National Cancer Institute

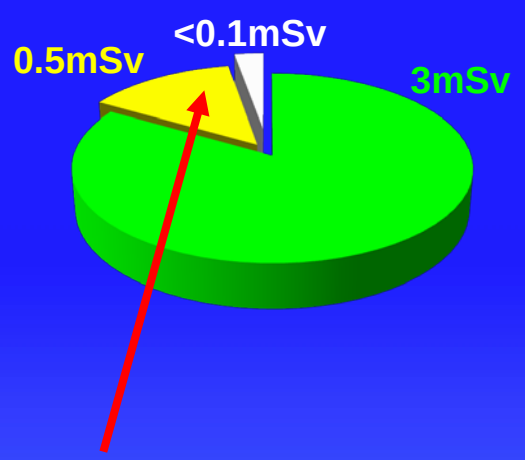
Diagnostic Imaging, Screening and Cancer Risk

Amy Berrington de Gonzalez, DPhil
Radiation Epidemiology Branch
DCEG/NCI/NIH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

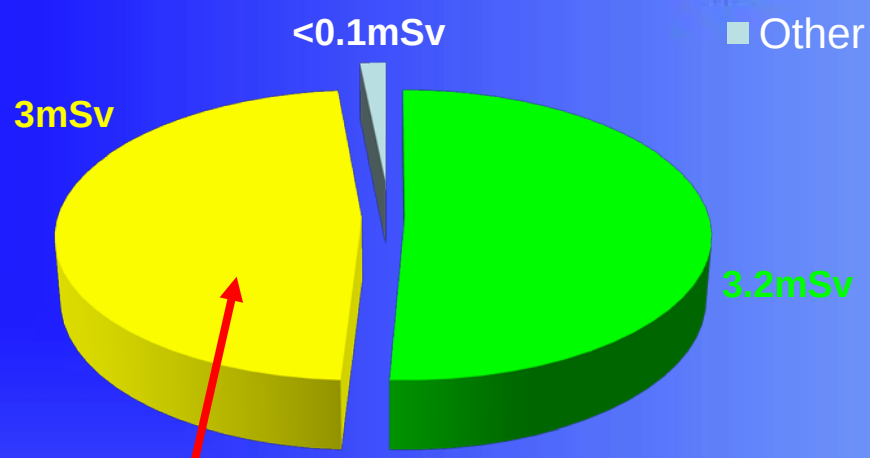
Radiation Exposure in the U.S.

1980



CT scans 3 million
Nuclear medicine 6 million

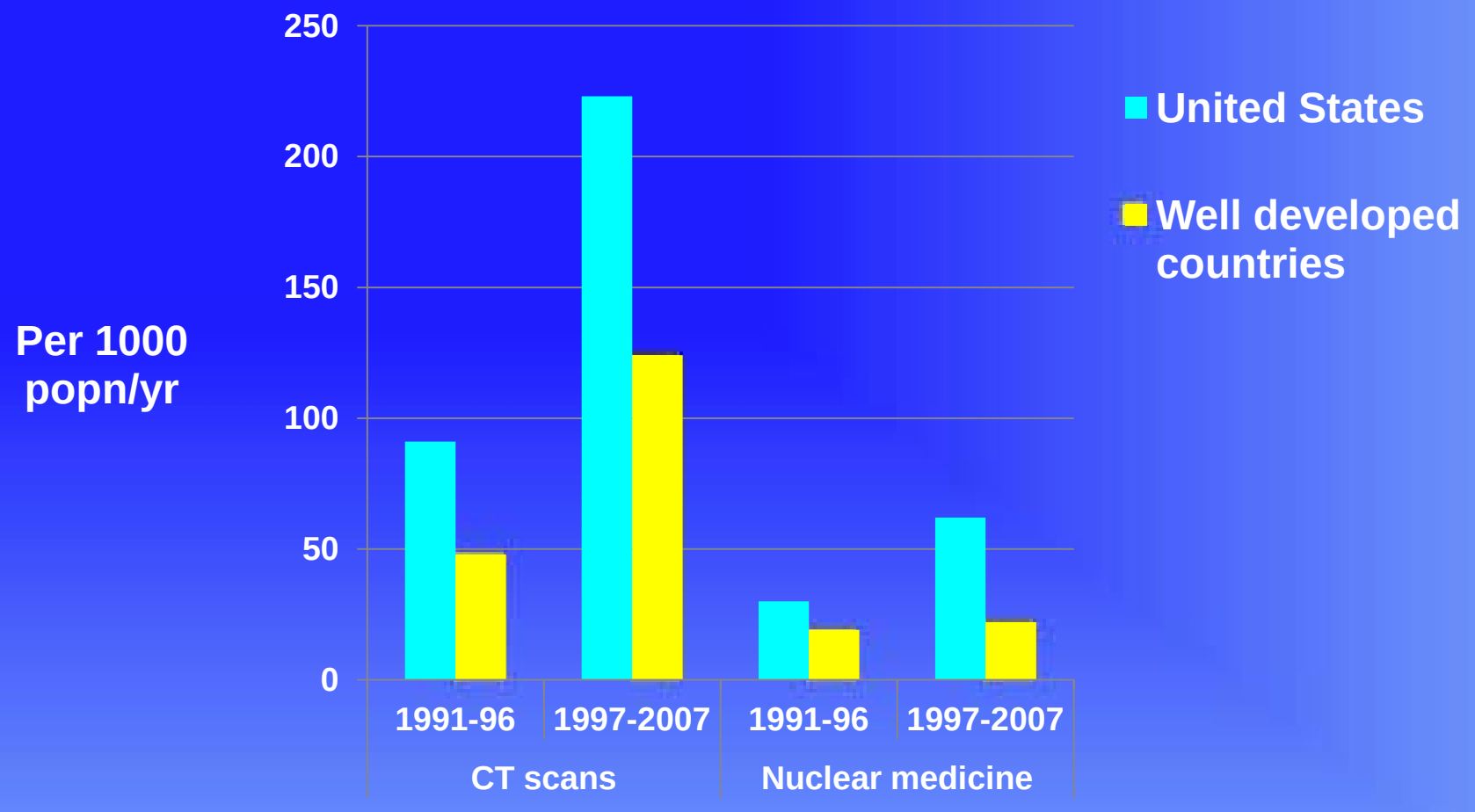
2006



CT scans 70 million
Nuclear medicine 18 million

NCRP report 160 (2009)

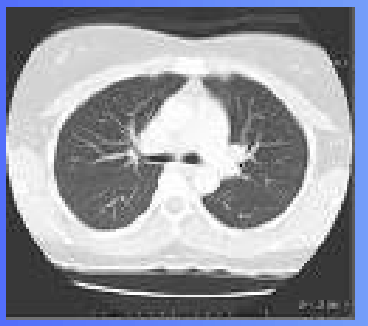
International Trends in Diagnostic Imaging



Mettler et al (Radiology 2009)

Diagnostic Imaging - Effective & Organ Doses

Procedure	X-ray	CT scan
Skull	0.1 mSv	2 mSv
Chest	0.1 mSv	7 mSv
Abdomen	0.7 mSv	8 mSv



CT scan	Brain	Lung	Stomach
Skull	40 mGy	0 mGy	0 mGy
Chest	0 mGy	20 mGy	6 mGy
Abdomen	0 mGy	3 mGy	20 mGy

Mettler et al (Radiology 2009)

Variation in Effective dose – 4 US hospitals

Scan type	Mettler	Smith-Bindman Median [range]
Head	2 mSv	2 [0.3-7] mSv
Chest	7 mSv	8 [2-25] mSv
Abdomen-pelvis	12 mSv	15 [3-45] mSv

Smith-Bindman et al (Arch Int Med 2009)

Diagnostic Radiation & Cancer: Rationale

- Radiation carcinogenesis
  - Medical records – exposure history
  - Wide dose-range
  - Any organ & exposure age
- Public health
- Clinical decision making

Methodological Issues

- Case-control vs cohort
- Sample size
- Exposure assessment
  - Medical records
  - Self-reported
  - Dose reconstruction
  - Organ doses
- Timing of exposure
  - Age at exposure
  - Latency period
- Confounding by indication

o2 mammograms at age 35 (10mGy)

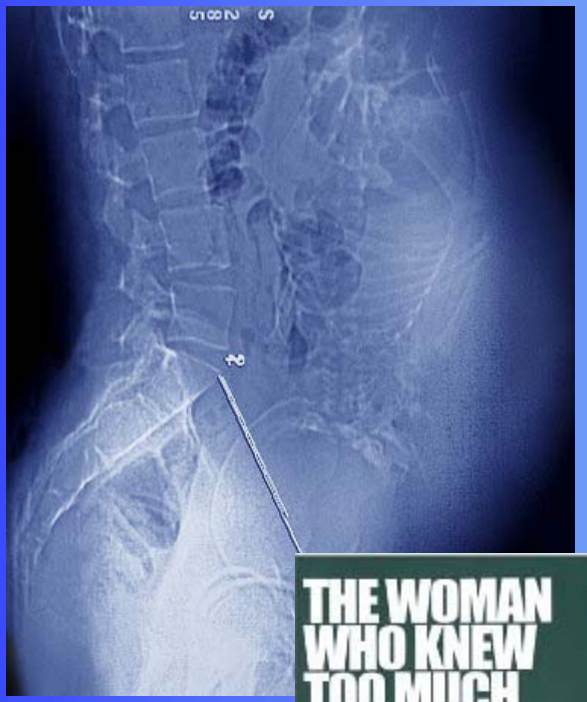
o20 years follow-up

o60 million women for 50% power (Land, 1981)

In Utero Exposures

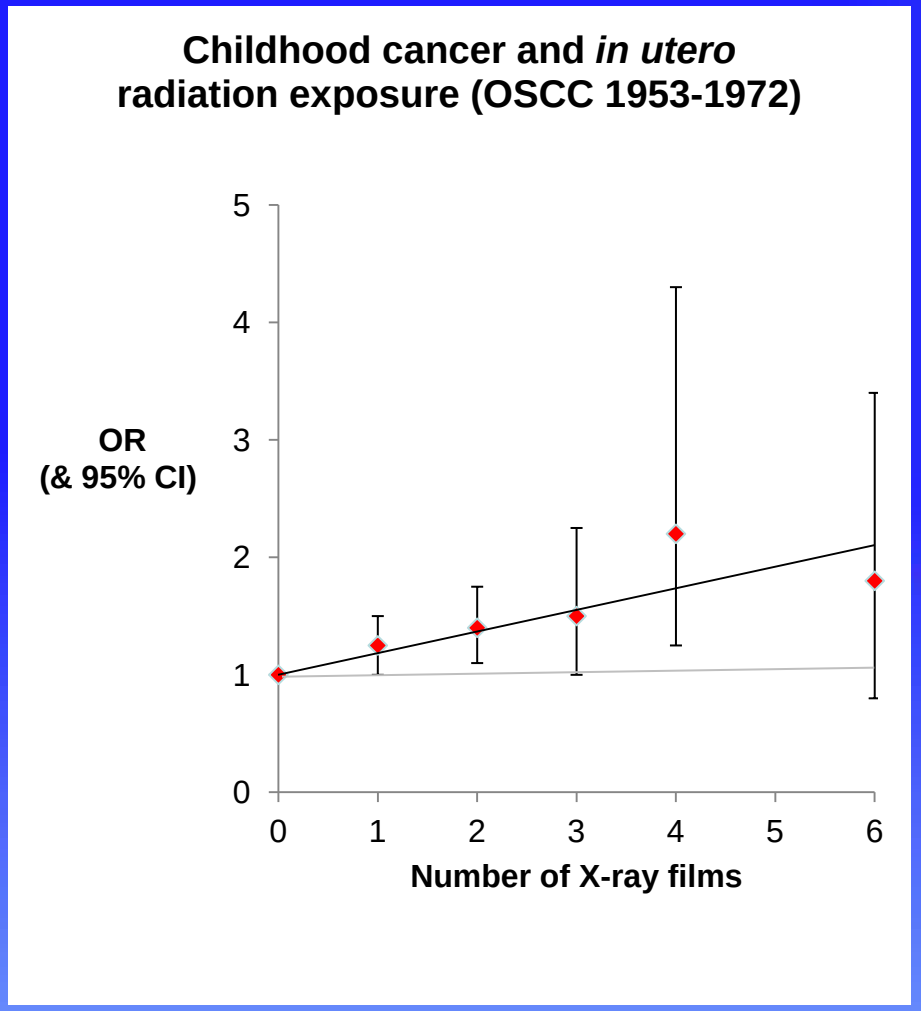
- OSCC 15,300 case-control pairs
  - Self-reported exposures
  - OR=1.39 (1.30-1.49)
- US medical records
  - OR=1.47 (1.22-1.77)
- Meta-analysis RR=1.38 (1.31-1.47)
  - similar for Leukemia & other cancers

- Cohort studies RR=1.13 (0.84-1.53)
  - 25 cases



Doll and Wakeford (Br J Radiology 1997); Wakeford (Radiat Prot Dosimetry 2008)

In Utero Exposures cont.



- Dose per film
  - 15mGy 1940s
  - 3mGy 1960s
- Decline in risk by birth cohort

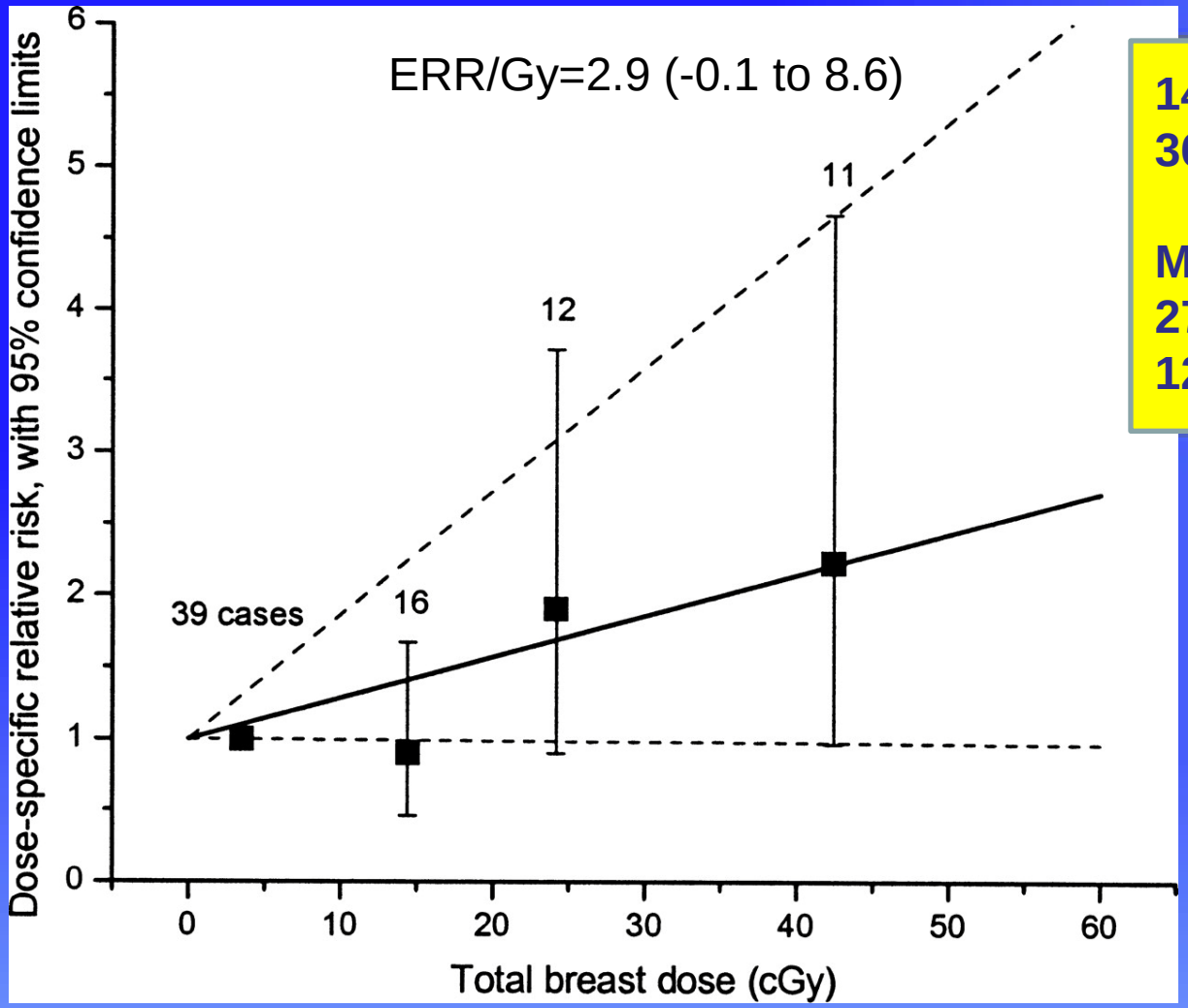
Doll and Wakeford (Br J Radiology 1997)

In Utero Exposures – Recent Studies

- 1997-2006 CT scan use ↑ 25% per year
- UK Childhood Cancer Study
  - Medical records (1976-1996)
  - 64% pelvimetry, 2698 cases
  - All cancers OR=1.14 (0.90-1.45)
  - Leukemia OR=1.36 (0.91-2.02)
- Canadian record linkage
  - 1.8 million women-child pairs
  - 1 in 250 CT scans
  - 4 cancers RR=0.69 (0.26-1.82)

Lazarus et al (2009); Rajaraman et al (BMJ 2011) ; Ray et al (PLOS 2010)

Radiation Dose Response for Breast Cancer Multiple Spine X-rays in 3,002 Scoliosis Patients



140,000 X-rays
36 years follow-up

Mean (range):
27 (0-332) X-rays
120 (0-1110) mGy

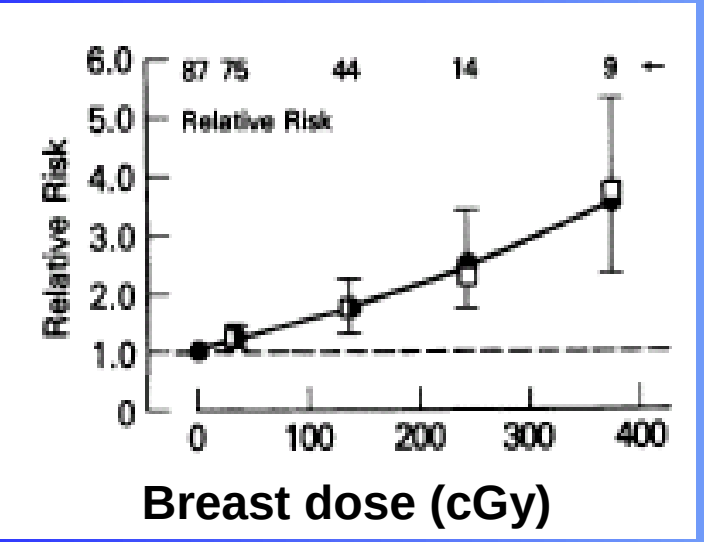
Ronckers et al (Cancer Epidemiol Biomarkers Prev 2008)

©2008 by American Association for Cancer Research

AACR Cancer Epidemiology, Biomarkers & Prevention

Tuberculosis & Multiple Fluoroscopies

- Massachusetts 4940 women (1925-54)
- Mean dose 0.8Gy (88 exposures)
- 234 breast cancers
- RR=1.61 at 1Gy



- Canadian TB 31,710 women (1930-1952)
- 688 breast cancer deaths
- Mean dose 1Gy RR=1.36 (1.11-1.67) at 1Gy

Boice et al (Radiat Res 1991); Howe and McLaughlin (Radiat Res 1996); Howe (Radiat Res 1995) ;

TB & Multiple Fluoroscopies – Lung cancer

- Massachusetts 13,572 patients (Mean dose 0.8Gy)
- 357 lung cancer deaths by 2002
- Lung cancer ERR/Gy -0.04 (-0.11 to 0.14)

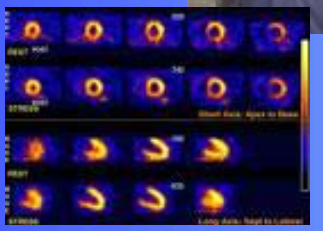
- Canadian TB
- 688 breast cancer deaths (Mean dose 1Gy)
- 1178 lung cancer deaths (ERR/Gy -0.00 (-0.04 to 0.07)

- Confounding by indication?
  - TB ERR/Gy -0.27 (-0.31 to -0.22)
  - TB risk factor for lung cancer
  - Negative confounding
  - Misclassification of cause of death (dose-dependent)?

Brenner (Conference Abstract Radiat Res 2010) ; Howe (Radiat Res 1995) ;

Canadian Cardiac Imaging Cohort

- 82,861 Acute MI patients (1996-2006)
- Record linkage – imaging claims, cancer
- Average effective dose 5mSv
- 12,020 incident cancers
- RR=1.003 per mSv (1.002-1.004)



- Organ-specific results?
- By latency period (mean FU 5yrs)?
- Adjustment for co-morbidities?

Eisenberg et al (CMAJ 2011)

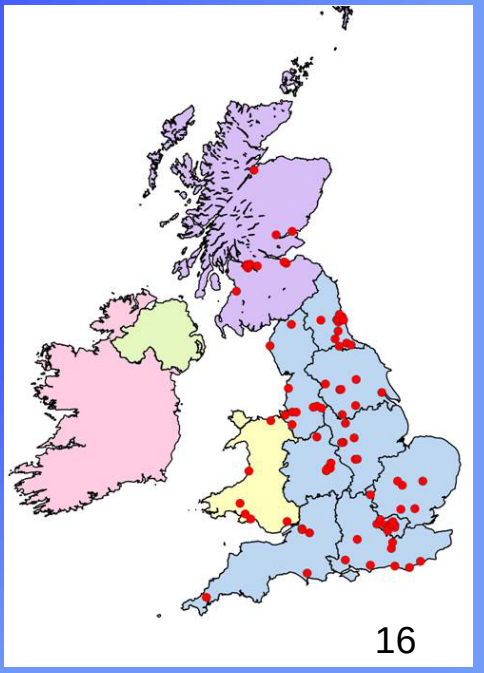
Pediatric CT scans

- Higher doses & risks for children
  - Patient size
  - Adult settings
  - Head CT 60 mGy brain
  - Chest CT 30 mGy breast

- NCI-UK Cohort – 250,000
- European Study EPI-CT – 1,000,000
- Canada, Israel and Australia cohorts

NCI-UK Pediatric CT scans

- 1990-2003 800,000 CT scans aged 0-20 yrs
- Link to cancer registrations, vital status
- Organ dose estimates – generic dosimetry
- Leukemia, brain, thyroid etc dose-response
- Nested case-control studies
  - Individual CT parameters
  - Accurate organ dose reconstruction



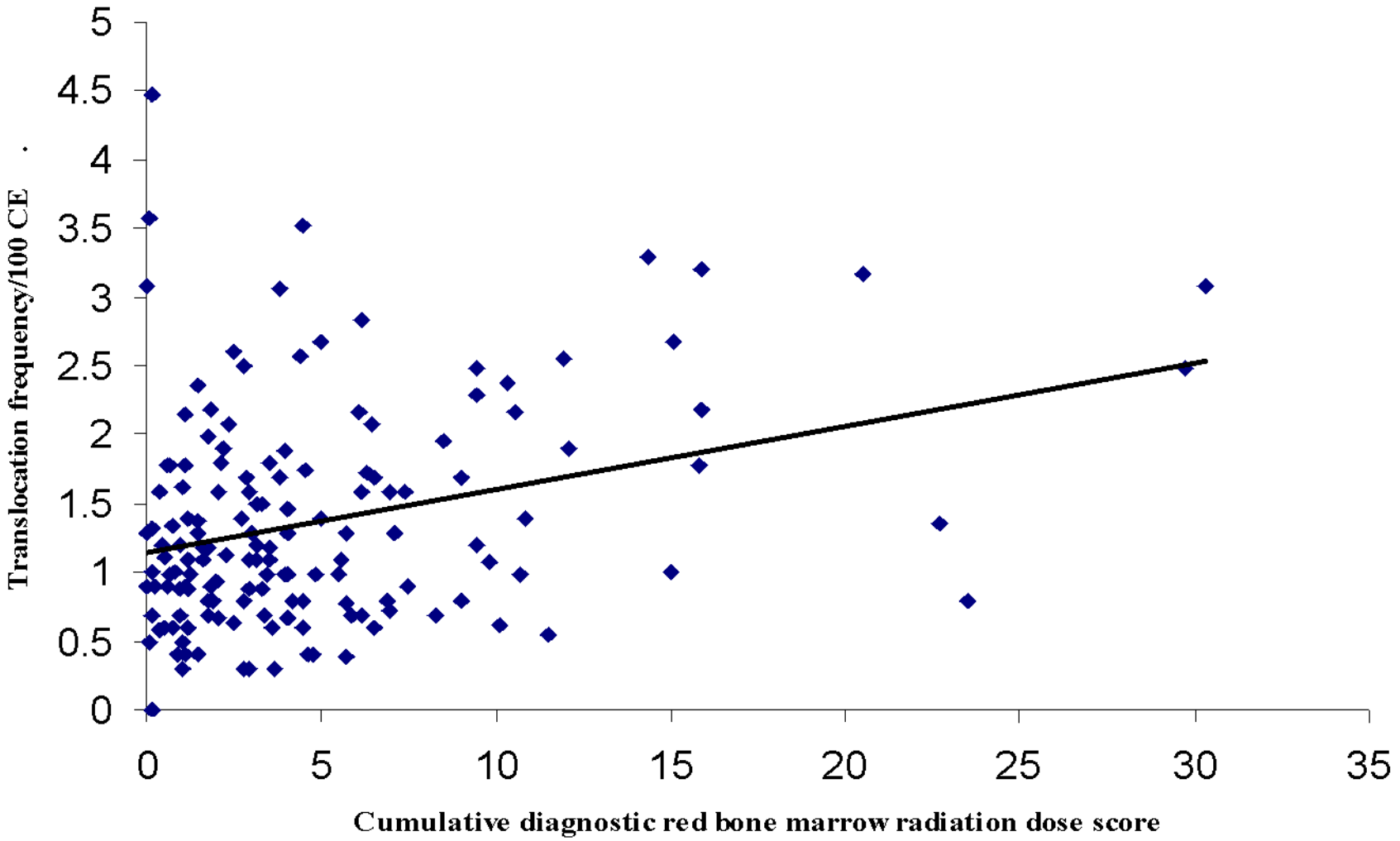
Pearce et al (Pediatric Radiology, in press)

USRT – Personal diagnostic X-rays

- Self-reported diagnostic exposures by type and calendar period
  - Biodosimetry for 152 technologists
  - Dose scores for red bone marrow
  - FISH whole chromosome painting for translocations
  - Expressed per 100 cell equivalents (CE)

Sigurdson et al (Cancer Res, 2008)

Translocation frequency versus personal diagnostic radiation red bone marrow dose "score"

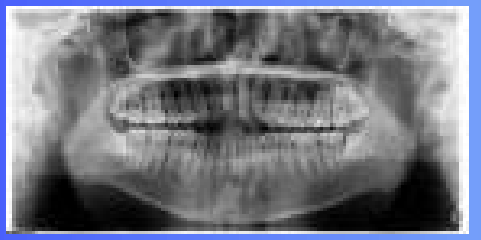


0.04 excess translocations/100 CE/dose score, P = 0.003

Case-control studies: adulthood exposure

- Leuk, NHL & MM
- Parotid gland tumors
- Glioma & meningioma
- Thyroid cancer

Dental X-rays



- Parotid gland tumors
- 269 benign & 139 malignant tumors
- 408 neighbourhood controls
- OR=3.4 (1.02-11.5) for 50 rad vs 0 (p-trend<0.05)

- Glioma (202 pairs) and meningioma (70 pairs)
- OR=1.5-3.0 for full-mouth dental x-rays

- Recall similar for cases and controls

Preston-Martin et al (JNCI 1988); Preston-Martin et al (Cancer Res 1989)

Dental X-rays cont

- Australian case-control study
- Glioma OR 0.42 (0.24-0.76)
- Meningioma adult males – possible association

- Swedish case-control study
- Meningioma OR 2.1 (1.0-4.3) for annual age 25+
- Other CNS - no association

- Australian case-control study
- Childhood brain tumors – no association

Ryan et al (Eur J Cancer B Oral Oncol 1992); Rodvall et al (Oral Oncol 1998);

McCredie et al (Int J Cancer 1994)

Leuk, NHL & MM Case-control study

- Kaiser NW and Kaiser NC Health Plans
- 565 Leuk, 318 NHL and 208 MM cases & 1390 controls
- Matched on age, sex, years in plan, year entered plan
- 25,000+ X-rays from medical records
- Bone marrow dose score
- 52% exposures were chest X-ray (0.1mGy)
- No clear evidence of association
  - Especially with 2+ years lag period

Lag	1	2	3	4	p-trend
3 mths	1.3	1.3	2.0	1.8	0.06
2 yrs	1.0	0.9	1.6	1.2	0.32

Boice et al (JAMA 1991)

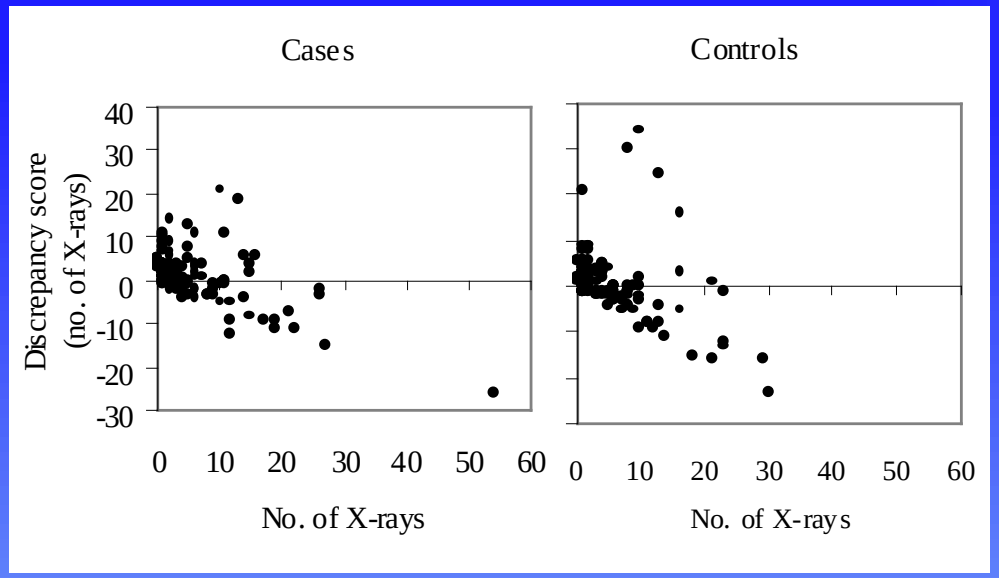
Thyroid Cancer & Diagnostic X-rays

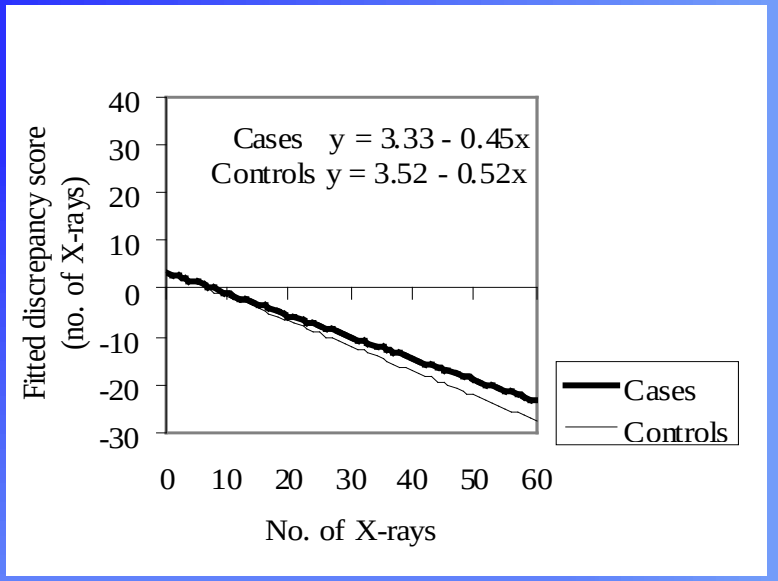
- 3 questionnaire based studies suggested associations
- Swedish medical records study
- 484 cases and matched popn controls
- Residential histories constructed
- Radiology records from hospitals
- 6148 X-rays 5+ yrs before diagnosis
- Generic thyroid dose estimates
- No risk associated with past X-rays
  - Dose 7-75 mGy OR=1.05 (0.7-1.5) P-trend=0.8
  - Similar results <age 20 exposure

Inskip et al (JNCI 1995)

Recall of Diagnostic X-rays

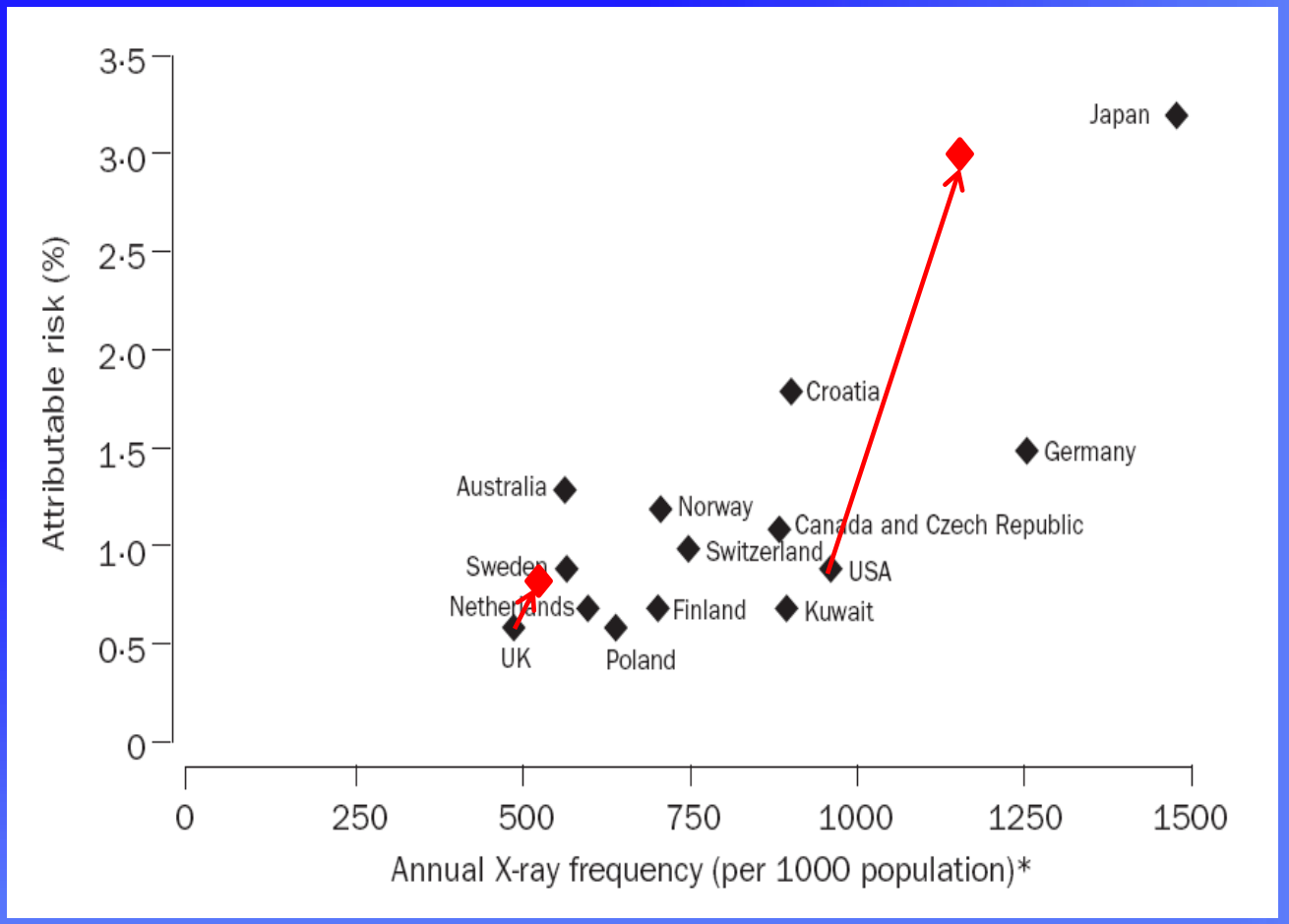
- 123 cases & controls Sweden
- 50 cases & controls US
- Medical records vs Telephone interview





Berrington de Gonzalez et al (AJE 2003)

Risk Projection: Attributable Cancer Risk



Berrington de González & Darby (Lancet 2004); Berrington de González et al (Arch Int Med, 2009); Berrington de González et al (Circulation, 2010)

Screening Examinations: Risk Projection

- Younger screening ages
  - Higher radiation risks & lower absolute mortality reduction
- Radiation risks ≥ benefits
  - Mammography BRCA carriers < age 35
  - Lung CT < age 50
- Benefits > radiation risks
  - CT colonography > age 50

Berrington de González et al (J Natl Can Inst 2009) Berrington de González (J Med Screen 2007)
Berrington de González et al (J Med Screen 2009)

Summary

Key studies

- ***In utero*** **exposures and childhood cancer**
- **Fluoroscopy TB and breast cancer**
- **Scoliosis X-rays and breast cancer**
- **Pediatric CT scans and childhood cancer?**

Key attributes

- **Relatively high exposure levels**
- **Or high risk sub-group (eg children, radio-sensitive?)**
- **Medical records for dose reconstruction**

Risk projection

- **Alternative for timely assessment of potential risks**

Acknowledgments

- Alina Brenner (NCI)
- Martha Linet (NCI)
- Preetha Rajaraman (NCI)
- Alice Sigurdson (NCI)