Cancer Risks from CT Scans: Now We Have Data… What Next?

David J. Brenner, PhD, DSc
Center for Radiological Research
Columbia University Medical Center

djb3@columbia.edu

There is no question that CT has revolutionized medical practice

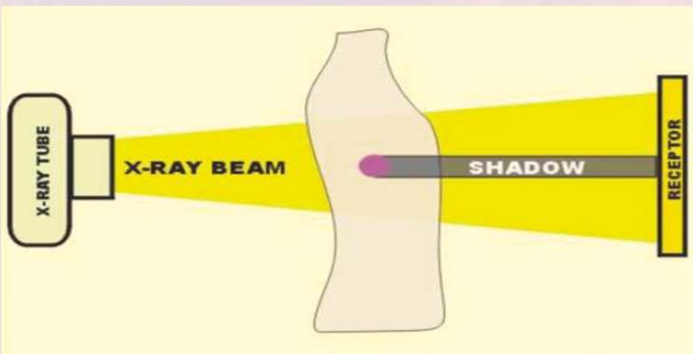
- ✓ *More effective surgical treatment*
- ✓ *Shorter hospital stays*
- ✓ *Elimination of exploratory surgeries*
- ✓ *Better diagnosis and treatment of cancer*
- ✓ *More efficient treatment after injury*
- ✓ *Better treatment of stroke*
- ✓ *Better treatment of cardiac conditions*

Why are we particularly interested in CT?

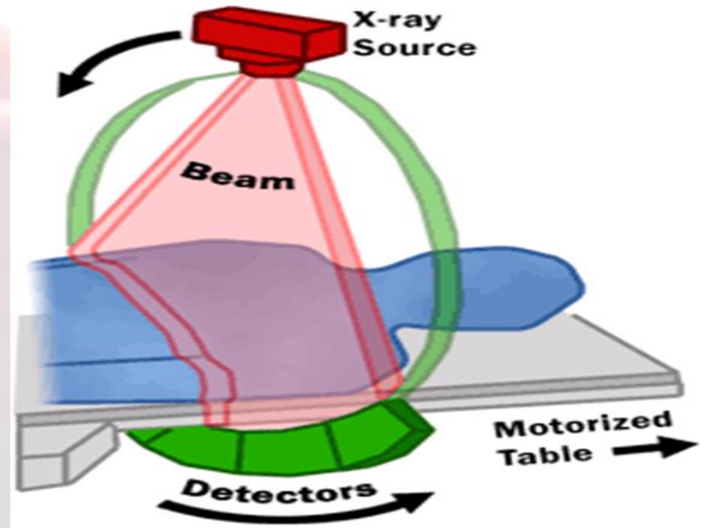
Examination	Relevant organ	Relevant organ dose (mGy)
Dental x ray	Brain	0.005
PA Chest x ray	Lung	0.01
Lateral chest x ray	Lung	0.15
Screening mammogram	Breast	3
Adult abdominal CT	Stomach	11
Adult head CT	Brain	13
Child abdominal CT	Stomach	10-25
Child head CT	Brain	20-25
Adult ^{18}F-FDG PET	Bladder	18

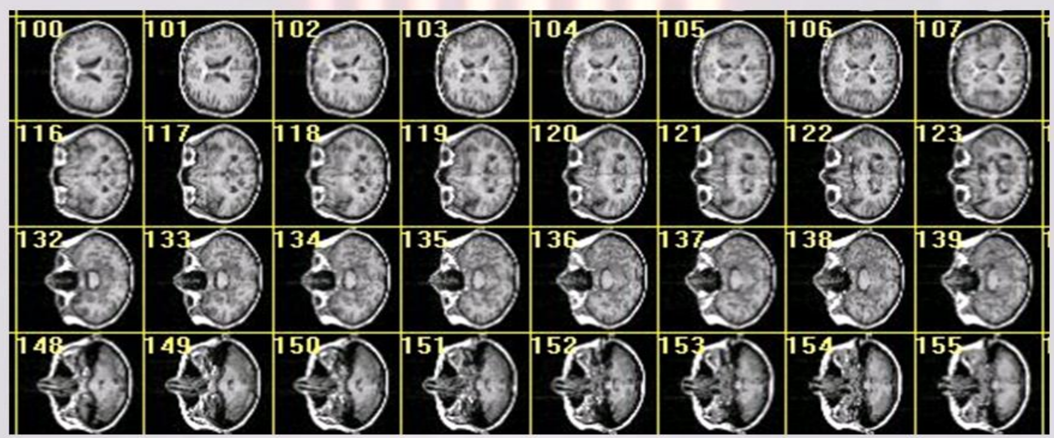
Why are we particularly interested in CT?

Conventional Radiograph



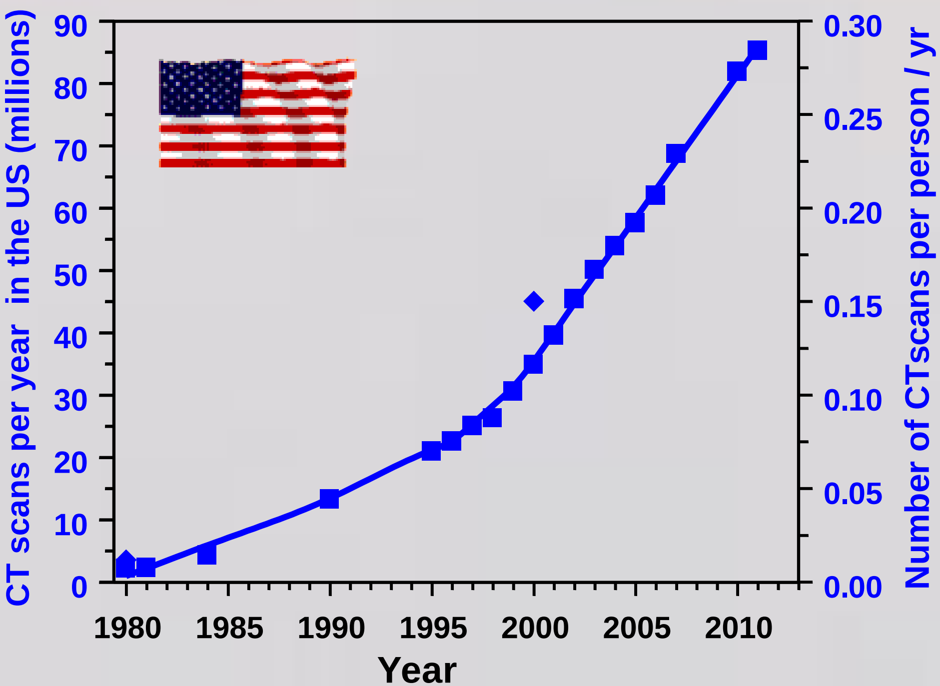
CT

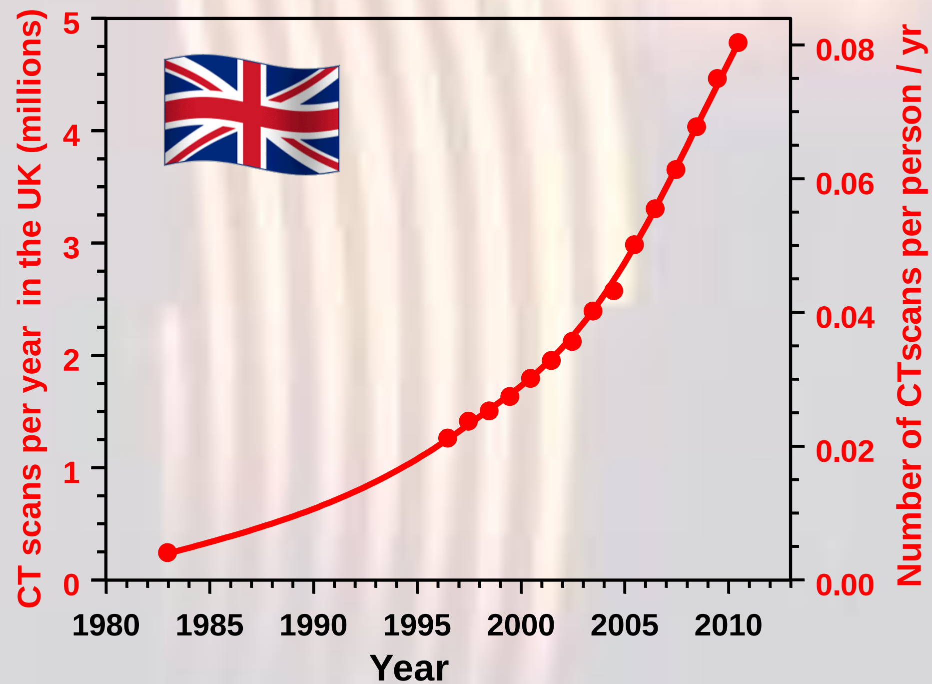




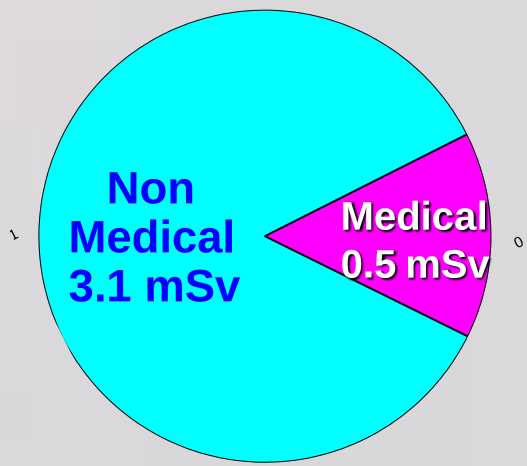
Why are we particularly interested in CT?

Frequency of CT scans per year

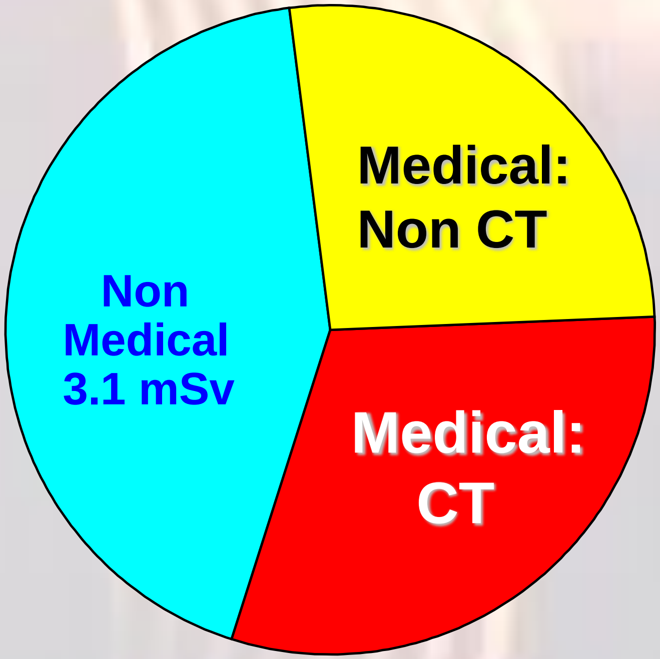




Mean individual total radiation dose in the US: 1980 vs. 2011

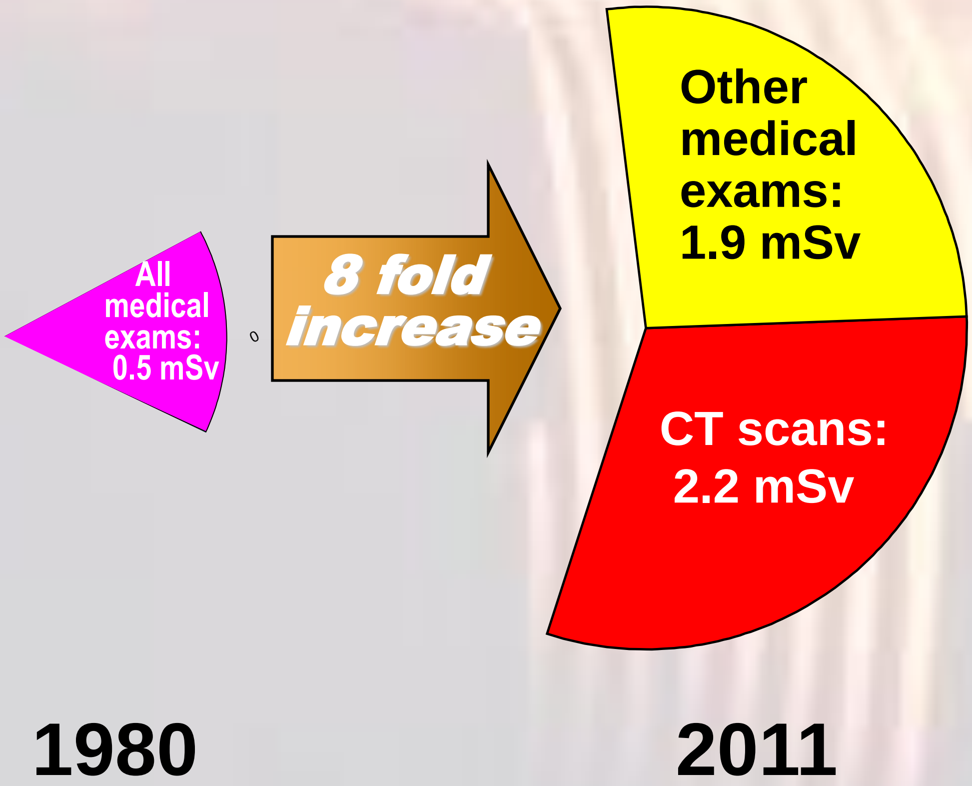


1980: 3.6 mSv



2011: 7.2 mSv

Average individual dose from medical imaging USA: 1980 vs. 2011



The key organ-dose ranges of relevance for CT

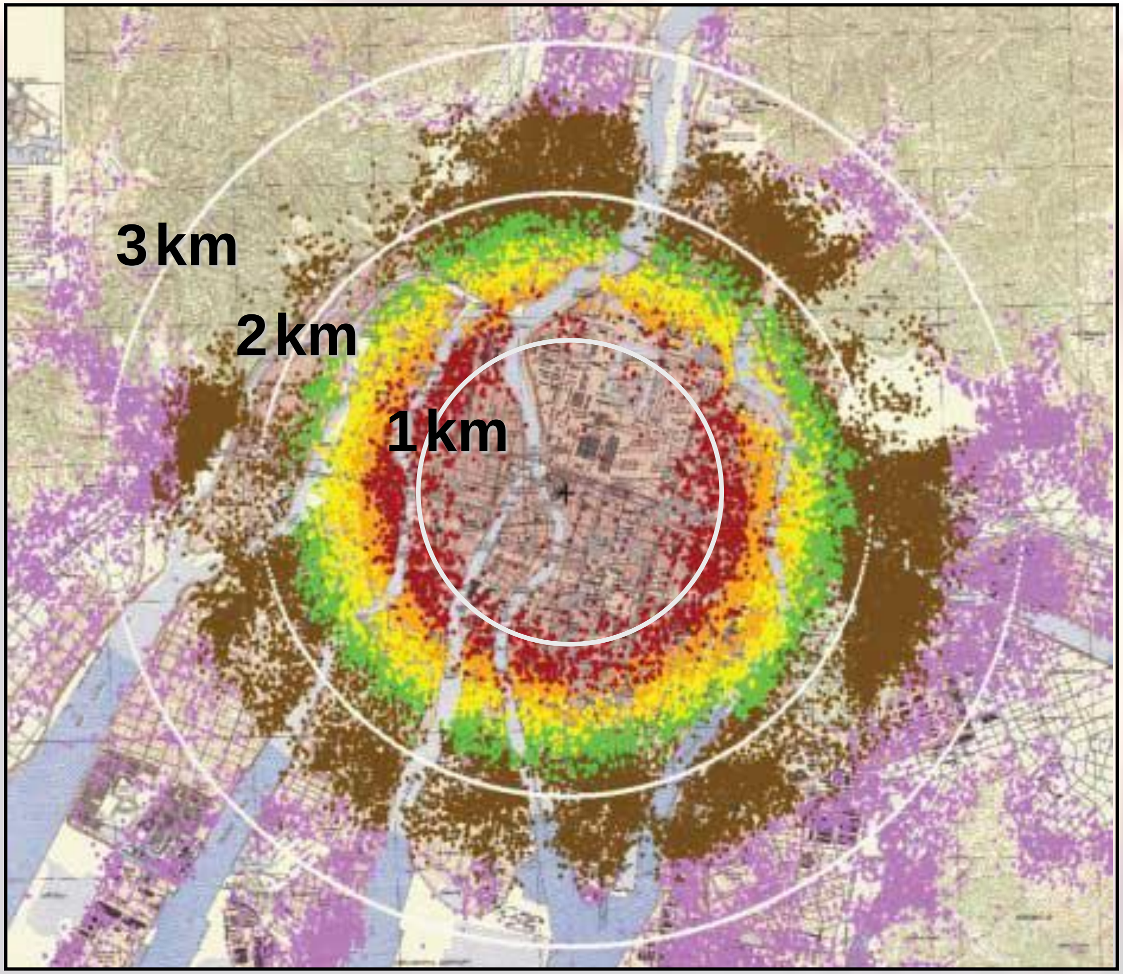
Taking into account

* Machine variability,
* Usage variability,
* Age variability,
* Scans done with and without contrast
* Multiple scans

Relevant organ dose ranges for CT are

5 - 100 mSv for a single series of scans

Atomic bomb survivor locations by dose



Green dots: Individuals exposed to between 100 and 200 mGy

Brown dots: Individuals exposed to between 5 and 100 mGy (~25,000)

Douple *et al* 2011

Number of solid cancers in A-bomb survivors exposed to doses between 5 and 100 mSv

Small but statistically significant increase in risk

	Cancer incidence (1958-98)
Study population (5-100 mSv)	27,789
Total solid cancers observed	4,406
Solid cancers expected (controls)	4,325
Radiation-related excess solid cancers	81

Preston *et al* 2007

Estimating the radiation-induced cancer risks from CT exams

- Direct epidemiology on people who received CT scans

- Risk estimation based on organ doses and A-bomb survivor data

Risk estimation based on organ doses and A-bomb survivor data

1. Estimate the dose to each organ, as a function of age, gender, and type of CT exam

2. Apply estimates of age-, gender-, and organ-specific risks-per-unit dose

   (low-dose risks from A-bomb survivors, "transferred" to a Western population)

3. Sum the estimated risks for all organs

Risk estimates based on organ doses and A-bomb survivor data - 2001

AJR American Journal of Roentgenology
Diagnostic Imaging and Related Sciences

Estimated Risks of Radiation-Induced Fatal Cancer from Pediatric CT

David J. Brenner[1]
Carl D. Elliston[1]
Eric J. Hall[1]
Walter E. Berdon[2]

OBJECTIVE. In light of the rapidly increasing frequency of pediatric CT examinations, the purpose of our study was to assess the lifetime cancer mortality risks attributable to radiation from pediatric CT.

MATERIALS AND METHODS. Organ doses as a function of age-at-diagnosis were estimated for common CT examinations, and estimated attributable lifetime cancer mortality risks (per unit dose) for different organ sites were applied. Standard models that assume a linear extrapolation of risks from intermediate to low doses were applied. On the basis of current standard practice, the same exposures (milliampere-seconds) were assumed, independent of age.

RESULTS. The larger doses and increased lifetime radiation risks in children produce a sharp increase, relative to adults, in estimated risk from CT. Estimated lifetime cancer mortality risks attributable to the radiation exposure from a CT in a 1-year-old are 0.18% (abdominal) and 0.07% (head)—an order of magnitude higher than for adults—although those figures still represent a small increase in cancer mortality over the natrual background rate. In the United States, of approximately 600,000 abdominal and head CT examinations annually performed in children under the age of 15 years, a rough estimate is that 500 of these individuals might ultimately die from cancer attributable to the CT radiation.

CONCLUSION. The best available risk estimates suggest that pediatric CT will result in significantly increased lifetime radiation risk over adult CT, both because of the increased dose per milliampere-second, and the increased lifetime risk per unit dose. Lower milliampere-second settings can be used for children without significant loss of information. Although the risk–benefit balance is still strongly tilted toward benefit, because the frequency of pediatric CT examinations is rapidly increasing, estimates that quantitative lifetime radiation risks for children undergoing CT are not negligible may stimulate more active reduction of CT exposure settings in pediatric patients.

The use of CT has increased rapidly in the past two decades, fueled in part by the development of helical CT [1]. For example, the estimated annual number of CT examinations in the United States rose approximately sevenfold from 2.8 million in 1981 [2] to 20 million in 1995 [3]. By their nature, CT examinations contribute disproportionately to the collective diagnostic radiation dose to the population; for example, in Britain it has been estimated that approximately 4% of diagnostic radiology procedures are CT examinations, but their contribution to the collective dose is approximately 40% [4].

Figure 1 shows a breakdown of the number of CT examinations by age at examination, based on the results of a 1989 British survey [5]; in this survey, approximately 4% of CT examinations (which corresponds to about 10^6/year in the United States) were performed on children under the age of 15 years. The proportion of childhood CT examinations is rapidly increasing (indeed, an average value of 6% was estimated in 1993 [6]); for example, Coren et al. [7] reported a 63% increase in requests for pediatric CT between 1991 and 1994.

The recent increase in pediatric CT examinations is particularly marked in the United States. Figure 2 shows the number of abdominal and pelvic CT examinations of children under a given age at a major American children's hospital for 1996 through 1999. This figure shows, for example, a 92% increase between 1996 and 1999 in abdominal and pelvic CT examinations on children less

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[1]Center for Radiological Research, Columbia University, 630 W. 168th St., New York, NY 10032. Address correspondence to D. J. Brenner.

[2]Department of Radiology, Division of Pediatric Radiology, Columbia-Presbyterian Medical Center, 630 W. 168th St., New York, NY 10032.

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Super Bowl

Let the hype begin

Clock is ticking toward Sunday. Full report, 1-4C
▸ 10 years ago, war was on our minds, 1C
▸ Coming Friday: Bonus Section

The Golden Globes

'Gladiator' wins best drama film

Julia Roberts, Tom Hanks honored for drama roles; *Almost Famous* named best comedy film ■ 1-2D
▸ The red carpet, 5D

Roberts: Smiles for *Erin Brockovich.*

Monday, January 22, 2001

Newsline

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■ Asia stocks mixed overnight

Japan's Nikkei average is down 137 points, 1.0%, to 13,852 early today. Hong Kong's Hang Seng index is up 136 points, 0.9%, to 16,069.

CT scans in children linked to cancer later

By Steve Sternberg
USA TODAY

Each year, about 1.6 million children in the USA get CT scans to the head and abdomen – and about 1,500 of those will die later in life of radiation-induced cancer, according to research out today.

What's more, CT or computed tomography scans given to kids are typically calibrated for adults, so children absorb two to six times the radiation needed to produce clear images, a second study shows. These doses are "way bigger than the sorts of doses that people at Three Mile Island were getting," David Brenner of Columbia University says. "Most people got a tenth or a hundredth of the dose of a CT."

Both studies appear in February's *American Journal of Roentgenology*, the nation's leading radiology journal. The first, by Brenner and colleagues, is the first to estimate the risks of "radiation-induced fatal cancer" from pediatric CT scans. Until a decade ago, CT scans took too long to perform on children without giving them anesthesia to keep them still. Today's scanners spiral around the patient in seconds, providing cross sections, or "slices," of anatomy.

Doctors use CT scans on children to search for cancers and ailments such as appendicitis and kidney stones.

"There's a huge number of people who don't just receive one scan," says Fred Mettler of the University of New Mexico, noting that CT scans are used for diagnosis and to plan and evaluate treatment. "The breast dose from a CT scan of the chest is somewhere between 10 and 20 mammograms. You'd want to think long and hard about giving your young daughter 10 to 20 mammograms unless she really needs it."

Mettler recently published a study showing that 11% of the CT scans at his center are done on children younger than 15, and they get 70% of the total radiation dose given to patients. Children have more rapidly dividing cells than adults, which are more susceptible to radiation damage. Children also will live long enough for cancers to develop.

Researchers led by Lane Donnelly at Cincinnati's Children's Hospital found that children often get radiation doses six times higher than necessary. Cutting the adult dose in half would yield a clear image and cut the risk a like amount, Brenner says. "Radiologists genuinely believe the risks are small," he says. "I suspect they've never been confronted with numbers like this."

Not everyone was convinced…

AJR American Journal of Roentgenology

Taking Care of Children

I read with dismay the article by Brenner et al. [1] in the February issue. The claim that using CT in the pediatric population results in an increased risk of cancer is unfounded. Their claim is based on the use of "relative risk models" that have never been proven. Moreover, their calculations are based on a setting of 404 mAs for abdominal CT, much more than is now used for adult CT scanning. This figure was taken from a 1989 survey of CT practice in Britain and does not reflect settings that are used in the United States today. This spurious claim of increased cancer risk has been trumpeted by the media and [illegible] considerable unwarranted anxiety among the parents of our patients.

Certainly, as emphasized in the articles by Paterson et al. [2] and Donnelly et al. [3] in the same issue, we should all use the minimum exposure necessary to obtain a diagnostic examination. This is a good reason for children's imaging to be done by pediatric radiologists.

Nancy S. Rosen
Memorial Sloan-Kettering Cancer Center
New York, NY 10021

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Not everyone was convinced…

"Risks of medical imaging at effective doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be non-existent"

The American Association of Physicists in Medicine

54th Annual Meeting & Exhibition
July 29 - August 2 • Charlotte, NC

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Professional/Education/Science Policies

POLICY NUMBER	POLICY NAME	POLICY DATE	SUNSET DATE
PP 25-A	AAPM Position Statement on Radiation Risks from Medical Imaging Procedures	12/13/2011	12/31/2016

Policy source

Policy text

The American Association of Physicists in Medicine (AAPM) acknowledges that medical imaging procedures should be appropriate and conducted at the lowest radiation dose consistent with acquisition of the desired information. Discussion of risks related to radiation dose from medical imaging procedures should be accompanied by acknowledgement of the benefits of the procedures. Risks of medical imaging at effective doses below 50 mSv for single procedures or 100 mSv for multiple procedures over short time periods are too low to be detectable and may be nonexistent. Predictions of hypothetical cancer incidence and deaths in patient populations exposed to such low doses are highly speculative and should be discouraged. These predictions are harmful because they lead to sensationalistic articles in the public media that cause some patients and parents to refuse medical imaging procedures, placing them at substantial risk by not receiving the clinical benefits of the prescribed procedures.

Could we design an epidemiological study of CT risks in the US?

The 2012 UK CT Study

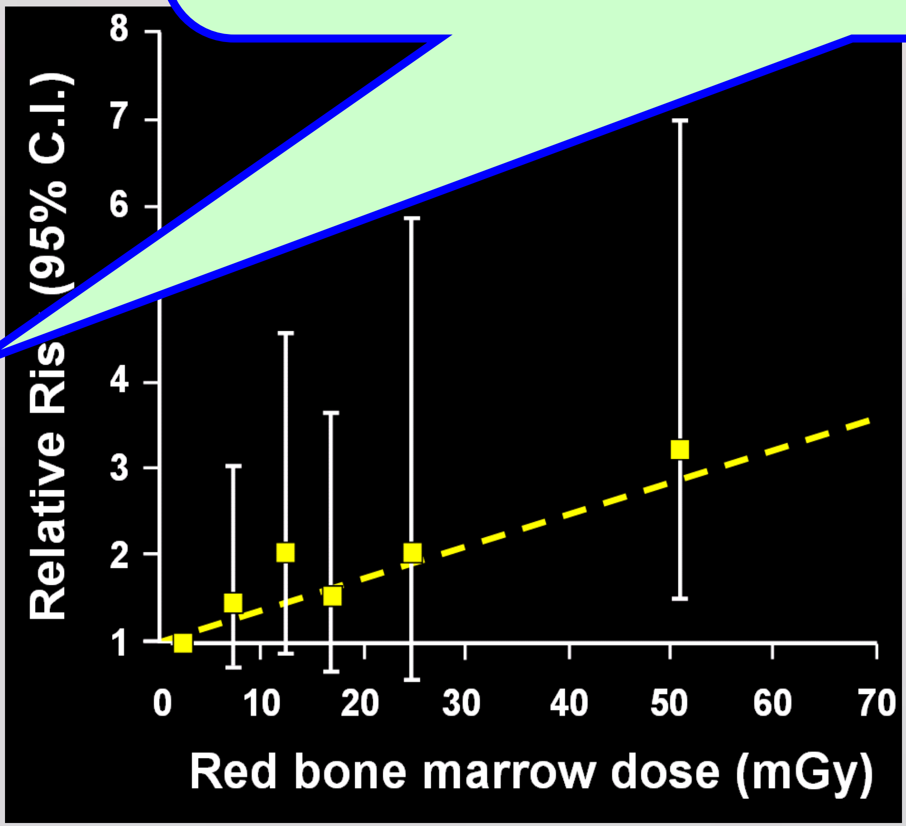
Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study

Mark S Pearce, Jane A Salotti, Mark P Little, Kieran McHugh, Choonsik Lee, Kwang Pyo Kim, Nicola L Howe, Cecile M Ronckers, Preetha Rajaraman, Sir Alan W Craft, Louise Parker, Amy Berrington de González

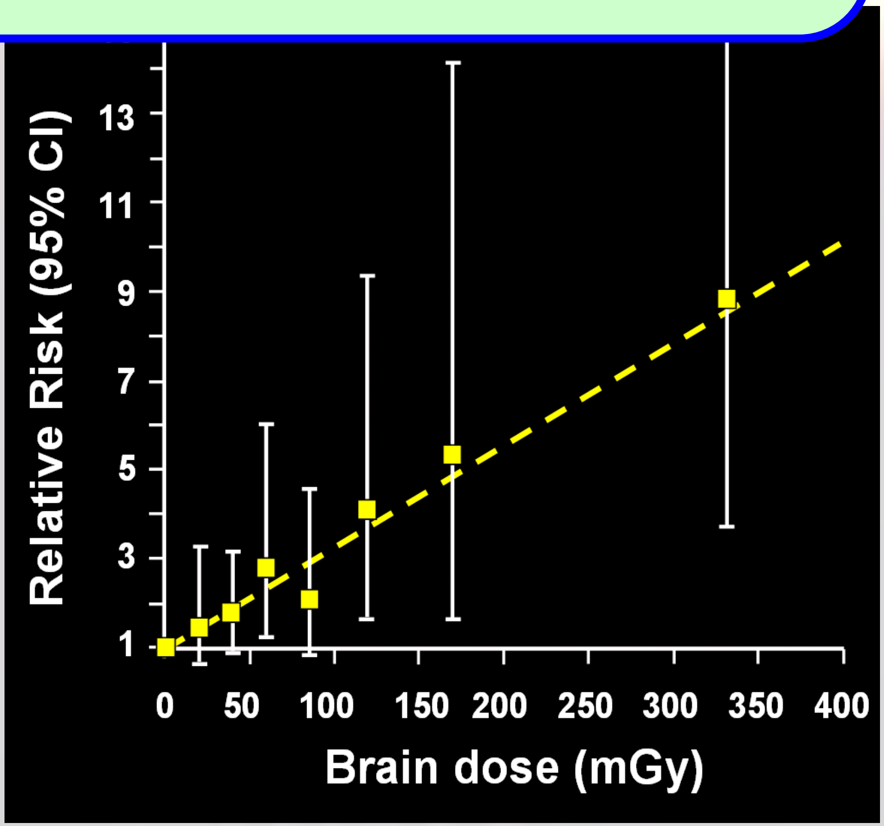
www.thelancet.com **Published online June 7, 2012 DOI:10.1016/S0140-6736(12)60815-0**

~10 year follow-up of 175,000 patients who received CT scans in the UK, age <22, between 1985 and 2002

- Statistically significant linear associations were seen between brain dose and brain tumor risk ($p<0.0001$), and between bone-marrow dose and leukemia risk ($p=0.01$)



Leukemia



Brain tumors

Could the reason for the CT also be a cause of cancer?

- **Reverse causation….**
- **For example does head trauma causes cancer?**

Cancer Causes Control. 2001 Oct;12(8):733-7.

Primary brain tumors following traumatic brain injury--a population-based cohort study in Sweden.

Nygren C, Adami J, Ye W, Bellocco R, af Geijerstam JL, Borg J, Nyrén O.

Department of Rehabilitation Medicine, Karolinska Institute, Danderyd Hospital, Stockholm, Sweden. catharina.nygren@mbox304.swipnet.se

Abstract

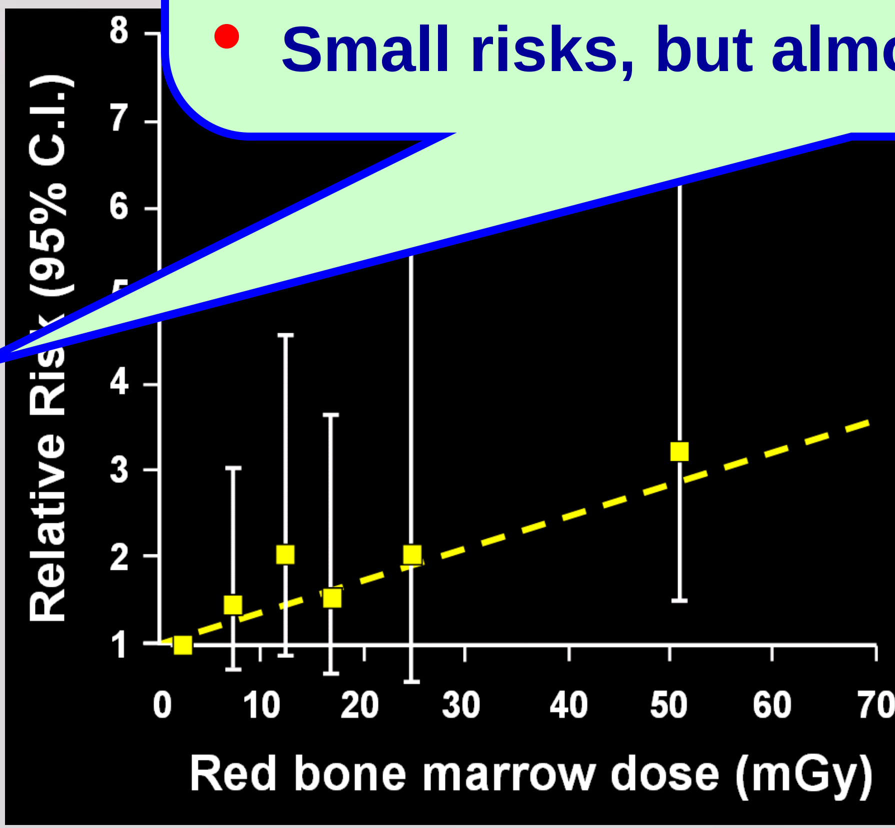
OBJECTIVES: The aim of this study was to explore the association between traumatic brain injury and brain tumor development.

METHODS: A cohort of patients hospitalized for traumatic brain injury during 1965-1994 was compiled using the Swedish Inpatient Register. Complete follow-up through 1995 was attained through record linkage with the Swedish Cancer Register, the Cause of Death Register, and the Emigration Register. Standardized incidence ratios (SIRs), defined as the ratios of the observed to the expected numbers of brain tumors, were usec as the measure of relative risk. The expected number of brain tumors was calculated by multiplying the observed person-time by age-, gender- and calendar year-specific incidence-rates derived from the general Swedish population.

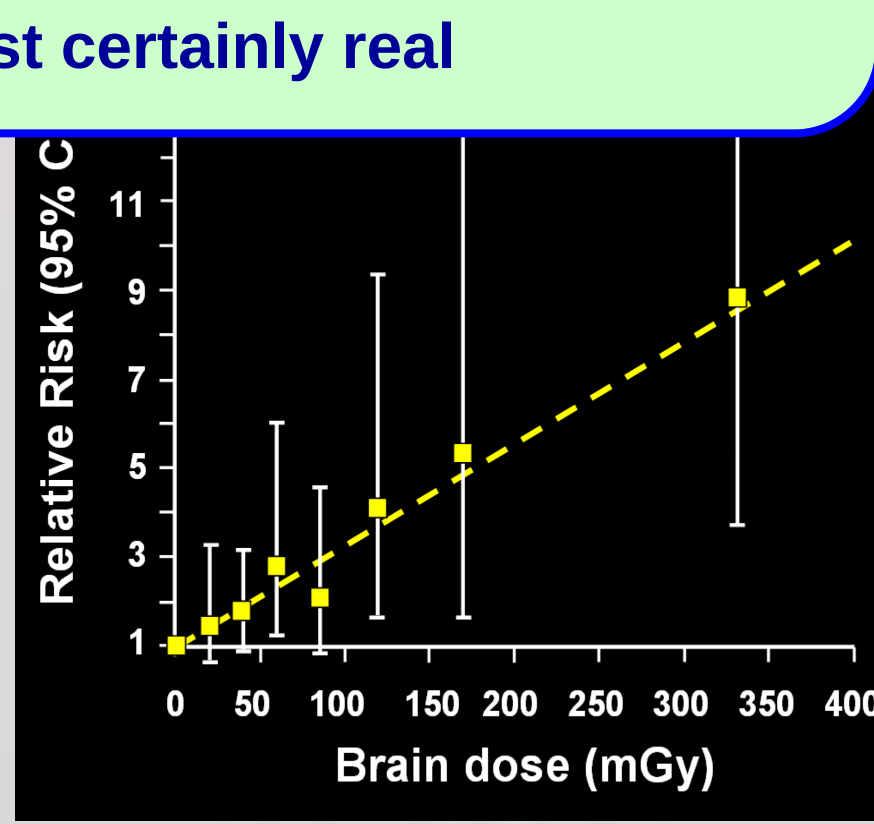
RESULTS: The cohort included 311,006 patients contributing 3,225,317 person-years. A total of 281 cases of brain tumors were diagnosed during follow-up. No associations were found between traumatic brain injury and the risk of primary brain tumors, neither overall (SIR: 1.0; 95% confidence interval (CI): 0.9-1.2), nor in analyses broken down by main groups of brain tumors. Stratified analyses according to age at entry into the cohort, yea of follow-up, and severity of the brain injury all showed essentially the same null results.

CONCLUSION: No association between traumatic head injury and primary brain tumors has been found.

- Statistically significant linear associations were seen between brain dose and brain tumor risk ($p<0.0001$), and between bone-marrow dose and leukemia risk ($p=0.01$)
- **Small risks, but almost certainly real**



Leukemia



Brain tumors

The UK CT Study: A pretty important event in our field

- **We have now passed a watershed in the field, where it is no longer reasonable to suggest that CT risks are "*too low to be detectable and may be non-existent*"**

The UK CT Study
Absolute risk estimates

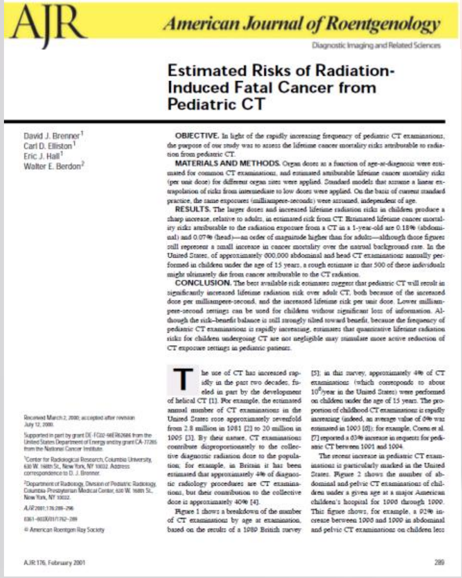
- **Pearce *at al* estimated absolute risks of about 1 in 10,000 per head CT scan, both for leukemia and for brain tumors**

The UK CT Study:
CT Risks are real but small

- **So the results of the study imply that if a CT exam is clinically justified, its benefits by far exceed its risks**
  - ***No real need for any complicated benefit-risk calculations***

The UK CT Study
Absolute risk estimates

- Pearce *at al* estimated absolute risks of about 1 in 10,000 per head CT scan, both for leukemia and for brain tumors
- How does this compare with lifetime risk estimates based on organ doses and A-bomb survivor data?



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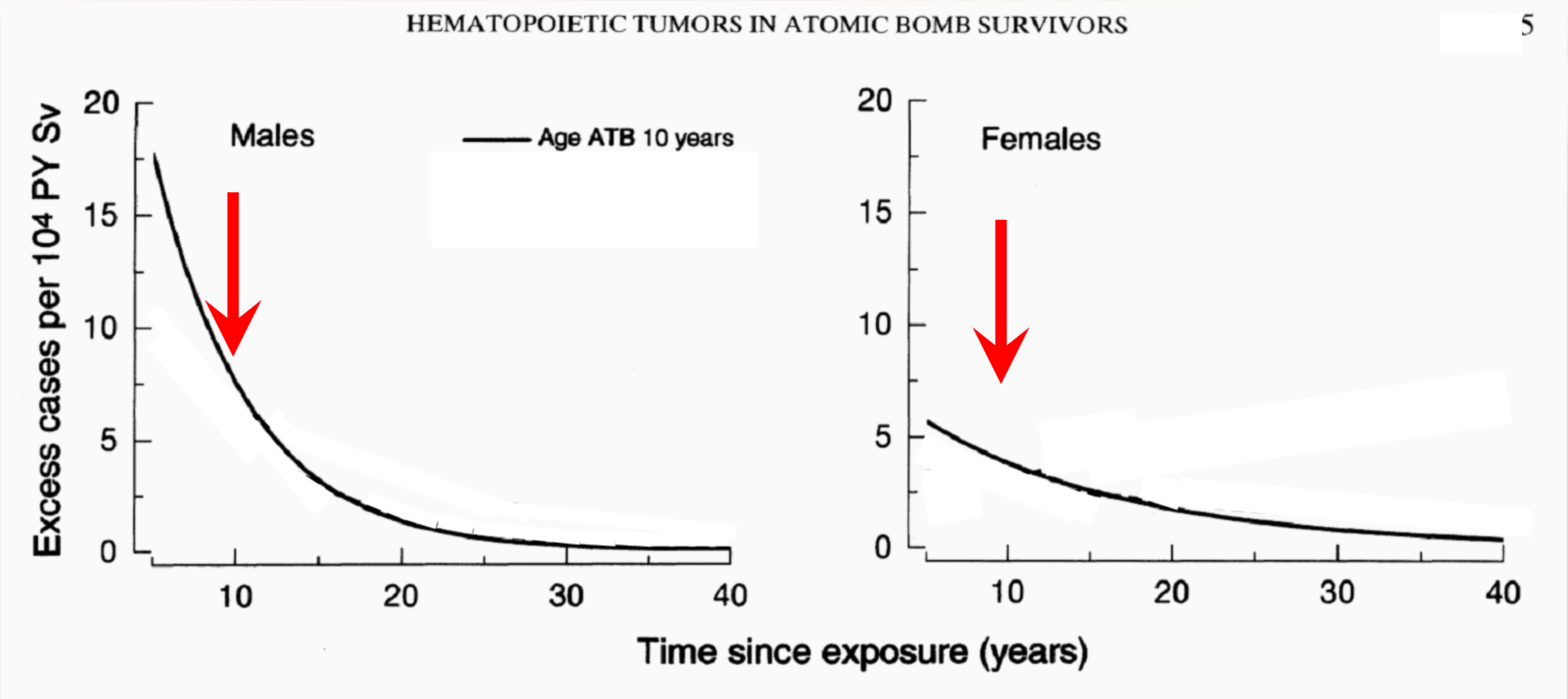
The UK CT Study
Absolute risk estimates

- **The mean follow-up time in the Pearce study was less than 10 years**
  - **From studies of other irradiated populations, we expect that not all the radiation-induced cancers that are going to appear, have actually yet appeared**

Cancer Incidence in Atomic Bomb Survivors. Part III: Leukemia, Lymphoma and Multiple Myeloma, 1950-1987

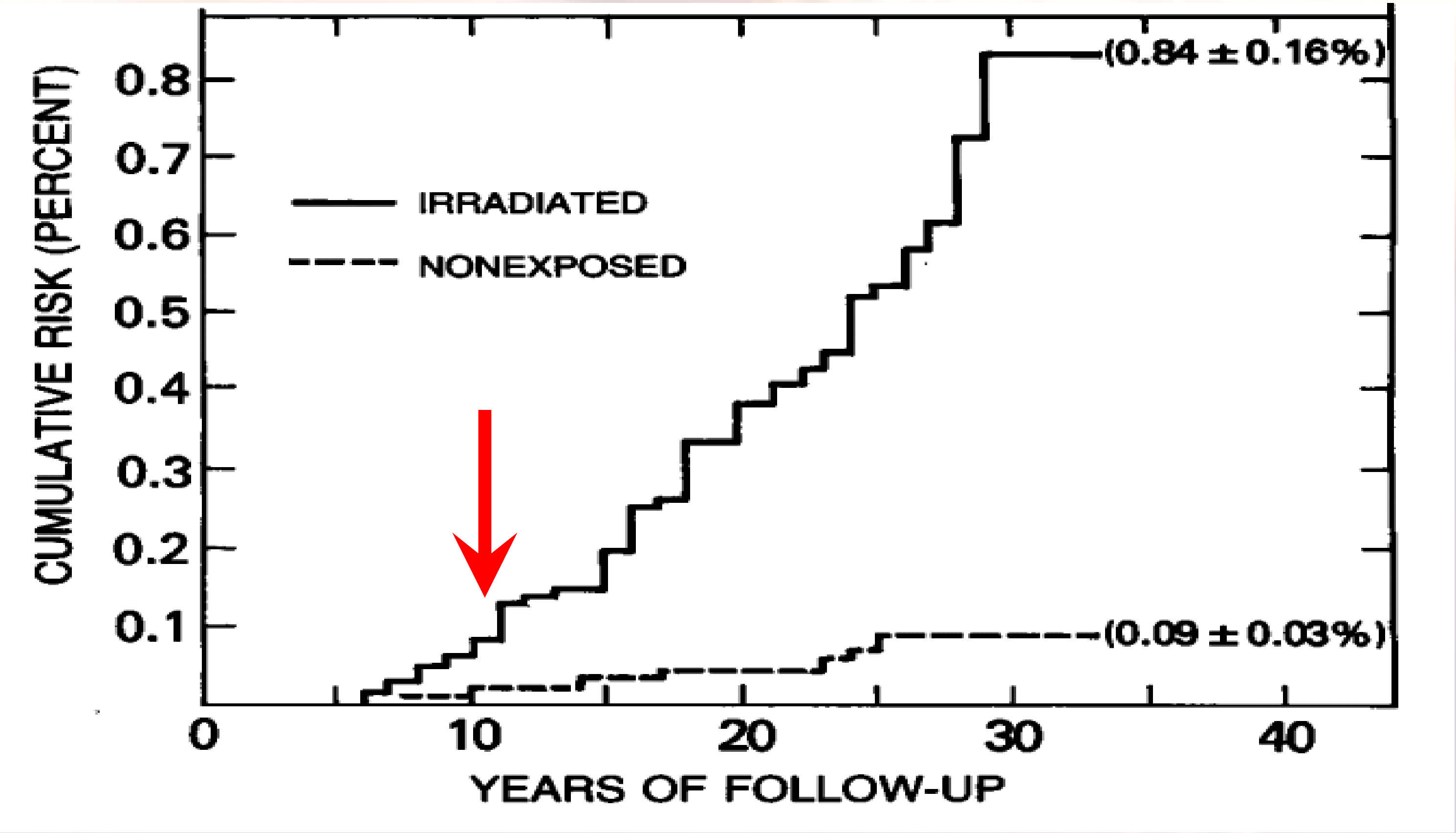
Preston et al. 1994



Percent of total radiation induced leukemias after 10 years follow up: 73%

Tumors of the Brain and Nervous System after Radiotherapy in Childhood

Ron et al NEJM 1988



Percent of total radiation induced brain tumors after 10 years follow up: 8%

UK CT study: Absolute risks *vs.* A-bomb based estimates

For a pediatric head CT scan, done around 1995

	UK CT study (10 yrs follow-up)	*UK CT study (corrected to lifetime follow-up)*	*A-bomb estimates, (corrected to lifetime follow-up)*
Leukemia	**1 in 10,000**	**1 in 7,500**	**1 in 10,000**
Brain tumor	**1 in 10,000**	**1 in 1,000**	**1 in 2,000**

Based on Pearce et al 2012

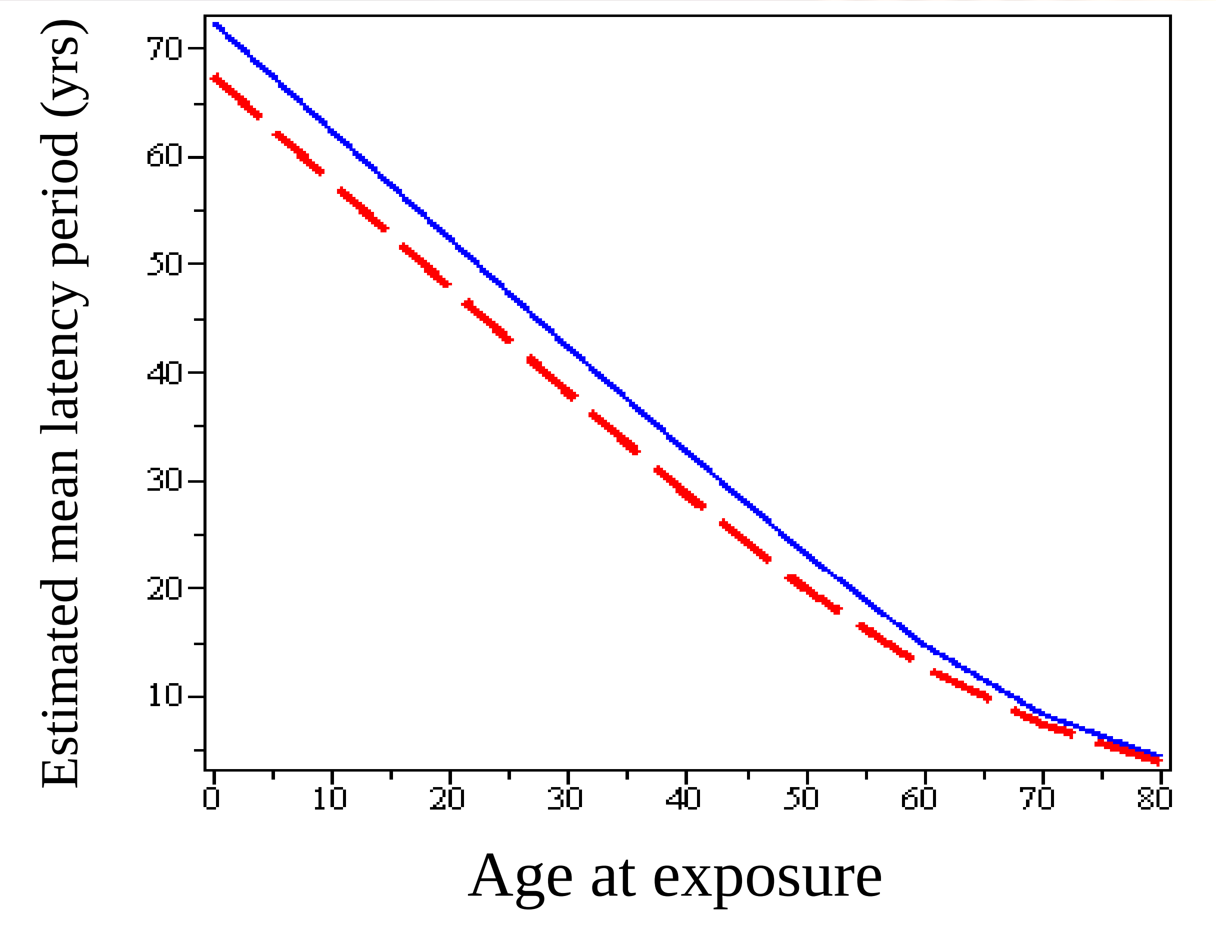
Based on Brenner et al 2001

The UK CT Study
Absolute risk estimates

- The various risk estimates for CT that have appeared in the past decade seem to have been pretty near the mark
- So the standard methodology of estimating low-dose radiological risks from A-bomb survivor data and physical dosimetry is probably not unreasonable
- … which is just as well, because we are going to have to wait a long time for the full epidemiological-based story
  - Other cancers
  - Lifetime risks
  - Adult CT

How long would a CT epi study need to be to estimate lifetime risks?

Median latency time: The time required to accumulate 50% of the predicted total lifetime radiation-induced absolute cancer risk



We are going to be reliant for quite a while on dosimetrically-based methods to estimate CT risks

1. Estimate the dose to each organ, as a function of age, gender, and type of CT exam

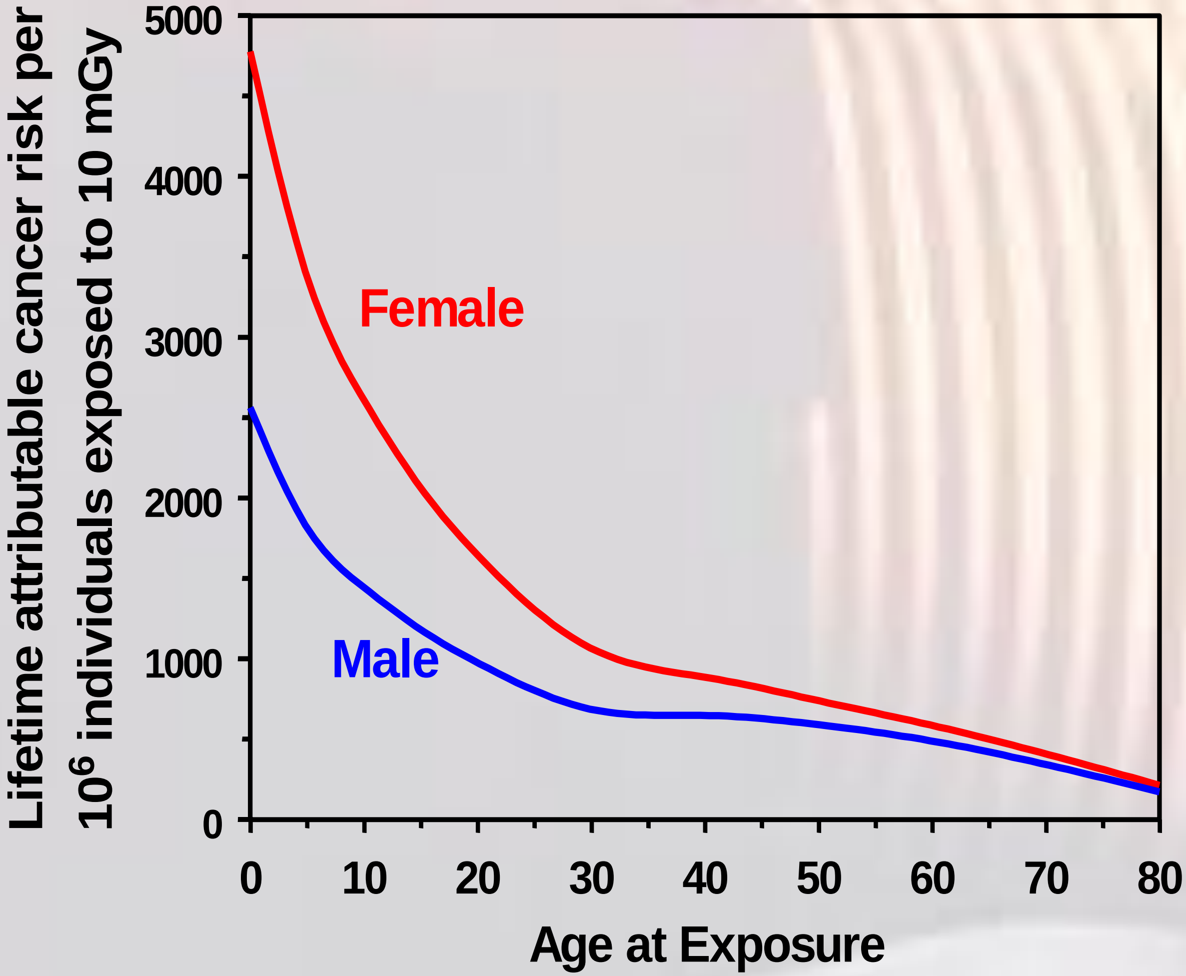
2. Apply estimates of age-, gender-, and organ-specific risks-per-unit dose

   (low-dose risks from A-bomb survivors, "transferred" to a Western population)

3. Sum the estimated risks for all organs

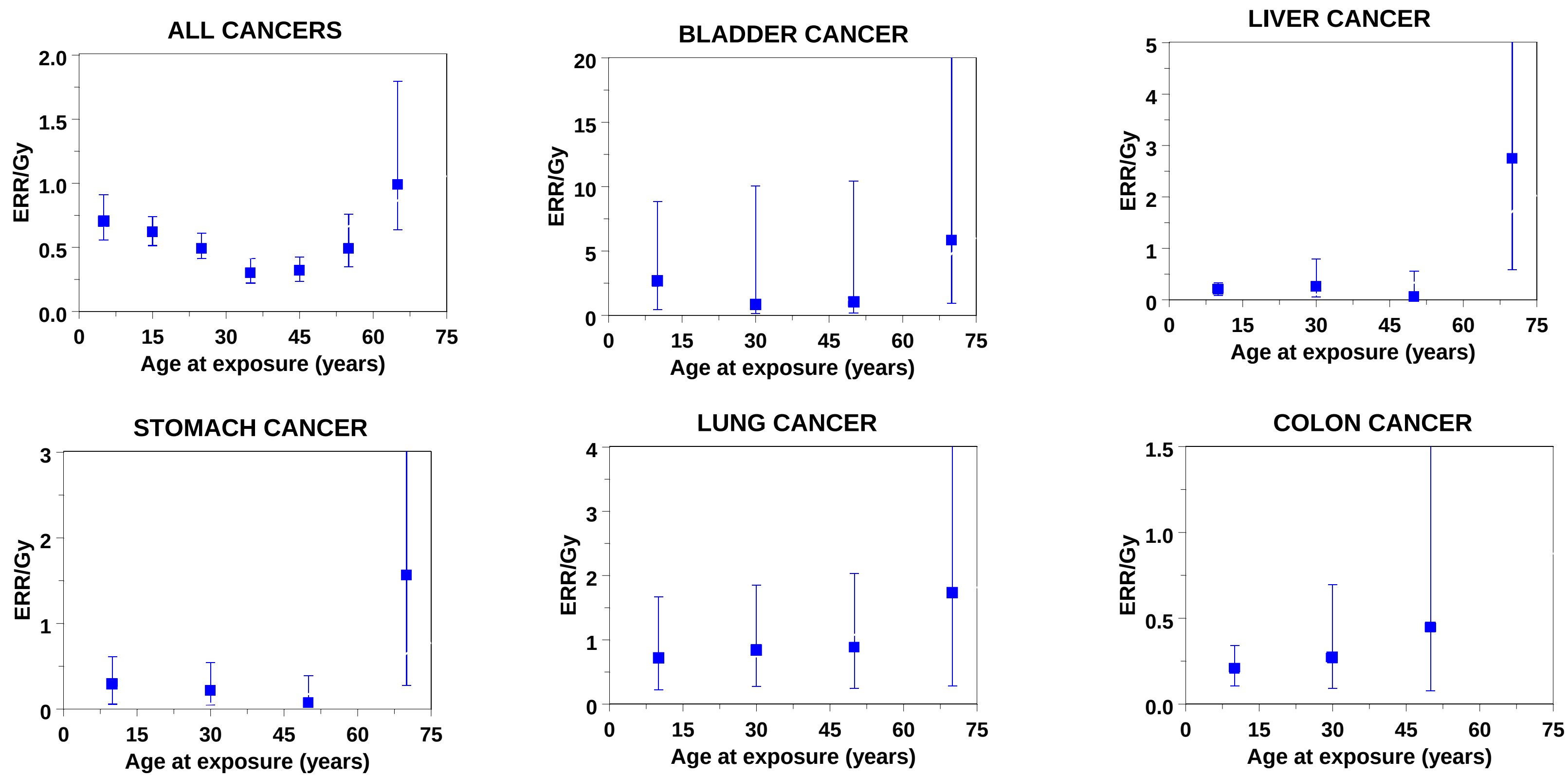
Should we be primarily concerned about children and young adults?

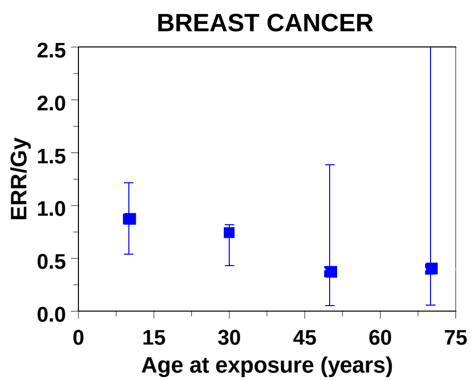
Estimated radiation-induced lifetime cancer risks as a function of age at exposure, from BEIR-VII



From BEIR-VII (2006)

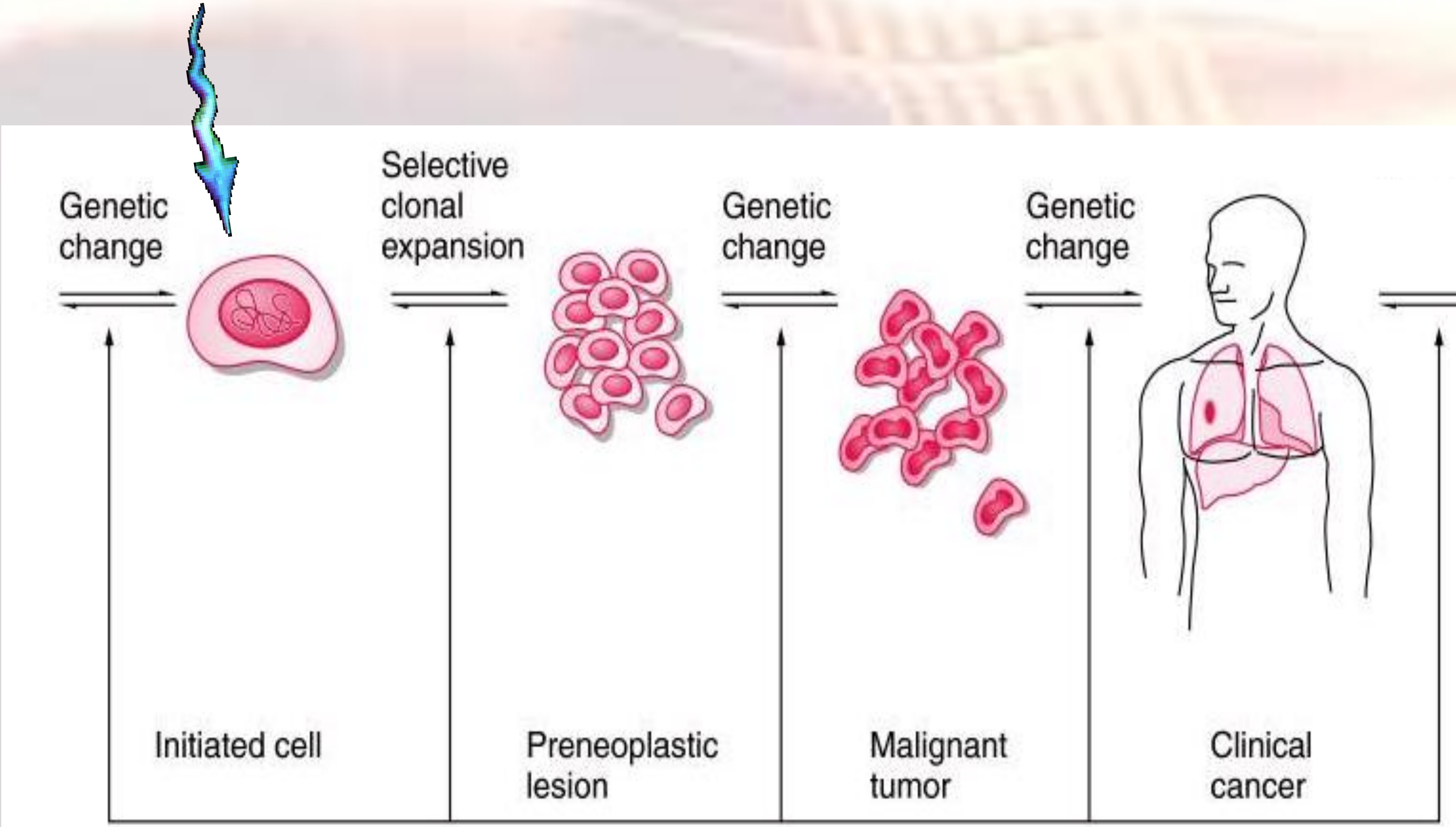
Lifetime cancer risk patterns among A-bomb survivors as a function of age-at-exposure





The actual data show very different age-at-exposure patterns relative to the monotonically decreasing risks modeled in BEIR VII

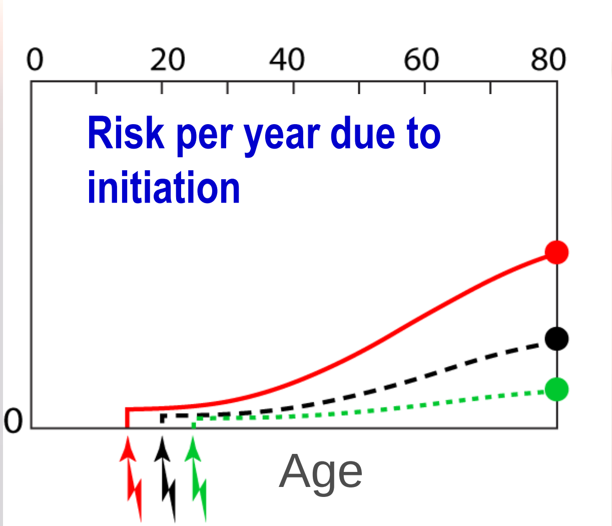
Multistage Carcinogenesis

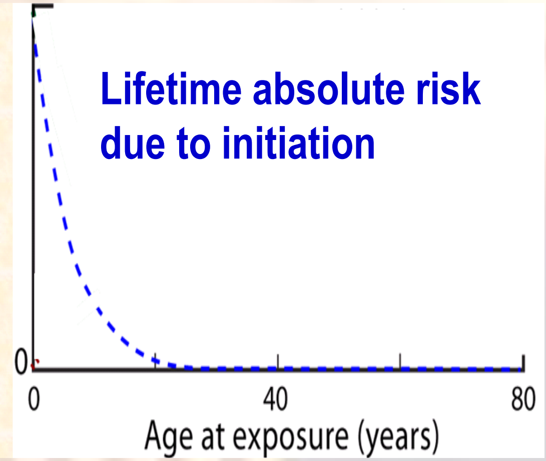


INITIATION PROMOTION MALIGNANT CONVERSION TUMOR PROGRESSION

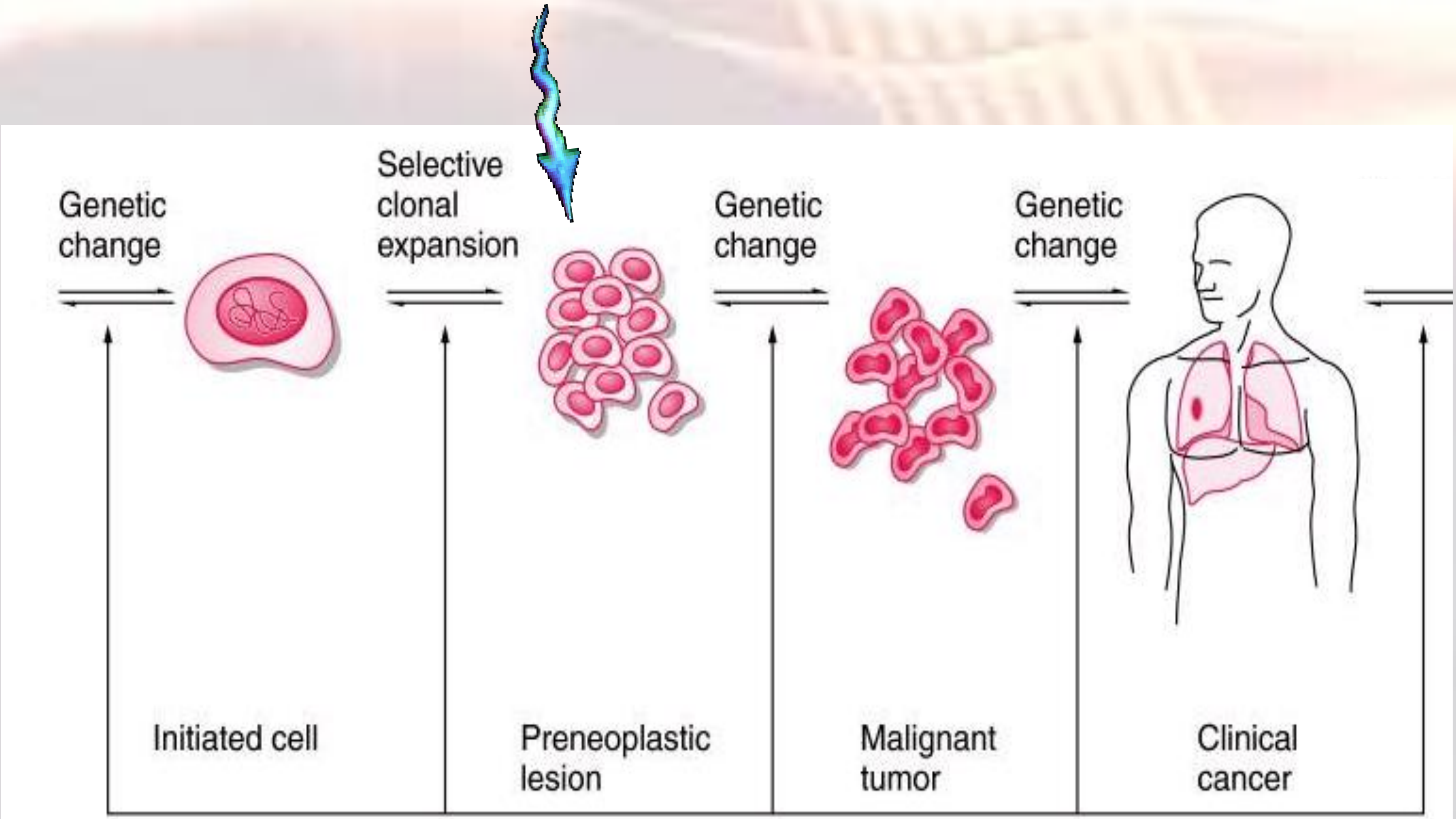
Lifetime cancer risk patterns as a function of age-at-exposure

Initiation: Here lifetime risk *decreases* with increasing age at exposure, because initiated cells have less time to exploit their growth advantage





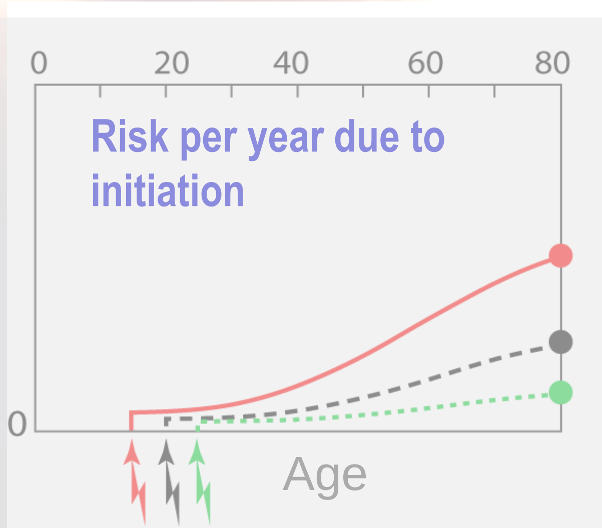
Multistage Carcinogenesis

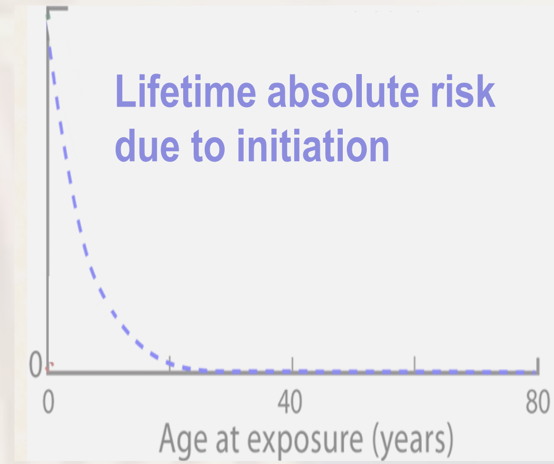


INITIATION **PROMOTION** **MALIGNANT CONVERSION** **TUMOR PROGRESSION**

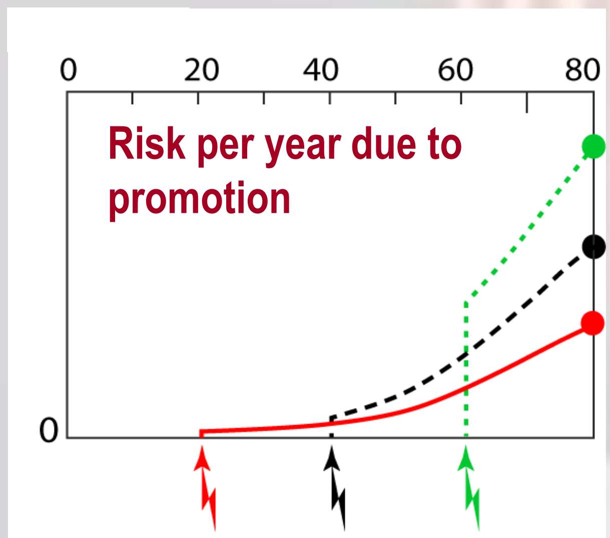
Lifetime cancer risk patterns as a function of age-at-exposure

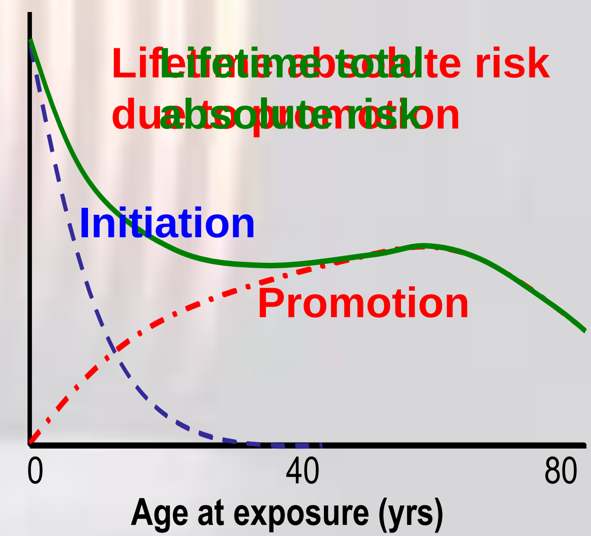
Initiation: Here lifetime risk *decreases* with increasing age at exposure, because initiated cells have less time to exploit their growth advantage.



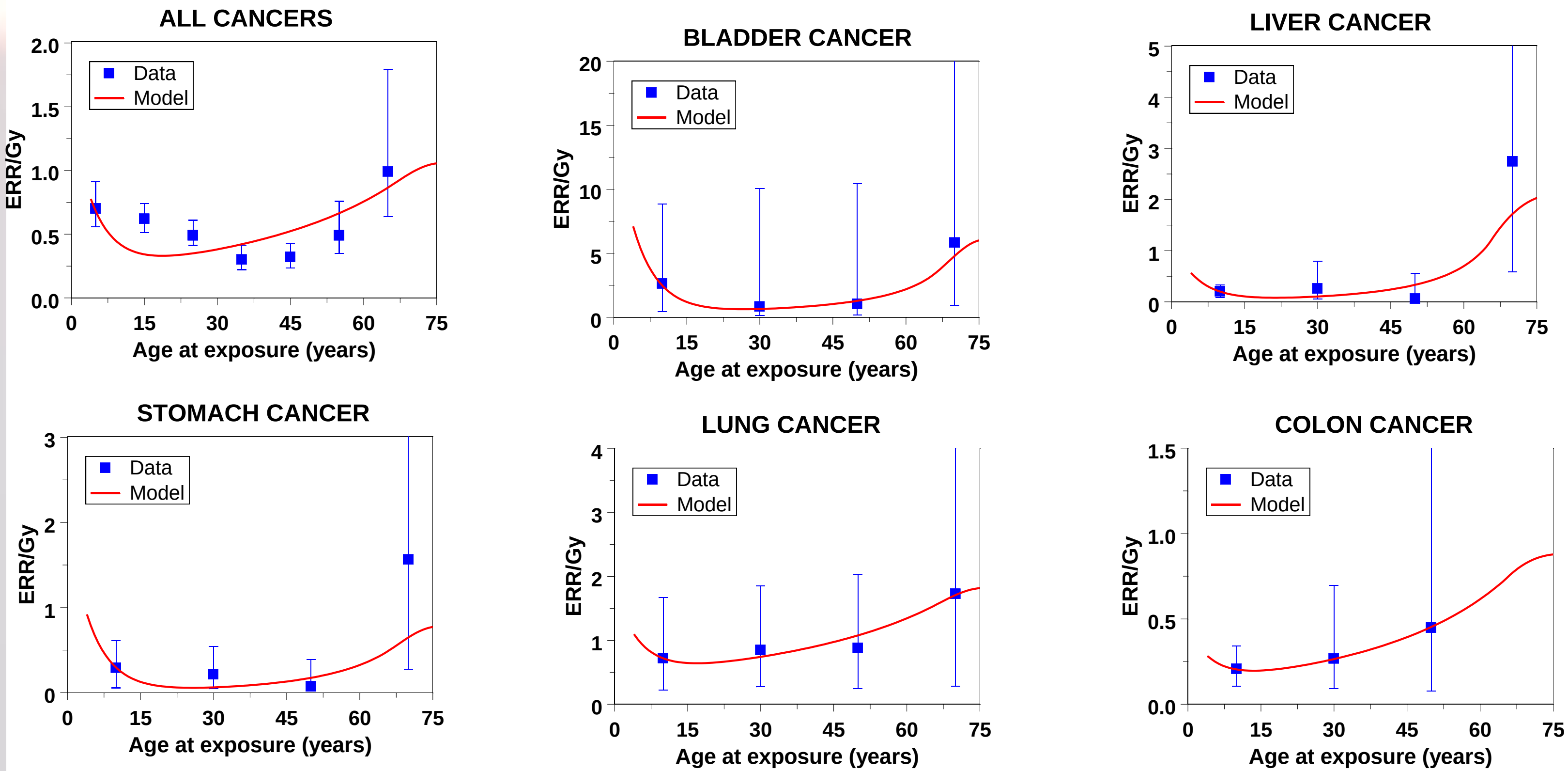


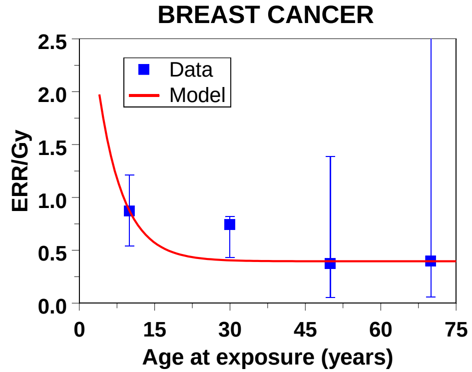
Promotion: In middle age, there are increasing numbers of pre-malignant cells to promote, so lifetime risk *increases* with increasing age at exposure.





Observed age-at-exposure risk dependencies can be explained by an age-dependent balance between initiation and promotion

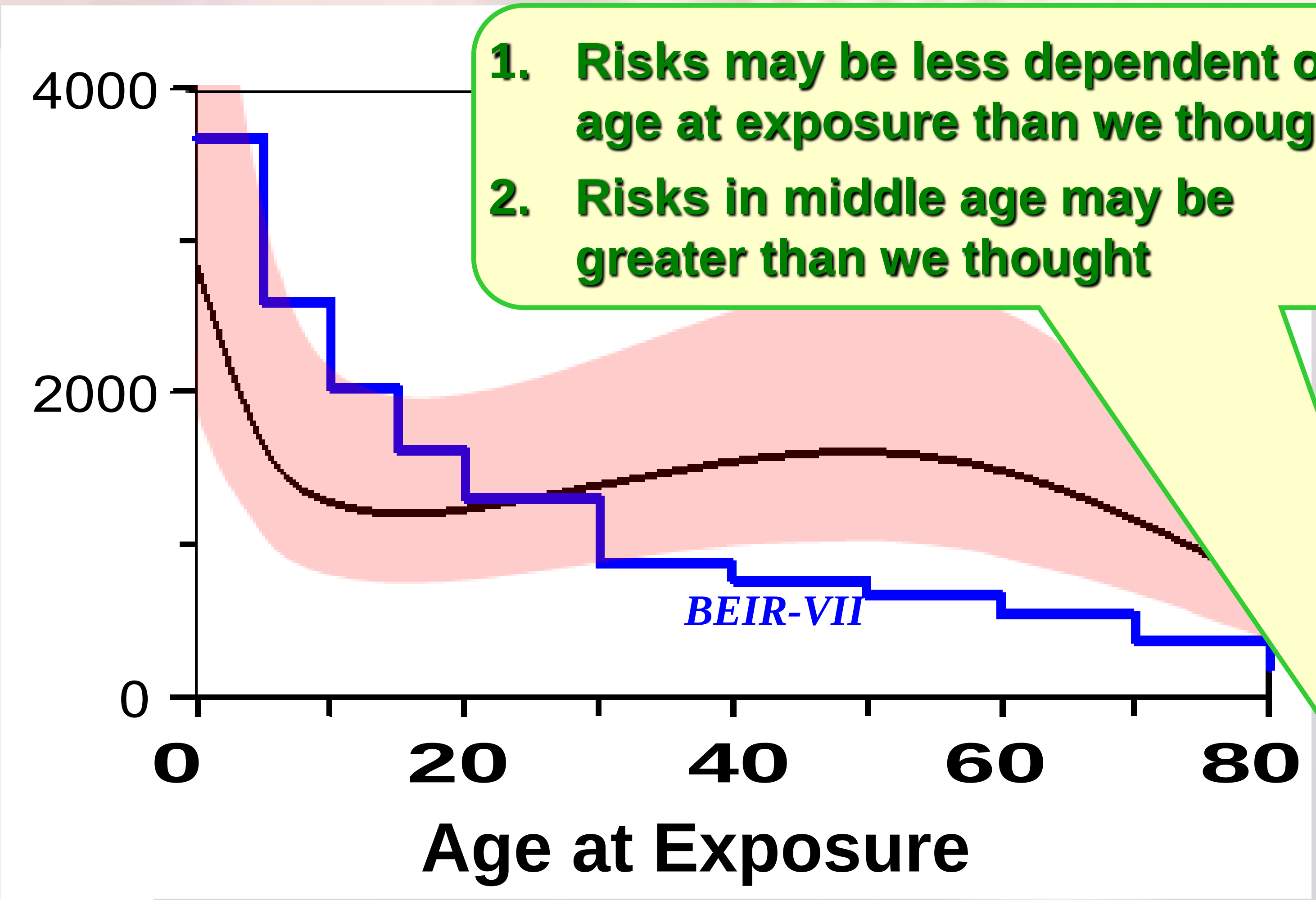




Red curves are the results from a radiation-induced initiation + promotion model

Shuryak et al JNCI 2010

Lifetime absolute risks, compared with BEIR-VII

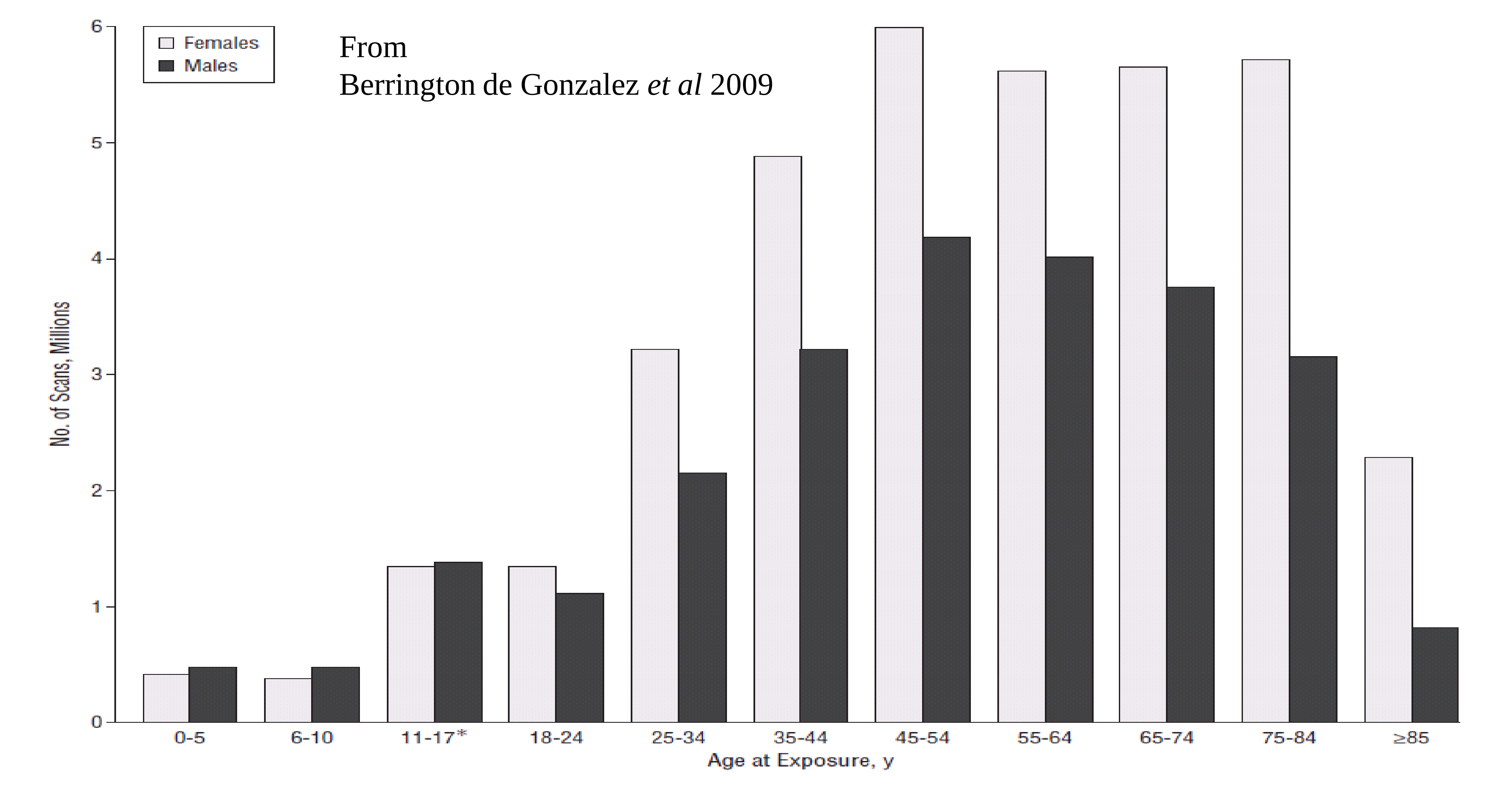


1. Risks may be less dependent on age at exposure than we thought
2. Risks in middle age may be greater than we thought

Shuryak et al JNCI 2010

… and of course most CT scans are given in middle age

Age distribution of CT scans, US, 2007



What do we know about risks from CT scans?

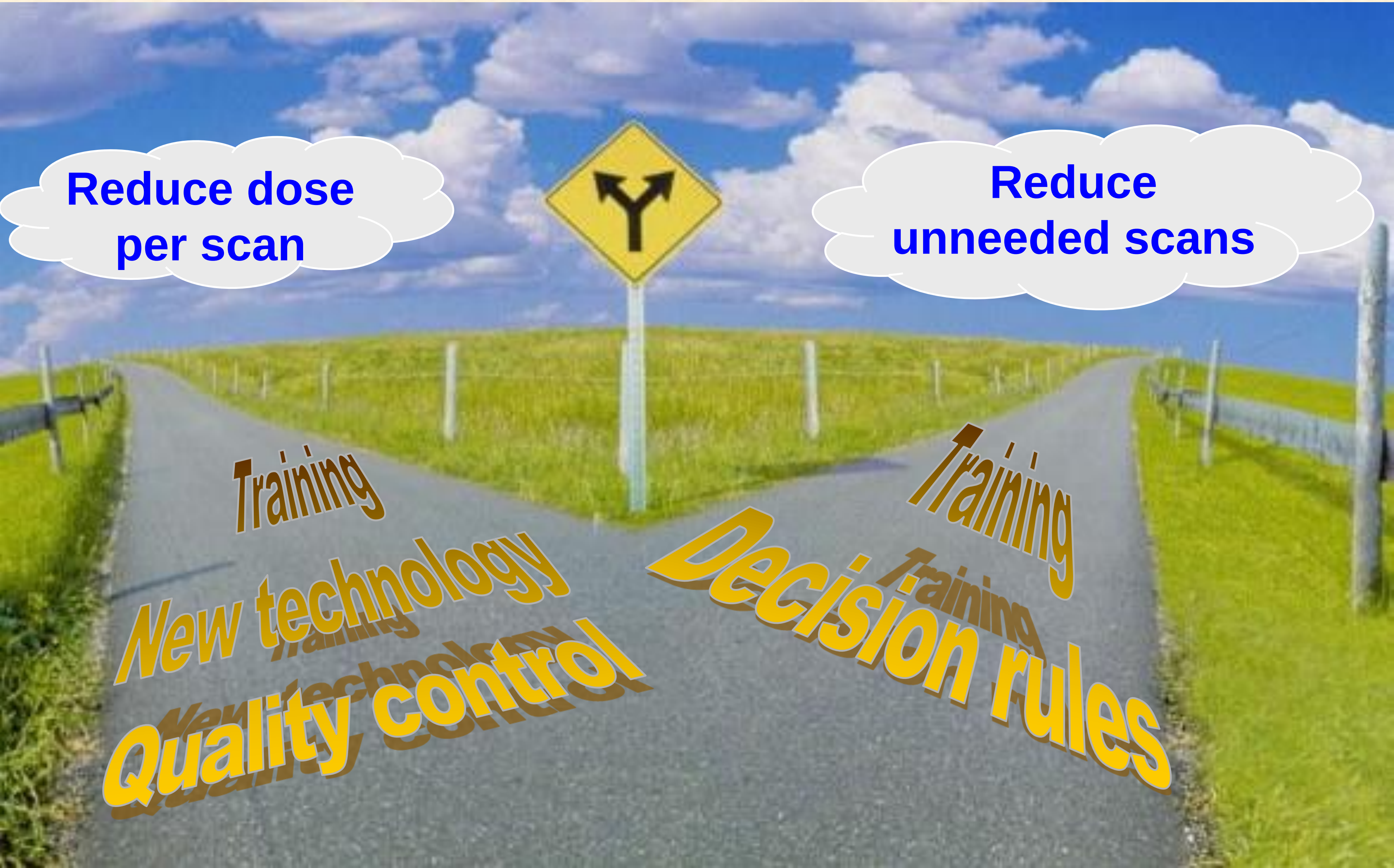
- **We have now passed a watershed in our field where it is no longer reasonable to suggest that CT risks are "*too low to be detectable and may be non-existent*"**
  - **We now know (almost) for sure that individual CT risks are small but real**
  - **Earlier CT risk estimates based on organ doses and A-bomb data have proved to be not unreasonable**

- **Because the individual risks are small, the individual benefits of any clinically-justified CT scan will by far outweigh the individual radiation risks**
  - **No need for super-accurate benefit-risk analyses for clinically-justified scans**

- **The CT risk issue is not confined to children**
  - **Radiation risks in middle age are probably somewhat larger than previously thought**
  - **Because there are far more adult CT scans, the population risks are larger for adults than for children**

- **While individual risks are small, because the number of CT scans is very large, and increasing, there will be significant population risks associated with CT**
  - **This population risk can be minimized by justifying and optimizing every CT scan**

A roadmap to reduce the long-term health consequences of radiation exposure from radiological exams



Inappropriate CT prescriptions rates:

Primary care physicians….
based on ACR Appropriateness Criteria

CT Exam	*Percent inappropriate*
Head / brain	**62**
Maxillofacial	**36**
Spine	**53**
Chest	**12**
Chest/abdomen/pelvis	**30**
Abdomen / pelvis	**18**
Miscellaneous + angiography	**21**
All CT exams	***27***

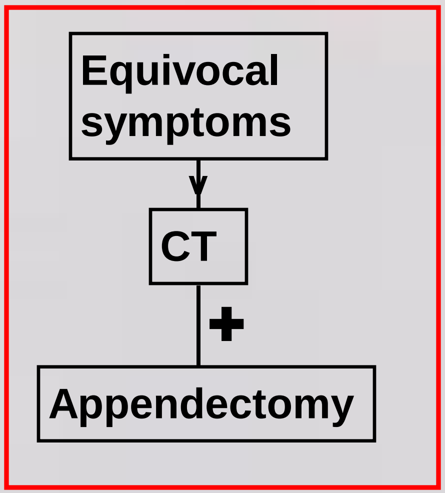
Lehnert and Bree 2010

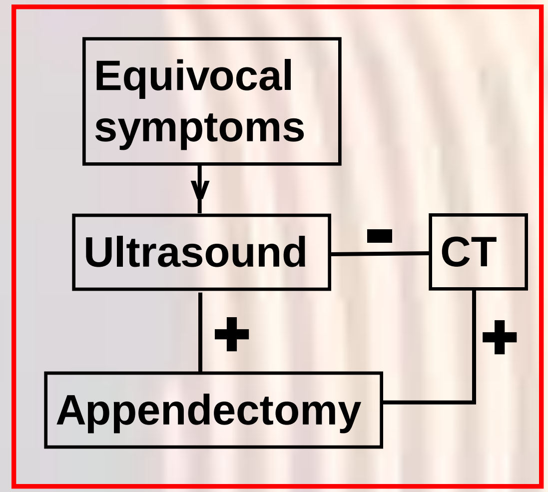
Potential gains from CT justification…

- **~82 million CT scans done last year in the US**
- **~4 million pediatric CT scans / yr**
- **~2.5 million pediatric head CT scans / yr**
- **~1.5 million clinically-unnecessary pediatric head CT scans / year**
- ***1,500 unnecessary radiation-induced brain tumors produced each year***

Approaches for diagnosing pediatric appendicitis

100% CT





70% CT

Based on Garcia Pena 2004

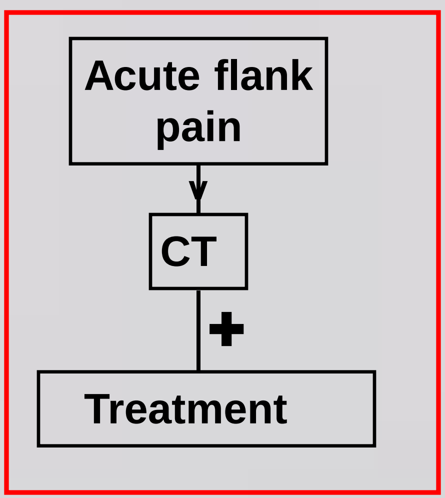
Approaches for imaging patients with acute flank pain

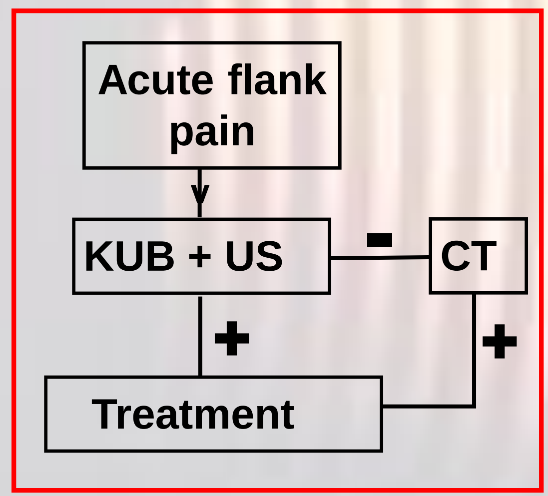
AJR Am J Roentgenol. 2002 Feb;178(2):379-87.

Suspected Ureteral Colic: Primary Helical CT Versus Selective Helical CT After Unenhanced Radiography and Sonography

Orlando Catalano[1,2]
Antonio Nunziata[3]
Francesco Altei[1]
Alfredo Siani[1]

100% CT





?% CT

Can CT usage be reduced?
(or the rate of increase slowed?)
without compromising patient care....

- **A significant fraction of CT scans (at least ¼ ??) could practically be replaced by alternate approaches, or need not be performed at all**

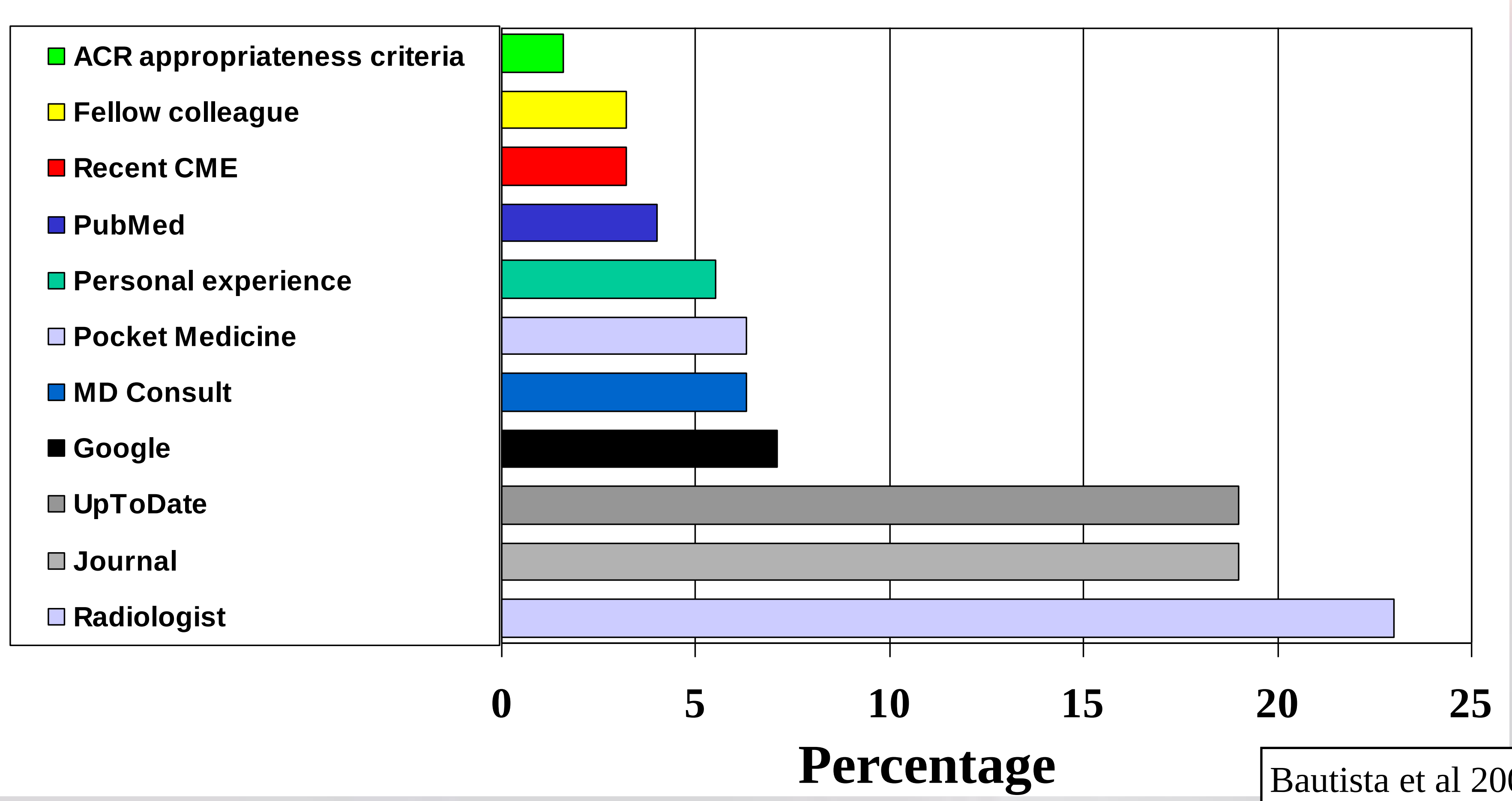
- **Targeting this "one quarter" is a [illegible]**

- **Physicians are subject to significant pressures**
  - **Throughput**
  - **Legal**
  - **Economic**
  - **From patients**

Clinical Decision Rules

Do physicians actually use ACR appropriateness criteria?

- *What is your primary information resource in making imaging decisions for your patients?*



Bautista et al 2009

Radiology Decision-Support System

MGH Radiology Order Entry

Patient Name: **TEST, IGNORE** MRN: **0000006** Ordering Physician: [redacted]

[Proceed with Order] [Cancel Exam]

Head CT has low utility for the clinical indications provided

9	8	7	6	5	4	3	2	1

Indicated 7-9 Marginal 4-6 Low Utility 1-3

Alternate procedures to consider:

MR	PET	CTA	MRA
8	8	1	1

Options:

- Proceed with exam
- Cancel or select new exam
- Change indications and resubmit

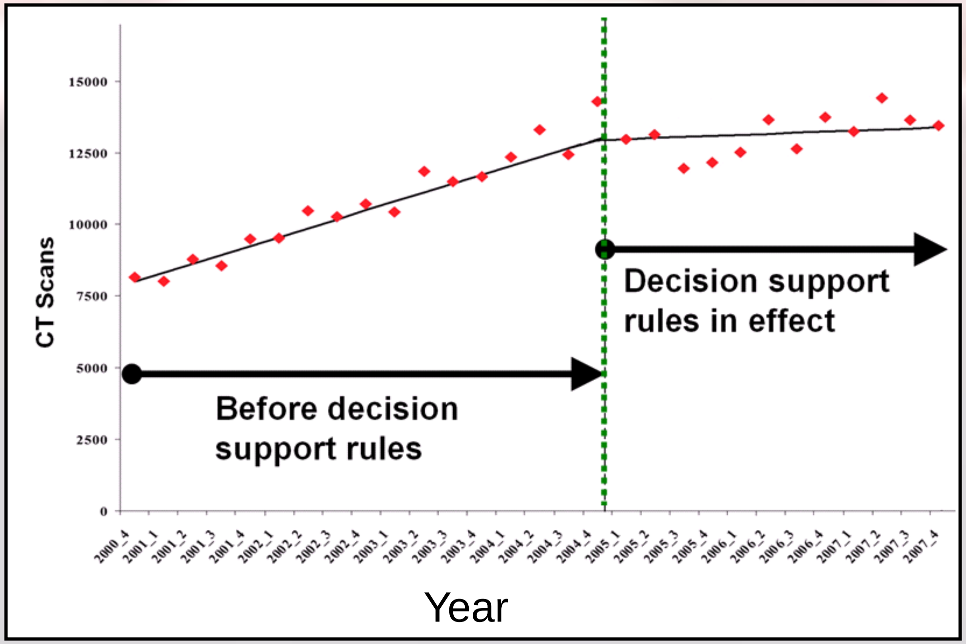
At least one box MUST be selected from either of the following groups

SIGNS / SYMPTOMS

- [ ] Acromegaly
- [ ] Speech changes (or Aphasia), new or progressive
- [ ] Concussion mild or moderate acute, no neurological deficit
- [ ] Coordination changes, new or progressive
- [x] Dementia
- [ ] Head injury mild or moderate acute, no neurological deficit
- [ ] Headache
- [ ] Hyperprolactinemia
- [ ] Pain in face
- [ ] Weakness- right side / left side / both
- [ ] Acute visual deficit (other than photophobia and aura)
- [ ] Syncope/fainting
- [ ] Signs of meningeal irritation (such as stiff neck)
- [ ] Ammenorrhea
- [ ] Abnormal gait (Ataxia)
- [ ] Seizures new or progressive
- [ ] Cranial nerve palsy (specify):
- [ ] Dizziness
- [ ] Head injury moderate or severe acute, stable
- [ ] Hearing changes
- [ ] Mental Status change (after trauma)
- [ ] Sensation loss
- [ ] TIA with transient neurological disturbance
- [ ] Mass or lump
- [ ] Vision changes
- [ ] Signs of increased intracranial pressure (such as fundascopic exam)

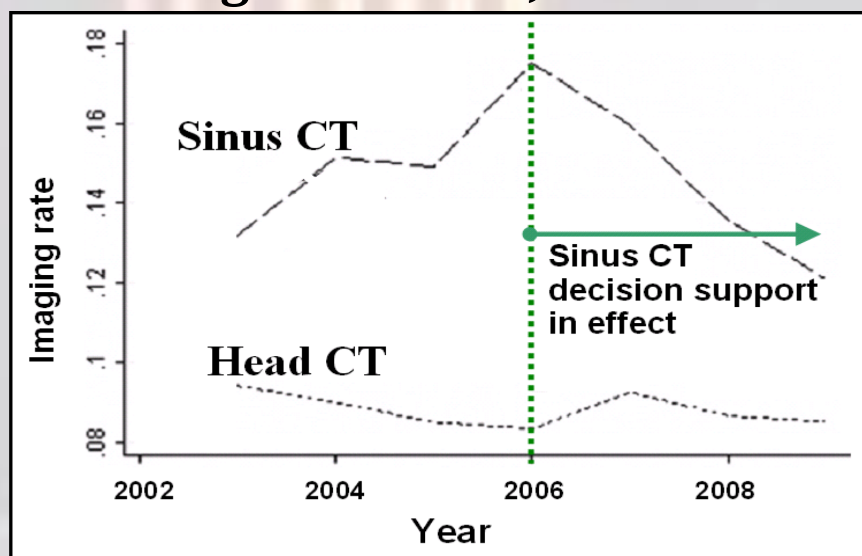
Sistrom, C. L. et al. Radiology 2009;251:147-55

Does putting decision support into order entry help?



MGH outpatients

Virginia Mason, Seattle



Conclusions

I: Are CT radiation risks real?

Yes

Conclusions

II. The individual risks are very small

- **When a CT scan is clinically warranted, the benefit will by far outweigh any possible individual radiation risk**
- ***(though of course we can and should continue to lower doses per scan)***

Conclusions

III. Reducing clinically unwarranted CT scans

- The main concern is really about the population exposure from the roughly ¼ of CT scans that may not be clinically warranted

Conclusions

IV. Reducing doses per scan is hard but doable; Reducing unwarranted CT scans is harder