

Imaging Wisely

Improving the Value of Medical Imaging

Rebecca Smith-Bindman, MD

Professor Radiology and Biomedical Imaging

Epidemiology and Biostatistics

Philip R Lee Institute for Health Policy

Obstetrics Gynecology and Reproductive Sciences

Director of the Radiology Outcomes Research Lab

The University of California San Francisco



Conflicts of Interest

- Federal and PCORI Grants
- No other conflicts

Advanced Diagnostic Imaging

- Improvements in imaging US, CT, MRI have been spectacular
- These tests are important and beneficial for our patients
- But the use of imaging comes with tradeoffs – just like everything else in medicine – and its important to consider potential harms of imaging in addition to potential benefits – as both need to include your imaging choices

Use of Diagnostic Imaging

- I am a big fan of advanced imaging
- I am not the only one enamored with imaging – everyone is
- And the use of imaging has soared over the last two decades

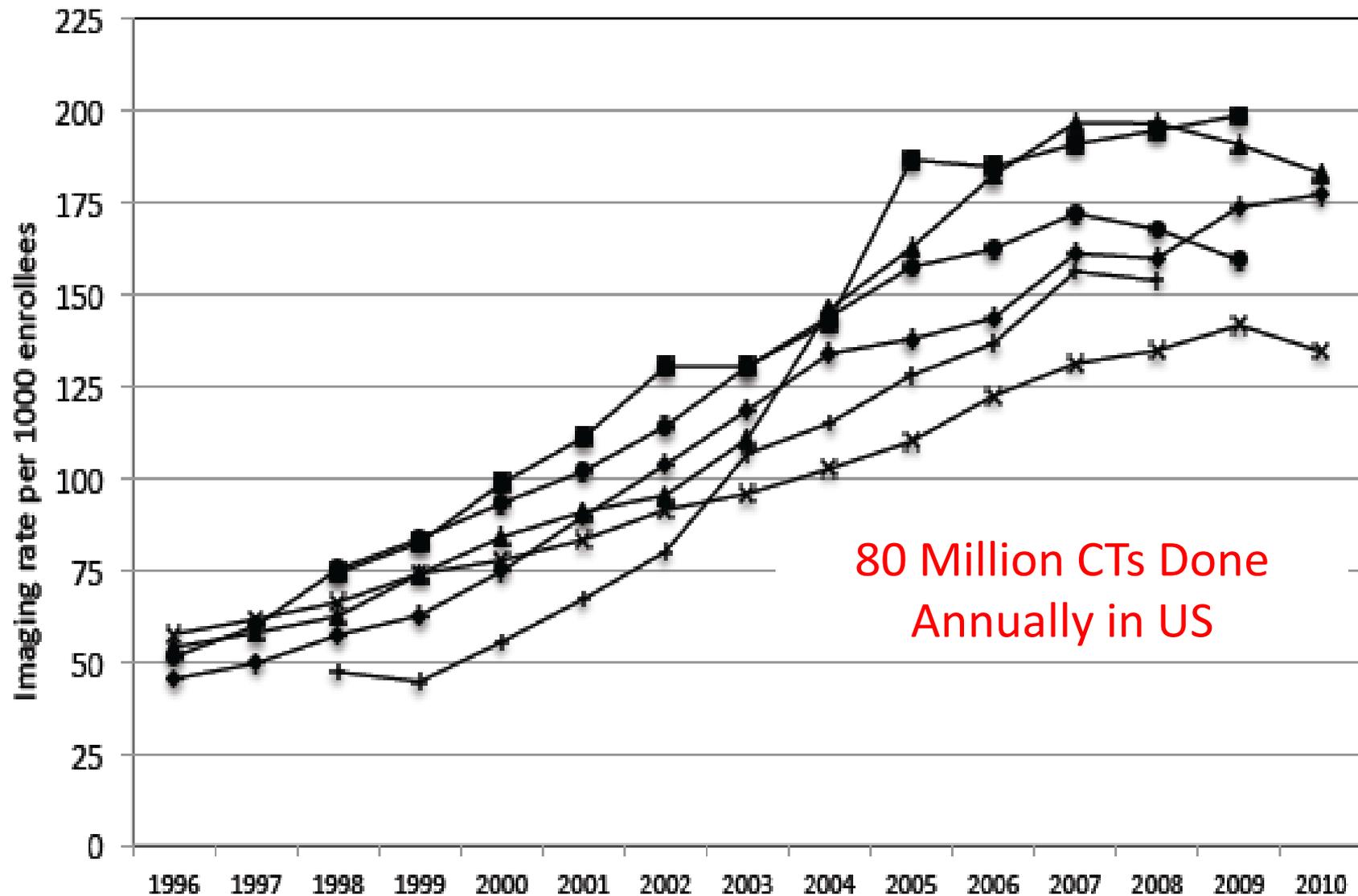
How Many Patients Undergo CT imaging per Year

- 1 CT per 5 patients per year
- 1 CT per 10 patients per year
- 1 CT per 100 patients per year
- 1 CT per 500 patients per year

Imaging Utilization Among Patients Enrolled in Large Integrated Health Systems

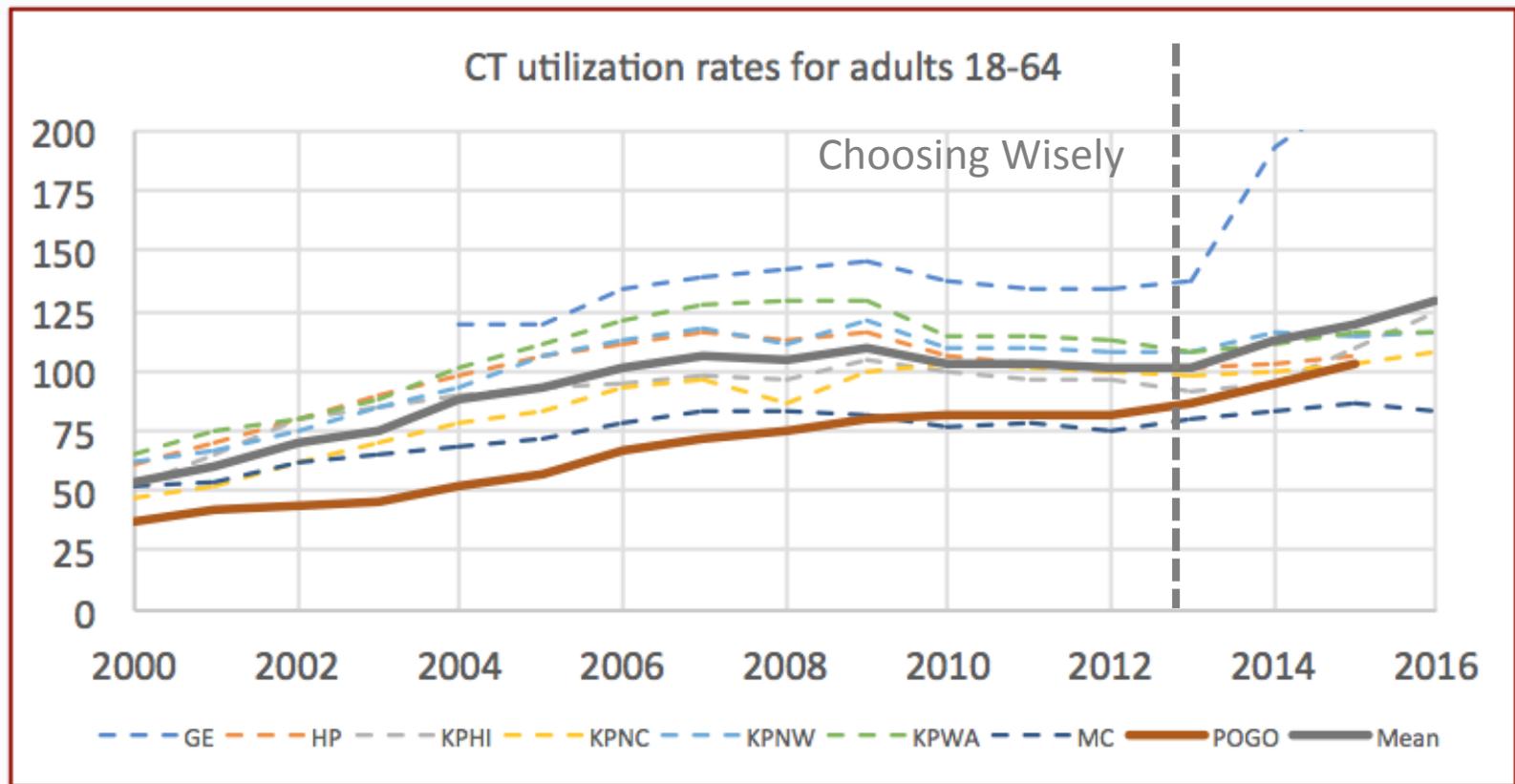
- Retrospect study, patients enrolled in one of 6 large integrated health care systems, 1996 – 2010
- 2 million HMO members each year, followed for 15 years

CT Examinations per 1000 HMO enrollees / Year



80 Million CTs Done
Annually in US

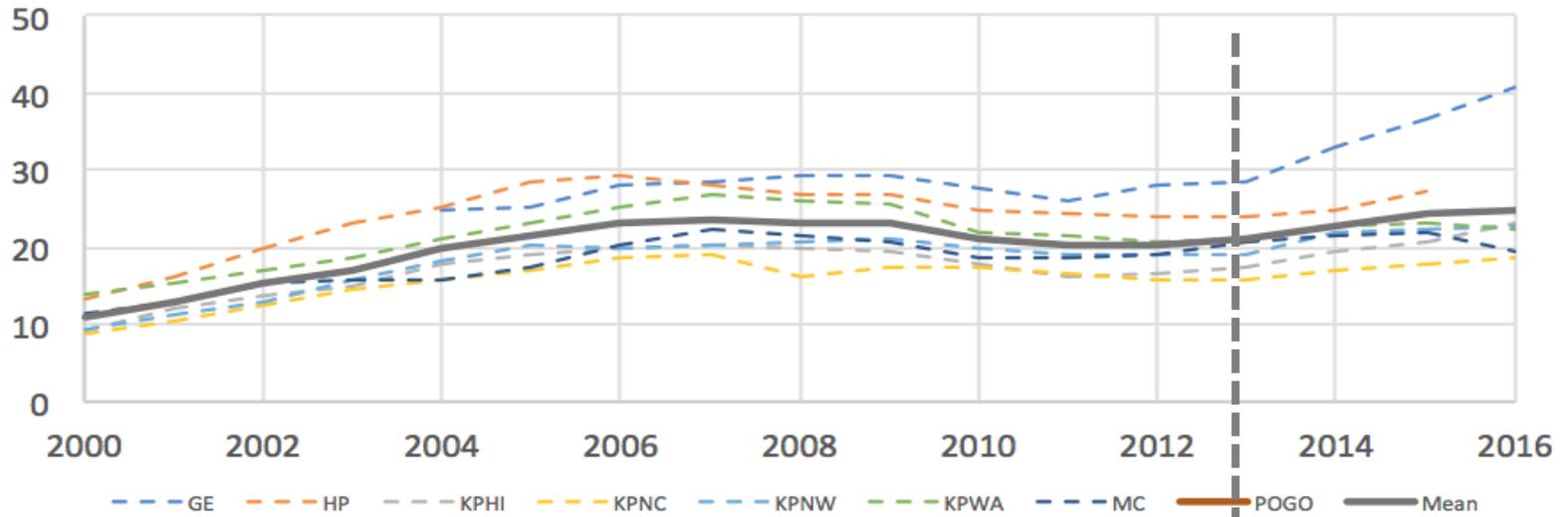
Imaging Trends: Different Integrated Systems and More Current Data



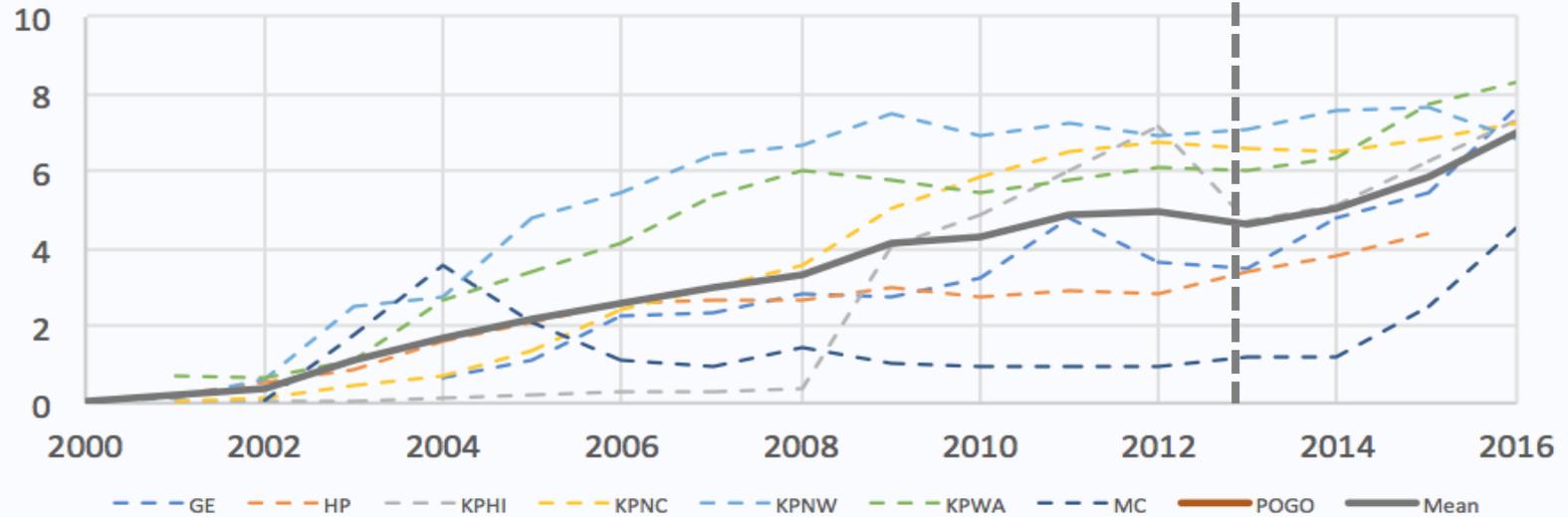
Imaging Trends in Last 15 Years

	Abdomen CT Scans / 1000			
	2002	2007	2012	2016
All ages*				
Rate per 1000	28	45	42	55
		12%	-1%	7%
Children <18 years				
Rate per 1000	3	6	4	5
		18%	-7%	5%
Adults 18-64				
Rate per 1000	26	44	41	55
		14%	-1%	8%
Adults 65+				
Rate per 1000	73	111	105	128
		10%	-1%	5%

Age-standardized non-vascular CHEST CT utilization rates



Age-standardized vascular CHEST CT utilization rates



Drivers and Costs of Medical Imaging

- Imaging utilization is high, 100-200 billion dollars spent annually
- It has grown at twice the rate of total health costs
- Drivers of medical imaging multifactorial
 - Improvement in technology
 - Patient Demand : no perceived disincentives to imaging
 - Physician Demand : testing often easier than seeing patient
 - Fear of malpractice
 - Profitability
 - Increased capacity resulting for a proliferation of equipment

How Much Imaging Is (Un) Necessary

- It's a difficult question to answer, with no good studies
- It's widely believed / cited that upwards of 30% of all advanced imaging is unnecessary
- There are many factors that drive unnecessary imaging:
 - Lack of evidenced based guidelines
 - Strong incentives to use imaging
 - Few disincentives to use imaging
- There is always a balance in the use of health care, and if there are few benefits, than risks and potential harms dominate

Potential Risks and Benefits of Imaging

- Potential benefit: rapid and accurate treatable diagnoses
- Potential harms
 - False positives / Incidental findings / Over diagnosis
 - Radiation Exposure
 - Wasting time and missing the opportunity to treat the patient
 - Unsustainable costs

False positives / Incidental findings / Over-diagnosis

- These are all different, but have important similarities
- None help our patients
- All lead to a cascade of testing
- All lead to labeling (some short term, some for a lifetime)
- All lead to anxiety, costs, and can be a huge distraction

Dr. Casarella, Radiology Chair, Letter to the Editor, Radiology

Underwent a screening CT Colonography – (results negative)

- + Renal mass : additional CT confirmed a benign cyst (FP)
- + Liver mass: additional CT and CT bx - showed benign (incidental)
- + Pulmonary nodules: PET negative: surgical resection- old infect

Cost:	\$50,000
Recovery:	5 weeks out of work
Disease diagnosed:	None
Reassurance:	The test cleared up the disease it caused
Benefit:	Ruled out colon cancer
Harms:	Costs, false positives, unnecessary Rx, Radiation, a a huge waste of time

Over Diagnosis : A Complex Problem

- Large problem and hard to fix or explain
- This reflects disease under the microscope (often cancer) but will not progress, so not really what patients or MDs think of as disease
- Often described as dying with a cancer, not from the cancer
- Imaging leads to a profound increase in detection in these cases, and by definition will not lead to the reduction in advanced disease
- For a given patient – its not currently possible to differentiate over-diagnosed dz from real disease- although we can improve what we do as radiologists and pathologists and to categorize disease better
- This must be thought of as a harm of imaging -

False Positives: Chasing Imaging Findings

- In some cases, there is no way to decide if a finding is important
- In many cases, it is possible to know that a finding is likely not important – but its still hard to ignore
- We often find lesions of the thyroid, when looking at the chest, findings in the kidneys when looking at the spine, brain when looking at neck vessels
- Its important to keep the important management decisions at the forefront of how we spend out time

Radiation Exposure: A Substantial Potential Harm

- Radiation is energy
 - High-speed particles and electromagnetic waves
- There are many sources of radiation - some naturally occurring, others are used in science, industry, medicine
- **Ionizing radiation** is one type – and its effect on cells is known. It can remove tightly bound electrons from their orbits – break chemical bonds – change DNA
- Ionizing radiation exposure cannot be eliminated, but to the degree we can minimize exposures we have made decisions to do so - many organizations – ICRP, NCRP, IAEC- are dedicated to this task

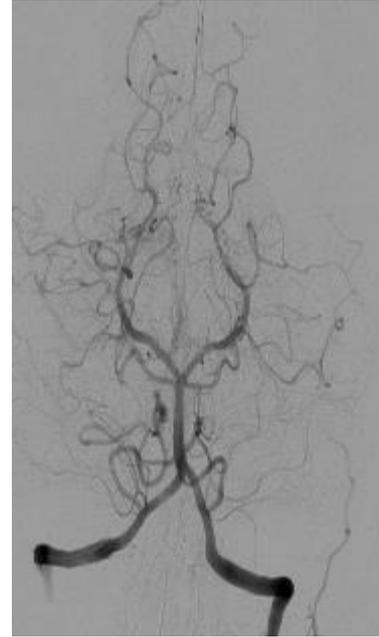
Radiation from Imaging



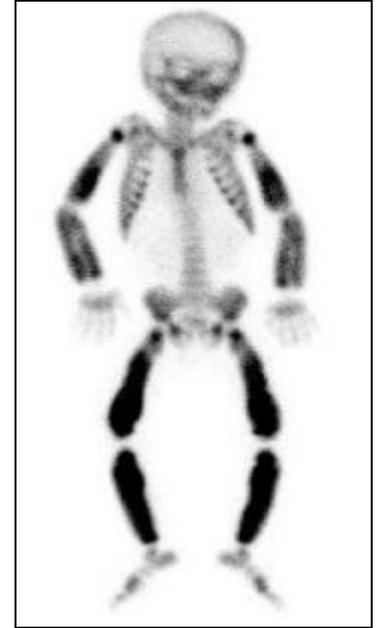
Radiographs
(x-rays)



Fluoroscopy



Angiography

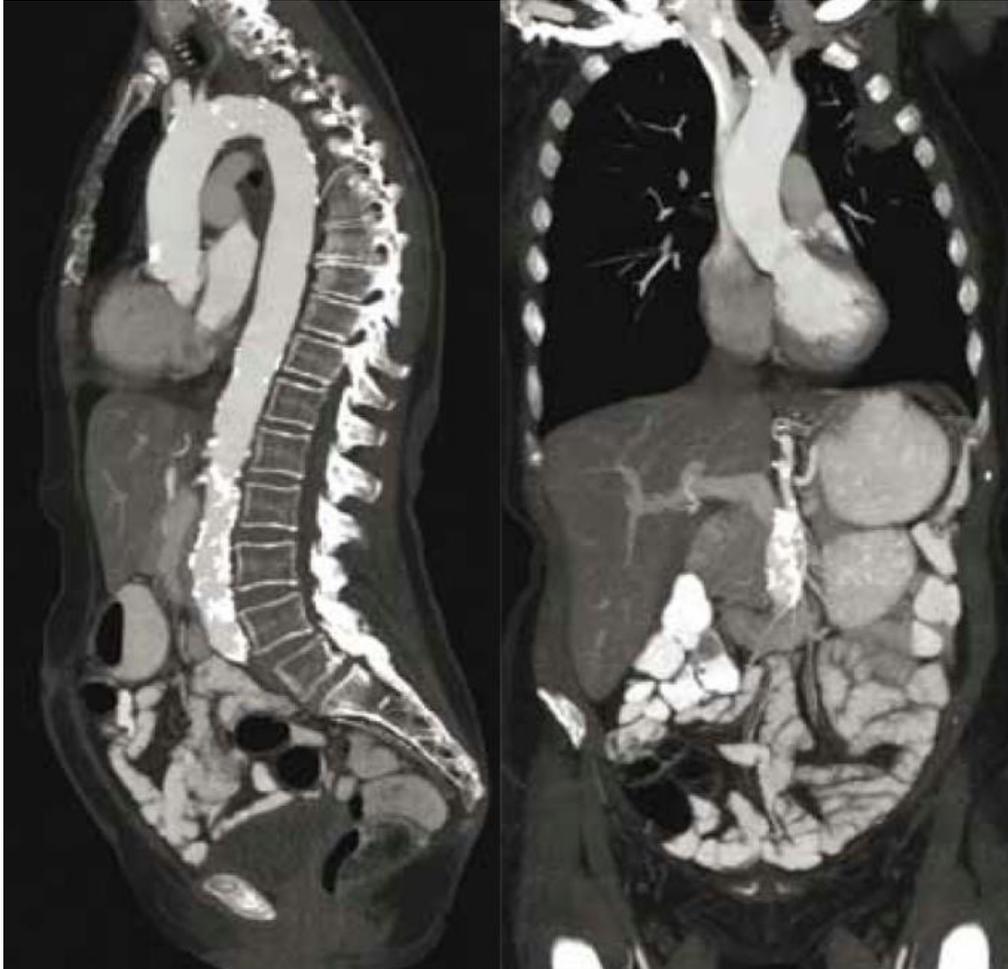


Nuclear
Medicine

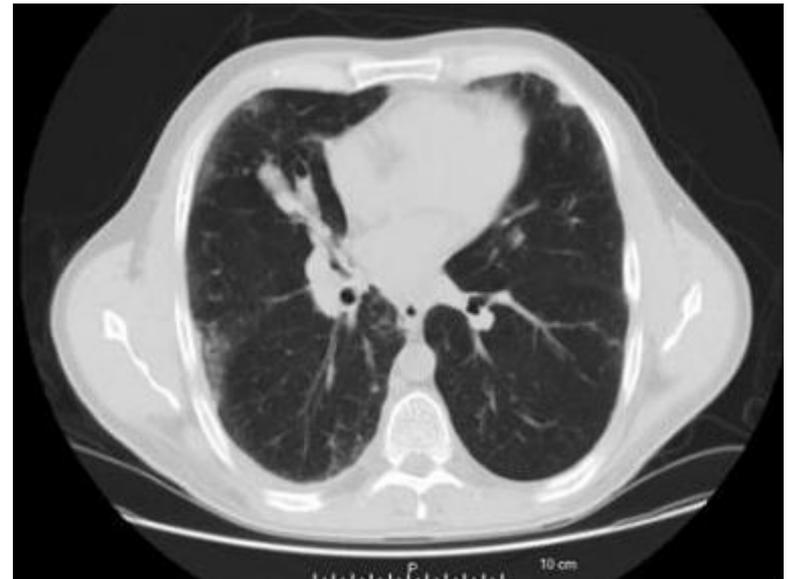
X-Rays

Gamma Rays

Radiation from Imaging: CT: 75% of all exposure



CT Scans are used frequently
CT doses per scan are high



Radiation Effects

- Very high levels can lead to burns, hair loss, immediate harms
- The dose we use in imaging are lower, but can nonetheless damage DNA and the impact can take years or decades to become apparent as cancers
- Substantial evidence on the harmful effects of radiation
- Modeling suggests 2-5% of all cancers come from imaging
- Because risks are delayed, they are harder for patients to comprehend, but no less important as long as a patient has a life expectancy > few years

What Do We Know About the Harmful Effects of Radiation

- Direct studies showing DNA damage follow one CT Scan
- Numerous (hundreds) of epidemiological studies

Biological Response to Radiation From CT

Nguyen, JACC Cardiovasc Imaging, 2015

- Exposure of cells to *therapeutic* radiation triggers a complex network of signal transduction pathways, changes gene expression, protein structure: results in cell cycle arrest & DNA repair activation
- Does *diagnostic* CT cause DNA damage?
- Prospective cohort, 67 patients, 2012-2013, underwent cardiac CT
- Biomarkers of DNA damage/ cell death measured before and several times after imaging

CT caused many biological effects that persisted 1 month

- Mean exposure 30 mSv
- 3% of lymphocytes had DNA damage
- Apoptosis-increased 3 fold
- Genome : changes in expression of 39 transcription factors, 33 signaling metabolic pathways, and 17 biological processes involved in regulation of cell cycle and DNA repair ; Genes in DNA repair (DDB2, XRCC4, BAC) sig increased expression
- Measureable change, and a dose response with dose ≥ 7.5 mSv
- While many damaged cells were repaired, a small percent of cells did not

Summaries of Published Data on Ionizing Radiation

HEALTH RISKS
FROM EXPOSURE TO
LOW LEVELS OF
IONIZING
RADIATION
BEIR VII PHASE 2

NATIONAL RESEARCH COUNCIL ON ENVIRONMENTAL HEALTH EFFECTS



Risk of Solid Cancers following Radiation Exposure: Estimates for the UK Population

Report of the independent Advisory Group on Ionising Radiation



Epidemiology on the Harmful Effects of Low Dose Radiation

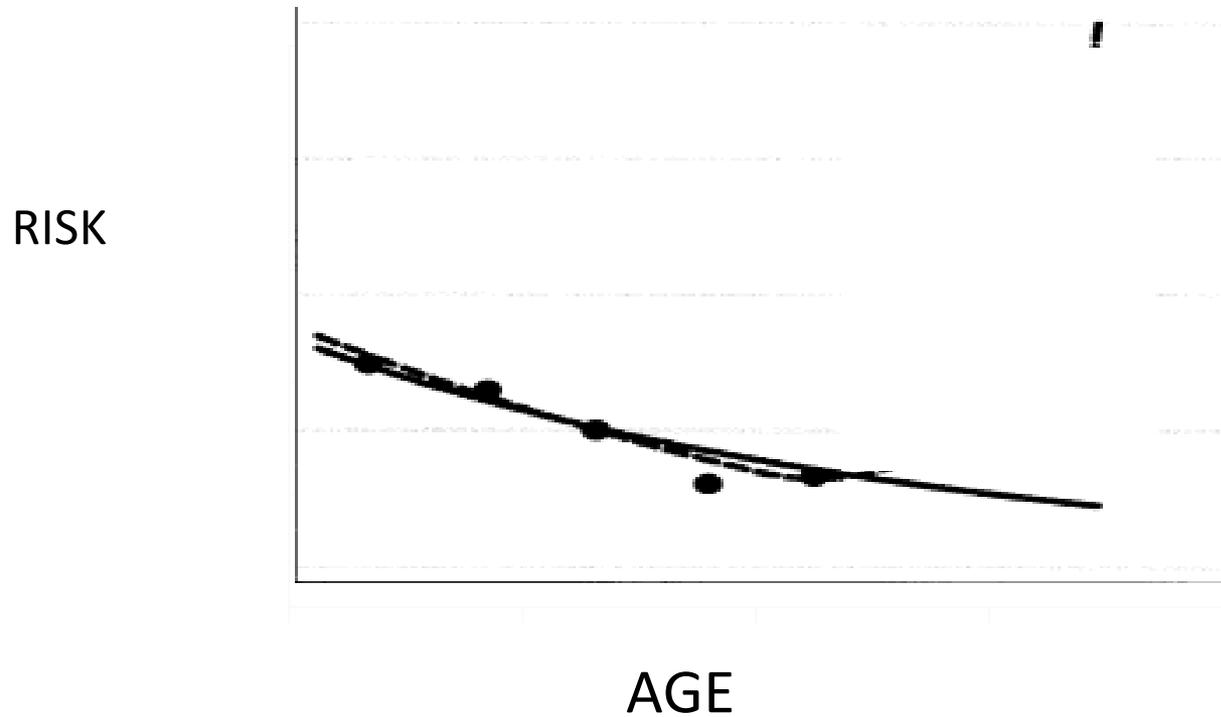
- 120,000 survivors of the Atomic bombs
- Patients treated for cancer
- Patients treated for benign conditions
- Patients who received repeated X-rays
- Radiation workers, such as in the nuclear power industry
- Environmental accidents (Chernobyl, Techa River)
- Direct studies of CT (these were not included in BEIR review)

Japanese Atomic Bomb Survivors: Life Span Study

Preston 2007, Ozasa 2011, 2012

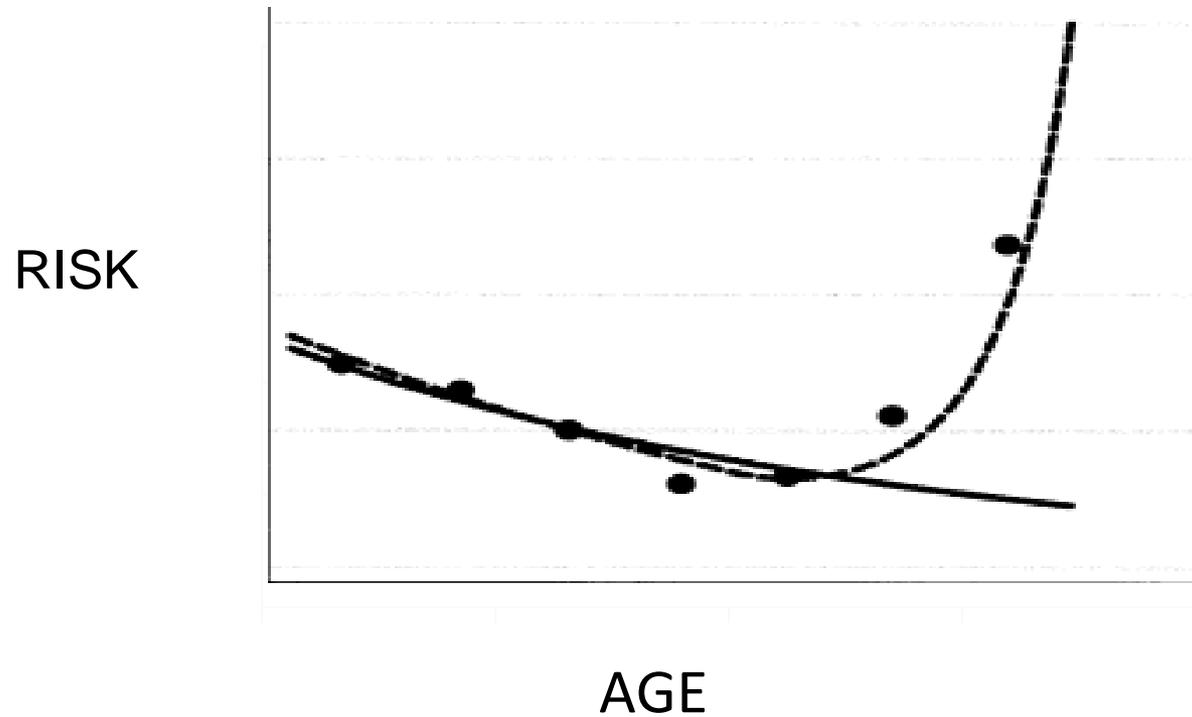
- The median dose of survivors was **40 mSv**
- Radiation doses ≥ 10 mSv associated \uparrow with leukemia & solid CA
- 11% of the solid cancers among individuals who received a dose above 5 mGy were associated with their exposure
- Modeling risk based on the Japanese survivor data has complexities when applying to imaging, but nonetheless the overwhelming consensus support these results

Typical Summary of Cancer Risks by Age at Exposure

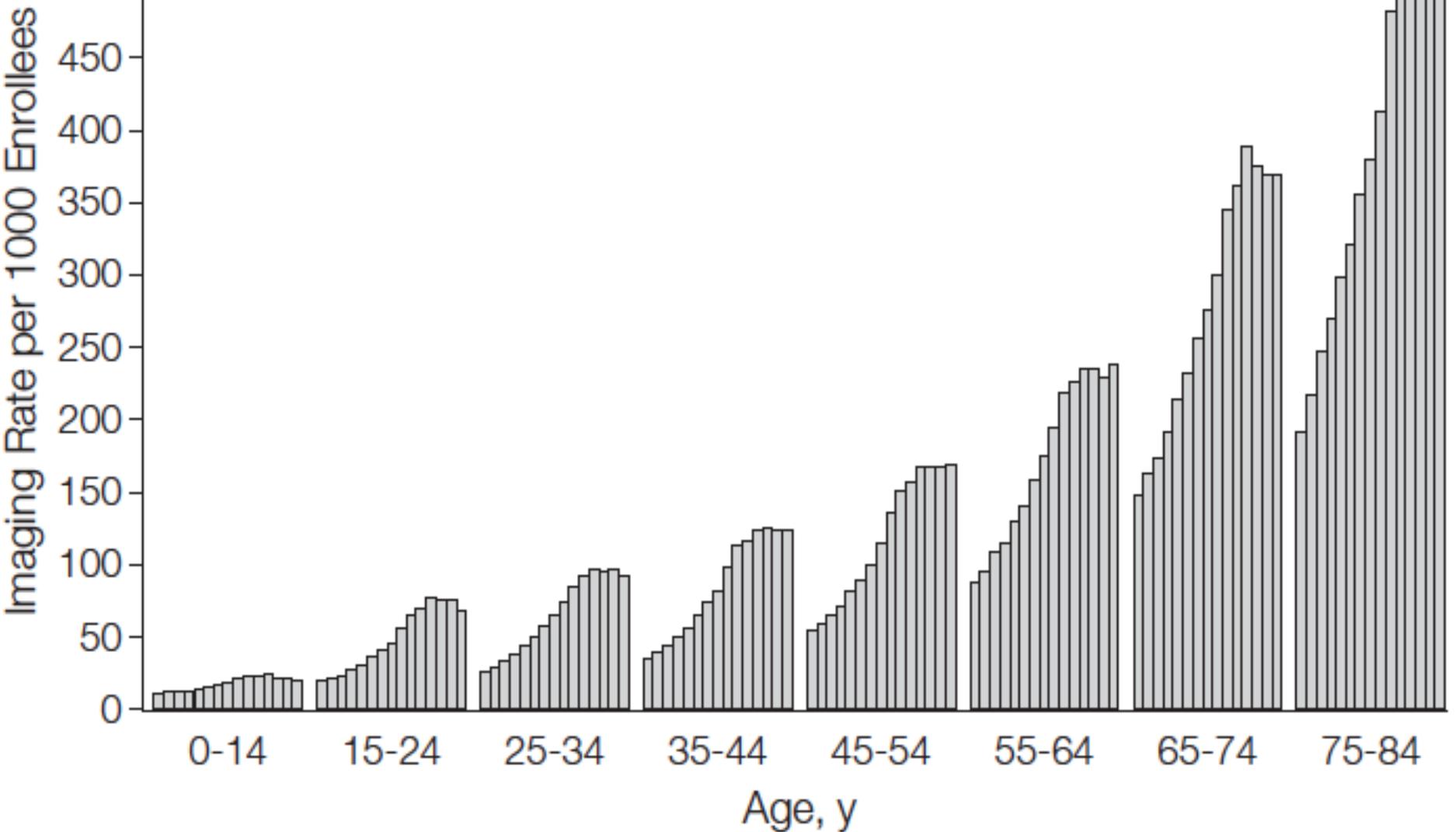


Cancer Risks Actually Follow a U -Shaped Distribution

Preston 2007, Shuryak 2010



Utilization of CT By Age and Year



Radiation Exposure from CT Scans in Childhood and Risk of Leukemia and Brain Cancer

- 178,604 children in the UK
- Underwent CT between 1985 – 2002, followed until 2008
- 74 leukemias, 135 brain cancers
- Assessed relationship between dose and cancer
- Within 10 years of CT, children who received doses 30 – 50 mSv **tripled their risks** of brain cancer and leukemia
- 10 – 20% of children receive these doses from 1 CT scan

What Are the Radiation Doses Used for CT?

- I have participated in many studies assessing the doses patients receive when they undergo CT
- The doses for CT are high and highly variable, vary tremendously across institutions for patients imaged for the same problem
- The doses are far higher than needed for diagnosis
- While higher dose can lead to prettier images, there is no evidence that higher doses lead to more accurate diagnosis
- Variation in dose reflects practice preferences, not evidence

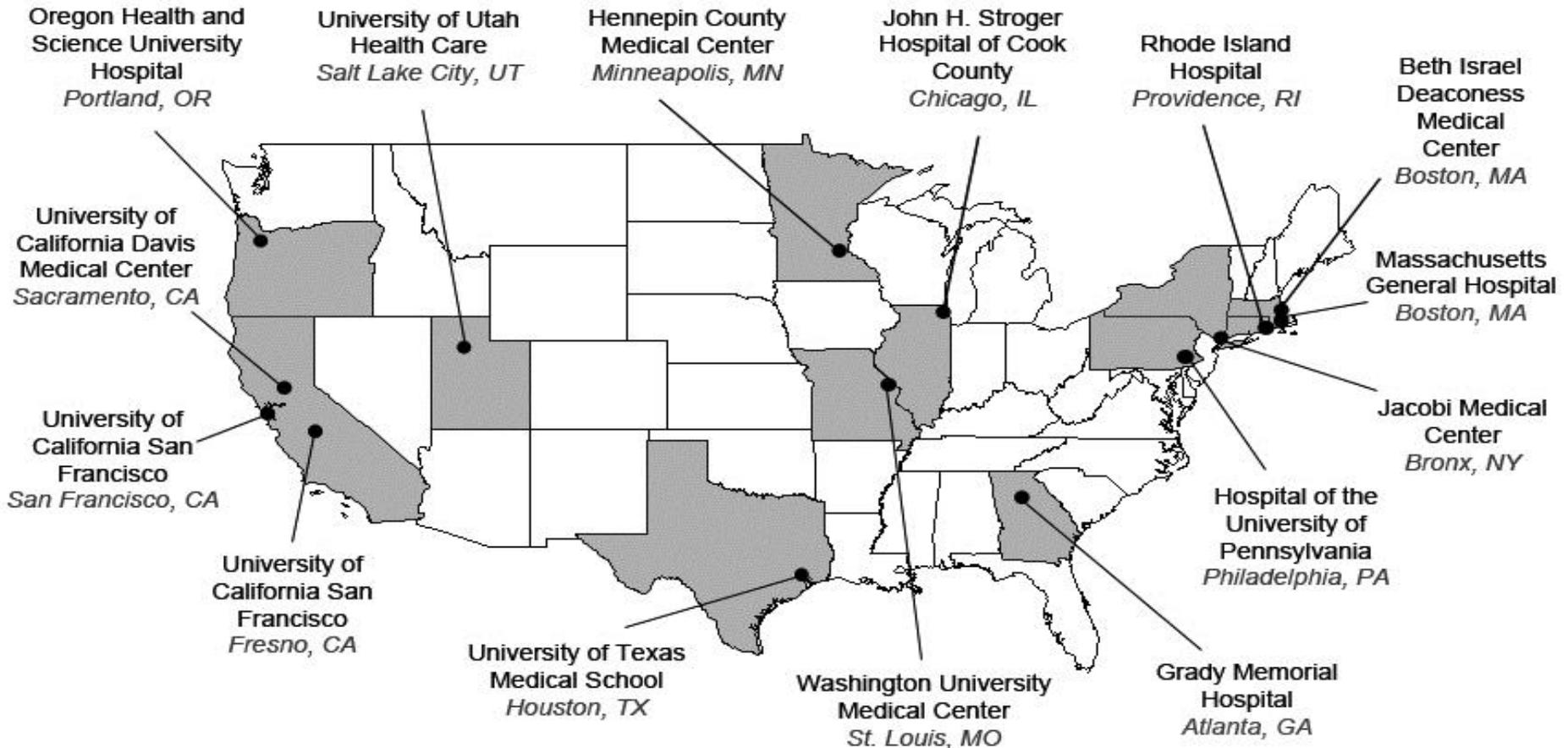
[JAMA Internal Medicine 2009](#); [JAMA 2012](#) , [JAMA Pediatrics 2013](#), [Radiology 2015](#)

Study of Tomography of Nephrolithiasis Evaluation

- 15-center randomized pragmatic comparative effectiveness trial comparing initial imaging with ultrasound versus CT (AHRQ)
- Patients were randomized to one of three study arms [point-of-care ultrasound; radiology ultrasound and CT] and
- Pts followed for 6 months



Participating Centers



Study Outcomes: Measurements that Matter

Primary Outcomes

High risk diagnosis with complications

Radiation Exposure

Costs

Secondary Outcomes

Serious Adverse Events (dx, hospital admit, etc.)

Related SAE (judged by 2 to be possibly related to trial)

Hospital readmission, ED readmission

Pain scores

Diagnostic Accuracy

Patients contacted at 3, 7, 30, 90, 180 days



Primary Study Results

	Point of Care US	Radiology US	CT	P Value
High risk diagnosis with complications N / (%)	6 (0.7%)	3 (0.3%)	2 (0.2%)	.30
Radiation Exposure, mSv	10.1	9.3	17.2	.0001

Secondary Study Outcomes

	Point of Care US	Radiology US	CT	P Value
Serious Adverse Events	113 (12%)	96 (11%)	107 (11%)	0.50
Related Serious Adverse Events	3 (0.3%)	4 (0.4%)	5 (0.5%)	0.88

Conclusion: CT or Ultrasound

- **Ultrasound should be the first test** in patients with suspected stones and can be done by whomever has expertise
- Ultrasound patients received lower radiation exposure with no significant difference in high risk diagnoses with complications, total serious adverse events or related serious adverse events.
- Secondary outcomes did not differ significantly across arms
- Our results do not imply that patients should undergo *only* ultrasound imaging, but rather that ultrasound should be used *as the initial diagnostic imaging test* with further imaging studies at physician discretion

Radiation Used For CT: What Were The Doses

- We prospectively collected radiation dose metrics on all patients who underwent CT (CTDIvol, DLP, scan length)
- We estimated effective dose
- We assessed how many patients were imaged using low dose techniques, whether this varied by risk factors for stones, and assessed differences across facilities in average doses

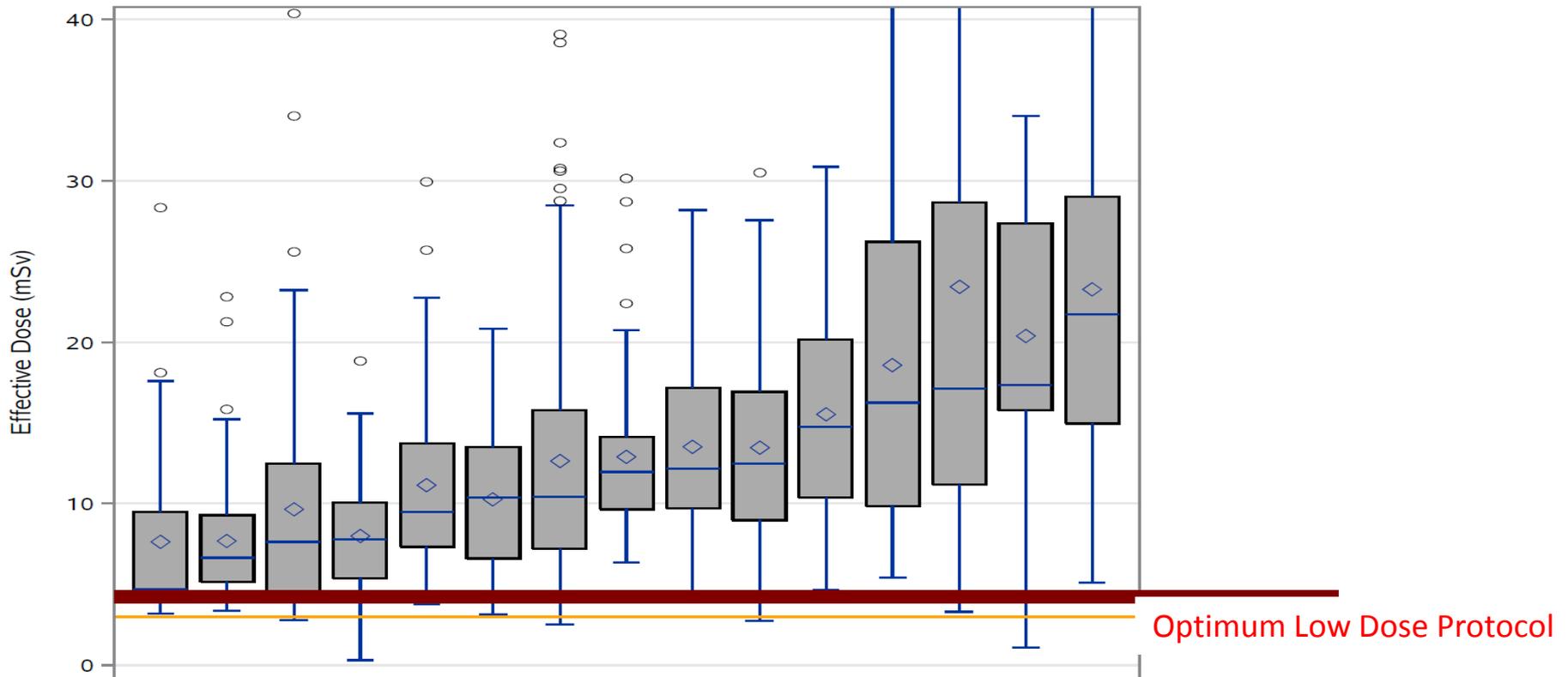
Results

- 1582 abdominal CT Scans, 15 institutions
- 7.6% (n=121) had doses ≤ 4 mSv

This did not improve when stratified by risk factors or outcomes

- Median Effective Dose = 11 mSv (range, 0.3 to 73 mSv)
- Median CTDIvol 14 mSv (range 0.5 to 100 mSv)
- Large variation across hospitals (median 4 – 19 mSv)
- Patient weight did not explain hospital variation in doses

Imaging Patients With Suspected Stones



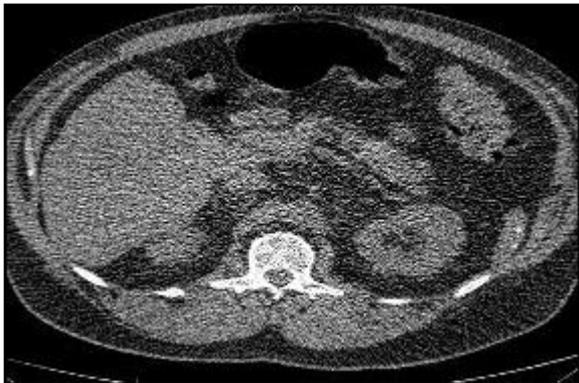
Two CTs Done on the Same Patient: Different Dose Higher Dose NOT Better Diagnoses



Low Dose Chest CT
ED 1.5 mSv



Routine Chest CT
ED 15.9 mSv



Smith-Bindman, New Engl J Med 2010

Why Are CT Doses so Variable?

- No comprehensive standards or guidelines on CT - there is the sense that everyone should be free to choose
- Doses should be as low as reasonably achievable -ALARA , but there are few guidelines for what doses are reasonable or achievable
- In the absence of explicit guidelines, practice variation introduces unnecessary harm from excessive radiation
- Each MD trying to keep to ALARA is not a strategy
- No organization responsible for collecting dose data

UCDOSE

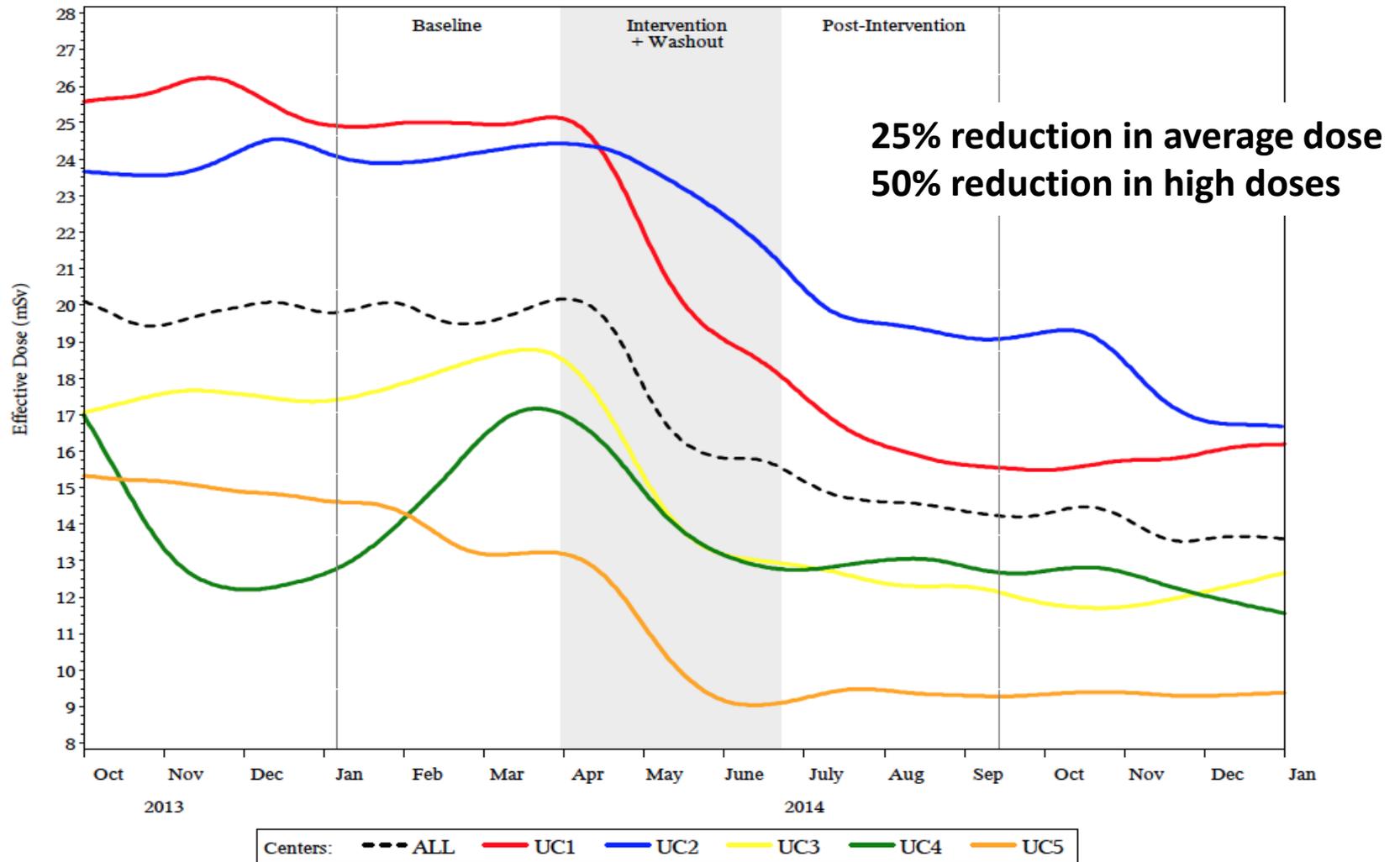
- Collaboration across 5 University of California Medical Centers
- Medical physicists, radiologists, technologists, biostatisticians
- Primary goal was to pool data and improve practice- we used dose monitoring software to collect dose
- We found considerable variation in the radiation doses
- While some of the variation could be explained by patient and scanner factors, most due to differences by campuses in how they preferred to do CT (i.e. personal preferences)

Using Results to Drive Practice

- We convened an in-person meeting and invited the clinical leads, technologists; physicists; researchers to participate
- Each site was provided with their doses ahead of time
- Section heads were asked to come prepared to explain, defend, or change practice
- We Identified areas where dose reduction was possible, and asked sites to identify specific changes
- Concrete lists of changes to be made were created at meeting

Abdomen Radiation Doses 2014

JAMA Internal Medicine 2017



UC DOSE

- Collaboration
- Develop audits
- Dose metric feedback

N=5

\$750,000

\$500,000

\$2,000,000

CDC: Pediatric -DOSE

- Focuses on Children
- Diverse hospitals
- Refine audits

N=10

\$7,000,000

PCORI CT-DOSE Registry

- Increase international collaboration, observational cohort
- Survey site-specific change process
- Revise benchmarks using large dose dataset

NIH CT-DOSE Collaboratory

- RCT to assess intervention strategies to optimize practice
- Study organizational factors successfully resulting in change
- Widely disseminate benchmarks & standardized protocols

N= 155

International CT DOSE Collaboration

- 5 year study
- Academic and non-academic medical centers, US and non-US, a total of 20 different institutions and > 150 facilities
- Expands on our previous work
 - Create broader dose benchmarks (what is the right dose)
 - Study what works and what does not to optimize dose in RCT
 - Learn from a broader group of institutions
 - Provide strategy for providing feedback to sites (Audit)

Current Status of Project

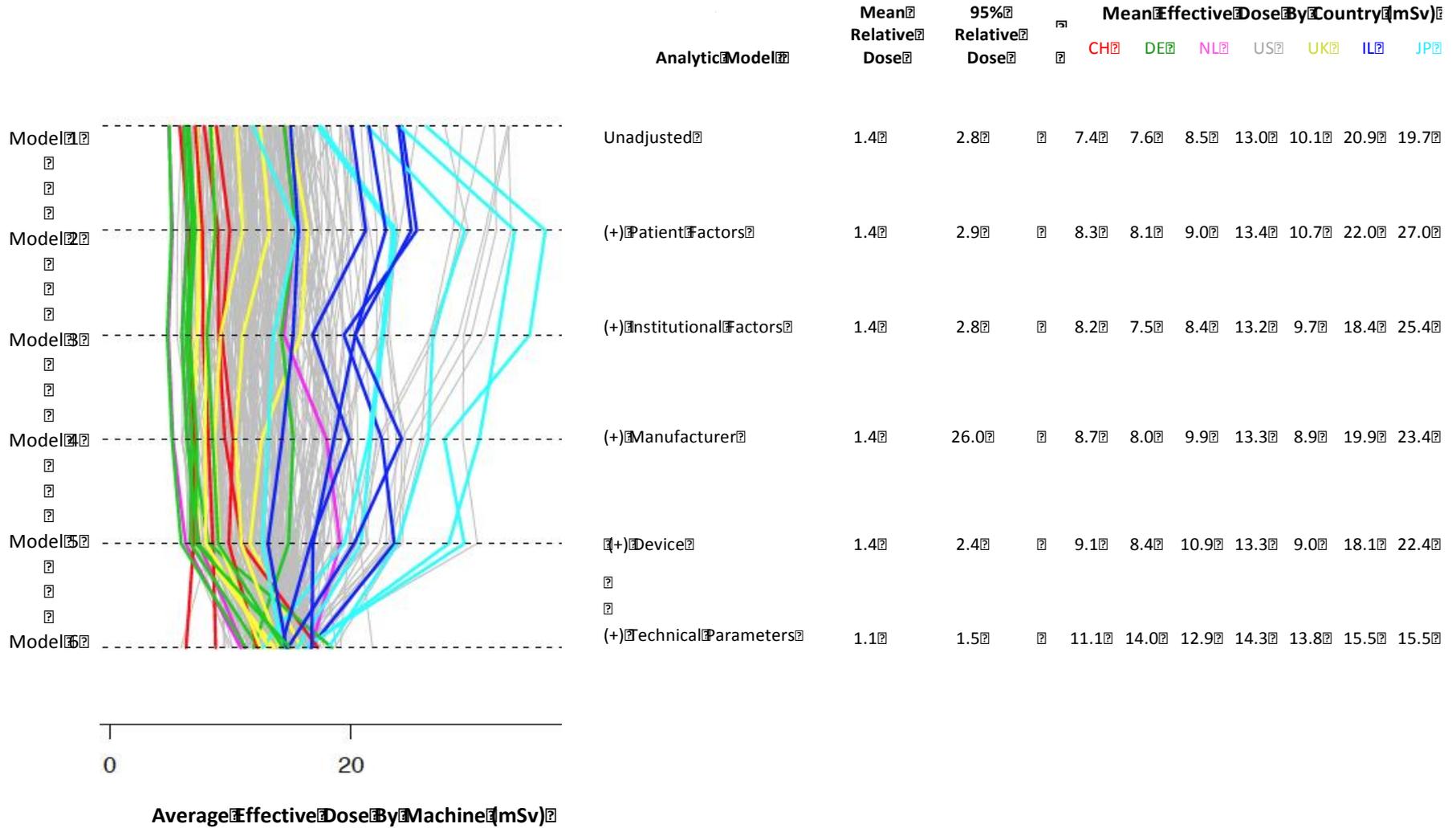
- Registry is established at UCSF, CT doses are flowing into the registry 4,000 CTs / day, total > 4 million thus far
- Our analyses are teaching us a lot (6 PhD Biostatisticians)
 - There is profound variation in dose!!
 - Its not primary the equipment that matters, but how its used
 - We have generated very detailed reports to provide specific feedback to each facility to guide their improvement, and response has been positive
 - The RCT is nearly complete and the results are exciting

	Abdomen Effective Dose			
	Dose		Over Benchmark	
	Mean	SD	Relative Dose	Relative Proportion of High Dose Examinations
Switzerland	5.7	(3.2)	-	-
Netherlands	7.0	(6.5)	1.2	6
Germany	5.8	(4.0)	1.0	2
UK	9.5	(7.8)	1.6	11
USA	10.5	(6.6)	1.8	10
Israel	19.4	(12.2)	3.4	38
Japan	25.9	(16.5)	4.5	48

What Accounts For Variation in Dose

- We have looked at the variation in doses within specific categories, such as suspected pulmonary embolism, or HA
- Variation by patient characteristics – such as body circumference is a relatively small contributor to differences across facilities
- Variation by manufacturer and machine make and model is real, but also relatively small
- Variation by how machines are used, the specific settings, is very strongly associated with dose
- **Communicate with radiologists that you care about dose!**

Abdomen



How To Lower Doses

- Institutions need to know how they are performing
- They need to target concrete acceptable benchmarks
- They should be held accountable to reach these benchmarks
- The focus on specific clinical indications – while good – makes it in many ways much more complicated than it needs to be ‘
- Basically most scans can be done using (routine) and lower dose scans and a few indications need very high higher or very low doses
- 3 protocols – rather than 300 different protocols - in each anatomic area would make it simpler to reach targets

What Do The Data Look Like?

Should They Inform Practice?

Variation in PE Protocols – All on the Same Scanner Type

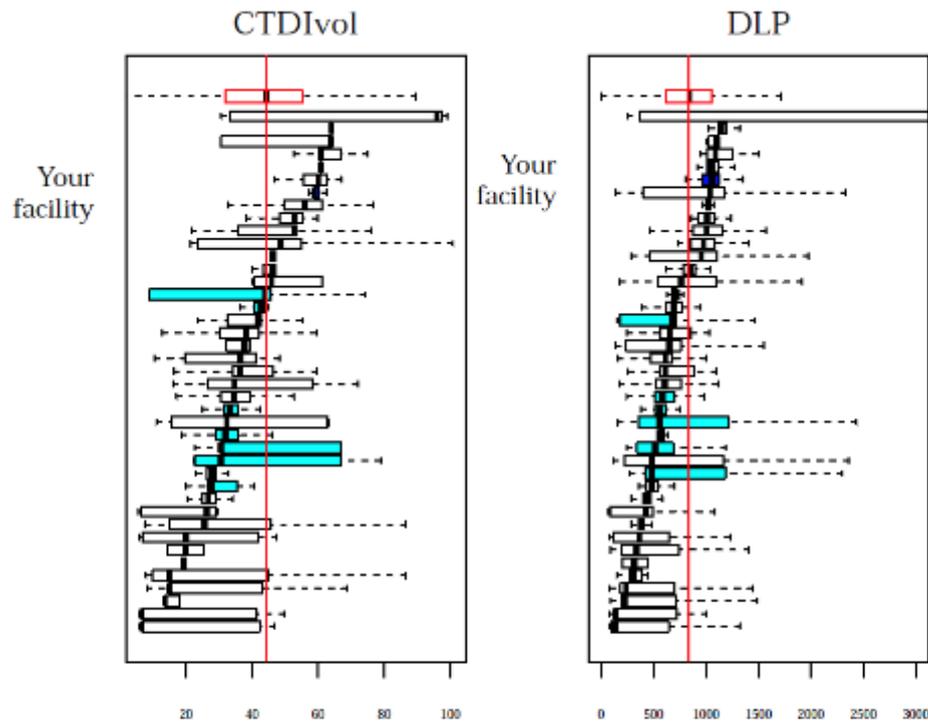
SIEMENS SOM DEF AS

	protocolname	ED	Scan length average	slice adverage	KVP average	mAs Average	Pitch Mode	collimatn Mode	Phase average
s0011 : Swiss	CT Chest Pulmonary Embolus w]	2.2	34	2	100	129	1.5	38	1.0
s0018 : German	PULMONALIS_SAFIRE	2.2	33	2	103	108	1.4	19	1.0
s0023 : USA	PE_SAFIRE	3.3	30	2	101	95	0.9	19	1.0
AVERAGE TOP 3		2.6	32	2	101	111	1.3	26	1.0
s0013 : USA	CH3_CHST_W_PE	5.5	32	1	114	105	0.8	19	1.0
s0011 : Swiss	CT Chest Pulmonary Embolus w]	7.5	32	3	114	161	1.0	27	1.2
s0012 : USA	CH_PE_	7.8	32	2	115	163	0.8	38	1.0
s0022 : USA	PE	7.8	35	5	116	295	1.0	11	1.0
s0019 : USA	PE_CHEST	8.2	29	4	116	144	0.9	18	1.2
s0019 : USA	PE_CHEST_ACR	8.3	29	2	112	204	0.9	18	1.2
s0013 : USA	CH3_CHST_W_PE	9.6	31	1	119	170	0.9	19	1.1
s0023 : USA	_CTA_PE	12.8	14	5	100	193	1.0	11	4.4
s0019 : USA	PE	13.1	18	3	109	269	1.0	25	2.2
s0022 : USA	PE_ABD	17.7	41	5	111	296	1.0	11	2.0
s0012 : USA	CHEST_PE_APWITHIV	34.2	43	3	116	212	0.8	38	2.9
AVERAGE BOTTOM 3		21.7	34	4	112	259	0.9	25	2.3

Seeing Results and Improving Practice – 8 week calls

- Understanding where there are opportunities to improve
- Knowing the impact of particular changes
- Sharing best practices – do those parameters work for others
- Within the context of our grant, we provide guidance on how to perform quality improvement – small tests of change
- We convene weekly meetings where individuals share best practices
- Ask sites to create a local or larger collaborative group to share best practices

Dose Audits – What Feedback Looks Like (a small peak)



Head CT
Doses on the high end

	25%tile	median	75%tile	%>median	%>benchmark
overall CTDIvol	32	44	55	52	27
your CTDIvol	59	59	60	95	79

How Are Your Doses Compared with Others Who Use Your Machine

HEAD

BRIGHTSPEED

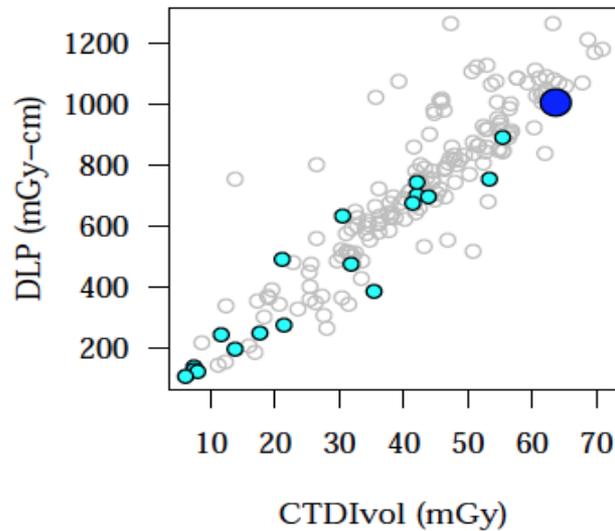


Table 10: BRIGHTSPEED ~ MODPCT1

metric	BestDose	AvgDose	YourDose	YourRank
CTDIvol (mGy)	27	33	64	188
DLP (mGy-cm)	363	588	1004	163

Preliminary Results: Results of Intervention and RCT

	Change in Mean Dose			Change in High Dose		
	Model Estimate	<i>p</i>		Model Estimate	OR	<i>p</i>
Abdomen	Preaudit estimate dose	14.3		-1.3		
	Audit	-1.2	<.0001	-0.3	0.77	<.0001
	Multicomponent Collaborative	-2.7	<.0001	-(19%)	0.54	<.0001
Chest	Preaudit estimate dose	8.2		-1.6		
	Audit	-0.4	<.0001	-0.2	0.84	<.0001
	Multicomponent	-0.9	<.0001	-(11%)	0.70	<.0001
Chest and Abdomen	Preaudit estimate dose	19.0		-1.8		
	Audit	-1.9	<.0001	-0.5	0.61	<.0001
	Multicomponent	-3.7	<.0001	-(20%)	0.43	<.0001
Head	Preaudit estimate dose	2.0		-1.6		
	Audit	0.0	0.05	0.0	1.00	0.92
	Multicomponent	-0.1	0.00	-(5%)	0.81	<.0001

reduction of 2.7 mSv from the baseline, accounting for time trends and clustering

Impact of Reducing the Highest Doses in Children

Miglioretti, JAMA Pediatrics, 2013

- We completed a study of imaging patterns and radiation doses in children ages 15 and younger enrolled in an HMO – the study included a very large number of children: 4.8 million patient-years
- Over 10 % of children received doses for single scan that the UK authors showed tripled their risk of cancer
- We estimate that national use of CT in children in 2010 will result in **4,870 future cancers**.
- Reducing the highest outlier doses to the average to the median would **prevent 44% of these cancers (or 2090 cases.)**