Low Dose CT for Lung Cancer Screening

Evidence | Cost-effectiveness | Implications

Delivering Affordable Cancer Care in the 21st Century

Institute of Medicine October 2012

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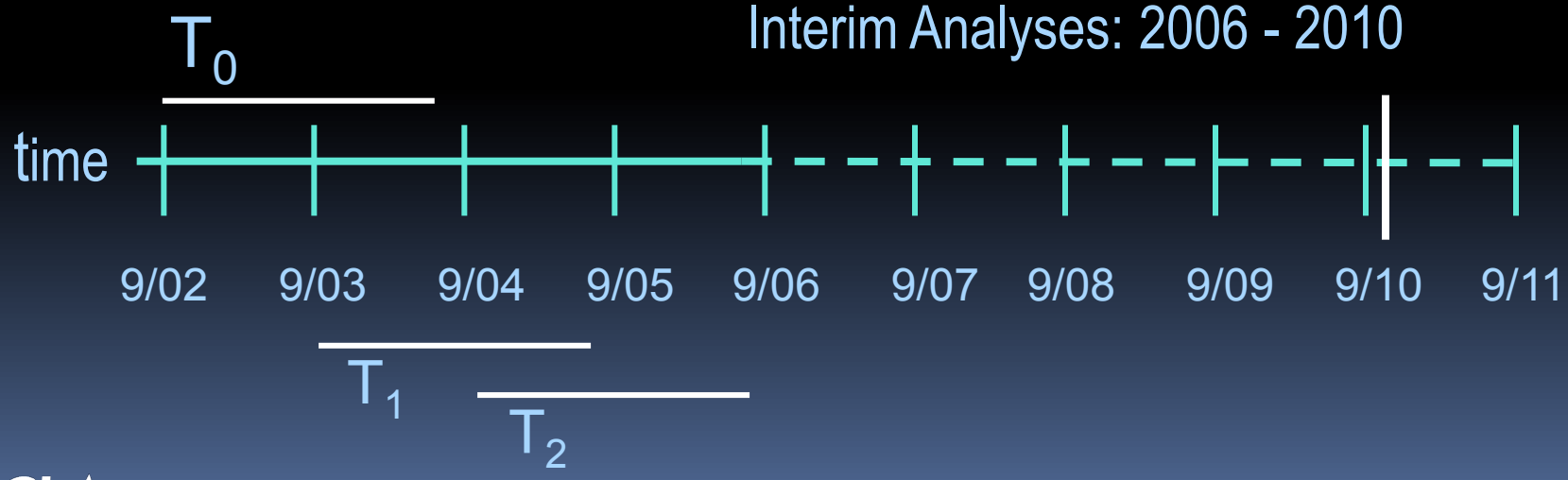
overview

- RCT involving 53, 454 individuals
  - 90% power to detect 20% difference in lung cancer mortality; α = 0.05
  - 1:1 randomization to LDCT or CXR | 3 annual screens
  - Median follow-up for outcomes ~ 6.5 years (Maximum: 7.4)
  - Vital status known for 97% LDCT | 96% CXR



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screening results by screening round

Round	LDCT Screens		CXR Screens	
	Screened	Positive N (%)	Screened	Positive N (%)
T0	26,309	7191 (27.3%)	26,035	2387 (9.2%)
T1	24,715	6901 (27.9%)	24,089	1482 (6.2%)
T2	24,102	4054 (16.8%)	23,346	1174 (5%)
TOTAL	75,126	18,146 (24.2%)	73,470	5043 (6.9%)

Positive Screens were > 3-fold higher in the LDCT arm

Among those who received all 3 LDCT screens: 39% had ≥ [+] screen

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NLST Investigators; NEJM 2011

lung cancers diagnosed in NLST

Screen Result and Time Period	CT (%)	CXR (%)
Total T0-T2 Screen [+] lung cancers	649 (61.2%)	279 (29.6%)
Total T0-T2 Screen [-] lung cancers	44 (4.2%)	137 (14.6%)
Total *NO* screen lung cancers	367 (34.6%)	525 (55.8%)
Total lung cancers in arm	1060 (100.0%)	941 (100%)

892 *NO* screen cancers include: post-screen time period (N = 802 | 90%)
never screened (N= 35) | due for screen (N = 55)

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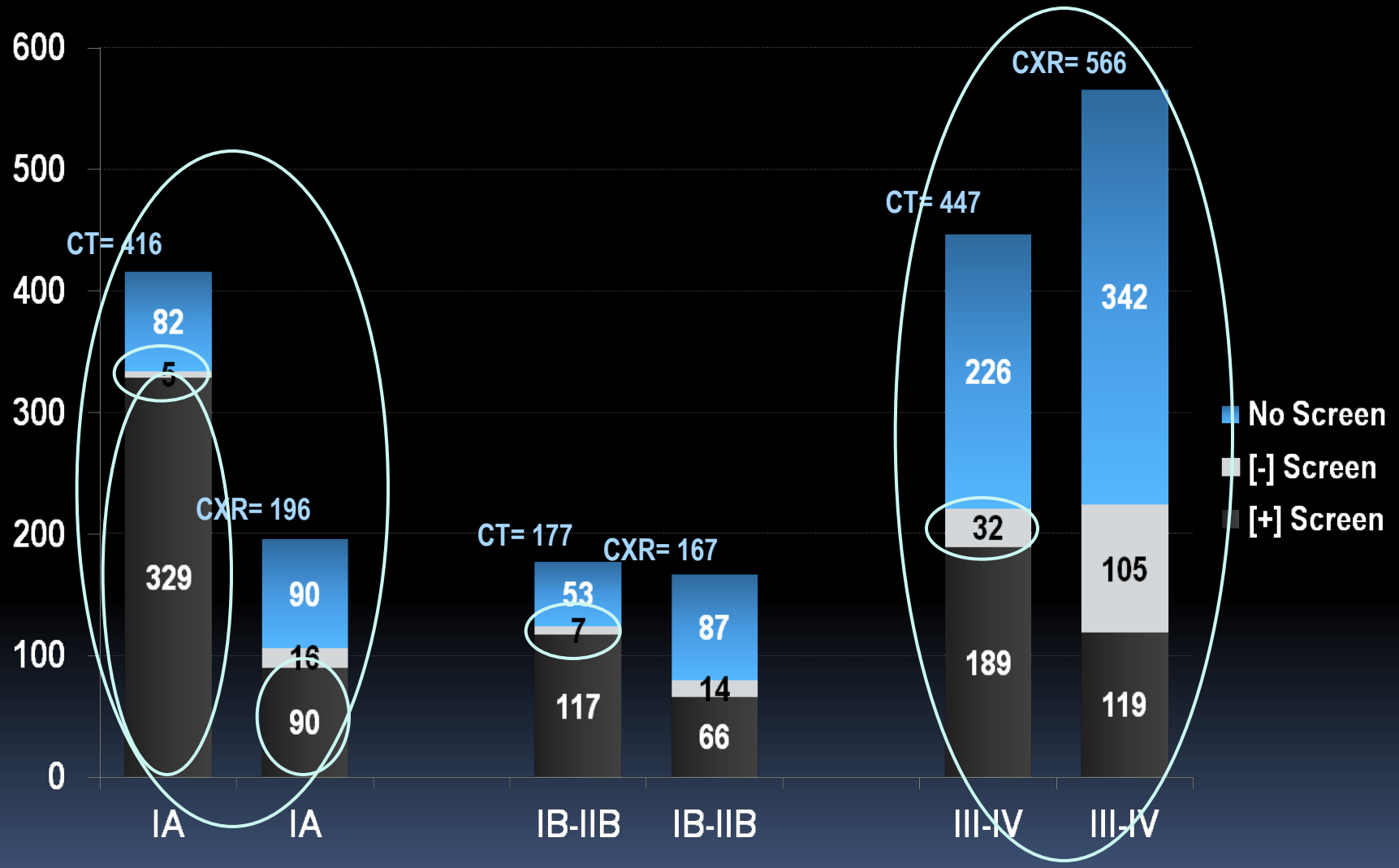
NLST Investigators; NEJM 2011

stage distribution of lung cancers



Numbers reflect only lung cancers of *known* stage

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complications in positive screens

Major complications:

Respiratory or Cardiac failure | MI | PE

Surgical complications: BPF | Empyema | Injury to vital organ

	CT lung cancer		CT NO cancer		CXR lung cancer		CXR No cancer	
	N	%	N	%	N	%	N	%
Positive screens	649	100	17,053	100	279	100	4,674	100
Major complication	75	11.6	12	0.1	24	8.6	4	< 0.1
Death 60 days after *invasive* procedure	10	1.5	6	< 0.1	10	3.8	0	0

Overall complications were low.

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cause of death by trial arm (DC)

	LDCT	CXR	Total
Neoplasm of lung and bronchus	427 (22.9%)	503 (25.3%)	930 (24.1%)
Neoplasm OTHER	416 (22.3%)	442 (22.2%)	858 (22.3%)
Cardiovascular illness	486 (26.1%)	470 (23.6%)	956 (24.8%)
Respiratory illness	175 (9.4%)	226 (11.4%)	401 (10.4%)
Complications (medical | surgical)	12 (0.6%)	7 (0.4%)	19 (0.5%)
Other	349 (18.7%)	343 (17.2%)	692 (17.9%)
Unknown	12 (-)	7 (-)	19 (-)
Total death certificates reviewed	1877 (100.0%)	1998 (100.0%)	3875 (100.0%)

Lung cancer deaths per 100,000 person yrs: LDCT = 247 | CXR = 309

With LDCT: 20% relative decrease lung cancer mortality | Absolute Reduction = 4 per 1000

6.7% decrease in *all cause mortality* in LDCT

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summary

- More lung cancers detected with CT than CXR
- True stage shift observed in CT arm
- 20% relative decrease in lung cancer mortality CT vs. CXR
- Few major complications
- 6.7% all cause mortality reduction with CT vs. CXR

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screening harms

- Radiation
- Overdiagnosis
  - Indolent lung cancer that will not result in death
  - Lung cancer diagnosis but death from competing cause
- High false positivity rates

background and excess risks of lung cancer

Background risk (age 50)	Background Risk	
	Men	Women
Never smokers	0.2%	0.4%
Former smokers	8.9%	9.5%
Current smokers	15.8%	16.9%

Excess risk from screening (current smokers)		
Single LDCT (60 mAs | 5.2 mGy)	0.017%	0.057%
Serial *annual* LDCT (from 50-75 yrs)	0.23%	0.85%

Risks vary by sex | smoking history | age

LDCT doses in NLST were ~ 20-50% that reported by Brenner.

Brenner DJ. Radiology 2004; 231:440-445.
Brennan P. Am J Epidemiol 2006; 164:1233-1241.

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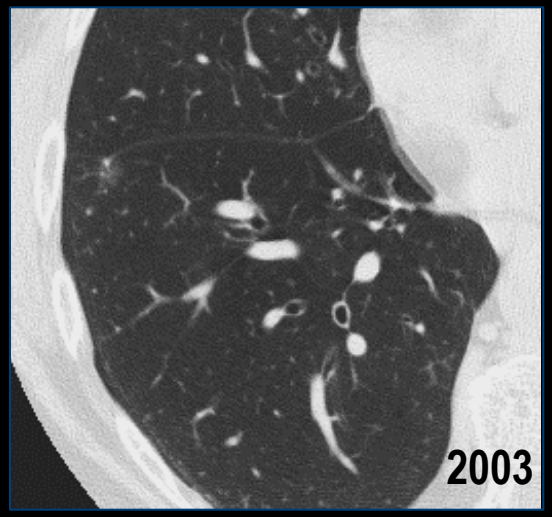
the conundrum of overdiagnosis…



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reducing false [+] screens

- Redefine [+] screen
  - Threshold criteria of nodule size | attenuation
  - Interpretation approach: Dichotomous vs. graduated

reducing false [+] screens

- Redefine [+] screen
  - Threshold criteria of nodule size | attenuation
  - Interpretation approach: Dichotomous vs. graduated
- Better define who should be screened
  - Identify higher risk population
- Define who will *develop* lung cancer
  - Diagnostic prediction: In those with indeterminate nodules
    - Epidemiologic
    - Physiologic
    - Imaging
    - Molecular

Combine variables across biological scales

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back of the napkin CEA

- Incremental cost effectiveness ratio (ICER): Δ Costs / Δ Life Years
- Costs: $US (reference 2008)
- LDCT to No Screen
  - Perspective: Societal | Time horizon: Lifetime
  - Discount rate: 3%
- Assumptions
  - 3 annual LDCT screens
  - 40% of screenees had a [+] screen
  - Per [+] screen: 2 additional CTs
  - Treatment costs cancel out

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Montes RP. The Cancer Letter 2011; 37(26):15-16.
Calculations by Bill Black, MD | Dartmouth-Hitchcock

cost per screenee

Variable	Baseline
LDCT	$300
Non-medical costs	$100
Total costs per screen	$400
Per 3 screens	$1200
Follow-up CT (.4 x $800)	$320
TOTAL	$1520

1. http://www.cms.gov/apps/physician-fee-schedule/
2. Heitman et al. J Am Coll Radiol 2010;7:943-8

life years per screenee

Variable	Baseline
Risk of lung cancer death [1]	0.017
RRR (Relative risk reduction) [1]	0.200
ARR (Absolute risk reduction)	0.0034
YLL (Years life lost) [2,3]	12.000
LYG (Life years gained)	0.041

1. http://www.cancer.gov/images/DSMB-NLST.pdf
2. Brown ML et al. Annu Rev Public Health 2001;22:91-113
3. With adjustment for 3% discount rate

preliminary ICER: LDCT vs. no screen

Variable	Baseline
Cost	$1520
Life Years Gained	0.040
Incremental cost effectiveness ratio	$38,000

- Caveats: Factors that could affect CEA
  - NLST cohort: healthy volunteer effect
  - CEA will be based on data from longer term follow-up
  - Assumptions on life expectancy do not factor smoking
  - Costs based on screening compliance and actual utilization (medical abstraction)

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Montes RP. The Cancer Letter 2011; 37(26):15-16.

implementation: address major stakeholders

- Screening programs: transdisciplinary
  - Risk assessment | smoking cessation | chemoprevention
  - Radiology: Standardization | Image analysis | Workflow | FU
- Primary care: Education | Workflow | Prioritization | FU
- Individuals at risk
  - Diffusion across all socioeconomic strata
  - Stigma | Education | Access

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preventing indiscriminant use

- Communication | education of all stakeholders
  - Physicians in screening programs
  - Primary care
  - Patients
- Regulation
  - Standards for acquisition | interpretation | FU
  - Mandatory QC
  - Requirement for multidisciplinary approach
- Vendor development of comprehensive tracking systems

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thanks

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