Cost-effectiveness and Thoracic Imaging: The Goals, the Methodology, and Review of Recent Literature

Anna Rozenshtein, MD

Objectives:
- The questions answered by cost-effectiveness analysis
- The methodology: the gold standard and the statistical modeling techniques
- The current debate on cost-effectiveness in CT screening for lung cancer

Medical decision making in the age of limited resources
- What is the efficacy of the intervention?
- Does the intervention provide good value for cost?
- How does the intervention compare with other alternatives (“bang per buck”)?

Cost-effectiveness
- An economic concept
  - Not “does it work?” but “Can we afford it?”
- Cost in USD per each life year in perfect health gained as a result of medical intervention
  - Quality Adjusted Life Year (QALY)

Cost-effectiveness
- Any intervention that gives same or greater benefit at lower cost when compared to the standard of care is cost-saving
- For interventions that give greater benefit at higher cost, the cost/benefit ratio is measured

UK National Institute for Health and Clinical Excellence
- Incremental cost-effectiveness ratio (ICER)
  - Cost per QALY
  - Cost-effective under £20,000 ($32,000) per QALY
  - Merits consideration between £20,000-£30,000 ($32,000 to $48,000) per QALY

Poon SC. A brief commentary on cost-effectiveness analysis in Radiologic research. AJR 2008; 191:1320-1322

Canada

- Incremental cost effectiveness as an evidence for adoption and utilization
  - Compelling evidence below CAD 20,000 per QALY
  - Moderate evidence between CAD 20,000 and CAD 100,000 per QALY
  - Weak evidence above CAD 100,000 per QALY


The relative values of medical intervention

- Universal precautions to prevent HIV transmission to healthcare workers CAD 565,000/QALY
- Dialysis $45,000/QALY
- Colorectal cancer screening with fecal occult blood testing $18,000/QALY
- Cholesterol lowering statin therapy $10,000/QALY

United States

- No fixed cutoff values
  - Most commonly quoted
    - Under $50,000/QALY cost-effective
    - Over $100,000/QALY as not cost-effective

How are costs and benefits calculated?

Gold standard

- An empiric randomized controlled study of long duration
  - Time-consuming
  - Expensive
  - Ethical issue of withholding potentially beneficial therapy from the control group

Acceptable substitutes

- Statistical modeling
  - Decision trees
  - Multivariate analysis models

Cost-effectiveness of Treatment Y for Disease X

- 60 year old male LE 20.7 years Disease X
- Treatment Y $20,000/year
- Survival p 0.90 Utility 0.70 LE 10 years
- No treatment $0.00
- Death p 1.00

Utility score

- Years of life with disease are imperfect
- Quality of life adjustment from 1 for perfect health to 0 for death
- Utility scores estimated for multiple diseases
  - MI: .8 first year, .86 all years afterwards
  - Lung cancer: .62 all, .88 for non-fatal disease
- Disease X has a utility score of .7

Cost for a cohort of 100

- $20,000/ year for 10 years discounted over 10 years at 3% = $17,572,000

Health benefit

- 9 x 10 LY x 100 = 900 LY
- 900 LY x .7 = 630 QALY
- Discounting over 10 years at 3%
  - 63/1.03 + 63/1.03² + ... + 63/1.03¹⁰ = 537.39 QALY

Cost/QALY

- $17,572,000/537.39 QALY = $32,624/QALY

- Not cost saving, but cost-effective
  - Dialysis $90,000/QALY
  - Cholesterol lowering therapy $30,000/QALY
  - Universal precautions HIV $565,000/QALY

Cost-effectiveness of imaging

- Indirect impact on outcomes
  - Screening is now the hotly debated topic
- Cost-effectiveness does not equal absolute affordability
  - Screening a population of one million is different from screening a population of 100M
Virtual colonoscopy at center of policy debate
Will Medicare pay for the procedure even though there’s no consensus about its effectiveness?

“This may be a bellwether for how the hard choices around expanding access and controlling costs will play out,” said Dr. Sean Tunis, who was chief medical officer at the Centers for Medicare and Medicaid Services in the last Bush administration.

Cost-effectiveness of mammography: estimates

- $16,000/year of life saved in 50-79 year olds and $20,000/year of life saved in 40-49 year olds
- $66,773/year of life saved in 70-79 year olds

Cost-effectiveness of mammography: reality

- $36,764/QALY

Virtual colonoscopy

- Review of 12 studies
  - The incremental cost-effectiveness ratios of colonoscopy and CT-colonography versus no screening remained under €20,000 and €30,000 per life year gained, respectively.

Cost-effectiveness of lung cancer screening

- Review of 12 studies
  - Two randomized controlled trials (RCTs)
  - No evidence that CT screening reduces lung cancer-related mortality
  - RCTs of short duration (1 year)
  - Ten trials without comparator groups
  - Overall quality adequate
  - High rate of Stage I resectable tumors

Wide variation of reported findings

- Abnormalities reported in 5-51%
- Lung cancer prevalence 0.4-3.2%
- Number screened to detect 1 cancer 31-249
- Incidence rate 0.1-1% per year
- Adverse effects poorly reported
- Incidental findings requiring medical follow-up reported as high as 49%
Favorable estimates

- $2,500/year of life saved
  - $4167/QALY
- Decision tree model
- Single screening CT, 60 year old smokers


Favorable estimates

- Incremental cost effectiveness for screen-detected lung cancer
  - From -$1,000/year of life (screening cost-saving) to $10,000/year of life (screening cost-effective)
  - From cost-saving to incremental cost of $17,000/QALY


Unfavorable estimates

- $113,000/QALY active smokers
- $558,600/QALY quitting smokers
- $2,322,700/QALY former smokers
  - Assumptions: 50% stage shift, 13% lung cancer-specific mortality reduction


Unfavorable estimates

- $42,5000/QALY gained in current smokers
  - “...if extremely favorable estimates were used for all influential parameters simultaneously.”


Unfavorable conclusions based on

- Survival curves of smokers, rather than the general US population
- The cost of high % of findings requiring follow-up included in the calculation


Whynes model

- Cost of screening
  - Screening CTs
  - Evaluating true positives
  - Evaluating false positives
- Incremental cost of screening
  - Total cost of treating cancer detected by screening minus cost of treating cancer which would have presented symptomatically

**Additional cost of screening**

- Total cost of CT-detected lung cancer (Csds) minus (Probability of survival until the age of presentation times total cost of screen-detected lung cancer)/(1+0.3) lead time

**Whynes model**

\[
\text{ICER} = \frac{Cs + PrSn(Cp + Csds) + (1-Pr)(1-Sp)Cp}{PrSnQALY}
\]

- \(Cs\): cost of initial screening
- \(Cp\): cost of investigating positive results
- \(Csds\): cost
- \(Pr\): disease prevalence
- \(Sn\): sensitivity of the screening test
- \(Sp\): specificity of the screening test
- \(QALY\): average QALYS gained per screen detected cancer

**Health benefit**

- Life years gained by a hypothetical cohort of 60 year old male smokers as a result of screening over the life years gained in the unscreened cohort

**Symptom-detected lung cancer**

- Mean age at presentation: 66 years in males
- Mean survival for symptom detected lung cancer is 1.2 years
- A 60 year old destined to develop lung cancer has average survival of 7.2 life years
  - This assumption is favorable to screening. In reality, the 60 year old cohort will develop cancer later than the average US male and will therefore survive longer

**Screen-detected lung cancer**

- Mortality curves suggest that a 60 year old male smoker
  - Average life expectancy to 75 years
  - Has a 90.5% probability to survive to at 66

**Health benefit for smokers with screen-detected lung CA**

- 75 years = 67.2 years = 7.8 life years gained
- Utility .88 for non-fatal lung cancer
- Benefit discounted over 7.8 years starting age 67.7 years
- Total health benefit 5.06 QALY
### Incremental cost of screening

\[
\text{ICER} = \frac{Cs + PrSn(Cp + Csds) + (1-Pr)(1-Sp)Cp}{PrSnQALY}
\]

### Whyne model in 60 year old US smokers

\[
\text{ICER} = \frac{Cs + PrSn(Cp + Csds) + (1-Pr)(1-Sp)Cp}{PrSnQALY}
\]
- Base estimate $14,000/QALY
- Sensitivity analysis from $84,000 to $10,000
- Highly sensitive to test parameters, prevalence, and cost of initial screening

### Take home points
- Cost effectiveness analysis is a useful tool for determining not only if an intervention is efficacious but whether it is affordable
- Statistical models used in the absence of randomized controlled trials

### Lung cancer CT screening in the US
- May be cost-effective
  - Await better estimates of mortality reduction
- High sensitivity and specificity (90-93%)
  - Modern equipment and subspecialty expertise
- High prevalence (2.7%)
  - Rigid enrollment criteria and age cutoffs
- Low costs
  - Economies of scale