Abdominal Aortic Aneurysm (AAA)

- An abdominal aortic aneurysm (AAA) is an abnormal expansion of the abdominal portion of the aorta, the largest artery in the body.
- AAAs usually develop slowly and most often do not cause symptoms.
- The eventual endpoint of AAA expansion is rupture, a catastrophic situation in which the artery bursts, causing severe internal bleeding.
- AAA is largely undetected and untreated.
- A common condition, particularly among men over 60.

AAA is a Candidate for Screening

- A common condition
  - 5% of men over 60 have AAA
- Long asymptomatic period of development
- Detection of AAA through ultrasound is non-invasive, low-cost and both sensitive and specific.
- If an AAA ruptures, death is likely (up to 90%)
  - Kills 9000-15,000 in US every year
  - Between 1 and 2% of deaths among men
- Surgery prior to rupture prevents a rupture
  - Complications from surgery kill 4%
  - Probability of rupture increases with size
  - Traditionally open aneurysm repair, but endovascular aneurysm repair became common recently.
Policy Question

• On February 1, 2005, the United States Preventive Services Task Force recommended screening for Abdominal Aortic Aneurysm (AAA) for men aged 65-75 who smoked.

• Screening Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act Effective Jan 1, 2007:
  – Medicare will pay for one time screening for anyone over 65 with family history of AAA, risk factors for cardiovascular disease (such as smoking or hypertension), or artherosclerotic vascular disease.

• Does this law improve the welfare of the country?
  – What information is needed to answer this question?

What information is needed for a cost-effectiveness analysis

• Screening costs $400
• Operation costs $20,000
  – Costs of surgery complications
• How many screens and how many AAAs detected?
• How many would need the operation and how many would be watched for AAA growth?
• What are the costs of not screening?
• How many deaths avoided from screening?

Cost-effectiveness Analysis

• Brings all of this information together to describe the tradeoff between costs and effectiveness of screening compared to usual care
  – Decision model (Frame, 1993)
  – Markov Decision model (Lee, 2002)
  – Economic evaluation within a clinical trial (MASS, 2002; Kim, 2007)
• How should we go about critically evaluating these studies?
Critical Evaluation of CE Studies
Drummond’s checklist

1. Well defined question:
   a. Does the study consider both costs and effects?
   b. Is there an appropriate comparison group?
   c. Is the point of view clear and relevant?

2. Are all relevant treatment alternatives considered?
   a. Is program applicable to the setting of the reader where an alternative standard of care may apply?
   b. Are alternative patient subgroup relevant?

3. Is the evidence for effectiveness well established?
   a. Clinical trial vs. evidence in literature vs. observational study
   b. Is the evidence representative of the population of interest?
   c. Is the evidence biased?

Is the estimation of costs well established?

4. Is the scope of costs considered sufficient?
   a. Health sector, other sectors, patient/family, productivity

5. Are the resources that make up costs measured accurately?
   a. Units consistent, no double counting, time horizon

6. Are the resources valued credibly?
   a. Do they use market values or proxies that represent opportunity cost?
   b. Are sources clearly identified and related to viewpoint?

7. Discounting?
8. Are costs incremental relative to valid alternative?
Critical Evaluation of CE Studies

Drummond’s checklist

9. Was the uncertainty in the estimates properly addressed?
   a. Different types of uncertainty
      a. Data used in the analysis
      b. Parameter uncertainty (decision analysis)
      c. Extrapolation of data
      d. Generalizing to other settings
   b. Sensitivity analysis
      a. Were uncertain parameters identified
      b. Did they specify plausible ranges
      c. One-way sensitivity or combined variability considered?

Critical Evaluation of CE Studies

Properties of Good Decision Models

- Transparency of structure and incorporated data
- Internal consistency in mathematical logic (no outcomes out of logical range)
- Reproducibility
- Interpretability
- Exploration of uncertainty

Frame (1993)

Comparison

- Intervention: One-time screen with elective repair of AAA $\geq 4$ cm
- Alternative: Elective repair of incidentally discovered AAA and emergency repair of ruptured AAA
- Hypothetical Population: men aged 60-79
- Time horizon: 20 years
Frame (1993)
Decision Model

- Follows cohort over time in different states with probabilities of transitioning between states
  - States: (noAAA, smallAAA-undetected, largeAAA-undetected, smallAAA-detected, largeAAA-detected, dead)
  - Transition probabilities come from literature
  - Different probabilities with and without screening

Frame (1993)
Measures and Result

- Effectiveness: Life years saved
- Unit Costs: From Canadian Health system (perspective)
- Sensitivity analysis: compared results between pessimistic and optimistic range of estimate
- Discount rate: 5%
- Result: $41,550 per life-year for one-time screen with ultrasound vs. “regular care”
  - “regular care” = elective surgery for incidental cases

Frame (1993) Table 2

<table>
<thead>
<tr>
<th></th>
<th>Total Cost Life year</th>
<th>Incremental Cost Life year</th>
<th>Cost/Life year</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Medical care</td>
<td>0</td>
<td>8.5341</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency surgery only</td>
<td>180.651</td>
<td>8.5457</td>
<td>180.651</td>
<td>0.0116</td>
</tr>
<tr>
<td>Elective surgery for incidental cases</td>
<td>479.751</td>
<td>8.5547</td>
<td>498.107</td>
<td>0.0198</td>
</tr>
<tr>
<td>+ one-time screen with ultrasound</td>
<td>916.263</td>
<td>8.5647</td>
<td>499.107</td>
<td>0.0198</td>
</tr>
<tr>
<td>+ second screen 5 years later</td>
<td>1007.270</td>
<td>8.5747</td>
<td>90.6789</td>
<td>1E-04</td>
</tr>
</tbody>
</table>

Cost-effectiveness curve

- $15,573/LY Emergency surg vs. no medical care
- $26,269/LY elective surg for incidental cases vs. emergency surg only
- $41,550/LY one time screen with ultrasound vs. incidental elective surg
Frame (1993)
Questions

• Are all relevant alternatives considered?
  – What about evaluating screen with ultrasound using the alternative of one-time screen with exam instead of elective surgery for surfacing cases.
  – In this case the CER is:
    \[
    \frac{(9.2-7.4)}{(85704-85667)} = \frac{1.8}{37} = 48,474
    \]

The best alternative will be the one that reflects current practice

What about surveillance of smaller aneurisms as an alternative?

Frame (1993)
Questions

• Was the effectiveness well established?
  – "some of the data can be accepted with a high degree of confidence whereas others are speculative.
• What was the source of the cost data? Is it relevant to the perspective of interest?
• What is the bias from not considering complications from surgery?
• Are results generalizable to other populations?
  – Women? Smokers?
  – Aneurisms >=5.5 cm
• What about the sensitivity analysis?
  – From 5,389 / LY to a net loser. Pretty sensitive!

Lee (2002)
Comparison

• Intervention: One-time screen with elective repair of AAA >=5cm plus surveillance if between 3 and 5 cm.
  – A "quick screen" also evaluated
• Alternative: Elective repair of incidentally discovered AAA and emergency repair of ruptured AAA
• Hypothetical Population: men aged 70
• Time horizon: lifetime
Lee (2002)
Markov Decision Model

Lee (2002)
Measures and Result

- Effectiveness: QALYs saved
- Unit Costs: Hospital study and lit review
- Considers complications in costs and QALYs
- Discount rate: 3% used
- Result: $11,215 per QALY for one-time screen with ultrasound vs. regular care

Lee (2002)
Sensitivity Analysis
Lee (2002)
Questions
- Why is this estimate so much more cost-effective than the Frame estimate?
  - Prevalence higher (7% >3 cms) vs. (5.4>3 cms)
  - Risk of rupture also much higher
- Is short term diminished QALYs from surgery underestimated?
- Were there problems with the quick screen analysis?
  - No power – estimated sensitivity and specificity of 100%
- Source of cost data? Accounting data from one hospital

Comparison
- Intervention: One-time screen with elective repair of AAA >=5.5 cm plus surveillance if between 3 and 5.5 cm
- Alternative: Elective repair of incidentally discovered AAA and emergency repair of ruptured AAA
- Population: men aged 65-74 in UK
- Time horizon: 4 years (MASS)
  7 years (KIM)
  [10 years – Thompson, 2009]

Economic Evaluation in MASS Clinical Trial
- 67,000 patients randomized to an invitation for a screen or no screen invitation
- Censored
  - those lost to follow-up prior to year 4 (or 7)
  - those who died of other causes
- Resource units collected:
  - Invitations for scans, scans, surgery consultations, elective surgeries, and emergency surgeries.

Measures

- Effectiveness: Life years saved based on AAA-related mortality
- Unit Costs: From Hospitals in 4 UK centers
  - Perspective of health service
  - Unit cost of surgery estimated from sample of patients
- Discount rate:
  - MASS: 1.5% for effects and 6% for costs
  - KIM: 3.0% for effects and costs


Results

- MASS (4 years): £28,389 per life-year for one-time screen with ultrasound vs. regular care (95% CI: £15,000 to £145,000 per LY)
  - $44,900 per LY (1 £=1.58)
  - CI: $24,000 to $231,000
- KIM (7 years):
  - $19,500 per LY (1 £=1.58)
  - ($16,400 per LY with 2000/01 financial data as in MASS)
  - CI: $12,400 to $39,800

MASS (2002)

Sensitivity Analysis

- Cost effectiveness improves over 10 year horizon to $12,640 per LY based on projection in Kim (very close to Thompson (2009) direct estimate when converted to pounds)
- Using 3% discount rate for both costs and effects does not change conclusion
- Cost effectiveness improves with all cause mortality
  - But clinical difference in all cause mortality was not statistically significant in the trial
- QALY measures did not show a disutility from screening surveillance or surgery, but QALY adjusted Lys makes results less cost effective
**Kim (2007)**

**Sensitivity Analysis**

- Base-case: $19,500 per LY
- QALYs: $24,600 per QALY
- U.S.-based costs $29,600 per LY
- Consultation costs 50% higher
  - U.S. based $30,800 (19,700 to 62,600)
- (Note: U.S. based costs are low compared to Frame)

- $7,600 cost per YL using all cause mortality
  - But upper bound of confidence interval is infinite

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**Issues**

- Sample uncertainty
- External validity
  - Smokers?
  - Centers where scanning is not as common

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**Should the Screening Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act be expanded or should it be limited to a more specific population?**
What happened when SAAAVE was implemented in Medicare?

- 65 year old men use of abdominal ultrasonography increased 2.0 percentage points
  - 7.6% in 2004 to 9.6% in 2008
  - But increased .7 to .9 pp in other comparison groups
  - Only 3% of abdominal ultrasounds are reimbursed through SAAAVE
- No detectible differences in AAA ruptures, repairs, or mortality

General Questions

- Is the perspective and setting of the studies appropriate for the policy decision?
- What is the right prevalence rate for screening to be cost-effective?
  - Could screening be used only for high risk groups?
- How should the uncertainty around the estimates be factored in to decision making?
- Is compliance an issue?
- When people live longer that costs money, especially if they are old people? Should that be added to analyses?
- If this is such a good idea, why is no one paying for this screening out-of-pocket?

Assignment

- Critique more recent papers (Ehlers, 2009 and Henriksson, 2005) using the checklist or this talk as guide
  - Why do the models come up with such different results? Is the checklist adequate to understand the discrepant results?
- Compare and contrast modeling with the MASS trial (2002, 2007, 2009)
  - Do data from trial look like what went into the models? Which data are preferred? What should we believe? Why?
  - What are the implications of the similarities and differences in approach and results
    - for AAA screening policy?
    - for cost-effectiveness analysis evidence in general?