Appraisal of CT Colonography

The Institute for Clinical and Economic Review
(ICER)
Structure of the Day

- Introduction to ICER and purpose of today
- Introduction to CTC
- Comparative Clinical Effectiveness
- Comparative Value
- Evidence Ratings
- Close
ICER

- Diverse Funding
- Collaborative academic model
- First cycle of appraisals
  - IMRT for localized prostate cancer
  - Virtual colonoscopy
  - Pegfilgrastim
Goals of ICER

- Stimulate broader national policy to integrate value considerations into comparative effectiveness initiatives
- Test new methods for making technology assessments more accessible and actionable
- Support public dialogue
ICER Appraisal Process

- Topic selection
- Scoping committee
- Technology assessment
  - Clinical effectiveness
  - Comparative value
- Presentation to Evidence Review Group (ERG)
- Final Report with Integrated Evidence Rating
Integrated Evidence Rating

Comparative Clinical Effectiveness

Superior A
Incremental B
Comparable C
Pot/Unprov P/U
Inadequate I

Comparative Value

a High
b Reasonable/Comparable
c Low
Comparative Clinical Effectiveness

Compared tech ___ vs. ____

High Confidence

- D
- C
- B
- A

Limited Confidence

- I
- I
- P/U
- P/U

Low Confidence

- I

Inferior Net Benefit
Comparable Net Benefit
Small Net Benefit
Mod-Large Net Benefit
Integrated Evidence Rating

Comparative Clinical Effectiveness
- Superior A
- Incremental B
- Comparable C
- Pot/Unprov P/U
- Inadequate I

Comparative Value
- a High
- b Reasonable/Comparable
- c Low
Comparative Value Rating

<table>
<thead>
<tr>
<th>Cost-saving</th>
<th>$0</th>
<th>$50K</th>
<th>$100K</th>
<th>$150K</th>
<th>$200K</th>
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</table>

Cost/QALY

High Value

Low Value

Reasonable/Comp

Other considerations:

• Cost per key outcome(s)
• Relative cost to similar treatments/situations
## Integrated Evidence Rating

### Comparative Clinical Effectiveness

<table>
<thead>
<tr>
<th>Superior</th>
<th>A</th>
<th>Aa</th>
<th>Ab</th>
<th>Ac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incremental</td>
<td>B</td>
<td>Ba</td>
<td>Bb</td>
<td>Bc</td>
</tr>
<tr>
<td>Comparable</td>
<td>C</td>
<td>Ca</td>
<td>Cb</td>
<td>Cc</td>
</tr>
<tr>
<td>Pot/Unprov</td>
<td>P/U</td>
<td>Pa</td>
<td>Pb</td>
<td>Pc</td>
</tr>
<tr>
<td>Inadequate</td>
<td>I</td>
<td>I</td>
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<td>I</td>
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</tbody>
</table>

### Comparative Value

- High
- Reasonable/Comparable
- Low
## Radiation treatments for prostate cancer

### Comparative Clinical Effectiveness

<table>
<thead>
<tr>
<th>Superior A</th>
<th>Aa</th>
<th>Ab</th>
<th>Ac</th>
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<tbody>
<tr>
<td>Incremental B</td>
<td>Brachytherapy</td>
<td>Bb</td>
<td>IMRT</td>
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<tr>
<td>Comparable C</td>
<td>Ca</td>
<td>Cb</td>
<td>Cc</td>
</tr>
<tr>
<td>Pot/Unprov P/U</td>
<td>Pa</td>
<td>Pb</td>
<td>Pc</td>
</tr>
<tr>
<td>Inadequate I</td>
<td></td>
<td></td>
<td>Proton Beam Therapy</td>
</tr>
</tbody>
</table>

### Comparative Value

- a: High
- b: Reasonable/Comparable
- c: Low
Purpose of the Day

- What is the structure and role of the Evidence Review Group?
  - Independent
  - Composition
  - Review of Draft Assessment
  - Recommend ratings of comparative clinical effectiveness and value
Introduction to CT Colonography

Mike Zalis, M.D.
Appraisal of CT Colonography

Background
Scope

- Patient population
- Comparator(s)
- Key questions
  - Technical issues
  - Sensitivity and specificity vs. OC
  - Safety
  - Patient acceptance
  - Extracolonic findings
  - Impact on population screening
  - Cost-effectiveness vs. no screening and vs. alternatives
Background

- Colorectal cancer screening
  - ~50% of eligible get screened
  - Non-invasive methods
  - Invasive methods: screening = prevention
  - Polyps
    - ≥ 10 mm
    - 6-9 mm
    - ≤ 5 mm
CT Colonography

- **Potential benefits**
  - Minimally invasive = fewer complications, no sedation
  - Availability and acceptance = More patients screened overall
  - ? Less costly overall

- **Potential harms**
  - False negatives
  - False positives
  - Hassle for patients of dual-phase testing
  - Loss to follow-up between positive CTC and OC
  - ? More costly overall
Assessing a diagnostic technology

- Evolution of data on devices/procedures
  - Technical effectiveness in selected patients and best hands
  - Generalizability to community patients and practice
Previous HTA on CTC

- MSAC (2006)
- ICSI (2006)
- NICE (2005)*
- CTAF (2004)

* Found evidence adequate to support its use
Clinical Guidelines

- NCCN (2007)
- ACR (2006)
  - CTC = 6 on appropriateness scale of 1-9
- ACS (2003)
- USPSTF (2002)
- ACG (2002)
Systematic Review of the Literature

Roberta Scherer, Ph.D
Draft Integrated Evidence Rating
Interpretation of Key Findings

- Safe, well accepted
- Test characteristics compare favorably to alternative screening methods other than OC
- Comparable to OC for large polyps
- Less sensitive for medium polyps but with q 5y strategy unlikely to miss many significant lesions
- Cost per LYS vs. no screening = $1,500
- Cost/LYS vs. OC
  - $630,000 if cost of CTC = colonoscopy
  - $100,000 if cost of CTC half price of colonoscopy
  - <$50,000 if cost of CTC one third of colonoscopy
### Draft Integrated Evidence Ratings

**CT Colonography vs. no screening and OC**

#### Comparative Clinical Effectiveness

<table>
<thead>
<tr>
<th>Superior A</th>
<th>Incremental B</th>
<th>Comparable C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTC</strong></td>
<td><strong>Ba</strong></td>
<td><strong>CTC 1/3-price</strong></td>
</tr>
<tr>
<td><strong>Ab</strong></td>
<td><strong>Bb</strong></td>
<td><strong>CTC half-price</strong></td>
</tr>
<tr>
<td><strong>Ac</strong></td>
<td><strong>Bc</strong></td>
<td><strong>CTC full-price</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Pot/Unprov P/U</th>
<th><strong>Pa</strong></th>
<th><strong>Pb</strong></th>
<th><strong>Pc</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I</strong></td>
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<td></td>
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</table>

#### Comparative Value

<table>
<thead>
<tr>
<th>a</th>
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</tr>
</thead>
<tbody>
<tr>
<td>b</td>
<td>Reasonable/Comparable</td>
</tr>
<tr>
<td>c</td>
<td>Low</td>
</tr>
</tbody>
</table>
ERG Feedback

- ICER format: useful?
- What information would you have liked?
  - Draft ratings before the meeting?
- What information did you not find useful?
- Process: a vote, consensus, or some blend for rating determination?
- Best role for patients, clinical experts, and manufacturers?
- Other?
Thank you!
Systematic review of CT colonography versus colonoscopy

Roberta W. Scherer, PhD
Evidence Review Group Meeting
October 9, 2007
Institute for Clinical and Economic Review
Boston, Massachusetts
Objectives of clinical review

- To compare the sensitivity and specificity of computed tomography (CT) colonography with that of optical colonoscopy for detection of polyps and colorectal neoplasia
- To assess harms associated with CT colonography
- To assess patient acceptance of CT as a screening tool
Inclusion Criteria

- Prospective diagnostic accuracy studies of CT colonography
- Colonoscopy used as reference standard
- Endoscopists unaware of index test results; CT readers unaware of reference test results
- Study participants:
  - Adults who have undergone CT colonography and colonoscopy
  - No active bowel disease (e.g., Crohn’s disease, irritable bowel syndrome, etc.)
Outcomes

- Outcomes:
  - Sensitivity & specificity to detect a lesion $\geq 10$ mm, $\geq 6$ mm, and 6 to 9 mm by patient
  - Sensitivity & specificity to detect a lesion $\geq 10$ mm, $\geq 6$ mm, and 6 to 9 mm by lesion
  - Harms associated with CT colonography
    - Perforation or other adverse event
    - Radiation
  - Extracolonic findings with CT colonography
  - Patient acceptance of CT colonography
Search Results

PubMed; n = 1,888 → 79 articles
The Cochrane Library; n = 646 → 5 articles
EMBASE; n = 895 → 65 articles

149 articles identified

Reference lists; n = 4 articles → Excluded 56 duplicates

Unique records identified; n = 97

Excluded: 36 studies
not prospective,
no comparison with colonoscopy
observer not blinded
duplicate study population

Awaiting assessment:
non-English language (7)
article being requested (2)

Articles included in review; n = 52
Criteria used to select studies

- Multi-detector CT scanners with collimation < 5 mm;
- Scan acquired within a single breath hold of ≤ 30 seconds;
- Reference standard of combined CT colonoscopy and colonoscopy results (segmental unblinded colonoscopy or second look colonoscopy);
- Observers had read at least 30 CT scans or receiving CTC training before study start.
<table>
<thead>
<tr>
<th>Author</th>
<th>Scanner</th>
<th>Time</th>
<th>Training</th>
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</thead>
<tbody>
<tr>
<td>Ginnerup</td>
<td>Marconi M x 8000, Marconi Medical Systems</td>
<td>2 x 17 s</td>
<td>approximately 100</td>
</tr>
<tr>
<td>Hoppe</td>
<td>Asterion 4- channel multi-detector</td>
<td>30 s</td>
<td>30-60</td>
</tr>
<tr>
<td>Iannaccone</td>
<td>Somatom Plus 4 Volume Zoom, Siemens Medical Solutions</td>
<td>12-18 s</td>
<td>&gt; 300, 200, 100</td>
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<tr>
<td>Iannaccone</td>
<td>Somatom Plus 4 Volume Zoom, Siemens Medical Solutions</td>
<td>14-20 s</td>
<td>&gt; 400, 200, 100</td>
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<tr>
<td>Johnson</td>
<td>Lightspeed Ultra, GE Healthcare</td>
<td>28 s</td>
<td>&gt; 1,000</td>
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<tr>
<td>Pickhardt</td>
<td>GE Lightspeed or LightSpeed Ultra, GE Medical Systems</td>
<td>NR</td>
<td>&gt; 25 for training or &gt; 1,000 scans</td>
</tr>
<tr>
<td>Rockey</td>
<td>4- or 8-slice multi-detector CT scanners</td>
<td>NR</td>
<td>&gt; 50 or training module</td>
</tr>
<tr>
<td>Taylor</td>
<td>Lightspeed Plus, GE Medical Systems</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Van Gelder</td>
<td>Mx8000, Philips</td>
<td>22 s</td>
<td>&gt; 50</td>
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Study Quality

- QUADAS Tool
  - Used to assess diagnostic accuracy studies
  - 14 items assessing internal validity
- 5 “high” quality studies
- 4 “fair” quality studies
Description of Studies

- **Population**
  - N = 3,141
  - Age range (56-69 years)
  - Men: women = 1,924:1,234
  - Asymptomatic, symptomatic, mixed
- **Bowel cleansing methods** fairly uniform
- **Routine use of contrast media** in 3 studies
- **Image reconstruction**
  - 2-D for initial review and 3-D for problem solving
  - 3-D for initial review and 2-D for problem solving
Sensitivity & specificity for lesions ≥ 10 mm per patient

Sensitivity
- Ginnerup 2003
- Hoppe 2004a
- Iannaccone 2004
- Iannaccone 2005
- Johnson 2007
- Pickhardt 2003
- Rocky 2005
- Rockey 2005
- Taylor 2003
- Van Gelder 2004
- Pooled sensitivity

NR

Sensitivity: 82%, (95% CI, 76-87%)

Specificity
- Pooled sensitivity

NR

Specificity: 96%, (95% CI, 95-97%)
Sensitivity & specificity for lesions ≥ 10 mm per patient

Sensitivity:
- 82%, (95% CI, 76-87%)
- 92%, (95% CI, 86-95%)

Specificity:
- 96%, (95% CI, 95-97%)
- 96%, (95% CI, 95-97%)
Predictive values in asymptomatic populations

- For lesions ≥ 10 mm per patient
- Pickhardt reported:
  - Positive Predictive Value = 49% (45/92)
  - Negative Predictive Value = 99.7% (1138/1141)
- Johnson reported:
  - Positive Predictive Value = 76% (16/21)
  - Negative Predictive Value = 98.6% (205/208)
CT colonography sensitivity

- By patient:
  - Lesions ≥ 6 mm: **77% (73-80%)**

- By lesion:
  - Lesions ≥ 10 mm: **83% (77-87%)**
  - Lesions 6 to 9 mm: **73% (68-77%)**
Extracolonic findings

<table>
<thead>
<tr>
<th>Author</th>
<th>Population</th>
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<th>Important</th>
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<tbody>
<tr>
<td>Cotton 2004</td>
<td>asymptomatic</td>
<td>--</td>
<td>1.3%</td>
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<tr>
<td>Dachman 1998</td>
<td>symptomatic</td>
<td>70%</td>
<td>--</td>
</tr>
<tr>
<td>Iannaccone 2004</td>
<td>mixed</td>
<td>13%</td>
<td>5.4%</td>
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<tr>
<td>Kalra 2006</td>
<td>symptomatic</td>
<td>57%</td>
<td>--</td>
</tr>
<tr>
<td>Laghi 2002</td>
<td>symptomatic</td>
<td>68%</td>
<td>--</td>
</tr>
<tr>
<td>Miao 2000</td>
<td>symptomatic</td>
<td>12%</td>
<td>--</td>
</tr>
<tr>
<td>Pickhardt 2003</td>
<td>asymptomatic</td>
<td>--</td>
<td>1.3%</td>
</tr>
<tr>
<td>Rockey 2005</td>
<td>symptomatic</td>
<td>57%</td>
<td>4.6%</td>
</tr>
<tr>
<td><strong>Xiong</strong> *</td>
<td><em>Review; 17 studies</em></td>
<td>55%</td>
<td>2.7%</td>
</tr>
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</table>
Harms

- None observed in 8 studies that reported on harms
- Rate of perforation in a survey of 50 institutions = 0.08% (9 in 17,067 CT exams) (Burling et al, 2006)
- Rate of perforation in a survey of 11 institutions = 0.06% (7 in 11,870 CT exams) (Sosna et al, 2006)
- Rate of perforation in colonoscopy = 0.13% (Burling et al, 2006)
Radiation

- Radiation dose reported in 11 of included studies ranged from 0.7 to 12 mSv.
- Current radiation risk of CT colonoscopy is between 1.2 to 11.7 mSv, with a median of 5.1 mSv (Jensch et al, 2006).
- Lower radiation doses (about 0.5 mSv) appear to detect lesions as well as standard radiation doses (Van Gelder 2004, Iannaccone 2003b).
Patient Acceptance

- After having experienced both CT colonography and colonoscopy, of 1883 patients in 4 included studies:
  - 48.7% preferred CT colonography
  - 41.3% preferred colonoscopy
  - 9.9% had no preference

- But, it is not known if unscreened patients who refuse colonoscopy would accept CT colonography as a screening option
Implications and Summary

- CT colonography appears equivalent to colonoscopy as a screening option, given:
  - Use of current best technology
  - Adequate training of readers
  - That lesions ≥ 10 mm are the ones that are clinically important

- CT colonography appears to be safe