Three Paradigms in Health Technology Assessment:
Experiences of the Committee to Evaluate Drugs (CED) in Ontario

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Outline

• What is the CED and CCO subcommittee
• How does the CED make decisions
• What are the Three Paradigms
• How have the Three Paradigms
  – Changed process
  – Affected decisions
New Drug Funding Program

• Ontario’s IV Cancer Drug Formulary

• est 1995 to ensure equitable access to IV cancer drugs
  – 75% of IV cancer drugs
  – Most IV drugs administered in hospitals

• Through the NDFP, CCO has agreements in place with over 90 hospitals.

• Require hospitals to use new drugs according to guidelines developed by CCO's Program in Evidence-Based Care.
NDFP: Original Drug Approval Process

Evidence:

Program in Evidence-based Care → Disease Site Groups (14) → Draft Practice Guideline or Evidence Summary → Practitioner Review Draft Practice Guideline or Evidence Summary → Practice Guideline/Evidence Summary Revised by DSG, Approved by PGCC, and posted on Website/publication

Policy:

Policy Advisory Committee → MOH Approval of $ → Develop Electronic Eligibility Forms → Reimbursement Decision Implemented

Ontario Drug Benefit
## NDFP Performance: 1997/98 to 2004/05

<table>
<thead>
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</thead>
<tbody>
<tr>
<td><strong>Expenditures ($ million)</strong></td>
<td>$8.00</td>
<td>$14.30</td>
<td>$23.40</td>
<td>$37.90</td>
<td>$50.80</td>
<td>$56.60</td>
<td>$62.40</td>
<td>$82.00</td>
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<tr>
<td><strong>% Growth</strong></td>
<td>79%</td>
<td>64%</td>
<td>62%</td>
<td>34%</td>
<td>11%</td>
<td>10%</td>
<td>31%</td>
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</tr>
<tr>
<td><strong>Total Patients</strong></td>
<td>2,425</td>
<td>4,811</td>
<td>6,785</td>
<td>8,716</td>
<td>11,339</td>
<td>12,943</td>
<td>14,211</td>
<td>16,488</td>
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<tr>
<td><strong>% Growth</strong></td>
<td>98%</td>
<td>41%</td>
<td>28%</td>
<td>30%</td>
<td>14%</td>
<td>10%</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td><strong>Treatments</strong></td>
<td>9,259</td>
<td>26,898</td>
<td>42,478</td>
<td>59,162</td>
<td>80,536</td>
<td>87,702</td>
<td>94,468</td>
<td>105,783</td>
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<tr>
<td><strong>% Growth</strong></td>
<td>191%</td>
<td>58%</td>
<td>39%</td>
<td>36%</td>
<td>9%</td>
<td>8%</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td><strong>Number of Approved Drugs</strong></td>
<td>6</td>
<td>10</td>
<td>10</td>
<td>14</td>
<td>14</td>
<td>16</td>
<td>16</td>
<td>18</td>
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<tr>
<td><strong>% Growth</strong></td>
<td>67%</td>
<td>0%</td>
<td>40%</td>
<td>0%</td>
<td>14%</td>
<td>0%</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td><strong>Number of Treatment Indications</strong></td>
<td>8</td>
<td>16</td>
<td>17</td>
<td>24</td>
<td>27</td>
<td>31</td>
<td>31</td>
<td>35</td>
</tr>
<tr>
<td><strong>% Growth</strong></td>
<td>100%</td>
<td>6%</td>
<td>41%</td>
<td>13%</td>
<td>15%</td>
<td>0%</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>

* Expenditure Values from CCO Finance. Other treatment data from DS-Web Data Cube.
NDFP Annual Expenditures and Cases

Reference: NDFP Microstrategy iPort May, 2006
NDFP Program: 2004 Challenges

...Time for a change

• NDFP expenditure growth surpassing MOHLTC funding

• Many new anti-cancer agents in development and close to launch

• Pharmacoeconomic Analysis was not used for recommending drugs

• No formal relationship to existed between the drug approval processes for the cancer and non-cancer formularies, allowing for inconsistent policy decisions
Backgrounder
Renseignements

Ministry of Health and Long-Term Care
Ministère de la Santé et des Soins de longue durée

APPROVING DRUGS IN ONTARIO

Ontario’s drug review process

When considering funding for new drugs, Ontario relies on the expert advice of medical professionals who are members of the Drug Quality and Therapeutics Committee (DQTC). The DQTC thoroughly reviews and evaluates the clinical evidence, scientific data and cost-effectiveness of drug products and makes a recommendation to the Minister of Health and Long-Term Care on whether funding should be provided.

Cancer drug review process

In early 2005, the DQTC and Cancer Care Ontario (CCO), the Ontario government’s principal advisor on cancer care, formed a sub-committee resulting in a more efficient review process for new cancer drugs. This sub-committee provides expert advice to the DQTC, whose recommendation on whether to provide funding is made to the minister of Health and Long-Term Care.

This new joint advisory body streamlines the cancer drug approval process. It means Cancer Care Ontario no longer independently submits recommendations for new cancer drug funding directly to the ministry. It also means the province can update its cancer drug coverage more frequently as new drugs are recommended and approved.
CCO Subcommittee

- Recommendations to CED

- Members- (~12)
  - Oncologists (~8)
  - Health economics (1-2)
  - MOH employees (~2)
  - CCO representatives (1)

  - Same process
  - Same listing recommendations
CED- CCO Subcommittee

• For each submission, one member presents
  – Clinical data (now, often CDR data)
  – PE data (now, often CDR data)

• Recommendation for
  – No listing
  – Listing
    • Full
    • Limited use (criteria) (conditional listing)
    • Individual Clinical Review (reviewed by expert)
Three Paradigms

• Evidence based medicine

• Economic evaluation

• Bioethics
What is a paradigm?

• a word too often used by those who would like to have a new idea but cannot think of one."

• —Mervyn Allister King, then–Deputy Governor, Bank of England
What is a (scientific) paradigm?

• “an entire constellation of beliefs, values and techniques......shared by the members of a given community”

Scientific Paradigm

- **what** is to be observed and scrutinized,
- the kind of **questions** that are supposed to be asked and probed for answers in relation to this subject,
- how these questions are to be **structured**, 
- how the results of scientific investigations **should be interpreted**.

Scientific Paradigm

• Intellectual construct(s)
  – Values, beliefs, techniques

• Social construct
  – Set of ideas represented in social institutions
    • Societies, journals, public institutions
Evidence Based Medicine

Clinimetrics
Clinical Epidemiology
Outcomes /Health Services Research
Knowledge Translation

Paradigm 1
Evidence Based Medicine

- Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.

_Sackett D. BMJ 1996;312:71-72_
Evidence based medicine: what it is, and what it is not.
To Improve the Evidence of Medicine: the 18th Century British Origins of a Critical Approach

• “The intellectual basis was essentially the emergence of a climate of `rational empiricism', a general emphasis on observation rather than theory, and also the profusion of medical societies allowing these views to be propagated. “
EBM...ideas about evidence...

- **Context-free**
  - Efficacy
  - Diagnosis

- **Context-sensitive**
  - Effectiveness
  - Prognosis
  - ethics
  - economic

- **Colloquial**
  - values
  - politics
EBM…techniques
EBM...ideas about how to apply evidence
Patron saints....

Archie Cochrane

Alvan Feinstein

David Sackett
Shrines....
Economic Evaluation

Cost effectiveness analysis
Pharmacoeconomics
Health Economics
Clinical Decision Analysis
Preference/utility measurement
Consumer decision support

Paradigm 2
Definition

• comparative analysis of alternative courses of action in terms of both their costs and consequences“.

(Drummond et. Al. Methods for the Economic Evaluation of Health Care Programmes)
Economic evaluation... ideas about evidence...

- **Context-free**
  - Efficacy
  - Effectiveness
  - Diagnosis
  - Prognosis

- **Context-sensitive**
  - Ethics
  - Economic

- **Colloquial**
  - Values
  - Politics
Economic evaluation techniques

Patron saints....

Milt Weinstein

Michael Drummond

George Torrance
Institutions....

Journals....
Shrines....
Bioethics
Accountability for Reasonableness
Ethics of Resource Allocation
Resource Allocation Decision Making
Bioethics

Paradigm 3
Definition- A4R

• Framework for priority setting that has 4 components
  • Publicity- (transparency)
  • Relevance- (reasons that are relevant and adequate)
  • Appeals
  • Enforcement

Hasman and Holm-
Accountability for Reasonableness.
Opening the black box of process
Health Care Analysis 2005
• In the absence of consensus on principles, a **fair process** allows us to agree on what is legitimate and fair. Key elements of fair process will involve transparency about the grounds for decisions; appeals to rationales that all can accept as relevant to meeting health needs fairly; and procedures for revising decisions in light of challenges to them. Together these elements assure "accountability for reasonableness."

• Daniels *BMJ* 2000;321:1300-1301
Comparisons

<table>
<thead>
<tr>
<th>Criterion based</th>
<th>Process based</th>
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<tbody>
<tr>
<td>Evidence based medicine</td>
<td>Accountability for reasonableness</td>
</tr>
<tr>
<td>Economic evaluation</td>
<td></td>
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## Comparisons

### Goals

<p>| | |</p>
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<thead>
<tr>
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<tbody>
<tr>
<td>EBM</td>
<td>Base decisions on best evidence</td>
</tr>
<tr>
<td>Economic evaluation</td>
<td>Maximal health benefit given resource constraints</td>
</tr>
<tr>
<td>A4R</td>
<td>Fair process</td>
</tr>
<tr>
<td>Decisions for</td>
<td>Efficacy/Effectiveness</td>
</tr>
<tr>
<td>---------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>EBM</td>
<td>Patient</td>
</tr>
<tr>
<td>Economic evaluation</td>
<td>Classes of patients populations</td>
</tr>
<tr>
<td>A4R</td>
<td>either</td>
</tr>
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</table>
Three Paradigms

• In the context of decision making around new technology/drugs

• A useful framework for
  – Decision making process
  – Criteria for individual decisions
Decision Making Process

• Paradigm I: Evidence Based Medicine-
  – Rigorous evidence reviews
  – Drugs must pass threshold of
    • EFFECTIVENESS
      In order to be funded
Existing drug with new indication

Evidence-based reports developed by CCO/DSG

Submission information and guidelines reviewed

CCO/CED Subcommittee recommendation to CED

Through government approval process, to formalize funding status

JODR Recommendation to Provinces

Hospital-based IV medications

Available through NDFP

Negative decision, no reimbursement

Community-based PO, injectable medications

List on ODB formulary

DSG – disease site group
NCE – New Chemical entity
CED – Committee to Evaluate drugs
Evidence-based Series #2-25: Section 1
The Role of Bevacizumab (Avastin™) Combined With Chemotherapy in the Treatment of Patients With Advanced Colorectal Cancer:
A Clinical Practice Guideline
S. Welch, W. Kocha, R.B. Rumble, K. Spithoff, J. Maroun,
and the Gastrointestinal Cancer Disease Site Group
A Quality Initiative of the Program in Evidence-based Care (PEBC), Cancer Care Ontario (CCO)
Developed by the Gastrointestinal Cancer Disease Site Group
Report Date: December 12, 2005
What’s new

• Not much...

• Still the dominant paradigm...
  – Most discussion related to
    • Quality of evidence (of efficacy)
    • Quantity of evidence (of efficacy)
Decision Making Process

• Paradigm 2: Cost effectiveness analysis

• Growing in importance...
  • 1. NDFP now part of CED
  • 2. Rigorous PE reviews
  • 3. PE education
  • 4. PE unit at Cancer Care Ontario
1. NDFP integrated into provincial decision making process

– Subcommittee of the Committee to Evaluate Drugs (CED)

– Members- (~12)
  • Oncologists (~8)
  • Other clinicians (1-2)
  • Health economics (1-2)
  • MOH employees (~2)

• Same process
• Same listing recommendations
Thus...

- Cost effectiveness of new drugs formally considered...

- A criterion in the reimbursement decision
• 3. Education in principles of cost effectiveness analysis/pharmacoeconomics
  – Substantial interest from committee members (n=4) and MOHLTC staff.
  – Workshop- Sept. 06

• “DECONSTRUCTING THE ICER”
Deconstructing the ICER

• A workshop for users of pharmacoeconomic evaluations
Bayoumi (overview)

Krahn (utilities)

John-Baptiste

Naimark (life expectancy)

Sander (quality-adjusted life expectancy)

\[ \frac{COST_a - COST_b}{QALY_a - QALY_b} \]
USING THE ICER

• Bell- bias
• Hoch- finding a threshold
• Decision paradigms:
  – Bell: Evidence
  – Sander: Health economics
  – Berry: Ethical frameworks
• Evans: integrating the ICER into decision making...some examples
4. A New CCO Pharmacoeconomics Unit

- Scientist (Health Economist)
- 2 RA’s

- Mandate
  - Service: support decision making at CCO subcommittee
  - Research- improve methods of integrating health economic evidence into decision making
Decision Making Process

• Paradigm 3: Bioethics/ A4R
  • 1. Transparency
  • 2. Stakeholder involvement
System-wide review of provincial drug system, June 2005

- 250 experts
- 3 countries
- 100 written submissions
5 Recommendations: Five Key Areas

• Improving access for patients to drugs
• Strengthening our position as a customer to get value-for-money
• Promoting appropriate use of drugs
• Rewarding innovation
• Strengthening the governance and operations of the public drug system
Changes to process

• Transparency...communication of reasons for decisions to public

• 2 patient representatives on CED
Citizens Council

– Involvement of public in “priority setting”
– Considerable "behind-the-scenes" work has been done, to determine the recruitment and selection process, ideal composition of the Council, etc.
– Advisory Committee being formed to advise on the questions, context, meeting format
– Recruitment of Council members expected to begin within next six weeks
Three Paradigms

• Decision making process

• Criteria for individual decisions
Methods

• Review of meeting CED meeting minutes Jan-Dec 06

• Coding by theme
  (evidence/pharmacoeconomics/ethics)

• And attribute (e.g. no RCT)

• 2 Reviewers
CED Decisions-
Jan 06-Jan 07

37 decisions

* Some change in funding

21 not funded

16 funded*

43%
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Number</th>
<th>Percent Successful</th>
</tr>
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<tbody>
<tr>
<td>Hematological</td>
<td>10</td>
<td>40%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Myeloma</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Solid Tumors</td>
<td>25</td>
<td>35%</td>
</tr>
<tr>
<td>GI</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>6</td>
<td></td>
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<tr>
<td>Ovarian</td>
<td>6</td>
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<td>Endometrial</td>
<td>1</td>
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<td>Breast</td>
<td>3</td>
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<tr>
<td>Prostate</td>
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<tr>
<td>Kidney</td>
<td>1</td>
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<tr>
<td>Other</td>
<td>1</td>
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## Evidence-related factors

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<tr>
<th>Factor</th>
<th>N=21</th>
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<tr>
<td>No RCT/Phase I-II only</td>
<td>11</td>
<td>52%</td>
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<tr>
<td>“not good quality studies”</td>
<td>5</td>
<td>24%</td>
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<tr>
<td>No bioequivalence data</td>
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<td>14%</td>
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<tr>
<td>Unpublished, or abstract only</td>
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<tr>
<td>Interim analysis</td>
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<tr>
<td>Surrogate/intermediate endpoints only</td>
<td>2</td>
<td>10%</td>
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<tr>
<td>Patient selection/generalizability</td>
<td>1</td>
<td>5%</td>
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<tr>
<td>Safety</td>
<td>7</td>
<td>33%</td>
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<tr>
<td>Potential for off-label use</td>
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<td>19%</td>
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<tr>
<td>Other</td>
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Pharmacoeconomics-related factors

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<th></th>
<th>N=21</th>
<th>%</th>
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<tbody>
<tr>
<td>No PE data</td>
<td>3</td>
<td>14%</td>
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<tr>
<td>“weak PE analysis”</td>
<td>7</td>
<td>33%</td>
</tr>
<tr>
<td>Cost of drug data only</td>
<td>5</td>
<td>24%</td>
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<tr>
<td>Cost per life year gained, or cost per disease free year gained only</td>
<td>4</td>
<td>19%</td>
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<tr>
<td>Design other than CEA or CUA</td>
<td>1</td>
<td>5%</td>
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<tr>
<td>Inappropriate comparator</td>
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<tr>
<td>Calculation error</td>
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<td>10%</td>
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<tr>
<td>Other*</td>
<td>9</td>
<td>43%</td>
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<tr>
<td>ICER too high</td>
<td>6</td>
<td>29%</td>
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<tr>
<td>*mostly projections based on weak clinical data</td>
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## Ethics-related factors

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<td>Cancer drugs should be held to same standards as other drugs, wrt cost effectiveness</td>
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<td>5%</td>
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<tr>
<td>Rare cancer*</td>
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<tr>
<td>No alternative treatment</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>*cited...but weighed neither for nor against</td>
<td></td>
<td></td>
</tr>
<tr>
<td>**cited...weighed for reimbursement</td>
<td></td>
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</tr>
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</table>
Factors associated with denial of reimbursement

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<tr>
<th>Reason</th>
<th>Count</th>
<th>Percentage</th>
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<tr>
<td>Evidence a reason</td>
<td>18</td>
<td>86%</td>
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<tr>
<td>Evidence the main reason</td>
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<td>33%</td>
</tr>
<tr>
<td>Pharmacoeconomics a reason</td>
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<td>71%</td>
</tr>
<tr>
<td>Pharmacoeconomics the main reason</td>
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<td>15%</td>
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<tr>
<td>Ethics a reason</td>
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<td>5%</td>
</tr>
<tr>
<td>Ethics the main reason</td>
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<td>5%</td>
</tr>
<tr>
<td>Multifactorial</td>
<td>10</td>
<td>48%</td>
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Summary

• Each paradigm comes from a distinct intellectual tradition

• Optimal decision making involves using all three
  – Each reflects an important social value
    • Basing practice on best evidence
    • Using scarce resources wisely
    • Making decisions fairly
Complementary

• A4R- focuses on fair process
  – Agnostic about criteria

• EBM and EE offer criteria
  – agnostic about process
Competing goals

• Best evidence ≠ maximizing benefit
  – Using evidence criteria for quality= rationing by evidence
  – BUT....using evidence as a major criterion will likely decrease efficiency

• Most efficient mix
  – Lower quality evidence, higher expected value
Competing goals

• Fair process...
  • Less good evidence
  • Less effect for constrained resources

  – Less rigorous process
  – More prominent role for influential stakeholders
    – Advocacy groups, industry,
Challenges

• Modeling tradeoffs
• Evidence-setting appropriate thresholds
• Economic evaluation
  – Quality of evidence- context sensitive evidence very low
  – Quality of PE evaluations-bias
  – Producer/Receptor capacity
  – Thresholds- setting lambda or setting a budget
• Fair process-
  – Incorporating citizens/citizens’ values effectively into process