Comparing Benefits and Risks: Challenges and Approaches From Environmental Risk Analysis

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Background

• Traditional framework for environmental risk management
  – Reduce risks to “acceptable” levels
  – For large regulations - compare benefits to economic costs
    • E.g., Regulatory impact statements

• Comprehensive framework
  – Recognize that risks do not occur in a vacuum
  – Compare risks and benefits of alternative interventions
  – If there were no tradeoff issues, managing risks would be easy!
Quantifying Tradeoffs Challenging in Practice

- Case Study #1 - Pesticides
  - Difficulties encountered with tradeoff analysis

- Case Study #2 - Mercury and fish
  - Problem encountered using EPA’s approach
  - Alternative approach to compare risks and benefits
Case Study #1 – Ban on Organophosphate and Carbamate Pesticides

• Evaluated the impact of a ban on all OP and carbamate pesticides for 14 major crops

Effects Considered

Ban OP/Carb

Substitute Pesticides

Consumer Health Effects

Acute Impact – Farm Workers

Natural Toxins

Lower Income Effects

Dietary Shifts

Higher Costs
Challenges - Noncancer Risks

- Do not know probability of clinical response associated with reference dose
- May not know severity of clinical response associated with reference dose
- What happens above and below the reference dose?
Challenges - Cancer Risks

- Cancer risks have different degrees of health protective (“conservative”) assumptions
  - Cannot quantitatively compare different risk estimates
Case Study #2 - Mercury and Fish

• Tradeoff:

  – Fish contain mercury, a neurotoxin that affects unborn children in particular

  – Fish are a rich source of omega-3 fatty acids
    • Important to neurological development in the unborn
    • Reduce the risk of coronary heart disease and stroke
FDA 2004 Advisory

- Women of childbearing age should limit fish consumption to two meals a week and avoid fish high in mercury (shark, swordfish, king mackerel, tilefish)

- Other adults do not need to worry about mercury
FDA 2004 Advisory
Policy Questions

• Will people reduce their fish consumption?
  – Women of childbearing age?
  – Other adults to reduce fish consumption?

• Tradeoff between:
  – Impact of mercury on neurological development
  – Neurological benefit of the omega-3 fatty acids?

• Tradeoff between:
  – Neurological benefits of lower Hg exposure in pregnant women
  – Coronary health risks from lower fish consumption among other adults
EPA Reference Dose Approach Discourages Comparison of Risks and Benefits

• EPA approach
  – Identify reference dose (dose above which exposure may be associated with risk)

• Impact
  – Exposure > reference dose assumed unacceptable
  – Exposure < reference dose assumed “safe”
Preoccupation with Fish Consumption Resulting in Exposure > RfD

• National Research Council (2000)* estimated
  – “… that over 60,000 children are born each year at risk for adverse neurodevelopmental effects due to in utero exposure to MeHg” (p. 327).
  – Value corresponds to number of children above RfD

• Environmental Working Group**
  – “… an average woman following [FDA’s] advice… would exceed a safe dose of mercury (the reference dose) by 30 percent…”

* Ibid.
** Environmental Working Group. 2003. Data Quality Act Challenge: Request for Correction of FDA’s “Advice for Women Who Are Pregnant, or Who Might Become Pregnant, and Nursing Mothers, About Avoiding Harm to Your Baby or Young Child From Mercury in Fish and Shellfish
Reality:
The Reference Dose Is Not a Threshold

• The identification of the benchmark dose has nothing to do with identifying a threshold

• There is no evidence of an effect threshold
  – More Hg somewhat worse
  – Less Hg somewhat better

FIGURE 7-5 Dose-response curves fitted to cord-blood Hg data for the linear, square root, and log transformations. Source: E. Barch-Jensen, University of Copenhagen, unpublished material, November 12, 1999.
Alternative Approach

• Harvard Center for Risk Analysis project for the National Food Processors Association Research Foundation (2002 to 2005)*

  – Goal: To evaluate tradeoffs associated with shifts in fish consumption

Harvard Approach: Develop Dose Response Relationship

• Identify nutritional benefits of fish consumption
  – Reduced coronary heart disease and stroke risk
  – Cognitive development benefits from prenatal intake

• Identify risks associated with mercury exposure
  – Adverse cognitive development effects
  – Reflect science indicating mercury poses risks even below the RfD

• Characterize health impacts in a way that makes it possible to compare them
QALYs (Quality Adjusted Life Years)

• A QALY is a life year weighted to reflect quality of life during that period
  – A year of life in perfect health is worth 1 QALY
  – No QALYs accrue after death
  – A year of life in less than perfect health is worth between 0 and 1 QALY
QALYs Accumulated
Example 1 – Illness Followed by Recovery
QALYs Accumulated
Example 2 – Illness Followed by Death

Value of Each Life Year

Age

Illness

Death
QALYs are Well-Accepted in the Health Economics Literature

• Around one thousand cost-effectiveness analyses of medical interventions in the academic literature use QALYs

• UK National Institute for Clinical Excellence (NICE) accepts the methodology
Coronary Effects

Notes: Area of each circle is proportional to data point’s weight. Red lines represent the 95% confidence interval for the best-fit dose-response.
Cognitive Effects

• Complicated by epidemiological study use of multiple test domains
  – Domains - visuospatial/visuomotor, motor, attention, language, memory, intelligence, learning and achievement
Annual Results for the U.S. Population

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<th>Optimistic</th>
<th>Pessimistic</th>
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<td>Natural units&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Stroke mortality</td>
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<td>Nonfatal stroke incidence</td>
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<td>Total</td>
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<td>Discounted QALYs&lt;sup&gt;b&lt;/sup&gt;</td>
<td>CHD mortality</td>
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<td>Stroke mortality</td>
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<td>Nonfatal stroke incidence</td>
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- Optimistic scenario – Women of childbearing age maintain current level of fish consumption but shift to low mercury fish. Other adults do not amount of fish consumed
- Pessimistic scenario – All adults cut fish consumption by 1/6th
Closing Thoughts

• Compare pharmaceuticals (and other medical interventions) to a realistic alternative
  – Placebo is a good starting point to “screen” a drug

• Quantify outcome probabilities
  – Critical if probabilities differ across members of the population
    • Different doses
    • Different underlying risk factors

• Quantify outcome severity
  – Use clinical outcomes – not intermediate measures (e.g., biomarkers)
  – Report both “natural unit” and common metric estimates
The Good News: We Have the Technology

• Keep in mind those one thousand cost-effectiveness analyses
  – Models include medical intervention benefits
  – They quantify uncertainty

• Must add risks