FDA's current consumption advisory for fish
Is a change warranted?

NO

Presentation Outline

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II. Fish Consumption and MeHg Exposure--J. T. Heimbach
III. Risk/Risk Tradeoffs in Risk Management--G. M. Gray
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V. Industry Impact--Companies
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Re-evaluation of the NRC Methylmercury Committee Estimate

F. Jay Murray, Ph.D.
Murray & Associates

Introduction

- Asked by NFPA:
  - To assess the scientific validity of the estimate of 60,000 newborns "at risk" of neurodevelopmental defects
  - To examine the underlying assumptions
  - To provide a better estimate

Overview

- Basis and assumptions of estimate are unclear
- No definition of "at risk"
- Gross overestimate of the number of newborns "at risk"
- Not scientifically defensible

Topics of Discussion

- Why is the estimate wrong?
- Better estimates
- Choice of critical study
- Potential risks and benefits of fish consumption

Why Is the Committee Estimate Wrong?

- Uncertainty factors
- Fish consumption (100 g per day)
- Based solely on the Faroe Islands study
- Disregards Seychelles study

"Best Guess" of Committee Estimate

No. of U.S. women age 15-44 consuming fish	18,363,440
Top 5% fish consumption	918,172
No. of newborns born to top 5% annually	60,232
Fish consumed by top 5%	100 g per day
MeHg in fish	0.1-0.2 ppm
Estimated dose of MeHg	10-20 μg per day

Uncertainty Factor

- Estimate presumed to be based on Reference Dose (RfD) of 6 μg per day
- 2 uncertainty factors
- Inappropriate uncertainty factor
- "Adjusted Reference Dose"
- BMDL

Number of Newborns at Risk (Committee Exposure Estimates)

Basis	Dose of MeHg (μg per day)	No. at risk at 95th percentile
RfD	6	60,232
Adjusted RfD	20	0
BMDL	44-73	0

Fish Consumption and MeHg Exposure at 95th Percentile

Organization	Fish (g per day)	MeHg (μg per day)
Committee (2000)	100	10-20 ?
EPA (1997)	--	7.8
Environ (2000)	46	5.7

Number of Newborns at Risk (Environ Exposure Estimates)

Basis	Dose of MeHg (μg per day)	No. at risk at 95th percentile
RfD	6	0
Adjusted RfD	20	0
BMDL	44-73	0

Limitations of Faroe Islands Study for Estimating Risk in U.S.

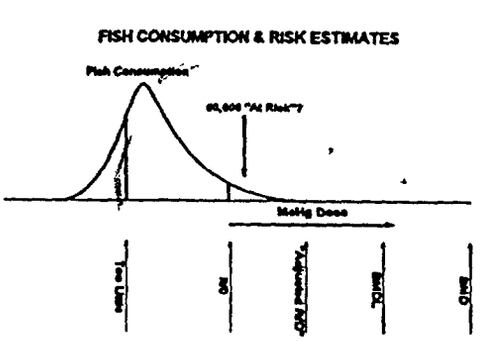
- Controversial choice
- Exposure to MeHg is far higher
- Whale meat and blubber is major source of exposure (2+ ppm)
- Pattern of exposure (episodic binge)
- PCBs and other chemicals are significant confounders

PCBs as a Confounder in the Faroe Islands Study

- PCB levels in whale meat and blubber are very high
- Exposure exceeds RfD by 600-fold
- Synergism between PCBs and MeHg
- JECFA (2000) recommended reassessing the confounding role of PCBs in this study

No Effect in Seychelles Study

- No adverse neurodevelopmental effects
- Fish consumption and MeHg exposure greater than in U.S.
- No confounding problem with PCBs
- Committee disregarded Seychelles study on the basis of policy, not science
  - Other agencies disagree



Conclusions

- Newborns are not at risk for neurodevelopmental effects from fish consumption at 95th percentile
- The Committee Estimate is scientifically unjustified
- It is important to weigh the benefits and risks of fish consumption

Fish Consumption and MeHg Exposure

J. T. Heimbach, Ph.D.
ENVIRON International Corp.

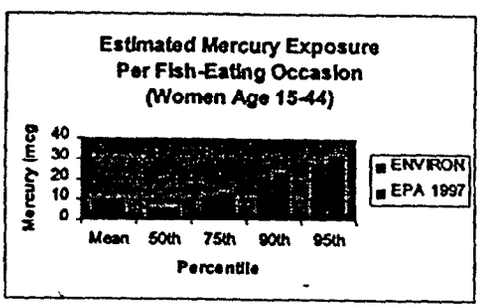
EPA Suggestion of Basis for Committee Estimate

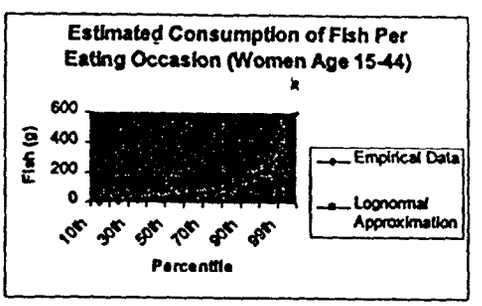
EPA Information

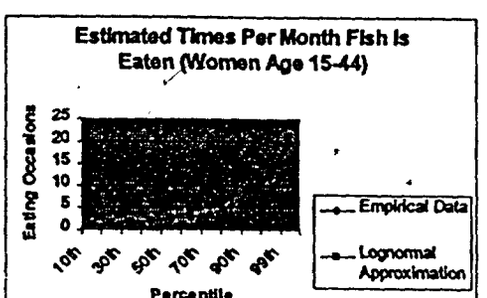
- 30.5% of women age 15 to 44 report fish consumption
- 95th percentile of consumption is 100g fish/day
- Data source: 1989/90 CSFII

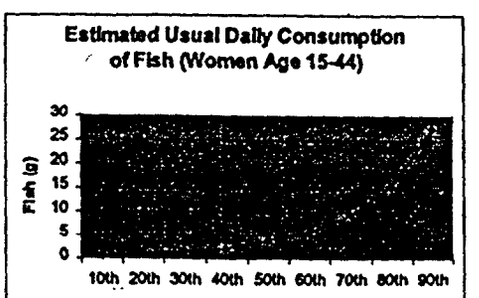
ENVIRON Comments

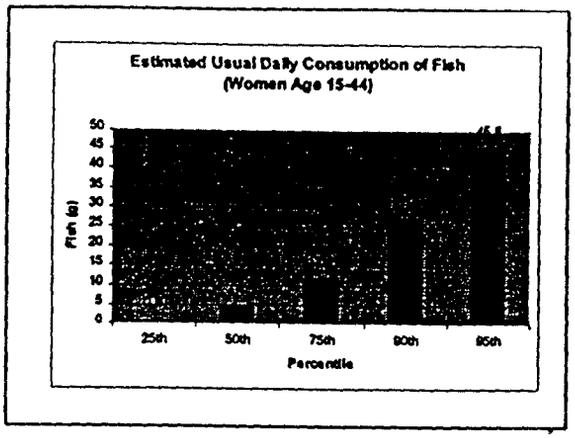
- Other data indicate that approximately 86% of women age 15 to 44 eat fish
- EPA appears to have used "3-day average" intake
- Method leads to severe overestimates of intake of infrequently consumed food
- Why use 89/90 CSFII?

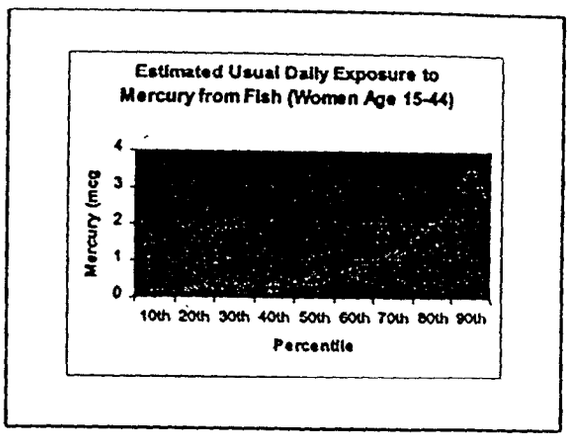


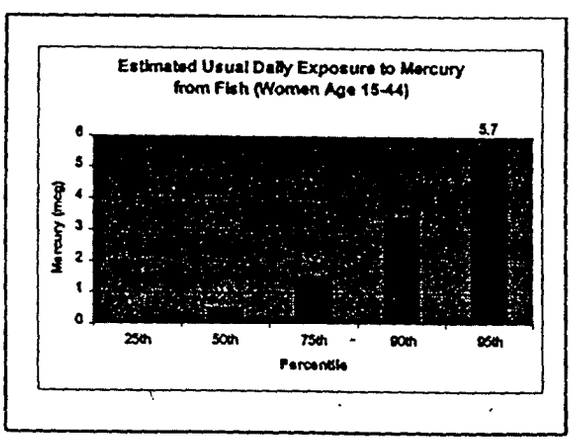












American Heart Association - Dietary Guidelines -

Two (2) servings of fish per week:

- About 1/2 fresh fish (RACC = 85g)
- About 1/2 canned/smoked fish (RACC = 55g)
- Average portion = 70g
  - Actual average for women age 15 to 44 = 71g

American Heart Association - Dietary Guidelines -

Two (2) servings of fish per week:

= 140g fish/week

= 20g fish/day

- 85th percentile of current consumption
- Twice current mean (11.3g) consumption
- Five times current median (4.1g) consumption
- AND... 14% of women age 15 to 44 do not eat fish at all

Risk/Risk Tradeoffs in Risk Management

George M. Gray, Ph.D
Harvard Center for Risk Analysis
Harvard School of Public Health

What are Risk/Risk Tradeoffs?

- Occur when risk reducing action may have risky consequences
- Target risk is often only focus of analytic and management efforts
- "Side effects" may offset, or outweigh, the benefits of a risk management policy

Confronting Risk/Risk Tradeoffs

- More commonly recognized and addressed in personal decisions
  - Osteoporosis *vs.* cancer risk for hormone treatment
  - Psychological effects of restricting elderly driver
- Rarely considered in broader social decisions
  - Increased benzene exposure with phase-out of lead in gasoline
  - Fish consumption advisories

Risk/Risk Tradeoffs with Methylmercury and Fish

- Target risk
  - Neurodevelopmental effects
  - Maybe others? (Cardio, immuno)
- Countervailing risks
  - Decreased fish consumption
    - Chronic heart disease risk
    - Neurodevelopmental effects
    - Immune system effects
  - Substitute foods
    - Increased fat intake
    - Contaminant in other foods

Risk Tradeoff Analysis

- Qualitative
  - Highlight areas of concern
  - Communication - looking after "common sense" questions
- Quantitative
  - Necessary for sense of magnitude of tradeoffs
  - Only way to know if risk management action helping or doing more harm than good

Summary

- Risk tradeoffs are pervasive
- Tradeoffs often transform risks or change population at risk
- Ignoring tradeoffs may reduce efficiency of risk management actions or even make things worse
- Need careful evaluation and risk comparison
- First--DO NO HARM

Comparison of Risks and Benefits from Fish Consumption

James R. Coughlin, Ph.D.
Coughlin & Associates

Omega-3 Fatty Acids in Fish

- Protective effect in cardiovascular disease risk:
  - Lower plasma triglycerides
  - Inhibit plaque formation
  - Decrease platelet aggregation
  - Alter arrhythmogenesis
- Eicosapentaenoic acid (EPA) and docosahexenoic acid (DHA) found in fatty fish
- Fish consumption also provides high quality protein and other nutrients (niacin, B12, vitamins A and D, Se)
- *Amer. J. Clin. Nutr. Suppl.* (Jan. 2000) - "Highly Unsaturated Fatty Acids in Nutrition and Disease Prevention," 38 articles from Barcelona Conference, 1996.

Beneficial Health Effects of Fish Consumption

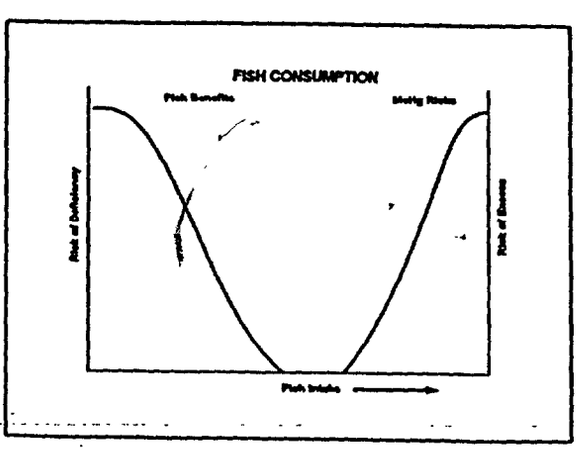
- Decreased risk of CHD and MI
- Enhanced immune and nervous system development
- Reduced risk of stroke and arthritis
- More long-term studies and randomized controlled clinical trials are needed to further confirm these observations
- If individuals do reduce their consumption of fish and replace it with other non-fish foods, these dietary changes may actually result in greater overall health risks.

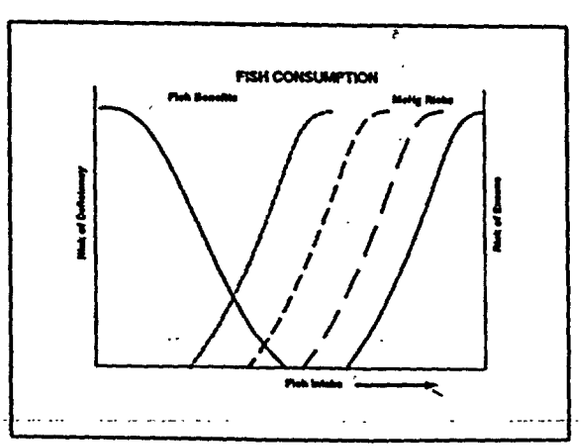
Risks and Benefits of Fish Consumption

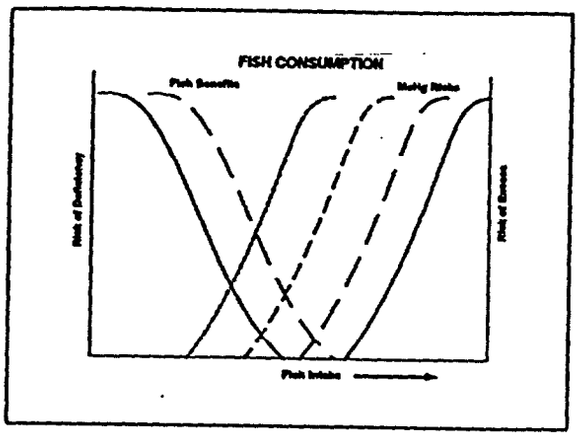
- Ponce et al., *Risk Analysis* (2000)
  - FDA's Clark Carrington and Michael Bolger as co-authors
  - Use of Quality Adjusted Life Years (QALYs) to compare risks of two different disease endpoints:
    - Increase in neurodevelopmental risk of delayed talking versus decrease in myocardial infarction
- Alternative Approach:
  - Directly compare risks and benefits for same adverse effects or diseases
  - This approach was not considered by the NRC Committee

Toxic Effects of MeHg versus Health Benefits of Fish Consumption

Effect	RfD	Health Benefit
Neurodevelopment	• Toxicity Endpoint for BMDL • UF = 2-3	Membrane function and brain/retina development
Cardiovascular Disease	Contributes to database UF	Reduced risk
Immune System	Contributes to database UF	Immunoinflammatory function improved
	TOTAL UF = 10	







In closing...

A change in FDA's current advisory for fish consumption is not scientifically justified:

- 60,000 children are not at risk for neurodevelopmental defects
  - Uncertainty factors, as apparently used in deriving the estimate, are inappropriate
  - Faroe Islands Study, alone, is inappropriate
    - Consumption patterns of population studied
    - Confounding role of PCBs

In closing...

A change in FDA's current advisory for fish consumption is not scientifically justified (cont'd):

- Seychelles Study is not considered in the analysis
- The harm of reducing/eliminating fish consumption in women of child bearing age and the public in total is real (not theoretical)
  - adverse neurodevelopmental effects
  - loss of cardiovascular health benefits
  - adverse impact to immune system

In closing...

A change in FDA's current advisory for fish consumption is not scientifically justified (cont'd):

- Conflicting dietary guidance
  - Confused public--who do they believe?
- Adverse impact to an Industry and the livelihood of many--nationally and internationally
- View of the International Community
  - Precautionary Principle?
  - There they go again...

In closing...

"...the Committee recommended that methylmercury be re-evaluated in 2002, when the 96-month evaluation of the Seychelles cohort and other relevant data that may become available can be considered." (Methylmercury, JECFA 2000)

In closing...

Data to date do not support a change in FDA's current consumption advisory for fish.

Before any change is considered:

- Risk comparison (risk/risk tradeoffs) must be done
- Seychelles Study, in total, must be considered