

A Quantitative Risk-Benefit Analysis of Changes in Population Fish Consumption

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Questions Related to the 2004 Fish Advisory

1. What is the basis for the advisory – why those specific limits?
2. Does adherence to this recommendation improve child health?
 - What about the nutritional benefits of long chain n-3 polyunsaturated fatty acids (LC n-3 PUFAs)?
 - What happens if compliance is imperfect?
3. How might other adults be affected by the advisory?

Part 1 - Basis for the 2004 Fish Advisory

FDA and EPA Development
of a Joint Advisory for
Methylmercury-containing
Fish Consumption for Women
of Childbearing Age and
Children
July 2003

Risk Management Decision-making

- NHANES indicates approx. 8% of at-risk population above the RfD
- How much can this percentage of the at-risk population be reduced, and still provide consumers with a variety of good sources of protein for a healthy diet?

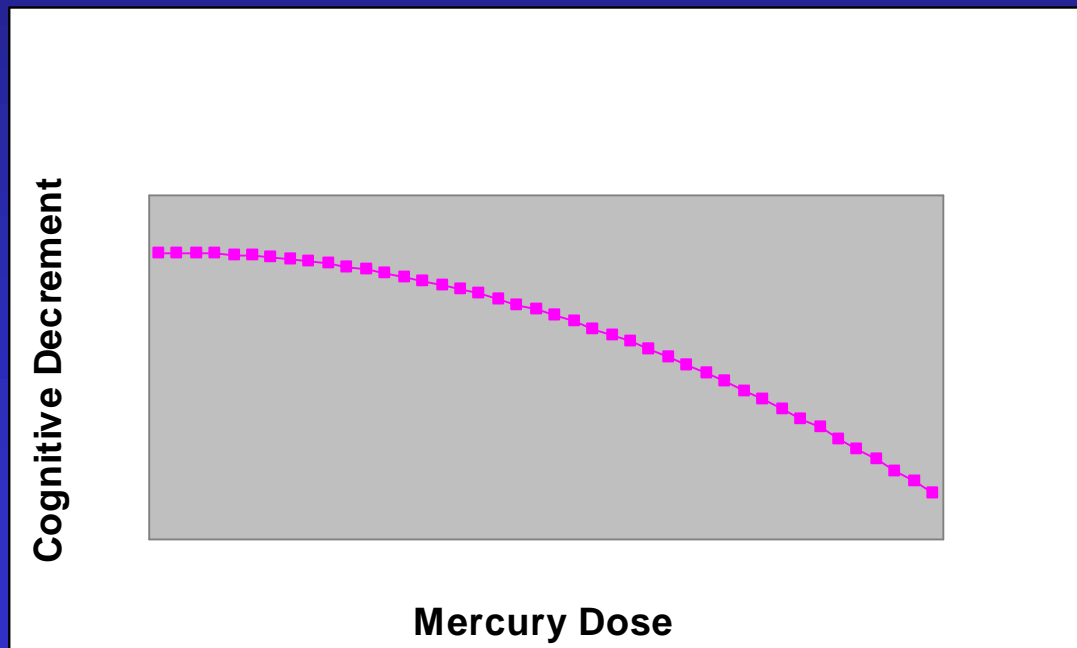


- Interpretation

- Exposure $>$ reference dose assumed unacceptable
- Exposure $<$ reference dose assumed “safe”

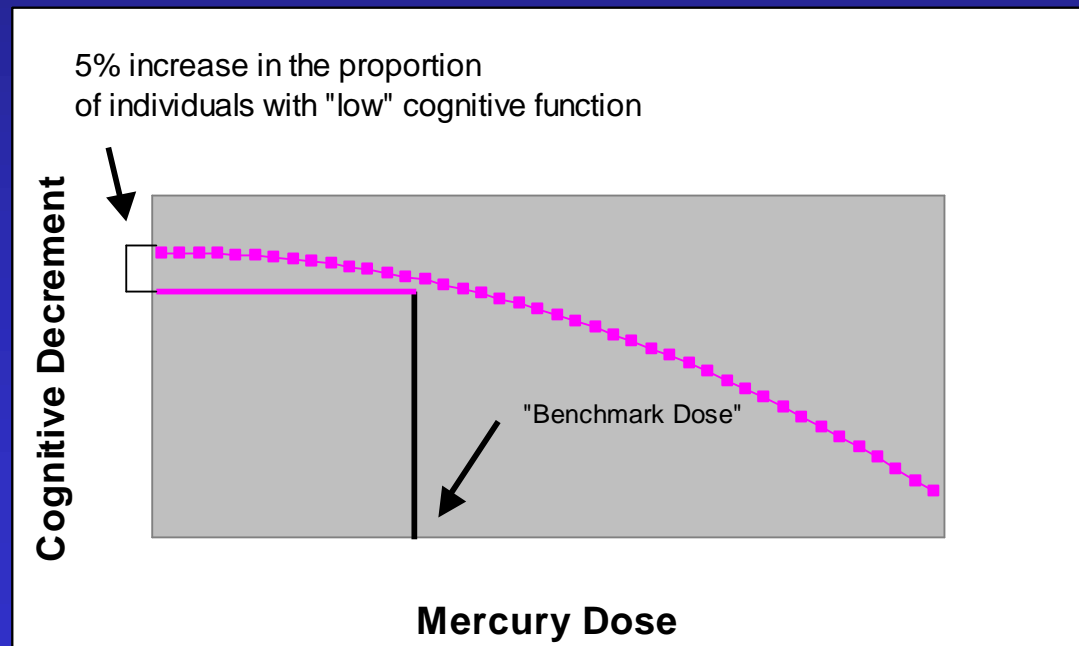
What is the Basis for FDA's Advisory?

- Epidemiology data – Mercury vs. cognitive decrement



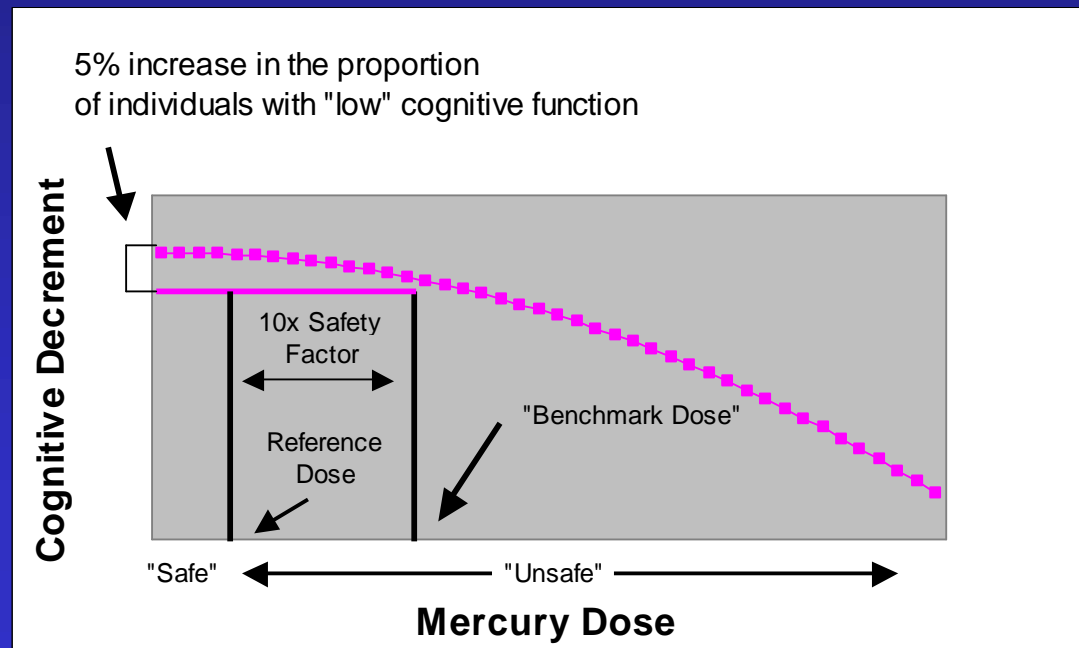
The “Benchmark dose”

- Smallest mercury exposure associated with an “important” cognitive decrement



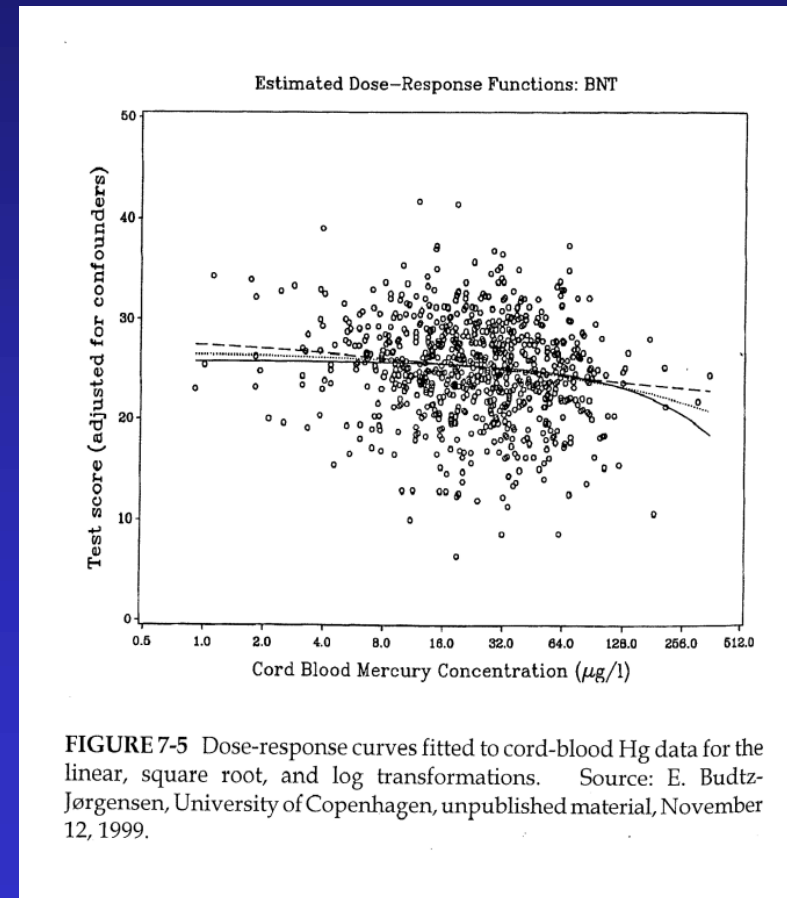
Reference Dose

- Divide by a “safety factor” of 10



Reference Dose is an Artificial Line

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



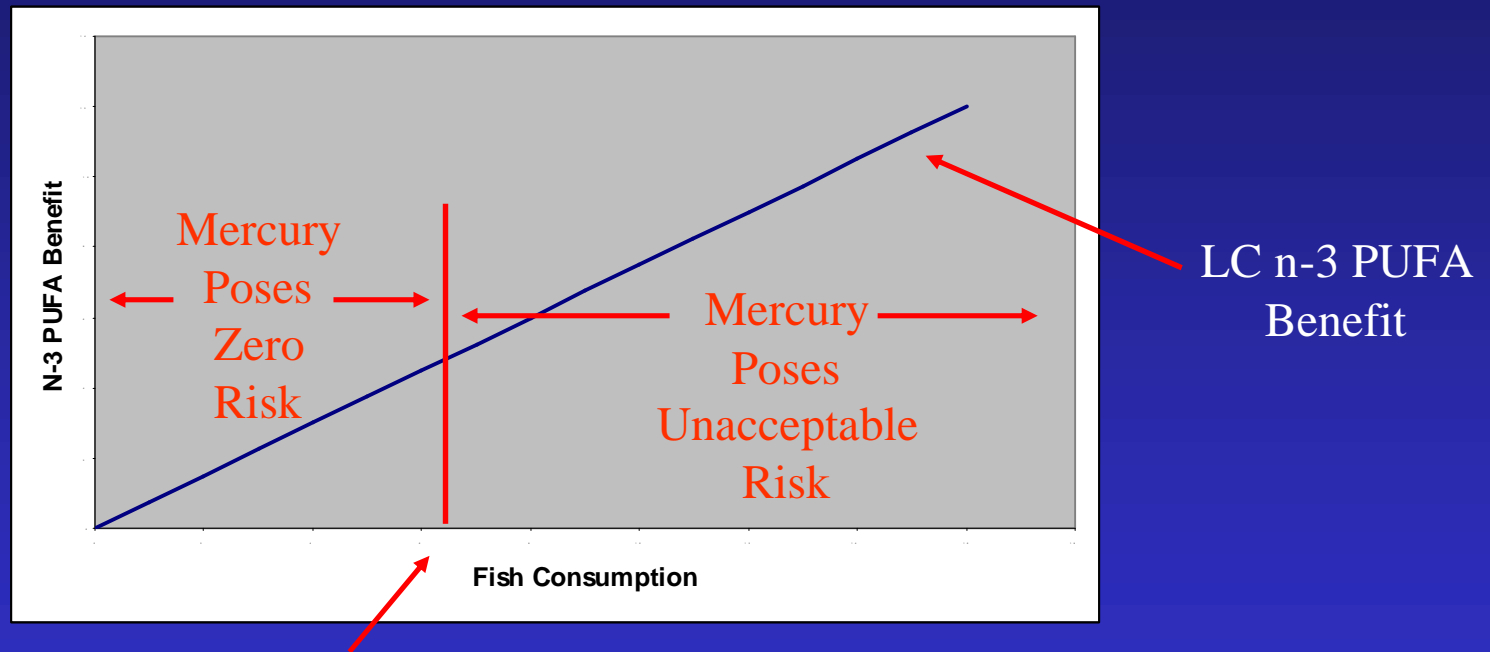
Preoccupation with Fish Consumption Resulting in Exposure > RfD

- National Research Council* 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 the reference dose
- Environmental Working Group**
 - “... an average woman following [FDA’s] advice... would exceed a safe dose of mercury (the reference dose) by 30 percent...”

•National Research Council (2000). Toxicological Effects of Methylmercury. Washington, DC

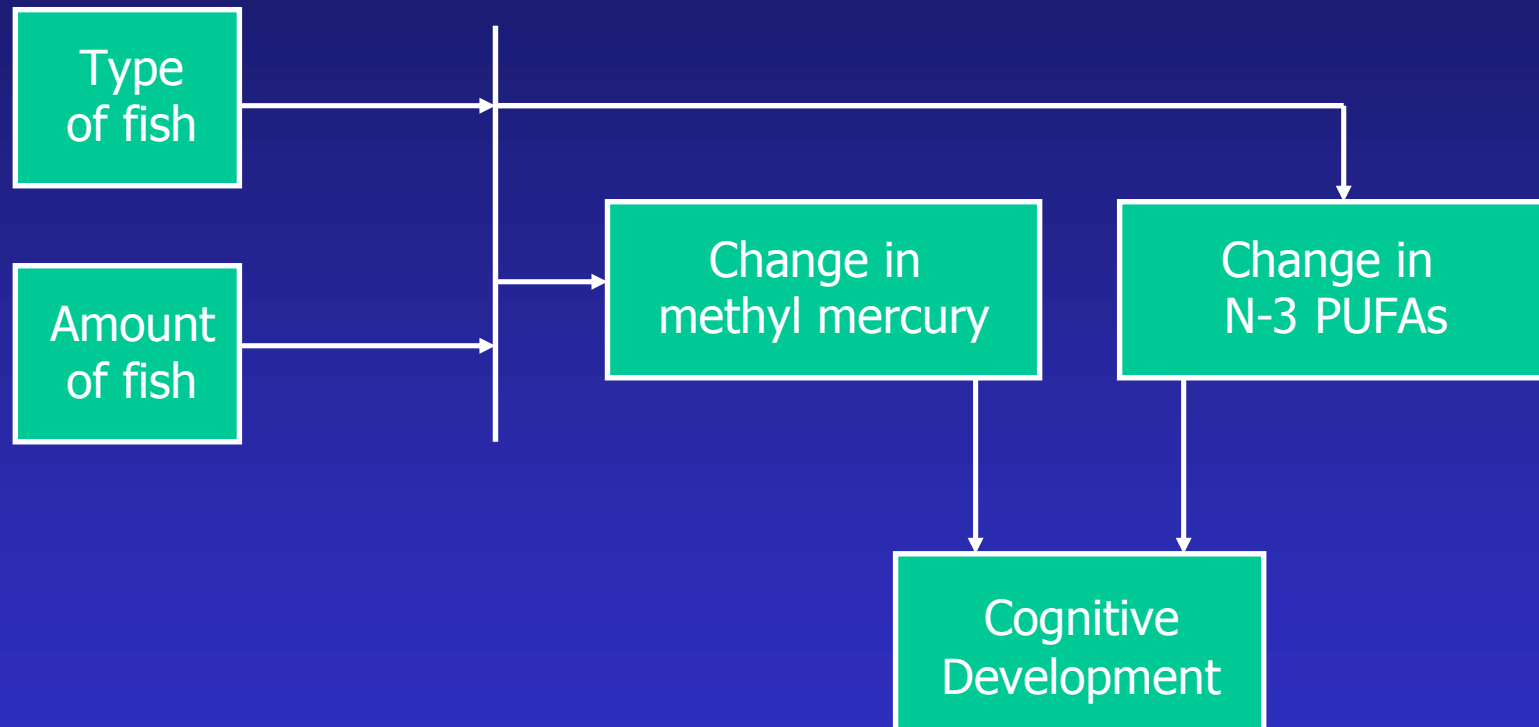
•Environmental Working Group. 2003. Data Quality Act Challenge: Request for Correction of FDA’s “Advice for Women Who Are Pregnant, or Who Might Become Pregnant, and Nursing Mothers, About Avoiding Harm to Your Baby or Young Child From Mercury in Fish and Shellfish

The Reference Dose Complicates Comparison of Risks and Benefits



Methyl Mercury
Reference
Dose

Part 2 –Advisory’s Implications for Child Health



Potential Scenarios Considered

- Challenge: We don't know advisory's actual impact on fish consumption
- Approach: Consider a range of plausible scenarios

	Scenario	
	Optimistic	Pessimistic
Women of childbearing age	Shift to low mercury fish but maintain same intake	Decrease total intake 17%*

* Estimate based on: Oken, E., et al. 2003. Obstet. Gynecol. "Decline in fish consumption among pregnant women after a national mercury advisory." 102:346-51.

Estimating MeHg – IQ Dose Response

- Weight standardized results from each test domain
- Weight corresponds to extent to which domain informs estimate of change in terms of IQ

Domain	Subjective Weight
Motor	0.2
Attention	0.3
Visuospatial/ Visuomotor	0.4
Language	0.6
Memory	0.6
Intelligence	1
Learning / Achievement	0.6

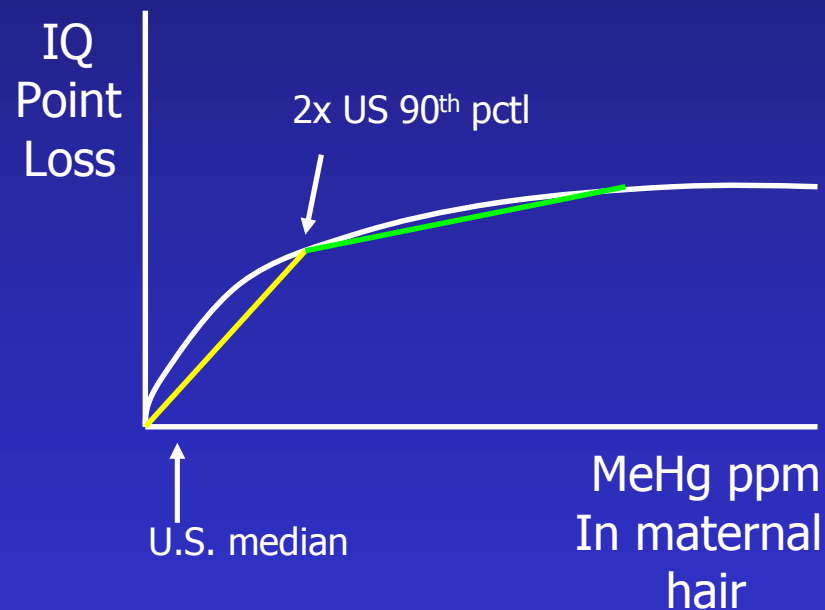
Within Each Test Domain

- Limit attention to 3 main longitudinal studies
- Weight by sample size
 - Proxy for precision

Population	Weight
Faroe Islands	734
Seychelles	643
New Zealand	115

Cohen JT et al. 2005. Am J. Prev Med “A quantitative analysis of prenatal methyl mercury exposure and cognitive development.” 29(4):353-65 .

Linearization of Faroe Islands Results



**Use FI slope over first quartile:
0.7 IQ points/ppm MeHg**

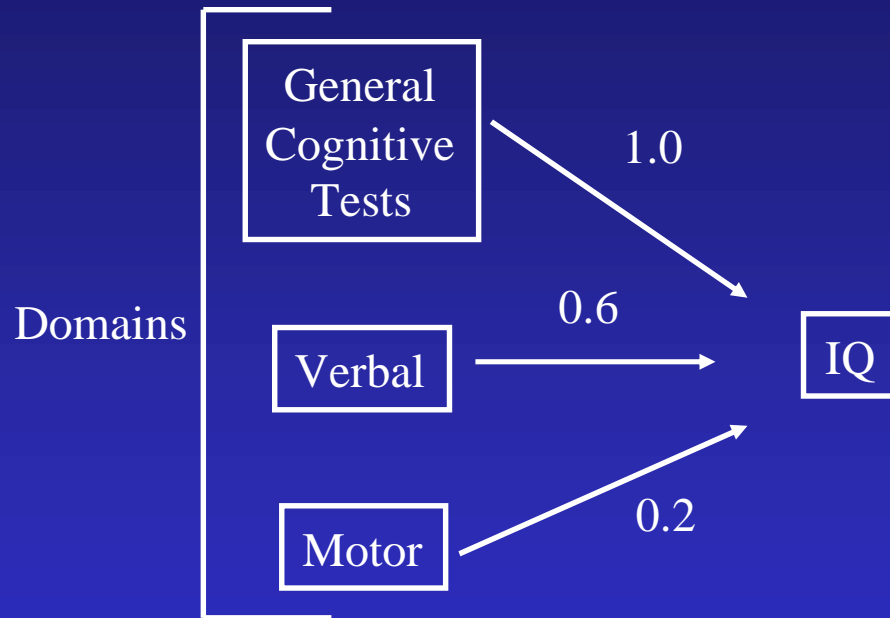
**Use FI slope over 1st to 3rd quartile:
0.2 IQ points/ppm MeHg**

**EPA analysis (Louise Ryan) with
original data from FI study: 0.13 IQ
points/ppm MeHg**

N-3 PUFA Benefits

Combining Results Across Studies

Using Different Types of Tests



Weighted influence :

$$\frac{\text{GenCog} + 0.6(\text{Verbal}) + 0.2(\text{Motor})}{1.8}$$

Cohen JT et al. 2005. Am J. Prev Med “A quantitative analysis of prenatal intake of n-3 polyunsaturated fatty acids and cognitive development.” 29(4):366-74 .

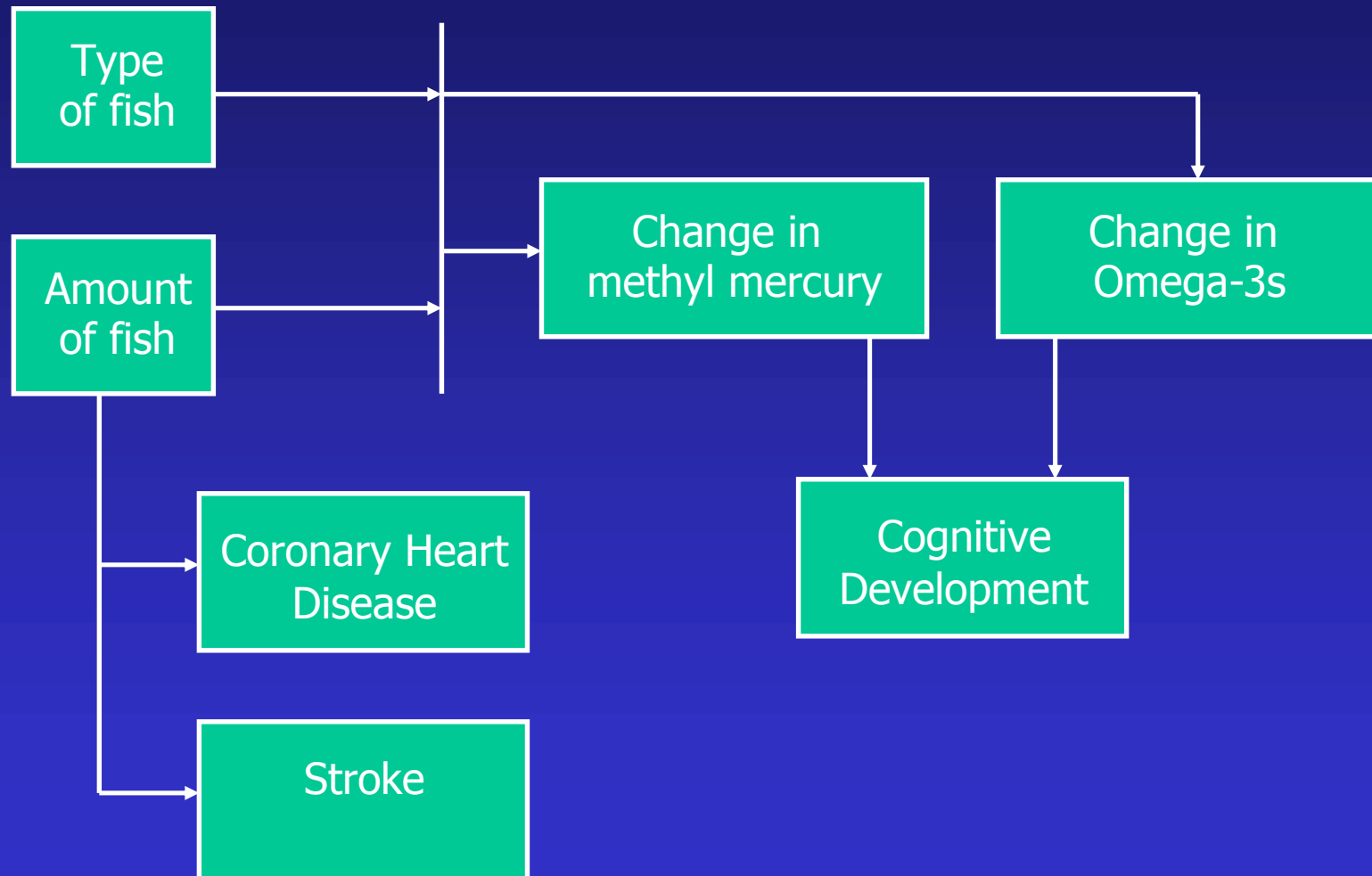
Individual Risks and Benefits

	Scenario	
	Optimistic	Pessimistic
IQ gain per child	0.1 points	0.02 points

Aggregate U.S. Population Risks and Benefits

	Scenario	
	Optimistic	Pessimistic
IQ gain	410,000 points	92,000 points

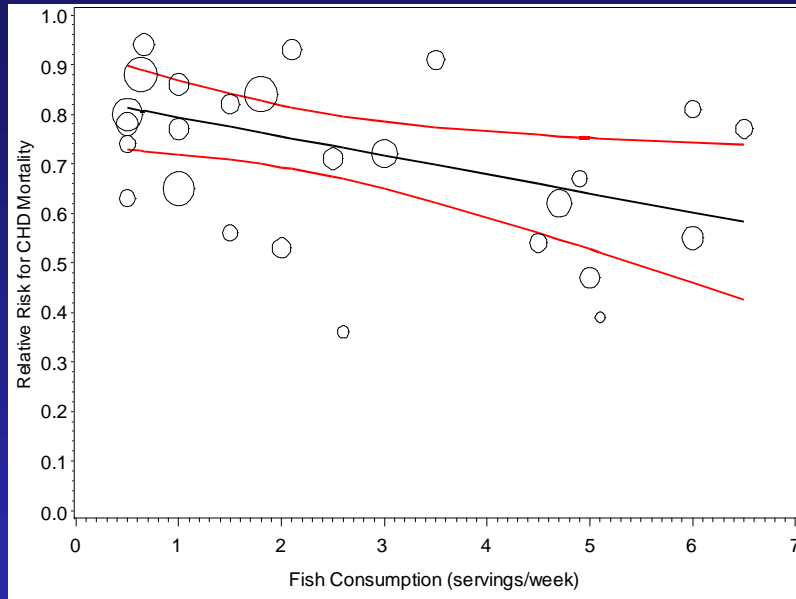
Part 3 – Impact on Other Groups



Scenarios

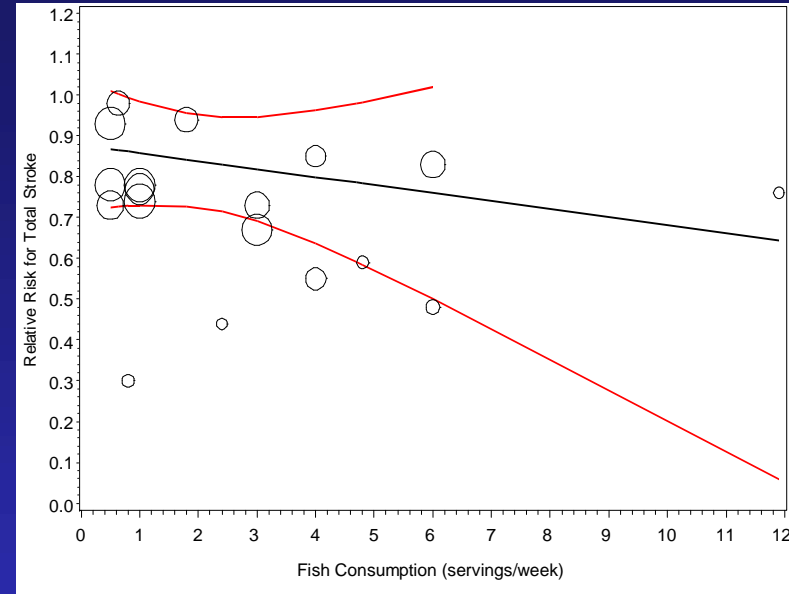
	Scenario		
	Optimistic	Middle	Pessimistic
Women of childbearing age	Shift to low mercury fish but maintain same intake	Decrease total intake 17%	Decrease total intake 17%
Other adults	No change	No change	Decrease total intake 17%

Stroke and Coronary Heart Disease



CHD Mortality

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.



Stroke Incidence

Bouzan C et al. 2005. Am J. Prev Med "A quantitative analysis of fish consumption and stroke risk ." 29(4):347-52 .

Konig, A et al. 2005. Am J. Prev Med "A quantitative analysis of fish consumption and coronary heart disease mortality

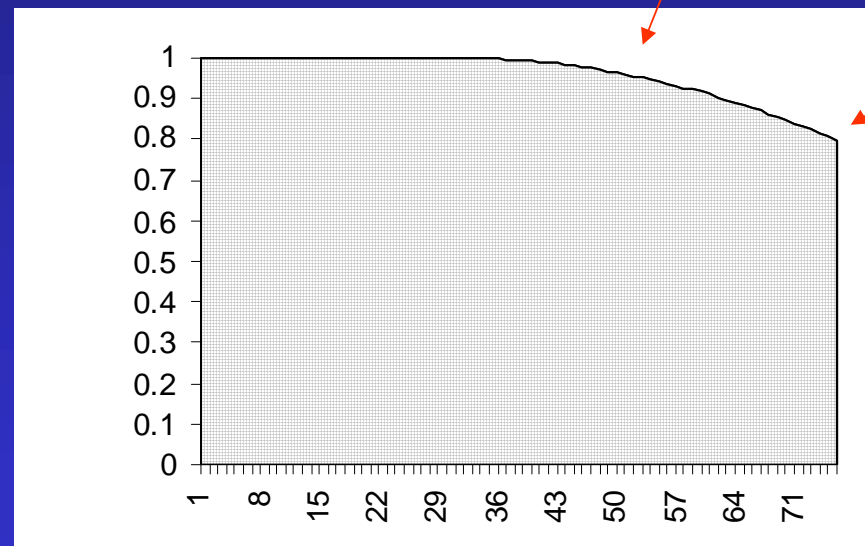
Health Effects Compared by Conversion to QALYs

- Value of year in perfect health = 1
- Value of death = 0
- Other health states between 0 and 1
- QALYs used extensively in the health economics literature

Value of Each Life Year

Example 1 – Typical Life

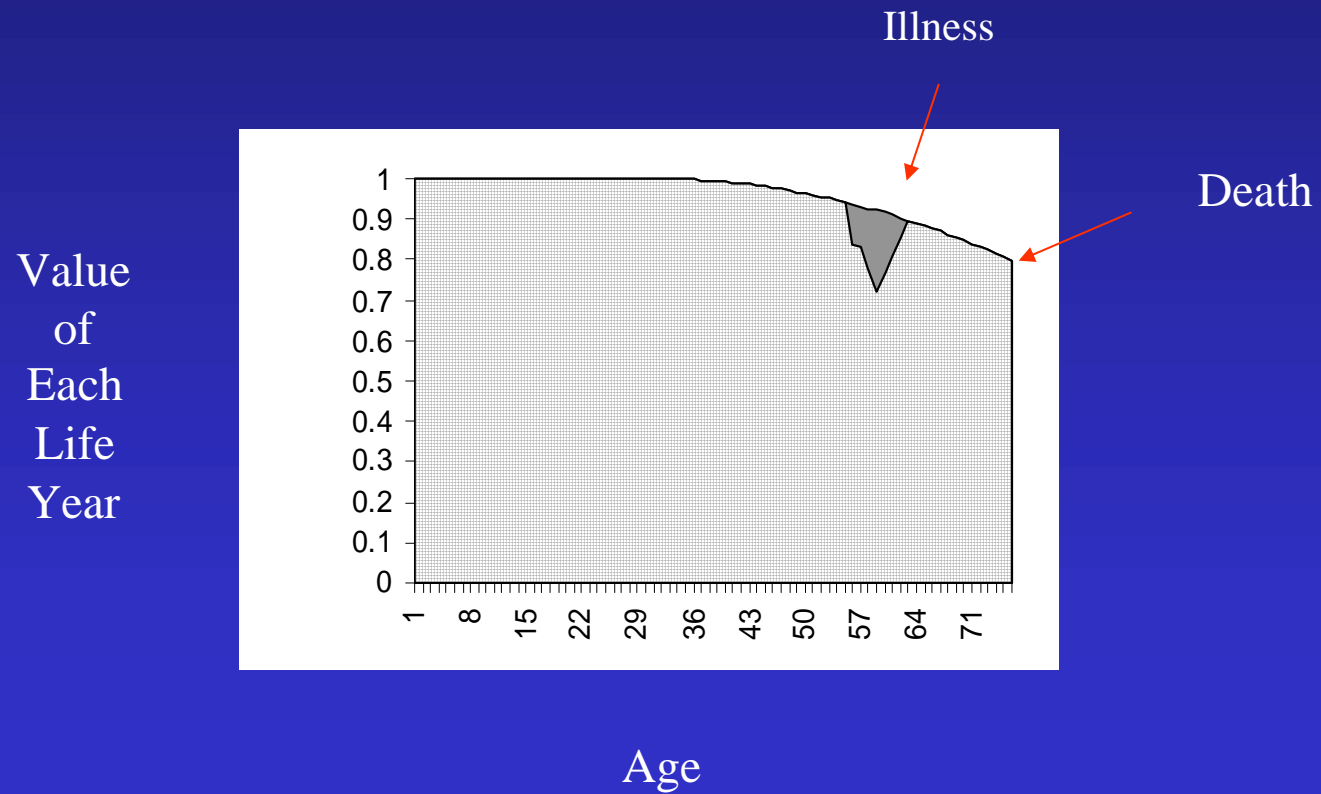
Declining health in later years



Age

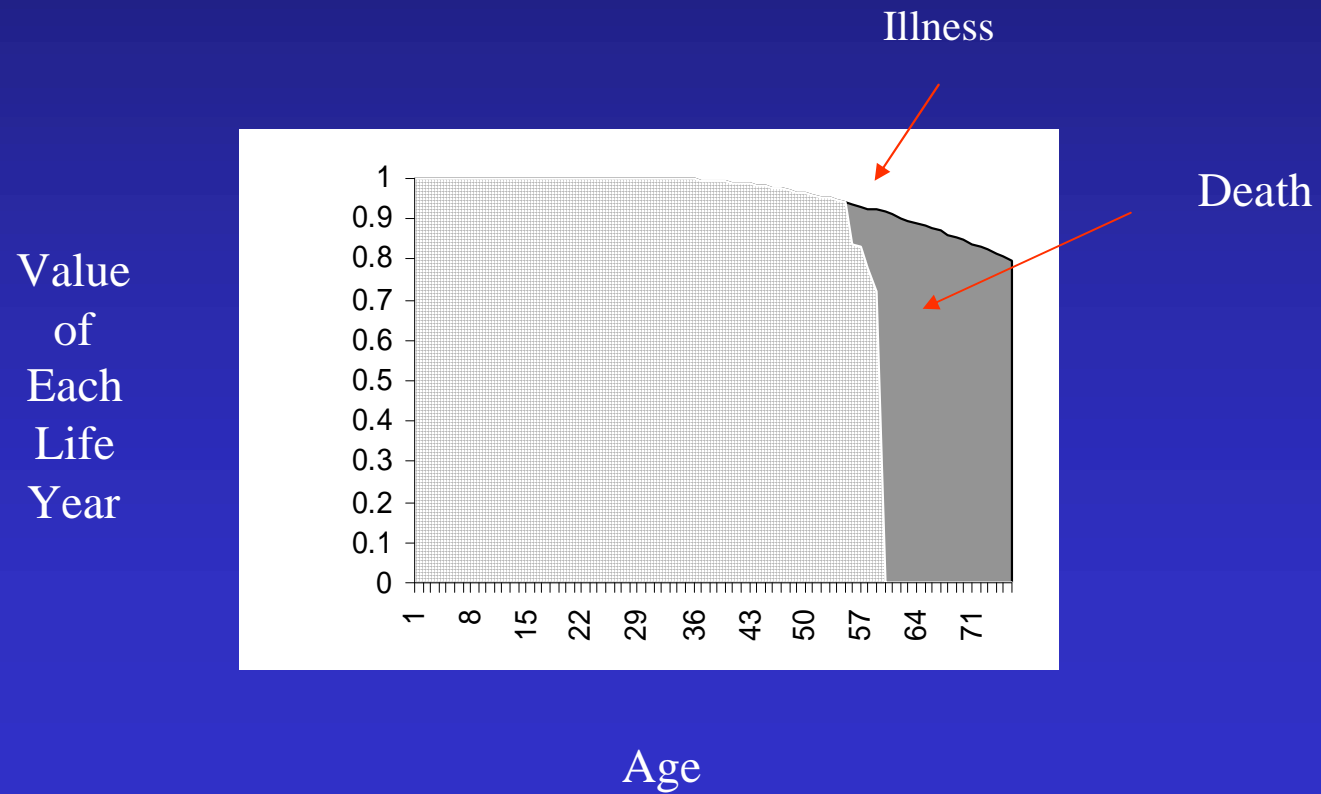
QALYs (continued)

Example 2 – Illness followed by recovery



QALYs (continued)

Example 3 – Illness followed by death

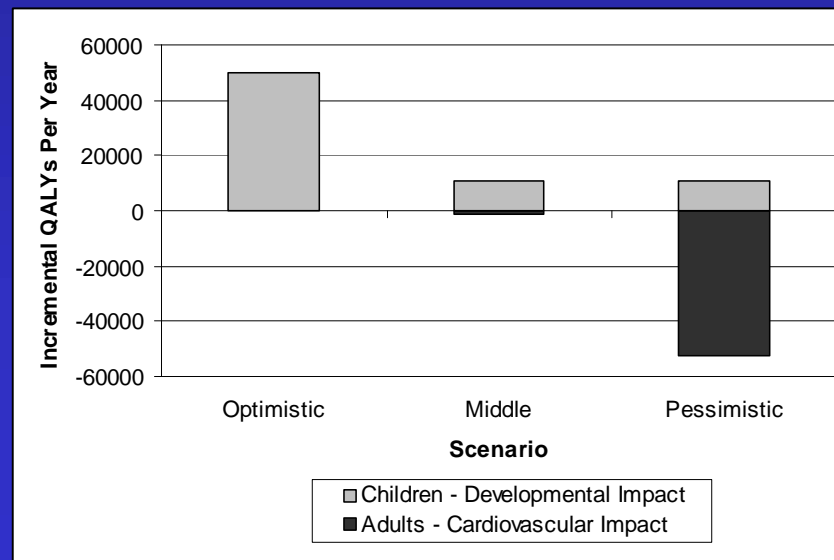


Results

Natural
Units

	Scenario		
	Optimistic	Middle	Pessimistic
Fish Consumption			
Women of childbearing age	Shift to Low Hg	Decrease	Decrease
Other adults	No change	No Change	Decrease
Change in Health			
Cognitive – Net IQ points gained	410,000	92,000	92,000
CHD and stroke –fatalities/yr	14	71	7,900
Non-fatal stroke – incidence	14	68	1,500

QALYs



Conclusions

- Advisory is beneficial to child health if women of childbearing age follow advice as intended
 - Maintain fish consumption
 - Shift to lower mercury fish
- Benefits remain positive if women reduce fish consumption instead of shift to low mercury fish
 - Net benefits substantially smaller

Conclusions (2)

- Small decreases in fish consumption among other adults (3% to 4%) can eliminate net benefits
- Assumed slope of MeHg-IQ dose response from Faroe Islands study is a key source of uncertainty