



Quantitative Modeling of Benefits and Risks And the Implications for Managing Risk from Mercury in Commercially Caught Fish

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FDA's Mission Relating to Fish

- **FDA has Federal regulatory responsibility for safety of fish marketed in the U.S.**
 - Fish may be removed from interstate commerce if they present a reasonable possibility of injury to health.
- **The challenge**: does a reasonable possibility of injury exist from commercial fish due to the MeHg in them, and if so, to whom?

Prenatal Exposure: FDA's Dilemma Involving MeHg

- The fetus is generally more sensitive to MeHg than adult (per the Japan and Iraq poisoning events);
- But unlike the Japan and Iraq events, no reported overt, clinical effects (e.g., cerebral palsy, mental retardation) from prenatal exposure.
- ***Are subtle, subclinical effects occurring? If they are, under what circumstances and how significant are they?***

Traditional “Safety Assessment” Model Does Not Address This Question

- **U.S. National Academy of Sciences (2000):** 60,000 babies born each year “at risk” of developmental deficits.
- In response to inquiry from FDA about meaning of ‘at risk:’
 - *“The committee does not believe it is possible to estimate a meaningful number of children that might be affected within the at risk population.”*

2001: FDA Opts for Advice to Pregnant Women as a Matter of Prudence

- ***Should not eat more than 12 oz of fish per week during pregnancy.***
 - Risk (likelihood & severity) over 12 oz: *not estimated.*
 - Risk (likelihood & severity) at 12 oz: *not estimated.*
 - Risk (likelihood & severity) below 12 oz: *not estimated.*
- **12 oz/wk ceiling retained in 2004 update. Risks (likelihood and severity) still not estimated.**

FDA Started Considering Quantitative Risk Assessment for MeHg (2004-5)

- To estimate:
 - likelihood of neurodevelopmental effects; and
 - size of those effects

through range of U.S. exposures resulting from mothers' consumption of commercial fish during pregnancy.

But Then....

Studies Published Beginning in 2004

- Eating fish during pregnancy associated with better cognitive outcomes in offspring.
 - Most reported outcomes appeared to be improvements.
 - Eating more than 12 oz/wk could be better than eating less.

- But MeHg still appeared to adversely affect outcomes in most of the studies that measured MeHg exposure in addition to “fish” consumption.
 - Could reduce the size of the benefit
 - Could cause the effect to be adverse

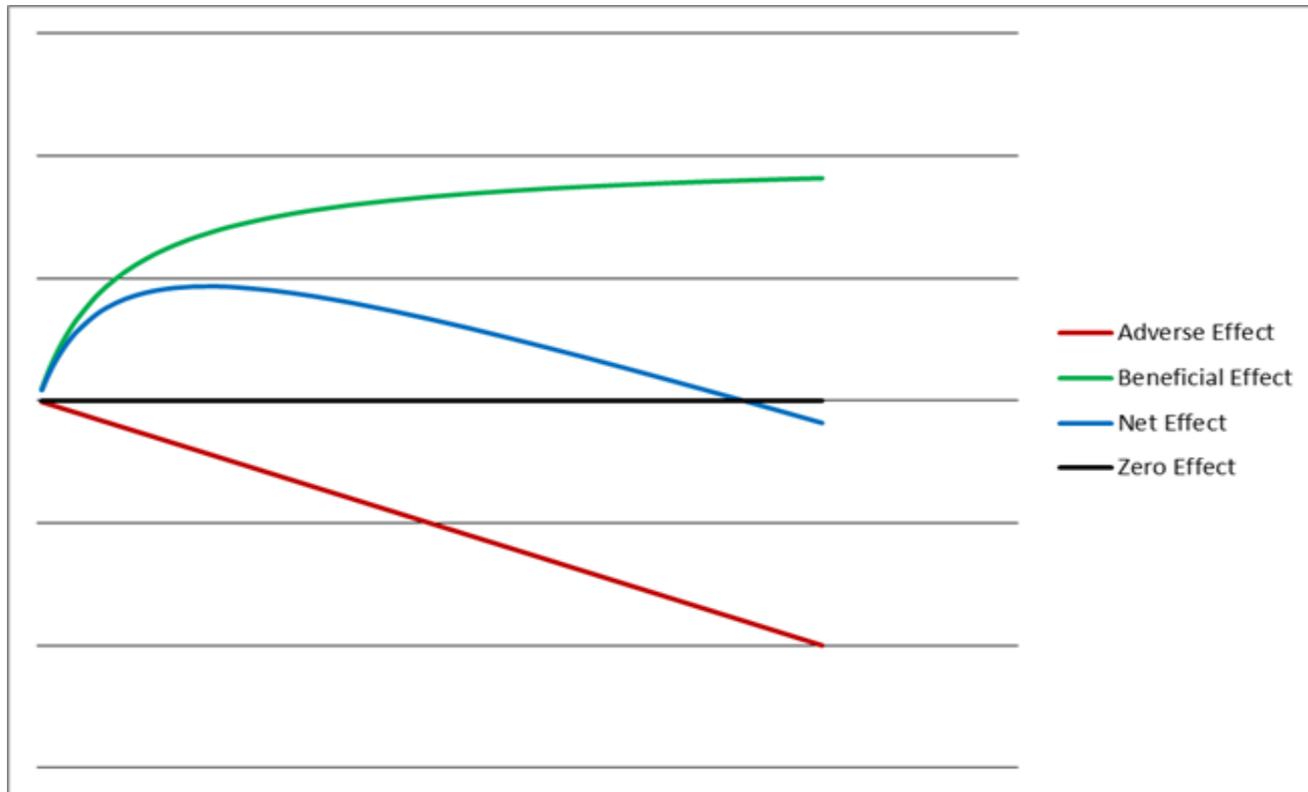
A Major “Take-Away” for Us

- We needed a new approach to assessing risk.
- The approach should take into account both:
 - Adverse contributions from MeHg; and
 - Beneficial contributions from... “fish”
- The approach should assess “*net effects*” from eating fish.

Our “Net Effects” Approach

1. Calculate dose-response function(s) for adverse effects on cognitive development from MeHg, independent of any benefit;
2. Calculate D/R function(s) for beneficial effects on cognitive development (presumably from one or more nutrients), independent of MeHg.
3. Calculate D/R function(s) for net effects (adverse and beneficial effects added together).

What D-R's Could Look Like for a Typical Fish From the Research Evidence



Net Effects Estimates in the FAO/WHO Risk Benefit Assessment

More than 70 species of fish:

- All species net beneficial through at least 24 oz/week with lower bound estimate for MeHg.
- All species below 0.5ppm MeHg net beneficial through at least 24 oz/week with upper bound estimate for MeHg.
 - Some high MeHg fish are net adverse immediately when upper bound for MeHg is used (marlin, orange roughy, bigeye tuna, king mackerel, shark, swordfish).

Potential Effect on Consumption Advice

- **Focus of U.S. advice in 2001 & 2004:**
 - How pregnant woman could *minimize risk* from MeHg without avoiding fish.

- **How advice could be re-focused now:**
 - How pregnant woman could **minimize risk** from MeHg while *maximizing benefit* that fish could provide to the developing nervous system.

Dietary Guidelines for Americans, 2010 (HHS/USDA)

Now includes a minimum consumption target:

- *Pregnant women should eat 8-12 oz/wk. of varieties lower in MeHg.*
 - Other aspects of the advice are the same as in FDA/EPA 2004 advice.
 - E.g., avoid same 4 high-MeHg species.

Conclusions

- Fish during pregnancy could benefit cognitive development or hurt cognitive development depending on amounts and types of fish.
- Public health entities can design risk management strategies to both maximize potential benefits and minimize potential risks.
- Public health entities can do this through a “net effects” approach that includes both adverse and beneficial effects.