Harvard Center for Risk Analysis

Using Decision Sciences to Promote Public Health

JANUARY 2006
Volume 14
Issue 1

Risk in Perspective

MATTERS OF THE HEART AND MIND: RISK-RISK TRADEOFFS IN EATING FISH CONTAINING METHYLMERCURY

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Introduction

In 2004, the U.S. Food and Drug Administration (FDA) and the U.S. Environmental Protection Agency (EPA) issued an advisory about the risks of methylmercury in fish and shellfish. Methylmercury is a neurotoxin that can cause developmental delays when young or unborn children are exposed. The advisory therefore targeted parents of young children, pregnant women, women who may become pregnant, and nursing mothers.

On the other hand, fish are an excellent nutrition source, rich in omega-3 fatty acids. The omega-3 fatty acids are thought to reduce the risk of coronary heart disease and stroke, and may also be good for the neurodevelopment of young and unborn children. The FDA and EPA advisory therefore had to walk a fine line. The advisory states that fish are an important part of a healthy diet, and that the advisory is not aimed at the large majority of the population for whom mercury poses little health risk. For those targeted by the advisory the message is nuanced: 1) avoid those types of fish with high mercury concentrations (shark, swordfish, king mackerel, and tilefish); 2) eat no more than one meal a week of fish with moderate mercury levels, such as albacore tuna; 3) eat no more than two

The Harvard Center for Risk Analysis recently conducted two projects evaluating public-health interventions to address methylmercury exposure. This issue of *Risk in Perspective* describes a project by Joshua Cohen and colleagues that estimates the net impact of the 2004 FDA/EPA advisory warning women of childbearing age about mercury in fish. Cohen *et al.* take the amount of mercury in the environment as given and evaluate the net effects of the 2004 advisory on public health, including both the cognitive benefits of lower mercury exposure and the forgone nutritional benefits from reduced fish consumption. Earlier work, conducted by HCRA Director James K. Hammitt and graduate student Glenn Rice, quantified the monetary value of health improvements associated with reducing mercury emissions from coal-fired power plants in the U.S. That project, to be described in a future issue of *Risk in Perspective*, took population fish consumption patterns as given and evaluated the impact of reducing the amount of mercury released to the environment.

meals a week of fish with low mercury concentrations (*e.g.* shrimp, canned light tuna, salmon, pollock, and catfish); and 4) check local advisories about the safety of non-commercially caught fish.

The consequences of the 2004 advisory, however, remain an open question. First, because mercury poses a risk to the cognitive development of young and unborn children but omega-3 fatty acids can help cognitive development, does the recommended shift in maternal fish consumption help or hurt children? Second, could unintended shifts in fish consumption among other members of the population lead to substantial increases in stroke and coronary heart disease? More generally, how should decision makers evaluate this and other public-health interventions that may involve tradeoffs?

Evaluating these tradeoffs in the context of the 2004 fish advisory depends on quantifying the impact of the advisory on fish-consumption patterns, estimating the extent to which the resulting changes in consumption affect nutrient intake and contaminant exposure, and quantifying the relationship between changes in these intakes and the resulting health effects. Finally, the different types of health effects must be aggregated to determine the net impact.

To study these questions, the Harvard Center for Risk Analysis (HCRA) was awarded a grant by the National Food Processors Association Research Foundation and the Fisheries Scholarship Fund. HCRA convened a scientific panel chaired by Steven Teutsch (now at Merck & Co, Inc., and formerly with the Centers for Disease Control and Prevention). Other panel members were David Bellinger (Department of Neurology, Children's Hospital, Boston), William Connor (Division of Endocrinology, Diabetes and Clinical Nutrition, Oregon Health Sciences University), Penny Kris-Etherton (Department of Nutritional Sciences, Pennsylvania State University), Robert Lawrence (Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University), David Savitz (Department of Epidemiology, School of Public Health, University of North Carolina), and Bennett Shaywitz (Department of Pediatrics and Neurology, Yale University). Harvard scientific staff included Colleen Bouzan, Joshua Cohen, Ariane König, and principal investigator George Gray.

This *Risk in Perspective* summarizes the full report, which has been peer reviewed and appears in the *American Journal of Preventive Medicine* 2005;29(4):325-334.

The Impact of Fish Advisories on Fish Consumption

Estimating the impact of advisories on fish consumption patterns is difficult because relevant studies are limited. One study reported that following the release of a similar fish advisory by the federal government in 2001, pregnant women in eastern Massachusetts decreased their fish consumption by 17%. Beyond this study, the evidence is fragmentary. Although no study in the scientific literature reports the impact of advisories on consumption among the broader population, it is not difficult to imagine that disturbing headlines, such as those below, may lead some individuals to avoid fish:

- E.P.A. says mercury taints fish across U.S. (New York Times, August 25, 2004);
- Study finds mercury levels in fish exceed U.S. standards (New York Times, August 4, 2004);
- Proposal would require warnings about mercury dangers in fish restaurants, markets would be forced to post trilingual signs (San Francisco Chronicle, October 4, 2005).

Rather than estimating exactly how the 2004 advisory affects consumption, we consider three representative scenarios. Our "optimistic" scenario assumes that only women of childbearing age change their consumption in response to the advisory, and that they do so by shifting consumption from the typical mix of fish for U.S. consumers to a mix that replaces fish high in mercury with fish low in mercury.

This scenario is optimistic because it assumes women reduce mercury exposure while essentially preserving the omega-3 fatty acid health benefits.

Our "middle" scenario also assumes that only women of childbearing age react to the advisory. In this case, however, we assume they reduce their consumption of fish by 17% without changing the mix of fish consumed. Unlike the optimistic scenario, this scenario envisions a loss of some neurological development benefits to unborn children because of decreased maternal intake of omega-3 fatty acids.

Our "pessimistic" scenario assumes that all adult members of the population reduce their fish consumption by 17%. In this case, all adults lose some protection against coronary heart disease and stroke.

In addition to these scenarios, we examined how an increase in fish consumption would affect public health.

The Impact of Fish Consumption on Omega-3 Fatty Acid Intake and Mercury Exposure

We use data on omega-3 fatty acid concentrations in fish, together with a model developed by the FDA, to quantify the impact of the shifts in fish consumption envisioned in our three scenarios on omega-3 fatty acid intake and mercury exposure.

Health Effects Due to Shifts in Fish Consumption, Omega-3 Fatty Acid Intake, and Mercury Exposure

Quantifying the health effects associated with shifts in fish consumption, omega-3 fatty acid intake, and mercury exposure has proven to be the most challenging aspect of the project. For mercury, typical risk assessments conducted by the federal government are not helpful because they identify a safe level of mercury exposure (referred to as the "reference dose"), rather than quantifying the incremental risk associated with changes in exposure. Although we could translate changes in fish consumption into changes in the proportion of individuals above and below the reference dose, we could not determine the impact of such shifts on measurable outcomes, such as cognitive ability as measured by IQ.

The second problem is the sheer number of potential health effects to consider. For example, in addition to aiding cognitive development in children and reducing the risk of coronary heart disease and stroke in adults, omega-3 fatty acids may also protect against Alzheimer's disease, depression, and low birth weight. In addition to compromising cognitive development, mercury may affect coronary health, harm the immune system, and adversely affect the kidneys. The HCRA panel reviewed the scientific literature and identified those effects judged both reasonably plausible given the available scientific evidence and likely to be substantial relative to the other health effects under consideration.

A related problem concerns other contaminants in fish. For example, some fish have elevated concentrations of organic chemicals, such as polychlorinated biphenyls (PCBs), which may cause cancer. However, because we judged their impact to be small when compared to other health effects included in our analysis, the effects of these compounds are not included.

Ultimately, our analysis includes four health effects: 1) the impact of mercury exposure during pregnancy on cognitive development, as measured by IQ; 2) the impact of omega-3 fatty acids on cognitive development, also measured in terms of IQ; 3) the net impact of fish consumption (*i.e.,* the effects of both omega-3 fatty acids and mercury) on coronary heart disease mortality; and 4) the net impact of fish consumption on stroke incidence and mortality.

Aggregating Different Types of Health Effects

Integrating the fish consumption scenarios, their modeled impact on fish consumption, mercury exposure and omega-3 fatty acid intake, and the estimated impact of these shifts on the health outcomes yields projected changes in population mortality (due to stroke and coronary heart disease), non-fatal stroke incidence, and IQ. In order to aggregate these impacts, we convert them to a common metric: the quality-adjusted life year (QALY). QALYs provide a method to account for changes in both mortality and morbidity. One QALY is defined as a year of life in perfect health, while death is assigned a value of zero QALYs. A year of life in less-than-perfect health has a value between zero and one QALY. The QALY has a well-defined theoretical foundation and has been used extensively in the scientific literature to evaluate the costs, risks, and benefits of many hundreds of health interventions.

Results

Our analysis shows, not surprisingly, that the impact of the 2004 advisory depends heavily on how it affects fish-consumption patterns. The table summarizes our findings for the U.S. population in terms of "natural units" – *i.e.,* changes in annual mortality (due to coronary heart disease and stroke), annual non-fatal stroke incidence, and total IQ (*i.e.,* the sum of the gains and losses in IQ among all four million babies born in the U.S. each year).

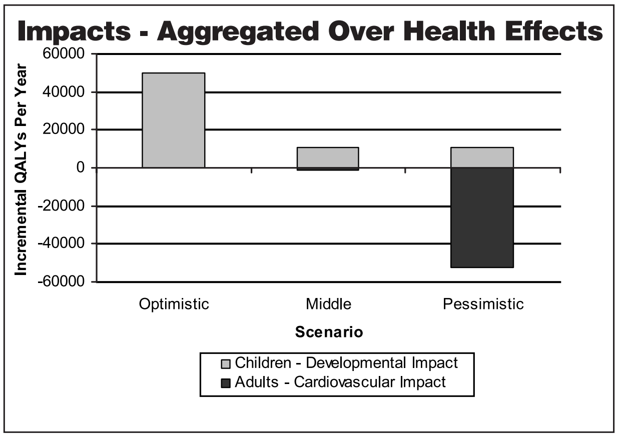
Impacts - By Health Effects

HEALTH EFFECT	SCENARIO OPTIMISTIC	 MIDDLE	 PESSIMISTIC
Cognitive Development – Net IQ Points Gained	410,000	92,000	92,000
CHD and stroke mortality – Additional annual fatalities	14	71	7,900
Non-fatal stroke incidence – Additional annual cases	14	68	1,500

Under our optimistic scenario (women of childbearing age shift to low mercury fish, but do not change total fish consumption, as effectively recommended by the 2004 advisory), there is a gain of more than 400,000 IQ points among newborn babies each year. There are slight increases in mortality and non-fatal strokes, but these are small because women of child-bearing age are at low risk of these effects. To help put these numbers into perspective, it is useful to think of them on an individual basis. The cognitive-development benefit averages 0.1 IQ points per newborn baby and the increase in individual annual mortality risk is less than one in 1 million for women between the ages of 35 and 44.

Under our middle scenario (women of childbearing age decrease fish consumption by 17%), the positive effects of omega-3 fatty acids on cognitive development are reduced and the net gain in IQ drops to 92,000 points per year for all newborn babies in the U.S. (approximately 0.02 points per child). The mortality and non-fatal stroke risks remain small.

Our pessimistic scenario (all adults decrease fish consumption by 17%) results in the same cognitive-development benefits to newborn babies because this scenario is identical to our middle scenario for women of childbearing age. The decrease in fish consumption among other members of the adult population, with much higher baseline risks for coronary heart disease and stroke, results in approximately 8,000 additional deaths and 1,500 non-fatal strokes each year. On an individual basis, the risks differ by age group because of differences in baseline risks. For example, we estimate that the 17% decrease in fish consumption would increase annual mortality risk by approximately 3 per 100,000 for males aged between 55 and 64, by 8 per 100,000 for males aged 65 to 74, and by 28 per 100,000 for males aged 75 to 84.



Converting IQ points, fatalities, and non-fatal strokes into QALYs makes it possible to aggregate these outcomes and determine if the overall impact on public health is positive or negative. The figure shows that, under our optimistic scenario, the cognitive-development gains among newborns are the dominant factor and that population well-being improves. Under the middle scenario, cognitive development remains the dominant factor, although the countervailing loss due to lower omega-3 intake contributes to reducing this gain by a factor of five. Under our pessimistic scenario, the cognitive impact for newborns remains beneficial but is dominated (in QALY terms) by the increased cardiovascular impact among adults.

Finally, we found that an *increase* in fish consumption would decrease both stroke and coronary heart disease risk. In the case of coronary heart disease, our evaluation of the epidemiologic data suggests substantial benefits are associated with consumption of at least some fish (*e.g.,* one meal per week), rather than no fish.

Uncertainty

Our evaluation includes an extensive analysis to identify assumptions that have a substantial impact on our findings. We review several here. First, our estimate of the impact of mercury on cognitive development is more pessimistic (*i.e.,* we believe mercury is *more* harmful) than the estimate developed for U.S. EPA in 2005 in their evaluation of proposed rules for coal burning power plants (the "Clear Skies" Initiative). Using an assumption closer to that of the EPA reduces the net benefits projected under our optimistic scenario by a factor of three. Under our middle scenario, the net effect of the advisory becomes negative.

Second, our evaluation of the epidemiologic literature leads us to conclude that people who consume a small amount of fish gain a great deal of protection against coronary heart disease compared with people who eat no fish (defined as less than one meal per month). We assume that increasing fish consumption even more affords further incremental protection against coronary heart disease, though in our analysis most of the benefit occurs with a single fish meal per week. If we drop the first assumption (that there is a substantial benefit associated with eating at least some fish), our projected losses for the pessimistic scenario decrease from 41,000 to 23,000 QALYs annually. If we instead retain that first assumption but drop our second assumption (that further fish consumption confers additional benefits), then projected losses for the pessimistic scenario decrease to 6,600 QALYs annually.

Finally, it is useful to explore the extent to which our findings depend on the scenarios we define. For example, the net loss projected for the pessimistic scenario is driven in large part by the 17% drop in fish consumption among adults who are <u>not</u> women of childbearing age and the resulting increase in mortality from coronary heart disease and stroke. Even if the assumed decrease in fish consumption among this group is as small as 4%, however, the adverse impact outweighs the residual cognitive development benefits resulting from decreased fish consumption among women of childbearing age.

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RECOMMENDED READING:

Cohen, J.T., Connor, W.E., Kris-Etherton, P.M., Lawrence, R.S., Savitz, D.A., Teutsch, S.M., and Gray, G.M. (2005). A quantitative risk-benefit analysis of changes in population fish consumption. *American Journal of Preventive Medicine.* 29(4):325-334.

Graham, J. D. and Wiener, J. B. (1995). *Risk versus Risk: Tradeoffs in Protecting Health and the Environment.* Cambridge, MA, Harvard University Press.

National Research Council (2000). *Toxicological Effects of Methylmercury.* Washington, DC., National Academy Press.

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Conclusions

The scientific literature on the adverse effects of mercury and the benefits of omega-3 fatty acids is extensive. Yet this literature alone is not sufficient for decision makers to evaluate potential interventions to address exposure to mercury in fish. The analysis described here is an effort to synthesize the available information to determine under what conditions the 2004 advisory might improve public health.

Our optimistic scenario approximates net health effects if the public correctly understands and complies with the 2004 advisory. Net health effects for this scenario are positive and large, suggesting that the advisory as promulgated by FDA/EPA appropriately balances health benefits and risks.

However, using plausible assumptions about how people might react to the 2004 advisory, we find that the net impact on public health could be negative. For that reason, *it is critical that additional information be gathered on how people are actually reacting to the 2004 advisory.* Actual patterns of fish consumption in the general population as well as for subpopulations of concern (such as women of child-bearing age and pregnant women) ultimately will determine whether the net health effects of the 2004 advisory are positive or negative. We note that our analysis does not address all tradeoffs associated with changes in fish consumption (including, for example, ecological implications and the nutritional characteristics of food people might eat in place of fish). Nonetheless, we hope that this analysis demonstrates both the value and the feasibility of quantitatively evaluating the benefits and countervailing risks of this, and other, public health interventions.

Decision makers must typically rely on incomplete data and imperfect science. We addressed this challenge in part by convening a panel of experts to guide and advise us. The panel helped us identify important health effects, make suitable assumptions, estimate the dose-response relationships, and combine these relationships to arrive at an aggregate estimate of risk. We also endeavored to make our analysis as transparent as possible so that people can understand which assumptions most strongly influence our findings. Even so, we acknowledge that the science underpinning our analysis is uncertain. Waiting for the science to resolve definitively these areas of uncertainty is not an option, however. Mercury exposure continues and decision makers must determine an appropriate course of action now. We believe that the analysis described here offers an approach to identify a reasonable course of action with present knowledge, and also identifies the key questions that must be answered to improve the confidence in our findings. As better information is developed, the analysis should be refined and, if necessary, interventions such as the 2004 advisory can be modified accordingly.