

Reviewer's report

Title: Reproductive outcomes in the Swedish Fishermen's Families Cohorts - A Review

Version: 1 **Date:** 14 November 2007

Reviewer: Michael Gochfeld

Reviewer's report:

General

Review of Reproductive outcomes in the Swedish Fishermen's Families Cohorts - A Review

for the Open Access Journal: Environmental Health by Anna Axmon, Lars Rylander

Anna Rignell-Hydbom

Reviewed by Michael Gochfeld 11/14/07

This is a well-written and interesting review of previously published papers about an elaborately organized long-term study---the kind we need more of.

There is great interest in exposure to contaminants such as persistent organic pollutants (mainly PCBs) and mercury from consumption of fish, and the balancing of the risks of intake against the benefits from the consumption of omega-3 fatty acids (n-3 PUFAs) for which fish is an excellent source. The authors provide an extensive review of their prior publication on reproductive outcomes in fisher cohorts from Sweden, and have made good use of their ability to juxtapose populations from the two coasts of Sweden which they report differ generally in levels of contamination. Inevitably questions arise. Some of the reproductive endpoints show no adverse (or even a protective) effect of being part of a Fisher group (and presumably therefore eating a lot of fish) or having higher levels of PCB-153 or DDE. The authors don't mention the growing literature on the reproductive benefits of fish consumption and/or omega-3 consumption. Nor (in the original MS) is there mention of a possible role of other contaminants, such as mercury. This seemed like a missed opportunity, but these same authors have just published a paper on mercury in this cohort in Environmental Health, which needs to be cited. There are of course other health endpoints which will be of great interest in a long-term study of these well-established cohorts.

I have made some specific editorial comments on the abstract and introduction in track changes. The editor or authors should pay attention to the agreement between subject and verb with regards to singular or plural (I have marked two of these).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

There seem to be some discrepancies in numbers that need to be clarified.

With regard to the following paragraph:

“Collecting information:

In 2000, a self-administered questionnaire was sent to the 2096 east and 4854 west

coast fishermen in the original cohorts who were alive as of December 31, 1999 [18]. The

questionnaire was mainly aimed at investigating a possible association between dietary PCB exposure and osteoporosis. However, it also contained a question on whether the man was interested in more information on a study of male reproductive function. Among the 2614 east and 1766 west coast fishermen who responded to the question concerning further studies, 171 east and 308 west coast men wanted more information.”

If 2096 questionnaires were sent to East Coast fishermen how did 2614 respond, and why the discrepancy in response rates between East and West. This paragraph needs clarification.

Likewise the numbers of wives or former wives doesn't seem to match the numbers in the cohorts. Were their twice as many divorces in the west? Why so many more West Coast women per fisherman.

“Thus, 2175 east and 7062 west coast women who were, or had been, married to a man in one...”

Also need to mention and cite.

Dietary exposure to methyl mercury and PCB and the associations with semen parameters among Swedish fishermen. Rignell-Hydbom A, Axmon A, Lundh T, Jönsson BA, Tiido T, Spano M. Environ Health. 2007 May 8;6:14

Otherwise readers will wonder why a possible mercury boat was missed.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Overall this is an interesting study of a reasonably sized population. There are a few methodologic issues that should be clarified. I would very much like to see a table (in this review) of the distribution of PCB-153 and DDE so that the results can be compared with other published studies that use these biomarkers. Also some statement about the back-extrapolation model. What were the levels likely to have been 10 and 20 years earlier. Also a statement about the presumed total PCB concentration, for which PCB-153 (usually the most common isomer) is the indicator.

With regard to the following paragraph, it would be helpful to explain why blood was collected from only 57 of 72 LBW mothers and only 135 of 162 normal BW mothers. Presumably this reflected non-participation. Were the non-participants representative? Was an attempt made to follow-up or ascertain whether there were differences between participants and non-participants.

Also what volume of blood was obtained. We drew 300 ml to measure serum TCDD (on lipid basis) in Viet Nam vets.

These are good participation rates, but it would be nice to know why there is a discrepancy.

“Using the information from the MBR, 72 east coast women who had given birth to a low birth-weight infant (1500-2750 g) were selected as cases in a case-control-study, using 162 east coast women with normal birth-weight infants (3250-4500 g) as controls [25]. The participating women were telephone interviewed during May and June 1994. Information was collected on fish consumption and having grown up in a fisherman’s family and/or fishing village. In addition, questions were asked on dietary habits, smoking and level of education. From June to November 1995, blood samples were collected from 57 case and 135 control mothers [26]. In connection to this, face-to-face interviews were performed, when information was collected on estimated consumption of fatty fish from the Baltic Sea.”

The use of biomarkers (a PCB and DDE) and the back-extrapolation to former levels, is a strength of the paper.

Sperm motility, sperm concentration, semen volume and total sperm count

In this paragraph reporting reductions in motility only, there is no mention of sperm morphology. When I was studying male reproduction many years ago, morphology was considered a useful endpoint and abnormal morphology appeared to be sensitive. I haven’t researched this in years. Is sperm morphology no longer of interest?

With regard to the following statement, I was taught (years ago) that we don’t use log transforms for percentages (perhaps arcsin). It would be good to know whether the transformation made a difference in the outcome, particularly since there was no association with the independent variables entered as continuous variables. It would be good to know whether there was an association with the untransformed percentages.

“Since the distributions of %DFI and %HDS were skewed, both variables were transformed using the natural logarithm (ln) before inclusion in any models.”

Fix the following by changing “neither” to “either”

“With respect to the other outcomes investigated, no associations were found with neither biomarker of exposure.”

With regard to controversy over the utility of lipid-adjusted blood levels versus fat biopsy (see quote below), we (Kahn et al. 1988) found a high correlation (+0.89) between 2,3,7,8 TCDD concentration in a 10-20 g fat biopsy and in the lipid-adjusted serum concentration. However, we drew at least 300 ml of blood to obtain sufficient lipid to provide adequate precision. The volume of the blood samples should be report.

However, if the results based on blood are biased it might be reasonable to assume that the blood level is more useful than the fat depot concentration, which may be less physiologically active (except in periods of starvation or voluntary weight loss).

Kahn PC, Gochfeld M, Nygren M, Hansson M, Rappe C, Velez H, Ghent-Guenther T, Wilson WP. Dioxins and dibenzofurans in blood and adipose tissue of Agent Orange-exposed Vietnam veterans and matched controls. JAMA. 1988 Mar 18;259(11):1661-7.

“Thus, theoretically, the body burden of POP may be estimated by calculating the lipid standardized serum concentrations. However, Schisterman et al [53] have recently shown that this method is highly prone to bias. Nevertheless, the correlations between wet weight and lipid adjusted concentrations

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.