

## Underestimation of developmental methylmercury neurotoxicity in the Faroes study

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**Introduction and Objectives** Misclassification of individual exposure levels would tend to bias the results of a dose-effect study toward the null hypothesis. We have examined the impact of this issue in a birth cohort of 1,000 methylmercury-exposed children born in 1987-1987. At age 7 years, the cohort members were examined with a battery of domain-specific neuropsychological tests. The cord-blood mercury concentration was used as the prenatal exposure biomarker, but maternal hair-mercury levels were also available. Exposure-related dysfunction was apparent on tasks assessing the domains of attention, language, and verbal memory, with less obvious decrements in scores on tasks assessing executive function, motor speed, and visuospatial constructions.

**Methods** Exposure imprecision can be estimated by factor analysis, but it requires three different measures of the same unknown exposure parameter. We then used the questionnaire information on the number of pilot whale dinners per month as the third exposure indicator. Supplementary analyses were carried out using structural equations. The imprecisions found were then used in sensitivity analyses.

**Results** As expected, the cord-blood mercury concentration showed the highest loading factor, but the estimated variance for the log transformation was 0.0175, which translates to a coefficient of variation (CV) of 30%. The hair-mercury concentration had a CV of 52%. These imprecisions greatly exceed the laboratory imprecision, which is usually below 5%. Structural equations analyses were carried out where the latent exposure variable was based on the same exposure information and, at the same time, was optimized to obtain the best possible association with the outcome variables. This analysis rendered essentially the same imprecisions. Given the estimated level of imprecision, sensitivity analyses were carried out to obtain adjusted regression coefficients for the mercury effects. This adjustment resulted in a deattenuation of about 15% for the mercury effects. Thus, a doubling of the prenatal exposure level results in decrements that are slightly larger than previously reported, i.e., a delay in development of about two months at age 7 years.

**Conclusions** These results support the notion that the cord-blood mercury concentration is the best available marker of prenatal methylmercury exposure. Still, this parameter is also subject to considerable imprecision, thus causing an underestimation of the exposure-related effects. While current estimates of the impact of methylmercury neurotoxicity must take into regard several uncertainties, the results obtained demonstrate that imprecision of the exposure assessment can now be quantified.