Exposure misclassification is major obstacle when developing dose-response relationships for risk assessment. We have determined the imprecision of biomarkers of methylmercury exposure and the resulting underestimation of exposure-associated effects.

In a study of a birth cohort from the Faroe Islands, we measured the mercury concentrations in cord blood and in maternal hair (sampled at the time of parturition). The laboratory imprecision on both chemical analyses was minimal and could not account for a correlation coefficient of only 0.78. As a third independent indicator, we used the frequency of maternal pilot whale dinners during pregnancy. With three exposure parameters reflecting the same 'true' exposure, a factor analysis could be performed to estimate the imprecision of each variable.

The calculated total imprecisions much exceeded the known laboratory variations: The coefficient of variation (CV) was 30% for the cord-blood concentration and 52% for the maternal hair concentration. However, taking into regard sample characteristics and methylmercury toxicokinetics, they seem realistic.

Dose-response associations based on cord-blood concentrations could then be adjusted by sensitivity analyses. The imprecision-adjusted impact on nervous system function for each increment of mercury concentration in cord blood was about 15% higher than previously reported. Thus, for each doubling of the prenatal methylmercury exposure level, a child would lose about 2 months in nervous system development by age 7 years.

For comparison, structural equation analyses were also carried out. Here the latent exposure variable took into account the same exposure information, but was optimized in regard to the outcomes. This approach confirmed the results from the factor analysis.

These findings are in accordance with the observation that the cord blood concentration is a better risk indicator than hair-mercury with regard to neurobehavioral deficits at age 7 years. They also emphasize that a risk may be underestimated or overlooked if the exposure variable is imprecise and proper adjustment is neglected.