Joint Analysis of Two Faroese Birth Cohorts to Assess the Effect of Prenatal Mercury Exposure in 7-Year-Old Children

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Background

Methylmercury and PCB are common contaminants in seafood. Due to measurement error and correlation between these exposures, the individual effects are difficult to determine. Information from two cohort studies conducted on the Faroe Islands were combined in structural equation analysis to achieve a more precise estimate of the effects of prenatal exposures to mercury and PCB.

Two Faroese Birth Cohorts

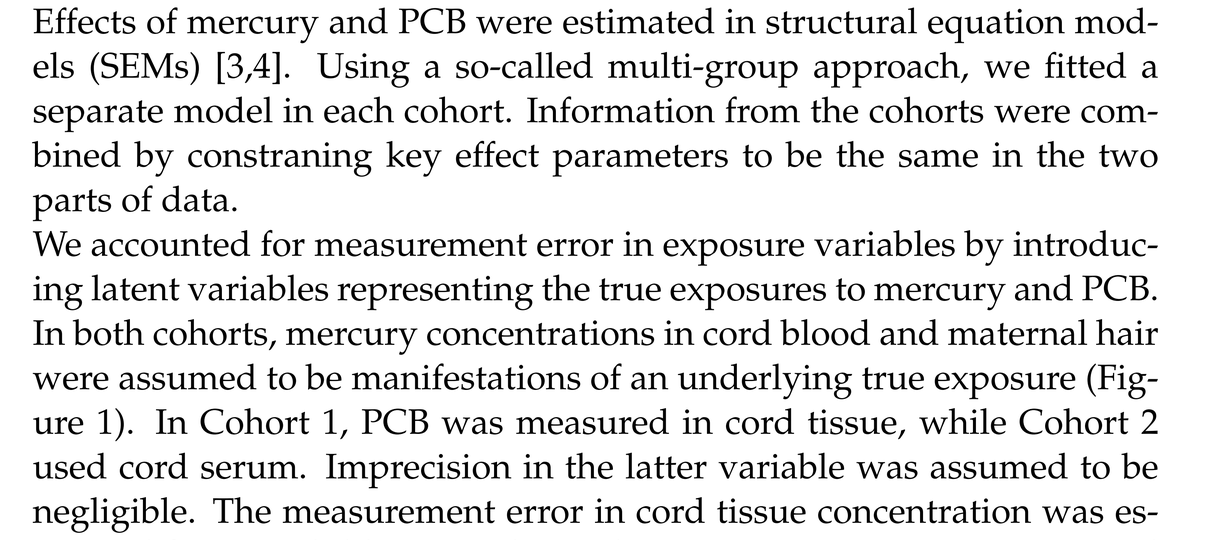
Cohort 1 consisted of 1022 children [1], while Cohort 2 included 180 children [2] born in the Faroe Islands, where meals included frequent consumption of contaminated whale meat and fish. In both cohorts the prenatal mercury exposure was assessed based on mercury concentrations in maternal hair and cord blood. In Cohort 1, PCB was measured in only half of the children using cord tissue samples. Cohort 2 provided PCB measurements in serum in almost all children. At 7 years, both sets of children underwent a detailed neurobehavioral examination. The smaller cohort plays an important role in the joint analysis as it has superior assessment of the PCB exposure.

Structural equation modeling

Effects of mercury and PCB were estimated in structural equation models (SEMs) [3,4]. Using a so-called multi-group approach, we fitted a separate model in each cohort. Information from the cohorts were combined by constraning key effect parameters to be the same in the two parts of data.

We accounted for measurement error in exposure variables by introducing latent variables representing the true exposures to mercury and PCB. In both cohorts, mercury concentrations in cord blood and maternal hair were assumed to be manifestations of an underlying true exposure (Figure 1). In Cohort 1, PCB was measured in cord tissue, while Cohort 2 used cord serum. Imprecision in the latter variable was assumed to be negligible. The measurement error in cord tissue concentration was estimated from 50 children in cohort 1 having PCB measurements in cord tissue *and* cord blood (Figure 2).

Covariates and true exposures to mercury and PCB were assumed to affect neurobevioral outcomes at age 7. Exposure effects were compared between cohorts and if they were consistent, effect parameters were constrained to be equal.



Cohort 1: $var(\epsilon_P) = 0.03$ Cohort 2: $var(\epsilon_P) = 0$

Figure 1: Path diagram showing the model fitted in each cohort. Mercury concentrations in cord blood (BHG) and hair (HHG) are indicators of true exposure (HG). In cohort 2, the serum PCB (SPCB) concentration has no error, while the error variance for cord tissue PCB (CTPCB) was fixed at 0.03 in cohort 1. Latent exposures are correlated and together with covariates they may affect the outcome.

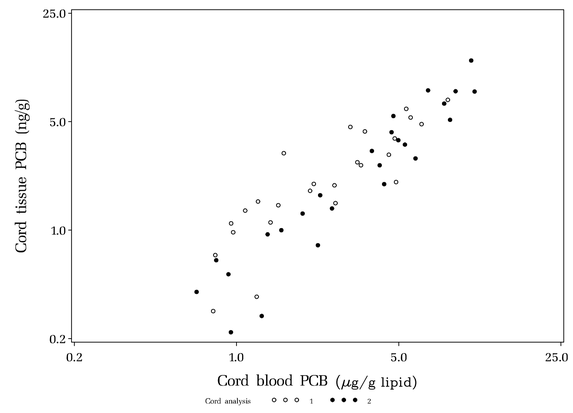


Figure 2: Association between PCB in cord tissue and cord blood.

Estimation of imprecision in cord tissue PCB concentration

We viewed cord blood concentration as the 'truth' and estimated error variance ($var(\epsilon_P)$) in cord tissue from the model:

$$\log(\text{CT-PCB}) = \alpha + \beta \log(\text{CB-PCB}) + \epsilon_P$$

Error variance in $\log$(CT-PCB) : $var(\epsilon_P) = 0.03$. In the original scale this corresponds to an error C.V. $\approx 40\%$

Results

Exposure effects were consistent in the two cohorts (data not shown). Even after adjusting for a possible PCB effect, the mercury effect remained negative for all outcomes and it was statistically significant for two of seven outcomes. In contrast, the direction of the PCB effects varied and non were close to being statistically significant. A joint test based on all outcomes showed a significant effect of mercury (p=0.032), while the evidence for a PCB effect was much weaker (p=0.51).

	Mercury		PCB	
Outcome	β	p	β	p
Boston Naming Test				
No cues	-1.399	0.062	-1.250	0.21
Cues	-1.622	0.028	-1.053	0.28
WISC(R)				
Similarities	-0.147	0.77	0.219	0.71
CVLT-Children				
Learning	-0.947	0.45	-0.015	0.99
Short-term delay	-0.926	0.015	0.840	0.088
Long-term delay	-0.347	0.39	-0.311	0.55
Recognition	-0.159	0.61	0.064	0.88

Effect of 10 fold increase in prenatal exposure to mercury and PCB

Conclusions

Estimated effects of prenatal exposures to mercury and PCB in two cohorts were consistent. A combined analysis showed that the mercury effect remained significant after PCB adjustment. The PCB effect was less certain.

Adjustment for error in confounders are required for unbiased estimation of exposure effects. Structural equation models are useful for analysis of environmental data, because they provide flexible approaches to measurement error adjustments. Information form different cohorts can be combined in a multi-group analysis.

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