

Benchmark doses after PCB correction

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In this document mercury benchmark doses are calculated after correction for PCB. Here the PCB exposure is given as $PCB=2 \cdot (PCB138+PCB153+PCB180)$ in wet weight cord tissue. The PCB exposure was only measured on children examined in 1993. This means that only about half of the observations are used when correcting for the PCB effect. When the number of observations is reduced the estimation uncertainty will increase which will lead to wider confidence bands and thereby lower BMDLs.

1. PCB as a covariate

1a. Blood mercury

BMDs and BMDLs (for cord-blood mercury in $\mu\text{g/l}$) calculated after adding $\log(PCB)$ as a covariate. $P_0 = 5\%$. Further, $-2 \cdot \log(L)$ indicates minus twice the log of the likelihood function.

Finger tapping (preferred hand)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	3620.74		3619.57		3618.38	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	149.20	65.80	77.25	23.59	9.13	2.54
BMR=0.10	249.86	110.20	198.93	57.21	47.29	7.32

CPT (reaction time)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	5544.51		5541.94		5540.28	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	82.76	48.58	31.07	14.53	3.40	1.63
BMR=0.10	138.60	81.35	76.59	34.10	10.97	4.04

Boston Naming (total score after cues)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	3219.83		3218.60		3218.00	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	184.22	71.41	90.57	24.96	13.21	2.83
BMR=0.10	308.52	119.60	234.65	60.76	84.13	8.47

CVLT (short-term reproduction)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	2935.98		2934.00		2931.95	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	224.29	77.76	82.55	24.52	7.61	2.38
BMR=0.10	375.62	130.22	213.13	59.61	35.77	6.70

1b. Hair mercury

BMDs and BMDLs (maternal hair-mercury in $\mu\text{g/g}$) calculated after adding $\log(\text{PCB})$ as a covariate. $P_0 = 5\%$. Further, $-2 \cdot \log(L)$ indicates minus twice the log of the likelihood function.

Finger tapping (preferred hand)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	3708.66		3708.41		3708.27	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	16.88	8.70	12.75	4.86	6.62	1.93
BMR=0.10	28.27	14.57	29.63	10.42	29.00	5.06

CPT (reaction time)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	5683.81		5683.77		5683.66	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	27.82	10.96	29.90	6.91	27.00	2.90
BMR=0.10	46.61	18.35	73.56	15.28	264.10	8.76

Boston Naming (total score after cues)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	3317.03		3316.60		3316.72	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	24.30	10.27	19.49	5.76	14.83	2.43
BMR=0.10	40.70	17.20	46.69	12.53	101.13	6.86

CVLT (short-term reproduction)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	3015.24		3014.16		3013.04	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	38.74	12.30	22.52	6.19	8.80	2.13
BMR=0.10	64.87	20.60	54.46	13.56	44.71	5.76

1c. Comments on the results

- **Finger tapping:** Both the BMDs and the BMDLs decrease as a result of the PCB correction. In addition to the reduced number of observations this decrease is due to the fact that for this response variable the PCB effect is very weak (PCB p -value > 0.9 when correcting for the usual set of confounders but *not* for mercury). Further, the mercury coefficient is de-attenuated when the regression is restricted to the 1993 data.
- **CPT reaction time:** For this variable the benchmark calculations not corrected for PCB is also based only on the 1993 data. The PCB correction has a relatively small effect on the benchmark results.
- **Boston Naming:** Since the PCB correction attenuates the mercury coefficient for this variable (see Grandjean et al. 1997 or Budtz-Jørgensen et al. 1999) the BMDs increase as a result of the PCB correction. However, because of the reduced number of observations the BMDLs are almost unchanged.
- **CVLT Short-term reproduction:** Section 3 of this document gives BMDs and BMDLs for this additional variable not corrected for PCB.

Although the hair-mercury concentration corresponds to a 5-fold higher cord-blood mercury concentration, the results for the latter only reflect this difference in the linear curve function.

2. Calculations restricted to children with PCB exposure in the lowest tertile

In this section the PCB correction is performed by restricting the benchmark calculations to children with PCB exposure in the lowest tertile.

2a. Blood Mercury

BMDs and BMDLs (for cord-blood mercury in $\mu\text{g/l}$) for children with PCB exposure in the lowest tertile and $P_0 = 5\%$. Further, $-2\cdot\log(L)$ indicates minus twice the log of the likelihood function.

Finger tapping (preferred hand)

DR-model	Linear		Square root		Logarithmic	
$-2\cdot\log(L)$	1027.12		1029.10		1030.63	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	41.20	24.07	21.44	8.06	5.00	1.37
BMR=0.10	69.00	40.31	51.69	18.05	19.07	3.25

CPT (reaction time)

DR-model	Linear		Square root		Logarithmic	
$-2\cdot\log(L)$	1660.62		1659.79		1659.26	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	53.23	27.88	20.05	7.80	2.65	1.07
BMR=0.10	89.14	46.69	48.13	17.43	7.76	2.38

Boston Naming (total score after cues)

DR-model	Linear		Square root		Logarithmic	
$-2\cdot\log(L)$	900.22		900.07		900.22	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	127.41	40.47	87.34	13.93	31.38	2.02
BMR=0.10	213.38	67.77	225.99	32.59	337.21	5.38

CVLT (short-term reproduction)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	804.74		804.27		803.69	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	393.05	51.92	127.69	15.59	13.67	1.76
BMR=0.10	658.23	86.96	334.73	36.79	88.78	4.47

2b. Hair Mercury

BMDs and BMDLs (maternal hair-mercury in $\mu\text{g/g}$) for children with PCB exposure in the lowest tertile and $P_0 = 5\%$. Further, $-2 \cdot \log(L)$ indicates minus twice the log of the likelihood function.

Finger tapping (preferred hand)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	1081.30		1083.40		1084.91	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	6.74	3.86	5.19	2.12	4.07	1.06
BMR=0.10	11.29	6.46	11.19	4.21	14.15	2.35

CPT (reaction time)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	1748.88		1749.05		1749.11	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	13.03	5.38	10.55	2.83	6.52	1.21
BMR=0.10	21.82	9.02	24.16	5.79	28.31	2.77

Boston Naming (total score after cues)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	962.14		962.20		962.42	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	20.95	6.32	22.29	3.44	61.43	1.65
BMR=0.10	35.08	10.58	53.87	7.15	1014.69	4.11

CVLT (short-term reproduction)

DR-model	Linear		Square root		Logarithmic	
$-2 \cdot \log(L)$	853.04		852.32		851.53	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	32.46	7.09	13.18	2.99	4.37	1.07
BMR=0.10	54.35	11.88	30.72	6.14	15.68	2.37

2c. Comments on the results

Overall, the results are much in accordance with the unrestricted analyses corrected for PCB, although particularly the logarithmic curve predicts lower BMDLs due to the decreased number of observations.

3. BMDs and BMDLs for CVLT short term reproduction

Here BMDs and BMDLs are calculated for the response variable: CVLT short term reproduction. The calculations are based on all observations. For this variable the PCB effect is very weak (PCB p -value > 0.7 when correcting for the usual set of confounders but *not* for mercury).

3a. Blood mercury

CVLT (short-term reproduction)

BMDs and BMDLs (for cord blood mercury in $\mu\text{g/l}$) for all children and $P_0 = 5\%$.

Further, $-2\cdot\log(L)$ indicates minus twice the log of the likelihood function.

DR-model	Linear		Square root		Logarithmic	
$-2\cdot\log(L)$	6772.99		6771.02		6769.36	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	218.05	98.87	141.45	46.99	29.38	6.39
BMR=0.10	365.17	165.58	372.00	118.38	302.98	27.51

3b. Hair mercury

CVLT (short-term reproduction)

BMDs and BMDLs (maternal hair-mercury in $\mu\text{g/g}$) for all children and $P_0 = 5\%$.

Further, $-2\cdot\log(L)$ indicates minus twice the log of the likelihood function.

DR-model	Linear		Square root		Logarithmic	
$-2\cdot\log(L)$	6966.69		6965.61		6964.77	
	BMD	BMDL	BMD	BMDL	BMD	BMDL
BMR=0.05	35.23	15.23	32.31	10.34	26.16	4.76
BMR=0.10	59.01	25.51	79.82	23.65	251.04	17.80

3c. Comments on the results

The overall tendencies when compared to the other results for this outcome are similar to those seen with other outcomes.

References

- Grandjean P., Weihe P., White R.F., Debes F., Araki S., Yokoyama K., Murata K., Sørensen N., Dahl R. and Jørgensen P.J. (1997). Cognitive Deficit in 7-Year-Old Children with Prenatal Exposure to Methylmercury, *Neurotoxicology and Teratology* **19**, 417-428.
- Budtz-Jørgensen E., Keiding N., Grandjean P., White R.F. (1999). Methylmercury Neurotoxicity Independent of PCB Exposure, *Environmental Health Perspectives* **107**, A236-A237.