

THE UNIVERSITY OF MICHIGAN DIOXIN EXPOSURE STUDY
An Investigation of Serum Outliers for TEQ,
2,3,7,8-TCDD, 2,3,4,7,8-PeCDF and PCB-126

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Background to Outlier Investigations

- The 29 congeners of polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and dioxin-like polychlorinated biphenyls (PCBs) that have consensus toxic equivalency factors (TEFs) were measured in serum of 946 subjects who were a representative sample of the general population in five Michigan counties; similar measurements were completed in soil (n=766 homes) and house dust (n=764 homes).
- The study was motivated because of concerns about possible human exposure to dioxin-contaminated sediments in the Tittabawassee River (TR) and the plume area downwind of the Dow facilities in Midland, Michigan.

Serum Outlier Investigations

- For this investigation an 'outlier' is defined to be someone whose serum concentration is among the top 15 out of 946 for at least one of the following:
 - TEQ
 - 2,3,7,8-TCDD
 - 2,3,4,7,8-PeCDF
 - PCB-126
- This corresponds to approximately 2.5 studentized residuals above the mean (after adjustment for age, age², and BMI)

Serum Outliers - Goals

- The goal of the following analyses is to identify possible sources and/or pathways of exposure to dioxins that may be associated with being a serum outlier, with particular focus on:
 - Contamination in soil
 - Contamination in house dust
 - Eating wild game from contaminated regions
 - Eating fish from contaminated bodies of water

Outlier Summary – Comparisons of Serum Levels

	TEQ Outliers	TCDD Outliers	PeCDF Outliers	PCB-126 Outliers	Other UMDES
	n=15	n=15	n=15	n=15	n=904
TEQ, ppt [median/mean (range)]	71.4/72.5 (48.8-211) ***	54.4/54.6 (27.9-211) ***	38/40.1 (17.8-211) ***	68/65.2 (40.8-211) ***	19.2/22.6 (3.8-109)
TCDD, ppt [median/mean (range)]	6.1/7.1 (3.5-65.4) ***	13.5/15.2 (8.1-65.4) ***	3/4.2 (1.2-65.4) ***	3.5/5.5 (2.5-65.4) ***	1.6/2.4 (0.2-24.1)
PeCDF, ppt [median/mean (range)]	17.5/16.8 (10.2-50) ***	11.7/10.9 (6.6-50) ***	16.9/18.2 (7.7-50) ***	13.9/14.4 (9.8-50) ***	5.5/6.4 (0.3-29.8)
PCB126, ppt [median/mean (range)]	258/220.8 (38.5-378) ***	58.9/71 (6.5-309) ***	14.1/36.5 (9.4-339)	270/261.6 (170-325) ***	16.6/27.1 (1.9-394)

All results based on survey linear regression

*** *p-value* < 0.01; ** *p-value* < 0.05; * *p-value* < 0.10 compared to 'Other UMDES'

Outlier Summary – Demographic Factors

	TEQ Outliers	TCDD Outliers	PeCDF Outliers	PCB-126 Outliers	Other UMDES
	n=15	n=15	n=15	n=15	n=904
Age, yrs [med/mean (range)]	58.1/57.5 (43.9-86.6) ***	53.1/55.5 (32.4-77.9) **	48.5/48.6 (24.5-82.3)	57.4/58.7 (43.9-78.7) **	50.4/51 (18-91.2)
BMI change, kg/m ² [med/mean (range)]	-1.3/-1.1 (-3.2-0) **	0/-0.6 (-3-2.3)	-1.1/-1.3 (-24.3-4.6)	0/-0.2 (-3.7-1.6)	0/-0.2 (-9.4-9.1)
Smoking, pack-yrs [med/mean (range)]	0/10.3 (0-40)	0/7.7 (0-30)	10.5/11.7 (0-52.5)	3/9.3 (0-40)	0.4/12.5 (0-145)
No. of children [med/mean (range)]	2/1.7 (1-4) (n=6)	1/1.3* (0-6) (n=12)	3/2.9*** (1-5) (n=6)	1/1.3** (1-5) (n=4)	2/2.2 (0-12)
Months breast feeding [med/mean (range)]	6/8.3 (0-36) (n=6)	0/5.2 (0-39) (n=12)	1/1.2*** (0-12) (n=6)	4/3.4*** (0-4) (n=4)	0/6.3 (0-120)

All results based on survey linear regression or survey Poisson regression

*** *p*-value < 0.01; ** *p*-value < 0.05; * *p*-value < 0.10 compared to 'Other UMDES'

Outlier Summary – Recent Game & Fish

	TEQ Outliers	TCDD Outliers	PeCDF Outliers	PCB-126 Outliers	Other UMDES
	n=15	n=15	n=15	n=15	n=904
Recent fish meals from contaminated regions [%]					
-never	89.9	96.5	87.6	90.5	88.7
-less than one meal/month	9.3	3.5	7	8.5	9.3
-more than one meal/month	0.8	0	5.4	1	1.9
Recent game meals from contaminated regions [%]					
-never	90.8	90.3	98	91.7	92.6
-less than one meal/month	0.5	0	0	0.5	5.6
-more than one meal/month	8.7	9.7	2	7.8	1.8

'Recent' = previous five years

Contaminated regions: Tittabawassee River, Saginaw River, and Saginaw Bay

All results based on survey ordered logistic regression

*** *p-value* < 0.01; ** *p-value* < 0.05; * *p-value* < 0.10 compared to 'Other UMDES'

Outlier Summary – Residence

	TEQ Outliers	TCDD Outliers	PeCDF Outliers	PCB-126 Outliers	Other UMDES
	n=15	n=15	n=15	n=15	n=904
Current residence [%] [@]					
- Floodplain	1.2	0.5 *	14.2**	1	1.1
- Near Floodplain	2.8	1.5	12.2*	1.6	1.1
- Other M/S	31.7	83.9	59.9	44.1	43.8
- Midland Plume	8.4	14	0 ^e	0 ^e	3.4
- Jackson/Calhoun	55.9	0 ^e	13.6	53.3	50.7
Ever resided in Plume [%] [#]	8.4	38.3***	0 ^e	0 ^e	5.5

[@]results based on survey multinomial (polytomous) logistic regression

[#]results based on survey logistic regression

^ecannot test because of zero cell

*** *p-value* < 0.01; ** *p-value* < 0.05; * *p-value* < 0.10 compared to 'Other UMDES'

Outlier Summary – Employment

	TEQ Outliers	TCDD Outliers	PeCDF Outliers	PCB-126 Outliers	Other UMDES
	n=15	n=15	n=15	n=15	n=904
Ever worked at Dow [%] [#]	1.3*	0 ^e	6.5	1.2*	5.8
Ever worked at other chemical Co. [%] [#]	0.8	0 ^e	2	0.7	4

[#]results based on survey logistic regression

^ecannot test because of zero cell

*** *p-value* < 0.01; ** *p-value* < 0.05; * *p-value* < 0.10 compared to 'Other UMDES'

Outlier Summary – Soil & Household Dust

Outliers	TEQ	TCDD	PeCDF	PCB-126
HP Soil Top 1"	6.3/26.5 (1.4-257)	3.6/18.6 (0.3-117)**	68/72.5 (1.2-147)***	3.1/5 (1-42.8)
Other UMDES	4.4/14.1 (0.4-2300)	0.4/2.7 (0-97.4)	1.3/9 (0.1-3340)	4.1/12.8 (0.1-1330)
Highest Soil	6.4/36.8 (1.8-816)	4.7/22 (0.5-140)**	101/731 (9.4-6670)***	3.1/5.3 (1.3-195)
Other UMDES	5.2/38.5 (0.4-11200)	0.5/3.1 (0-187)	1.7/46.7 (0.1-18600)	4.6/16.6 (0.1-1330)
House Dust	36.8/26.5 (3.9-85.3)	0.9/2.2 (0.2-8.4)*	1.5/4.3 (1.1-44.2)	22.4/24.7 (4.3-71.8)
Other UMDES	16.1/34.4 (1.4-1750)	0.4/0.8 (0-12.3)	1.9/3.7 (0.2-512)	12.9/53.7 (1.5-2580)

[median/mean (range)]; #Outlier results do not include imputed values; Results based on survey linear regression on log scale; *** *p-value* < 0.01; ** *p-value* < 0.05; * *p-value* < 0.10 compared to 'Other UMDES'

Distributions – Of House Dust & Soil

House Dust *	Mean	Median	75 th %ile	95 th %ile
TEQ	36.7	16.2	29.7	126
2378-TCDD	0.8	0.5	0.9	2.7
23478-PeCDF	3.6	1.9	3.3	10.9
PCB-126	68.9	13.3	27.8	103

HP Soil Top 1"@	Mean	Median	75 th %ile	95 th %ile
TEQ	14.3	4.5	10.3	59.4
2378-TCDD	2.8	0.4	1.3	13.1
23478-PeCDF	8.7	1.3	4.3	24.5
PCB-126	13.8	4.1	9.6	36.4

All values shown are parts per trillion.

The TEQ is calculated using 2005 TEFs.

Results based on 764 homes for dust and 766 homes for soil

Conclusions - Demographics

- TEQ, TCDD and PCB-126 outliers tend to be older, while PeCDF outliers do not differ in age from the rest of the UMDES population
- Change in BMI appears to have little relationship to outlier status, except possibly in a few TEQ outlier cases
- Smoking appears to have little relationship to outlier status
- Breastfeeding may be inversely related to outlier status among females for PeCDF and PCB-126, but the numbers are small

Conclusions – Recent Game & Fish

- About 90% of all outliers reported no recent (i.e., in the last five years) fish or game consumption from contaminated regions
- None of the outlier groups reported recent fish or game consumption significantly more frequently from contaminated regions than the rest of the UMDES
- Fish and game consumption from contaminated regions appears to make little or no contribution to outlier status

Conclusions - Residence

- PeCDF outliers are significantly more likely to currently reside in the floodplain or near-floodplain compared to the rest of the UMDES
- TEQ and PCB-126 outliers did not differ significantly from the rest of the UMDES in terms of current residence
- Being a TCDD outlier is strongly associated with having ever resided in the plume area (and possibly 'other Midland/Saginaw'), and TCDD outliers appear to be less likely to reside in the control area (Jackson/Calhoun)

Conclusions - Employment

- Outlier status is not related to having worked at Dow or at another chemical company

Conclusions – Dust

- Household dust contamination appears to have no association with outlier status

Conclusions - Soil

- House perimeter top 1" soil and maximum soil measurements are associated with TCDD and PeCDF outliers, but these soil measurements are NOT associated with TEQ or PCB-126 outliers
- The explanation for these discrepancies among congeners is unclear – confounding may be playing a role
 - The absence of an association of outlier status with dust would also be consistent with confounding of the soil relationships for TCDD and PeCDF
 - Further investigations are underway

Overall Conclusions

- Overall, TEQ and PCB-126 outlier status are not associated with soil or dust contamination, or with consumption of fish or game from contaminated regions in the last 5 years
- TCDD and PeCDF outliers are not associated with recent game or fish consumption from contaminated regions, or with household dust contamination
- While there is an association between TCDD and PeCDF serum outlier status with soil, these associations should be interpreted with caution due to possible confounding
- TCDD outlier status is significantly associated with having ever resided in the plume area

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