

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
retrospective cohort ADVA (2005b) Vietnam veterans	Cause of death in 59,179 Australian Vietnam veterans(100% male) vs. general male Australian population from end of Vietnam service to December 31, 2001(6,166 total deaths)	diabetes (death certificate) *report notes selection bias because diabetics would have not been permitted to serve in Vietnam	Vietnam service (veteran status)	Australian Vietnam veterans vs Australian population [55 diabetes deaths, 6,166 total deaths]	SMR = 0.52 (0.38-0.66)	
				Navy, 12 diabetes deaths/1,435 total deaths	0.54 (0.28-0.94)	
				Army, 37 diabetes deaths/4,045 total deaths	0.52 (0.35-0.69)	
				Air Force, 6 diabetes deaths/686 total deaths	0.46 (0.17-0.98)	
retrospective cohort ADVA (2005a) Vietnam veterans	Australian Army National Service, 59,179 Australian Vietnam veterans (100% male) deployed vs. non-deployed from end of Vietnam service to December 31, 2001 (6,166 total deaths)	diabetes (death certificate)	Agent Orange (deployment status)	deployed vs. non-deployed [6 diabetes deaths; 1,052 total deaths]	SMR = 0.3 (0.1-0.7)	
prospective cohort AFHS (2005) Vietnam veterans	Air Force Health Study, 2002 examination cycle in Ranch Hand veterans 776 C-123 crew members in Operation Ranch Hand and 1,173 comparison pool who also served in SE Asia during the same period matched by age, race, and military occupation.	diabetes (verified history of diabetes or a 2-hour postprandial glucose \geq 200 mg/dL or greater on two separate occasions, FG \geq 126 mg/dL or greater on two separate occasions, or one 2-hour postprandial glucose \geq 200 mg/dL or greater and a fasting glucose level of 126 mg/dL or greater on separate occasions)	Agent Orange (serum TCDD, lipid adjusted) 1987 dioxin levels: low: \leq 7.8 ppt; medium: $>$ 7.8-19.2 ppt; high: $>$ 19.2 ppt	Ranch Hand: n=776; (18.2%) 141 with diabetes /635 without diabetes Comparison: n=1,173; 226 (19.3%) with diabetes/948 without diabetes Total: n=1,929; 367 (19%) with diabetes/1562 without diabetes	Rand Hand vs. Comparison adjusted RR: 0.93 (0.72-1.19) Within the 776 Ranch Hand participants, 1987 dioxin adjusted : RR = 1.3 (1.1-1.5), p\leq0.010 with 2-fold increase in 1987 serum TCDD	BMI at the time of blood dioxin measurement
retrospective cohort US, 3M plant (AL) (Alexander <i>et al.</i> 2003) occupational	Cause of death in 2,083 workers at perfluorooctanesulphonyl fluoride (POSF) plant in Decatur, AL (83% male; median age 50.9 years). Employees had at least 1 year cumulative employment at plant by December 31, 1997. 145 deaths total; 65 deaths in "high" exposure group	cardiovascular disease (death certificate – "all heart disease")	PFOS (job description, serum) relative differences in serum PFOS by job based on 1998 biological monitoring survey	all heart disease all cohort vs state of Alabama (35 deaths) ever employed in high exposure job vs state of Alabama (14 deaths)	SMR (95%CI) 0.56 (0.39-0.78) 0.56 (0.31-0.95)	age, gender, calendar period
cross-sectional US, West Virginia community Anderson-Mahoney <i>et al.</i> (2008) environmental	566 white residents who were plaintiffs or potential plaintiffs in a lawsuit	diabetes, heart disease (self-report) Expected rates from NHANES 2001-2002 using sampling weights to calculate an unbiased estimate of national rates while adjusting for non-response, survey design, and sampling technique	PFOA (drinking water, ppb) range of PFOA in water sources: 0.05 – 8.6 ppb; 64% of study sample consumed source water with 0.4-4.3 ppb	Standardized Prevalence Ratio [SPR (95%CI)] compared to expected disease rate of general US population cardiovascular problems diabetes high blood pressure	4.29 (3.47-5.29) 1.54 (1.16-2.05) 1.18 (0.97-1.43)	age, gender
retrospective cohort	Children residing in Seveso during the	diabetes	TCDD	101 children with chloracne	1 case of diabetes	

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Seveso, Italy Baccarelli et al. (2005) environmental	1976 accident assessed from 1993 to 1998.	(self-report)	(chloracne status)	211 children without chloracne 2 case of diabetes study not included in forest plot database		
retrospective cohort Beard et al. (2003) occupational	514 pesticide application workers (100% male) exposed to DDT during 1955-1962 compared with 1) 209 unexposed workers and 2) the Australian population; age not reported	death certificate, Medicare records, self-report	pesticides	pesticide workers vs. unexposed workers [n=723; 12 diabetes deaths (1.7%)/711 non-diabetes deaths) pesticide workers vs. Australian population SIR: 4.88 (0.90-26.45) *standardized incidence ratio SMR: 1.22 (0.45-2.65)	SIR: log age SMR: age, period of follow-up	
prospective cohort Seveso, Italy Bertazzi et al. (2001) environmental	Mortality in residents of Seveso, Italy during 1976-1996: Zone A (n=804; 414 ♀, 390 ♂), Zone B (n=5,941; 2,924 ♀, 3,017 ♂), and Zone R (n=38,624; 19,424 ♀, 19,200 ♂) and a referent population of (n=232,745; 118,775 ♀ and 113,970 ♂)	diabetes mellitus (death certificate)	TCDD (1976/77 serum, lipid adjusted) median levels Reference: NA Zone A: 447 ppt Zone B: 94 ppt Zone R: 48 ppt	Rate ratios for cause of death versus reference population, 1976-1996 Zone A (2 diabetes deaths) 0.8 (0.2-3.3) Zone B (24 diabetes deaths) 1.4 (0.9-2.1) Zone A+B (26 diabetes deaths) 1.3 (0.9-2.0) ♀(20 diabetes deaths) 1.7 (0.1-2.7) ♂(6 diabetes deaths) 0.8 (0.3-1.7) Rate ratios for cause of death and years since 1st exposure (latency) for zones A+B versus reference population, 1976-1996 0-4 (7 diabetes deaths) 2.0 (0.9-4.2) ♀(4 diabetes deaths) 2.0 (0.8-5.5) ♂(3 diabetes deaths) 1.8 (0.6-5.8) 5-9 (3 diabetes deaths) 0.6 (0.2-2.0) ♀(1 diabetes deaths) 0.3 (0.04-2.5) ♂(2 diabetes deaths) 1.1 (0.3-4.4) 10-14 (8 diabetes deaths) 1.6 (0.8-3.2) ♀(7 diabetes deaths) 2.2 (1.0-4.6) ♂(1 diabetes deaths) 0.6 (0.1-4.1) 15-20 (8 diabetes deaths) 1.4 (0.7-2.8) ♀(8 diabetes deaths) 2.4 (1.2-4.8) ♂(0diabetes deaths)	age, gender, calendar period	
cross-sectional USA Calvert et al. (1999) occupational	541 workers: 281 workers with > 15 years occupational exposure to TCDD and 260 unexposed referents (95% male; mean age 55-56 years). Workers employed at one of two plants in Newark, NJ and Verona, MO	diabetes (fasting serum glucose ≥ 7.8 mmol/l, physician diagnosis)	TCDD (serum, lipid adjusted)	referents (<20 ppt TCDD) [n=260; 18 diabetics (7%)/242 non-diabetics] All workers 1.49 (0.77-2.91) <20 ppt (7 diabetics/69 non-diabetics) 2.11 (0.77-5.75) 20-74(6 diabetics/59 non-diabetics) 1.51 (0.53-4.27) 75-237 (3 diabetics/62 non-diabetics) 0.67 (0.17-2.57) 238-3400 ppt (n=65; 10 diabetics/55 non-diabetics) 1.97 (0.79-4.90) *60% of workers with current serum TCDD concentrations >1500 ppt had diabetes	age, gender, race, BMI, family history of diabetes, medical treatment that affects serum glucose	
retrospective cohort CDC (1988) Vietnam veterans	Random subsample of 15,288 enlisted men who entered Army from 1965-1971 (7,924 Vietnam and 7,364 non-Vietnam veterans) who participated in a telephone interview and random sample of 4,464 who underwent complete physical exam (2,490 Vietnam vets vs. 1,972 non-	diabetes (self-report)	Vietnam service	Deployed vs non-deployed (n=15,288 (7,924 Vietnam) and 7,364 non-Vietnam veterans). 1.9% exposed cases (155 cases reported in 2008 IOM Agent Orange Report (2009) subset with physical exam, diabetes n=4,462(2,490 Vietnam vets vs. 1,972	adjOR = 1.2, NS 1.1, NS	the six entry characteristics: age at enlistment, race, year of

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	Vietnam vets)			non-Vietnam vets); 1.7%, or 42 exposed cases) subset with physical exam, fasting serum glucose, mmol/L (mg/dL) n= 4,462 (2,490 Vietnam vets vs. 1,972 non-Vietnam vets)	enlistment, enlistment status (volunteer vs draftee), score on general technical test, and primary military occupation al specialty																				
cross-sectional Taiwan Chang et al. (2010) environmental	1,234 non-diabetic people living near a deserted pentachlorophenol (PCP) factory (25-80 years; 52% male)	<u>Insulin Resistance:</u> Matthews method FG (mmol/L) x fasting insulin (mU/L)/22.5 <u>β-cell function</u> 20 x fasting insulin (mU/L)/[FG (mmol/L)-3.5] <u>Metabolic syndrome</u> any 3 of the following: (1) WC >90 cm (♂) and >80 cm (♀); TG >150 mg/dL; HDL < 40 mg/dL (♂) and <50 mg/dL (♀); BP >130/85 mm Hg; FG >100 mg/dL.	dioxins (PCDDs/PCDFs) (serum, lipid adjusted)	<u>Insulin resistance</u> , based on percentile categories of serum PCDD/F levels (pg WHO ₉₈ -TEQ _{DF} /g lipid)[n= 1,234; 178 cases (14.4%)/1056 non-cases] <table border="1"> <tr> <td><10th (<9.6ppt)</td> <td>adjOR = 1.00</td> </tr> <tr> <td>10th to <25th (9.6- 13.0) [n=305 <25th percentile]</td> <td>~2.2 (not significant)</td> </tr> <tr> <td>25th to <50th (13.1- 20.4) [n=310]</td> <td>~2.3 (not significant)</td> </tr> <tr> <td>50th to 75th (20.5- 33.8) [n=311]</td> <td>2.7 (1.0-7.8)</td> </tr> <tr> <td>75th to <90th (33.9-54.0)[n=308 ≥ 75th percentile]</td> <td>3.5 (1.1-12)</td> </tr> <tr> <td>≥90th (≥54.1 ppt)</td> <td>5.0 (1.5-18), p-trend <0.001</td> </tr> <tr> <td><75% versus ≥75th percentile</td> <td>1.7 (1.2-2.4)</td> </tr> </table> <u>Metabolic syndrome</u> The 20.7% (255/1,234) of participants diagnosed with metabolic syndrome had higher median serum PCDD/PCDFs than those without the syndrome [27.7 (5.3-355.2) vs.19.6 (4.5-403) pgWHO ₉₈ -TEQ _{DF} /g lipid), not reported if difference was statistically significant <u>β-cell function (HOMA-β)</u> <75% versus ≥75 th percentile 1.3 (0.9-1.8)	<10 th (<9.6ppt)	adjOR = 1.00	10 th to <25 th (9.6- 13.0) [n=305 <25 th percentile]	~2.2 (not significant)	25 th to <50 th (13.1- 20.4) [n=310]	~2.3 (not significant)	50 th to 75 th (20.5- 33.8) [n=311]	2.7 (1.0-7.8)	75 th to <90 th (33.9-54.0)[n=308 ≥ 75 th percentile]	3.5 (1.1-12)	≥90 th (≥54.1 ppt)	5.0 (1.5-18), p-trend <0.001	<75% versus ≥75 th percentile	1.7 (1.2-2.4)	age, sex						
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cross-sectional Canada Chateau-Degat et al. (2010) environmental	723 adult non-pregnant Nunavik Inuit in Northern Quebec exposed to PFOS through consumption of fish and game (mean age: 36.9 years, 45%male)	Blood lipids: total cholesterol, HDL-C, LDL-C, and triglycerol	PFOS (plasma) geometric mean = 18.6 µg/L (20.4 ♂; 16.8 ♀)	<u>R² model and adjusted β coefficients for association of PFOS with blood lipids</u> <table border="1"> <tr> <td>total cholesterol (mmol/L)^an=663</td> <td>R²=0.17; β=0.0009 (p=0.086)</td> </tr> <tr> <td>HDL (mmol/L)^b</td> <td></td> </tr> <tr> <td>♀, n=384</td> <td>R²=0.12; β=0.0042 (p=0.001)</td> </tr> <tr> <td>♂, n=309</td> <td>R²=0.12; β=0.0016 (p<0.001)</td> </tr> <tr> <td>TC/HDL ratio^c, n=663</td> <td>R²=0.09; β= -0.0035 (p<0.001)</td> </tr> <tr> <td>triglycerides (mmol/L)^d</td> <td></td> </tr> <tr> <td>♀, n=365</td> <td>R²=0.20; β= -0.0014 (p=0.040)</td> </tr> <tr> <td>♂, n=284</td> <td>R²=0.16; β= -0.0009 (p=0.162)</td> </tr> <tr> <td>LDL (mmol/L)^e, n=651</td> <td>R²=0.17; β= -0.0020 (p=0.242)</td> </tr> <tr> <td>non-HDL^e, n=670</td> <td>R²=0.082; β= -0.0011 (p=0.315)</td> </tr> </table>	total cholesterol (mmol/L) ^a n=663	R²=0.17; β=0.0009 (p=0.086)	HDL (mmol/L) ^b		♀, n=384	R²=0.12; β=0.0042 (p=0.001)	♂, n=309	R²=0.12; β=0.0016 (p<0.001)	TC/HDL ratio ^c , n=663	R ² =0.09; β= -0.0035 (p<0.001)	triglycerides (mmol/L) ^d		♀, n=365	R²=0.20; β= -0.0014 (p=0.040)	♂, n=284	R²=0.16; β= -0.0009 (p=0.162)	LDL (mmol/L) ^e , n=651	R²=0.17; β= -0.0020 (p=0.242)	non-HDL ^e , n=670	R ² =0.082; β= -0.0011 (p=0.315)	see notes in previous column
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cross-sectional Taiwan Chen et al. (2006) environmental	1034 volunteers living near 12 municipal waste incinerators in Taiwan for at least 5 years recruited between 2000 and 2001 (51% male; ≥18 years of age)	diabetes, physician diagnosis	PCDDs, PCDFs (serum, lipid adjusted)	PCDD/PCDF concentration and diabetes (n= 1034; 29 diabetics (2.8)/1 non-diabetics) *serum percentiles in comparison not specified (“increased PCDD/Fs”) PCDD/PCDF concentration and serum glucose adjOR=2.44 (0.21-31.90) β=0.349 (p=0.009)	age, sex, smoking status, and BMI age, sex, and BMI
cross-sectional Taiwan Chen et al. (2008) environmental	40 non-diabetic pregnant women (between 28 and 32 weeks of gestation) living in an area of southwestern Taiwan known to be contaminated by chemicals from a large PCP-manufacturing plant (0% male; mean age = 28.2)	serum insulin insulin sensitivity (22.5EXP[-ln(glucose)]/insulin QUICKI 1/[log(FG)+log (fasting insulin)])	PCDDs, PCDFs, PCBs (serum, pg-TEQ/g-lipid)	adjusted Pearson correlations (r) with insulin sensitivity (*no significant correlations with serum insulin or QUICKI results in adjusted models) PCDDs PCDFs 2,3,7,8-TCDD; r=-0.10, ns 2,3,7,8-TCDF; r=-0.26, ns 1,2,3,7,8-PeCDD; r=-0.14, ns 1,2,3,7,8-PeCDF; r=-0.18, ns 1,2,3,4,7,8-HxCDD; r=-0.29, p=0.09 2,3,4,7,8-PeCDF; r=-0.17, ns 1,2,3,6,7,8-HxCDD; r=-0.24, ns 1,2,3,4,7,8-HxCDF; r=-0.13, ns 1,2,3,7,8,9-HxCDD; r=-0.21, ns 1,2,3,6,7,8-HxCDF; r=-0.17, ns 1,2,3,4,6,7,8-HpCDD; r=-0.38, p=0.07 2,3,4,6,7,8-HxCDF; r=-0.27, ns OCDD; r=-0.12, ns 1,2,3,7,8,9-HxCDF; r=-0.07, ns PCDDs TEQ; r=-0.16, ns 1,2,3,4,6,7,8-HpCDF; r=-0.11, ns 1,2,3,4,7,8,9-HpCDF; r=0.06, ns OCDF; r=-0.29, p=0.11 PCDDs/PCDFs TEQ; r=-0.17, ns PCDFs TEQ; r=-0.18, ns Total TEQ; r=-0.32, p=0.06	age, pre-pregnancy, BMI
PCBs					
	3,4,4',5'-TeCB 81; r=-0.28, p=0.13	2,3',4,4',5,5'-HxCB 167; r=-0.35, p=0.06			
	3,3',4,4'-TeCB 77; r=-0.33, p=0.09	2,3,3',4,4',5-HxCB 156; r=-0.34, p=0.10			
	2',3,4,4',5-PeCB 123; r=-0.46, p=0.01	2,3,3',4,4',5'-HxCB 157; r=-0.34, p=0.08			
	2,3',4,4',5-PeCB 118; r=-0.40, p=0.05	3,3',4,4',5,5'-HxCB 169; r=-0.42, p=0.04			
	2,3,4,4',5-PeCB 114; r=-0.32, p=0.12	2,3,3',4,4',5'-HpCB 189; r=-0.33, p=0.12			
	2,3,3',4,4'-PeCB 105; r=-0.42, p=0.06	PCBs TEQ; r=-0.42, p=0.02			
	3,3',4,4',5-PeCB 126; r=-0.37, p=0.05				
cross-sectional US Codru et al. (2007) environmental	352 Mohawk adults (38% male) who lived at or near Akwesasne for ≥5 years; mean age=48.8 years; range=30-85 years [71 diabetes cases (25.3%)/281 non-cases]	diabetes (FG value >125 mg/mL, use of diabetes medication)	PCB, PCB153, PCB74, DDE, mirex, HCB (serum, lipid adjusted ng/g lipid)	Diabetes, highest tertile vs lowest tertile, OR (95%CI) based on lipid standardized measurements Total PCBs: 756.2 vs 448.6 ppb 3.2 (1.4-7.5) PCB-153: 104.4 vs. 59.8 ppb 2.4 (1.0-5.6) PCB-74: 38.7 vs 19.2 ppb 4.5 (1.3-15.6) DDE: 544.6 vs 246.1 6.2 (1.8-21.9) HCB: 13 vs 9.1 ppb 6.8 (2.3-20.3)* Mirex: 19.6 vs. 8.3 ppb 0.9 (0.4-2.2) *remained significant after adjusting for other analytes in addition to the adjustment model: HCB: 4.8 (1.7-13.9)	age, BMI, serum lipid levels, gender, and smoking
retrospective cohort US Collins et al. (2009) occupational	Cause of death in 662 trichlorophenol workers with occupational exposure to TCDD compared to the US population(% male not reported (based on vital records for 1942-2003)	death certificate	TCDD (serum, historical TCDD levels estimated by serum survey of workers)	all trichlorophenol workers vs US population [n=662; 16diabetes deaths in workers/646 non-diabetes deaths in workers] SMR=1.1 (0.6-1.8) trichlorophenol workers excluding those with pentachlorophenol exposure vs US population [n=567; 15 diabetes deaths in workers/552 non-diabetes deaths in workers] 1.2 (0.7-1.9)	
prospective cohort Seveso, Italy Consonni et al. (2008)	37,187 subjects residing in any of 3 contamination zones (A, B, R) on the day of the 1976 Seveso industrial accident followed for 25 years (1976-2001);	death certificates and government records	TCDD median serum (1976-1977), lipid adjusted	diabetes deaths, 25-year mortality in residents of Seveso area at time of accident. Reference territory vs zones A, B, or R (221 diabetes deaths/6802 deaths in total; zone A: 3 diabetes deaths/115 non-diabetes deaths; zone B: 26 diabetes deaths/724 non-diabetes deaths; zone R: 192 diabetes deaths/5742 non-diabetes	gender, age, and time period

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				<22.81 vs. 39.10-58.60	
				β-HCH	
				1.00 vs. ≥1.00 ppb	2.3 (1.0-4.3) ^a
				<1.00 vs. 1.00-2.10	1.7 (1.1-2.8) ^a
				<1.00 vs. >2.10	2.7 (0.9-8.2)^a
retrospective cohort USA Cranmer et al. (2000) environmental	69 healthy adults (68% male) living within 25 miles of the Vertac/Hercules Superfund site in Jacksonville, AK	insulin and glucose response at fasting and during OGTT	TCDD (serum, lipid corrected)	>15 ppt (90th percentile) versus < 15ppt	Age, pre-pregnancy BMI
				glucose	no difference in levels, FG or OGTT
				insulin	
				high fasting insulin (>4.5 μU/ml)	adjOR = 8.5 (1.49-49.4)
				high insulin during OGTT, 30 minutes (>177 μU/ml)	7 (1.26-39.0)
				high insulin during OGTT, 60 minutes (>228 μU/ml)	12 (2.23-70.1)
				high insulin during OGTT, 120 minutes (>97.7 μU/ml)(n=69; 12 with hyperinsulinemia (17.4%); 57 without hyperinsulinemia)	56 (5.7-556)
prospective cohort Mexico Cupul-Uicab et al.(2010) environmental	778 male infants born during 2002-2003 and their mothers from Chiapas, Mexico; age of mothers 15-35 years; median age of children during follow-up= 18 months	height and weight measurements, measured as a standard deviation score (SDS)	DDE, DDT (maternal serum within a day of delivery) median DDE = 2.7 μg/g lipid median DDT = 0.3 μg/g lipid	Adjusted β-coefficients(95% CI)	gestational age, smoking during pregnancy, hospital of recruitment, rural residence at recruitment, maternal education, pre-pregnancy BMI
				DDE and change of height (age-standardized and expressed as standard deviation scores, SDS)	0.555 (0.344-0.766)
				3.01-6.00 vs. ≤3.00 (referent)	-0.121 (-0.28-0.42)
				6.01-9.00vs. ≤3.00	-0.30 (-0.27-0.21)
				>9.00vs. ≤3.00	0.069 (-0.13-0.27)
				DDT and change of height (age-standardized and expressed as standard deviation scores, SDS)	no statistically significant associations (data not shown)
				DDE and change of BMI (age-standardized and expressed as standard deviation scores, SDS)	Intercept: -0.017 (-0.25-0.22)
				3.01-6.00 vs. ≤3.00 (referent)	-0.112 (-0.29-0.07)
				6.01-9.00 vs. ≤3.00	-0.183(-0.45-0.08)
				>9.00 vs. ≤3.00	0.073 (-0.15-0.297)
				DDT and change of BMI (age-standardized and expressed as standard deviation scores, SDS)	no statistically significant associations (data not shown)
cross-sectional Belgium Dhooge et al. (2010) environmental	1679 adolescents (887 boys and 762 girls), 775 men and 808 women from Flanders (densely populated area of Europe); adolescents aged 14- to 15-years ; adults aged 50-65 years	length and body weight measured by a study nurse	PCB 118, PCB 138, PCB 153, PCB 180, HCB, p,p'-DDE (serum) Median (10th-90th percentile) Men: PCB 118 in serum: 22.8 (10.4-46.8) μg/g	Change (95%CI) in BMI for doubling of exposure	age, height of father, height of mother, smoking, sexual maturation , and food intake
				HCB (ng/g fat)	
				boys:22.8 (15.2-34.5)	-0.69 (-0.20 to -1.18)*
				girls: 18.3 (12.3-26.6)	-0.64 (-0.03 to -1.25)
				men: 44.2 (23.7-90.9)	1.642(1.26 to 2.02)
				women: 71.9 (36.2-143.3)	2.73 (2.29 to 3.17)
				Marker PCBs (ng/g fat)	
				boys: 79.8 (42.7-141.3)	-2.45 (-2.07 to -2.82)
				girls: 53.1 (30.3-98.5)	-2.01 (-1.62 to -2.41)
				men: 354 (222-552)	-3.20 (-2.61 to -3.79)

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			fat	women: 335 (203-521) PCB118 (ng/g fat)	-6.18 (-5.48 to -6.87)	
			Sum of marker PCBs in serum: 354 (222-552) µg/g fat	boys: 7.28 (2.85-13.58) girls: 6.00 (2.37-11.59) men: 22.8 (10.4-46.8) women: 28.8 (12.9-52.9)	0.56 (0.27 to 0.85) 0.74 (0.41 to 1.07) 0.824 (0.463 to 1.19) 1.28 (0.83 to 1.72)	
			HCB in serum: 44.2 (23.7-90.9) µg/g fat	p,p'-DDE (ng/g fat) boys: 103.6 (46.8-403.9) girls: 84.0 (39.3-247.1)	NR NR	
			p,p'-DDE in serum: 443 (123-1398) ng/g fat	men: 443 (123-1398) women: 556 (167-1818)	0.609 (0.404 to 0.815) 0.674 (0.445 to 0.902)	
			<u>Women:</u> PCB 118 in serum: 28.8 (12.9-52.9) µg/g fat	dioxin fraction of dioxin-like activity TEQ (pg/g fat) boy girls men women	NR NR 0.273 (0.071-0.476) NR	
			Sum of marker PCBs in serum: 335 (203-521) µg/g fat	*not included in forest plot because the study didn't assess developmental exposure and BMI later in life		
			HCB in serum: 71.9 (36.2-143.3) µg/g fat			
			p,p'-DDE in serum: 556 (167-1818) ng/g fat			
cross-sectional USA, NHANES Everett et al. (2007) environmental	1830 adults from NHANES 1999-2002 (% male not stated); age ≥20 years	diagnosed diabetes by self-report; undiagnosed diabetes by HbA1c > 6.1% prevalence of total diabetes = 226/1,830 (12.3%) prevalence of diagnosed diabetes: not reported prevalence of undiagnosed diabetes: not reported	PCB 126,p,p'-DDT, HxCDD (serum, lipid adjusted)	PCB126, pg/g (ppt) 31.3-83.8 vs ≤31.2 >83.8 vs ≤31.2 p,p'-DDT, ng/g (ppb) 20.8-26.6vs≤20.7 >26.6vs≤20.7 HxCDD, pg/g (ppt) 42.1-99.1vs≤42.0	adjOR (95% CI) diagnosed 1.77 (0.91-3.43) undiagnosed 1.43 (0.60-3.37) total 1.67 (1.03-2.71) combined model 1.36 (0.78-2.40) diagnosed 3.28 (1.73-6.22) undiagnosed 3.32 (1.15-9.58) total 3.68 (2.09-6.49) combined model: 2.57 (1.33-4.95) diagnosed 3.01 (1.27-7.11) undiagnosed 1.78 (0.51-6.15) total 2.69 (1.35-5.36) combined model 2.52 (1.26-5.02) diagnosed 2.14 (1.03-4.46) undiagnosed 2.58 (1.25-5.33) total 2.46 (1.45-4.15) combined 2.74 (1.44-5.23) diagnosed 2.43 (1.22-4.83) undiagnosed 0.87 (0.40-1.91)	age, gender, race, country of birth, education, poverty income ratio (PIR), BMI, waist circumference, physical activity *combined model includes all three compounds as well as control

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
				total 1.77 (1.10-2.84) combined model 1.33 (0.73-2.44)	variables.
			>99.1 vs ≤42.0	diagnosed 2.98 (1.07-8.30) undiagnosed 0.74 (0.22-2.42) total 1.99 (0.91-4.37) combined model 1.14 (0.49-2.66)	
cross-sectional USA, NHANES Everett et al. (2010) environmental	3,049 adults from NHANES 1999-2004 (% male not stated); age ≥20 years Diabetes: 334/2715 Pre-diabetes: 462/2349	diagnosed diabetes: self-report undiagnosed diabetes: HbA1c ≥6.5% pre-diabetes: HbA1c 5.7-6.4%	β-HCH, <i>p,p'</i> -DDE, <i>p,p'</i> -DDT, oxychlorane, trans-nonachlor, heptachlor epoxide, mirex, dieldrin (serum, lipid adjusted)	adjOR (95% CI) for total diabetes (diagnosed + undiagnosed diabetes) β-hexachlorocyclohexane <9.36 vs. ≥9.36 ng/g lipid 2.67 (1.59-4.49) combined model 1.65 (0.99-2.74) pre-diabetes 1.11 (0.76-1.63) <i>p,p'</i> -DDE <168 vs ≥168.6 ng/g lipid 1.90 (1.13-3.18) combined model 1.08 (0.58-2.03) pre-diabetes 1.59 (0.98-2.55) <i>p,p'</i> -DDT <20.7 vs ≥20.7 ng/g lipid 1.96 (1.29-2.98) combined model 1.59 (0.99-2.55) pre-diabetes 1.55 (1.03-2.32) combined model pre-diabetes 1.48 (0.97-2.27) Oxychlorane <14.5 vs ≥14.5 ng/g lipid 2.90 (1.78-4.71) combined model 1.90 (1.09-3.32) pre-diabetes 1.28 (0.88-1.88) Trans- <i>nonachlor</i> <14.5 vs ≥14.5 ng/g lipid 2.36 (1.48-3.76) combined model 1.28 (0.72-2.27) pre-diabetes 1.30 (0.88-1.90) Heptachlor epoxide <14.6 vs ≥14.6 ng/g lipid 2.09 (1.46-3.00) combined model 1.70 (1.16-2.49) pre-diabetes 1.45 (1.04-2.01) combined model pre-diabetes 1.40 (1.00-1.95) Mirex <14.6 vs ≥14.6 ng/g lipid 1.65 (0.93-2.92) combined model = not reported pre-diabetes 1.15 (0.65-2.03) Dieldrin <10.6 vs ≥10.5 ng/g lipid 1.19 (0.70-2.04) combined model = not reported pre-diabetes 0.89 (0.61-1.29)	age, gender, race/ethnicity, education, poverty income ratio, BMI, waist circumference, physical activity, and family history of diabetes *combined model includes all three compounds as well as control variables.
				Adjusted association of number of organochlorine pesticides elevated with total diabetes	
				None of 6 pesticides elevated adjOR (95% CI)=1.00 (reference)	
				1 of 6 pesticides elevated 1.30 (0.47-3.55)	
				2 of 6 pesticides elevated 1.56 (0.64-3.81)	
				3 of 6 pesticides elevated 2.05 (0.88-4.78)	
				4 of 6 pesticides elevated 3.99 (1.47-10.86)	
				5 of 6 pesticides elevated 8.15 (3.49-10.05)	
				6 of 6 pesticides elevated 8.17 (2.56-26.09)	
cross sectional Belgium Fierens et al. (2003) environmental	257 adults from five areas of Belgium living near iron and steel plant (n=58), waste dumping sites (n=52), municipal solid waste incinerator in an industrial area (n=33) or rural area (51), referent group (n=63) living in rural areas in	self-report (T2D) 9 with diabetes/248 without diabetes	dioxins (PCDD/PCDFs), PCBs (serum, lipid corrected)	≥90 th percentile for dioxin versus <90 th percentile (serum levels at these percentiles not presented) 17 dioxins or PCDD/Fs adjOR=5.07 (1.18-21.7) 4 coplanar PCBs (77, 81, 126, 169) 13.3 (3.31-53.2) 12 other PCBs (3, 8, 28, 52, 101, 118, 138, 153, 180, 194, 206, 209) 7.58 (1.58-36.3)	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For																																																																																																			
	Southern Belgium with no known source of dioxins and PCBs (45% male)																																																																																																							
cross-sectional US, West Virginia community Frisbee et al. (2010) environmental	12,476 children and adolescents (aged 1 to 17.9 years) of six communities participating in the C8 Health Project where the drinking water was contaminated with PFOA (51% male; mean age = 11.1 years)	serum lipids (total cholesterol, HDL, LDL, fasting triglycerides)	PFOS and PFOA *author's report that effects tend to be non-linear with largest increases in total cholesterol and LDL-C occurring in the lowest range, especially for PFOA	<p>PFOA, adjusted estimated marginal mean (EMM) between 1st and 5th quintiles [β(SE) for quintile trend]</p> <table border="1"> <thead> <tr> <th>1-11.9 years, n</th> <th>total cholesterol</th> <th>LDL</th> </tr> </thead> <tbody> <tr> <td>both sexes, n=3857</td> <td>5.8 [1.3 (0.3); p<0.001]</td> <td>4.9 [1.0 (0.3); p=0.001]</td> </tr> <tr> <td>girls, n=1886</td> <td>5.8 [1.1 (0.4); p<0.001]</td> <td>5.4 [0.8 (0.4); p=0.04]</td> </tr> <tr> <td>boys, n=1971</td> <td>5.8 [1.1 (0.4); p<0.001]</td> <td>4.8 [1.1 (0.4); p=0.004]</td> </tr> <tr> <th>12-17.9 years, n</th> <th>total cholesterol</th> <th>LDL</th> </tr> <tr> <td>both sexes, n=5293</td> <td>4.2 [1.1 (0.3); p<0.001]</td> <td>3.2 [0.7 (0.2); p=0.004]</td> </tr> <tr> <td>girls, n=2520</td> <td>3.9 [1.0 (0.4); p=0.02]</td> <td>3.2 [0.7 (0.4); p=0.05]</td> </tr> <tr> <td>boys, n=2773</td> <td>4.8 [1.1 (0.4); p=0.005]</td> <td>3.5 [0.7 (0.3); p=0.03]</td> </tr> <tr> <td></td> <td>pooled EMM = 4.6 mg/dL increase per quintile</td> <td>pooled EMM = 3.8 mg/dL increase per quintile</td> </tr> <tr> <th>1-11.9 years, n (fasting)</th> <th>HDL</th> <th>fasting triglycerides</th> </tr> <tr> <td>both sexes, n=3857 (803)</td> <td><1.0 [-0.02 (0.1); NS]</td> <td>2.0 [2.0 (1.3); p=0.10]</td> </tr> <tr> <td>girls, n=1886 (397)</td> <td><1.0 [0.02 (0.2); NS]</td> <td>16.2 [4.0 (1.9); p=0.04]</td> </tr> <tr> <td>boys, n=1971 (406)</td> <td><1.0 [-0.06 (0.2); NS]</td> <td>5.3 [0.4 (1.9); NS]</td> </tr> <tr> <th>12-17.9 years, n (n fasted)</th> <th>HDL</th> <th>fasting triglycerides</th> </tr> <tr> <td>both sexes, n=5293 (1428)</td> <td><1.0 [0.1 (0.1); NS]</td> <td>3.8 [1.5 (1.1); p=0.10]</td> </tr> <tr> <td>girls, n=2520 (687)</td> <td><1.0 [0.3 (0.2); 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p<0.001]	4.8 [1.1 (0.4); p=0.004]	12-17.9 years, n	total cholesterol	LDL	both sexes, n=5293	4.2 [1.1 (0.3); p<0.001]	3.2 [0.7 (0.2); p=0.004]	girls, n=2520	3.9 [1.0 (0.4); p=0.02]	3.2 [0.7 (0.4); p=0.05]	boys, n=2773	4.8 [1.1 (0.4); p=0.005]	3.5 [0.7 (0.3); p=0.03]		pooled EMM = 4.6 mg/dL increase per quintile	pooled EMM = 3.8 mg/dL increase per quintile	1-11.9 years, n (fasting)	HDL	fasting triglycerides	both sexes, n=3857 (803)	<1.0 [-0.02 (0.1); NS]	2.0 [2.0 (1.3); p=0.10]	girls, n=1886 (397)	<1.0 [0.02 (0.2); NS]	16.2 [4.0 (1.9); p=0.04]	boys, n=1971 (406)	<1.0 [-0.06 (0.2); NS]	5.3 [0.4 (1.9); NS]	12-17.9 years, n (n fasted)	HDL	fasting triglycerides	both sexes, n=5293 (1428)	<1.0 [0.1 (0.1); NS]	3.8 [1.5 (1.1); p=0.10]	girls, n=2520 (687)	<1.0 [0.3 (0.2); p=0.09]	1.8 [0.8 (1.4); NS]	boys, n=2773 (741)	<1.0 [0.03 (0.1); NS]	5.9 [2.4 (1.6); p=0.10]		pooled EMM HDL not reported	pooled EMM fasting triglyceride not reported		PFOS, adjusted estimated marginal mean (EMM) between 1st and 5th quintiles [β(SE) for quintile trend]		1-11.9 years, n	total cholesterol	LDL	both sexes, n=3857	5.5 [1.3 (0.3); p<0.001]	3.4 [0.9 (0.3); p=0.002]	girls, n=1886	4.6 [1.3 (0.5); p=0.004]	2.6 [0.8 (0.4); p=0.04]	boys, n=1971	6.2 [1.2 (0.5); p=0.01]	4.1 [0.9 (0.4); p=0.03]	12-17.9 years, n	total cholesterol	LDL	both sexes, n=5293	9.5 [2.1 (0.3); p<0.001]	7.5 [1.7 (0.2); p<0.001]	girls, n=2520	9.4 [1.9 (0.4); p<0.001]	6.9 [1.5 (0.4); p<0.001]	boys, n=2773	9.3 [2.1 (0.4); p<0.001]	7.9 [1.8 (0.3); p<0.001]		pooled EMM cholesterol = 8.5 mg/dL increase per quintile	pooled EMM LDL = 5.8 mg/dL increase per quintile	1-11.9 years, n (fasting)	HDL	fasting triglycerides	both sexes, n=3857 (803)	1.6 [0.3 (0.1); p=0.007]	2.8 [0.1 (1.4); NS]	girls, n=1886 (397)	<1.0 [0.1 (0.2); NS]	7.6 [0.6 (1.9); NS]	boys, n=1971 (406)	2.6 [0.5 (0.2); p=0.003]	-1.4 [-0.3 (2.0); NS]	12-17.9 years, n (fasting)	HDL	fasting triglycerides	age, estimated time of fasting, body mass index z score, sex, and regular exercise; sex-stratified models were not adjusted for sex
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both sexes, n=5293 (1428)	<1.0 [0.1 (0.1); NS]	3.8 [1.5 (1.1); p=0.10]																																																																																																						
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Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates		Adjusted For
				both sexes, n=5293 (1428)	1.5 [0.4 (0.1); p=0.001]	<1.0 [-0.1 (1.0); NS]
				girls, n=2520 (687)	1.8 [0.3 (0.2); p=0.06]	-13.4[-3.0(1.3);p=0.02]
				boys, n=2773 (741)	1.1 [0.4 (0.1); p=0.003]	11.1 [2.2 (1.6); NS]
				pooled EMM HDL not reported		pooled EMM fasting triglyceride not reported
retrospective cohort Fujiyoshi et al. (2006) Vietnam veterans	313 veterans: 129 Vietnam Operation Ranch Hand Veterans and 184 non-Vietnam Southeast Asia Veterans (100% male; 1997 assessment)	diabetes (physician diagnosis or 2-hr postprandial glucose ≥200 mg/dL) <u>Operation Ranch Hand Veterans:</u> 19 diabetics (14.7%)/110 non-diabetics <u>Comparison Veterans:</u> 28 diabetics (15.2%)/156 non-diabetics	TCDD (serum collected in 1987 and 1992)	Correlation between serum dioxin levels and the GLUT4: NFκB mRNA ratio (an inflammatory marker): Operation Ranch Hand group (r=0.21, p=0.02) Comparison group (r=-0.12, p=0.11). Correlations between serum dioxin and fasting blood glucose: Operation Ranch Hand group: r=0.07, p=0.40 Comparison group: r= 0.17, p=0.02)		age and percent body fat
retrospective cohort Gilliland et al. (1993) occupational	2,788 male workers and 749 female workers employed at a Minnesota plant that has produced PFOA since 1947, employed for at least 6 months between January 1, 1947 and December 31, 1981	death certificates	exposed: worked ≥ 1 month in chemical division unexposed: never worked or worked < 1 month in chemical division	Males (n=2788; 1339 in chemical division (48%)/1449 elsewhere 145 deaths from cardiovascular disease among all workers (41.8%, n=347)/339 deaths from other causes 54 deaths from cardiovascular disease among workers exposed to PFOA (36.5%, n=148)/94 deaths from other causes Females (n=749; 245 in chemical division (32.7%)/504 elsewhere 10 deaths from cardiovascular disease (20%, n=50)/40 deaths from other causes	SMR (95% CI) , standardized to mortality rates of white males in Minnesota 0.68 (0.58-0.80) 0.70 (0.53-0.92) 0.81 (0.49-1.29)	
cross-sectional US, Minnesota Gilliland et al. (1996) occupational	Serum lipids in workers at a PFOA production plant employed during 1985-1989 (115 total subjects)	Total serum fluorine in workers	PFOA (total fluoride, serum) 5 categories: <1, ≥1-3, >3-10, >10-15, >15-26 ppm	serum lipid cholesterol HDL HDL LDL	β coefficient or results from ANOVA non-significant ANOVA across 5 exposure categories non-significant ANOVA across 5 exposure categories β=-1.61 ± 0.77, p=0.04 non-significant ANOVA across 5 exposure categories	age, BMI, smoking, testosterone, alcohol use
prospective cohort US, Philadelphia Gladen et al. (2000) environmental	594 subjects in the NC Infant Feeding Study with prenatal and lactational exposures previously measured (1978-1982), followed up 1992-1997 – until final pubertal stages attained	anthropometric and pubertal measures in adolescents	PCB and DDE (ppm in maternal serum)	Adjusted mean height and weight at 14 years by transplacental exposure categories girls PCB (ppm) height (cm) and weight (kg) 0-1; n=22 165.4 ± 1.6 51.6 ± 1.9 1-2; n=178 163.6 ± 0.5 53.0 ± 0.6 2-3; n=85/87 163.5 ± 0.8 52.9 ± 0.9 boys PCB (ppm) height (cm) and weight (kg) 0-1; n=17 169.0 ± 2.0 59.6 ± 2.2 1-2; n=165/163 168.9 ± 0.6 56.9 ± 0.7 2-3; n=65 169.8 ± 1.0 56.8 ± 1.1		weight is adjusted for height

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates		Adjusted For	
				≥3; n=27	164.2 ± 1.3 57.0 ± 1.6	≥3; n=30	166.2 ± 1.5 56.1 ± 1.5
				p-trend	height: p=0.75 weight: p=0.09	p-trend	height: p=24 weight: p=0.64
				DDE (ppm)		DDE (ppm)	
				0-1; n=19/18	162.7 ± 1.7 54.2 ± 2.1	0-1; n=21/20	163.9 ± 1.8 53.7 ± 2.0
				1-2; n=97	163.7 ± 0.7 52.5 ± 0.8	1-2; n=75	168.3 ± 0.9 56.1 ± 1.0
				2-3; n=100/103	163.5 ± 0.7 54.0 ± 0.8	2-3; n=80	169.6 ± 0.9 57.4 ± 1.0
				3-4; n=55	164.6 ± 0.9 53.3 ± 1.1	3-4; 56/55	169.0 ± 1.1 55.6 ± 1.2
				≥4; n=41	164.0 ± 1.2 51.5 ± 1.4	≥4; n=45	170.2 ± 1.3 60.6 ± 1.4
				p-trend	height: p=0.81 weight: p=0.51	p-trend	height: p=0.054 weight: p=0.025
prospective cohort US, Philadelphia Gladen et al. (2004) environmental	304 males born in Philadelphia in the early 1960s enrolled in the Philadelphia BP Project (PBPP; this project followed some of the children enrolled in Collaborative Perinatal Project during adolescence and early adulthood until 20 years of age)	height, BMI, triceps skinfold thickness, central adiposity (%), and skeletal age (study also measured blood testosterone and DHEAS levels)	<i>p,p'</i> -DDE, <i>p,p'</i> DDT, <i>o,p'</i> -DDT Prenatal (maternal serum from the 3 rd trimester)	<i>p,p'</i>-DDE, ≥12 µg/g lipid vs. <3 µg/g lipid and anthropometric measures at ages ~11 to 20 years		regression coefficients ± SEM	
				height (cm)		0.4 cm ± 1.8, NS	
				height ratio (%)		0.0% ± 0.3, NS	
				BMI (kg/m ²)		-0.4 kg/m² ± 0.9, NS	
				triceps (log mm)		-0.01 log mm ± 0.11, NS	
				central adiposity (%)		0.6% ± 1.2, NS	
				skeletal age (years)		0.2 years ± 0.3, NS	
				<i>p,p'</i> DDT		no significant effects (data not shown)	
				<i>o,p'</i> -DDT		no significant effects (data not shown)	
							Mothers: <i>p,p'</i> -DDE serum levels, BMI, height, race, smoking during pregnancy, age at menarche, age at enrollment
							Boys: Family size, number of older siblings, breast fed, age at measurement, correlation among multiple measurements of the same boy
cross-sectional China	85 male production workers of Chinese descent who worked on an assembly line	serum insulin (serum steroid hormones)	TCE (using urine levels of	correlation between urine TCA and serum insulin (n=78 workers)		0.277* (p<0.05)	age, smoking

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
Goh et al. (1998) occupational	in an electronic factory where trichloroethylene (TCE) was used; age range = 22 to 39 years; mean = 27.8 years	levels also assessed but not summarized here) TCE mean environmental exposure levels for an 8-hour workday = 20.4 ppm (excludes an outlier)	trichloroacetic acid, TCA, as a marker; years of employment)	insulin levels based on years of exposure <2 years (n=10) vs 2-4 years (n=9) <2 years (n=10) vs 4-6 years (n=21) <2 years (n=10) vs >6 years (n=45)	*mean in normal non-exposed men cited as 9.6 mIU/l 40.8 vs 11.7 mIU/l*(p<0.001) 40.8 vs 16.4 mIU/l*(p<0.05) 40.8 vs 20.5 mIU/l (NS)	history and size of testis
retrospective cohort; USA; Henriksen et al, (1997) Vietnam veterans	2265 male veterans, including 989 Vietnam Air Force Veterans from Operation Ranch Hand compared with 1,276 unexposed Air Force Veterans who served in Southeast Asia during the same period	physician diagnosed during post-Vietnam period (from end of veteran's last tour of duty to June 1995)	TCDD [serum, ppt; current (D) and initial (I)] Referent = D ≤10 Ranch Hand Background = D ≤10 Low = D <10 & I ≤94 High = D <10 & I >94	<i>Diabetes</i> (n=2265; 315 diabetics (13.9%)/1950 non-diabetics) Referent (n=1,276) RR=1.00 Background, Ranch Hand (n=422) 0.7 (0.5-1.0) Low, Ranch Hand (n=284) 1.3 (1-1.7) High, Ranch Hand (n=283; 57 diabetics, 20.1%) 1.5 (1.2-2.0) *time to develop diabetes decreased with TCDD exposure Glucose abnormalities for High, Ranch Hand (60 cases, 25.6%) 1.4 (1.1-1.8) Use of controls for diabetes (diet, oral medication, insulin) for High, Ranch Hand (40 cases, 15%) 1.8 (1.3-2.6) Serum insulin abnormalities for High, Ranch Hand (18 cases, 8.4%) 3.4 (1.9-6.1)	comparison group matched on age, race, and military occupation	
cross-sectional Greenland Jorgensen et al. (2008) environmental	692 Greenlanders (44% male) with at least one Inuit parent, ≥ 35 years old, living in three areas of West Greenland. 1999 – 2002; mean age for men= 50 years, mean age for women=49 years	diabetes (OGTT or FG, 10.3% diabetics in cohort) Insulin resistance (HOMA)	3 dioxin-like PCBs, 10 non-dioxin-like PCBs, and 11 OC pesticides (plasma)	Diabetes(n=692; 72 (10.3%) with diabetes/620 without diabetes) 1st (referent) vs 4th quartile dioxin-like PCBs (ng/g lipid) PCB 105: 44 vs 6.5 PCB 118 300 vs 43 PCB 156 13 vs 20 non-dioxin like PCBs (ng/g lipid) PCB 28: 8.5 vs 4.9; PCB 52: 14 vs 7.2; PCB 99: 190 vs 35; PCB 101: 17 vs 4.6; PCB 128 6.5 vs 1.6; PCB 138: 730 vs 130; PCB 153: 1700 vs 290; PCB 163: 390 vs. 54; PCB 170: 310 vs 46; PCB 180: 1100 vs 150 OC pesticides (ng/g lipid) Aldrin 0.7 vs 0.44; Mirex: 83 vs 7.9 HCB: 770 vs 120; β-HCH: 66 vs 15; α-Chlordane: 1.20 vs. 0.31; γ-Chlordane: 1.15 vs 0.15; Oxychlordane: 620 vs 54; <i>trans</i> -nonachlor: 1200 vs 120; <i>cis</i> -Nonachlor: 190 vs 23; DDT: 67 vs 12; DDE: 3400 vs 490	adjOR (95% CI)*ORs for individual congeners not presented 1.2 (0.4-3.6), p-trend = 0.37 1.2 (0.4-3.2), p-trend = 0.42 1.8 (0.6-5.5), p-trend = 0.4	Age, sex, ethnicity, waist circumference, physical activity, alcohol consumption, smoking, and educational level
	IGT (n=692; 73 (10.5%) with IGT/619 without IGT) dioxin-like PCBs 0.7 (0.2-1.8), p-trend = 0.82 non-dioxin like PCBs 0.5 (0.2-1.3), p-trend = 0.4 OC pesticides 0.6 (0.2-1.8), p-trend = 0.55 mean 2 hour insulin in subjects without diabetes (n=621) dioxin-like PCBs: range from 129 to 90 pmol/l from 1 st to 4 th exposure quartiles p-trend=0.04 non-dioxin like PCBs: range from 122 to 90 pmol/l from 1 st to 4 th exposure quartiles p-trend=0.01 OC pesticides: range from 133 to 87 pmol/l from 1 st to 4 th exposure quartiles p-trend=0.03					
prospective cohort US, San Francisco	399 mothers and children who participated in the Child Health and	Birth weight (n=371), gestational age, birth length	Maternal levels during pregnancy,	adj mean adjusted difference(95% CI), 75th vs 25th percentile birth weight (g)	At delivery: maternal	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
Jusko et al. (2006) environmental	Development Study (CHDS)	(n=370), head circumference (n=369) and gestational age-adjusted birth weight Five Year Growth standardized height (n=390), standardized weight (n=391), and head circumference (n=383)	mostly 2 nd trimester, (25 th , 75 th percentile) p,p'-DDE (3.90, 8.56), p,p'-DDT (1.11, 2.30), o,p' DDT (0.12, 0.35), ΣDDT (5.68, 11.15)	p,p'-DDE	6 (-54 to 66)	BMI, height, parity, race, alcohol intake, father's education and occupation At 5-years: maternal BMI, height, race, and quality of prenatal care
				p,p'-DDT	1 (-58 to 59)	
				o,p' DDT	-9 (-70 to 51)	
				ΣDDT	5 (-58 to 68)	
				adjusted birth weight (z-score)		
				p,p'-DDE	0.01 (-0.11 to 0.14)	
				p,p'-DDT	0.01 (-0.12 to 0.13)	
				o,p' DDT	-0.03 (-0.17 to 0.10)	
				ΣDDT	0.01 (-0.12 to 0.15)	
				birth length (cm)		
				p,p'-DDE	0.0 (-0.4 to 0.3)	
				p,p'-DDT	0.1 (-0.3 to 0.4)	
				o,p' DDT	-0.3 (-0.7 to 0.1)	
				ΣDDT	0.0 (-0.4 to 0.4)	
				birth head circumference (mm)		
				p,p'-DDE	1 (-1 to 2)	
				p,p'-DDT	1 (-1 to 3)	
				o,p' DDT	0 (-1 to 2)	
				ΣDDT	1 (-1 to 3)	
				5-year standardized height (z-score)		
				p,p'-DDE	0.59 (-0.32 to 1.50)	
				p,p'-DDT	0.38 (-0.75 to 1.51)	
				o,p' DDT	0.28 (-0.96 to 1.53)	
ΣDDT	0.60 (-0.37 to 1.58)					
5-year standardized weight (z-score)						
p,p'-DDE	0.68 (-0.16 to 1.51)					
p,p'-DDT	0.95 (-0.33 to 2.23)					
o,p' DDT	0.19 (-1.03 to 1.41)					
ΣDDT	0.80 (-0.10 to 1.70)					
5-year head circumference (mm)						
p,p'-DDE	2 (0 to 4)					
p,p'-DDT	0 (-1 to 2)					
o,p' DDT	1 (-2 to 3)					
ΣDDT	2 (0 to 4)					
retrospective cohort US Army Kang et al. (2006) Vietnam veterans	US Army Chemical Corps 2927 men; 1499 Vietnam veterans exposed to herbicides compared with 1428 non-Vietnam veterans assigned to chemical operations branch (median age 51-53 years) year= 1994-2000	diabetes (self-report)	deployment status, spaying of herbicides in Vietnam, & lipid adjusted serum TCDD for 897 veterans	deployed vs. non-deployed, diabetes OR=1.16 (0.91-1.49) <u>Vietnam:</u> n=1499; 226 with diabetes/1273 without diabetes <u>non-Vietnam:</u> n=1428; 136 with diabetes/1292 without diabetes herbicide spraying: <u>Vietnam sprayers:</u> n=662; 123 with diabetes/539 without diabetes <u>non-Vietnam sprayers:</u> n=811; 99 with diabetes/712 without diabetes	Age, race, BMI, rank, and smoking	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				<p>sprayed herbicides in Vietnam vs. never 1.50 (1.15-1.95)</p> <p>mean (range) serum TCDD sprayed herbicides in Vietnam: 4.3(0.5-85.8) ng/g serum lipid did not spray herbicides and was in Vietnam: 2.70 (0.6-27.7) ng/g serum lipid did not spray herbicides and was not in Vietnam: 2.1 (0.4-12.5) ng/g serum lipid</p>		
prospective cohort US, Michigan Karmaus et al. (2009) environmental	176 adult female offspring of mothers from the Michigan fish-eater cohort. 151 daughters participated in 2001/02 and 129 participated in 2006/07. They were born between 1950 and 1980 and were 20-50 years of age at assessment.	BMI, weight	PCB, DDE (maternal serum, pregnancy 1950-1980)	<p># mothers = 101; # participants = 169, # of observations = 267</p> <p>Maternal DDE (µg/l)</p> <p><1.503 referent</p> <p>1.503-2.9 BMI: 1.65 (0.33); p<0.05 weight: 5.93 (1.79); p<0.05</p> <p>>2.9 BMI: 2.88 (0.92), p<0.05 weight: 9.22 (3.06); p<0.05</p> <p>Maternal PCBs, µg/l</p> <p><0.05 referent</p> <p>0.05-1.94 BMI: -0.39 (0.74); NS weight: 0.93 (2.35); NS</p> <p>>1.94 BMI: 1.28 (1.18), NS weight: 2.29 (3.43); NS</p>	maternal height, maternal BMI, breastfed as a child, birth weight of offspring, height of offspring, age of adult female offspring, number of offspring's pregnancies, having the same mother	
cross-sectional Kim et al. (2003) Vietnam veterans (Korean)	1398 Korean veterans: 1,244 with service in Vietnam and 154 non-Vietnam veterans	diabetes (clinical exam, 1995-1996)	Agent Orange service in Vietnam y/n	<p>Korean Vietnam veterans vs. Korean non-Vietnam veterans</p> <p>154 exposed diabetics (12.4%)/1090 exposed non-diabetics</p> <p>9 non-exposed diabetics (5.8%)/145 non-exposed non-diabetics</p> <p>*diabetes was not significantly associated with TCDD exposure levels, but samples were collected in 1995-1996-and pooled across subjects in the same "exposure." The exposure categories were based on estimated total cumulative exposure during service and "personal" exposure based on self-reported extent and frequency of Agent Orange contact (TCDD levels did not show a linear correlation with ordinal exposure category)</p>	<p>OR=2.69 (1.09-6.67)</p> <p>β=0.989</p>	age, smoking, alcohol, body mass index, education, and marital status.
prospective cohort AFHS Kern et al. (2004) Vietnam veterans	<p>1997 exam: 29 matched pairs of male Southeast Asia Veterans, 29 Operation Ranch Hand veterans and 29 veterans who did not spray herbicides (mean age= 57years)</p> <p>2002 exam: 71 matched pairs of male Southeast Asia Veterans. 71 Operation Ranch Hand veterans and 71 veterans who did not spray herbicides (mean age= 58 years)</p>	insulin sensitivity [ivGTT, quantitative insulin sensitivity check index (QUICKI)]	TCDD (serum, lipid adjusted; mostly based on 1987 measurements or else in 1992 or 1997 and extrapolated to 1987 using first-order kinetics and half-life of 7.6 years)	<p>Within pair differences for lower insulin sensitivity in Operation Ranch Hand veterans*</p> <p>1997 (29 pairs) β = -0.368 (-0.645 to -0.091), p = 0.01</p> <p>2002 (71 pairs) β = -0.00639 (-0.012 to -0.001), p = 0.02</p> <p>no associations with HbgA1c, triglycerides, cholesterol, HDL, fasting insulin, FG, TNFα, adiponectin</p> <p>*no difference between groups with paired t-test, but pairs with the greatest difference in TCDD levels had the largest decrease in insulin sensitivity</p>	matched cases and controls	
retrospective cohort East Slovakia	240 workers from a PCB production factory (21% male; age range: 26-65)	anti-glutamic acid decarboxylase (anti-GAD)		Frequency of anti-GAD antibodies >1.21 U/ml in exposed and unexposed subject (Yates Chi-square test)		

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
Langer et al. (2002) environmental	years) compared with 704 subjects from not heavily polluted areas of East Slovakia (38% male; age range: 21-72 years)	antibody serum levels >1.21 U/mL		PCB factory employee ("exposed") vs. unexposed	"exposed" 97/240 vs "unexposed" 74/704 (40.4% versus 10.5%); p<0.001	
cross-sectional Slovakia Langer et al. (2009) environmental	2,046 men and women aged 21-75 from heavily and "background" polluted areas in Slovakia (41% male) Upper PCBs level for each quintile Q1: 627 ppb; Q2: 906 ppb; Q3: 1341 ppb; Q4: 2343 ppb; Q5: 101,413 (overall range: 149-101,413 ng/g lipid)	glucose, insulin, lipids, BMI	PCBs (lipid adjusted serum levels of Σ 15 PCB congeners and <i>p,p'</i> -DDE, HCB; PCB exposure levels used as surrogate for <i>p,p'</i> -DDE and HCB)	Chi-square for number of "adverse" health cases per quintile: range of PCB 149 vs 101,413 ng/g lipid ↑FG, >5.6 mmol/l[100 mg/dl] 1163 cases (56.8%) 883 non-cases ↑ fasting insulin, >10 mIU/ml 495 cases (24.2%)1551 non-cases ↑ cholesterol, >6.0 mmol/l 611 cases (29.9%)1435 non-cases ↑ triglycerides, >2.0 mmol/l 611 cases (29.9%)1435 non-cases ↑ BMI, 75 th percentile for each appropriate sex and age group 744 cases (36.4%)1302 non-cases	110.55; p<0.0001 11.89; p=0.0182 8.76; p=0.0673 19.36; p=0.0007 5.84; p=0.2118	not reported
cross-sectional US, NHANES Lee et al. (2006) environmental	2,016 adults participants from NHANES 1999-2002; ≥20 years [% male not reported]	diabetes (fasting plasma glucose ≥126 mg/dl, non-fasting plasma glucose ≥200 mg/dl, or self-report)	PCB153, DDE, HpCDD, oxychlorodane, trans-nonachlor, OCDD	adj OR (95%CI) for diabetes, ≥90th percentile versus not detectable (ND) PCB153, 164 ppb vs. ND exposed cases/non-cases= 164; 30/134 referent = 413; 10/403 (n=577) HpCDD, 170 pg/g vs. ND exposed cases/non-cases= 177; 46/131 referent= 263; 12/251 (n=440) OCDD, 1,485 pg/g vs. ND exposed cases/non-cases= 166; 31/135 referent= 390; 13/377 (n=556) Oxychlorodane, 65.5 ng/g vs. ND exposed cases/non-cases= 166; 49/117 referent= 359; 11/348(n=525) DDE, 3,700 ng/g vs. ND exposed cases/non-cases= 202; 53/149 referent= 502; 16/486 (n=704) trans-nonachlor, 114 ng/g vs. ND exposed cases/non-cases= 182; 54/128 referent= 203; 4/199 (n=385) Σ 6 chlorinated POPs exposed cases/non-cases= 246; 63/183 referent= 463; 2/461 (n=709)	adjOR=6.8 (3.0-15.5) ,p trend <0.001 2.7 (1.3-5.5) ,p trend =0.007 2.1 (0.9-5.2) ,p trend=0.094 6.5 (2.0-21.4) ,p trend <0.001 4.3 (1.8-10.2) ,p trend <0.001 11.8 (4.4-31.3) ,p trend <0.001 37.7 (7.8-182.0) , p trend <0.001	Sex, race/ethnicity, age, poverty income ratio, BMI, and waist circumference
cross-sectional US, NHANES Lee et al. (2007a) environmental	NHANES 1999-2002: 749 non-diabetic participants, ≥ 20 years old (46.3% male)	insulin sensitivity (HOMA)	>90 th percentile PCDDs, PCDFs, dioxin-like PCBs, nondioxin-like PCBs, OC pesticides	serum level, ≥75th vs. <25th percentile PCDDs exposed cases/non-cases= 187; 26/161 referent= 187; 13/174 (n=374) 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin exposed cases/non-cases= 137; 16/121 referent= 198; 22/178 1,2,3,4,6,7,8-heptachlorodibenzo-p-dioxin	adjOR HOMA >90th percentile (95% CI) 2.3 (0.9-6.0)p=0.14 for trend 1.3 (0.5-3.4); p=0.57 for trend 2.0 (0.6-6.4), p=0.30 for trend	Age, sex, race, poverty income ratio, BMI, waist circumference, cigarette smoking,
	PCB-170 exposed cases/non-cases= 125; 15/110 referent= 253; 20/233	3.8 (1.2-11.5); p=0.02 for trend				
	PCB-180 exposed cases/non-cases= 142; 19/123	2.3 (0.8-7.0); p=0.24 for trend				

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
	referent= 179; 18/161			exposed cases/non-cases= 161; 23/138 referent= 103; 6/97	serum cotinine, alcohol consumption, and exercise	
	PCB-187 exposed cases/non-cases= 112; 18/94 referent= 229; 22/207	4.2 (1.5-11.7); p=0.01 for trend		1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin exposed cases/non-cases= 143; 16/127 referent= 178; 14/164	1.3 (0.5-3.5), p=0.53 for trend	
	OC pesticides exposed cases/non-cases= 187; 31/156 referent= 187; 12/175	7.5 (2.3-23.9); p<0.01 for trend		PCDFs exposed cases/non-cases= 187; 24/163 referent= 187; 13/174	1.7 (0.7-4.0); p=0.46 for trend	
	Oxychlorane exposed cases/non-cases= 153; 22/131 referent=140; 8/132	8.7 (2.3-33.3), p<0.01 for trend		Dioxin-like PCBs exposed cases/non-cases= 187; 22/165 referent= 186; 15/171	1.4 (0.5-4.1); p=0.60 for trend	
	Trans-nonachlor exposed cases/non-cases= 166; 26/140 referent= 86; 4/82	5.4 (1.3-23.1), p=0.02 for trend		Nondioxin-like PCBs exposed cases/non-cases= 187; 23/164 referent= 187; 18/169	2.3 (0.8-6.4); p=0.10 for trend	
	p,p'-DDT exposed cases/non-cases= 187; 22/167 <25 th percentile= 187; 15/172	1.4 (0.5-3.7), p=0.33 for trend		PCB-138 exposed cases/non-cases= 139; 16/123 referent= 193; 20/173	1.5 (0.6-4.0); p=0.35 for trend	
	β-Hexachlorocyclohexane (β-HCH) exposed cases/non-cases= 138; 21/117 referent= 198; 15/183	1.7 (0.6-5.1), p=0.56 for trend		PCB-153 exposed cases/non-cases= 148; 17/131 referent= 155; 17/138	1.5 (0.5-4.2); p=0.51 for trend	
cross-sectional US, NHANES Lee et al. (2007b) environmental	NHANES 1999-2002: 721 non-diabetic participants; ≥20 years; % male not reported (175, or 24.3%, cases of metabolic syndrome)	<u>Metabolic syndrome:</u> Three or more of the following five criteria: Waist ≥ 102 (♂), 88 (♀) cm; serum triglycerides ≥1.7 mmol/l; HDL <1.1 (♂), <1.4 (♀) mmol/l ; BP ≥ 130/85; or FG ≥5.6 mmol/l/[100 mg/dl]	PCDDs, PCDFs, dioxin-like PCBs, non-dioxin-like PCBs, OC pesticides (lipid-adjusted serum levels of 19 POPs in five subclasses)	≥75th versus <25th percentile PCDDs (n=360) referent = 180; 29/151 exposed cases/non-cases = 180; 57/123 PCDFs referent = 180; 30/150 exposed cases/non-cases = 180; 56/124 PCDD03 PCDD05 PCDD07 PCDF03 PCDF04 PCDF08 Dioxin-like PCBs referent= 180; 27/153 exposed cases/non-cases= 180; 61/119 PCB074 PCB118 PCB126 PCB169 Non-dioxin-like PCBs referent= 180; 29/151 exposed cases/non-cases= 180; 47/133 PCB138	Odds Ratios (95% CI), model 2 1.3 (0.7-2.5), p trend=0.35 1.6 (0.9-2.8), p-trend=0.11 0.6 (0.3-1.1), p-trend=0.48 2.0 (0.9-4.1), p-trend=0.13 1.3 (0.7-2.5), p-trend=0.67 1.0 (0.5-1.8), p-trend=0.56 2.0 (1.1-3.6), p-trend<0.01 1.0 (0.6-1.7), p-trend=0.87 2.1 (1.0-4.3), p-trend=0.01 2.0 (0.9-4.2), p-trend<0.01 2.5 (1.3-5.1), p-trend<0.01 2.7 (1.5-5.0), p-trend<0.01 0.4 (0.2-0.8), p-trend=0.10 1.0 (0.5-1.9), p-trend<0.01 1.1 (0.6-2.1), p-trend=0.03	model 2: Age, sex, race, poverty income ratio, cigarette smoking, serum cotinine, alcohol consumption and exercise model 3 included BMI and did not appreciably change when included, but model 2 is used as summary value here

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
				PCB153 1.0 (0.5-2.2), p-trend<0.01 PCB170 0.8 (0.4-1.7), p-trend<0.01 PCB180 1.0 (0.4-2.1), p-trend<0.01 PCB187 1.3 (0.7-2.7), p-trend<0.01 OC pesticides 5.3 (2.5-11.3), p-trend <0.01 referent= 180; 20/150 exposed cases/non-cases= 180; 79/101 oxychlordane 1.9 (0.8-4.2), p-trend=0.12 trans-Nonachlor 1.8 (0.8-4.3), p-trend=0.17 p,p'-DDE 1.0 (0.5-1.9), p-trend=0.67 β -HCH 3.1 (1.4-6.5), p-trend<0.01	because data for model 3 for the individual congeners was not presented
nested case control US. multi-center Lee et al. (2010) environmental	The Coronary Artery Risk Development in Young Adults (CARDIA) cohort (a multi-center study). Baseline (year 0) was in 1985/86 with follow-up at years 2, 5, 7, 10, 15 and 20 (2005/06) Subjects were 90 cases / 90controls matched for BMI during year 0	diabetes (FG _≥ 126 mg/dL, medications) cases: non-diabetic at year 1 and 2 and subsequently became diabetic (116 new cases during study and 90 randomly selected as cases) controls: randomly selected from those who had FG<100 mg/dL at all times when glucose measured (years 0, 7, 10, 15, 20)	55 POPs (serum levels of 31 POPs at year 2, 1987-88)	2nd quartile versus 1st quartile, OR (95% CI) of incident diabetes (2nd quartile exposure categories in CARDIA in 1987/88 considered ≈ exposure levels in higher current NHANES percentiles) oxychlordane [n= 88; Q2=30 (56.6%)/23; Q1=13(37.1%)/22] Q2 (111-157pg/g) vs. Q1 (≤110pg/g) 1.7 (0.7-4.3) trans-nonachlor [n= 85; Q2=33 (58.9%)/23; Q1=7(24.1%)/22] Q2 (110-174pg/g) vs Q1 (≤109pg/g) 4.3 (1.5-12.6), non-linear trend HCB [n=88; Q2=18 (43.9%)/23; Q1=25 (53.2%)/22] Q2 vs Q1 (levels not reported) 0.5 (0.2-1.3) β-HCH [n= 90; Q2= 23 (50.0%)/23; Q1= 22(37.1%)/22] Q2 (76-108pg/g) vs Q1 (≤75pg/g) 1.0 (0.4-2.5) γ-HCH [n=85; Q2= 21 (47.7%)/23; Q1= 19 (46.3%)/22] Q2 vs Q1 (levels not reported) 1.2 (0.5-3.0) p,p'-DDE [n= 86; Q2=23 (50.0%)/23; Q1=18(37.1%)/22] Q2 (2154-3312pg/g) vs Q1 (≤2153pg/g) 1.2 (0.5-3.0) p,p'-DDT [n=78; Q2=16 (41.0%)/23; Q1=17 (43.6%)/22] Q2 vs Q1 (levels not reported) 0.8 (0.3-2.2) Mirex [n=79; Q2=18 (52.9%)/16; Q1=16(35.6%)/29] Q2 (≤ 21pg/g) vs Q1 (not reported) 2.0 (0.7-5.5) PCB74[n=95; Q2=33 (58.9%)/23; Q1=17 (43.6%)/22] Q2 (59-98pg/g) vs Q1 (≤58pg/g) 2.8 (1.0-7.3), non-linear trend PCB87 [n=84; Q2=18 (45%)/22; Q1=22 (50%)/22] Q2 vs Q1 (not reported) 1.1 (0.4-2.8) PCB99 [n=84; Q2=18 (43.9%)/23; Q1= 21 (48.8%)/22] Q2 vs Q1 (not reported) 0.7 (0.3-1.8)	age, sex, race, and year 2 BMI, triglycerides, and total cholesterol (model 2) p-cubic used to assess trends; allows the outcome curve to rise, fall, and rise again

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
			PCB105 [n=91; Q2=18 (42.9%)/24; Q1=28 (57.1%)/21] Q2 vs Q1 (not reported)	0.3 (0.1-0.8)	
			PCB118 [n=89; Q2=18 (43.9%)/23; Q1=26 (54.2%)/22] Q2 vs Q1 (not reported)	0.5 (0.2-1.3)	
			PCB146 [n=90; Q2=32 (59.3%)/22; Q1=14 (38.9%)/22] Q2 vs Q1 (not reported)	1.7 (0.7-4.5)	
			PCB153 [n=95; Q2=35 (51.5%)/23; Q1=15 (40.5%)/22] Q2(205-349pg/g) vs Q1(≤204 pg/g)	2.0 (0.8-5.2)	
			PCB156 [n=91; Q2=29 (54.7%)/24; Q1=17 (44.7%)/21] Q2 vs Q1 (not reported)	1.3 (0.5-3.5)	
			PCB157 [n=93; Q2= 29 (55.8%)/23; Q1=20 (48.8%)/21] Q2 vs Q1 (not reported)	1.0 (0.4-2.5)	
			PCB138-158 [n=91; Q2=26 (54.2%)/22; Q1=20 (46.5%)/23] Q2 vs Q1 (not reported)	1.2 (0.5-2.9)	
			PCB167 [n=92; Q2= 23 (50%)/23; Q1=24 (52.2%)/22] Q2 vs Q1 (not reported)	0.9 (0.4-2.2)	
			PCB170[n=93; Q2=35 (60.3%)/23; Q1=13 (37.1%)/22] Q2 vs Q1 (not reported)	2.2 (0.8-6.1)	
			PCB178 [n=97; Q2=38(62.3%)/23; Q1=14 (38.9%)/22] Q2(9-15pg/g) vs Q1(≤8pg/g)	2.7 (1.0-7.0), non-linear trend	
			PCB180 [n=98; Q2=41 (64%)/23; Q1= 12 (35.3%)/22] Q2 vs Q1 (not reported)	2.8 (1.0-7.6), non-linear trend	
			PCB183 [n=91; Q2=31 (57.4%)/23; Q1=15 (40.5%)/22] Q2 vs Q1 (not reported)	1.7 (0.7-4.2)	
			PCB187 [n=98; Q2=41 (64.1%)/23; Q1=12 (35.3%)/22] Q2(45-78pg/g) vs Q1(≤44pg/g)	2.8 (1.1-7.4), non-linear trend	
			PCB194 [n=93; Q2= 32 (58.2%)/23; Q1=16 (42.1%)/22] Q2 vs Q1 (not reported)	1.6 (0.6-4.3)	
			PCB195 [n=93; Q2=34 (60.7%)/22; Q1=15 (40.5%)/22] Q2 vs Q1 (not reported)	1.9 (0.7-5.1)	
			PCB199 [n=96; Q2=35 (60.3%)/23; Q1=16 (42.1%)/22] Q2 vs Q1 (not reported)	2.2 (0.8-5.6)	
			PCB196-203 [n=99; Q2=39 (62.9%)/23;	2.3 (0.9-6.1)	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				Q1= 15 (40.5%)/22] Q2 vs Q1 (not reported) PCB206 [n=84; Q2=19 (45.2%)/23; Q1=20 (47.6%)/23] Q2 vs Q1 (not reported) PCB209 [n=96; Q2=35 (57.4%)/26; Q1=16 (45.7%)/19] Q2 vs Q1 (not reported) PBB153 [n=94; Q2=29 (55.8%)/23; Q1=10(31.3%)/22] Q2(10-16pg/g) vs Q1(≤9pg/g) All 31 POPS, sextile 2 vs sextile 1 16 POPs with OR≥1.5 in 2nd quartile comparison, sextile 2 vs sextile 1	0.7 (0.3-1.9) 1.1 (0.4-3.0) 2.5 (0.9-6.9) 2.8 (1.0-8.8), p-cubic = 0.03 5.4 (1.6-14.3), p-cubic = <0.01	
retrospective cohort US, DuPont plant (WV) Leonard et al. (2008) occupational	Mortality in 6,027 employees who worked between 1948 and 2002 at a DuPont company plant in Washington Works, WV that manufactured PFOA manufacturing (773deaths through 2002; 23 diabetic deaths/784 non-diabetic deaths)	death certificate	PFOA (employment)	WV cohort had 22 diabetes deaths WV cohort versus US population (25.9 diabetes deaths expected) WV cohort versus WV population (31.5 diabetes deaths expected) WV cohort versus DuPont region 1 (11.2 diabetes deaths expected)	sex, calendar period (SMR) SMR = 85 (53.3-128.7) SMR = 69.9 (43.8-105.8) SMR = 196.9 (123.4-298.1)	
cross-sectional US, NHANES Lim et al. (2008) environmental	NHANES 2003-2004: 1367 participants; 47.3% male;(156 or 11.4% diabetic); 637 participants with morning fasting urine (237 or 37.2% cases of metabolic syndrome)	<u>Diabetes:</u> FG≥ 126 mg/dl; non-FG≥ 200 mg/dl; anti-diabetic medication n=1367; 156 (11.4%)/1211 <u>Metabolic syndrome:</u> Waist Circ≥ 102 (♂), 88 (♀) cm; FTrig≥150 mg/dL; HDL < 40 (♂), 50 (♀) mg/dL; BP≥ 130/85 or anti-hypertensive medication; FG≥100 mg/dL or anti-diabetes medication n=637; 237 (37.2%)/400	PBB, PBDE (serum, lipid adjusted)	≥75th versus not detectable (ND), adjOR (95% CI) of prevalent diabetes PBB153 (n= 466; exp = 49 (16.3%)/251; ref = 11(6.62%)/155 ≥75th (13.1 ng/g) vs. ND PBDE-28 (n=550; exp=37(13.7%)/234; ref= 37 (13.3%)/242 ≥75 th (5.4 ng/g) vs. ND PBDE-47 (n=369; exp=37(11.1%)/296; ref= 2 (5.56%)/34 ≥75 th (73.3 ng/g) vs. ND PBDE-99 (n=684; exp=27(11.8%)/201; ref= 45 (9.87%)/411 ≥75 th (26.9 ng/g) vs. ND PBDE-100 (n=410; exp=37(11.7%)/278; ref= 10 (10.6%)/84 ≥75 th (16.8 ng/g) vs. ND PBDE-153 (n=420; exp=31(9.71%)/288; ref= 9 (8.91%)/92 ≥75 th (24.6 ng/g) vs. ND ≥75th versus not detectable (ND) adjOR (95% CI) of prevalent metabolic syndrome PBB153 (n= 218; exp = 57 (41.9%)/79; ref = 18(22.0%)/64 ≥75th (13.1 ng/g) vs. ND PBDE-28 (n=265; exp=52 (42.3%)/71; ref= 50 (35.2%)/92 ≥75 th (5.4 ng/g) vs. ND PBDE-47 (n=164; exp=54 (37.5%)/90;	1.9 (0.9-4.0) , p-trend = <0.01 0.8 (0.5-1.4) , p-trend=0.93 2.7 (0.6-12.5) , p-trend=1.00 1.3 (0.7-2.2) , p-trend=0.57 1.4 (0.6-3.0) , p-trend=0.50 1.8 (0.8-4.0) , p-trend=0.15 3.1 (1.4-6.9) , p-trend<0.01 1.3 (0.7-2.4) , p-trend=0.09 1.1 (0.3-3.6) , p-trend=0.70	age, sex, race/ethnicity, poverty income ratio, and BMI metabolic syndrome age, sex, race/ethnicity, poverty income ratio, BMI, smoking, cotinine concentrations (ng/ml), alcohol consumption (g/day), and leisure-time physical activity)

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				ref= 6(30.0%)/14 ≥75 th (73.3 ng/g) vs. ND PBDE-99 (n=328; exp=34 (32.4%)/71; ref= 82 (36.8%)/141 ≥75 th (26.9 ng/g) vs. ND PBDE-100 (n=193; exp=54(38.3%)/87; ref= 16 (30.8%)/36 ≥75 th (16.8 ng/g) vs. ND PBDE-153 (n=199; exp=47(32.0%)/100; ref= 19(836.5%)/33 ≥75 th (24.6 ng/g) vs. ND	0.8 (0.5-1.5), p-trend=0.75 1.7 (0.7-3.8), p-trend=0.68 1.7 (0.7-3.8), p-trend=0.69	
Cross-sectional USA, NHANES Lin et al. (2009) environmental	NHANES 1999-2000, 2003-2004:1443 participants aged ≥12 years with complete data 474 adolescents, ≥ 12 - 20 years; 56.1% male; (38 or 8.0% with metabolic syndrome) 969 adults, >20 years; 49.1% male; (382 or 39.4% with metabolic syndrome)	metabolic syndrome In adolescents, 3 of 5 criteria: WC ≥ sex-specific 90 th percentile; FTrig>1.24mmol/l (110 mg/dL); HDL ≤1.04mmol/l (41 mg/dL); BP>sex-specific 90 th percentile or antihypertensive medication; FG>5.55 mmol/l (100 mg/dL) or anti- hyperglycemic medications In adults: WC>100 (♂), 88 (♀) cm; FTrig>1.69mmol/l (150 mg/dL); HDL <1.03mmol/l (40 mg/dl) (♂), 1.29mmol/l (50 mg/dl) (♀);BP> 130/85 or antihypertensive medication; FG> 6.10 mmol/l (110 mg/dL) or anti- hyperglycemic medication	PFHS, PFNA, PFOS,PFOA (serum, log scale) Mean levels Adolescents (≥12 years, <20 years) PFHS (log ng/ml): 0.95 ± 0.10 PFNA (log ng/ml): -0.35 ± 0.07 PFOA (log ng/ml): 1.51 ± 0.05 PFOS (log ng/ml): 3.11 ± 0.05 Adults (20 years) PFHS (log ng/ml): 0.60 ± 0.04 PFNA (log ng/ml): -0.21 ± 0.07 PFOA (log ng/ml): 1.48 ± 0.04 PFOS (log ng/ml): 3.19 ± 0.04	glucose PFHS, adolescent PFHS, adult PFNA, adolescent PFNA, adult PFOA, adolescent PFOA, adult PFOS, adolescent PFOS, adult insulin(log) PFHS, adolescent PFHS, adult PFNA, adolescent PFNA, adult PFOA, adolescent PFOA, adult PFOS, adolescent PFOS, adult HOMA-IR (log) PFHS, adolescent PFHS, adult PFNA, adolescent PFNA, adult PFOA, adolescent PFOA, adult PFOS, adolescent PFOS, adult β-cell function (log) PFHS, adolescent PFHS, adult PFNA, adolescent PFNA, adult PFOA, adolescent	β-coefficients (SEM), * p<0.05 $\beta = -0.01 \pm 0.03$ $\beta = -0.02 \pm 0.06$ $\beta = 0.07 \pm 0.04$ $\beta = 0.00 \pm 0.04$ $\beta = -0.03 \pm 0.05$ $\beta = -0.09 \pm 0.08$ $\beta = -0.03 \pm 0.06$ $\beta = -0.03 \pm 0.07$ β-coefficients (SEM), * p<0.05 $\beta = 0.06 \pm 0.03$ $\beta = 0.01 \pm 0.03$ $\beta = -0.10 \pm 0.05$ $\beta = -0.04 \pm 0.03$ $\beta = 0.08 \pm 0.07$ $\beta = 0.07 \pm 0.03$ $\beta = 0.15 \pm 0.08$ $\beta = 0.14 \pm 0.05^*$ β-coefficients (SEM), * p<0.05 $\beta = 0.05 \pm 0.03$ $\beta = 0.00 \pm 0.04$ $\beta = -0.08 \pm 0.04$ $\beta = -0.04 \pm 0.04$ $\beta = 0.08 \pm 0.05$ $\beta = 0.06 \pm 0.04$ $\beta = 0.15 \pm 0.07$ $\beta = 0.14 \pm 0.05^*$ β-coefficients (SEM), * p<0.05 $\beta = 0.05 \pm 0.03$ $\beta = 0.01 \pm 0.03$ $\beta = -0.12 \pm 0.06$ $\beta = -0.04 \pm 0.03$ $\beta = 0.08 \pm 0.05$	adjβs: age, sex, race, smoking status, alcohol intake, household income, waist circumference, CRP, HOMA/insulin, and medication *metabolic syndrome endpoints (waist, glucose, HDL, triglycerides) also adjusted for other components of the metabolic syndrome adjOR, model 4: age, sex, race, health behaviors (smoking status,

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
			PFOA, adult	$\beta = 0.07 \pm 0.03^*$	alcohol intake, and household income), measurement data (CRP and HOMA/insulin), medication model 5: model 4 + other component of metabolic syndrome
			PFOS, adolescent	$\beta = 0.13 \pm 0.09$	
			PFOS, adult	$\beta = 0.15 \pm 0.05^*$	
		metabolic syndrome, prevalence		adjOR (95% CI) per 1-unit increase in log PFC, model 4	
			PFHS, adolescent	OR=0.56 (0.22-1.45)	
			PFHS, adult	OR= 0.93 (0.73-1.19)	
			PFNA, adolescent	OR=0.37 (0.21-0.64)	
			PFNA, adult	OR= 0.92 (0.69-1.24)	
			PFOA, adolescent	OR=0.79 (0.30-2.12)	
			PFOA, adult	OR= 1.07 (0.73-1.57)	
			PFOS, adolescent	OR= 0.49 (0.18-1.30)	
			PFOS, adult	OR= 1.25 (0.86-1.82)	
		metabolic syndrome, waist		adjOR (95% CI), model 5	
			PFHS, adolescent	OR= 0.64 (0.45-0.91)	
			PFHS, adult	OR= 0.80 (0.58-1.10)	
			PFNA, adolescent	OR= 1.09 (0.61-1.95)	
			PFNA, adult	OR= 1.34 (0.93-1.92)	
			PFOA, adolescent	OR= 0.58 (0.34-1.00)	
			PFOA, adult	OR= 0.97 (0.65-1.46)	
			PFOS, adolescent	OR= 0.37 (0.16-0.82)	
			PFOS, adult	OR= 0.91 (0.59-1.41)	
		metabolic syndrome, glucose		adjOR (95% CI), model 5	
			PFHS, adolescent	OR= 0.98 (0.44-2.17)	
			PFHS, adult	OR= 0.76 (0.54-1.07)	
			PFNA, adolescent	OR= 3.16 (1.39-7.16)	
			PFNA, adult	OR= 0.86 (0.66-1.12)	
			PFOA, adolescent	OR= 0.55 (0.24-1.25)	
			PFOA, adult	OR= 0.87 (0.61-1.26)	
			PFOS, adolescent	OR= 0.58 (0.28-1.14)	
			PFOS, adult	OR= 0.84 (0.62-1.05)	
		metabolic syndrome, HDL		adjOR (95% CI), model 5	
			PFHS, adolescent	OR=0.93 (0.60-1.43)	
			PFHS, adult	OR= 1.00 (0.73-1.37)	
			PFNA, adolescent	OR=0.67 (0.45-0.99)	
			PFNA, adult	OR= 0.81 (0.65-1.00)	
			PFOA, adolescent	OR= 1.50 (0.67-3.36)	
			PFOA, adult	OR=1.22 (0.86-1.71)	
			PFOS, adolescent	OR= 1.38 (0.61-3.14)	
			PFOS, adult	OR= 1.61 (1.15-2.26)	
		metabolic syndrome, triglycerides		adjOR (95% CI), model 5	
			PFHS, adolescent	OR= 1.08 (0.83-1.40)	
			PFHS, adult	OR= 0.78 (0.60-1.02)	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				PFNA, adolescent PFNA, adult PFOA, adolescent PFOA, adult PFOS, adolescent PFOS, adult	OR=0.71 (0.37-1.34) OR= 0.99 (0.81-1.19) OR=1.15 (0.54-2.47) OR= 0.86 (0.65-1.13) OR= 0.78 (0.41-1.49) OR= 0.86 (0.65-1.16)	
Cross-sectional USA, NHANES Lin et al. (2010) environmental	2,216 adults from the NHANES 1999-2000 and 2003-2004.	PFOA and liver enzymes + interactions with BMI, metabolic syndrome and insulin resistance	PFC (serum level)	alanine aminotransferase (ALT, UI) overall BMI BMI 25-30 BMI ≥30 metabolic syndrome, no metabolic syndrome, yes HOMA-IR ≤1.61 HOMA-IR 1.61-2.91 HOMA-IR >2.91	unit increase per 1 unit increase in log PFOA (SE) 1.86 (95%CI 1.24-2.48) -0.65 (0.57) NS 3.85 (1.91), p=0.053 2.99 (0.95), p=0.004 1.73 (0.85), p=0.052 2.45 (1.12), p=0.036 -1.16 (0.88), p=0.194 3.46 (1.98), p=0.091 5.95 (2.27), p=0.014 Note: This study is not included in forest plot database	age, gender, race / ethnicity, smoking status, drinking status, education level), and measurement data (BMI, HOMA-IR, metabolic syndrome, and iron saturation status
	log- γ glutamyltransferase (GGT) overall BMI <25 BMI 25-30 BMI ≥30 metabolic syndrome, no metabolic syndrome, yes HOMA-IR ≤1.61 HOMA-IR 1.61-2.91 HOMA-IR >2.91	unit increase per 1 unit increase in log PFOA (SE) 0.08 (95%CI 0.05-0.11) 0.03 (0.04), p=0.56 0.09 (0.08), p=0.313 0.10 (0.04), p=0.24 0.07 (0.04), p=0.130 0.07 (0.04), p=0.144 -0.00 (0.06), p=0.96 0.16 (0.07), p=0.029 0.14 (0.05), p=0.015				
cross-sectional AFHS Longnecker et al. (2000) Vietnam veterans	1,197 male veterans in the Air Force Health Study (1997 examination cycle). One group participated in Operation Ranch Hand and was exposed to Agent Orange (n=169). The comparison group was individually matched by age, race, and military occupation and did not participate in Operation Ranch Hand (n=1028)	diabetes (self-report of physician diagnosed-diabetes or post challenge glucose of ≥200 mg/dL)	TCDD (Operation Ranch Hand status & serum TCDD, lipid adjusted)	adjOR (95% CI) for diabetes 1 st quartile (referent; <2.8 ng/kg lipid) [n=298, 26 diabetics (8.7%)/272 non-diabetics] [n=305, 25 diabetics (8.2%)/280 non-diabetics] [n=295, 57 diabetics (23.9%)/238 non-diabetics] 4 th quartile (≥5.2 ng/kg lipid) [n=299, 61 diabetics (20.4%)/238 non-diabetics] per 4 ng/g	1.00 0.91 (0.50-1.68) 1.77 (1.04-3.02) OR=1.56 (0.91-2.67) 1.37 (0.96-1.97)	Age, race, BMI, waist size, family history of diabetes, BMI at the time dioxin was measured, military occupation, serum triglycerides
cross-sectional US, multi-site Longnecker et al. (2001) #1440 environmental	2245 pregnant women from the Collaborative Perinatal Project (CPP) 44 diabetics (1.2%)/2201 without diabetes (37 had diabetes before pregnancy and with the young age most cases are type 1)	diabetes (self-report, suggested to be mostly T1D)	PCB (serum, lipid adjusted)	serum PCB <2.5 µg/l n=935; 9 diabetics (0.096%)/926 non-diabetics 2.5-3.75 µg/l n=679; 13 diabetics (1.95%)/666 non-diabetics 3.75-5 µg/l	adjOR (95% CI) OR=1.00 2.9 (1.1-7.3) 4.4 (1.6-12.5)	age, race, socioeconomic index, center, serum triglycerides, and cholesterol

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				n=318; 9 diabetics (2.91%)/309 non-diabetics ≥5.0 µg/l n=313; 13 diabetics (4.33%)/300 non-diabetics		
retrospective cohort US, 3M plant (MN) Lundin et al. (2009) occupational	Mortality in 3,993 employees who worked ≥ 1 year prior to Dec. 31, 1997 to 2002 at a 3M company plant in Cottage Grove, MN that manufactured PFOA manufacturing (807 total deaths; 23 diabetic deaths/784 non-diabetic deaths)	diabetes (death certificate)	PFOA (job classification and employment duration)	Diabetes SMR for exposure category probable versus general population of Minnesota 368 total deaths, 18 diabetes (4.9%)/350 non-diabetes Hazard ratio by job classification “moderate” versus “low” exposure “low”: 5 diabetes deaths “moderate”: 18 diabetes deaths *no diabetes deaths in “high” group so HR not calculated Hazard ratio by cumulative exposure (years) 1-4.9 (5 diabetes deaths) versus <1 (14 diabetes deaths) ≥5 (4 diabetes deaths) versus <1 (14 diabetes deaths) Pancreatic Cancer SMR for exposure category 368 total deaths, 7 pancreatic cancer deaths/361 non-pancreatic cancer Hazard ratio by job classification “moderate” versus “low” exposure “low”: 5 pancreatic cancer deaths “moderate”: 8 pancreatic cancer deaths *no pancreatic cancer deaths in “high” group so HR not calculated Hazard ratio by cumulative exposure (years) 1-4.9 (4 pancreatic cancer deaths) versus <1 (7 pancreatic cancer deaths) ≥5 (2 pancreatic cancer deaths) versus <1 (7 pancreatic cancer deaths) Heart Disease SMR for exposure category 368 total deaths, 93 ischemic heart disease deaths (25.3%)/275 non-ischemic heart disease deaths Hazard ratio by job classification	5.1 (1.9-13.8) SMR=2.0 (1.2-3.2) HR=3.7 (1.4-10.1) HR= 1.3 (0.5-3.7) HR= 1.3 (0.4-4.1) SMR=0.9 (0.4-1.8) HR=1.7 (0.5-5.2) HR= 2.3 (0.7-8.1) HR= 1.3 (0.3-6.4) SMR=1.0 (0.4-2.1)	sex, calendar period (SMR) or year of birth (HR)

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
				"moderate" versus "low" exposure HR=1.2 (0.9-1.7) "high" versus "low" exposure HR=0.9 (0.4-2.1) "low": 92 ischemic heart disease deaths "moderate": 103 ischemic heart disease deaths "high": 6 ischemic heart disease deaths <hr/> Hazard ratio by cumulative exposure (years) <hr/> 1-4.9 (42 ischemic heart disease deaths) versus <1 (138 ischemic heart disease deaths) HR= 1.2 (0.9-1.8) <hr/> ≥5 (21 ischemic heart disease deaths) versus <1 (42 ischemic heart disease deaths) HR=0.8 (0.5-1.2) <hr/> SMR for exposure category SMR=0.8 (0.6-0.9) 368 total deaths, 110 all heart disease deaths (29.9%)/258 non- all heart disease deaths	
cross-sectional US, West Virginia community MacNeil et al. (2009) environmental	53,346 residents, ≥ 20 years old, of six communities participating in the C8 Health Project where the drinking water was contaminated with PFOA (48% male) At least 10 years exposure prior to diagnosis (20 years residence): 1,055/ 12,508 (1035 cases and 12,106 controls available for regression analysis)	diabetes self-report or "validated" (self-report confirmed by medical records)	PFOA (serum)	Prevalence of validated type II diabetes among subjects residing in water district of interest for at least 20 years >191.2 versus <7.9ng/ml PFOA n=2098 OR=0.72 (0.52-1.00) Exposed: 189(18%)/861 Ref: 65(6.2%) /983 <hr/> Prevalence of self-report type II diabetes, no restriction on length of residence >191.2 versus <7.9 ng/ml PFOA n=8535 OR=0.61 (0.52-0.71) Exposed: 453(10.6%)/3821 Ref: 473(11.1%)/3788 <hr/> Prevalence of validated type II diabetes, no restriction on length of residence >191.2 versus <7.9 ng/ml PFOA n=7018 OR=0.62 (0.53-0.74) Exposed: 397(11.3%)/3116 Ref: 375(10.7%)/3130 <hr/> Regression model for outcome for the log of fasting glucose (based on 21,642 subjects) >191.2 versus <7.9 ng/ml PFOA -0.005 (p=0.29)	age, gender, race, BMI, regular exercise, family history of T2D, use of cholesterol -or blood-pressure-lowering medicine
cross sectional Saskatchewan, Canada Masley et al. (2000) environmental	Population-based survey in Saskatchewan; 511 men, 499 women, and 393 children (<18 years) living on a farm (52.2%, in a town (43.8%), or both (4%).	diabetes (self-report)	self-reported use of pesticides and fertilizers	n= 1010 (28 with diabetes (2.77%)/ 982 without diabetes) NR results not included in forest plot database	
cross sectional (three studies) Melzer et al. (, 2010 #1829}	3,974 adults (≥20 years) from NHANES 1999-2000, 2003-2004, and 2005-2006.	diabetes (self-report) heart disease (self-report of coronary heart disease, and/or angina,	PFOS, PFOA (serum)	PFOA OR (95% CI), p-value Diabetes (ever) n=3964; 456 with diabetes (8.7%) <hr/> Q1, n=1314; 186 with diabetes (10.9%) 1.00 <hr/> Q2, n=1035; 127 with diabetes (9.2%) 0.80 (0.55-1.17), p=0.242 <hr/> Q3, n=857; 83 with diabetes (7.7%) 0.74 (0.48-1.15), p=0.177	age, sex, race/ethnicity, education, smoking status, BMI, and alcohol intake

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
		and/or heart attack)		<p>Q4, n=758; 63 with diabetes (7%) 0.69 (0.41-1.16), p=0.158</p> <hr/> <p>Heart disease (ever) n=3,966; 321 with heart disease (5.8%)</p> <hr/> <p>Q1, n=1,314; 93 with heart disease (5.7%) 1.00</p> <hr/> <p>Q2, n=1,037; 93 with heart disease (6.1%) 0.95 (0.59-1.51), p=0.816</p> <hr/> <p>Q3, n=857; 78 with heart disease (5.9%) 1.02 (0.65-1.61), p=0.917</p> <hr/> <p>Q4, n=758; 57 with heart disease (5.4%) 1.08 (0.70-1.69), p=0.715</p> <hr/> <p>PFOS</p> <hr/> <p>Diabetes (ever) n=3964; 456 with diabetes (8.7%)</p> <hr/> <p>Q1, n=1,133; 122 with diabetes (8.6%) 1.00</p> <hr/> <p>Q2, n=1,012; 119 with diabetes (9.3%) 1.02 (0.70-1.47), p=0.928</p> <hr/> <p>Q3, n=916; 103 with diabetes (7.7%) 0.76 (0.50-1.18), p=0.218</p> <hr/> <p>Q4, n=903; 115 with diabetes (9.4) 0.87 (0.57-1.31), p=0.491</p> <hr/> <p>Heart disease (ever) n=3,966; 321 with heart disease (5.8%)</p> <hr/> <p>Q1, n=1,134; 69 (4.8%) 1.00</p> <hr/> <p>Q2, n=1,013; 85 (5.1%) 0.77 (0.49-1.23), p=0.270</p> <hr/> <p>Q3, n=916; 80 (5.7%) 0.83 (0.46-1.51) p=0.540</p> <hr/> <p>Q4, n=903; 87 (7.4%) 0.91 (0.50-1.64), p=0.745</p>	
retrospective cohort Michalek et al (1999) Vietnam veterans	1992 male Vietnam veterans (871 Vietnam Operation Ranch Hand Veterans and 1121 other Air Force veterans in Southeast Asia not involved in Operation Ranch Hand) mean age at assessment in 1992 examination=51-55 years	<p>Relationship between insulin and FG by TCDD category and diabetic status*</p> <p>*diabetes diagnosis before July 1995: verified medical diagnosis, 2-hr post-prandial glucose \geq 200 mg/dL</p> <p>diabetes cases/non-cases: total cohort: n=1992; 236 (11.8%)/1756 Operation Ranch Hand: total n=871; 111 (12.7%)/760 "high" n=248; 43 (17.3%)/205 Reference group: n=1121; 125 (11.1%)/996</p>	TCDD (1987 serum, lipid adjusted)	<p>Geometric mean insulin and fasting glucose in 1992 based on 1987 TCDD categories of "high" (45.8 ppt in 1987, range: 18-617.8) vs. referent (3.9ppt, range: 0-10)</p> <hr/> <p>Insulin</p> <hr/> <p>non-diabetics: "high" vs. referent 67.7 vs. 81.1 μU/mL, p=0.004</p> <hr/> <p>diabetics: "high" vs. referent 63.6 vs. 48.5 μU/mL, p=0.21</p> <hr/> <p>fasting glucose</p> <hr/> <p>non-diabetics: "high" vs. referent 99 vs. 98.6 mg/dL, p=0.52</p> <hr/> <p>diabetics: "high" vs. referent 137.4 vs. 156.1 mg/dL, p=0.03</p>	age and percent body fat
retrospective cohort Michalek et al (2003) Vietnam veterans	343 Vietnam Operation Ranch Hand veterans (100% male); mean age in 1982=42.1	<p>diabetes (medical diagnosis, 2-hr post-prandial glucose \geq 200 mg/dL)</p> <p>92 with diabetes (26.8%)/251 without diabetes</p>	<p>TCDD (1982-1997 serum, lipid adjusted)</p> <p>1982 median (range) 40.8 (11.5-422.7)ppt</p>	<p>Proportional hazard model of time to onset of diabetes and TCDD elimination rate (λ)</p> <hr/> <p>Logistic and ANCOVA models of diabetes prevalence and TCDD elimination rate (λ)</p> <hr/> <p>no relationship after adjustment for covariates</p> <hr/> <p>no relationship after adjustment for covariates</p> <hr/> <p>Number and percentage of veterans with diabetes by TCDD elimination rate stratum</p>	age, BMI at tour/percent change, smoking, and family history

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				TCDD elimination rate stratum	diabetes prevalence	
				$\lambda \leq 5^{\text{th}}$ percentile	n=17, 6 diabetics (35.3%), p = 0.41	
				$\lambda > 5^{\text{th}}$ percentile	n=325, 85 diabetics (26.2%)	
				$\lambda > 95^{\text{th}}$ percentile	n=20, 6 diabetes (30%), p=0.72	
				$\lambda \geq 95^{\text{th}}$ percentile	n=322, 85 diabetics (26.4%)	
retrospective cohort Michalek et al (2008) Vietnam veterans	2469 male Vietnam veterans; 1020 Operation Ranch Hand veterans (AFHS follow-up of 2469 through 2004) (exposed) and 1449 Southeast Asia (SEA) Veterans (100% male; median age of groups, 62 to 65 years)	medical diagnosis or 2-hr post-prandial glucose ≥ 200 mg/dL n=2469; 1305 diabetics (52.9%)/1164 non-diabetics	serum TCDD, lipid adjusted anch Hand veterans (median TCDD = 12.6 ppt in diabetics and 10.6 ppt in non-diabetics) vs. SEA comparison group (median TCDD = 4.0 ppt in diabetics and 3.9 ppt in non-diabetics)	adjRR for diabetes, AFHS versus SEA Ranch Hands: n= 1020, 180 cases (17.7%) SEA: n= 1449, 259 cases (17.9%) Calendar period in Vietnam During or before 1969 (130 cases) background, ≤ 10 ppt (39 cases/274 total) low, 10-91 ppt (40 cases/176 total) high, >91 ppt (51 cases/207 total) After 1969 (50 cases) Spraying during tour ≥ 90 days (170 cases) background, ≤ 10 ppt (42 cases/364 total) low, 10-91 ppt (60 cases/269 total) high, >91 ppt (68 cases/275 total) < 90 days (10 cases) Stratified by calendar period of service and days of spraying ≤ 1969 and ≥ 90 d (229 cases)	RR=1.21, p=0.16 RR=1.65 (p=0.005) RR = 1.26 (0.8-1.98) 1.87 (1.21-2.89) 1.97 (1.26-3.06) 0.85 (p=0.45) RR=1.32 (p=0.04) 0.97 (0.66-1.43) 1.45 (1.04-2.02) 1.58 (1.12-2.24) RR=0.57 (p=0.12) HR=1.39 (1.21-1.58)	adjusted for BMI at blood draw, smoking history (pack-year), family history of diabetes, BMI at tour, year of birth, last calendar year of service in Southeast Asia, Vietnam days/SEA days, occupation.
prospective cohort US, Iowa & North Carolina Montgomery et al. (2008) occupational	31,787 licensed private pesticide applicators (97.4% male) who did not have diabetes at baseline in the Agricultural Health Study. Follow-up interviews were conducted 5 years later(1999-2003); 34% < 40 years old, 28% 40-49yrs, 22% 50-59yrs, 13% were 60-69yrs, and 3% were > 70 years old.	Self-reported of doctor diagnosed incident diabetes (patients with diabetes at/prior to enrollment were excluded) n=31,787; 1,176 diabetics and 30,611 non-diabetics	50 pesticides (self-report at enrollment of "ever" use and cumulative days of use)	Organochlorine, "ever" use n = 15,325 (666 diabetics/14,659 non-diabetics); 380 exposed cases (57%) Aldrin, "ever" use n = 5,678 (261 diabetics/5,417 non-diabetics) 70 exposed cases (27%) Aldrin, never vs. >100 days of use n=241 (16 diabetics/225 non-diabetics) Chlordane, "ever" use n = 7,737 (372 diabetics/7,365 non-diabetics) 141 exposed cases (38%) Chlordane, never vs. >100 days of use n=174 (15 diabetics/159 non-diabetics) Dieldrin, "ever" use n=2,127 (96 diabetics/2,031 non-diabetics) 9 exposed cases (10%) DDT, "ever" use	OR=1.01 (0.91-1.16) 1.14 (0.97-1.33)* 1.51 (0.88-2.58), p-trend=0.08 1.16 (1.01-1.34) 1.63 (0.93-2.86), p-trend=0.05 1.03 (0.83-1.30) 1.09 (0.94-1.27)	age, state, BMI
	Herbicides, "ever" use n=30,286 (1,102 diabetics/29,184 non-diabetics) 1035 exposed cases (94%)				0.92 (0.72-1.18)	
	2,4,5-T, "ever" use n=6,493 (273 diabetics/6,220 non-diabetics) 76 exposed cases (28%)				1.02 (0.88-1.19)	
	2,4,5-TP "ever" use				1.04 (0.85-1.27)	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
n=2,682 (120 diabetics/2,562 non-diabetics) 15 exposed cases (13%)				n=7,519 (409 diabetics/7,110 non-diabetics) 167 exposed cases (41%)	
2,4-D, "ever" use n=23,733 (822 diabetics/22,911 non-diabetics) 600 exposed cases (73%)	0.92 (0.79-1.06)			Heptachlor, "ever" use n=4,778 (209 diabetics/4,569 non-diabetics) 45 exposed cases (22%)	1.20 (1.01-1.34)
Alachor, "ever" use n=15,779 (585 diabetics/15,194 non-diabetics) 339 exposed cases (58%)	1.14 (1.00-1.30)			Heptachlor, never vs. >100 days of use n=158 (11 diabetics/147 non-diabetics)	1.94 (1.02-3.69), p-trend=0.02
Alachor, never vs. >100 days of use n=5,214 (240 diabetics/4,974 non-diabetics)	1.31 (1.11-1.55), p-trend=0.001			Lindane, "ever" use n=5920 (192 diabetics/5728 non-diabetics) 38 exposed cases (20%)	0.94 (0.80-1.11)
Atrazine, "ever" use 22,373 (796 diabetics/21,577 non-diabetics) 557 exposed cases (70%)	1.07 (0.93-1.23)			Toxaphene, "ever" use n=4,235 (224 diabetics/4,011 non-diabetics) 51 exposed cases (23%)	1.14 (0.97-1.33)
Atrazine, never vs. >100 days of use n=9,375 (370 diabetics/9,005 non-diabetics)	1.15 (0.98-1.36), p-trend=0.02			Toxaphene, never vs. >100 days of use n=250 (13 diabetics/237 non-diabetics)	0.82 (0.46-1.46), p-trend=0.80
Butylate, "ever" use n=9,437 (328 diabetics/9,109 non-diabetics) 111 exposed cases (34%)	1.07 (0.93-1.24)				
Chlorimuron-ethyl, "ever" use n=10,803 (339 diabetics/10,494 non-diabetics) 118 exposed cases (35%)	1.01 (0.88-1.16)				
Cyanazine, "ever" use n=12,442 (408 diabetics/12,034 non-diabetics) 163 exposed cases (40%)	1.27 (1.09-1.47)			Carbamates, "ever" use n=20,071 (804 diabetics/19,267 non-diabetics) 546 exposed cases (68%)	1.00 (0.88-1.14)
Cyanazine, never vs. >100 days of use n=3,294 (115 diabetics/3,179 non-diabetics)	1.38 (1.10-1.72), p-trend=0.004			Aldicarb, "ever" use n=3,174 (163 diabetics/3,011 non-diabetics) 27 exposed cases (17%)	1.10 (0.91-1.34)
Dicamba, "ever" use n=15,073 (434 diabetics/14,639 non-diabetics) 186 exposed cases (43%)	0.99 (0.85-1.15)			Aldicarb, never vs. >100 days of use n=274 (15 diabetics/259 non-diabetics)	0.97 (0.56-1.68), p-trend=0.90
EPTC, "ever" use n=5,913 (180 diabetics/5,733 non-diabetics) 32 exposed cases (18%)	1.10 (0.93-1.31)			Carbaryl, "ever" use n=16,900 (702 diabetics/16,198 non-diabetics) 477 exposed cases (68%)	1.10 (0.95-1.28)
EPTC, never vs. >100 days of use n=980 (31 diabetics/949 non-diabetics)	1.07 (0.74-1.56), p-trend=0.56			Carbaryl, never vs. >100 days of use n=1,694 (94 diabetics/1,600 non-diabetics)	0.95 (0.72-1.25), p-trend=0.67
Glyphosate, "ever" use n=23,937 (865 diabetics/23,072 non-diabetics) 657 exposed cases (76%)	0.85 (0.74-0.98)			Carbofuran, "ever" use n=8,267 (330 diabetics/7,937 non-diabetics) 108 exposed cases (33%)	1.05 (0.91-1.20)
Metolachlor, "ever" use n=13,648 (444 diabetics/13,204 non-diabetics) 195 exposed non-cases (44%)	1.05 (0.92-1.19)				
Metribuzin, "ever" use n=13,398 (400 diabetics/12,998 non-diabetics) 168 exposed cases (42%)	0.96 (0.83-1.10)				
Metribuzin, never vs. >100 days of use	1.44 (0.94-2.21), p-trend=0.06				

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
n=599 (25 diabetics/574 non-diabetics)					
Paraquat, "ever" use n=6,882 (313 diabetics/6,509 non-diabetics) 100 exposed cases (32%)	1.01 (0.87-1.18)			Pyrethroids, "ever" use n=7,241 (235 diabetics/7,006 non-diabetics) 47 exposed cases (20%)	1.07 (0.92-1.25)
Pendimethalin, "ever" use n=12,907 (453 diabetics/12,454 non-diabetics) 208 exposed cases (46%)	1.04 (0.92-1.19)			Permethrin (crops), "ever" use n=3,999 (150 diabetics/3,849 non-diabetics) 22 exposed cases (15%)	1.09 (0.91-1.31)
Petroleum oil, "ever" use n=13,894 (479 diabetics/13,415 non-diabetics) 239 exposed cases (50%)	1.13 (0.99-1.29)			Permethrin (animals), "ever" use n=4,103 (106 diabetics/3,997 non-diabetics) 11 exposed cases (11%)	1.04 (0.84-1.29)
Petroleum oil, never vs. >100 days n=912 (30 diabetics/882 non-diabetics)	0.93 (0.63-1.37), p-trend=0.72			Fungicides, "ever" use n=11,011 (496 diabetics/10,515 non-diabetics) 208 exposed cases (42%)	1.01 (0.88-1.15)
Trifluralin, "ever" use n=15,625 (493 diabetics/15,132 non-diabetics) 241 exposed cases (49%)	1.01 (0.88-1.16)			Benomyl, "ever" use n=2,926 (144 diabetics/2,782 non-diabetics) 20 exposed cases (14%)	0.90 (0.74-1.10)
Organophosphates, "ever" use n=27,307 (978 diabetics/26,329 non-diabetics) 811 exposed cases (83%)	1.02 (0.86-1.20)			Captan, "ever" use n=3,476 (115 diabetics/3,361 non-diabetics) 13 exposed cases (12%)	1.00 (0.82-1.23)
Chlorpyrifos, "ever" use n=13,173 (466 diabetics/12,707 non-diabetics) 191 exposed cases (41%)	1.03 (0.91-1.17)			Chlorothalonil, "ever" use n=2,409 (132 diabetics/2,277 non-diabetics) 15 exposed cases (12%)	1.04 (0.85-1.27)
Chlorpyrifos, never vs. >100 days n=2,818 (123 diabetics/2,695 non-diabetics)	1.24 (1.02-1.52), p-trend=0.04			Maneb, "ever" use n=2,863 (146 diabetics/2,717 non-diabetics) 21 exposed cases (15%)	0.96 (0.79-1.16)
Coumaphos, "ever" use n=2,639 (111 diabetics/2,528 non-diabetics) 12 exposed cases (11%)	1.26 (1.03-1.55)			Metalaxyl, "ever" use n=6,818 (322 diabetics/6,496 non-diabetics) 103 exposed cases (32%)	1.02 (0.88-1.20)
Coumaphos, never vs. >100 days n=456 (16 diabetics/440 non-diabetics)	0.94 (0.56-1.56), p-trend=0.79			Ziram, "ever" use n=466 (19 diabetics/447 non-diabetics) 1 exposed case (2%)	0.92 (0.57-1.47)
Diazinon, "ever" use n=9,509 (387 diabetics/9,122 non-diabetics) 154 exposed cases (40%)	0.98 (0.85-1.13)			Fumigants "ever" use n=7,095 (357 diabetics/6,738 non-diabetics) 107 exposed cases (30%)	1.04 (0.90-1.19)
Diazinon, never vs. >100 days of use n=471 (36 diabetics/435 non-diabetics)	1.59 (1.09-2.31) p-trend=0.006			Aluminum phosphide, "ever" use n=1,422 (59 diabetics/1,363 non-diabetics) 33 exposed cases (6%)	1.18 (0.90-1.55)
Dichlorvos, "ever" use n=3,215 (110 diabetics/3,105 non-diabetics) 12 exposed cases (11%)	1.21 (0.98-1.49)			Aluminum phosphide, never vs. >10 days n=241 (10 diabetics/231 non-diabetics)	1.10 (0.57-2.12), p-trend=0.69
Dichlorvos, never vs. >100 days of use n=1,231 (44 diabetics/n=1,187 non-diabetics)	1.26 (0.91-1.73), p-trend=0.15			Carbon tetrachloride, "ever" use n=1,672 (73 diabetics/1,599 non-diabetics) 5 exposed cases (7%)	1.03 (0.80-1.33)
Fonofos, "ever" use n=6,486 (193 diabetics/6,293 non-diabetics) 36 exposed cases (19%)	1.02 (0.86-1.21)			Ethylene dibromide, "ever" use n=1,033 (43 diabetics/990 non-diabetics) 1 exposed case (4%)	0.82 (0.60-1.13)
Malathion, "ever" use n=21,163 (766 diabetics/20,397 non-diabetics) 574 exposed cases (75%)	1.10 (0.95-1.27)			Methyl bromide, "ever" use n=4,889 (268 diabetics/4,621 non-diabetics) 64 exposed cases (24%)	0.99 (0.84-1.16)

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For																
Parathion, "ever" use n=4,497 (218 diabetics/4,279 non-diabetics) 50 exposed cases (23%)	1.03 (0.88-1.22)																				
Phorate, "ever" use n=9,655 (345 diabetics/9,310 non-diabetics) 124 exposed cases (36%)	1.22 (1.06-1.42)																				
Phorate, never vs. >100 days of use n=671 (27 diabetics/644 non-diabetics)	1.05 (0.70-1.58), p-trend=0.68																				
Terbufos, "ever" use n=11,669 (392 diabetics/11,277 non-diabetics) 152 exposed cases (39%)	1.17 (1.02-1.35)																				
Terbufos, never vs. >100 days of use n=3,352 (116 diabetics/3,236 non-diabetics)	1.14 (0.93-1.41), p-trend=0.19																				
Trichlorfon, "ever" use n=182 (13 diabetics/169 non-diabetics) 1 exposed cases (1%)	1.85 (1.03-3.33)																				
Trichlorfon, never vs. >10 days of use n=82 (7 diabetics/75 non-diabetics)	2.47 (1.10-5.56) p-trend=0.02																				
longitudinal intervention trial Czech Republic Mullerova et al. (2008) environmental	27 obese adult women, aged 21-74 years, BMI>30kg/m ² were randomly recruited from patients of Centre for Obesity Treatment. 9 non-obese healthy control women volunteers, aged 21-64 years, BMI=19-25 kg/m ² were recruited as controls. Obese women were put on a 3 month low-calorie-diet intervention (n=22 measured post-intervention)	HOMA index: fasting glucose (mmol/l) x fasting insulin (mIU/ml)/22.5 Immuno reactive adiponectin, C-reactive protein, and interleukin-6	PCB153 (plasma) Obese: 0.15 ng/ml Control: 0.14 mg/ml Obese post-intervention: 0.16ng/ml	Correlation between adiponectin (ln [µg/ml] and PCB153 (pooled analysis of all subjects, including those <0.02ng/ml QL) Obese subjects (n=27) r=-2.59, (R²=0.335, p<0.001) Control subjects (n=9) r=-5.99 (R² = 0.0268, p<0.337) Obese post-intervention (n=22) r=3.803 (R² = 0.0782, p<0.139) There was no correlation between PBC153 and study group (P-value > 0.05), C-reactive protein, interleukin-6, insulinemia or HOMA (data not shown)	None reported																
cross-sectional US, NHANES Nelson et al. (2010) environmental	data from 860 participants (12-80 years old) in NHANES 2003-2004	HOMA = [fasting insulin (µU/mL) x fasting glucose (mmol/L)/22.5]	serum PFOS, PFOA	difference in log-HOMA Q4 vs Q1 (ages20-80, ♂+♀, n=524), β and p-trend PFOS +0.12 log-HOMA, p-trend = 0.25 PFOA +0.15 log-HOMA, p-trend = 0.31 PFNA +0.05 log-HOMA, p-trend = 0.59 PFHxS +0.18 log-HOMA, p-trend = 0.14 total cholesterol, β (95% CI) by age and gender Q4 vs Q1, β (95%CI), p-trend <table border="1"> <thead> <tr> <th></th> <th>12-19</th> <th>20-59</th> <th>60-80</th> </tr> </thead> <tbody> <tr> <td>PFOS, ♂</td> <td>3.61 (-8.48, 15.70) p-trend=0.49</td> <td>10.54 (-4.79, 25.88) p-trend=0.10</td> <td>13.30 (-19.33, 45.92) p-trend=0.22</td> </tr> <tr> <td>PFOS, ♀</td> <td>-0.38 (-9.32, 8.57) p-trend=0.88</td> <td>0.64 (-13.52, 14.80) p-trend=0.56</td> <td>0.18 (6.00, 39.34) p-trend=0.01</td> </tr> <tr> <td>PFOA, ♂</td> <td>4.95 (-0.233, 12.24)</td> <td>6.2 (-10.14, 22.54)</td> <td>19.97 (-10.91, 50.86)</td> </tr> </tbody> </table>		12-19	20-59	60-80	PFOS, ♂	3.61 (-8.48, 15.70) p-trend=0.49	10.54 (-4.79, 25.88) p-trend=0.10	13.30 (-19.33, 45.92) p-trend=0.22	PFOS, ♀	-0.38 (-9.32, 8.57) p-trend=0.88	0.64 (-13.52, 14.80) p-trend=0.56	0.18 (6.00, 39.34) p-trend=0.01	PFOA, ♂	4.95 (-0.233, 12.24)	6.2 (-10.14, 22.54)	19.97 (-10.91, 50.86)	Age, gender, race/ethnicity, socioeconomic status, saturated fat intake, exercise, time in front of a TV or computer, alcohol consumption (≥20 years),
	12-19	20-59	60-80																		
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difference in lipids, Q4 versus Q1, β and p-trend																					
PFC (median µg/L in Q4 /Q1)	total cholesterol (mg/dL)	HDL (mg/dL)	non-HDL (mg/dL)	LDL (mg/dL)																	
PFOS (37.5 vs 9.9 µg/L)	+13.4, p-trend = 0.01	+0.9, p-trend = 0.78	+12.6, p-trend = 0.02	+8.5, p-trend = 0.27																	
PFOA (6.9 vs 2.1 µg/L)	+9.8, p-trend = 0.07	-1.3, p-trend = 0.34	+11.0, p-trend = 0.05	+2.9, p-trend = 0.84																	
PFNA (2 vs 0.4 µg/L)	+13.9, p-trend = 0.04	-2.0, p-trend = 0.31	+15.9, p-trend = 0.04	+13.3, p-trend = 0.08																	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For				
PFHxS (5.3 vs 0.8 µg/L)	-7.0, p-trend = 0.07	+2.3, p-trend = 0.11	-9.3, p-trend = 0.04	-9.7, p-trend = 0.10	p-trend=0.26	smoking (≥20 years), and parity (≥20 years)			
					PFOA, ♀		3.34 (-4.15, 10.83) p-trend=0.33	1.52 (-12.51, 15.55) p-trend=0.82	7.98 (-14.97, 30.93) p-trend= 0.14
					PFNA, ♂		4.05 (-8.48, 16.58) p-trend=0.24	7.52 (-3.74, 18.25) p-trend=0.29	21.56 (-11.51, 54.62) p-trend=0.19
					PFNA, ♀		8.19 (-3.89, 20.26) p-trend=0.19	11.50 (-2.51, 25.51) p-trend=0.16	17.96 (-11.79, 47.71) p-trend=0.08
					PFHxS, ♂		-3.18 (-15.37, 9.02) p-trend=0.38	-3.68 (-17.52, 10.17) p-trend=0.55	-27.09 (-61.92, 7.75) p-trend=0.21
					PFHxS, ♀		-12.72 (-23.44, -1.99) p-trend=0.02	-8.12 (-22.43, 6.19) p-trend=0.04	-8.85 (-28.12, 10.41) p-trend=0.30
cross-sectional US, 3M plant (MN) Olsen et al. (2000) occupational	265 male fluorochemical production workers assessed in 1993 (n=111), 1995 (n=80), and/or 1997 (n= 74)	serum lipids (voluntary medical surveillance)	PFOA (serum, ppm) 1993: 0 to <1 ppm (n=52), 1 to <10 (n=39), ≥10 (n=29) 1995: 0 to <1 ppm (n=46), 1 to <10 (n=26), ≥10 (n=34) 1997: 0 to <1 ppm (n=13), 1 to <10 (n=15), ≥10 (n=11)	ANOVA comparisons across 0 to <1, 1 to <10, ≥10 ppm categories Cholesterol for 1993, 1995, and 1997 PFOA F value=0.8 to 2.7, p = NS HDL for 1993, 1995, and 1997 PFOA F value=0.4 to 1.2, p = NS LDL for 1993, 1995, and 1997 PFOA F value=0.1 to 2.3, p = NS Triglycerides for 1993, 1995, and 1997 PFOA F value=0.3 to 2.7, p = NS Serum lipids F value=0.1 to 2.7, p = NS Multiple regression analysis HDL for 1993, 1995, and 1997 PFOA βs -1.61 to -0.10, NS except for 1990 (p=0.04)	Age, alcohol use, cigarette use, testosterone (1993, 1995)				
cross-sectional US, 3M plants Olsen et al. (2007) occupational	506 Fluorochemical production workers (93% male) taking part in the 2000 medical surveillance program at 3M locations in Antwerp, Belgium (n=196), Cottage Grove, MN (n=122), and Decatur, AL (n=188)	serum lipids (voluntary medical surveillance)	PFOA (serum, concurrent with samples for lipid analysis) mean µg/ml (range) all: 2.21 (0.01-92.03) <u>Antwerp:</u> 1.02 (0.01-7.04) <u>Cottage Grove:</u> 4.63 (0.01-92.03) <u>Decatur:</u> 1.89 (0.04- 12.70)	all locations cholesterol 0.05, NS LDL 0.006, NS HDL -0.17, p<0.0001 triglycerides 0.21, p<0.0001 Mean levels by location (all, Antwerp, Cottage Grove, Decatur) significantly different (p<0.05) from ^a Antwerp, ^b Cottage Grove, ^c Decatur cholesterol 214, 217, 210, 214 (NS) LDL 136, 139 ^b , 130 ^a , 136 HDL 49, 55 ^{b,c} , 46 ^a , 44 ^a triglycerides 159, 120 ^{b,c} , 187 ^a , 182 ^a all locations adjOR (95%CI), 10th vs 1st decile cholesterol ≥200 mg/dl 1.1 (0.5-2.6), model 1 LDL ≥130 mg/dl 1.1 (0.5-2.6), model 2 LDL ≥130 mg/dl 1.2 (0.5-2.8), model 1 LDL ≥130 mg/dl 1.4 (0.6-3.3), model 2 HDL ≤40 mg/dl 2.6 (1.0-6.8), model 1	OR model 1 (and βs): age, BMI, alcohol OR model 2: age, BMI, alcohol, location OR model 3: age				
	adjβ (SE); *p < 0.05								
	all locations	Antwerp, Belgium	Cottage Grove, MN	Decatur, AL					
In cholesterol	0.0076 (0.0059)	0.013 (0.0096)	0.0021 (0.01)	0.00266 (0.0141), p=0.06					
In LDL	0.0021 (0.009)	0.0106 (0.0147)	0.0049 (0.0145)	0.0302 (0.0200)					

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
In HDL	-0.0183 (0.0069)*	-0.0095 (0.0131)	-0.0192 (0.0120)	-0.0207 (0.0141)	1.8 (0.7-4.8), model 2	
In triglycerides	0.0711 (0.0169)*	0.0980 (0.0270)*	0.0280 (0.0314)	0.0689 (0.0376), p=0.07	triglycerides ≥150 mg/dl 2.4 (1.0-5.8), model 1 1.8 (0.8-4.4), model 2 metabolic syndrome 1.0 (0.3-3.6), model 3	
cross-sectional Germany, BASF plant Ott et al. (1994) occupational	138 employees who had been potentially exposed to TCDD following a 1953 trichlorophenol autoclave accident and 6474 referents. Results of 34 clinical tests were analyzed, but only fasting glucose summarized here (mean age=61 years)	fasting glucose	TCDD (serum and chloracne status) current <1 - 553 ppt and log TCDD (back calculated to time of exposure): 3.3-12,000ppt	Fasting glucose (n=134 in study group; 6475 in referent group) current TCDD β=0.062 (p<0.15) log (TCDD) back calculated or chloracne status data not shown, NS	age, BMI, smoking	
cross-sectional Germany, BASF plant Ott et al. (1994) occupational	42 men; 34 male production employees and 8 technical support personnel who were potentially exposed to PBDDs and PBDFs during production of resins containing PBDEs. Referents were 42 men from other resin producing plant that did not use PBDEs	fasting glucose	2,3,7,8-TBDD (serum)	fasting glucose (log transformed); study group (n=41) versus referent group (n=42) fasting glucose (log transformed), regression slope TBDD estimate	103.4 vs. 103.7 mg/dl, p=0.81 β=-0.00023 (SD=0.00016), NS	
case control South Korea, Uljin County Park et al. (2010) environmental	100 subjects ≥40 years of age: 50 non-diabetic subjects (28% male) with metabolic syndrome and 50 age and sex matched non-diabetic controls without metabolic syndrome taking part in community-based health survey from June-December 2006 in Uljin county, South Korea	metabolic syndrome (diabetes excluded) waist ≥ 90 (♂), 80 (♀) cm FTrig≥150 mg/dL HDL < 40 (♂), 50 (♀) mg/dLBP≥ 130/85mmHG or medication FG≥110 mg/dL insulin resistance (HOMA-IR)	organochlorine pesticides (serum, lipid adjusted; ng/g lipid, ppb) β-HCH, hexachlorobenzene, oxychlorodane, trans-nonachlor, heptachlor epoxide, o,p'-DDE, p,p'-DDE, p,p'-DDT what is evidence for stronger associations at lower levels of exposure?	(OR (95% CI) for 3rd tertile versus 1st tertile (referent) [median serum ppb 1st (reference), 2nd, 3rd tertiles] and correlation between HOMA-IR and log-transformed serum β-HCH 21.4, 39.3, 66.8 ppb 3 rd tertile: 26 cases (60.4%)/17 non-cases 1 st tertile (ref): 6 cases (26%)/17 non-cases OR (95% CI) or correlation Model 1: 4.4 (1.4-13.5) Model 2: 1.6 (0.4-71), p-trend = 0.51 0.7 (0.2-3.0), model 2 2.9 (0.6-13.5), model 2 0.7 (0.2-3.3), model 2 5.1 (0.6-46.2), model 2 0.3 (0.1-1.4), model 2 Pearson correlation with HOMA-IR cases (0.22, NS); non-cases (0.16, NS), model 2 Hexachlorobenzene 13.3, 20.6, 31.1 ppb 3 rd tertile: 15 cases (46.9%)/17 non-cases 1 st tertile (ref): 25 cases (59.5%)/17 non-cases correlation with HOMA-IR cases (0.20, NS) and non-cases (0.13, NS), model 2 Oxychlorodane 4.4, 7.7, 12.6 ppb 3 rd tertile: 19 cases (52.8%)/17 non-cases 1 st tertile (ref): 18 cases (51.4%)/17 non-cases correlation with HOMA-IR cases (0.25, NS) and non-cases (0.08, NS), model 2 Trans-nonachlor 9.6, 17.9, 37.2 ppb Model 1: 1.6 (0.5-4.9)	Model 1: age, sex, alcohol, and smoking Model 2: age, sex, alcohol, smoking, and BMI	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
				<p>3rd tertile: 20 cases (54.1%)/17 non-cases 1st tertile (ref): 14 cases (45.2%)/17 non-cases correlation with HOMA-IR</p> <p>Model 2: 0.8 (0.2-3.5), p-trend = 0.81</p> <p>cases (0.20, NS) and non-cases (0.06, NS), model 2</p> <p>Heptachlor epoxide</p> <p>3.0, 5.3, 12.7 ppb 3rd tertile: 27 cases (61.4%)/17 non-cases 1st tertile (ref): 5 cases (22.7%)/17 non-cases</p> <p>Model 1: 6.0 (1.8-20.2) Model 2: 4.60(0.9-23.5), p-trend = 0.10</p> <p>waist ≥ 90(♂), 80 (♀) cm: 1.6 (0.3-8.0), model 2 high BP (≥130/85 mmHg or medication): 6.6 (1.3-34.7), model 2 high Trig(≥150 mg/dL): 3.9 (0.8-20.1), model 2 high FG(≥100 mg/dL): 3.5 (0.8-15.3), model 2 low HDL [<40 (♂), 50 (♀) mg/dL]: 1.9 (0.4-7.9) correlation with HOMA-IR: cases (0.32, p<0.05) and non-cases (0.20, NS), model 2</p> <p>o,p'-DDE</p> <p>0.2, 0.9, 2.0 ppb 3rd tertile: 13 cases (43.3%)/17 non-cases 1st tertile (ref): 23 cases (57.5%)/17 non-cases</p> <p>Model 1: 0.5 (0.2-1.4) Model 2: 0.4 (0.1-1.6), p-trend = 0.15</p> <p>correlation with HOMA-IR: cases (0.22, NS) and non-cases (0.07, NS)</p> <p>p,p'-DDE</p> <p>161, 314.6, 723.8 ppb 3rd tertile: 19 cases (52.8%)/17 non-cases 1st tertile (ref): 16 cases (48.5%)/17 non-cases</p> <p>Model 1: 1.1 (0.4-3.1) Model 2: 0.6 (0.2-2.3), p-trend = 0.48</p> <p>correlation with HOMA-IR: cases (0.13, NS) and controls (-0.01, NS), model 2</p> <p>p,p'-DDT</p> <p>10.7, 18.0, 33.6 ppb 3rd tertile: 20 cases (54.1%)/17 non-cases 1st tertile (ref): 18 cases (51.4%)/17 non-cases</p> <p>Model 1: 1.2 (0.4-3.1) Model 2: 1.4 (0.3-5.9), p-trend = 0.64</p> <p>correlation with HOMA-IR: cases (0.10, NS) and controls (0.04, NS), model 2</p>	
prospective cohort Netherlands (Patandin <i>et al.</i> 1998) environmental	207 mother-infant pairs, infants born at term from 1990-1992 without congenital anomalies or diseases were recruited. Mothers selected intended to use either formula (FF group, N=102) or to breast-feed (BF, N=105) their child for at least 6 weeks were included. FF infants received formula from the same batch from birth until 7 months of age.	<u>Growth</u> Weight was measured at birth, and weight, length or height, and head circumference were measured at 10 days, 3, 7, 18, and 42 months. Data converted into SDS using weight, height and head circumference standards of healthy Dutch children as reference data.	PCBs cord and maternal during pregnancy serum , ΣPCB118, PCB138, PCB153, PCB180 breast milk : total TEQ (the 17 most abundant 2,3,7,8-substituted PCDD and PCDF congeners, three planar PCBs (77, 126, and 169); three mono-ortho PCBs (105, 118, 156); two di-ortho	<p>ln(ΣPCB)</p> <p>birth weight (cord blood) -119.4 (±53.7), p=0.027 birth weight (maternal serum) -123.1 (±64.4), p=0.057</p> <p>ln(ΣPCB)</p> <p>formula fed group, prenatal exposure to PCBs</p> <p>body weight change, birth/d10 to 3 months -0.37 (±0.09), p=0.0001 body length change, birth/d10 to 3 months -0.36 (±0.08), p<0.0001 head circumference change, birth/d10 to 3 months -0.25 (±0.07), p=0.0008 growth rates for 3-7,7-18 or 18-42 months NS (data not presented)</p> <p>breast fed group, pre- and post-natal exposure</p>	parity, gestational age, TH, smoking, and alcohol use during pregnancy.

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
			PCBs (170, 180); and 18 other nonplanar PCBs (28, 52, 66, 70, 99, 101, 128, 137, 138, 141, 151, 153, 177, 183, 187, 194, 195, and 202)	body weight change, birth/d10 to 3 months body length change, birth/d10 to 3 months head circumference change, birth/d10 to 3 months growth rates for 7-18 or 18-42 months Total TEQ in breast milk x breast feeding period body weight change, birth/d10 to 3 months body length change, birth/d10 to 3 months body length change, 3 -7 months head circumference change, birth/d10 to 3 months growth rates for 7-18 or 18-42 months	-0.30 (± 0.14), p=0.03 -0.28 (±0.09), p=0.002 -0.19 (±0.09), p=0.05 NS (data not presented) -0.72 (±0.46), p=0.12 -0.05 (±0.31), p=0.88 -0.21 (SE not reported), p=0.04 -0.49 (±0.37), p=0.19 NS (data not presented)	
cross-sectional US, NHANES (EWAS) Patel et al. (2010) environmental	NHANES 1999-2006 (total of four individual cohorts: 1999-2000, 2001-2002, 2003-2004, 2005-2006); Sample sizes ranged from 507-3,318	T2 diabetes (FG ≥126 mg/dL)	heptachlor epoxide and PCB170	OR (95% CI) based on change in log exposure by 1-SD; "lo-hi" range of exposure = ±1 SD of the average logged exposure level Heptachlor Epoxide 1999-2000: n=681; 46 T2 diabetics (6.8%)/635 without T2 diabetes "lo-hi" range: 0.02-0.09 ng/g 2003-2004: n=876; 67 T2 diabetics (7.6%)/809 without T2 diabetes 1999-2004: n=2545; 178 T2 diabetics (7.0%)/2,367 without T2 diabetes PCB170 1999-2000: n=761; 45 T2 diabetics(5.9%)/716 without T2 diabetes 2003-2004: n=826; 53 T2 diabetics(6.4%)/773 without T2 diabetes 1999-2004: n=2591; 165 T2 diabetics (6.4%)/2,426 without T2 diabetes	OR=3.2 (2.4-4.4) p=0.002 1.9 (1.3-2.6) p=0.01 1.7 (1.3-2.1) p<0.001 2.3 (1.5-3.6) p=0.02 4.5 (2.1-9.9) p=0.01 2.2 (1.6-3.2) p<0.001	age, sex, ethnicity, BMI, SES
retrospective cohort Seveso, Italy Pesatori et al.(1998) environmental	15 year mortality in Seveso residents followed from 1976-1991 in Zone A (n=805), Zone B (n=5943), Zone R (n=38,625), and the reference Lombardy region (n=232,747)	diabetes (death certificates)	TCDD (1976-77 serum, lipid adjusted) median levels measured in a subset in 1976-7: reference: NA Zone A (n=177): 443 pg/g Zone B (n=54): 87 pg/g Zone R (n=17): 15 pg/g	Zone A, B, and R versus population of Lombardy region Zone R males: 37 diabetes deaths/1898 total deaths females: 74 diabetes deaths/1589 total deaths Zone B males: 6 diabetes deaths/255 total deaths females: 13 diabetes deaths/176 total deaths	RR = 1.1 (0.8-1.6) 1.2 (1.0-1.6) 1.3 (0.6-2.9) 1.9 (1.1-3.2)	age, calendar year

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				Zone A		
				males: 0 diabetes deaths/39 total deaths	not calculated	
				females: 2 diabetes deaths/30 total deaths	1.8 (0.4-7.3)	
prospective cohort US Ribas-Fito et al. (2006) environmental	1712 children (51% boys) born between 1959 and 1966 participating in the Multicenter US Collaborative Perinatal Project (CPP); data collected at pre-natal visits, delivery, age 24hours, 4 months, 8 months, and 1, 3, 4, 7, and 8 years	growth (height at ages 1, 4, and 7 years; BMI not reported)	p,p'-DDE, p,p'-DDT and several PCB congeners (serum, µg//l)	adjβ for p,p'-DDE (µg/l) and (SE) relative height (cm)* *ratio of adjusted mean height among those in given exposure group to those in referent exposure group	age at examination, gender, race, SEI, tobacco exposure, center location, maternal cholesterol, maternal triglycerides, maternal pre-pregnancy BMI, maternal age, maternal height, and parity	
				age 1, ≥60 µg/l versus <15 µg/l (n=1540)	-0.72 cm (0.37), p<0.05	
				age 4, ≥60 µg/l versus <15 µg/l (n=1289)	-1.14 cm (0.56), p<0.05	
				age 7, ≥60 µg/l versus <15 µg/l (n=1371)	-2.19 cm (0.46), p<0.05	
				height at age 7, whites + African American (n = 1,371)		
				reference <15 µg/l (n=300)	Intercept: 119.43 (0.59)	
				15-29 µg/l	0.37 (0.38)	
				30-44 µg/l	-0.16(0.46)	
				45-59 µg/l	0.12 (0.58)	
				≥ 60 µg/l (n=111)	2.21 (0.67), p<0.05	
				height at age 7, whites only (n=625)		
				reference <15 µg/l	Intercept: 118.74 (0.84)	
				15-29 µg/l	0.27 (0.45)	
				30-44 µg/l	0.26 (0.66)	
				45-59 µg/l	-0.50 (0.97)	
				≥ 60 µg/l	0.31 (2.19)	
				height at age 7, African Americans only (n=698)		
				reference <15 µg/l	Intercept: 119.14 (1.27)	
				15-29 µg/l	0.28 (0.68)	
				30-44 µg/l	0.03 (0.73)	
				45-59 µg/l	0.50 (0.84)	
				≥ 60 µg/l	-2.19 (0.87), p<0.05	
cross-sectional Sweden Rignell-Hydbom et al. (2007) environmental	543 fishermen's wives from the Swedish east and west coasts (from previously established cohorts) born 1945 or later; median age=50 years 15 cases (2.8%)/528 non-cases	T2 diabetes (self-report)	PCB153, p,p'-DDE (serum, lipid adjusted)	PCB153 per 100 ng/g lipid increase in serum level median (5 th , 95 th percentile): non-cases: 82 ng/g lipid (30, 220) cases: 110 ng/g lipid (56, 250) prevalence in relation to quartiles of serum ≤58 ng/g lipid, n=136, 1 case (0.7%) >58 -84 ng/g lipid, n=136, 0 cases >84-118 ng/g lipid, n=135, 7 cases (5%) >118 ng/g lipid, n=136, 7 cases (5%) p,p'-DDE per 100 ng/g increase in serum level median (5 th , 95 th percentile): non-cases: 140 ng/g lipid (49, 500) cases: 240 ng/g lipid (93, 970) prevalence in relation to quartiles of	OR (95th CI)=1.4 (0.8-2.5) p for prevalence trend = 0.004 1.3 (1.1-1.5)	age, BMI (excluded*), and PCB153 or p,p'-DDE *potential confounders included in effect estimate changed by ≥10%; excluded if their exclusion changed effect

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
				serum	estimate by 5%	
				≤91 ng/g lipid, n=136, 0 cases		
				>91-144 ng/g lipid, n=136, 2 cases (1.5%)		
				>144-240 ng/g lipid, n=135, 5 cases (3.7%)		
				>240 ng/g lipid, n=136, 8 cases (5.9%)	p for prevalence trend = 0.002	
case control Sweden Rignell-Hydbom et al. (2009) environmental	371 cases and 371 matched controls from participants of the Women's Health In the Lund Area cohort (WHILA) diagnosed with T2D after baseline assessment (aged 50-59 years). Cases and controls were matched for age, calendar-year, BMI, and positive or negative selection criteria for OGTT at baseline.	diabetes (OGTT)	PCB153, <i>p,p'</i> -DDE (serum collected at baseline, not lipid adjusted)	PCB153 (pg/ml) >1790 versus ≤1790 at baseline	OR (95% CI)	None, but matched on age, calendar-year, and BMI.
				all (371 sets)	0.99 (0.71-1.4)	
				<1 year after baseline (208 sets)	0.91 (0.59-1.4)	
				>1 year (163 sets)	1.1 (0.66-1.9)	
				>3 year (107 sets)	1.4 (0.72-2.6)	
				>5 year (74 sets)	1.4 (0.67-3.1)	
				>7 year (39 sets)	1.6 (0.61-4.0)	
				<i>p,p'</i>-DDE (pg/ml)		
				>4,600 versus ≤4,600 at baseline		Other potential risk factors (heredity, country of birth, education, smoking history, alcohol intake, hormone replacement therapy, and physical activity) were similar between the cases and controls.
				all (371 sets)	1.1 (0.76-1.5)	
				<1 year after baseline (208 sets)	0.90 (0.57-1.4)	
				>1 year (163 sets)	1.3 (0.78-2.2)	
				>3 year (107 sets)	1.5 (0.80-2.8)	
				>5 year (74 sets)	2.5 (0.97-6.4)	
				>7 year (39 sets)	5.5 (1.2-25)	
case control Sweden (Rignell-Hydbom et al. 2010)	300 children, 150 T1D cases and 150 controls, matched for gender and day of birth. Sample collected from biobank Malmö, a city in southern Sweden. Children were born from February 1970 to December 1990 and developed T1D before 2002, most (88%) diagnosed before the age of 18	T1 diabetes (medical diagnosis, diabetes registry)	PCB153, <i>p,p'</i> -DDE (maternal serum at delivery, not lipid adjusted)	PCB153 (pg/ml)	OR (95% CI)	gender, date of birth
				<1.9 (ref)	1.00	
				1.9-2.6	0.85 (0.45-1.63)	
				2.7-3.4	0.67 (0.35-1.31)	
				>3.4	0.64 (0.32-1.29); p-trend = 0.17	
				<i>p,p'</i>-DDE (pg/ml)		
				<5.8 (ref)	1.00	
				5.8-9.6	0.58 (0.28-1.20)	
				9.7-16.8	0.51 (0.24-1.07)	
				>16.8	0.64 (0.28-1.46); p-trend = 0.29	
prospective cohort US, North Carolina	858 children were followed from birth to 5 years of age with assessments at six	growth (weight)	PCBs, <i>p,p'</i> -DDE (estimate of mother's	weight gain at 1 year and <i>p,p'</i> -DDE (height not reported); estimated 0.31 to 23.8	data not shown, but authors reported no association	

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
Rogan et al. (1987) environmental	weeks, 3, 6, 12, and 18 months and yearly until age 5 in the North Carolina Breast Milk and Formula Project (1978-1982)		milk at birth)	ppm in mother's milk weight gain at 1 year and PCBs (height not reported); estimated 0.49 to 15.8 ppm in mother's milk	data not shown, but authors reported no association	
cross-sectional Sweden Rylander et al. (2005) environmental	380 Swedish fishermen (n=196) and fishermen's wives (n=184) from the Swedish Population Register 2000; Mean age for men = 60 years; mean age for women = 63 years men: 12cases (6.1%)/184 non-cases women: 10 cases (5.4%)/174 non-cases	diabetes (self-report)	PCB153, p,p'-DDE (serum, lipid adjusted)	PCB153 per 100 ng/g lipid increase in serum level median (5 th , 95 th percentile): non-cases (male): 360 ng/g lipid (110, 950) cases (male): 560 ng/g lipid (360, 1600) non-cases (female): 240 ng/g lipid (94, 620) cases (female): 230 ng/g lipid (110, 810) men, prevalence in relation to quartiles of serum ≤290 ng/g lipid, n=64, 0 cases 290 -475 ng/g lipid, n=64, 4 cases (6.3%) >475 ng/g lipid, n=64, 8 cases (12.5%) p for prevalence trend = 0.005 women, prevalence in relation to quartiles of serum ≤180 ng/g lipid, n=60, 3 cases (5%) 180 -290 ng/g lipid, n=61, 4 cases (6.6%) >290 ng/g lipid, n=63, 3 cases (4.8%) p for prevalence trend = 0.94 p,p'-DDE per 100 ng/g increase in serum level 1.05 (1.01-1.09) men: 1.05 (0.98-1.11), p prevalence trend = 0.04 women: 1.05 (1.01-1.10), p prevalence trend = 0.07 median (5 th , 95 th percentile): non-cases (male): 570 ng/g lipid (110, 2100); cases (male): 1100 ng/g lipid (390, 2400) non-cases (female): 590 ng/g lipid (100, 2300) cases (female): 990 ng/g lipid (300, 5300) men, prevalence in relation to quartiles of serum ≤410 ng/g lipid, n=64, 1 case (1.6%) 410 -850 ng/g lipid, n=65, 4 cases (6.2%) >850 ng/g lipid, n=67, 7 cases (10.4%) p for prevalence trend = 0.04 women, prevalence in relation to quartiles of serum ≤375 ng/g lipid, n=60, 1 case (1.7%) 375 -860 ng/g lipid, n=62, 3 cases (3.2%) >860 ng/g lipid, n=62, 6 cases (9.7%) p for prevalence trend = 0.07	OR (95 th CI)=1.16 (1.03-1.32) men: 1.20 (1.04-1.39), p prevalence trend = 0.005 women: 1.06 (0.75-1.50)	
prospective cohort US, West Virginia (Sakr et al. 2007) occupational	454 DuPont workers with industrial exposure to PFOA at the Washington Works site in West Virginia (data from an ongoing health and exposure monitoring	serum lipids (total cholesterol, LDL, HDL, triglycerides)	PFOA (serum) mean (SD):	lipids total cholesterol; n=1585 triglycerides; n=508	Coefficient (95% CI) for each 1 ppm increase in serum PFOA -1.06 (-0.24, -1.88), p=0.011 0.79 (-5.99, 7.57), NS	age, age-squared, gender, BMI, and

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
	program)		1.13 (2.1) ppm range: 0-22.66 ppm	HDL; n=509 LDL; n=504	0.16 (-0.39, 0.71), NS 0.46 (-0.87, 1.79), NS	decade of hire
prospective cohort US, Iowa & North Carolina (Saldana <i>et al.</i> 2007) environmental	11,273 women whose pregnancies occurred within 25 years of enrollment in the Agricultural Health Study (AHS). Women self-reported pesticide-related activities during the first trimester of most recent pregnancy.	gestational diabetes mellitus, GDM (self-report)	self-report 4 categories of exposure: none, indirect, residential, and agricultural	overall GDM [n=506] no GDM [n=10767] No exposure and N's (%) GDM [233 (46%)/273], no GDM [4918 (46%)/5849] indirect exposure and N's (%) GDM [157 (31%)/349], no GDM [3724 (35%)/7043] residential exposure and N's (%) GDM [84 (17%)/422], no GDM [1820 (17%)/8947] agricultural exposure and N's (%) GDM [32 (6%)/474], no GDM [305 (3%)/10462] Herbicides 2,4-D: n=327, exposed N's (%) GDM [10 (35%)/19], no GDM [125 (42%)/173] 2,4,5-TP: n=329, exposed N's (%) GDM [2(7%)/27], no GDM [3(1%)/297] 2,4,5-T: n=297, exposed N's (%) GDM [3(10%)/27], no GDM [8(3%)/259] Alachlor: n=329, exposed N's (%) GDM [7(24%)/22], no GDM [48(16%)/252] Atrazine: n=319, exposed N's (%) GDM [9(31%)/20], no GDM [55(19%)/235] Bulylate: n=296, exposed N's (%) GDM [5(17%)/24], no GDM [16(6%)/251] Cyanazine: n=329, exposed N's (%) GDM [6(21%)/23], no GDM [36(12%)/264] Dicamba: n=323, exposed N's (%) GDM [7(24%)/22], no GDM [50(17%)/244] Glyphosate: n=326, exposed N's (%) GDM [19(63%)/11], no GDM [219(74%)/77] Pendimethalin: n=312, exposed N's (%) GDM [5(17%)/24], no GDM [34(12%)/249] Petroleum Oil: n=324, exposed N's (%) GDM [5(17%)/24], no GDM [59(20%)/236] Trifluralin: n=324, exposed N's (%) GDM [6(21%)/23], no GDM [65(22%)/230] Insecticides Organophosphates Diazinon: n=318, exposed N's (%) GDM [13(43%)/17], no GDM [92(32%)/196] Malathion: n=327, exposed N's (%) GDM [12(39%)/19], no GDM [154(52%)/142] Terbufos: n=314, exposed N's (%) GDM [5(17%)/24], no GDM [37(13%)/248] Phorate: n=300, exposed N's (%) GDM [5(17%)/24], no GDM [19(7%)/252] Carbamates	AdjOR (95% CI) for GDM ref. 0.9 (0.7-1.1) 1.0 (0.8-1.3) 2.2 (1.5-3.3) AdjOR (95% CI) 1.01 (0.41-2.49) 6.69 (1.02-43.97) 4.67 (1.13-19.38) 2.05 (0.79-5.33) 2.35 (0.98-5.67) 3.92 (1.29-11.93) 2.45 (0.88-6.84) 2.27 (0.83-6.16) 0.72 (0.31-1.67) 1.80 (0.63-5.15) 0.93 (0.33-2.64) 1.13 (0.42-3.06) 2.35 (0.95-5.78) 0.59 (0.25-1.37) 1.74 (0.60-5.06) 3.57 (1.14-11.17)	Adjusted for: BMI at enrollment , mother's age at pregnancy, parity, race, state, and five commonly used pesticides

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For
				Carbaryl: n=324, exposed N's (%) GDM [16(52%)/15], no GDM [167(57%)/126] 0.76 (0.33-1.73)	
				Carbofuran: n=312, exposed N's (%) GDM [5(17%)/24], no GDM [17(6%)/266] 3.93 (1.28-12.02)	
prospective cohort Spain Smink et al. (2008) environmental	482 children born in Menorca, Spain (full term pregnancies) in 1997 – 1998 (sex not stated). Weight and height measured at birth and at age 6.5 years (total n=405 for analysis)	overweight (>85 th percentile of BMI) n=482; 77(16%)/405 obese (BMI criteria not defined) n=482; 58(12%)/424	HCB (cord serum; available for n=405) *units are expressed as log ng/ml in paper, but that is likely an error as the linear model fits for natural scale (ng/ml); p-values not presented in paper but calculated based on reported data	HCB cord blood (log ng/ml) and BMI, age β (\pm SE) 6.5 years continuous prenatal HCB (log ng/ml*) and BMI prenatal HCB (categorical) and BMI <0.46 ng/ml (reference) 14.53, intercept 0.46-0.67 0.10 (0.31) 0.68-1.03 0.50 (0.34) >1.03 0.83 (0.33), p=0.012* HCB cord blood (log ng/ml) and overweight/obese overweight, <0.46 vs \geq 0.46 log ng/ml 1.69 (1.05-2.72) obese, <0.46 vs \geq 0.46 log ng/ml 2.02 (1.06-3.85)	Maternal age, height, pre-pregnancy overweight /obese, education, parity; child's sex, current age, and birth weight
cross-sectional South Korea Son et al. (2010) environmental	80 Residents of Uljin County, South Korea; aged \geq 40 years (mean age=55.7 years; 52.5% male); 40 diabetics and 40 age-matched controls	diabetes (FG \geq 126 mg/dl, use of anti-diabetic medication)	10 organochlorine pesticides (serum, lipid adjusted)	3rd tertile versus 1st tertile (referent) <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p align="center">OR (95% CI)</p> <p>Oxychlorane: 13.5 versus 2.2 ng/g lipid 3rd (n=33); 20 cases (60.6%)/13 non-cases 1st (n=15): 2 cases (13.3%)/13 non-cases 26.0 (1.3-517.4), p-trend<0.01</p> <p>Trans-nonachlor: 33.1 versus 8.4 ng/g lipid 3rd (n=35); 22 cases (62.9%)/13 non-cases 1st (n=16): 3 cases (18.8%)/13 non-cases 8.1 (1.2-53.5), p-trend=0.02</p> <p>Heptachlor epoxide: 12.2 versus 2.9 ng/g lipid 3rd (n=44); 31 cases (70.5%)/13 non-cases 1st (n=18): 5 cases (27.8%)/13 non-cases 3.1 (0.8-12.1), p-trend=0.05</p> <p>Hexachlorobenzene (HCB): 27.3 versus 9.4 ng/g lipid 3rd (n=40); 27 cases (67.5%)/13 non-cases 1st (n=19): 6 cases (31.6%)/13 non-cases 6.1 (1.0-36.6), p-trend=0.03</p> <p>β-Hexachlorocyclohexane (β-HCH) 68.6 versus 20.9 ng/g lipid 3rd (n=38); 25 cases (65.8%)/13 non-cases 1st (n=15): 2 cases (13.3%)/13 non-cases 8.2 (1.3-53.4), p-trend=0.02</p> </div> <div style="width: 45%;"> <p align="center">OR (95% CI)</p> <p>Mirex: 4.5 versus 1.0 ng/g lipid 3rd (n=45); 22 cases (48.9%)/13 non-cases 1st (n=20): 7 cases (35%)/13 non-cases 3.7 (0.9-15.8), p-trend = 0.08</p> <p>p,p'-DDE: 667.4 versus 162.2 ng/g lipid 3rd (n=38); 25 cases (65.8%)/13 non-cases 1st (n=16): 3 cases (18.8%)/13 non-cases 12.7 (1.9-83.7), p-trend <0.01</p> <p>p,p'-DDD: 8.4 versus 2.7 ng/g lipid 3rd (n=34); 21 cases (61.8%)/13 non-cases 1st (n=21): 9 cases (42.9%)/13 non-cases 3.6 (0.8-16.3), p-trend=0.09</p> <p>p,p'-DDT: 36.2 versus 12.1 ng/g lipid 3rd (n=37); 24 cases (64.9%)/13 non-cases 1st (n=21): 8 cases (38.1%)/13 non-cases 10.6 (1.3-84.9), p-trend=0.02</p> <p>o,p'-DDT: 5.4 versus 0.9 ng/g lipid 3rd (n=36); 23 cases (63.9%)/13 non-cases 1st (n=18): 5 cases (27.8%)/13 non-cases 12.3 (1.3-113.2), p-trend=0.02</p> </div> </div>	age, sex, BMI, alcohol consumption, cigarette smoking.
retrospective cohort US, 12 chemical plants Steenland et al. (1999) occupational	5,132 chemical workers from 12 U.S. plants that produced TCDD-contaminated products from 1942 to 1984 (total deaths = 1,444). Data from 3,538 workers used in exposure-level cohort.	diabetes (death certificate)	TCDD 1. TCDD (μ g/g) in process materials, 2. Fraction of the day the worker worked on the specific	total cohort industrial cohorts (n=5,132; 1,444 deaths) versus the US population diabetes, underlying cause (26 deaths) 1.18 (0.77-1.73) diabetes, multiple causes and beyond (89 deaths) 1.08 (0.87-1.33) diabetes, chloracne sub-cohort (n=608; 271 deaths; 4 diabetes deaths) 1.06 (0.29-2.71)	year of birth and age

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For																																																	
			process, 3. Qualitative contact level (0.01-1.5) based on estimates of the amount of TCDD contamination reaching exposed skin areas or potential for inhalation of TCDD-contaminated dust.	<p>diabetes (underlying cause), SMRs (number of deaths) across septiles of exposure:</p> <table border="1"> <tr><td>Septile 1: 0 to <19</td><td>1.87 (4), referent</td></tr> <tr><td>Septile 2: 19-139</td><td>2.17 (5)</td></tr> <tr><td>Septile 3: 139-<581</td><td>1.36 (3)</td></tr> <tr><td>Septile 4: 581-<16.50</td><td>0.92 (2)</td></tr> <tr><td>Septile 5: 1650-<5740</td><td>1.33 (3)</td></tr> <tr><td>Septile 6: 5740-<20,000</td><td>1.10 (2)</td></tr> <tr><td>Septile 7: ≥20,200</td><td>0 (0)</td></tr> </table> <p>diabetes (underlying cause), Cox regression, risk ratios (95%CI) across septiles of exposure:</p> <table border="1"> <tr><td>Septile 1: 0 to <19</td><td>1.00, referent</td></tr> <tr><td>Septile 2: 19-139</td><td>1.27 (0.49-3.33)</td></tr> <tr><td>Septile 3: 139-<581</td><td>0.92 (0.33-2.53)</td></tr> <tr><td>Septile 4: 581-<16.50</td><td>0.81 (0.28-2.30)</td></tr> <tr><td>Septile 5: 1650-<5740</td><td>0.98 (0.36-2.65)</td></tr> <tr><td>Septile 6: 5740-<20,000</td><td>0.72 (0.23-2.21)</td></tr> <tr><td>Septile 7: ≥20,200</td><td>0.54 (0.15-1.89)</td></tr> </table>	Septile 1: 0 to <19	1.87 (4), referent	Septile 2: 19-139	2.17 (5)	Septile 3: 139-<581	1.36 (3)	Septile 4: 581-<16.50	0.92 (2)	Septile 5: 1650-<5740	1.33 (3)	Septile 6: 5740-<20,000	1.10 (2)	Septile 7: ≥20,200	0 (0)	Septile 1: 0 to <19	1.00, referent	Septile 2: 19-139	1.27 (0.49-3.33)	Septile 3: 139-<581	0.92 (0.33-2.53)	Septile 4: 581-<16.50	0.81 (0.28-2.30)	Septile 5: 1650-<5740	0.98 (0.36-2.65)	Septile 6: 5740-<20,000	0.72 (0.23-2.21)	Septile 7: ≥20,200	0.54 (0.15-1.89)	<p>p-trend=0.10, based on cumulative exposure</p> <p>p-trend=0.09, based on logarithm of cumulative exposure</p> <p>p-trend=0.02, based on cumulative exposure</p> <p>p-trend=0.12, based on logarithm of cumulative exposure</p>																					
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retrospective cohort Steenland et al. (2001) Vietnam veterans & occupational	2759 men; combined analysis of data from 2265 from Ranch Hand (990 US Air Force veterans and 1275 referents) and 494 from a NIOSH cohort of [264 chemical workers (TCDD data available for 259) and 227 referents]	diabetes [physician diagnosis, OGGT >200 mg/dl (Ranch Hand), or FG ≥ 126 mg/dl (NIOSH)]	TCDD (serum, “current” measured in 1980 & back extrapolated to end of exposure) median (range) serum TCDD Ranch Hand (n=990) 1980, 12 ppt (0-618) back extrapolated 94 ppt (27-3,290) NIOSH (n=259) 1980, 75 ppt (2-3,388) back extrapolated 584 ppt (35-19,744)	<p>Diabetes prevalence, logistic regression coefficient (95%CI), current TCDD</p> <table border="1"> <tr><td>Ranch Hand</td><td>0.0065 (0.0032-0.0099)</td></tr> <tr><td>NIOSH</td><td>0.0008 (0.0002-0.0015)</td></tr> </table> <p>Diabetes prevalence, logistic regression coefficient, current log TCDD</p> <table border="1"> <tr><td>Ranch Hand</td><td>0.2401 (0.1139-0.3663)</td></tr> <tr><td>NIOSH</td><td>0.0263 (-0.1428-1954)</td></tr> </table> <p>Diabetes prevalence, OR (95% CI) based on quartiles, current TCDD</p> <table border="1"> <thead> <tr> <th></th> <th>Ranch Hand</th> <th>NIOSH</th> </tr> </thead> <tbody> <tr><td>referent, <10 ppt</td><td></td><td></td></tr> <tr><td>Q1: 10-17 ppt</td><td>1.39 (0.91-2.14)</td><td>0.67 (0.07-6.24)</td></tr> <tr><td>Q2: 17-30 ppt</td><td>1.33 (0.85-2.10)</td><td>1.73 (0.57-5.26)</td></tr> <tr><td>Q3: 30-78 ppt</td><td>1.11 (0.67-1.88)</td><td>0.88 (0.28-2.78)</td></tr> <tr><td>Q4: ≥ 78 ppt</td><td>3.21 (1.81-5.72)</td><td>0.84 (0.40-1.77)</td></tr> <tr><td>exposed versus non-exposed</td><td>1.18 (0.91-1.52)</td><td>1.22 (0.65-2.29)</td></tr> <tr><td></td><td>147 exposed cases/990 total</td><td>28 exposed cases/264 total</td></tr> <tr><td>exposed versus non-exposed</td><td colspan="2">1.17 (0.92-1.48), combined</td></tr> </tbody> </table> <p>Diabetes prevalence by logistic regression coefficient (95%CI), back extrapolated TCDD</p> <table border="1"> <tr><td>Ranch Hand</td><td>0.0013 (0.0005 to 0.0020)</td></tr> <tr><td>NIOSH</td><td>0.0002 (0.0000 to 0.0003)</td></tr> </table> <p>Diabetes prevalence, logistic regression coefficient (95%CI), back extrapolated log TCDD</p> <table border="1"> <tr><td>Ranch Hand</td><td>0.3174 (0.0575 to 0.5773)</td></tr> <tr><td>NIOSH</td><td>0.1796 (-0.2044 to 0.5635)</td></tr> </table> <p>Diabetes prevalence, OR (95% CI), back extrapolated TCDD for Ranch Hand</p> <table border="1"> <tr><td>referent, <10 ppt</td><td>Ranch Hand</td></tr> <tr><td>Q1: 10-64 ppt</td><td>NR</td></tr> <tr><td>Q2: 64-140 ppt</td><td>1.02 (0.57-1.85)</td></tr> </table>	Ranch Hand	0.0065 (0.0032-0.0099)	NIOSH	0.0008 (0.0002-0.0015)	Ranch Hand	0.2401 (0.1139-0.3663)	NIOSH	0.0263 (-0.1428-1954)		Ranch Hand	NIOSH	referent, <10 ppt			Q1: 10-17 ppt	1.39 (0.91-2.14)	0.67 (0.07-6.24)	Q2: 17-30 ppt	1.33 (0.85-2.10)	1.73 (0.57-5.26)	Q3: 30-78 ppt	1.11 (0.67-1.88)	0.88 (0.28-2.78)	Q4: ≥ 78 ppt	3.21 (1.81-5.72)	0.84 (0.40-1.77)	exposed versus non-exposed	1.18 (0.91-1.52)	1.22 (0.65-2.29)		147 exposed cases/990 total	28 exposed cases/264 total	exposed versus non-exposed	1.17 (0.92-1.48), combined		Ranch Hand	0.0013 (0.0005 to 0.0020)	NIOSH	0.0002 (0.0000 to 0.0003)	Ranch Hand	0.3174 (0.0575 to 0.5773)	NIOSH	0.1796 (-0.2044 to 0.5635)	referent, <10 ppt	Ranch Hand	Q1: 10-64 ppt	NR	Q2: 64-140 ppt	1.02 (0.57-1.85)	<p><u>All analyses:</u> Family history of diabetes, BMI, year of birth, race, current taking of medications possibly contributing to diabetes or increased serum glucose, and education</p> <p><u>Time to diabetes analysis:</u> Plus age at last exposure</p>
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Ranch Hand	0.0013 (0.0005 to 0.0020)																																																					
NIOSH	0.0002 (0.0000 to 0.0003)																																																					
Ranch Hand	0.3174 (0.0575 to 0.5773)																																																					
NIOSH	0.1796 (-0.2044 to 0.5635)																																																					
referent, <10 ppt	Ranch Hand																																																					
Q1: 10-64 ppt	NR																																																					
Q2: 64-140 ppt	1.02 (0.57-1.85)																																																					

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For		
				Q3: 140-376 ppt Q4: ≥ 376 ppt			
				1.60 (0.83-3.06) Q4: 2.30(1.07-4.94)			
				Log serum fasting glucose (mmol/l), linear regression coefficient (95%CI), current TCDD			
				Ranch Hand NIOSH combined	0.00006(-0.00009 to 0.00021) 0.00004 (-0.00001 to 0.00009) 0.00004 (0.00001 to 0.00008)		
				Log serum fasting glucose (mmol/l), linear regression coefficient (95%CI), current log TCDD			
				Ranch Hand NIOSH combined	0.0016 (-0.0025 to 0.0057) 0.0033 (-0.0047 to 0.0113) 0.0025 (-0.0010 to 0.0060)		
				Change in log serum fasting glucose (mmol/l) by quartile of current TCDD (95%CI)			
				referent, <10 ppt	Ranch Hand NIOSH combined		
				Q1: 10-17 ppt	-0.001 (-0.016,0.016)	-0.016 (-0.077, 0.045)	-0.004 (-0.019, 0.013)
				Q2: 17-30 ppt	-0.001 (-0.017,0.014)	-0.017 (-0.065, 0.031)	-0.005 (-0.016, 0.011)
				Q3: 30-78 ppt	-0.011 (-0.028,0.004)	-0.033 (0.078, 0.012)	-0.017 (-0.033, 0.007)
				Q4: ≥ 78 ppt	0.014 (-0.024,0.038)	0.014 (-0.017,0.045)	0.018 (0.001,0.035)
				Time to diabetes, Cox's regression coefficient (95%CI), current TCDD			
				Ranch Hand NIOSH	0.0060 (0.0039 to 0.0082) 0.0008 (0.0001 to 0.0016)		
				Time to diabetes, Cox's regression coefficient (95%CI), current log TCDD			
				Ranch Hand NIOSH	0.1975 (0.0299 to 0.3650) -0.0308 (-0.3183 to 0.2567)		
				Time to diabetes, risk ratio (95%CI) by quartile of current TCDD			
				referent, <10 ppt	Ranch Hand NIOSH		
				Q1: 10-17 ppt	1.60 (0.99 to 2.58)	0.27 (0.03 to 2.70)	
				Q2: 17-30 ppt	1.76 (1.06 to 2.93)	0.90 (0.25 to 3.29)	
				Q3: 30-78 ppt	1.57 (0.89 to 2.79)	0.51 (0.13 to 2.04)	
				Q4: ≥ 78 ppt	4.48 (2.48 to 8.09)	0.42 (0.12 to 1.49)	
cross-sectional US, West Virginia community (Steenland <i>et al.</i> 2009) environmental	46,294 residents, ≥18 years old, of six communities participating in the C8 Health Project where the drinking water was contaminated with PFOA (46.1% male)	lipid profile in adults not taking cholesterol-lowering medication	PFOS, PFOA, PFNA, PFHxS (serum, concurrent with lipid analysis) PFOA, ng/ml: mean=80.3 median=26.6 range=0.25-17,556.6 PFOS, ng/ml: mean=22.4 median=19.6	OR (95% CI) for high cholesterol (total cholesterol ≥ 240 mg/dL) PFOA, Q4 vs Q1 PFOS, Q4 vs Q1 PFNA, Q4 vs Q1 PFHxS, Q4 vs Q1 Linear regression using continuous exposure variables, log exposure Total cholesterol PFOA PFOS	age, gender, BMI, education, smoking, regular exercise, current alcohol consumption		
				1.38 (1.28-1.50), p-trend < 0.0001 1.51 (1.40-1.64), p-trend < 0.0001 data not presented, but showed a monotonic increase data not presented, but showed a monotonic increase Logged coefficient (SD), t statistic 0.01112 (0.00076), t statistic = 14.5 0.02660 (0.00140), t statistic = 19.0			

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For																																																																
			range=0.25-759.2	HDL cholesterol PFOA 0.00276 (0.00094), t statistic = 2.9 PFOS 0.00355 (0.00173), t statistic = 2.1 LDL cholesterol PFOA 0.01499 (0.00121), t statistic = 12.4 PFOS 0.04176 (0.00221), t statistic = 18.9 Triglycerides PFOA 0.00169 (0.00219), t statistic = 7.7 PFOS 0.01998 (0.00402), t statistic = 5.0 Total cholesterol/HDL cholesterol ratio PFOA 0.00831 (0.00110), t statistic = 7.5 PFOS 0.02290 (0.00202), t statistic = 11.3 Non-HDL-C PFOA 0.01406 (0.00104), t statistic = 13.6 PFOS 0.03476 (0.00190), t statistic = 18.3	*6-hour fasting status was also included as covariate in TG analyses																																																																
prospective cohort Taiwan Su et al. (2010) environmental	92 mother and newborn pairs were recruited from the general population in central Taiwan and were followed up at year 2 and year 5.	Low exposure: <15 pg-TEQ/g lipid (based on mother's PCDD/Fs TEQ levels) High exposure: > 15 pg TEQ/g lipid (based on mother's PCDD/Fs TEQ levels)	PCDD/PCDF (maternal serum) Low exposure: <15 pg-TEQ/g lipid (based on mother's serum PCDD/Fs TEQ levels) High exposure: > 15 pg TEQ/g lipid (based on mother's serum PCDD/Fs TEQ levels)	"Low" (15.1 pg-TEQ/g lipid) versus "high" (≥15.1 pg-TEQ/g lipid) ; p-values for group comparisons Year 2 ♂= 14 low, 15 high; ♀= 21 low, 20 high <table border="1"> <thead> <tr> <th></th> <th>male</th> <th>female</th> <th>overall</th> </tr> </thead> <tbody> <tr> <td>height (cm)</td> <td>NS</td> <td>p=0.0110 85.8 vs 88.7</td> <td>p=0.0029 86.8 vs 89.9</td> </tr> <tr> <td>weight (kg)</td> <td>NS</td> <td>p=0.0086 12.0 vs 13.7</td> <td>p=0.0076 12.3 vs 13.6</td> </tr> <tr> <td>BMI (kg/m²)</td> <td>NS</td> <td>NS 16.4 vs. 17.4</td> <td>NS 16.4 vs. 16.9</td> </tr> <tr> <td>head circumference (cm)</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>chest girth (cm)</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>bone age</td> <td>NS</td> <td>0.0461</td> <td>NS</td> </tr> <tr> <td>bone age/chronological age</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> </tbody> </table> Year 5 ♂= 6 low, 8 high; ♀= 15 low, 12 high <table border="1"> <thead> <tr> <th></th> <th>male</th> <th>female</th> <th>overall</th> </tr> </thead> <tbody> <tr> <td>height (cm)</td> <td>NS</td> <td>NS 110 vs 113</td> <td>p=0.0276 109.8 vs 113</td> </tr> <tr> <td>weight (kg)</td> <td>NS</td> <td>NS 19.6 vs 22.2</td> <td>NS 19.9 vs 21.6</td> </tr> <tr> <td>BMI (kg/m²)</td> <td>NS</td> <td>NS 17.8 vs. 19.3</td> <td>NS 18.0 vs. 18.8</td> </tr> <tr> <td>head circumference (cm)</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>chest girth (cm)</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>bone age</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> <tr> <td>bone age/chronological age</td> <td>NS</td> <td>NS</td> <td>NS</td> </tr> </tbody> </table>		male	female	overall	height (cm)	NS	p=0.0110 85.8 vs 88.7	p=0.0029 86.8 vs 89.9	weight (kg)	NS	p=0.0086 12.0 vs 13.7	p=0.0076 12.3 vs 13.6	BMI (kg/m ²)	NS	NS 16.4 vs. 17.4	NS 16.4 vs. 16.9	head circumference (cm)	NS	NS	NS	chest girth (cm)	NS	NS	NS	bone age	NS	0.0461	NS	bone age/chronological age	NS	NS	NS		male	female	overall	height (cm)	NS	NS 110 vs 113	p=0.0276 109.8 vs 113	weight (kg)	NS	NS 19.6 vs 22.2	NS 19.9 vs 21.6	BMI (kg/m ²)	NS	NS 17.8 vs. 19.3	NS 18.0 vs. 18.8	head circumference (cm)	NS	NS	NS	chest girth (cm)	NS	NS	NS	bone age	NS	NS	NS	bone age/chronological age	NS	NS	NS	infants' gender
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cross-sectional US Sweeny et al.(1997) occupational	281 workers employed more than 15 years earlier in the production of NaTCP,2,4,5-T ester or one of its derivatives (substances contaminated	diabetes (interview, medical exam) elevated fasting glucose	TCDD (current serum, lipid adjusted)	workers (n=281, mean 220 pg/g lipid) versus referents (n=260, mean 7 pg/g lipid) diabetes (prevalence not reported) OR=1.12, p.0.003 fasting glucose positive increase with increased serum TCDD (p<0.001)	body weight index, age, use of																																																																

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For																																																																																																																
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prospective cohort Finland Turunen et al. (2008) environmental	6410 fishermen and 4260 fishermen's wives compared with the general population from the same region of Finland; 60% male; age= 45-74 years	diabetes (death certificate) total deaths, male = 962 diabetes deaths, male =5 total deaths, female = 355 diabetes deaths, female =5	dioxins, PCBs (occupation)	SMR (95%CI) with national mortality rates after exclusion of the first 3 years of follow-up fishermen (5 diabetes deaths) 0.43 (0.14-0.99) fishermen wives (5 diabetes deaths) 0.83 (0.27-1.94)	Not reported																																																																																																																
prospective cohort US, Great Lakes Turyk et al. (2009a) environmental	471 individuals without diabetes in 1994 (baseline) from the Great Lakes Consortium for the Health Assessment of Great Lakes Sport Fish Consumption cohort study; Years=1994-2005; average 8.4 year follow-up 36 incident diabetes cases(25 men and 11 women)/435 did not develop diabetes	diabetes (self-report)	DDE, Σ PCBs, PCB118 (serum, ng/g wet weight)	diabetes incident RR (95%CI) <table border="1"> <thead> <tr> <th></th> <th>total</th> <th>men</th> <th>women</th> </tr> </thead> <tbody> <tr> <td>DDE, ng/g wet weight</td> <td>n=471</td> <td>n=279</td> <td>n=192</td> </tr> <tr> <td><LOD-2.2 n=153 (672, 81 ♀)</td> <td>1</td> <td>1</td> <td>1</td> </tr> <tr> <td>2 cases (1 ♂, 1 ♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>2.3-5.3 n=162 (94 ♂, 68 ♀)</td> <td>5.5</td> <td>6.8</td> <td>3.9</td> </tr> <tr> <td>12 cases (9 ♂, 3 ♀)</td> <td>(1.2-25.1)</td> <td>(0.9-54.4)</td> <td>(0.4-42.0)</td> </tr> <tr> <td>5.4-49.2(♂), 21.8 (♀)</td> <td>7.1</td> <td>7.3</td> <td>7.5</td> </tr> <tr> <td>n=156 (113 ♂, 43 ♀) 22 cases (15 ♂, 7 ♀)</td> <td>(1.6-31.9)</td> <td>(0.9-56.5)</td> <td>(0.7-78.3)</td> </tr> <tr> <td>p-trend</td> <td>p=0.008</td> <td>p=0.06*</td> <td>p=0.08</td> </tr> </tbody> </table> *significant after further adjusting for Σ PCBs tertiles ΣPCBs, ng/g wet weight <table border="1"> <tbody> <tr> <td><LOD-1.6 n=157 (62♂, 95♀)</td> <td>1</td> <td>1</td> <td>1</td> </tr> <tr> <td>6 cases (3♂, 3♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>1.6-4.3 n=157 (92♂, 65♀)</td> <td>2.0 (0.7-5.3)</td> <td>1.8</td> <td>2.3</td> </tr> <tr> <td>15 cases (10♂, 5♀)</td> <td></td> <td>(0.5-6.5)</td> <td>(0.5-11.4)</td> </tr> <tr> <td>4.3-29.8 (♂), 10.7 (♀)</td> <td>1.8 (0.6-5.0)</td> <td>1.5</td> <td>2.2</td> </tr> <tr> <td>n=157 (125♂, 32♀)</td> <td></td> <td>(0.4-5.5)</td> <td>(0.4-13.2)</td> </tr> <tr> <td>15 cases (12♂, 3♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>p-trend</td> <td>p=0.37</td> <td>p=0.72</td> <td>p=0.40</td> </tr> </tbody> </table> PCB118, ng/g wet weight <table border="1"> <tbody> <tr> <td><LOD n=187 (102♂, 85♀)</td> <td>1</td> <td>1</td> <td>1</td> </tr> <tr> <td>9 cases (5♂, 4♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>0.1-0.3 n=124 (63♂, 61♀)</td> <td>0.9 (0.4-2.4)</td> <td>2.1</td> <td>0</td> </tr> <tr> <td>8 cases (8♂, 0♀)</td> <td></td> <td>(0.7-6.7)</td> <td></td> </tr> <tr> <td>0.3-4.6 (♂), 1.1 (♀)</td> <td>1.3 (0.5-3.0)</td> <td>1.4</td> <td>1.1</td> </tr> <tr> <td>n=160 (114♂, 46♀)</td> <td></td> <td>(0.5-4.2)</td> <td>(0.2-5.3)</td> </tr> <tr> <td>19 cases (12♂, 7♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>p-trend</td> <td>p=0.54</td> <td>p=0.67</td> <td>p=0.51</td> </tr> </tbody> </table> years eating sports fish <table border="1"> <tbody> <tr> <td>0-15 n=158 (69♂, 89♀)</td> <td>1</td> <td>1</td> <td>1</td> </tr> <tr> <td>9 cases (6♂, 3♀)</td> <td></td> <td></td> <td></td> </tr> <tr> <td>16-35 n=160 (94♂, 66♀)</td> <td>1.1 (0.4-2.5)</td> <td>0.8</td> <td>1.7</td> </tr> </tbody> </table>		total	men	women	DDE, ng/g wet weight	n=471	n=279	n=192	<LOD-2.2 n=153 (672, 81 ♀)	1	1	1	2 cases (1 ♂, 1 ♀)				2.3-5.3 n=162 (94 ♂, 68 ♀)	5.5	6.8	3.9	12 cases (9 ♂, 3 ♀)	(1.2-25.1)	(0.9-54.4)	(0.4-42.0)	5.4-49.2(♂), 21.8 (♀)	7.1	7.3	7.5	n=156 (113 ♂, 43 ♀) 22 cases (15 ♂, 7 ♀)	(1.6-31.9)	(0.9-56.5)	(0.7-78.3)	p-trend	p=0.008	p=0.06*	p=0.08	<LOD-1.6 n=157 (62♂, 95♀)	1	1	1	6 cases (3♂, 3♀)				1.6-4.3 n=157 (92♂, 65♀)	2.0 (0.7-5.3)	1.8	2.3	15 cases (10♂, 5♀)		(0.5-6.5)	(0.5-11.4)	4.3-29.8 (♂), 10.7 (♀)	1.8 (0.6-5.0)	1.5	2.2	n=157 (125♂, 32♀)		(0.4-5.5)	(0.4-13.2)	15 cases (12♂, 3♀)				p-trend	p=0.37	p=0.72	p=0.40	<LOD n=187 (102♂, 85♀)	1	1	1	9 cases (5♂, 4♀)				0.1-0.3 n=124 (63♂, 61♀)	0.9 (0.4-2.4)	2.1	0	8 cases (8♂, 0♀)		(0.7-6.7)		0.3-4.6 (♂), 1.1 (♀)	1.3 (0.5-3.0)	1.4	1.1	n=160 (114♂, 46♀)		(0.5-4.2)	(0.2-5.3)	19 cases (12♂, 7♀)				p-trend	p=0.54	p=0.67	p=0.51	0-15 n=158 (69♂, 89♀)	1	1	1	9 cases (6♂, 3♀)				16-35 n=160 (94♂, 66♀)	1.1 (0.4-2.5)	0.8	1.7	age, sex, and BMI
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				12 cases (8♂, 4♀) 36-65 (♂), 56 (♀) n=153 (116♂, 37♀) 15 cases (11♂, 4♀) p-trend	(0.3-2.4) 0.8 (0.3-2.2) p=0.69	(0.4-84) 1.1 (0.2-6.7) p=0.95
				adjusted incident RR (95%CI) per one-tertile increase in serum levels by BMI		
				17-25	25-29	29-48
			DDE	3.0 (0.4-26.2)	1.7 (0.6-4.9)	2.2 (1.1-4.3)
				adjusted incident RR (95%CI) per one-tertile increase in serum levels by age		
				25-44	44-52	52-76
			DDE	1.5 (0.5-5.0)	1.5 (0.7-3.3)	2.6 (1.0-6.3)
cross-sectional US, Great Lakes Turyk et al. (2009b) environmental	503 individuals from the Great Lakes Consortium for the Health Assessment of Great Lakes Sport Fish Consumption cohort study re-contacted 2004-2005; 69% male; mean age=57.9 years	n=503; 61 self-reported diabetics (12.1%)/442 non-diabetics Diabetes and/or HA1c > 6.3% n=85 (16.9%)/418 non-diabetic and HA1c <6.3% Male: diabetes and/or HA1c > 6.3% n=75 (21.6%)/272 non-diabetic and HA1c <6.3% Female: diabetes and/or HA1c > 6.3% n=10 (6.4%)/146 non-diabetic and HA1c <6.3%	Self-reported diabetes diagnosis or diabetes medication use; HA1c > 6.3%	exposure categories DDE (ng/g) all (n=503) <LOD-1.2 (♂ = <LOD-1.1; ♀ = 0.2-2.3) 1.3-2.0 (♂ = 1.1-1.8; ♀ = 2.4-17.0) 2.1-4.0 (♂ = 1.9-1.8) 4.1-24.0 (♂ = 3.5-24.0) p-value trend ΣPCB (ng/g) <LOD-0.8 0.8-1.9 1.9-3.6 3.6-24.4 p-value trend ΣDioxin-like PCBs (ng/g) <LOD 0.2-0.3 (♂ = 0.2-0.3; ♀ = 0.2-0.8) 0.3-1.6 p-value trend ΣPBDEs (ng/g) <LOD-0.1 0.1-0.2 0.2-0.4 0.4-10.1 p-value trend Sports fish consumption (years) 0-18 20-37 38-50	ORs (prevalence) for diagnosed diabetes and/or HA1c>6.3% (85 cases, 16.9%) ♂ (n=347) ♀ (n=156) 1 (8.9%) 1.7 (16.3) 1.6 (22%) 3.6 (40%) p=0.009 1 (16.1%) 1.4 (26%) 2.1 (39%) P=0.05 1 (13.7%) 0.7 (15.6%) 0.9 (17.6%) 0.9 (20.6%) p=0.87	age, sex, and BMI *not significant with further control for ΣPCBs, DDE or years of sports fishing

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates			Adjusted For
				51-70	1.1 (27.6%)		
				p-value trend	p=0.91		
				Exposure, dichotomized or continuous			
				Modifications of exposure	66th percentile	50th percentile	continuous
				DDE and ΣPBDEs			
				p-value for interaction beta	0.03	0.02	0.02
				low DDE, low ΣPBDEs	OR= 1	OR= 1	
				low DDE, high ΣPBDEs	OR= 0.5	OR= 0.3	
				high DDE, low ΣPBDEs	OR= 1.2	OR= 0.9	
				high DDE, high ΣPBDEs	OR= 2.2	OR= 1.6	
				DDE and hypothyroid disease			
				p-value for interaction beta	0.054	0.80	0.32
				No hypothyroid disease	OR= 1.7	OR= 1.8	
				Hypothyroid disease	OR= 22.0	OR= 2.4	
				ΣPBDEs and hypothyroid disease			
				p-value for interaction beta	0.02	NE	0.02
				No hypothyroid disease	OR= 0.9	NE	
				Hypothyroid disease	OR= 13.8	NE	
							Logistic model with dichotomous main effects: adjusted for age, sex, BMI, triglycerides, and cholesterol
							*NE=could not estimate: for 38 persons with hypothyroidism, all 7 persons with diabetes had RPBDE > 50th percentile
cross-sectional Japan Uemura et al. (2008) environmental	1,374 people from the general population of Japan (from 75 different residential areas of 25 prefectures) who were not occupationally exposed to dioxins, and living throughout urban, farming, and fishing areas through 2002-2006 (46% male); 15-73 years	self-reported physician diagnosis, HbA1c > 6.1% 65 diabetics/1309 non-diabetics (4.7%)	7 PCDDs, 10 PCDFs, 12 dioxin-like PCBs (serum, lipid adjusted)	adjOR (95%CI)			ORs: age, gender, BMI, smoking, region, residential area, and survey year
				PCDDs+PCDFs, pg TEQ/g lipid			
				<12 [n=644, 13 (2%)/631]		1	
				≥12 to 18 [n=361, 16 (4.4%)/345]		1.24 (0.54-2.85)	
				≥ 18 [n=369, 36 (9.8%)/333]		2.21 (1.02-5.04)	
				Dioxin-like PCBs, pg TEQ/g lipid			
				≤7.60 [n=678, 7 (1%)/671]		1	
				≥7.60 to <13 [n=325, 14 (4.3%)/311]		3.07 (1.16-8.81)	
				≥13 [n=371, 44 (12%)/327]		6.82 (2.59-20.1)	
				Total dioxins, pg TEQ/g lipid			
				<20 [n=666, 9 (1.4%)/657]		1	
				≥20 to <31 [n=353, 17 (4.8%)/336]		2.10 (0.87-5.39)	
				≥31 [n=355 39 (11%)/316]		3.81 (1.56-10.1)	
cross-sectional Japan Uemura et al. (2009) environmental	1,374 people from the general population of Japan (from 75 different residential areas of 25 prefectures) who were not occupationally exposed to	160 have metabolic syndrome/1,214 do not have metabolic syndrome	Serum lipid levels of PCDDs, PCDFs, and dioxin-like PCBs	Exposure	adjOR metabolic syndrome (all, n=1374) [cases (prevalence)/total n]	adjOR metabolic syndrome (excl. 65 diabetics, n=1309) [cases (prevalence)/total n]	age, gender, smoking, drinking,
				PCDDspg TEQ/g lipid			

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates		Adjusted For	
cross-sectional Slovakia Ukropec et al. (2010) environmental	2,047 individuals (41% male) from the heavily polluted east Slovakian district and two adjacent districts; ages 21-75 years	<u>Metabolic syndrome:</u> defined as having three or more of the following five criteria: a) BMI≥25 kg/m ² ; b) serum triglycerides≥150 mg/dL; c) serum HDL<40mg/dL in men or <50 mg/dL in women; d) systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg, or self reported history of physician-diagnosed hypertension; e) HbA1c≥5.6%	Serum lipid levels of PCBs, HCB, p,p'-DDE, p,p'-DDT, βHCH	<4.6	1.00	1.00	regional block, residential area, and survey year
				<4.49 (w/o diab)	[15 (4.4%)/343]	[12 (3.7%)/325]	
				4.0-7.39	2.2 (1.2-4.4)	2.2 (1.1-4.8)	
				4.48-7.27 (w/o diab)	[39 (11.3%)/344]	[31 (9.4%)/329]	
				7.39-<11.20	2.1 (1.1-4.3)	2.1 (0.99-4.7)	
				7.27-<11.00 (w/o diab)	[38 (11.2%)/339]	[28 (9%)/311]	
				≥11.20	3.2 (1.6-6.7)	3.4 (1.6-7.6)	
				≥11.00 (w/o diab)	[68 (19.5%)/348]	[51 (14.8%)/344]	
				p-trend	<0.01	<0.01	
				PCDFspg TEQ/g lipid			
				<2.9	1.00	1.00	
				<2.83 (w/o diab)	[9 (2.7%)/330]	[9 (2.8%)/326]	
				2.9 to <4.5	4.0 (1.9-9.3)	3.5 (1.6-8.2)	
				2.83 to <4.4 (w/o diab)	[40 (11.5%)/347]	[31 (9.5%)/326]	
				4.5 to <6.80	4.1 (1.9-9.7)	3.8 (1.7-9.2)	
				4.4 to <6.6 (w/o diab)	[48 (13.6%)/352]	[37 (11.5%)/323]	
				≥6.80	4.4 (2.0-11)	3.8 (1.6-9.7)	
				≥6.6 (w/o diab)	[63 (18.3%)/345]	[45 (13.5%)/334]	
				p-trend	0.04	0.07	
				dioxin-like PCBs pg TEQ/g lipid			
				<4.40	1.00	1.00	
				<4.28 (w/o diab)	[14 (4.1%)/339]	[9 (2.8%)/327]	
				4.40 to 7.6	1.9 (0.95-4.0)	3.1 (1.4-7.4)	
				4.28 to 7.4 (w/o diab)	[27 (8%)/339]	[24 (7.5%)/320]	
				7.6 to <13	2.8 (1.3-6.2)	5.0 (2.1-13)	
				7.4 to <12.87 (w/o diab)	[39 (12%)/325]	[35 (10.5%)/334]	
				≥13	4.8 (2.2-11)	7.3 (2.9-20)	
				≥12.87 (w/o diab)	[80 (21.6%)/371]	[54 (16.5%)/328]	
				p-trend	<0.01	<0.01	
				Total TEQs pg TEQ/g lipid			
				<12.00 (both)	1.00	1.00	
					[10 (3.3%)/303]	[10 (3.3%)/303]	
				12 to <20	2.3 (1.1-5.3)	2.2 (0.98-5.0)	
12 to <19 (w/o diab)	[29 (8%)/363]	[22 (6.9%)/318]					
20 to <31	3.7 (1.7-8.7)	3.2 (1.4-7.6)					
19 to <30 (w/o diab)	[47 (13.3%)/353]	[35 (10.1%)/345]					
≥31	5.3 (2.3-13)	5.1 (2.1-13)					
≥30 (w/o diab)	[74 (20.8%)/355]	[55 (16%)/343]					
p-trend	<0.01	<0.01					
	Exposure	Odds Ratio (95% CI)					
	PCB (ng/g lipids)	pre-diabetes	diabetes				
		[cases (prevalence)/total n]	[cases (prevalence)/total n]				
	Q1: 148-627	1.00	1.00				
		[189 (46.2%)/409]	[30 (7.3%)/409]				

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates			Adjusted For
	1,220 with diabetes or pre-diabetes	diabetes (FPG>7.0 mmol/l; 2 h glucose >11.1 mmol/l)		Q2: 627-904 0.99 (0.73-1.35)	1.32 (0.77-2.26) [211 (51.2%)/409]	[47 (11.5%)/409]	residential area, and survey year
				Q3: 904-1,341	1.52 (1.11-2.09) [257 (62.3%)/410]	1.64 (0.96-2.80) [61 (14.9%)/410]	
HCB (ng/g lipids)	pre-diabetes [cases (prevalence)/total n]	diabetes [cases (prevalence)/total n]		Q4: 1,341-2,330	2.27 (1.64-3.15) [291 (71.2%)/409]	1.77 (1.05-3.02) [68 (16.6%)/409]	
Q1: 21-214	1.00 [192 (46.9%)/409]	1.00 [25 (6.1%)/409]		Q5: 2,330-101,413	2.74 (1.92-3.90) [321 (78.3%)/410]	1.86 (1.09-3.17) [90 (22.0%)/410]	
Q2: 214-499	1.20 (0.86-1.68) [220 (53.8%)/409]	0.63 (0.33-1.17) [28 (6.8%)/409]		p,p'-DDE (ng/g lipids)			
Q3: 499-838	1.30 (0.89-1.90) [260 (63.4%)/410]	0.94 (0.52-1.70) [61 (14.9%)/410]		Q1: 54-821	1.00 [175 (42.8%)/409]	1.00 [23 (5.6%)/409]	
Q4: 838-1,364	1.62 (1.07-2.46) [290 (70.9%)/409]	1.21 (0.66-2.23) [80 (19.6%)/409]		Q2: 821-1,410	1.30 (0.96-1.77) [226 (55.3%)/409]	1.43 (0.80-2.56) [43 (10.5%)/409]	
Q5: 1,364-17,927	1.86 (1.17-2.95) [307 (74.9%)/410]	1.25 (0.64-2.43) [102 (24.9%)/410]		Q3: 1,410-2,224	1.66 (1.21-2.28) [265 (64.6%)/410]	1.85 (1.06-3.21) [67 (16.3%)/410]	
β-HCH (ng/g lipids)				Q4: 2,224-3,605	1.93 (1.38-2.69) [284 (69.4%)/409]	1.34 (0.76-2.35) [61 (14.9%)/409]	
Q1: 3-23	1.00 [189 (46.2%)/409]	1.00 [26 (6.4%)/409]		Q5: 3,605-22,328	2.49 (1.74-3.57) [319 (77.8%)/410]	1.94 (1.11-3.78) [102 (24.9%)/410]	
Q2: 23-37	1.08 (0.79-1.50) [216 (52.8%)/409]	0.90(0.50-1.60) [37 (9.0%)/409]		p,p'-DDT (ng/g lipids)			
Q3: 37-56	1.25 (0.87-1.80) [254 (62.2%)/ 408]	0.77 (0.43-1.37) [49 (12.0%)/408]		Q1: 4-26	1.00 [177 (43.3%)/409]	1.00 [18 (4.4%)/409]	
Q4: 56-83	1.40 (0.95-2.06) [284 (69.1%)/411]	0.91 (0.51-1.62) [70 (17.0%)/411]		Q2: 26-39	1.17 (0.86-1.58) [220 (53.8%)/409]	1.57 (0.86-2.86) [42 (10.3%)/409]	
Q5: 83-781	1.97 (1.28-3.04) [326 (79.5%)/410]	1.08 (0.59-1.97) [114 (27.8%)/410]		Q3: 39-40	1.73 (1.27-2.36) [267 (65.1%)/410]	1.84 (1.03-2.27) [56 (13.7%)/410]	
				Q4: 60-103	1.88 (1.37-2.57) [285 (69.7%)/409]	2.51 (1.43-4.38) [80 (19.6%)/409]	
				Q5: 103-940	2.48 (1.77-3.48) [320 (78.1%)/410]	2.49 (1.42-4.35) [100 (24.4%)/410]	
prospective cohort US, Michigan Vasiliiu et al. (2006) environmental	1384 adults in the Michigan PBB cohort established in 1976 (25 years of follow-up); 48% male; ages ≥20 years	diabetes (self report) 180 diabetics (13%)/1204 without diabetes	PBBs, PCBs (serum at enrollment)	Incidence Density Ratios (95% CIs)			age, BMI, smoking status, alcohol consumption at enrollment
				PBB, ppb (cumulative incidence)	♂(n=688)	♀(n=696)	
				≤1.0 (♂12%; ♀14%)	1.00	1.00	
				1.1-3.0 (♂13%; ♀11%)	0.71 (0.33-1.56)	1.08 (0.61-1.89)	
				3.1-7 (♂14%; ♀17%)	0.63 (0.28-1.39)	1.20 (0.68-2.11)	
				>7 [♂n=225, 27 cases (12%); ♀n=101, 11 cases (11%)]	0.50 (0.23-1.12)	1.52 (0.74-3.14)	
				PCB, ppb(cumulative incidence)	♂(n=688)	♀(n=696)	
				≤5.0 (♂9%; ♀10%)	1.00	1.00	
				5.1-7.0 (♂12%; ♀12%)	1.59 (0.77-3.28)	2.04 (1.10-3.78)	
				7.1-10 (♂11%; ♀16%)	0.99 (0.48-2.01)	2.25 (1.19-4.26)	
				>10 [♂n=190, 35 cases (18%); ♀n=111, 22 cases (20%)]	1.74 (0.91-3.34)	2.33 (1.25-4.34)	
retrospective cohort	Mortality in the International Agency for	diabetes	TCCD, higher	Poisson regression analysis of diabetes mortality in the IARC international cohort study			age,

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
IARC international cohort study Vena et al. (1998) occupational	Research on Cancer (IARC) International Study 26,976 of phenoxyacid herbicide and chlorophenol production workers and sprayers from 36 cohorts in 12 countries followed from 1939-1992. 21,863 workers included in current analysis: 13,831 exposed to TCDD or higher chlorinated dioxins (HCD) 7,552 not exposed 479 unknown amounts of exposure	(death certificate)	chlorinated dioxins (HCD) (job records and company questionnaires with validation by biologic and environmental measures)	and indices of exposure to TCDD or HCD, RR (95% CI)	gender, country, calendar period, employment status, years since first exposure, and duration of exposure to phenoxy herbicides or chlorophenols	
				“yes” (33 cases) versus “no” (11 cases)		RR = 2.25 (0.53-9.50)
				years since first TCDD/HCD exposure		
				0-9 (reference, 3 cases)		1.00
				10-19 (14 cases)		2.34 (0.56-9.83)
				20+ (16 cases)		1.54 (0.30-7.82), p for trend=0.96
				years of TCDD/HCD exposure		
				< 1 (reference, 8 cases)		1.00
				1-4 (9 cases)		1.07 (0.39-2.94)
				5-9 (4 cases)		1.01 (0.28-3.62)
				10-19 (10 cases)		2.52 (0.89-7.11)
				20+ (2 cases)		1.13 (0.20-6.43), p for trend=0.18
				year of first TCDD/HCD exposure		
before 1955 (reference, 16 cases)	1.00					
1955-1964 (10 cases)	0.97 (0.41-2.30)					
1965+ (7 cases)	1.76 (0.58-5.31), p for trend= 0.42					
prospective cohort Belgium Verhulst et al. (2009) environmental	138 mother-infant pairs living in Flanders, Belgium, with follow-up until children were 3 years of age; Year=	growth (BMI standard deviation score, SDS)	DDE, HCBs, PCBs, dioxin-like compounds DDE mean: (range) 212 (24-1,816) ng/g lipid PCBs (congeners 118, 138, 153, 170, and 180): mean (range): 117 (9-442) ng/g lipids hexachlorobenzene: mean (range) 34.4 (4.3-108.3) ng/g lipid dioxin-like compounds: assessed by dioxin-responsive chemical activated luciferase expression assay (DR-CALUX) mean (range) 31 (6.0-78.7 pg CALUX-TEQ/g lipids)	Association between DDE and BMI SDS of children between 1-3 years of age	age of the child, BMI of both parents, maternal age at time of birth, birth weight SDS, any breastfeeding, maternal smoking before and/or during pregnancy, household income	
				DDE		β (SE)= -0.002 (0.001), p=0.2
				DDE x maternal smoking ever		β (SE)= -0.003 (0.001), p=0.06
				DDE x maternal smoking ever x age of child		β (SE)= 0.001 (0.001), p=0.04
				PCBs		β (SE)= 0.003 (0.001), p=0.03
				hexachlorobenzene		no association with BMI SDS (data not reported)
				dioxin-like compounds		no association with BMI SDS (data not reported)
				Least-square means for BMI SDS by age of child and maternal smoking status		
				Maternal smoking: no		Maternal smoking: yes
				10th percentile (63.7 ng/g lipid)		
				age 1; β (SE)= 0.74 (± 0.15)		age 1; β (SE)= 1.42 (± 0.17)
				age 2; β (SE)= 0.11 (± 0.14)		age 2; β (SE)= 0.38 (± 0.17)
				age 3; β (SE)= -0.53 (± 0.21)		age 3; β (SE)= -0.66 (± 0.24)
				90th percentile (450 ng/g lipid)		
				age 1; β (SE)= 1.03 (± 0.15)		age 1; β (SE)= 1.21 (± 0.30)
				age 2; β (SE)= 0.32 (±0.15)		age 2; β (SE)= 0.65 (±0.30)
				age: 3; β (SE)= -0.39 (±0.20)		age 3; β (SE)= 0.10 (±0.40)
Difference in BMI SDS for DDE level of 450 ng/g and 63.7 ng/g						
0.13, no maternal smoking	0.76, maternal smoking					
retrospective cohort Taiwan Wang et al. (2008) environmental	378 Yucheng subjects(155 ♂ and 223 ♀) and 370 matched referents (152 ♂ and 218 ♀) from the Yucheng cohort assessed 1993-2003; 24-year follow-up (41% ♂; ages ≥30 years)	diabetes (self-report of T2D, with and without therapy) total n=748; 144 diabetics	ΣPCBs (serum collected 1979-1983)	T2D and prevalence (Yucheng versus referent)	♀: age and BMI ♂: age, BMI, cigarette	
				PCBs levels = 73.3 vs 1.67 ppb*, ♂ 87.4 vs 1.67 ppb*, ♀ *based on pooled sample from 50 referents		
				T2D without therapy, ♂		1.0 (0.5-1.9)

Appendix Table for Epidemiology Studies of Persistent Organic Pollutant (POPs)

Study Design	Population	Diagnosis	Exposure	Risk Estimates	Adjusted For	
	(19.3%)/604 without diabetes			22 (14.4%) vs 22 (14.7%)	smoking, and alcohol drinking	
				T2D with therapy, ♂ 22 (14.3%) vs 17 (11.3%)		1.3 (0.7-2.7)
				T2D without therapy, ♀ 25 (11.3%) vs 12 (5.6%)		2.1 (1.1-4.5)*
				T2D with therapy, ♀ 17 (7.7%) vs 7(3.2%)		2.5 (1.0-6.5)*
				T2D diabetes based on chloracne status in Yucheng individuals aged ≥30 years, "positive" versus "negative"		
				♂, 12 cases (16.9%)/60 non-cases vs 11 (11.6%)/84 non-cases PCBs levels = 94.4 vs 53.9 ppb		1.7 (0.7-4.6)
				♀, 14 cases (24.1%)/44 non-cases vs 11 (5.9%)/175 non-cases PCBs levels = 121.4 vs 72.6 ppb	5.5 (2.3-13.4)*	

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