Exposure to Persistent Organic Pollutants and Metabolic Diseases

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MAJOR RISK FACTORS FOR CARDIOVASCULAR DISEASE:

- Type II diabetes
- Central obesity
- Hypertension
- Proinflammatory and prothrombotic state
- Hyper/Dyslipidemia
  - High total cholesterol and triglycerides
  - Low HDL-cholesterol

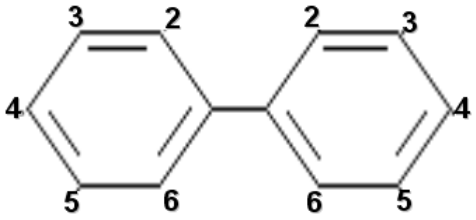
THE METABOLIC SYNDROME:

Defined as the presence ≥3 of metabolic diseases

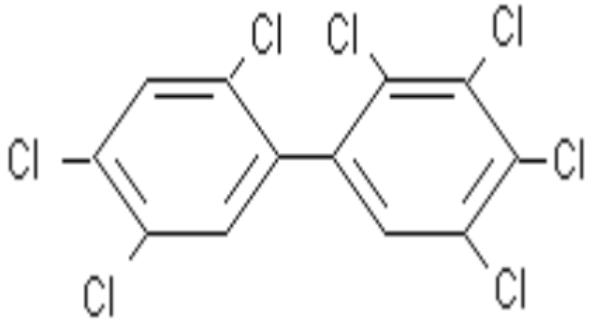
Does it really exist?

RISK FACTORS FOR METABOLIC DISEASES

- Age
- Genetic predisposition
- Positive energetic balance
  - Eat too much, especially high fat foods
  - Too little exercise
- Excessive alcohol consumption and smoking
- Exposure to toxic chemicals



(a)



(b)

Figure 2-1 Polychlorinated biphenyl molecule.

(a) shows a biphenyl molecule showing the 10 possible locations where a chlorine atom may be attached to the molecule.

(b) shows a PCB molecule with chlorine substitution at the 245 locations on one phenyl ring, and at the 2345 locations on the second phenyl ring. This particular PCB congener is referred to as 245-2345 CB or alternatively, PCB 180 (IUPAC nomenclature).

The populations studied:

- We investigated metabolic diseases in two populations:
- Anniston is a city of about 24,000 people. It is the home of one of two US plants operated by the Monsanto Corporation for the manufacture of polychlorinated biphenyls (PCBs), which were sold under the trade name, Aroclor, from 1929-1971. We obtained serum PCB and pesticide levels in 772 residents, ages 18-93 years, serum lipid concentrations and three measures of blood pressure.
- Akwesasne is a Native American community of about 12,000 living along the St. Lawrence River and exposed to PCBs because of industrial contamination. We obtained PCB. pesticide and serum lipid analysis from 601 residents ages 18-84

Results

Prevalence of metabolic diseases

	US, median %*	Anniston, %*	Mohawks, %
Obesity	24.4	**51**	**46**
CVD	4.0	**9**	**11**
Hypertension	25.5	**42**	**29**
Diabetes	7.3	**16**	**19**

*(Rosenbaum, 2012)

Statistical methods:

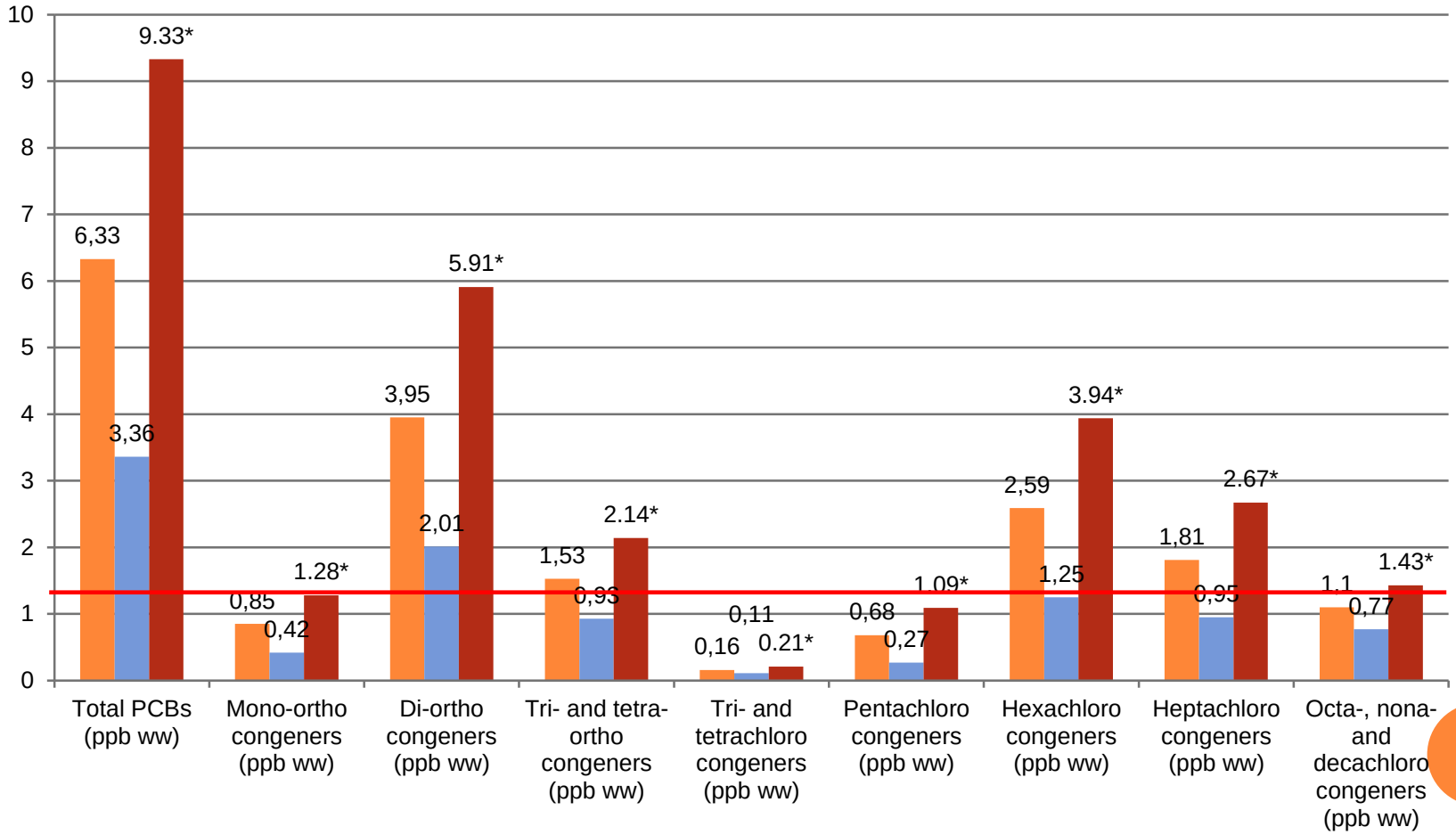
- PCBs were categorized by total concentration and by numbers and positions of chlorines. Pesticides were grouped by class.
- Multiple log-binomial and logistic regression were used to assess relationships between exposure variables and each metabolic disorder.
- Three models were applied. In Model 1 exposure variables were adjusted for covariates (age, gender, BMI and serum total lipids). In Model 2 in addition to the above covariates there was further adjustment total PCBs or total pesticides. In Model 3 there was adjustment for all other contaminants and/or contaminant groups.

Data collection

Variables	Anniston population	Mohawks of Akwesasne
Exposure	35 ortho-substituted PCBs, 9 OCPs	101 PCBs, 3 OCPs
Serum lipids	Total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides	Total cholesterol and triglycerides
BMI (obesity)	Weight and height	Weight and height
Diabetes	Self-reported diabetes or serum fasting glucose concentrations	Self-reported diabetes or serum fasting glucose concentrations
Hypertension	Three measurements of systolic and diastolic blood pressures	Self-reported hypertension
CVDs	Self-report of CVDs	Self-report of CVDs
Lifestyle	Physical exercise, alcohol consumption, smoking status and amount	Smoking status was available only for part of the study population
Medication	Complete information on medications	Medication data was collected for a part of the study population

Results

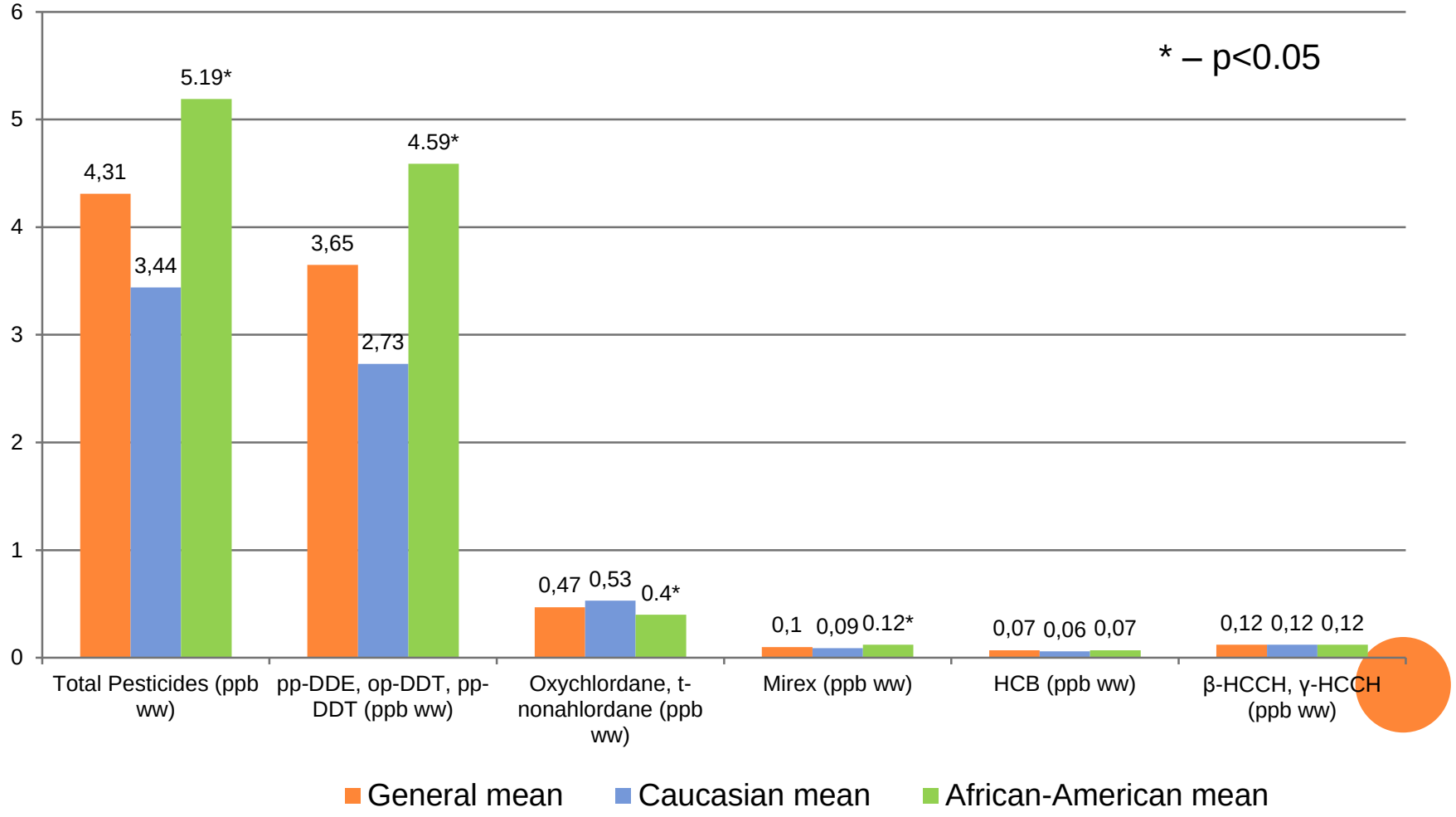
- Serum concentrations of PCBs (Anniston, AL)



*- Significant at p=0.05

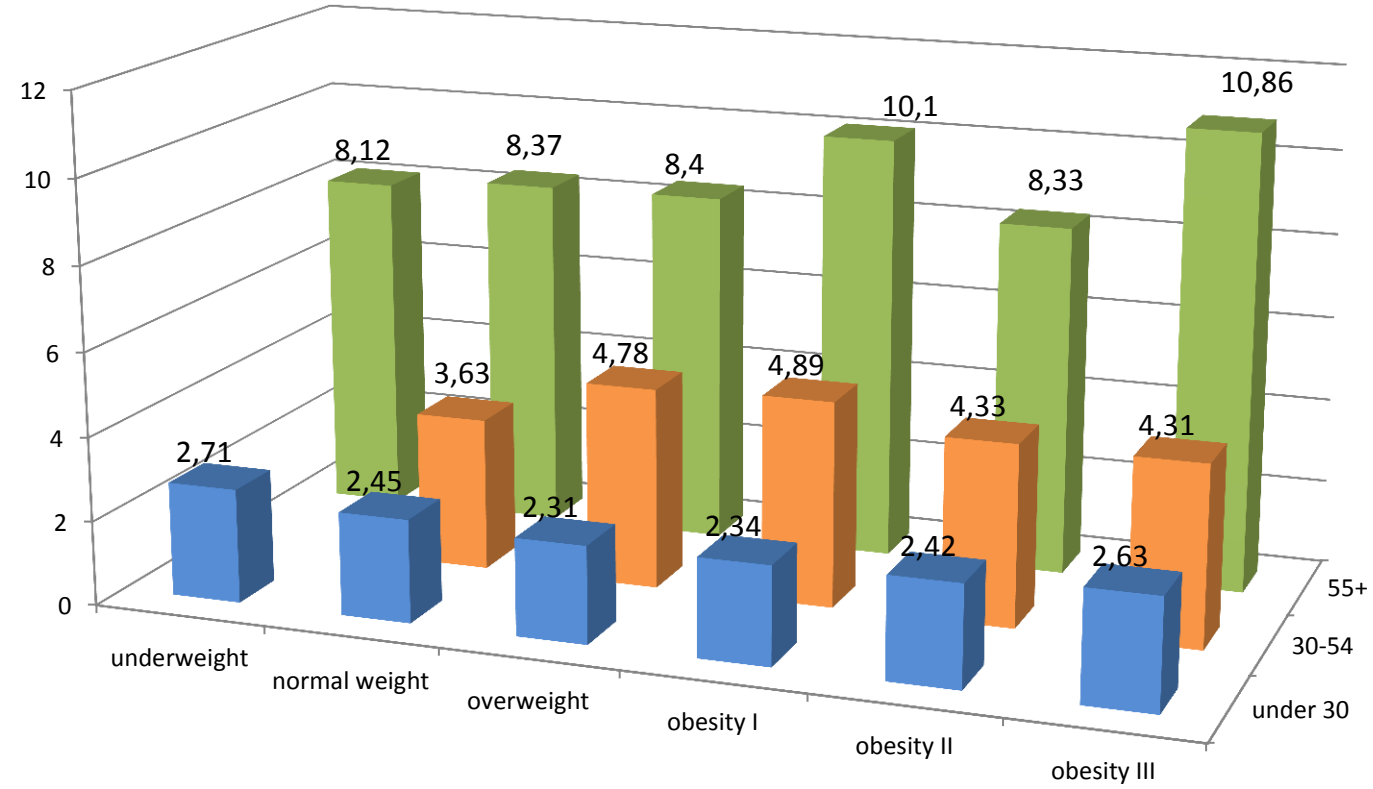
Results

- Serum concentrations of OCPs (Anniston, AL)



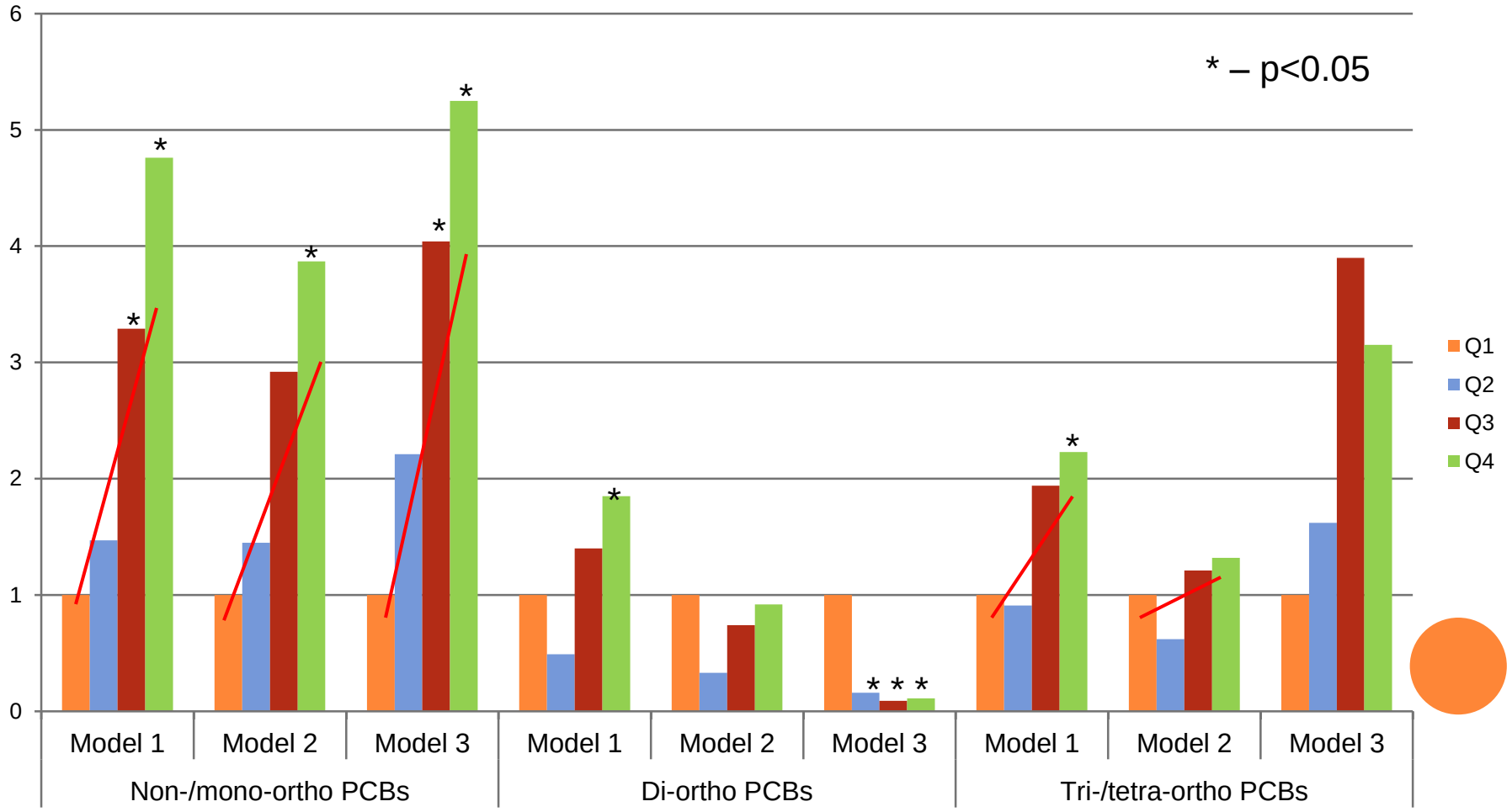
Results

- Serum concentrations of PCBs (ppb) by age and BMI (Mohawks)



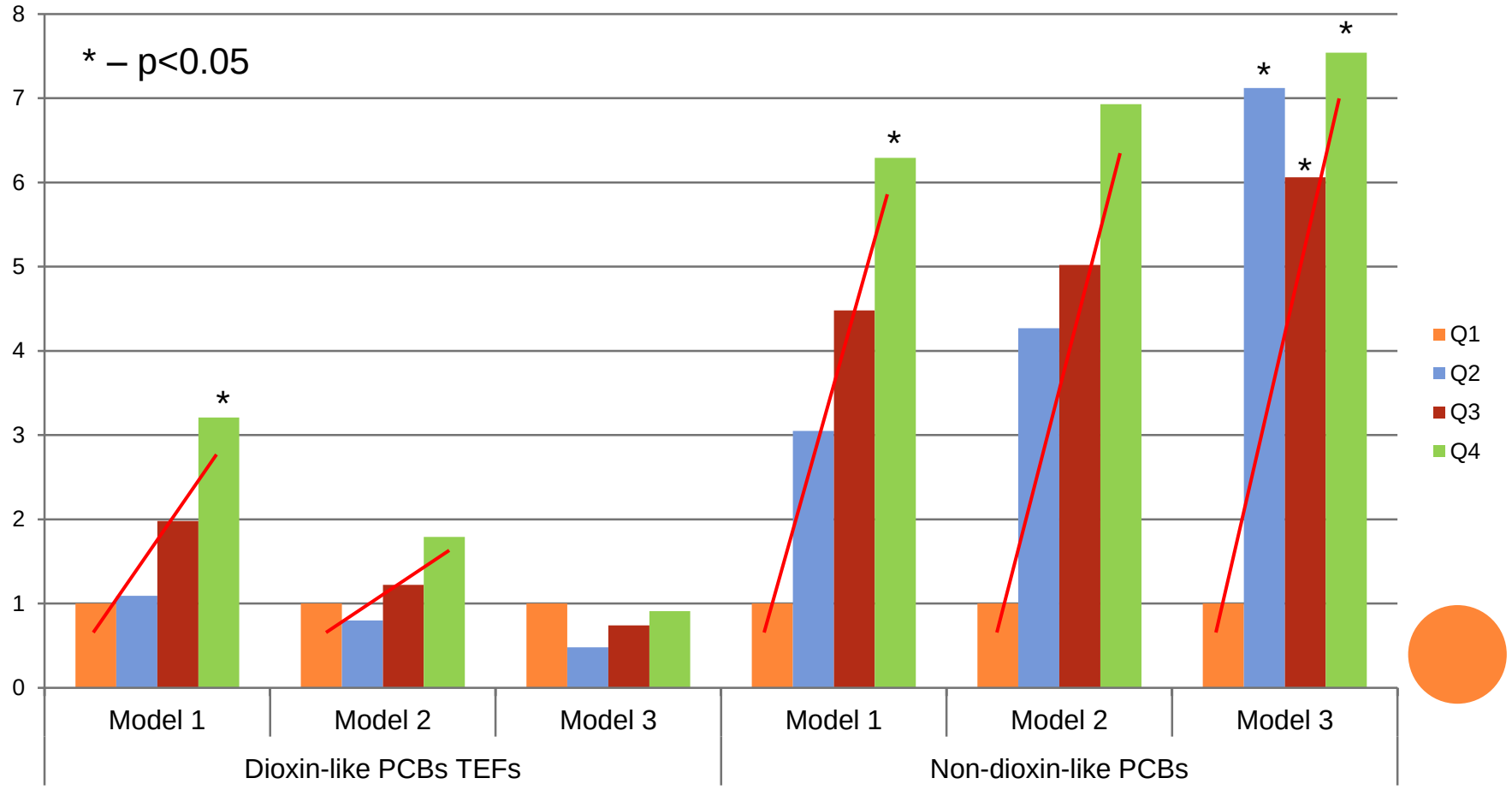
Results

- Exposure to PCBs and diabetes (Mohawks)



Results

- Exposure to non-/mono-ortho PCBs and diabetes (Mohawks)



Results

- Exposure to OCPs and diabetes (Mohawks)

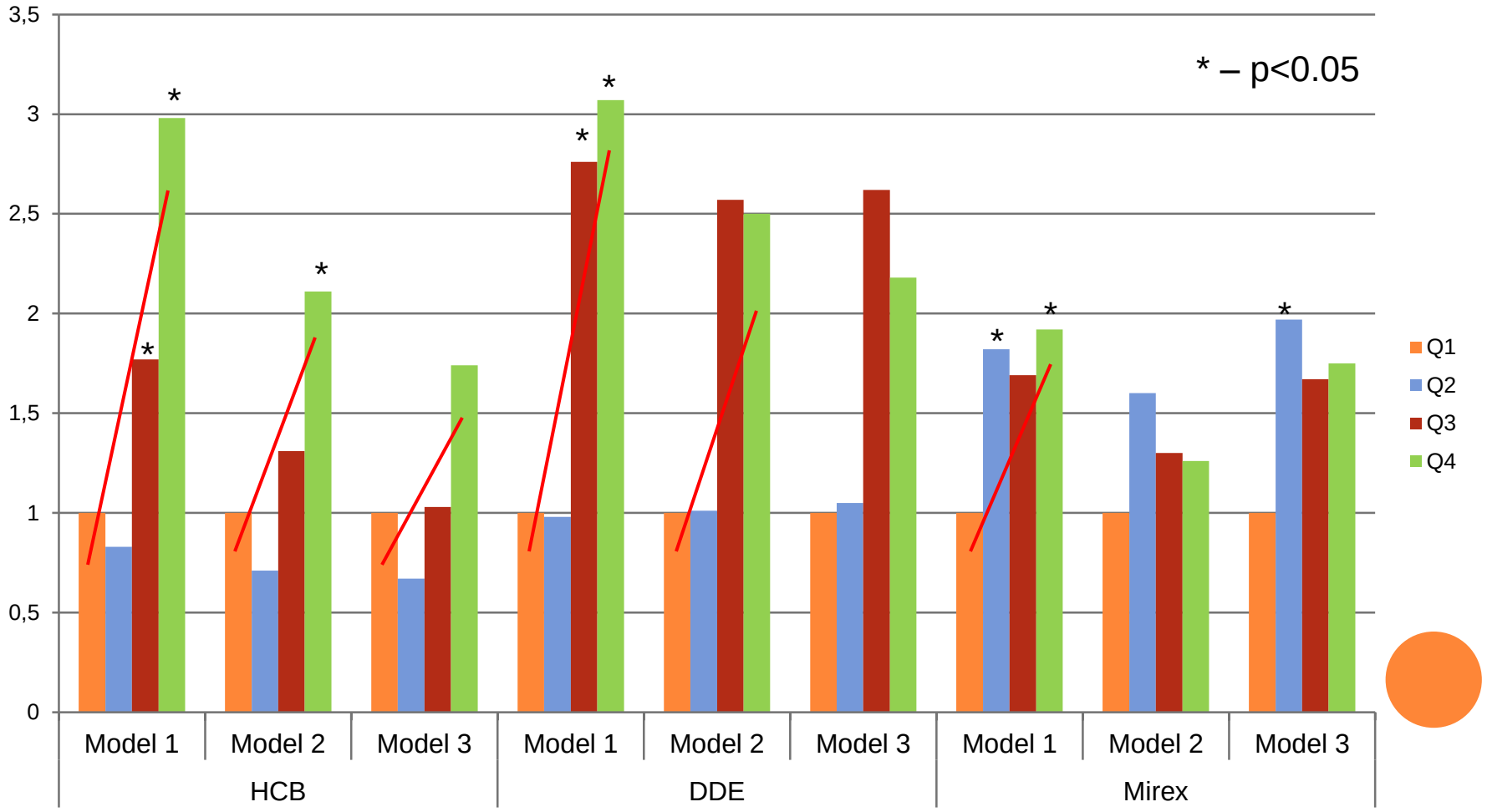


Figure 2. Linear regression of systolic and diastolic blood pressure on total PCBs concentration. The dashed lines show cut-off pressures for systolic (a) and diastolic (b) hypertension. Data from Anniston.

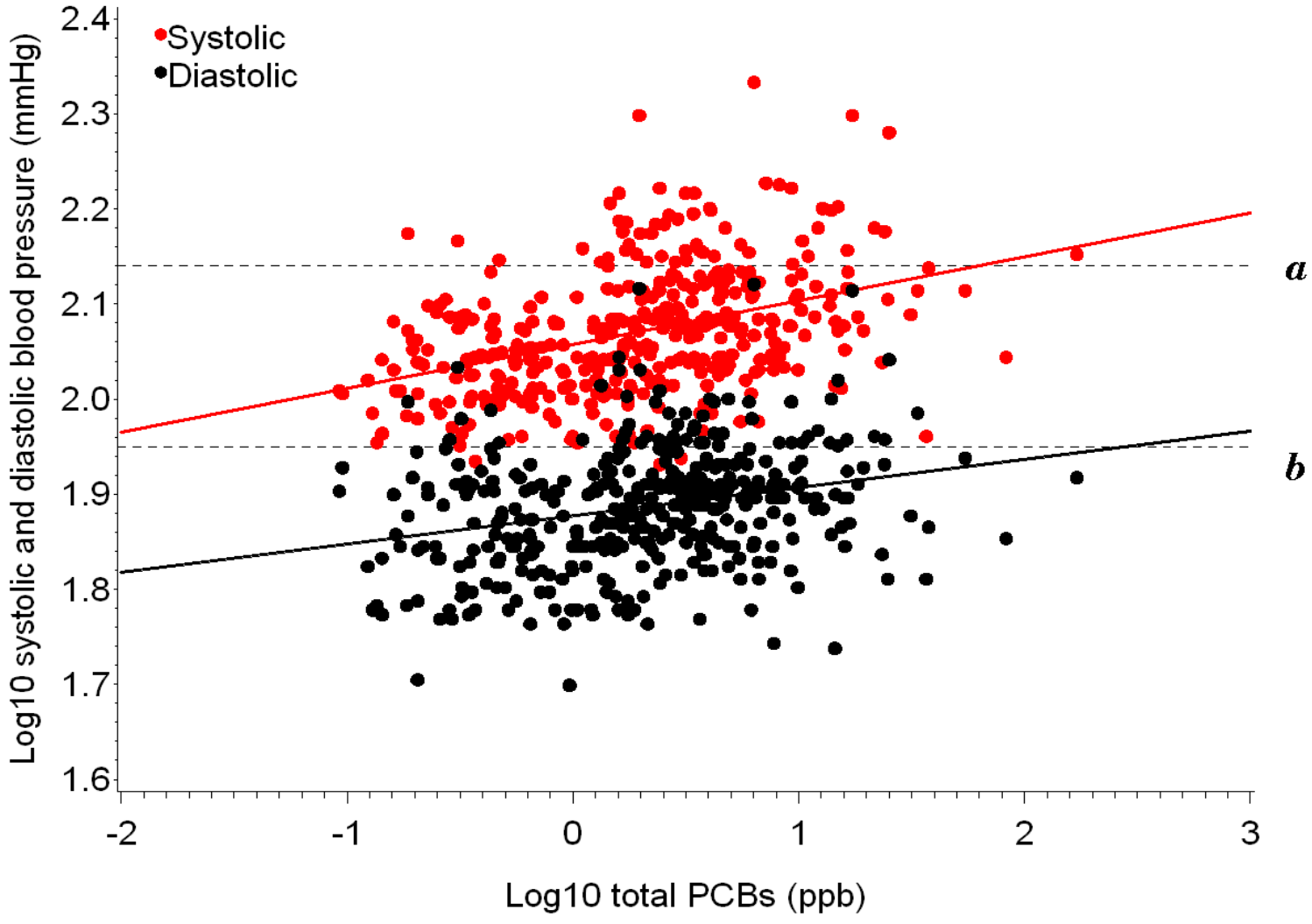
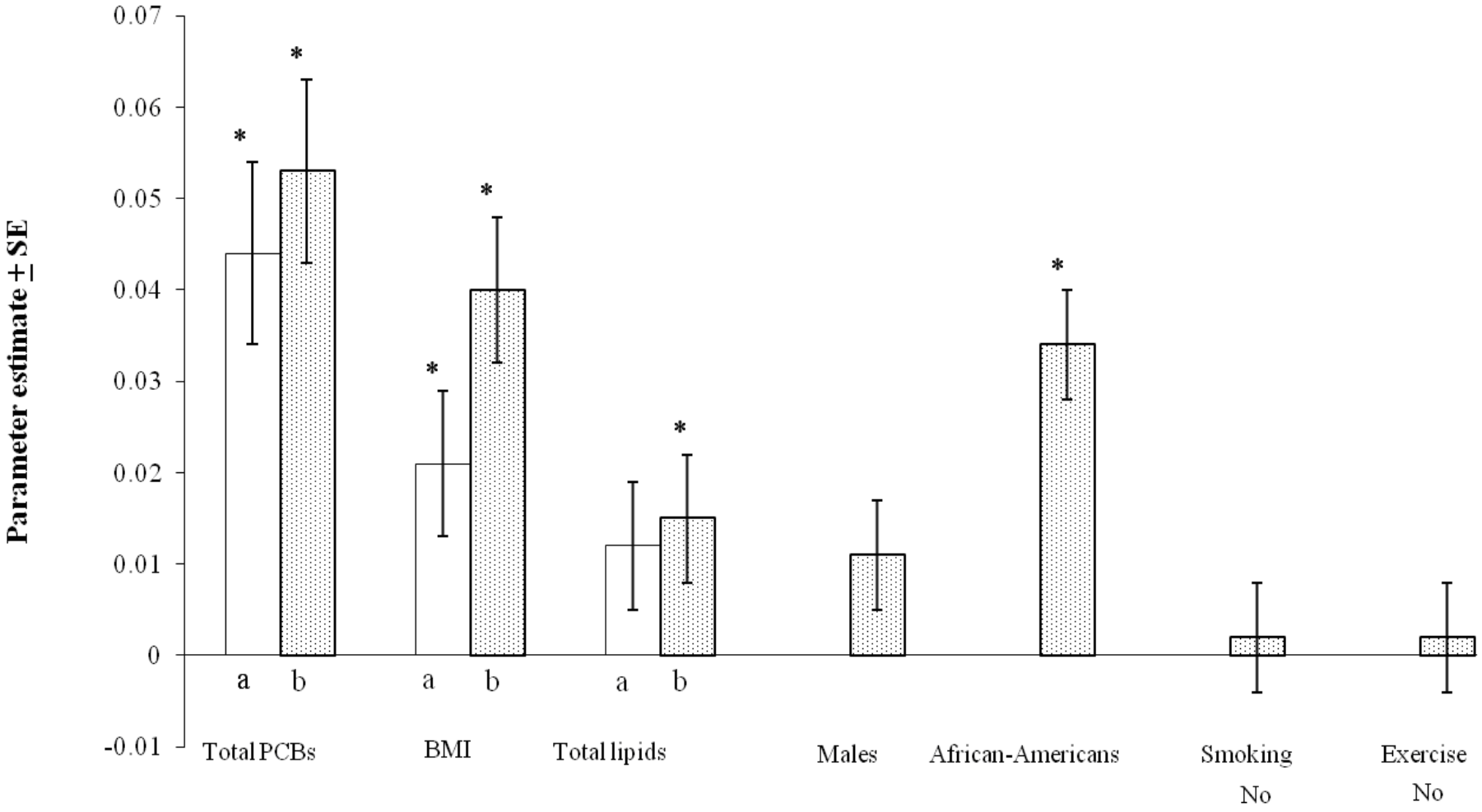


Table 2 **Odds ratios and 95% confidence intervals for clinical hypertension, diastolic hypertension, systolic hypertension, and systolic and diastolic hypertension in relation to total polychlorinated biphenyl concentrations by tertile after adjustment for age, BMI, total serum lipid (or lipid components), sex, race, smoking status, and physical activity in the participants who were not on medication**

PCBs tertiles (ppb)	Hypertensive/ normotensive	OR (95%CI)[a]	OR (95%CI)[b]
Clinical hypertension			
1st 0.1–1.2	7/124	1.0	1.0
2nd 1.3–3.6	32/100	3.90 (1.4–10.5)	3.58 (1.4–10.3)
3rd 3.7–170.4	33/98	4.09 (1.3–12.7)	3.86 (1.1–10.9)
Diastolic			
1st 0.1–1.2	7/124	1.0	1.0
2nd 1.3–3.6	24/108	4.27 (1.5–12.1)	3.66 (1.1–11.9)
3rd 3.7–170.4	25/106	4.49 (1.3–14.9)	4.15 (1.4–11.6)
Systolic			
1st 0.1–1.2	4/127	1.0	1.0
2nd 1.3–3.6	25/107	3.05 (0.7–12.0)	2.95 (0.7–11.4)
3rd 3.7–170.4	24/107	3.87 (1.1–13.1)	3.82 (1.1–12.8)
Systolic and diastolic			
1st 0.1–1.0	3/116	1.0	1.0
2nd 1.1–3.4	17/103	5.21 (1.2–21.5)	4.64 (1.0–21.9)
3rd 3.4–82.9	17/103	5.26 (1.0–25.8)	4.95 (1.2–20.1)

[a] ORs for total PCBs with total lipids as a model covariate. [b] ORs for lipid-

Parameter estimates +/- SE of mean diastolic blood pressure in those not on antihypertensive medication in relation to risk factors after adjustment for age (*p<0.05).

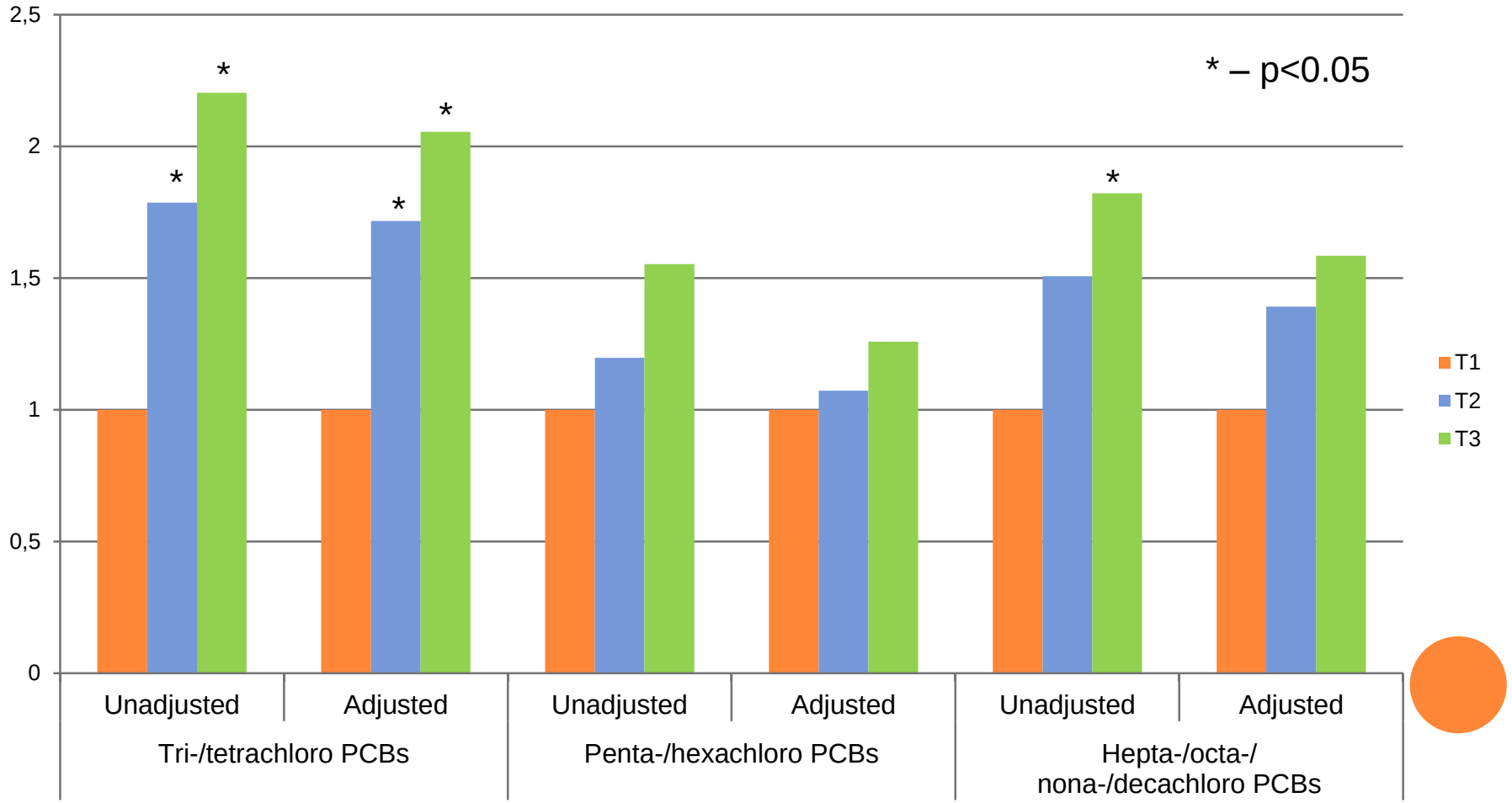


Pesticides and Blood Pressure

- We found no significant relationship between concentrations of hexachlorobenzene, β and γ hexachlorocyclohexane, oxychlordane, trans-nonachlor, pp'-DDE, op'- or pp'-DDT or mirex with either systolic or diastolic blood pressure in the Anniston population and no consistent significant relationship with DDE, HCB or mirex at Akwesasne.
- We conclude that PCBs alter blood pressure but chlorinated pesticides do not. Serum PCB concentration is a greater risk factor than any other monitored except age.

Results

- Exposure to PCBs and hypertension (Mohawks)



RESULTS

- Exposure to PCBs and serum lipids (Anniston, AL)

		Mono-ortho		Di-ortho		Tri-/Tetra-ortho	
		Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Total lipids	β	**0.04**	-0.05	**0.05**	**-0.09**	**0.06**	**0.12**
	p-value	**0.0005**	0.0814	**<0.0001**	**0.0433**	**<0.0001**	**<0.0001**
Total Cholesterol	β	**0.03**	-0.02	**0.03**	-0.08	**0.04**	**0.09**
	p-value	**0.0262**	0.5254	**0.0169**	0.0846	**0.0013**	**0.0047**
HDL cholesterol	β	0.01	**0.08**	-0.00	-0.05	-0.00	-0.02
	p-value	0.4722	**0.0297**	0.9741	0.4145	0.8036	0.6888
LDL cholesterol	β	0.02	-0.03	0.02	-0.09	**0.04**	**0.11**
	p-value	0.2997	0.4565	0.1728	0.2056	**0.0285**	**0.0133**
Triglycerides	β	**0.08**	**-0.16**	**0.09**	-0.20	**0.12**	**0.31**
	p-value	**0.0117**	**0.0219**	**0.0018**	0.0754	**<0.0001**	**<0.0001**

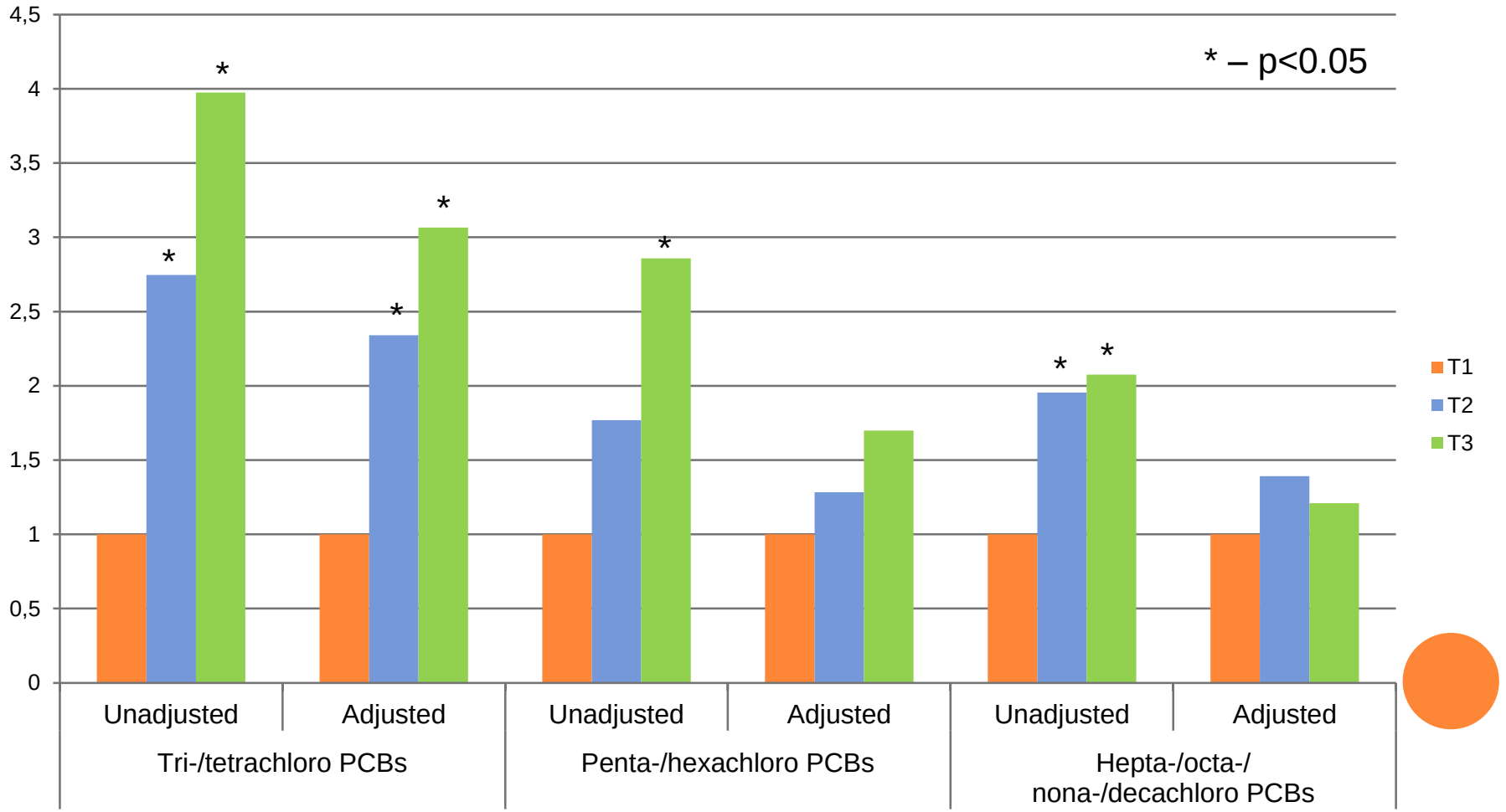
RESULTS

- Exposure to OCPs and serum lipids (Anniston, AL)

		DDT		Chlordane		Mirex		HCB		HCCH	
		Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Total lipids	β	**0.05**	0.00	**0.11**	**0.05**	**0.05**	0.02	**0.21**	**0.21**	**0.07**	-0.03
	p-value	**<0.0001**	0.8109	**<0.0001**	**0.0037**	**0.0002**	0.2608	**<0.0001**	**<0.0001**	**<0.0001**	0.1205
Total Cholesterol	β	**0.03**	0.00	**0.06**	0.02	**0.03**	0.01	**0.15**	**0.18**	**0.04**	-0.04
	p-value	**0.0124**	0.9873	**<0.0001**	0.3877	**0.0125**	0.3697	**<0.0001**	**<0.0001**	**0.0018**	0.0629
HDL cholesterol	β	-0.01	0.00	-0.03	-0.03	0.01	0.02	**-0.06**	**-0.08**	-0.01	0.02
	p-value	0.5831	0.9323	0.1309	0.3034	0.7112	0.4401	**0.0205**	**0.0267**	0.4439	0.5214
LDL cholesterol	β	0.02	0.00	**0.05**	-0.00	0.02	0.00	**0.17**	**0.25**	0.03	**-0.07**
	p-value	0.2229	0.9100	**0.0266**	0.9531	0.2846	0.8392	**<0.0001**	**<0.0001**	0.1862	**0.0198**
Triglycerides	β	**0.10**	-0.01	**0.26**	**0.18**	**0.09**	0.01	**0.44**	**0.39**	**0.18**	-0.02
	p-value	**0.0003**	0.8396	**<0.0001**	**<0.0001**	**0.0054**	0.8391	**<0.0001**	**<0.0001**	**<0.0001**	0.6926

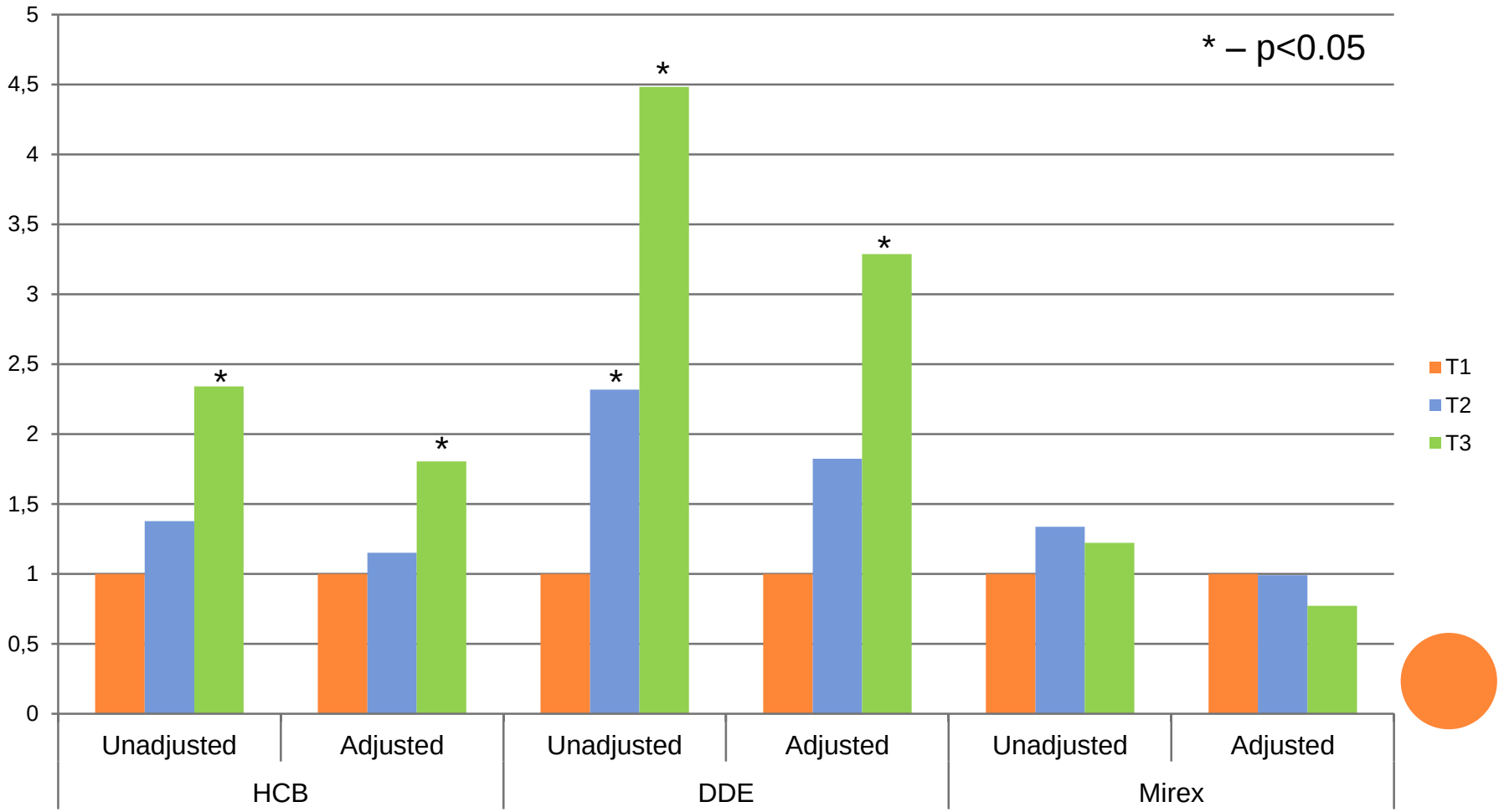
Results

- Exposure to PCBs and the MetS (Mohawks)



Results

- Exposure to OCPs and the MetS (Mohawks)



Discussion

- Some statistically significant relationships have been observed between exposure to POPs and metabolic diseases
- The relationships were not the same for all metabolic diseases
  - Diabetes showed stronger relationships with lower chlorinated and non-/mono-*ortho* PCBs
  - Hypertension had significant association with lower chlorinated, non-/mono-*ortho* as well as tri-/tetra- PCBs
  - Dys/hyperlipidemia was more strongly associated with highly chlorinated PCBs and those with multiple *ortho*-chlorines

Discussion

- All observed relationships with lower chlorinated and non-/mono-*ortho* PCBs were not related to dioxin-like activity
- There is emerging evidence to direct association between exposure to POPs and increased risk of CVD (Lee et al., 2012; Lind et al., 2012; Puga et al., 2011)
  - No direct associations have been observed in our study population (Mohawks)
  - CVD has shown strong associations with metabolic diseases
  - Aging was the strongest confounder in all analyses

Conclusion

- Our data suggest that exposure to various POPs increases risk of some metabolic diseases, but that the patterns are not the same.
- Diabetes and hypertension were associated primarily with low chlorinated, non-dioxin like PCBs, while hyperlipidemia was primarily higher chlorinated PCBs. There were not strong associations with cardiovascular disease or obesity.
- Since risks of the metabolic diseases were associated with different groups of POPs our results are consistent with the conclusion that the metabolic syndrome is not a single disease.