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Biomarkers of pesticide exposure and diabetes in the 1999–2004 National Health and Nutrition Examination Survey

Charles J. Everett *, Eric M. Matheson

Department of Family Medicine at the Medical University of South Carolina, United States

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The associations of 8 pesticides and pesticide metabolites with total diabetes (diagnosed and undiagnosed) and pre-diabetes (glycohemoglobin 5.7–6.4%) were evaluated using the National Health and Nutrition Examination Survey (NHANES), 1999–2004. Six of the pesticides were found to be associated with total diabetes in separate adjusted logistic regressions. These pesticides and pesticide metabolites were beta-hexachlorocyclohexane, *p,p′*-DDE, *p,p′*-DDT, oxychlordane, *trans*-nonachlor, and heptachlor epoxide. When the number of compounds elevated was tested, 4 or more, of the 6, elevated had an odds ratio of 4.99 (95% CI 1.97–12.61) compared to none elevated. When the 6 compounds were tested together in a single combined adjusted logistic regression only oxychlordane, a metabolite of chlordane, and heptachlor epoxide, a metabolite of heptachlor, were significantly associated with total diabetes. In the combined adjusted logistic regression, oxychlordane ≥14.5 ng/g lipid adjusted had an odds ratios of 1.90 (95% CI 1.09–3.32) compared to oxychlordane <14.5 ng/g lipid adjusted, and heptachlor epoxide ≥14.6 ng/g lipid adjusted had an odds ratio of 1.70 (95% CI 1.16–2.49) compared to heptachlor epoxide <14.6 ng/g lipid adjusted. Heptachlor epoxide and *p,p′*-DDT were significantly associated with pre-diabetes in separate adjusted logistic regressions. When these 2 compounds were tested together only heptachlor epoxide remained significantly associated with pre-diabetes. The evidence supporting the relationship between pesticides and pesticide metabolites, with diabetes, was strongest for heptachlor epoxide and oxychlordane, intermediate for *p,p′*-DDT, and least for beta-hexachlorocyclohexane, *p,p′*-DDE, and *trans*-nonachlor. Mirex and dieldrin were not associated with total diabetes or pre-diabetes.

1. Introduction

Pesticides or pesticide metabolites which have been shown to be associated with diabetes include beta-hexachlorocyclohexane, a metabolite of lindane (Lee et al., 2007c); oxychlordane and *trans*-nonachlor, both metabolites of chlordane (Lee et al., 2006, 2007c), hexachlorobenzene (Codru et al., 2007; Glynn et al., 2003), DDT (dichlorodiphenyltrichloroethane) (Everett et al., 2007; Morgan et al., 1980), and its metabolite DDE (dichlorodiphenyltrichloroethylene) (Lee et al., 2006, 2007c; Rignell-Hydbom et al., 2007; Rylander et al., 2005). The Agricultural Health Study has been used for a longitudinal study of incident diabetes among 31,787 licensed pesticide applicators (Montgomery et al., 2008). Participants enrolled at baseline (1993–1997) were contacted 5 years later for a follow-up interview (1999–2003). Persons having diabetes at baseline were excluded, and persons developing diabetes, by the follow-up interview, plus those without diabetes were evaluated for exposure to 49 pesticides. Ever-use of the organochlorines chlordane and heptachlor; organophosphates coumaphos, phorate, terbufos, and trichlorfon; and the herbicides alachlor and cyanazine was associated with incident diabetes in logistic regressions adjusted for age, state (Iowa versus North Carolina) and body mass index. In addition, a dose–response relationship with cumulative days of use was found for the organochlorine heptachlor, the organophosphates chlorpyrifos, diazinon, and trichlorfon, and the herbicides alachlor, and cyanazine.

States that precede diabetes, namely metabolic syndrome and insulin resistance have been shown to be related to some pesticide metabolites, but not all tested (Lee et al., 2007a,b). Gestational diabetes is considered an early stage in the progression to diabetes and risk factors are similar for both. Gestational diabetes has been shown to be associated with the reporting of ever-use of the herbicides 2,4,5-T; 2,4,5-TP/silvex; atrazine; and butylate; the organophosphate insecticides diazinon; and phorate; and the carbamate carbofuran among agriculturally exposed women (Saldana et al., 2007). The precise mechanisms through which pesticides induce diabetes remain unclear but several likely mechanisms have been proposed for organophosphates (Rahimi and Abdollahi, 2007). Organophosphates can affect glucose metabolism through blocking cholinesterase activity, oxidative stress, nitrosative stress, physiological stress, adrenal stimulation, and inhibition of paraoxanse.

The purpose of our study was to expand on previous analyses of pesticides and diabetes in the National Health and Nutrition

* Corresponding author. Department of Family Medicine, Medical University of South Carolina, 295 Calhoun Street, MSC 192, Charleston, SC 29425-1920, United States. Tel.: +1 843 792 3413; fax: +1 843 792 3598.
E-mail address: everettc@musc.edu (C.J. Everett).

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Examination Survey (NHANES) 1999–2002 (Everett et al., 2007; Lee et al., 2006, 2007c) by addition of the NHANES 2003–2004 data. We included heptachlor epoxide, mirex, and dieldrin in our study bringing the total number of pesticides and pesticide metabolites evaluated using the NHANES 1999–2004 to eight. In addition to evaluating total diabetes (diagnosed and undiagnosed) we also tested a precursor to diabetes called pre-diabetes or a "category of increased risk for diabetes" as defined by glycohemoglobin (HbA1c) 5.7–6.4% (ADA, 2010). We further tested all of the compounds significant in separate logistic regressions again in a single combined logistic regression to see which ones remained associated with diabetes or pre-diabetes. While it is desirable to evaluate dioxins, furans and polychlorinated biphenyls along with pesticides, this is not possible using the NHANES 2003–2004 data. Dioxins, furans and polychlorinated biphenyls were measured in "Subsample C," while pesticides were measured in "Subsample B."

2. Methods

Data used for this study were derived from the National Health and Nutrition Examination Survey (NHANES), 1999–2004. The NHANES 1999–2004 is a nationally representative sample of the noninstitutionalized U.S. population. The NHANES design includes an oversampling of minorities and an ability to make population estimates. More information on the methodology of the NHANES 1999–2004, including laboratory assessment, can be found at the National Center for Health Statistics (NCHS) website (CDC, 2009).

We investigated the association of 8 pesticides and pesticide metabolites with total diabetes (diagnosed plus undiagnosed). Diagnosed diabetes was assessed by self-report answer to the question: "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?" Persons who answered "borderline" were considered to not have diabetes. Undiagnosed diabetes was defined as persons who had glycohemoglobin (HbA1c) ≥6.5% who had not been diagnosed as having diabetes (ADA, 2010; Rohlfing et al., 2000). We did not use fasting plasma glucose for determination of undiagnosed diabetes because glucose was measured on a fasting subsample of participants and would have reduced the number of persons in our analyses by half. Total diabetes was defined as diagnosed plus undiagnosed diabetes. We also tested a precursor to diabetes called pre-diabetes or a "category of increased risk for diabetes" defined by HbA1c 5.7–6.4% (ADA, 2010).

Beta-hexachlorocyclohexane, *p,p′*-DDE, *p,p′*-DDT, oxychlordane, *trans*-nonachlor, heptachlor epoxide, mirex, and dieldrin were measured in nonfasting blood samples of a one third, stratified random, subsample of participants age 12 years and older. We evaluated persons in this subsample who were ≥20 years old. The unweighted number of participants assessed for total diabetes is listed in Table 1. When 6 chemicals were evaluated together for total diabetes (those significant in separate logistic regressions), the unweighted number of participants was 3049. There were 334 persons with diagnosed or undiagnosed diabetes in this logistic regression. In analyses of pre-diabetes, persons with diagnosed or undiagnosed diabetes were excluded. When 2 chemicals were tested together for pre-diabetes the unweighted number of participants was 2811. There were 462 persons with pre-diabetes in this logistic regression.

The eight pesticides and pesticide metabolites were measured in serum by high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry. Values are expressed on a lipid adjusted basis (Akins et al., 1989). The (maximum) limit of detection was 9.36 ng/g lipid adjusted for beta-hexachlorocyclohexane, 18.6 ng/g lipid adjusted for *p,p′*-DDE, 20.7 ng/g lipid adjusted for *p,p′*-DDT, 14.5 ng/g lipid adjusted for oxychlordane, 14.5 ng/g lipid adjusted for *trans*-nonachlor, 14.6 ng/g lipid adjusted for heptachlor epoxide, 14.6 ng/g lipid adjusted for mirex, and 10.5 ng/g lipid adjusted for dieldrin (CDC, 2005). For linear regressions and calculation of medians, values below the sample-specific limit of detection were set to the limit of detection divided by the square root of 2. For logistic regressions values below the (maximum) limit of detection were assigned to the lowest category.

It should be noted that all non-detectable pesticides have values below the (maximum) limit of detection, but that some detectable pesticides also have values below the (maximum) limit of detection. We chose to use values below the (maximum) limit of detection as our reference category, and classify values above the (maximum) limit of detection as having elevated pesticides. One exception to this procedure was *p,p′*-DDE, which had 99.6% of all measurements above the (maximum) limit of detection. In the case of *p,p′*-DDE, we used the first tertile as the reference category, and classified the second and third tertiles as elevated *p,p′*-DDE.

We tested the association of 8 pesticides and pesticide metabolites with total diabetes in logistic regressions adjusted for age, gender, race/ethnicity, education, poverty income ratio, body mass index, waist circumference, physical activity and family history of diabetes. Race/ethnicity was classified as Non-Hispanic White, Non-Hispanic Black, Mexican American, Other Race/Multi-Racial, and Other Hispanic. Education was classified as either less than high school, or high school graduate/at least some college. Poverty income ratio (PIR) was analyzed as a continuous variable, and was the ratio of a family's income to their appropriate poverty threshold based on family size (US Census Bureau, 2009a). PIR was top coded at 5, and values below 1.00 were below the official poverty threshold (US Census Bureau, 2009b). Body mass index (BMI) was derived from height and weight measurements (kg/m^2) collected in the NHANES physical examination. Waist circumference (cm) was also measured in the NHANES physical examination. Physical activity was defined as moderate or vigorous activity over the past 30 days, versus sedentary, from two questions (CDC, 2009). An individual was considered to have a family history of diabetes if one of their parents, grandparents, brothers or

Table 1
Unweighted number of participants and (maximum) limit of detection for organochlorine pesticides studied.

	Unweighted *N*	Maximum LOD[a] (ng/g lipid adjusted)	Below maximum LOD[a] (%)	Above maximum LOD[a] (%)
Beta-hexachlorocyclohexane	3414	9.36	56.0	44.0
p,p′-DDE	3456	18.6[b]	0.4[b]	99.6
p,p′-DDT	3235	20.7	93.9	6.1
Oxychlordane	3199	14.5	56.0	44.0
trans-Nonachlor	3432	14.5	37.1	62.9
Heptachlor epoxide	3171	14.6	88.9	11.1
Mirex	3364	14.6	92.3	7.7
Dieldrin	2341[c]	10.5	78.4	21.6

[a] Limit of detection.
[b] First tertile used for reference category (<168.6 ng/g lipid adjusted).
[c] Four years of data (2001–2004).

sisters had diabetes. Body mass index and waist circumference were used as control variables because these chemicals are lipophilic. In addition to testing the association of the 8 chemicals individually, we also evaluated combined models predicting total diabetes with 6 of the chemicals included at the same time (those significant in separate logistic regressions) and predicting pre-diabetes with 2 chemicals included at the same time. Finally, we evaluated the 6 pesticides and pesticide metabolites that were significantly associated with total diabetes in separate adjusted logistic regressions, by the number of compounds that were elevated compared to none of the 6 pesticides elevated.

We used SUDAAN software, for all analyses, to allow us to make appropriate estimates from the complex sample design used in the NHANES (Research Triangle Institute, 2005). Our analysis incorporated both the stratification and clustering aspects of the sampling design. The proper weighting procedures include adjustments for nonresponse and poststratification. Since minorities were over-sampled and a complex sampling design was employed, sampling weights provided by the NHANES for the pesticides subsample were used to compute population estimates based on weighted parameter estimates and standard errors (CDC, 2009).

3. Results and discussion

Preliminary regression model analyses were performed to determine if HbA1c, as a continuous variable, was linearly related to the 8 pesticides and pesticide metabolites. For 7 of the 8 pesticides a linear model was significant ($p<0.0001$), while the exception, *p,p′*-DDT, had a *p*-value of 0.0582 for a linear relationship. These results suggested that a smoothing procedure such as restricted cubic spline was not needed.

The proportion of each compound above the (maximum) limit of detection ranged from 6.1% to 99.6% (Table 1). Wide variation in the percentage of subjects above and below the (maximum) level of detection may have resulted in some of pesticides not being categorized in a biologically meaningful way. Having only 2 categories, reference and elevated pesticide seemed most appropriate for pesticides with 6.1–21.6% of values above the (maximum) limit of detection. However, significant differences were also found for pesticides with 44.0–67.0% of the sample in the elevated pesticide category.

Results of adjusted logistic regressions predicting total diabetes for the 8 pesticides and pesticide metabolites are given in Table 2. Six of the compounds, beta-hexachlorocyclohexane, *p,p′*-DDE, *p,p′*-DDT, oxychlordane, *trans*-nonachlor, and heptachlor epoxide, proved to be associated with total diabetes in separate logistic regressions. Beta-hexachlorocyclohexane ≥ 9.36 ng/g lipid adjusted had an odds ratio of 2.67 (95% CI 1.59–4.49) when compared to beta-hexachlorocyclohexane < 9.36 ng/g lipid adjusted. *p,p′*-DDE ≥ 168.6 ng/g lipid adjusted had an odds ratio of 1.90 (95% CI 1.13–3.18) compared to *p,p′*-DDE < 168.6 ng/g lipid adjusted. *p,p′*-DDT ≥ 20.7 ng/g lipid adjusted had an odds ratio of 1.96 (95% CI 1.29–2.98) compared to *p,p′*-DDT < 20.7 ng/g lipid adjusted. Oxychlordane ≥ 14.5 ng/g lipid adjusted had an odds ratio of 2.90 (95% CI 1.78–4.71) when compared to oxychlordane < 14.5 ng/g lipid adjusted. *trans*-Nonachlor ≥ 14.5 ng/g lipid adjusted had an odds ratio of 2.36 (95% CI 1.48–3.76) compared to *trans*-nonachlor < 14.5 ng/g lipid adjusted. Finally, heptachlor epoxide ≥ 14.6 ng/g lipid adjusted had an odds ratio of 2.09 (95% CI 1.46–3.00) compared to heptachlor epoxide < 14.6 ng/g lipid adjusted. These 6 pesticides and pesticide metabolites were further evaluated as the number elevated compared to none elevated. Exactly 4 compounds elevated had an odds ratio of 3.99 (95% CI 1.47–10.86) compared to none of the 6 elevated (Table 3). Four or more of the pesticides and pesticide metabolites elevated had an odds ratio of 4.99 (95% CI 1.97–12.61) compared to none elevated.

When the 6 pesticides and pesticide metabolites, associated with total diabetes in the entire sample, were tested in a single combined adjusted logistic regression the odds ratios declined. The only compounds which remained associated with total diabetes were oxychlordane and heptachlor epoxide. In the combined adjusted logistic regression oxychlordane ≥ 14.5 ng/g lipid adjusted had an odds ratio of 1.90 (95% CI 1.09–3.32) compared to oxychlordane < 14.5 ng/g lipid adjusted. Similarly, in the same combined adjusted logistic regression heptachlor epoxide ≥ 14.6 ng/g lipid adjusted had an odds ratio of 1.70 (95% CI 1.16–2.49) compared to heptachlor epoxide < 14.6 ng/g lipid adjusted. Of the compounds not significant in the combined adjusted logistic regression, *p,p′*-DDE, *trans*-nonachlor and beta-hexachlorocyclohexane had substantially higher median values in the elevated oxychlordane and elevated heptachlor epoxide categories compared to their medians in the reference oxychlordane and reference heptachlor epoxide categories (Table 4). These pesticides and pesticide metabolites appear to vary together with oxychlordane and heptachlor epoxide, and as shown in Table 3, contribute to the association with total diabetes.

A secondary line of evidence for the association of pesticides with diabetes is to consider any relationship with pre-diabetes. As suggested by the linearity of the association of HbA1c with most of the chemicals evaluated, pesticides should be related to a precursor to diabetes as well as diabetes itself. In separate adjusted logistic regressions both *p,p′*-DDT and heptachlor epoxide were associated with pre-diabetes (Table 5). The odds ratio for *p,p′*-DDT ≥ 20.7 ng/g lipid adjusted was 1.55 (95% CI 1.03–2.32) compared to *p,p′*-DDT < 20.7 ng/g lipid adjusted, and heptachlor epoxide ≥ 14.6 ng/g lipid adjusted had an odds ratio of 1.45 (95% CI 1.04–2.01) compared to heptachlor epoxide < 14.6 ng/g lipid adjusted. When these two compounds were tested together in a single adjusted logistic regression, only heptachlor epoxide remained significant, with an odds ratio of 1.40 (95% CI 1.00–1.95) for heptachlor epoxide ≥ 14.6 ng/g lipid adjusted compared to heptachlor epoxide < 14.6 ng/g lipid adjusted. However, when either heptachlor epoxide or *p,p′*-DDT were elevated the odds ratio for pre-diabetes was 1.70 (95% CI 1.26–2.30) compared to neither elevated. This result suggests a role for *p,p′*-DDT in the relationship with pre-diabetes.

The evidence supporting the relationship between pesticides and pesticide metabolites, with diabetes, was strongest for heptachlor epoxide and oxychlordane, intermediate for *p,p′*-DDT, and least for beta-hexachlorocyclohexane, *p,p′*-DDE, and

Table 2
Adjusted association of organochlorine pesticides with total diabetes in separate and combined models.[a]

	Total diabetes		Combined model for total diabetes	
	Odds ratio	95% CI	Odds ratio	95% CI
Beta-hexachlorocyclohexane ng/g lipid adjusted				
<9.36	1.00	–	1.00	–
≥9.36	2.67	1.59–4.49	1.65	0.99–2.74
p,p′-DDE ng/g lipid adjusted				
<168.6	1.00	–	1.00	–
≥168.6	1.90	1.13–3.18	1.08	0.58–2.03
p,p′-DDT ng/g lipid adjusted				
<20.7	1.00	–	1.00	–
≥20.7	1.96	1.29–2.98	1.59	0.99–2.55
Oxychlordane ng/g lipid adjusted				
<14.5	1.00	–	1.00	–
≥14.5	2.90	1.78–4.71	1.90	1.09–3.32
trans-Nonachlor ng/g lipid adjusted				
<14.5	1.00	–	1.00	–
≥14.5	2.36	1.48–3.76	1.28	0.72–2.27
Heptachlor epoxide ng/g lipid adjusted				
<14.6	1.00	–	1.00	–
≥14.6	2.09	1.46–3.00	1.70	1.16–2.49
Mirex ng/g lipid adjusted				
<14.6	1.00	–		
≥14.6	1.65	0.93–2.92		
Dieldrin ng/g lipid adjusted				
<10.5	1.00	–		
≥10.5	1.19	0.70–2.04		

[a] Logistic regressions adjusted for age, gender, race/ethnicity, education, poverty income ratio, body mass index, waist circumference, physical activity, and family history of diabetes. Combined model includes six compounds as well as control variables.

Table 3
Adjusted association of number of organochlorine pesticides elevated with total diabetes.[a]

	Odds ratio	95% CI	Percent of sample
None of 6 pesticides elevated	1.00	–	20.4
1 of 6 pesticides elevated	1.30	0.47–3.55	17.3
2 of 6 pesticides elevated	1.56	0.64–3.81	15.8
3 of 6 pesticides elevated	2.05	0.88–4.78	14.1
4 of 6 pesticides elevated	3.99	1.47–10.86	21.8
5 of 6 pesticides elevated	8.15	3.49–19.05	8.6
6 of 6 pesticides elevated	8.17	2.56–26.09	2.0

[a] Six organochlorine pesticides evaluated were: beta-hexachlorocyclohexane, *p,p′*-DDE, *p,p′*-DDT, oxychlordane, *trans*-nonachlor, and heptachlor epoxide. Logistic regression adjusted for age, gender, race/ethnicity, education, poverty income ratio, body mass index, waist circumference, physical activity, and family history of diabetes.

Table 4
Median organochlorine pesticides concentrations by oxychlordane and heptachlor epoxide categories.

	Oxychlordane		Heptachlor epoxide	
	Below maximum LOD[a]	Above maximum LOD[a]	Below maximum LOD[a]	Above maximum LOD[a]
	ng/g lipid adjusted			
Beta-hexachlorocyclohexane	4.52	15.86	6.66	29.69
p,p′-DDE	171.08	503.08	239.83	613.60
p,p′-DDT	6.01	6.78	6.19	8.69
Oxychlordane			11.07	34.24
trans-Nonachlor	11.47	35.64	17.12	52.72
Heptachlor epoxide	4.15	8.68		
Mirex	3.68	4.25	3.77	4.46
Dieldrin	4.99	8.74	5.72	15.29

[a] Limit of detection.

trans-nonachlor. Mirex and dieldrin were not associated with total diabetes or pre-diabetes. As shown in Table 3, the 6 compounds identified as significantly associated with total diabetes in separate adjusted logistic regressions may all contribute to the relationship between pesticides and diabetes. The proportion of the sample having 4 or more pesticides and pesticide metabolites elevated was 32.4%. In contrast, only 20.4% of the sample had none of the 6 elevated.

The main components of technical-grade chlordane are *cis*- and *trans*-chlordane, *trans*-nonachlor, and heptachlor (CDC, 2005). The use of chlordane in the United States was restricted to control of subterranean termites in 1983 and all commercial use ceased in 1988. In the mid-1970s the use pattern of chlordane was: 35% used by pest control operators, mostly on termites; 28% on agricultural crops, including corn and citrus; 30% for home lawn and garden use; and 7% on turf and ornamentals (ATSDR, 1994). Ever-use of chlordane or heptachlor among 31,787 licensed pesticide applicators was found to be associated with incident diabetes in the Agricultural Health Study (Montgomery et al., 2008). Hence, our finding of an association with 2 biomarkers in a cross-sectional study is confirmed in a longitudinal study of pesticide use.

Table 5
Adjusted association of organochlorine pesticides with pre-diabetes in separate and combined models.[a]

	Pre-diabetes		Combined model for pre-diabetes	
	Odds ratio	95% CI	Odds ratio	95% CI
Beta-hexachlorocyclohexane ng/g lipid adjusted				
<9.36	1.00	–		
≥9.36	1.11	0.76–1.63		
p,p′-DDE ng/g lipid adjusted				
<168.6	1.00	–		
≥168.6	1.59	0.98–2.55		
p,p′-DDT ng/g lipid adjusted				
<20.7	1.00	–	1.00	–
≥20.7	1.55	1.03–2.32	1.48	0.97–2.27
Oxychlordane ng/g lipid adjusted				
<14.5	1.00	–		
≥14.5	1.28	0.88–1.88		
trans-Nonachlor ng/g lipid adjusted				
<14.5	1.00	–		
≥14.5	1.30	0.88–1.90		
Heptachlor epoxide ng/g lipid adjusted				
<14.6	1.00	–	1.00	–
≥14.6	1.45	1.04–2.01	1.40	1.00–1.95
Mirex ng/g lipid adjusted				
<14.6	1.00	–		
≥14.6	1.15	0.65–2.03		
Dieldrin ng/g lipid adjusted				
<10.5	1.00	–		
≥10.5	0.89	0.61–1.29		

[a] Logistic regressions adjusted for age, gender, race/ethnicity, education, poverty income ratio, body mass index, waist circumference, physical activity, and family history of diabetes. Combined model includes two compounds as well as control variables.

References

Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological profile for chlordane. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service; 1994.

Akins JR, Waldrep K, Bernert Jr JT. The estimation of total serum lipids by a completely enzymatic 'summation' method. Clin Chim Acta 1989;184:219–26.

American Diabetes Association (ADA). Summary of revisions for the 2010 clinical practice recommendations. Diabetes Care 2010;33(Suppl 1):S3.

Centers for Disease Control and Prevention (CDC), National Center for Environmental Health. Third national report on human exposure to environmental chemicals. Atlanta, Georgia. N.C.E.H. Pub. No. 05-0570; 2005.

Centers for Disease Control and Prevention (CDC), National Center for Health Statistics. National Health and Nutrition Examination Survey, NHANES 1999–2004 [cited 2009 Feb 22]; 2009. Available from: URL: http://www.cdc.gov/nchs/nhanes.htm.

Codru N, Schymura MJ, Negoita S, The Akwesasne Task Force on the Environment, Rej R, Carpenter DO. Diabetes in relation to serum levels of polychlorinated biphenyls and chlorinated pesticides in adult Native Americans. Environ Health Perspect 2007;115:1442–7.

Everett CJ, Frithsen IL, Diaz VA, Koopman RJ, Simpson Jr WM, Mainous III AG. Association of a polychlorinated dibenzo-*p*-dioxin, a polychlorinated biphenyl, and DDT with diabetes in the 1999–2002 National Health and Nutrition Examination Survey. Environ Res 2007;103:413–8.

Glynn AW, Granath F, Aune M, Atuma S, Darnerud PO, Bjerselius R, et al. Organochlorines in Swedish women: determinants of serum concentrations. Environ Health Perspect 2003;111:349–55.

Lee D-H, Lee I-K, Jin S-H, Steffes M, Jacobs Jr DR. Association between serum concentrations of persistent organic pollutants and insulin resistance among nondiabetic adults: results from the National Health and Nutrition Examination Survey 1999–2002. Diabetes Care 2007a;30:622–8.

Lee D-H, Lee I-K, Porta M, Steffes M, Jacobs Jr DR. Relationship between serum concentrations of persistent organic pollutants and the prevalence of metabolic syndrome among non-diabetic adults: results from the National Health and Nutrition Examination Survey 1999–2002. Diabetologia 2007b;50:1841–51.

Lee D-H, Lee I-K, Song K, Steffes M, Toscano W, Baker BA, et al. A strong dose–response relation between serum concentrations of persistent organic pollutants and diabetes: results from the National Health and Examination Survey 1999–2002. Diabetes Care 2006;29:1638–44.

Lee D-H, Lee I-K, Steffes M, Jacobs Jr DR. Extended analyses of the association between serum concentrations of persistent organic pollutants and diabetes. Diabetes Care 2007c;30:1596–8.

Montgomery MP, Kamel F, Saldana TM, Alavanja MCR, Sandler DP. Incident diabetes and pesticide exposure among licensed pesticide applicators: Agricultural Health Study, 1993–2003. Am J Epidemiol 2008;167:1235–46.

Morgan DP, Lin LI, Saikaly HH. Morbidity and mortality in workers occupationally exposed to pesticides. Arch Environ Contam Toxicol 1980;9:349–82.

Rahimi R, Abdollahi M. A review on the mechanisms involved in hyperglycemia induced by organophosphorus pesticides. Pestic Biochem Physiol 2007;88:115–21.

Research Triangle Institute. SUDAAN: version 9.0.1 for SAS version 9. Research Triangle Park, North Carolina: Research Triangle Institute; 2005.

Rignell-Hydbom A, Rylander L, Hagmar L. Exposure to persistent organochlorine pollutants and type 2 diabetes mellitus. Hum Exp Toxicol 2007;26:447–52.

Rohlfing CL, Little RR, Wiedmeyer HM, England JD, Madsen R, Harris MI, et al. Use of GHb (HbA_{1c}) in screening for undiagnosed diabetes in the U.S. population. Diabetes Care 2000;23:187–91.

Rylander L, Rignell-Hydbom A, Hagmar L. A cross-sectional study of the association between persistent organochlorine pollutants and diabetes. Environ Health: Global Access Sci Source 2005;4:28.

Saldana TM, Basso O, Hoppin JA, Baird DD, Knott C, Blair A, Alavanja MCR, Sandler DP. Pesticide exposure and self-reported gestational diabetes mellitus in the Agricultural Health Study. Diabetes Care 2007;30:529–34.

US Census Bureau. Poverty thresholds [cited 2009 Feb 22]; 2009a. Available from URL: http://www.census.gov/hhes/www/poverty/threshld.html.

US Census Bureau. How the Census Bureau measures poverty [cited 2009 Feb 22]; 2009b. Available from URL: http://www.census.gov/hhes/www/poverty/povdef.html.