Published in final edited form as:

Sci Total Environ. 2015 April 15; 0: 337–344. doi:10.1016/j.scitotenv.2015.01.059.

Distribution and determinants of urinary biomarkers of exposure to organophosphate insecticides in Puerto Rican pregnant women

Ryan C. Lewis, M.S.¹, David E. Cantonwine, Ph.D.², Liza V. Anzalota Del Toro, M.D.³, Antonia M. Calafat, Ph.D.⁴, Liza Valentin-Blasini, Ph.D.⁴, Mark D. Davis⁴, M. Angela Montesano, Ph.D.⁴, Akram N. Alshawabkeh, Ph.D.⁵, José F. Cordero, M.D., M.P.H.³, and John D. Meeker, Sc.D.¹

Ryan C. Lewis: rclewis@umich.edu; David E. Cantonwine: dcantonwine@partners.org; Liza V. Anzalota Del Toro: liza.anzalota@upr.edu; Antonia M. Calafat: aic7@cdc.gov; Liza Valentin-Blasini: lvb5@cdc.gov; Mark D. Davis: msd7@cdc.gov; M. Angela Montesano: ahm2@cdc.gov; Akram N. Alshawabkeh: aalsha@coe.neu.edu; José F. Cordero: jose.cordero6@upr.edu; John D. Meeker: meekerj@umich.edu

¹University of Michigan School of Public Health, Department of Environmental Health Sciences, 1415 Washington Heights, Ann Arbor, MI 48109

²Brigham and Women's Hospital, Department of Obstetrics and Gynecology, 75 Francis Street, Boston, MA 02115

³University of Puerto Rico Graduate School of Public Health, Medical Sciences Campus, San Juan, Puerto Rico 00935

⁴Centers for Disease Control and Prevention, National Center for Environmental Health, Division of Laboratory Sciences, 4770 Buford Highway, Atlanta, GA 30341

⁵Northeastern University, College of Engineering, 360 Huntington Avenue, Boston, MA 02115

Abstract

Globally, human exposures to organophosphate (OP) insecticides may pose a significant burden to the health of mothers and their developing fetuses. Unfortunately, relevant data is limited in certain areas of the world concerning sources of exposure to OP insecticides in pregnant populations. To begin to address this gap in information for Puerto Rico, we studied repeated measures of urinary concentrations of 10 OP insecticide metabolites among 54 pregnant women from the northern karst region of the island. We also collected demographic data and self-reported information on the consumption of fruits, vegetables, and legumes in the past 48-hr before urine collection and home pest-related issues. We calculated the distributions of the urinary biomarkers and compared them to women of reproductive age from the general U.S. population. We also used

© 2015 Elsevier B.V. All rights reserved.

Correspondence to: John D. Meeker, meekerj@umich.edu.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

statistical models accounting for correlated data to assess within-subject temporal variability of the urinary biomarkers and to identify predictors of exposure. We found that for all but two metabolites (*para*-nitrophenol [PNP], diethylthiophosphate [DETP]), 50th or 95th percentile urinary concentrations (the metric that was used for comparison was based on the biomarker's detection frequency) of the other eight metabolites (3,5,6-trichloro-2-pyridinol [TCPY], 2-isopropyl-4-methyl-6-hydroxy-pyrimidine, malathion dicarboxylic acid, diethylphosphate, diethyldithiophosphate, dimethylphosphate, dimethylthiophosphate [DMTP], dimethyldithiophosphate) were somewhat lower in our cohort compared with similarly aged women from the continental United States. TCPY, PNP, DETP, and DMTP, which were the only urinary metabolites detected in greater than 50% of the samples, had poor reproducibility (intraclass correlation coefficient range: 0.19–0.28) during pregnancy. Positive predictors of OP insecticide exposure included: age; marital or employment status; consumption of cherries, grape juice, peanuts, peanut butter, or raisins; and residential application of pesticides. Further research is needed to understand what aspects of the predictors identified influence OP insecticide exposure during pregnancy.

Keywords

Biomarker; pesticides; pregnancy; urine; women

1. INTRODUCTION

The annual global use of pesticides in agricultural and non-agricultural (e.g., home, garden, commercial, government) settings is an estimated 5.2 billion pounds of active ingredients (EPA, 2011). On a weight basis, insecticides account for 17% of all pesticides (e.g., herbicides, fungicides, nematicides) used around the world (EPA, 2011). Organophosphate (OP) insecticides, such as chlorpyrifos, malathion, and diazinon, are one class of insecticide characterized by their potent acetylcholinesterase inhibitor activity (Clune et al., 2012). Use of OP insecticides in the United States has generally decreased over time (EPA, 2011). While this decrease is due in part to regulatory efforts (Clune et al., 2012), OP insecticides still account for 35% of all insecticides used in the U.S., which is equivalent to 33 million pounds of OP insecticides on an annual basis (EPA, 2011).

Due to widespread use, humans can be exposed to OP insecticides through multiple routes, including inhalation from spray drift, ingestion of residues on foods, dust, and soil, and dermal absorption from skin contact (Fortenberry et al., 2014). Human exposure to OP insecticides has been most notably associated with detrimental child neurodevelopment (Bouchard et al., 2010; Engell et al., 2011; Fortenberry et al., 2014; Marks et al., 2010). In addition, human exposure to OP insecticides has been linked with a wide variety of other adverse human health effects, including decreased gestational age (Eskenazi et al., 2004; Rauch et al., 2012; Wang et al., 2012), reduced birth weight (Rauch et al., 2012), altered serum hormone concentrations (Meeker et al., 2006a, 2008, 2006b), reduced semen quality (Swan et al., 2013), wheeze (Hopping et al., 2006), and lung cancer (Lee et al., 2004).

The rates of preterm birth (Martin et al., 2011; March of Dimes, 2012) and many other adverse human health conditions with potential environmental influences, such as childhood

obesity and asthma (Garza et al. 2011; Otero-González and García-Fragoso, 2008; Rivera-Soto et al., 2010), and adult obesity, metabolic syndrome, and diabetes (CDC, 2012; Pérez et al., 2008) are higher in Puerto Rico compared to the mainland U.S. and in some cases (e.g., preterm birth) most other parts of the world (Blencowe et al., 2012). Puerto Rico also has a history of pesticide drift, illegal use and applications of pesticides, and pesticide-contaminated land (EPA, 2001, 2003, 2004, 2008), including a Superfund hazardous waste site with elevated soil levels of OP insecticides (EPA, 2012). However, little is known regarding human exposures to environmental chemicals in Puerto Rico, including OP insecticides.

Our study had three primary objectives: to 1) describe distributions, 2) assess within-subject temporal variability, and 3) identify predictors of urinary concentrations of 10 OP insecticide metabolites in pregnant women from Puerto Rico. Studies on these aspects of OP insecticide exposure in pregnant women have been limited to date (especially #2 and #3), and may also directly assist with understanding the potential burden of OP insecticide exposure globally, identifying sources of exposure, and designing exposure characterization components of future epidemiology studies.

2. MATERIALS AND METHODS

2.1 Study participants

This analysis involved 54 pregnant women participating in the Puerto Rico Test site for Exploring Contamination Threats (PROTECT) project. PROTECT is an ongoing prospective birth cohort in the northern karst region of Puerto Rico designed to assess the potential relationship between environmental exposures and risk of preterm birth and other adverse pregnancy outcomes (Cantonwine et al., 2014; Meeker et al., 2013). Participants were recruited at approximately 14 ± 2 weeks of gestation at seven prenatal clinics and hospitals during 2010–2012. Pregnant women were eligible if they were 18–40 years of age, resided in a municipality within the northern karst region, received their first prenatal visit by the 20th week of pregnancy, did not use oral contraceptives three months prior to pregnancy or had in vitro fertilization as a method of assisted reproductive technology, and were free of known medical/obstetrics complications. Participants provided spot urine samples during three study visits at approximately 20 ± 2 weeks, 24 ± 2 weeks, and 28 ± 2 weeks of gestation. Questionnaires were also administered at each visit prior to collecting the urine to obtain information on demographics and self-reported consumption of fruits, vegetables, and legumes in the 48-hr prior to urine collection, and home pest-related issues. The study was described in detail to all participants who then gave informed consent. The Ethics and Research Committees of the University of Puerto Rico, the University of Michigan, and Northeastern University approved the research protocol. The involvement of the Centers for Disease Control and Prevention (CDC) did not constitute engagement in human subject research.

2.2 Urinary biomarkers of pesticide exposure

At each study visit, participants provided one spot urine sample, which was collected and processed using procedures that were comparable to those the CDC has developed for the

National Health and Nutrition Examination Survey (NHANES) and other studies. Urine samples were analyzed within about two years after collection at the National Center for Environmental Health of the CDC (Atlanta, GA, USA). The urine was analyzed for the following four metabolites of specific OP insecticides: 3,5,6-trichloro-2-pyridinol (TCPY), a metabolite of chlorpyrifos and chlorpyrifos-methyl; 2-isopropyl-4-methyl-6-hydroxypyrimidine (IMPY), a metabolite of diazinon; malathion dicarboxylic acid (MDA), a metabolite of malathion; and *para*-nitrophenol (PNP), a metabolite of parathion and methyl parathion. The urine was also analyzed for the following six metabolites that are common to many OP insecticides, not just the ones mentioned in the preceding sentence: diethylphosphate (DEP), diethylthiophosphate (DETP), diethyldithiophosphate (DEDTP), dimethylphosphate (DMP), dimethylthiophosphate (DMTP), and dimethyldithiophosphate (DMDTP). Quantification of TCPY, IMPY, MDA and PNP used solid phase extraction and high-performance liquid chromatography-isotope dilution tandem mass spectrometry (SPE-HPLC-MS/MS) as described previously (Davis et al., 2013). The six dialkyl substituted OP metabolites were measured using a modification of the analytical method of Odetokun et al. (2010) that also employs SPE-HPLC-MS/MS with isotope dilution calibration. Accuracy and precision for each analytical run were monitored through the use of calibration standards, reagent blanks, and quality control materials of high and low concentrations. Where applicable (Tables 1 and 2 and Figure 1), concentrations below the limit of detection (LOD) were assigned a value of LOD divided by the square root of 2. Where adjustment for urinary output was necessary (Table 2 and Figure 1), urinary concentrations were corrected for specific gravity (SG), which was measured at the University of Puerto Rico using a digital handheld refractometer (Atago Co., Ltd., Tokyo, Japan), using the following formula: $P_c = P_m[(SG_p - 1)/(SG_m - 1)]$, where P_c is the SG-corrected urinary concentration (ng/ml), P_m is the measured urinary concentration (ng/ml), SG_p is the median of the urinary SGs for the population (1.019), and SG_m is the measured urinary SG.

2.3 Statistical analysis

Statistical analysis was performed using SAS version 9.3 for Windows (SAS Institute, Cary, NC, USA). Distributions of urinary concentrations were calculated and compared to those measured most recently (either the 2007–2008 or 2009–2010 cycles) in U.S. women 18–40 years of age from NHANES (www.cdc.gov/nchs/nhanes.htm). Comparisons of urinary biomarker concentrations were made using the 50th percentile value for biomarkers with a sufficiently high frequency of detects (i.e., TCPY, PNP, and DMTP). For all other biomarkers, comparisons were made using the 95th percentile as the low frequency of detects for these biomarkers made it impossible to use the 50th percentile value. To assess between- and within-subject variability in urinary concentrations over the three study visits, intraclass correlation coefficients (ICCs) were calculated using variance components derived from linear mixed models with a random subject effect only for log-transformed analytes detected in at least 50% of the samples. The corresponding 95% confidence intervals (CIs) associated with the ICCs were also calculated (Hankinson et al., 1995). The magnitude of the ICCs was interpreted using the following criteria: poor reproducibility (ICC <0.40), fair to good reproducibility (0.40 ≤ ICC <0.75), and excellent reproducibility (ICC ≥ 0.75) (Rosner, 2000). We examined the associations between time of urine collection, demographic characteristics, select food items consumed in the past 48-hr (except for

Brussel sprouts, celery, and wine due to the low number of participants who reported consuming those items), and home pest-related issues (except for use of pet grooming products, pet flea/tick prevention applications, or pet flea/tick spray in the past 48-hr due to the low number of participants who reported use of those items) and urinary concentrations of the analytes using mixed effects models to account for repeated data. In particular, for analytes detected in at least 50% of the samples, we estimated the percent change in SG-corrected urinary metabolite concentrations and their associated 95% CIs in linear mixed effect models with a random subject effect and fixed effect for the predictor of interest (e.g., consumed strawberries in the past 48-hr). For analytes detected in fewer than 50% of the samples, we estimated the odds of having detectable urinary metabolite concentrations by calculating odds ratios (OR) and their associated 95% CIs using generalized estimating equations to account for repeated measures with a fixed effect for the predictor of interest. In other words, these statistical models relied on binary exposure data that assigned a participant a “yes” if the biomarker was detected or a “no” if the biomarker was not detected. In this case, we gave consideration to modeling urinary biomarker concentrations as a continuous variable, but we chose a binary outcome approach (i.e., detect or non-detect) as the former would require the imputation of too many left censored values for many of the biomarkers (e.g., 85.5% of the values for IMPY).

3. RESULTS

Demographic characteristics of these women have been described previously (Cantonwine et al., 2014). Briefly, participants had a mean age of 28 years, and were predominantly employed (60%), married or living with their partner (71%), and moderately educated (83% of women had college level education).

Table 1 shows the distributions of the urinary biomarkers relative to those among U.S. women ages 18–40 years from NHANES. Only four of the 10 biomarkers were detected in at least 50% of the samples: TCPY, PNP, DETP, and DMTP. Compared to the U.S. population-based sample, 50th percentile urinary concentrations of TCPY and DMTP and 95th percentile urinary concentrations of IMPY, MDA, DEP, DEDTP, DMP, and DMDTP were lower in our cohort of pregnant Puerto Rican women, whereas 50th percentile urinary concentrations of PNP and 95th percentile urinary concentrations of DETP were similar and slightly higher, respectively, in our sample.

ICCs for TCPY, PNP, DETP, and DMTP, the urinary biomarkers detected in at least 50% of the samples are shown in Figure 1. ICCs for both uncorrected (ICC range: 0.20–0.31) and SG-corrected (ICC range: 0.19–0.28) suggested poor reproducibility across all three study visits.

Table 2 shows the percent change in SG-corrected urinary concentrations of biomarkers in relation to select variables for biomarkers detected in at least 50% of the samples (TCPY, PNP, DETP, and DMTP). There were significant positive associations between women who consumed grape juice or raisins in the past 48-hr and TCPY, and suggestive inverse associations between women who consumed collards or spinach in the past 48-hr and PNP. Among demographic variables, there were suggestive positive associations for women who

were married and DMTP, or unemployed and PNP and DETP, and suggestive inverse associations between being younger and TCPY and DETP. There were no significant or suggestive associations between concentrations of the biomarkers and time of day at which urine was collected, education, the other food items consumed in the past 48-hr (apples, cherries, grapes, peanuts, peanut butter, strawberries, and tomatoes), or home pest-related issues (insects were a common nuisance inside the home, pesticides had been used at home by the participant or an exterminator, and pesticides were stored inside the home) (data not shown).

Table 3 shows the odds of having detectable urinary concentrations of biomarkers in relation to select variables for the six biomarkers detected in less than 50% of the samples: IMPY, DMA, DEDTP, DMDTP, DEP, and DMP. There were significantly increased odds for detecting DMDTP and MDA in the urine of women who consumed collards or grape juice in the past 48-hr, respectively. There were also suggestive decreased odds for detecting DMP in the urine of women who consumed grapes in the past 48-hr, and suggestive increased odds for detecting several other biomarkers in the urine of women who consumed cherries (DEDTP), collards (MDA and DEP), or peanuts (MDA and DEP) in the past 48-hr. Among demographic variables, there were significantly decreased odds for detecting IMPY and DEP in the urine of younger women. A significant decreased and suggestive increased odds for detecting IMPY and DMP, respectively, was also noted among married women. Regarding home pest-related issues, there were significant increased odds for detecting certain biomarkers in the urine of women who lived in homes where pesticides had been historically applied inside the home by an exterminator (MDA) or by the participant herself (DEP). A significant decreased odds for detecting IMPY was also observed for women reporting that insects were a common nuisance inside the home. If women applied pesticides to the home or lawn in the past 48-hr there was a suggestive increased odds for detecting DEP, whereas if they stored pesticides inside the home there was a suggestive decreased odds for detecting DMDTP. We found no associations between biomarker detection frequency and the other demographic variables and foods consumed in the past 48-hr (data not shown).

4. DISCUSSION

In this study, we collected repeated measures of urinary concentrations of 10 OP insecticide metabolites (TCPY, IMPY, MDA, PNP, DEP, DETP, DEDTP, DMP, DMTP, DMDTP) across pregnancy among 54 pregnant Puerto Rican women. We found that for all but two metabolites (PNP, DETP), 50th or 95th percentile urinary concentrations (the metric that was used for comparison was based on the biomarker's detection frequency) were somewhat lower in our cohort compared with similarly aged women from NHANES. TCPY, PNP, DETP, and DMTP, which were the only urinary metabolites detected in greater than 50% of the samples, had poor reproducibility across pregnancy. We also found that certain demographic and lifestyle variables are important determinants of exposure to OP insecticides. To our knowledge, this is the first biomarker study of OP insecticide exposure among pregnant women living in Puerto Rico.

Urinary metabolites of OP insecticides have been measured in pregnant women from around the world. Outside of the U.S., urinary metabolites have been measured in pregnant women from China (Shanghai (Wang et al., 2012); Shenyang (Zhang et al., 2014)), Mexico (Fortenberry et al., 2014), Netherlands (Ye et al., 2009, 2008), and Norway (Ye et al., 2009). Across these studies, urinary concentrations of OP insecticide metabolites varied widely; geometric mean (GM) urinary concentrations of TCPY ranged between 1.8 ng/ml (Mexico) and 3.6 ng/ml (Netherlands), whereas GM urinary concentrations of diethyl and dimethyl phosphates ranged between <LOD (1.0 ng/ml) (Shenyang, China) and 7.1 ng/ml (Shenyang, China) and 0.7 ng/ml (Netherlands) and 17.2 ng/ml (Shanghai, China), respectively. Urinary concentrations of OP insecticide metabolites were much higher in these other studies compared with those measured in our study. Differences by country may reflect geographic and/or temporal variability in the chemical content of insect control products and/or insect control practices in agricultural, community, and residential settings. This, combined with variability in the lifestyle behaviors of pregnant women (e.g., fruit and vegetable consumption, washing practices), may lead to different interactions with insecticide sources and, consequently, differences in the intensity, frequency, and duration of OP insecticide exposures.

The temporal reliability analysis of TCPY, PNP, DETP, and DMTP implies that more than one spot urine sample may be needed to characterize exposures from their respective parent compounds over pregnancy. Thus, epidemiology studies conducted in pregnant women where the exposure analysis component relies on a single spot measurement of any one of these four urinary metabolites will likely result in a moderate degree of exposure misclassification/measurement error, which, if non-differential, would most likely underestimate the true association. Similar to our findings, Fortenberry et al. (2014) and Whyatt et al. (2009) reported that within-subject variability of urinary concentrations of TCPY over pregnancy was large in cohorts of pregnant women from Mexico (ICC: 0.32) and New York City (ICC: 0.43), respectively. In addition, Meeker et al. (2005) observed poor reproducibility of repeated measures of urinary concentrations of TCPY (ICC: 0.21) over a three-month period in men from Boston, which supports the findings of the limited peer-reviewed studies conducted in pregnant women. We are aware of no other peer-reviewed studies in adults that have estimated ICCs for PNP, DEPT, or DMTP.

We identified several demographic and lifestyle predictors of urinary concentrations of OP insecticide metabolites in pregnant women. Consumption of cherries, grape juice, peanuts, peanut butter, or raisins in the past 48-hr was a positive predictor of levels of certain OP metabolites, which is consistent with the findings of a study of pregnant women from Cincinnati, Ohio that found a positive association between fresh fruit and vegetable intake and levels of urinary diethyl and dimethyl phosphates (Yolton et al., 2013) and a study of men and women from Israel that reported a positive relationship between fruit consumption and levels of urinary dialkyl phosphates (Berman et al., 2013). However, it is unclear why and contrary to our expectations that the consumption of collards, grapes, or spinach in the past 48-hr generated results that were inversely related to urinary concentrations of OP insecticide metabolites as residues of OP insecticides have been detected in samples of these food items, such as from the Total Diet Study, which is a market basket study conducted by the U.S. Food and Drug Administration (FDA, 2005). It is possible that collards, grapes, and

spinach consumed among this population in Puerto Rico were produced without the use of OP insecticides in comparison to the other foods and compared to samples of these foods tested by the US FDA, but this hypothesis could not be explored because information of this kind was not collected in our study. Chance findings as an explanation for significant inverse (or positive) associations also cannot be ruled out.

We found that being unemployed was a positive predictor of insecticide exposure. One hypothesis is that unemployed women spend more time outdoors attending to their lawns or gardens, thus necessitating the use of OP insecticides relative to working women. We had questionnaire information on weekly chore frequency and duration, which may correlate with outdoor activities, but additional investigation of these variables with respect to employment status did not reveal any noteworthy relationships (data not shown). It is also possible that unemployed women spend more time inside the home where OP insecticides may persist due to protection from moisture, sunlight, and other conditions that lead to chemical degradation (Shin et al., 2013), or have differences in diet and sources of food relative to employed women, which influence exposure. Although Yoltan et al. (2013) reported a relationship that was opposite of our study findings (unemployed women had lower OP metabolite urinary concentrations than other women), which may reflect differences in occupational exposures between pregnant women living in Cincinnati versus Puerto Rico. Younger women in our study also had lower concentrations of urinary OP insecticide metabolites relative to older women. Others have reported that the consumption of organic produce is inversely associated with age (Curl et al., 2013), thus it is plausible that younger women in our study consumed such foods with greater frequency compared to older women and, as a result, had lesser OP insecticide exposure. Another possibility is that younger women consumed less fruits and vegetables with OP insecticide residues resulting in lesser OP insecticide exposure relative to older women, but we did not observe differences in age by the total number of food items consumed in the past 48-hr (data not shown). In addition, residential applications of pesticides, whether by the participant or a professional exterminator, were positive predictors of exposure. Direct use of pesticides by the participant creates opportunities for exposure. Because OP insecticides are fairly persistent indoors (Shin et al., 2013), there are also opportunities for exposure long after the product has been applied. The associations identified with being married and the other home pest-related issues are difficult to explain and are perhaps chance findings. Nonetheless, Berman et al. (2013) also observed positive associations between marital status (higher levels for those that were married, divorced, or widowed relative to those that were single) and urinary levels of dialkyl phosphates in Israeli adults. Lastly, peer-reviewed studies on demographic predictors of OP insecticide exposure in pregnant women from Israel (Berman et al., 2011) and Netherlands (Ye et al., 2008) have also been published, but for some of the variables examined in our analysis, we observed relationships with exposure where they did not (age) or vice versa (education). However, these differences may be due to geographic-specific lifestyle behaviors of pregnant women, which could lead to variability in OP insecticide exposure profiles between countries and, consequently, different associations with demographic factors.

Several key strengths of this analysis included an understudied and potentially at-risk population, the breadth of OP insecticide exposure biomarkers examined, and the collection

of repeated measurements within women during pregnancy. Our study also significantly adds to the current state-of-the science as there have been a limited number of studies on OP insecticide exposures in pregnant women, especially on within-subjected temporal variability and predictors of exposures. One limitation was the lack of detailed information on the questionnaire that precluded further investigation of demographic variables and lifestyle factors that were associated with exposure. However, the increase in detail on the questionnaires would have increased participant burden and may have resulted in reduced participation and study compliance or potentially introduced added recall error. Similarly, because we could not find information on fruit, vegetable, or legume consumption in Puerto Rico and associated crop pesticide use patterns, we were limited in our ability to connect our findings to the people and insect control practices on the island. The selected biomarkers also cannot necessarily distinguish between exposure to the parent compound or the metabolite, which can also be found in the environment. Using an approach similar to Panuwet et al. (2009), we found that the Spearman's rho between pairs of specific metabolites and their associated common metabolites (TCPY-DEP/DETP/DMP/DMTP, IMPY-DMP/DMPT, MDA-DMP/DMTP/DMDTP, PNP-DEP/DETP) (CDC, 2013) was weak (range: 0.02–0.24). This suggests exposure to additional parent compounds that are metabolized to these common dialkyl phosphates. We also looked at the correlations between DMP and DMTP, and between DEP and DETP, since these pairs of dialkyl phosphates have shared parent compounds and strong correlations may reflect exposure to the parent compounds rather than the individual metabolites themselves. We found that the correlation between DMP and DMTP was moderately strong (0.56). Because DMP and DMTP share several parent OP insecticides as their precursors (aside from chlorpyrifos methyl, malathion, and methyl parathion), this may suggest that the participants were likely exposed to one or more of their shared parent dimethyl phosphates. On the other hand, the correlation between DEP and DETP was weak (0.07), which may suggest environmental exposure to one or both of these metabolites. Several additional limitations included a modest sample size, a small number of women that reported consumption of certain food items and performing certain home pest-related activities, and relatively low detection frequencies for six out of the 10 urinary biomarkers examined. Caution is needed if attempting to generalize these results to other populations, particularly non-pregnant adults and children, because their interaction with sources of OP insecticides and/or their metabolism of these chemicals may be different from those of pregnant women. Caution should also be employed when generalizing our findings that were based on a small sample size (i.e., those analyses with sparse cells pertaining to the consumption of collards, cherries, and spinach, and pesticides used inside the home by a professional exterminator).

5. CONCLUSIONS

Our findings suggest that pregnant Puerto Rican women are exposed to several OP insecticides during pregnancy, and certain demographic characteristics and lifestyle choices may play a role in exposure. Additional research is needed to understand what aspects of the identified predictors influence OP insecticide exposure during pregnancy.

Acknowledgments

Work was supported by grants P42ES017198 and P30ES017885 from the National Institute of Environmental Health Sciences, National Institutes of Health (NIH), and by grants G12MD007600 and U54MD007587 from the National Institute on Minority Health and Health Disparities, NIH. The content is solely the responsibility of the authors and does not necessarily represent the official position of NIH or CDC. We thank Carolina Fernandez, Do-Gyun Kim, William Roman, Erin Wade and Charlie Chambers of CDC for their technical support with the urinalysis.

ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CI	confidence interval
DEDTP	diethyldithiophosphate
DEP	diethylphosphate
DETP	diethylthiophosphate
DMDTP	dimethyldithiophosphate
DMP	dimethylphosphate
DMTP	dimethylthiophosphate
GM	geometric mean
ICC	intraclass correlation coefficient
IMPY	2-isopropyl-4-methyl-6-hydroxy-pyrimidine
LOD	limit of detection
MDA	malathion dicarboxylic acid
NHANES	National Health and Nutrition Examination Survey
OP	organophosphate
PNP	<i>para</i> -nitrophenol
PROTECT	Puerto Rico Test site for Exploring Contamination Threats
SG	specific gravity
SPE-HPLC-MS/MS	solid phase extraction and high-performance liquid chromatography-isotope dilution tandem mass spectrometry
TCPY	3,5,6-trichloro-2-pyridinol

References

- Berman T, Goldsmith R, Göen T, Spungen J, Novack L, Levine H, Amitai Y, Shohat T, Grotto I. Urinary concentrations of organophosphate pesticide metabolites in adults in Israel: demographic and dietary predictors. *Environ Int.* 2013; 60:183–9. [PubMed: 24064379]
- Berman T, Hochner-Celnikier D, Barr DB, Needham LL, Amitai Y, Wormser U, Richter E. Pesticide exposure among pregnant women in Jerusalem, Israel: results of a pilot study. *Environ Int.* 2011; 37:198–203. [PubMed: 20952069]

- Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *Lancet*. 2012; 379:2162–72. [PubMed: 22682464]
- Bouchard MF, Bellinger DC, Wright RO, Weisskopf MG. Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. *Pediatrics*. 2010; 125:e1270–7. [PubMed: 20478945]
- Cantonwine DE, Cordero JF, Rivera-González LO, Anzalota Del Toro LV, Ferguson KK, Mukherjee B, Calafat AM, Crespo N, Jiménez-Vélez B, Padilla IY, Alshawabkeh AN, Meeker JD. Urinary phthalate metabolite concentrations among pregnant women in Northern Puerto Rico: distribution, temporal variability, and predictors. *Environ Int*. 2014; 62:1–11. [PubMed: 24161445]
- CDC (U.S. Centers for Disease Control and Prevention). Organophosphorus insecticides: dialkyl phosphate metabolites. Atlanta, GA: U.S. Centers for Disease Control and Prevention; Dec 4. 2013 Biomonitoring summary.
- CDC (U.S. Centers for Disease Control and Prevention). Increasing prevalence of diagnosed diabetes – United States and Puerto Rico, 1995–2010. *MMWR Morb Mortal Wkly Rep*. 2012; 61:918–921. [PubMed: 23151951]
- Clune AL, Ryan PB, Barr DB. Have regulatory efforts to reduce organophosphorus insecticide exposures been effective? *Environ Health Perspect*. 2012; 120:521–5. [PubMed: 22251442]
- Curl CL, Beresford SA, Hajat A, Kaufman JD, Moore K, Nettleton JA, Diez-Roux AV. Associations of organic produce consumption with socioeconomic status and the local food environment: Multi-Ethnic Study of Atherosclerosis (MESA). *PLoS One*. 2013; 8:e69778. [PubMed: 23936098]
- Davis MD, Wade EL, Restrepo PR, Roman-Esteva W, Bravo R, Kuklenyik P, Calafat AM. Semiautomated solid phase extraction method for the mass spectrometric quantification of 12 specific metabolites of organophosphorus pesticides, synthetic pyrethroids, and select herbicides in human urine. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2013; 929:18–26.
- Engel SM, Wetmur J, Chen J, Zhu C, Barr DB, Canfield RL, Wolff MS. Prenatal exposure to organophosphates, paraoxonase 1, and cognitive development in childhood. *Environ Health Perspect*. 2011; 119:1182–8. [PubMed: 21507778]
- EPA (U.S. Environmental Protection Agency). News releases: in settlement with US, Puerto Rico farm pays fine and changes the way it applies pesticides; agrees to relief measures to protect local residents from drift. Washington, DC: U.S. Environmental Protection Agency; Aug 28. 2001
- EPA (U.S. Environmental Protection Agency). News releases: EPA adds Pesticide Warehouse III site in Manati to the Superfund National Priorities list. Washington, DC: U.S. Environmental Protection Agency; Apr 30. 2003
- EPA (U.S. Environmental Protection Agency). News releases: EPA draws attention to hazards of illegal pesticides in Puerto Rico. Washington, DC: U.S. Environmental Protection Agency; Sep 29. 2004
- EPA (U.S. Environmental Protection Agency). News releases: EPA cites pesticides practices of Puerto Rico agency. Washington, DC: U.S. Environmental Protection Agency; Oct 8. 2008
- EPA (U.S. Environmental Protection Agency). Pesticide industry sales and usage: 2006 and 2007 market estimates. Washington, DC: U.S. Environmental Protection Agency; Feb. 2011
- EPA (U.S. Environmental Protection Agency). NPL site narrative for Pesticide Warehouse III. Washington, DC: U.S. Environmental Protection Agency; Nov 27. 2012
- Eskenazi B, Harley K, Bradman A, Weltzien E, Jewell NP, Barr DB, Furlong CE, Holland NT. Association of in utero organophosphate pesticide exposure and fetal growth and length of gestation in an agricultural population. *Environ Health Perspect*. 2004; 112:1116–24. [PubMed: 15238287]
- FDA (U.S. Food and Drug Administration). 2004–2005 Summary of pesticide residues and industrial chemicals found in TDS foods, sorted by food: market baskets 2004-1 through 2005-4. Rockville, MD: U.S. Food and Drug Administration; 2005.
- Fortenberry GZ, Meeker JD, Sánchez BN, Barr DB, Panuwet P, Bellinger D, Schnaas L, Solano-González M, Ettinger AS, Hernandez-Avila M, Hu H, Tellez-Rojo MM. Urinary 3,5,6-trichloro-2-pyridinol (TCPY) in pregnant women from Mexico City: distribution, temporal variability, and

- relationship with child attention and hyperactivity. *Int J Hyg Environ Health*. 2014; 217:405–12. [PubMed: 24001412]
- Garza JR, Pérez EA, Prelip M, McCarthy WJ, Feldman JM, Canino G, Ortega AN. Occurrence and correlates of overweight and obesity among island Puerto Rican youth. *Ethn Dis*. 2011; 21:163–169. [PubMed: 21749019]
- Hankinson SE, Manson JE, Spiegelman D, Willett WC, Longcope C, Speizer FE. Reproducibility of plasma hormone levels in postmenopausal women over a 2–3-year period. *Cancer Epidemiol Biomarkers Prev*. 1995; 4:649–54. [PubMed: 8547832]
- Hoppin JA, Umbach DM, London SJ, Lynch CF, Alavanja MC, Sandler DP. Pesticides associated with wheeze among commercial pesticide applicators in the Agricultural Health Study. *Am J Epidemiol*. 2006; 163:1129–37. [PubMed: 16611668]
- Lee WJ, Blair A, Hoppin JA, Lubin JH, Rusiecki JA, Sandler DP, Dosemeci M, Alavanja MC. Cancer incidence among pesticide applicators exposed to chlorpyrifos in the Agricultural Health Study. *J Natl Cancer Inst*. 2004; 96:1781–9. [PubMed: 15572760]
- March of Dimes. Premature birth report cards. White Plains, NY: March of Dimes; 2012. Available from: www.marchofdimes.com/mission/prematurity_reportcard.html
- Marks AR, Harley K, Bradman A, Kogut K, Barr DB, Johnson C, Calderon N, Eskenazi B. Organophosphate pesticide exposure and attention in young Mexican-American children: the CHAMACOS study. *Environ Health Perspect*. 2010; 118:1768–74. [PubMed: 21126939]
- Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Kirmeyer S, Mathews TJ, Wilson EC. Births: final data for 2009. *Natl Vital Stat Rep*. 2011; 60:1–70. [PubMed: 22670489]
- Meeker JD, Barr DB, Hauser R. Thyroid hormones in relation to urinary metabolites of non-persistent insecticides in men of reproductive age. *Reprod Toxicol*. 2006a; 22:437–42. [PubMed: 16584866]
- Meeker JD, Barr DB, Ryan L, Herrick RF, Bennett DH, Bravo R, Hauser R. Temporal variability of urinary levels of nonpersistent insecticides in adult men. *J Expo Anal Environ Epidemiol*. 2005; 15:271–81. [PubMed: 15340359]
- Meeker JD, Cantonwine DE, Rivera-González LO, Ferguson KK, Mukherjee B, Calafat AM, Ye X, Anzalota Del Toro LV, Crespo-Hernández N, Jiménez-Vélez B, Alshawabkeh AN, Cordero JF. Distribution, variability, and predictors of urinary concentrations of phenols and parabens among pregnant women in Puerto Rico. *Environ Sci Technol*. 2013; 47:3439–47. [PubMed: 23469879]
- Meeker JD, Ravi SR, Barr DB, Hauser R. Circulating estradiol in men is inversely related to urinary metabolites of nonpersistent insecticides. *Reprod Toxicol*. 2008; 25:184–91. [PubMed: 18249523]
- Meeker JD, Ryan L, Barr DB, Hauser R. Exposure to nonpersistent insecticides and male reproductive hormones. *Epidemiology*. 2006b; 17:61–8. [PubMed: 16357596]
- Odetokun MS, Montesano MA, Weerasekera G, Whitehead RD Jr, Needham LL, Barr DB. Quantification of dialkylphosphate metabolites of organophosphorus insecticides in human urine using 96-well plate sample preparation and high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci*. 2010; 878:2567–74.
- Otero-González M, García-Fragoso L. Prevalence of overweight and obesity in a group of children between the ages of 2 to 12 years old in Puerto Rico. *P R Health Sci J*. 2008; 27:159–161. [PubMed: 18616044]
- Panuwet P, Prapamontol T, Chantara S, Thavornnyuthikarn P, Bravo R, Restrepo P, Walker RD, Williams BL, Needham LL, Barr DB. Urinary paranitrophenol, a metabolite of methyl parathion, in Thai farmer and child populations. *Arch Environ Contam Toxicol*. 2009; 57:623–9. [PubMed: 19365648]
- Pérez CM, Guzmán M, Ortiz AP, Estrella M, Valle Y, Pérez N, Haddock L, Suárez E. Prevalence of the metabolic syndrome in San Juan, Puerto Rico. *Ethn Dis*. 2008; 18:434–441. [PubMed: 19157247]
- Rauch SA, Braun JM, Barr DB, Calafat AM, Khoury J, Montesano AM, Yoltan K, Lanphear BP. Associations of prenatal exposure to organophosphate pesticide metabolites with gestational age and birth weight. *Environ Health Perspect*. 2012; 120:1055–60. [PubMed: 22476135]

- Rivera-Soto WT, Rodríguez-Figueroa L, Calderón G. Prevalence of childhood obesity in a representative sample of elementary school children in Puerto Rico by socio-demographic characteristics, 2008. *P R Health Sci J*. 2010; 29:357–363. [PubMed: 21261174]
- Rosner, B. Multisample inference. In: Rosner, B., editor. *Fundamentals of Biostatistics*. 5. Pacific Grove: Duxbury; 2000. p. 511-76.
- Shin HM, McKone TE, Tulve NS, Clifton MS, Bennett DH. Indoor residence times of semivolatile organic compounds: model estimation and field evaluation. *Environ Sci Technol*. 2013; 47:859–67. [PubMed: 23244175]
- Swan SH, Kruse RL, Liu F, Barr DB, Drobni EZ, Redmon JB, Wang C, Brazil C, Overstreet JW. Study for Future Families Research Group. Semen quality in relation to biomarkers of pesticide exposure. *Environ Health Perspect*. 2003; 111:1478–84. [PubMed: 12948887]
- Wang P, Tian Y, Wang XJ, Gao Y, Shi R, Wang GQ, Hu GH, Shen XM. Organophosphate pesticide exposure and perinatal outcomes in Shanghai, China. *Environ Int*. 2012; 42:100–4. [PubMed: 21601922]
- Whyatt RM, Garfinkel R, Hoepner LA, Andrews H, Holmes D, Williams MK, Reyes A, Diaz D, Perera FP, Camann DE, Barr DB. A biomarker validation study of prenatal chlorpyrifos exposure within an inner-city cohort during pregnancy. *Environ Health Perspect*. 2009; 117:559–67. [PubMed: 19440494]
- Ye X, Pierik FH, Angerer J, Meltzer HM, Jaddoe VW, Tiemeier H, Hoppin JA, Longnecker MP. Levels of metabolites of organophosphate pesticides, phthalates, and bisphenol A in pooled urine specimens from pregnant women participating in the Norwegian Mother and Child Cohort Study (MoBa). *Int J Hyg Environ Health*. 2009; 212:481–91. [PubMed: 19394271]
- Ye X, Pierik FH, Hauser R, Duty S, Angerer J, Park MM, Burdorf A, Hofman A, Jaddoe VW, Mackenbach JP, Steegers EA, Tiemeier H, Longnecker MP. Urinary metabolite concentrations of organophosphorous pesticides, bisphenol A, and phthalates among pregnant women in Rotterdam, the Netherlands: the Generation R study. *Environ Res*. 2008; 108:260–7. [PubMed: 18774129]
- Yolton K, Xu Y, Sucharew H, Succop P, Altaye M, Popelar A, Montesano MA, Calafat AM, Khoury JC. Impact of low-level gestational exposure to organophosphate pesticides on neurobehavior in early infancy: a prospective study. *Environ Health*. 2013; 12:79. [PubMed: 24034442]
- Zhang Y, Han S, Liang D, Shi X, Wang F, Liu W, Zhang L, Chen L, Gu Y, Tian Y. Prenatal exposure to organophosphate pesticides and neurobehavioral development of neonates: a birth cohort study in Shenyang, China. *PLoS One*. 2014; 9:e88491. [PubMed: 24551109]

HIGHLIGHTS

- We studied repeated urinary levels of OP insecticide metabolites during pregnancy.
- Detection frequencies for all 10 urinary metabolites ranged from 3–90%.
- Repeated measures of TCPY, PNP, DETP, and DMTP had poor reproducibility.
- Certain demographic and lifestyle variables are determinants of exposure.

Figure 1.

ICCs (95% CIs) for log-transformed uncorrected and SG-corrected urinary organophosphate insecticide metabolite concentrations across pregnancy. Dashed lines indicate the lower- and upper-ends of the ICC interpretation criteria (0.00–0.39 = poor reproducibility; 0.40–0.74 = fair to good reproducibility; 0.75–1.00 = excellent reproducibility).

Urinary concentrations of organophosphate insecticide metabolites (ng/ml, uncorrected for SG) in pregnant women from PROTECT (Puerto Rico) and comparison with women ages 18–40 years from NHANES (U.S. population-based sample)

Table 1

Parent compound(s)	Metabolite	LOD	Study and year	N	N (%)	LOD	GM	Percentiles				
								25 th	50 th	75 th	95 th	Max
Chlorpyrifos, chlorpyrifos-methyl	TCPY	0.1	PROTECT 10-12	152 ^a	131 (86.2)	0.4	0.2	0.2	0.5	0.9	2.0	3.3
		0.1	NHANES 09-10	355	302 (85.1)	0.8	0.5	0.5	1.0	2.0	4.4	23.8
Diazinon	IMPY	0.1	PROTECT 10-12	152 ^a	22 (14.5)	<LOD	<LOD	<LOD	<LOD	<LOD	0.3	1.6
		0.1	NHANES 09-10	355	65 (18.1)	<LOD	<LOD	<LOD	<LOD	<LOD	0.6	12.5
Malathion	MDA	0.2	PROTECT 10-12	152 ^a	16 (10.5)	<LOD	<LOD	<LOD	<LOD	<LOD	0.4	4.1
		0.5	NHANES 09-10	355	60 (16.9)	<LOD	<LOD	<LOD	<LOD	<LOD	2.3	20.0
Parathion, methyl parathion	PNP	0.1	PROTECT 10-12	152 ^a	137 (90.1)	0.5	0.3	0.5	1.1	3.2	11.4	11.4
		0.1	NHANES 09-10	355	283 (79.7)	0.5	0.1	0.5	1.1	3.1	39.8	39.8
Diethyl substituted OPs	DEP	0.5	PROTECT 10-12	150 ^b	49 (32.7)	0.9	<LOD	<LOD	<LOD	2.6	11.4	158
		0.4	NHANES 07-08	274	93 (33.9)	0.7	<LOD	<LOD	<LOD	1.23	14.5	78.6
	DETTP	0.3	PROTECT 10-12	150 ^b	77 (51.3)	0.5	<LOD	<LOD	<LOD	1.0	4.1	17.1
		0.6	NHANES 07-08	274	128 (46.7)	0.7	<LOD	<LOD	<LOD	1.0	3.8	32.0
Dimethyl substituted OPs	DEDTP	0.1	PROTECT 10-12	150 ^b	4 (2.7)	<LOD	<LOD	<LOD	<LOD	<LOD	0.1	0.8
		0.4	NHANES 07-08	274	1 (0.4)	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD	1.1
	DMP	0.5	PROTECT 10-12	150 ^b	69 (46.0)	1.4	<LOD	<LOD	<LOD	6.9	15.3	51.2
		0.5	NHANES 07-08	274	113 (41.2)	<LOD	<LOD	<LOD	<LOD	11.9	42.2	194
	DMTP	0.1	PROTECT 10-12	150 ^b	94 (62.7)	0.8	<LOD	<LOD	1.0	4.0	26.7	73.3
		0.6	NHANES 07-08	274	216 (78.8)	2.1	0.6	1.9	4.7	40.9	267	267
	DMDTP	0.1	PROTECT 10-12	150 ^b	58 (38.7)	0.2	<LOD	<LOD	<LOD	0.4	2.4	5.2
		0.5	NHANES 07-08	270	58 (21.5)	0.5	<LOD	<LOD	<LOD	<LOD	5.8	35.9

Abbreviations: GM, geometric mean; LOD, limit of detection; NHANES, National Health and Nutrition Examination Survey; PROTECT, Puerto Rico Testsite for Exploring Contamination Threats.

^a 152 samples from 54 women.

^b 150 samples from 54 women.

Table 2

Percent change in SG-corrected urinary concentrations of organophosphate insecticide metabolites for studied variables with at least one statistically significant or “suggestive” association (displaying results for metabolites detected in 50% of samples)

Category	Variable	TCPY		PNP		DETP		DMTP	
		N	% change (95% CI) ^a	N	% change (95% CI) ^a	N	% change (95% CI) ^a	N	% change (95% CI) ^a
Demographic characteristics	Age (years)								
	<24	76	-29.6 (-51.0, 1.2)*	76	-0.6 (-35.0, 52.0)	75	-30.5 (-54.9, 7.1)*	75	69.4 (-24.0, 277.6)
	24	71		71		70		70	
	Married								
Unemployed	Yes	67	-15.4 (-38.1, 15.4)	67	21.9 (-12.6, 69.9)	67	-2.6 (-32.8, 41.3)	67	86.3 (-6.1, 269.7)*
	No	79		79		77		77	
	Yes	43	24.4 (-17.3, 87.2)	43	47.5 (-6.3, 132.0)*	41	57.2 (-2.1, 152.5)*	41	4.9 (-57.0, 156.2)
	No	103		103		103		103	
Foods consumed in the past 48-hr	Collards								
	Yes	5	5.4 (-55.8, 151.5)	5	-55.7 (-82.6, 12.5)*	5	6.9 (-62.1, 201.4)	5	46.6 (-78.4, 892.6)
	No	135		135		133		133	
	Grape juice								
Raisins	Yes	55	59.9 (15.0, 122.2)**	55	20.4 (-16.6, 73.7)	53	12.3 (-25.1, 68.3)	53	-13.2 (-58.9, 83.5)
	No	85		85		85		85	
	Yes	15	69.5 (1.6, 182.6)**	15	22.0 (-30.3, 113.5)	15	30.6 (-29.6, 142.4)	15	146.0 (-20.8, 664.5)
	No	125		125		123		123	
Spinach	Yes	6	14.5 (-48.0, 152.0)	6	-51.1 (-79.0, 13.9)*	6	-40.4 (-76.7, 52.6)	6	-28.9 (-87.5, 305.0)
	No	134		134		132		132	

Abbreviations: CI, confidence interval.

^a Calculated using a linear mixed model with one random effect as the random intercept for each woman and a fixed effect for the variable of interest.

* 0.05 $p < 0.10$.

$p < 0.05$
**

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Odds ratios for detectable urinary concentrations of organophosphate insecticide metabolites for studied variables with at least one statistically significant or “suggestive” association (displaying results for metabolites detected in <50% of samples)

Table 3

Category	Variable	IMPY		MDA		DEDTP		DMDTP		DEP		DMP	
		N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a
Demographic characteristics	Age (years)												
	<24	80	0.1 (0.03, 0.4)**	80	0.7 (0.2, 2.3)	79	0.9 (0.1, 6.5)	79	0.9 (0.4, 2.1)	79	0.3 (0.1, 0.8)**	79	1.5 (0.8, 2.9)
	24	72	1.0	72	1.0	71	1.0	71	1.0	71	1.0	71	1.0
	Married												
Foods consumed in the past 48-hr	Yes	68	0.3 (0.1, 0.9)**	68	0.9 (0.4, 2.2)	68	0.6 (0.1, 6.3)	68	0.9 (0.5, 1.8)	68	0.9 (0.5, 1.7)	68	1.7 (0.9, 2.9)*
	No	80	1.0	80	1.0	78	1.0	78	1.0	78	1.0	78	1.0
	Cherries												
	Yes	9	— ^b	9	1.1 (0.2, 7.5)	9	16.3 (0.9, 289.3)*	9	2.0 (0.5, 7.1)	9	0.9 (0.3, 2.8)	9	0.9 (0.3, 2.5)
Collards	No	133	1.0	133	1.0	131	1.0	131	1.0	131	1.0	131	1.0
	Yes	5	1.4 (0.1, 15.0)	5	6.4 (0.8, 49.1)*	5	— ^b	5	6.4 (1.2, 35.4)**	5	8.0 (0.8, 75.8)*	5	1.7 (0.4, 7.1)
	No	137	1.0	137	1.0	135	1.0	135	1.0	135	1.0	135	1.0
Grapes	Yes	49	1.1 (0.4, 2.8)	49	1.8 (0.5, 6.3)	49	1.9 (0.1, 31.0)	49	0.7 (0.3, 1.7)	49	1.3 (0.7, 2.5)	49	0.6 (0.3, 1.1)*
	No	93	1.0	93	1.0	91	1.0	91	1.0	91	1.0	91	1.0
	Grape juice												
	Yes	55	1.1 (0.5, 2.6)	55	3.6 (1.1, 11.8)**	53	1.7 (0.1, 26.2)	53	1.3 (0.6, 2.5)	53	0.9 (0.4, 1.9)	53	1.1 (0.6, 1.9)
Peanuts	No	87	1.0	87	1.0	87	1.0	87	1.0	87	1.0	87	1.0
	Yes	22	1.3 (0.4, 5.2)	22	3.2 (0.8, 12.1)*	22	— ^b	22	1.0 (0.5, 2.3)	22	2.6 (0.9, 7.2)*	22	1.4 (0.6, 3.0)
	No	120	1.0	120	1.0	118	1.0	118	1.0	118	1.0	118	1.0
	Peanut butter												
Peanut butter	Yes	14	2.4 (0.6, 10.6)	14	4.3 (0.9, 20.7)*	14	— ^b	14	1.1 (0.4, 3.7)	14	1.0 (0.3, 3.4)	14	0.8 (0.3, 2.3)
	No	128	1.0	128	1.0	126	1.0	126	1.0	126	1.0	126	1.0

Category	Variable	IMPY		MDA		DEDTP		DMDTP		DEP		DMP	
		N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a	N	OR (95% CI) ^a
Home pest- related issues	Insects (inside) ^c												
	Yes	73	0.4 (0.1, 0.9) **	73	0.8 (0.3, 2.4)	73	— ^b	73	0.6 (0.3, 1.3)	73	1.2 (0.5, 2.8)	73	1.0 (0.5, 1.9)
	No	69	1.0	69	1.0	67	1.0	67	1.0	67	1.0	67	1.0
	Pesticides (inside) ^d												
	Yes	7	0.9 (0.1, 7.9)	7	7.7 (2.1, 28.7) **	7	— ^b	7	2.1 (0.6, 7.3)	7	1.4 (0.3, 7.8)	7	0.4 (0.1, 1.7)
	No	135	1.0	135	1.0	133	1.0	133	1.0	133	1.0	133	1.0
	Pesticides (inside) ^e												
	Yes	32	0.7 (0.2, 2.6)	32	1.3 (0.4, 4.0)	32	— ^b	32	0.7 (0.3, 1.7)	32	2.7 (1.1, 6.5) **	32	0.6 (0.3, 1.3)
	No	110	1.0	110	1.0	108	1.0	108	1.0	108	1.0	108	1.0
	Pesticides (home/lawn) ^f												
	Yes	17	0.7 (0.1, 3.3)	17	— ^b	17	— ^b	17	0.8 (0.2, 2.6)	17	2.3 (0.9, 6.3) *	17	0.7 (0.2, 2.3)
	No	125	1.0	125	1.0	123	1.0	123	1.0	123	1.0	123	1.0
	Pesticides(stored) ^g												
	Yes	97	0.6 (0.2, 1.9)	97	0.9 (0.3, 3.0)	95	— ^b	95	0.5 (0.2, 1.1) *	95	0.9 (0.4, 2.1)	95	0.9 (0.4, 2.0)
	No	45	1.0	45	1.0	45	1.0	45	1.0	45	1.0	45	1.0

Abbreviations: CI, confidence interval; OR, odds ratio.

^aCalculated using a generalized estimating equation with a fixed effect for the variable of interest.

^bUnable to calculate an odds ratio because there were 0 detects in one of the two compared groups.

^cInsects a common nuisance inside home.

^dPesticides historically applied inside home by a professional exterminator.

^ePesticides historically applied inside home by participant.

^fPesticides applied to home or lawn by participant in past 48-hr.

^gPesticides currently stored inside home.

* 0.05 p<0.10.

*
**
p < 0.05

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript