



Published in final edited form as:

Cancer Epidemiol. 2012 August ; 36(4): 375–380. doi:10.1016/j.canep.2011.12.009.

Reliability of Maternal-Reports Regarding the Use of Household Pesticides: Experience from a Case-Control Study of Childhood Leukemia

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Abstract

Introduction—Self-reported household pesticide use has been associated with higher risk of childhood leukemia in a number of case-control studies. The aim of this study is to assess the reliability of self-reported household use of pesticides and potential differences in reliability by case-control status, and by socio-demographic characteristics.

Methods—Analyses are based on a subset of the Northern California Childhood Leukemia Study population. Eligible households included those with children less than 8 years old who lived in the same residence since diagnosis (reference date for controls). The reliability was based on two repeated in-person interviews. Kappa, percent positive and negative agreements were used to assess reliability of responses to ever/never use of six pesticides categories.

Results—Kappa statistics ranged from 0.31 to 0.61 (fair to substantial agreement), with 9 out of the 12 tests indicating moderate agreement. The percent positive agreement ranged from 46–80% and the percent negative agreement from 54–95%. Reliability for all pesticide types as assessed by the three reliability measures did not differ significantly for cases and controls as confirmed by bootstrap analysis. For most pesticide types, Kappa and percent positive agreement were higher for non-Hispanics than Hispanics and for households with higher income versus lower income.

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Conflict of interest: None declared

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Conclusions—Reproducibility of maternal-reported pesticide use was moderate to high and was similar among cases and controls suggesting that differential recall is not likely to be a major source of bias.

Keywords

reliability; case-control study; leukemia; recall bias

1. Introduction

Household pesticide use has been associated with increased risk of childhood leukemia in most case-control studies that relied on self-reported exposure data [1]. Although specific biochemical mechanisms relating pesticide exposures to childhood cancer have yet to be established [2], insecticides and herbicides induce oxidative stress and have been shown to have direct genotoxic effects in both occupational [3] and residential [4] exposure settings. Exposure effects from household pesticide use could occur before conception through germline mutations that can be passed on to the child, during pregnancy through transplacental crossover, and postnatally through direct exposure to the child.

Most epidemiological studies conducted over the past two decades have indicated positive associations between self-reported home pesticides use and childhood leukemia. A study previously published by the Northern California Childhood Leukemia Study (NCCLS) reported a positive association between childhood leukemia and maternal reports of household use of pesticides [5]. In that study, Ma et al. reported that cases were exposed indoors to more pesticides than were the controls and that the highest odds ratio (OR) was seen for these exposures during pregnancy (OR = 2.2; 95% confidence interval (CI): 1.3–3.6) [5]. The authors also reported that more frequent indoor exposure to insecticides was associated with a higher risk, consistent with a dose response relationship. Similarly, eight other studies reported positive and significant results for the association between childhood leukemia and household pesticide use during pregnancy [6–12] and five studies reported significant results for exposure in early childhood [7–11]. In addition, five studies showed significant associations with garden products used during pregnancy [8, 10, 12] and early childhood [8, 10, 11, 13]. These studies, and six more, were included in a recent Meta-Analysis, by Turner et al. (2010) [14]. The authors found a positive association between residential pesticides exposures during pregnancy (summary OR = 1.54; 95% CI, 1.13–2.11), and during early childhood (summary OR = 1.38; 95% CI, 1.12–1.70) [14].

These previous studies on the association between pesticides and childhood cancer have been case-control in design and have relied on self-reported retrospective exposure assessment, for which there are concerns about recall bias. Recall bias, also called reporting bias or differential recall, is caused by differences in accuracy of recalling or reporting past events by cases and controls. Recall bias can be defined as a measurement error characterized by differences in the accuracy of subject recall or report between compared groups [15]. Recall bias can distort the measure of association between exposure and disease by any magnitude and direction, and this distortion is frequently difficult to predict [16]. It is difficult to evaluate the direction of the resulting bias, if it exists, because cases could over

or under report the exposure depending on whether recognition of past exposure or guilt about that exposure took precedence [12].

To our knowledge, no prior studies of childhood leukemia have measured the reliability of maternal-reported household pesticide. Previous reliability and validity studies of chemical exposures include studies of occupational epidemiology that compared the self-reported exposure with expert-assessed or exposure biomarkers [17–19] and studies that evaluated the reliability by comparing information from repeated interviews [20, 21]. In the absence of an objective reference, i.e., a “gold standard” to evaluate validity, we assessed the reproducibility of maternal-reported household pesticide use between cases and controls in a subset of the NCCLS.

2. Materials and Methods

2.1. Study population

The study population included in this reliability study is a subset of the parent NCCLS case-control study conducted from 1995 to 2008. A detailed description of the NCCLS design has been published elsewhere [22, 23]. In brief, the parent study recruited children with leukemia from hospitals in 35 counties in Northern and Central California, using rapid case ascertainment procedures to report cases usually within 72 hours after diagnosis. For each case, one or two control subjects were randomly selected from birth certificates through the California Office of Vital Records, matched on date of birth, sex, Hispanic ethnicity, and maternal race. Participating controls in the NCCLS were determined to be representative of the sampled population by parental age, parental education, and mother’s reproductive history; characteristics which indicate a reduced potential for selection bias [22]. Eligibility criteria for cases and controls participating in the parent NCCLS include: 1) residence in the 35-county study area; 2) less than 15 years of age at the time of case diagnosis (referent date for controls); 3) availability of an English or Spanish-speaking biological parent; and 4) no previous diagnosis of cancer. The reliability study was conducted for a subset of this study population between October 2001 - December 2006 and included subjects who met the following eligibility criteria: 1) less than 8 years of age at the time of case diagnosis (reference date for controls), and 2) residing at the same address since diagnosis for cases and corresponding date for matched controls. Approximately 55% of households enrolled in the parent NCCLS from 2001 to 2006 were eligible for the reliability study. Of those, 86% consented to participate providing 209 case and 235 control families for the present analysis.

The study was approved by the University of California Committee for the Protection of Human Subjects, the California Health and Human Services Agency Committee for the Protection of Human Subjects, the Institutional Review Board of the National Cancer Institute and of all the participating hospitals and institutions. A written informed consent was obtained from the parents or legal guardian of all participating subjects.

2.2. Data collection

Pesticide data were collected during two separate in-person interviews conducted by trained staff in English or Spanish. The initial interview (referred to as Tier 1) was scheduled as soon as consent was obtained and the follow-up interview (referred to as Tier 2) was

conducted within 3–12 months following the Tier 1 interview. In both interviews, respondents were asked questions about household use of pesticide products targeting fleas and ticks; ants, flies, and cockroaches; and outdoor weeds and insects. Respondents were also queried about the use of indoor foggers and the use of professional services for pest control and lawn and garden maintenance. A detailed description of the NCCLS Tier 1 interview process has been published previously [1]. Standardized questionnaires were used at the time of both interviews including show cards and calendars to elicit responses regarding exposure to a wide range of chemicals used at home and at work, for critical periods of the child's development. Information collected included the name of the products (household use only) or the name of the insect and pest treated (Tier 1 and 2). For each product or treatment the information regarding the timing of use and frequency of use (5 or more times during the past 12 months, less than 5 times during the past 12 months) was collected. Information regarding the time of use was collected in a more detailed description in the first interview. Specifically time windows for each product included the following: 3 months before pregnancy, 1st trimester, 2nd trimester, 3rd trimester, while breastfeeding, from birth to age 1, from age 1 to age 2, from age 2 to age 3, and in the past 12 months. In the repeated interview, time windows included 3 months before pregnancy, during pregnancy, from birth to 3 years, and the last 12 months.

Both the Tier 1 and 2 interviews asked questions regarding the same types of pest treatments; however, the methods of data collection differed slightly due to different study objectives. The main objective of the Tier 2 interview was to link EPA registration numbers obtained from pesticide products stored in the homes to publicly available EPA databases, thus allowing for identification of active ingredients, chemical composition, and intended target pest. Consistent with this objective, the Tier 2 interview began with an inventory of pesticide products found in and around the home using a standard questionnaire to record the name, EPA registration number, the purpose, period and locations the product was used. Once this information was recorded, a standardized questionnaire was used to collect information about additional pest treatments that were not ascertained during the home product inventory. The questions about “flea and ticks” and “weed and plant/tree insects/diseases” differed slightly between the interviews. Specifically, the Tier 1 questionnaire included three separate questions about “flea and tick” products while the Tier 2 included one multi-part question. Questions in the Tier 1 questionnaire were: 1) Did you use flea or tick soaps or shampoos?, 2) Did you use sprays, dusts, powders or skin applications for fleas or ticks?, and 3) Did you use flea or tick collars?. The Tier 2 question was “Did you have a pet that was treated for fleas or ticks using shampoos, soaps, collars, sprays, dusts, powders, or skin applications?” Both questionnaires obtained time-period specific use for each product reported as described above.

2.3. Statistical Analysis

Kappa statistics, percent positive and negative agreement (with 95% CI) were used to assess reliability of responses in Tier 1 to Tier 2 for ever or never pesticide use. Pesticide use was defined as pesticide use anytime from three months prior to conception until three years of age. Percent positive, percent negative, and Kappa statistics, were used to assess reliability of six categories of pesticide applications or services: 1) fleas or ticks, 2) ants, flies, or

cockroaches, 3) indoor foggers, 4) weeds and plant/tree insects/diseases, 5) professional pesticide services, and 6) professional lawn services. An overall measure of agreement was calculated for the three reliability measures using data from the six categories together (i.e. it combines data from all six categories providing an overall agreement). In order to assess the potential for differential recall between cases and controls these analyses were conducted by case-control status. To determine whether the reliability of self-reported household pesticide use was consistent across subgroups, tests of agreement were also calculated by Hispanic ethnicity, household income and parental education. Kappa statistics ranging from 0.21 to 0.40 were interpreted as “fair” agreement, from 0.41 to 0.60 as “moderate” agreement, 0.61 to 0.80 as “substantial” agreement, and those of 0.81 have been interpreted to indicate “almost perfect” agreement as suggested by Landis and Koch [24]. In addition, a bootstrap analysis [25] based on 2000 replicate samples was used to estimate the mean reliability differences by case/control status, Hispanic ethnicity, and other socio-economic characteristics. The 95% CIs and p-values of the bootstrap were computed based on the distribution of replications.

3. Results

Cases and controls in this analysis were comparable for all demographic characteristics evaluated (Table 1). In addition, the mean number of days between the two interviews was similar between cases (218.6 days) and controls (212.9 days) (p-value = 0.521). Table 2 presents the frequencies of self-reported pesticide use at the first interview (Tier 1) and at the second (repeated) interview (Tier 2). The category with the highest frequency of use was ants, flies, or cockroaches with reported use in 65.1% and 70.3% of Tier 1 and Tier 2 interviews, respectively.

Table 3 presents the results of the reliability assessment of self-reported pesticide use among cases and controls. Kappa statistics ranged from 0.35 to 0.61 among cases and from 0.31 to 0.58 among controls, indicating fair to substantial agreement. The lowest agreement was observed for self-reported use of products for ants, flies, or cockroaches among both cases and controls. The percent positive agreement ranged from 47–80% among cases and 46–77% among controls with self-reported use of products for ants and flies showed the highest agreement. Percent negative agreement ranged from 55–95% among cases and 54–94% among controls; indoor foggers showed the highest agreement for both cases and controls.

Reproducibility of responses for all pesticide categories using the three reliability measures was similar between cases and controls. Moreover, the overall reliability measures (using data from the six categories together) produced similar results, with an overall Kappa for cases and controls of 0.58 (95% CI: 0.52–0.62), and 0.56 (95% CI: 0.51–0.61), respectively. Importantly, there were no differences in reproducibility of responses between cases and controls for the overall percent positive agreement [72% (95% CI: 69–76%) and 72% (95% CI: 68–75%), respectively], and for the overall percent negative agreement [85% (95% CI: 83–87%) and 85% (95% CI: 83–86%), respectively]. Bootstrapping of the mean differences and their variances of the three measures also showed no apparent difference in the recall between the cases and controls.

Table 4 presents results of the reliability assessment of self-reported pesticide use by Hispanic ethnicity (n=173 Hispanic, n=271 non-Hispanic) for cases and controls combined. Similar results were obtained for household income (data not shown) and therefore these results are summarized together. Reproducibility of responses for the majority of the pesticide categories using Kappa and percent positive agreement were higher among non-Hispanics participants and participants with higher household incomes than among Hispanics and those with lower household incomes. Significant differences for both Kappa and percent positive agreement were observed only in the professional pest service category: Kappa (0.66 for non-Hispanic vs. 0.37 for Hispanic; and 0.37 for low income vs. 0.70 for high income) and percent positive agreement (79% for non-Hispanic vs. 57% for Hispanic; 52% for low income vs. 82% for high income). In addition, the overall percent positive agreement as well as the bootstrap estimates of the mean difference of percent positive agreement, revealed that both non-Hispanic participants and those with higher income had higher percent positive agreement than Hispanic participants (p-value = 0.004) and those with lower household income (p-value = 0.020).

Table 5 shows the results of the reliability assessment by two levels of maternal education, 12 or less years of education (high school or less) (n=134), and more than 12 years of education (some college, college or post graduate degree) (n=310). Reproducibility of responses by educational status was similar for all comparisons except for the overall percent negative agreement. Overall results of the percent negative agreement indicate a high concordance of negative responses among mothers with 12 or less years of education (88%; 95% CI: 85–89%) compared to those mothers with more than 12 years of education (84%; 95% CI: 82–85%). The reliability assessment by the same levels of paternal education produced similar results to those of maternal education (data not shown). In addition, no difference in reproducibility of responses was found when similar comparisons were done between urban and rural subgroups (data not shown).

The analyses stratified by Hispanic ethnicity (Table 3), maternal education (Table 4), and household income were performed separately for cases and controls. Although based on small numbers, the results also indicated that for most pesticide types, Kappa and percent positive agreement were higher for non-Hispanics, for households with higher income, and higher education regardless of case control status (data not shown).

4. Discussion

These analyses, conducted using data from an ongoing case-control study of childhood leukemia, are the first to assess reliability of self-reported home pesticide use in a childhood leukemia study. Based on the Kappa statistics, the overall agreement was fair to substantial depending on the type of pest treatment. Using all three reliability measures (Kappa, percent positive and negative) as well as the bootstrap analysis, we found no difference in reproducibility of responses between Tier 1 and Tier 2 interviews for cases and controls. These results suggest that perhaps differential recall bias may not explain the observed associations between childhood leukemia and residential use of pesticides as previously reported by the NCCLS [5] and other case-control studies with similar reliance on self-reported exposures and retrospective exposure assessment [1]. However, with the

observation of fair and moderate agreement in both cases and controls, potential non-differential recall of exposure that attenuates the ability to detect exposure–outcome associations and results in an estimated measure of association that is biased toward the null can not be ruled out.

Concordance of positive responses was somewhat lower among Hispanic families and those with lower socio-economic status especially for reporting of professional pesticide and lawn services. This difference in recall is difficult to explain as families might be expected to accurately report the use of professional services, which are memorable events. A possible explanation for this difference may be related the fact that more of the Hispanic parents engaged in lawn care as an occupation, and concepts related to interpretation of use of professional services for lawn care may have been commingled. Alternatively, the definition of professional pest control services and lawn services may have been unclear in the Spanish version of the questionnaire at the time of the initial and follow-up interview.

The estimated Kappa statistics generally ranged from 0.31 to 0.61 while the percent positive and negative agreements were much higher and generally ranged from 46 to 80% and from 55 to 95%, respectively. Although perfect agreement would generate a Kappa value of 1.0, values much lower still represent good agreement as the Kappa statistic is highly dependent on prevalence of the characteristic in the population. Thompson and Walter have shown that for factors with a true prevalence of 0.2 to 0.8 and with a high sensitivity and specificity (70–90%), Kappa statistics fall into a range 0.3–0.6 [26]. Thus, Kappa statistics can be low, and percent positive and/or negative agreements high for situations in which the factor is highly prevalent or extremely rare. This could have been the situation when we observed low Kappa statistics and high percent negative agreement for indoor flea foggers (used by only 8.8% of cases and controls) and high percent positive for ants, flies, and cockroach use (highly used in about 65.1% of cases and controls).

Previous studies provide some evidence that differential recall is not likely to explain observed pesticide associations. Several studies of childhood cancer indicated that the magnitude of the associations with pesticide use varies by histological type of leukemia and other hematopoietic malignancies [6, 12, 27, 28], suggesting that differential recall bias may not explain the observed associations. Indeed, if more accurate reporting by case mothers caused the positive associations with reported pesticide use, the risk estimates would be expected to be elevated for all histologic types.

A strength of this study is the use of in-person interviews that employed several tools to facilitate recall of cases and controls including standardized questionnaires, show cards and calendars to elicit responses regarding exposure to a wide range of chemicals and pesticides used at home and at work, for critical periods of the child’s development. However, even these methods are limited by an individual’s ability to correctly recall past events. Some limitations of this study must be considered. While both interviews at Tier 1 and Tier 2 asked questions regarding the same pesticides products, the methods of data collection were slightly different due to the interviews different objectives. While these differences may have contributed to a lower level of agreement it would not affect our conclusion regarding the non-differential recall bias between cases and controls. Because pest treatment

information was collected primarily from mothers, their knowledge about paternal use of pesticides may have been inaccurate. Therefore, some pesticide exposures may not have been ascertained, introducing additional misclassification.

In conclusion, our results indicate that the reliability of maternal-reported household pesticide use was similar among cases and controls, suggesting that differential recall of maternal-reported household use of pesticides may not be substantial. To directly assess differential recall in studies of childhood cancer, additional efforts to evaluate the validity of self-reported pesticide exposures are needed. Based on the Kappa statistics, the overall agreement was fair to substantial, indicating the potential for non-differential recall of exposure which may attenuate estimates of association. The similarity in reliability between cases and controls as observed in these analyses, supports previous findings by the NCCLS suggesting that exposure to household pesticides is associated with elevated risk of childhood leukemia.

Acknowledgments

This work was supported by the National Institute of Environmental Health Sciences (PS42 ES04705 and R01 ES09137). We thank the children and their families for their participation in the Northern California Childhood Leukemia Study, and participating hospitals and clinical collaborators including: University of California Davis Medical Center (Dr. Jonathan Ducore), University of California San Francisco (Dr. Mignon Loh and Dr. Katherine Matthay), Children's Hospital of Central California (Dr. Vonda Crouse), Lucile Packard Children's Hospital (Dr. Gary Dahl), Children's Hospital Oakland (Dr. James Feusner), Kaiser Permanente Sacramento (Dr. Vincent Kiley), Kaiser Permanente Santa Clara (Dr. Carolyn Russo and Dr. Alan Wong), Kaiser Permanente San Francisco (Dr. Kenneth Leung), and Kaiser Permanente Oakland (Dr. Stacy Month).

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Table 1

Characteristics of cases (n=209) and controls (n= 235), NCCLS, 2001–2006, included in the reliability study of self-reported pesticide use

Characteristics	Cases n (%)	Controls n (%)
Gender		
Male	125 (59.8)	139 (59.2)
Female	84 (40.2)	96 (40.8)
Age at diagnosis, years (reference date for controls)		
Mean (s.e.)	3.76 (0.13)	3.88 (0.12)
Race/ethnicity		
Non-Hispanic white	72 (34.4)	106 (45.1)
Hispanic	88 (42.1)	85 (36.2)
Non-Hispanic black	7 (3.4)	7 (3.0)
Non-Hispanic other races	42 (20.1)	37 (15.7)
Maternal age at child's birth, years		
Mean (s.e.)	30.3 (0.43)	30.5 (0.38)
Household income, \$		
< 29,999	53 (25.4)	37 (15.7)
30,000–44,999	30 (14.3)	27 (11.5)
45,000–59,999	27 (12.9)	34 (14.5)
60,000–74,999	16 (7.7)	26 (11.1)
75,000	83 (39.7)	111 (47.2)
Maternal education		
High school or less	66 (31.6)	68 (28.9)
Some college	60 (28.7)	68 (28.9)
College or postgraduate	83 (39.7)	99 (42.2)
Paternal education		
High school or less	82 (40.0)	82 (35.6)
Some college	40 (19.5)	63 (27.4)
College or postgraduate	83 (40.5)	85 (37.0)
Urban/rural residence		
Rural	22 (10.5)	36 (15.3)
Suburban	32 (15.3)	24 (10.2)
Urban	155 (74.2)	175 (74.5)
Days between interviews		
Mean (s.e.)	218.6 (7.2)	212.9 (5.4)

Table 2

Comparison of self-reported pesticide use^a among cases and controls combined (n=444) at the 1st interview (Tier 1) and the 2nd (repeated: Tier 2) interview, NCCLS, 2001–2006

	1 st interview n (%)	2 nd (repeated) interview n (%)
Fleas, ticks	159 (35.9)	169 (38.2)
Ants, flies, cockroaches	289 (65.1)	312 (70.3)
Indoor foggers	39 (8.8)	47 (10.6)
Weeds, insects, plants	191 (43.2)	195 (32.9)
Professional pest service	142 (32.2)	145 (32.9)
Professional lawn service	99 (22.5)	75 (17.1)

^a Pesticide use: from three months prior to conception until three years of age

Table 3

Comparison of reliability of self-reported pesticide use^a by case-control status (cases, n=209 and controls, n=235), NCCLS, 2001–2006

	Kappa (95% CI)		Percent positive (95% CI)		Percent negative (95% CI)	
	Cases	Controls	Cases	Controls	Cases	Controls
Fleas, ticks	0.53 (0.41–0.65)	0.58 (0.47–0.68)	70 (61–78)	74 (66–81)	83 (78–88)	84 (79–88)
Ants, flies, cockroaches	0.35 (0.22–0.49)	0.31 (0.18–0.43)	80 (75–85)	77 (71–82)	55 (45–66)	54 (44–63)
Indoor foggers	0.42 (0.21–0.63)	0.40 (0.21–0.58)	47 (28–67)	46 (28–63)	95 (92–97)	94 (91–96)
Weeds, insects, plants	0.52 (0.40–0.64)	0.47 (0.35–0.58)	70 (62–78)	72 (66–79)	81 (76–86)	74 (68–81)
Professional pest service	0.56 (0.44–0.68)	0.58 (0.47–0.69)	70 (61–79)	72 (64–80)	86 (81–90)	86 (82–90)
Professional lawn service	0.61 (0.48–0.74)	0.51 (0.36–0.66)	71 (61–81)	58 (45–72)	90 (87–94)	92 (90–95)
Overall	0.58 (0.52–0.62)	0.56 (0.51–0.61)	72 (69–76)	72 (68–75)	85 (83–87)	85 (83–86)
Mean difference (95% CI) ^b	-0.02 (-0.06, 0.01)		-1.5 (-4.2, 1.2)		-1.0 (-2.0, 0.1)	
p-value ^c	0.840		0.927		0.812	

^a Pesticide use: from three months prior to conception until three years of age

^b Bootstrap estimates for difference of means and variances between cases and controls

^c Bootstrap estimated p-value

Table 4

Comparison of reliability of self-reported pesticide use^a by Hispanic Status (Non-Hispanic, n=271 and Hispanic n=173), NCCLS, 2001–2006

	Kappa (95% CI)		Percent positive (95% CI)		Percent negative (95% CI)	
	Hispanics	Non-Hispanics	Hispanics	Non-Hispanics	Hispanics	Non-Hispanics
Fleas, ticks	0.49 (0.36–0.63)	0.59 (0.49–0.69)	66 (56–76)	75 (69–82)	83 (78–88)	84 (80–88)
Ants, flies, cockroaches	0.25 (0.10–0.40)	0.38 (0.26–0.49)	76 (70–82)	80 (75–84)	50 (38–61)	57 (49–66)
Indoor foggers	0.41 (0.20–0.62)	0.41 (0.22–0.59)	47 (28–67)	46 (28–63)	94 (91–96)	95 (93–97)
Weeds, insects, plants	0.46 (0.32–0.60)	0.48 (0.38–0.59)	63 (52–74)	75 (69–81)	83 (78–88)	73 (67–79)
Professional pest service	0.37 (0.21–0.53)	0.66 (0.57–0.75)	57 (44–70)	79 (73–85)	85 (80–89)	87 (83–91)
Professional lawn service	0.39 (0.19–0.59)	0.63 (0.52–0.74)	47 (28–65)	72 (63–80)	92 (89–95)	91 (88–94)
Overall	0.50 (0.44–0.55)	0.60 (0.56–0.64)	65 (60–69)	76 (73–78)	85 (83–87)	85 (83–87)
Mean difference (95% CI) ^b	0.13 (0.09;0.17)		11.8 (9.0; 14.6)		0.0 (-1.2; 1.2)	
p-value ^c	0.031		0.004		0.739	

^a Pesticide use: from three months prior to conception until three years of age

^b Bootstrap estimates for difference of means and variances between Hispanics and non-Hispanics

^c Bootstrap estimated p-value

Comparison of reliability of self-reported pesticide use^a by years of maternal education (< 12 years, n=134 and > 12 years n=310), NCCLS, 2001–2006

Table 5

	Kappa (95% CI)		Percent positive (%)(95% CI)		Percent negative (%)(95% CI)	
	12 yrs	> 12 yrs	12 yrs	> 12 yrs	12 yrs	> 12 yrs
Fleas, ticks	0.45 (0.29–0.62)	0.58 (0.49–0.67)	60 (47–74)	75 (69–81)	85 (80–90)	83 (76–87)
Ants, flies, cockroaches	0.29 (0.12–0.45)	0.34 (0.23–0.45)	74 (67–82)	80 (76–84)	54 (42–66)	54 (46–63)
Indoor foggers	0.57 (0.30–0.84)	0.36 (0.19–0.52)	60 (35–85)	42 (27–57)	97 (94–99)	93 (91–95)
Weeds, insects, plants	0.49 (0.33–0.65)	0.47 (0.37–0.57)	64 (52–77)	73 (68–79)	85 (80–91)	74 (68–79)
Professional pest service	0.51 (0.34–0.69)	0.58 (0.49–0.67)	62 (48–77)	73 (67–80)	89 (84–93)	85 (81–88)
Professional lawn service	0.44 (0.20–0.69)	0.59 (0.49–0.70)	50 (27–73)	68 (60–77)	94 (91–97)	90 (88–93)
Overall	0.54 (0.47–0.60)	0.57 (0.53–0.61)	66 (61–71)	74 (71–76)	88 (85–89)	84 (82–85)
Mean difference (95% CI) ^b	0.03 (–0.12;0.07)		–6.8 (–11.0; –2.6)		4.2 (3.3;5.0)	
p-value ^c	0.728	0.051			0.042	

^a Pesticide use: from three months prior to conception until three years of age

^b Bootstrap estimates for difference of means and variances between < 12 years and > 12 years

^c Bootstrap estimated p-value