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Residential agricultural pesticide exposures and risks of spontaneous preterm birth

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Abstract

Background—Pesticides exposures are aspects of the human exposome that have not been sufficiently studied for their contribution to risk for preterm birth. We investigated risks of spontaneous preterm birth from potential residential exposures to 543 individual chemicals and 69 physicochemical groupings that were applied in the San Joaquin Valley of California during the study period, 1998–2011.

Methods—The study population was derived from birth certificate data linked with Office of Statewide Health Planning and Development maternal and infant hospital discharge data. After exclusions, the analytic study base included 197,461 term control births and 27,913 preterm case births. Preterm cases were more narrowly defined as 20–23 weeks (n=515), 24–27 weeks (n=1792), 28–31 weeks (n=3098), or 32–36 weeks (n=22,508).

Results—The frequency of any (versus none) pesticide exposure was uniformly lower in each preterm case group relative to the frequency in term controls, irrespective of gestational month of exposure. All odds ratios were below 1.0 for these any vs no exposure comparisons. The majority of odds ratios were below 1.0, many of them statistically precise, for preterm birth and exposures to specific chemical groups or chemicals.

Conclusions—This study showed a general lack of increased risk of preterm birth associated with a range of agriculture pesticide exposures near women's residences.

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Conflict of Interest: None to declare.

Data Sharing: The data are publicly available from the Office of Statewide Health Planning and Development (OSHPD). The data are not available for replication because specific approvals from OSHPD and the California Committee for the Protection of Human Subjects must be obtained in order to access them.

Keywords

pesticides; environment; prematurity; endocrine disruptors; pregnancy

INTRODUCTION

Preterm birth (delivery before 37 weeks of gestation) is associated with substantial morbidity and mortality with >15 million babies born preterm every year in the world.[1] In the US, preterm birth occurs in ~12% of live births.[2] There are iatrogenic explanations of preterm birth, most of which can be attributed to maternal or fetal conditions requiring medical intervention to facilitate earlier delivery. Risk factors for *spontaneous* preterm birth, however, remain largely unexplained. Factors associated with spontaneous preterm birth have included race, infection, stress, genetics, and environmental toxicants.[3] Each of these broad factors has either explained only a small fraction of the population burden of spontaneous preterm birth or has been insufficiently studied to derive meaningful inferences.[2–5]

Despite some pesticides being known reproductive toxicants[6] and substantial public concern about pesticide exposures, few studies have investigated relations between specific pesticide exposures and pregnancy outcomes including spontaneous preterm birth. The few studies that have explored pesticide exposures and preterm birth suggest some associations, but extant data are insufficient to draw clear inferences.[7–9] Studies specifically investigating residential pesticide exposures and preterm birth risks are nearly non-existent.[8] In general, studies of preterm birth and pesticides have been limited by the exposure assessments employed, been small in size, or have not investigated finer gestational ages to define preterm birth other than simply <37 weeks. To overcome many of these limitations, we investigated population-based data on >200,000 births and proximal residential exposures to more than 500 commercial agricultural pesticide active ingredients and adjuvants during multiple gestational time points, to extend the limited extant literature on pesticides and spontaneous preterm birth. The study population derived from the San Joaquin Valley of California, one of the highest agricultural pesticide use areas in the US.

MATERIALS AND METHODS

Study population

This study was approved by the Stanford University Institutional Review Board and the California State Committee for the Protection of Human Subjects.

Data for this case–control study come from 1998–2011 California births to women residing in the San Joaquin Valley (Fresno, Kern, Kings, Madera, Merced, San Joaquin, Stanislaus, and Tulare counties). In this region and time period there were 892,088 livebirths delivered in non-military hospitals. We restricted the study to those with gestational ages 20–41 weeks (determined by obstetric estimate for 2007–11 and by last menstrual period for 1998–2006), whose birth weights were between 500 and 5000 grams, and were singleton births. Among 771,416 eligible births, there were 78,421 preterm, i.e., <37 weeks gestation (cases) and

692,995 term, i.e., ≥37 weeks gestation. From the term group, we randomly selected 235,263 births (controls) in a 3:1 control to case ratio.

For each case and control we extracted from the birth certificate the residential address at the time of birth. The California Environmental Health Tracking Program (CEHTP) Geocoding Service was used to geocode these addresses.[10,11] The CEHTP Geocoding Service standardizes, verifies, and corrects addresses before matching against multiple address-attributed reference databases. Successful geocoding was achieved for 73,736 (94%) preterm cases and for 221,651 (94%) term controls.

We further linked the 73,736 cases and 221,651 controls derived from birth certificate data with Office of Statewide Health and Planning (OSHPD) maternal and infant hospital discharge data. This linkage allowed for information on a range of maternal and pregnancy characteristics found on the birth certificate paired with clinical detail from the delivery hospitalization for practically all inpatient live births. The algorithm employed for this linkage is accurate and previously described.[12,13] Successful linkage was achieved for 72,907 (99%) preterm cases and 220,137 (99%) term controls.

Our analytic goal was to specifically investigate *spontaneous* preterm birth. Thus, the case group was further restricted to spontaneous preterm birth events based on information coded on hospital discharge or birth certificate records. Spontaneous preterm birth was identified as those births <37 weeks with preterm premature rupture of membranes (ICD-9-CM code 658.1 or birth certificate complication of labor/delivery code 10), premature labor (ICD-9-CM code 644), or the use of tocolytics (birth certificate complication/procedure of pregnancy code 28). This reduced the preterm cases to n=36,758 (excluded from the total were 368 deliveries at 20–23 weeks, 715 at 24–27 weeks, 2366 at 28–31 weeks, and 32,700 at 32–36 weeks). Further, we excluded women with the selected comorbidities of pregestational diabetes (n=888), gestational diabetes (n=2908), gestational hypertension (n=820), pre-eclampsia/eclampsia (n=4739), and chronic hypertension (n=1386) from each case group (except the 20–23 week group for which gestational diabetes was not considered an exclusion criterion because delivery occurred prior to gestational diabetes being typically diagnosed) and from controls (n=22676). These exclusions were motivated by our goal to determine whether “pesticide exposures” alone, i.e., not mediated by or through these comorbid conditions, contributed to spontaneous preterm birth risks. These comorbidities were identified from codes pertinent to the birth hospitalization in the form of ICD-9-CM diagnoses. Specifically, we applied methods similar to those used elsewhere[14] to assess maternal morbidity in pregnancy as follows: diabetes (250 and 648.0), gestational diabetes (648.8), chronic hypertension (401–405, 642.0, 642.1, 642.2, 642.7, and 642.9), gestational hypertension (642.3), and preeclampsia/eclampsia (642.4, 642.5, and 642.6). These refinements to the preterm case phenotype resulted in 197,461 term control births and 27,913 preterm birth case births serving as the analytic base. Preterm cases were more narrowly defined as, 20–23 weeks (n=515), 24–27 weeks (n=1792), 28–31 weeks (n=3098), or 32–36 weeks (n=22,508).

Pesticide and adjuvant compounds studied

We assessed exposure to 543 individual chemicals used as pesticides or as adjuvants in pesticide products or application mixtures and 69 physicochemical groupings having the same chemical classification and proven or putative mechanism of action (e.g., organophosphates) that were applied at >100 lb in any of the 8 San Joaquin Valley counties in any year during the study period (1998–2011).[15] Low-toxicity chemicals such as biopesticides (e.g., microbial pesticides, soaps, essential oils), low-toxicity inorganic compounds (e.g., sulfur, kaolin clay), and other compounds determined by the US Environmental Protection Agency (EPA) to have low toxicity, as described in US EPA Risk Assessment documents for each chemical[16] were excluded. In addition, compounds were flagged as having reproductive or developmental toxicity based on the California Proposition 65 list[17] or as endocrine disruptors.[18–20] Chemicals with a US EPA-determined Reference Dose based on a toxicologic study with a reproductive or developmental endpoint as described in EPA risk assessment documents were included.[16]

Pesticide exposure assessment

To estimate pesticide exposures, we assigned a time window of exposure for each case or control mother from one month before conception (B1) to date of delivery by every 4 weeks of pregnancy (P1–P9).

To estimate pesticide applications, we obtained statewide Pesticide Use Reporting (PUR) records from the California Department of Pesticide Regulation describing agricultural pesticide applications occurring between 1 January 1998 and 31 December 2011.[15] These data are submitted by county agriculture commissioners and are spatially referenced to public land survey sections (PLSS). During the study period, the total number of active ingredient daily production agricultural use records with a PLSS specified, and for the 543 chemicals that were present in PUR records, exceeded 24 million. Following the method of Rull and Ritz,[21] we spatially refined PLSS polygons through overlay of matched land-use survey field polygons provided by the California Department of Water Resources. We matched each PUR record to the land-use survey conducted closest in time to the application date (surveys are conducted roughly every 5–7 years in each California county). Matching is based on PLSS and crop type as specified in records. Infrequently rotated crops, such as orchard crops and vineyards, were matched one-to-one, while frequently rotated crops, such as field and truck crops, were grouped together in a single category, and non-agricultural land uses were subtracted from PLSS polygons when no crop types were matched to available polygons. Of the total applications (and active-ingredient poundage) recorded spanning 1998–2011 for the 543 chemicals of interest, >90% were successfully linked to polygons. For those where no field polygon was specified, no spatial refinement was possible. We determined temporal proximity by comparing recorded dates of applications (which are believed to be accurate within a few days) to the time window of exposure for each study subject.

To assign exposure, we utilized the CEHTP Pesticide Linkage Tool, a custom-developed Java (Oracle, Redwood Shores, CA) application that incorporates the PostGIS spatial and geographic objects library for PostgreSQL (http://www.postgis.net/) and the GeoTools Java

GIS Toolkit, version Release 12 (open source, http://www.geotools.org/) for GIS data management and spatial analysis.[10,11] We calculated pounds of pesticides used during the relevant time window within a 500 m radius of a geocoded point,[22] intersecting polygons with the buffer, and assuming homogeneous distribution of pesticides within each polygon.

Statistical analysis

Risks associated with pesticide exposures were estimated using logistic regression. Univariate analyses were conducted to estimate crude odds ratios and 95% confidence intervals (CI) reflecting associations between pesticide exposures and spontaneous preterm birth. We performed multivariable analyses adjusting for maternal age (years), race/ethnicity (non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other), education (less than high school, high school, more than high school), parity (1 or ≥2), prenatal care initiated by fifth month (yes vs no), payer source for care (Medi-Cal, private, or other). Additional analyses based on the availability of data beginning with 2007 births were performed adjusting for pre-pregnancy body mass index (BMI in kg/m^2, continuous) and neighborhood poverty derived from US Census data for census block groups. Given that the source of potential covariate information was derived from the birth certificate we determined that women's cigarette smoking was too incomplete to include in analyses.

To focus on comparisons likely to have the most precise estimates and to fully utilize available data, we did the following. For pesticides that had five or more exposed cases and controls, risks were estimated that compared any versus no exposure. Risks were not estimated for pesticides that had fewer than five exposed cases and controls. We also created overall exposure "scores." These scores were created by flagging studied chemicals as having reproductive or developmental toxicity based on the California Proposition 65 list[17] or as endocrine disruptors.[18–20] Chemicals with an EPA-determined reference dose based on an acute toxicological study with a reproductive or developmental endpoint as described in EPA risk assessment documents were also included.[16] We created overall exposure scores by summing the total number of chemical groups, endocrine disruptors, Proposition 65 chemicals, or chemicals in EPA lists. For the exposure scores, we examined the associations of specific preterm birth phenotypes with these scores specified as categorical variables; that is, exposed subjects were divided into tertiles based on the control distributions.

Analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, 2015–2016).

RESULTS

Compared to term controls, mothers of preterm infants were more likely to be Black, initiate prenatal care after the fifth month of pregnancy, have their delivery paid under MediCal benefits, be nulliparous, or more likely to deliver male infants (Table 1).

Frequencies of preterm cases and term controls with any vs no exposure assignments for the B1–P9 month periods are shown in Table 2. The frequency of any exposure was uniformly lower in each preterm case group, and month time period, relative to the frequency in term controls. The corresponding odds ratios (crude and adjusted) are shown in Table 3. All odds

ratios were below 1.0 for these any vs no exposure comparisons. Stratum-specific analyses by male and female births did not reveal substantially different results.

As noted in the Methods, we employed a minimum sample size criterion for risk estimation, i.e., pesticides (groups or specific chemicals) that had five or more exposed cases *and* controls for each phenotype. This produced upwards of 54,000 comparisons based on four preterm case groups (20–23, 24–27, 28–31, and 32–36 gestational weeks), as many as 9 exposure months (i.e., B1–P9), 313 chemical groups with exposure, 61 chemical classes of exposure, crude and adjusted odds ratios, and stratification by sex of the infant (this latter stratification motivated by higher frequency of males among preterm births and some pesticides having endocrine disruptor mechanisms). Owing to this large number of comparisons (not easily conveyed in journal tables), we have limited our presentation of results as follows, but summarize in text the general pattern of findings not specifically shown. We show adjusted odds ratios for chemical groups and specific chemicals for which 1) there were at least five cases exposed (this criterion biases toward identifying elevated risks) and 2) only for the exposure month closest to the time of delivery (e.g., for preterm cases 20–23 weeks at delivery the odds ratios shown are for month P5). These results are displayed in Table 4 for chemical groups, and eTable 1 for specific chemicals.

As shown in Table 4, there was only a single comparison (aryloxyphenoxy proprionic acid) that showed a statistically precise (confidence interval did not include 1.0) increased risk. Indeed, the majority of adjusted odds ratios were below 1.0 (crude estimates were similar), many of them statistically precise. Results for the “months of exposure” not shown were not substantially different than those that are shown. Stratum specific analyses by male and female births did not reveal substantially different results than those that appear in Table 4.

In eTable 1 are the adjusted odds ratios associated with specific chemicals. Similar to results for chemical groups, only a small number of elevated risks was observed with the majority of adjusted odds ratios observed to be below 1.0 (crude estimates were similar). The 18 comparisons observed to have elevated odds ratios ranged in magnitude from 1.17 (diacylhydrazine) to 2.94 (silicone). The observed elevated odds ratios were associated with a variety of chemicals and reflected the spectrum of preterm case phenotypes. Stratum specific analyses by male and female births did not reveal substantially different results with but a few exceptions. That is, specific chemicals that were associated with more than a 2-fold (only an elevated risk direction) observed OR differential between males and females were: 1) for males, polyalkyloxy compound exposure for gestational age at delivery 20–23 weeks, OR=3.09 (1.27–7.53), pyrethroids (cypermethrin) exposure for gestational age at delivery of 24–27 weeks, OR=2.35 (1.04–5.29), quaternary ammonium compound (dimethylbenzyl ammonium chloride) exposure for gestational age at delivery of 32–36 weeks, OR=4.65 (1.72–12.59); urea (thidiazuron) exposure for gestational age at delivery of 24–27 weeks, OR=2.15 (1.14–4.04) and 2) for females dithiocarbamate-MITC (potassium n-methyldithiocarbamate) exposure for gestational age at delivery of 28–31 weeks, OR=3.13 (1.38–7.09), thiocarbamate (cycloate) for gestational age at delivery of 28–31 weeks, OR=4.02 (1.88–8.60), alkyl phthalate (chlorthal-dimethyl) exposure for gestational age at delivery of 28–31 weeks, OR=3.57 (1.57–8.12), and spirotetramat exposure for gestational age at delivery of 28–31 weeks, OR=2.55 (1.04–6.22).

To estimate potential effects associated with a sum of multiple exposures we explored "scores" to various chemical classifications, including number of chemical groups, endocrine disruptors, Proposition 65-listed reproductive toxicants, or EPA listed reproductive or developmental toxicants. Increasing numbers of exposures to any of these classifications did not show elevated risks, but rather decreasing risks of preterm birth with increasing sums of exposures (Table 5).

For a subset (2007–11) of the overall data (1998–2011) we had information about body mass index and poverty (see Table 1 for description and frequency). These additional variables were added as covariates to adjusted models. Results of these additional analyses did not show substantially different findings from those displayed in Tables 2–4.

As sensitivity analyses, we re-analyzed data without the exclusions of women with diabetes or pre-eclampsia as well as re-analyzed data excluding women with a prior history of preterm birth. Results of these additional sets of analyses did not show substantially different findings from those displayed in Tables 2–4 (not shown).

DISCUSSION

We examined associations between women's residential proximity to agriculture-related pesticide applications in the San Joaquin Valley of California during pregnancy and risk of spontaneous preterm birth. Despite a very large study population, consideration of the preterm phenotype into narrower categories than simply <37 gestational weeks, and consideration of a variety of gestational exposure definitions such as chemical groups, specific chemicals, and number of pesticides, there was a notable lack of association between pesticide exposures and elevated risk of spontaneous preterm birth. Indeed, owing to the large number of comparisons we would have expected many more elevated risks to emerge by chance alone. Results were not materially influenced by presented potential confounders (e.g., maternal age and race/ethnicity) or by those not presented (e.g., year of birth).

Previous research on *residential* proximity to pesticide applications and risks of preterm birth phenotypes is nearly non-existent. To our knowledge there has been one study that has investigated residential proximity to pesticides. Willis et al.,[23] in a small cohort study of 535 women, observed women who reported living near land used for agricultural purposes were not at increased risk to deliver preterm.

Although there has been limited investigation of residential proximity and preterm birth, there have been observed associations between other measures of pesticide exposures and preterm birth. These other measures of exposure have included individual-level estimations such as serum measures of DDE[24] or chlordecone,[25] as well as more ecologic-level estimations such as county-level pesticide use.[26,27] However, findings from these study designs are not directly comparable to those in the current study.

The explanation of our overall observed results is not obvious. Many of the analytic comparisons indicated reduced risks of spontaneous preterm birth and various pesticide exposure estimations. Clearly, it is difficult to believe that such exposures, given the

manifold toxicities these various compounds have, could be beneficial to reducing the likelihood of preterm birth. It also seems unlikely that these observations arose from a lack of control for suspected confounders, namely, cigarette smoking, proximity to greenspace,[28] and better air quality. That is, 60% of our study population was Hispanic women, a population subgroup known to have very low use of cigarettes, the study region is one of extensive agricultural land use (not greenspace) and the study region has very poor air quality with noted increased risks observed by us previously for preterm birth from exposures to selected air pollutants.[29]

Given the unexpected direction of our overall results, one might posit that what is being observed here is that pesticide exposures in pregnancy before 20 weeks (the earliest a birth would be identified in vital statistics files) selectively increase the odds of earlier loss or stillbirth of fetuses destined to be born preterm and therefore not observable when only live birth data are the analytic substrate. Others have described the construct of live-birth selection bias.[30] Although this selection bias proposition seems plausible, and has been advanced for studies of congenital anomalies,[31,32] the extant data investigating potential associations between miscarriage and residential pesticide exposures is also quite sparse.[8] Thus, further investigation to understand whether such a selective culling of pregnancies, from the overall population cohort of pregnancies, that would otherwise be born preterm based on pesticide exposures could lead to potentially biased reduced risks (among births), seems clearly warranted.

Among the strengths of our study is the specificity with which we defined the outcome of spontaneous preterm birth, although this is also a source of nuance when considering our primary findings. As noted, we required delivery prior to 37 complete weeks with spontaneous onset of labor and absence of co-morbidities such as maternal pre-diabetes or diabetes, hypertension, or pre-eclampsia. We did conduct sensitivity analyses by re-analyzing data without the exclusions of women with diabetes or pre-eclampsia. These additional sets of analyses did not show substantially different findings. Although the outcome definition we employed maximized the specificity of our findings, further studies might examine other clinical scenarios such as indicated preterm birth with associated co-morbidities not specifically investigated here.

Our study has several other strengths as well, including its population-based design, large sample size, and an exposure assessment that was highly detailed and spatially and temporally specific (to multiple gestational periods), and captured a broad spectrum of pesticide compounds.

Our study also had challenges. Our assessment of residential proximity to agricultural pesticide applications was thorough, but it did not take into account other factors such as qualities of the pesticides and individuals' behaviors that could affect actual exposures (e.g., chemical half-lives and vapor pressure, wind patterns, accumulative exposures over time a woman may have had before pregnancy, and other sources of pesticide exposure such as occupation or home use). That is, the basis of pesticide exposure considered here was proximity to pesticide applications associated with women's residence at delivery. Exposure attribution was based on residence address at delivery rather than at other points in

pregnancy. Misclassification of exposure could have occurred for women who moved during gestation. If moving was unrelated to preterm vs term birth status, results would be biased toward the null; if not, the direction cannot be predicted. Further, duration of time spent at the given address is unknown and likely reflective of only a portion of what a woman may encounter in her broader environment. Although many pesticides are prone to drift and detectable in air samples at locations beyond the application site,[33] and residential proximity to pesticide-treated fields has been associated with household dust and urine levels,[34,35] there are certainly other exposure sources such as in food or water that were not considered here, whereby individuals could be exposed. For example, atrazine levels in drinking water have been associated with small increased risks of preterm birth.[26] These various sources of misclassification would be expected to be non-differential, reducing our precision to estimate potential associations. Our analyses, although extensive, did not investigate risks to specific pesticides independent of other pesticides nor did it investigate specific pesticide combinations. Exploration of such independent and combinatorial exposures may be the focus of future unsupervised analytic queries.

In addition, an individual's ability to metabolize the various types of chemicals in pesticides would certainly affect actual tissue exposures. It has been demonstrated that genetic polymorphisms in detoxification pathways for many pesticides may contribute to preterm birth risks.[36,37] Such genetic inquiries were beyond the scope of this initial investigation.

Our study rigorously adds to the scant literature on this topic, particularly in its effort to investigate numerous pesticide compounds.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Descriptive characteristics (percentages)[a] of preterm case and term control infants, California, 1998–2011 (n=225,374)

Characteristic	Gestational age in weeks at delivery				
	CASES				CONTROLS
	20–23 n=515	24–27 n=1,792	28–31 n=3,098	32–36 n=22,508	37–41 n=197,261
Maternal age (years)					
<20	19.2	19.4	20.1	16.2	14.2
20–24	24.7	27.2	28.3	28.8	29.9
25–29	23.1	23.8	23.2	25.7	28.0
30–34	18.8	17.4	16.3	18.2	18.4
>35	14.2	12.2	12.1	11.1	9.5
Missing	0	0	0.1	<0.1	<0.1
Maternal race/ethnicity					
White, nonHispanic	19.8	22.7	24.1	28.4	29.4
White, Hispanic	60.6	57.1	54.9	54.8	57.0
Black	9.5	9.4	9.6	6.3	4.5
Asian	7.0	8.7	8.8	8.3	7.1
Other	1.9	1.6	1.9	1.8	1.5
Missing	1.2	0.4	0.6	0.6	0.6
Maternal education					
Less than high school	36.9	34.0	37.1	33.7	32.6
High school	32.8	34.2	33.8	31.0	31.8
More than high school	27.8	29.4	26.8	33.6	34.0
Missing	2.5	2.5	2.3	1.8	1.6
Prenatal care initiation by fifth month of gestation					
Yes	85.2	88.2	85.9	88.4	91.8
No	8.9	7.2	10.3	8.6	6.4
Missing	5.8	4.6	3.8	3.0	1.8
Parity					
1	41.8	45.1	38.1	35.8	34.8

Characteristic	Gestational age in weeks at delivery				
	CASES				CONTROLS
	20–23 n=515	24–27 n=1,792	28–31 n=3,098	32–36 n=22,508	37–41 n=197,261
≥2	57.9	54.9	61.8	64.1	65.2
Missing	0.4	<0.1	0.2	<0.1	0.1
Payer type for delivery					
Medi-Cal	63.5	61.9	63.7	60.0	56.9
Private	28.9	30.5	30.2	35.5	39.7
Uninsured	6.2	6.2	4.5	2.9	1.7
Other	1.0	1.0	1.2	1.3	1.5
Missing	0.4	0.4	0.4	0.3	0.2
Infant sex					
Male	56.5	57.1	58.5	55.1	50.6
Female	43.5	42.8	41.5	44.9	49.4
Missing	0	<0.1	0	<0.1	<0.1
Infant Birth Year					
1998	5.8	5.7	6.3	4.9	6.7
1999	6.4	5.5	6.3	4.7	6.7
2000	7.4	6.8	6.4	5.1	6.9
2001	5.6	6.3	7.0	5.7	6.9
2002	5.6	5.7	6.6	5.9	7.1
2003	5.1	5.9	6.3	6.2	7.4
2004	9.5	6.9	6.9	6.4	7.9
2005	8.7	7.5	9.0	6.9	9.1
2006	8.0	7.9	8.4	7.7	9.5
2007	8.0	8.5	8.8	9.4	6.8
2008	5.4	8.8	7.6	10.0	6.7
2009	8.4	7.8	7.1	9.1	6.3
2010	7.4	7.6	6.5	9.0	6.1
2011	8.7	9.2	7.0	9.1	6.0
Years 2007–2011	195	751	1141	10452	63021

Characteristic	Gestational age in weeks at delivery				
	CASES				CONTROLS
	20–23 n=515	24–27 n=1,792	28–31 n=3,098	32–36 n=22,508	37–41 n=197,261
Prepregnancy body mass index (kg/m2) (2007–2011)					
Underweight (BMI<18.5)	2.1	5.5	5.0	4.7	3.1
Normal (18.5≤BMI<25)	30.3	30.8	38.9	42.6	40.2
Overweight (25≤BMI<30)	19.5	26.1	22.8	23.0	24.7
Obese (BMI≥30)	27.2	24.1	20.0	18.0	20.3
Missing	21.0	13.6	13.3	11.8	11.8
Poverty (2007–2011)[b]					
≤107.25	20.5	16.1	16.5	17.5	19.4
107.26 – ≤180.14	13.3	17.7	17.3	18.2	19.4
180.15 – ≤260.29	20.0	19.4	18.6	19.0	19.5
260.30 – ≤365.66	21.0	21.0	22.4	20.8	19.6
>365.66	21.5	23.0	22.4	21.6	19.3
Missing	3.6	2.7	3.0	2.9	2.7

[a] Percentages may not equal 100 owing to rounding

[b] Quintile cutoffs were determined among term births. The highest quintile reflects the highest degree of poverty.

Table 2

Any (as percentage of total) gestational pesticide exposure per month among women of preterm cases and term controls

		Count and percentage of any exposure (% yes vs no) per month[a]									
	Gestational Weeks at Delivery (total No.)	**B1**	**P1**	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**	**P9**
Pre-term	20–23 (n=515)	129 (25.0)	112 (21.7)	139 (27.0)	127 (24.7)	133 (25.8)	124 (24.1)				
	24–27 (n=1,792)	413 (23.0)	407 (22.7)	432 (24.1)	416 (23.2)	439 (24.5)	430 (24.0)	415 (23.2)			
	28–31 (n=3,098)	790 (25.5)	789 (25.5)	815 (26.3)	806 (26.0)	816 (26.3)	792 (25.6)	764 (24.7)	772 (24.9)		
	32–36 (n=22,508)	5850 (26.0)	5900 (26.2)	5937 (26.4)	5911 (26.3)	5966 (26.5)	5976 (26.6)	5871 (26.1)	5921 (26.3)	5782 (25.7)	
Term	37–42 (n=197,461)	55136 (27.9)	55507 (28.1)	55770 (28.2)	56019 (28.4)	55834 (28.3)	56029 (28.4)	56079 (28.4)	56000 (28.4)	55662 (28.2)	54960 (27.8)

[a] B1=month before conception, P1–P9=each successive month from first to ninth month of pregnancy,

Table 3

Risks (odds ratios) for any vs no gestational pesticide exposure (per month) among women of preterm cases and term controls

Gestational Weeks at Delivery	Month of Exposure[a]	Case (Preterm) (exposed/not-exposed)	Control (Term) (exposed/not-exposed)	Crude OR (95%CI)	Adjusted[b] OR (95%CI)
20–23	B1	129/386	55136/142325	0.86 (0.71–1.05)	0.86 (0.70–1.06)
	P1	112/403	55507/141954	0.71 (0.58–0.88)	0.73 (0.59–0.91)
	P2	139/376	55770/141691	0.94 (0.77–1.14)	0.94 (0.77–1.16)
	P3	127/388	56019/141442	0.83 (0.68–1.01)	0.84 (0.68–1.04)
	P4	133/382	55834/141627	0.88 (0.72–1.08)	0.89 (0.72–1.10)
	P5	124/391	56029/141432	0.80 (0.65–0.98)	0.83 (0.67–1.03)
24–27	B1	413/1379	55136/142325	0.77 (0.69–0.86)	0.82 (0.73–0.92)
	P1	407/1385	55507/141954	0.75 (0.67–0.84)	0.78 (0.70–0.88)
	P2	432/1360	55770/141691	0.81 (0.72–0.90)	0.84 (0.75–0.94)
	P3	416/1376	56019/141442	0.76 (0.68–0.85)	0.80 (0.71–0.90)
	P4	439/1353	55834/141627	0.82 (0.74–0.92)	0.86 (0.77–0.96)
	P5	430/1362	56029/141432	0.80 (0.71–0.89)	0.82 (0.73–0.92)
	P6	415/1377	56079/141382	0.76 (0.68–0.85)	0.79 (0.71–0.89)
28–31	B1	790/2308	55136/142325	0.88 (0.81–0.96)	0.93 (0.86–1.01)
	P1	789/2309	55507/141954	0.87 (0.81–0.95)	0.91 (0.83–0.99)
	P2	815/2283	55770/141691	0.91 (0.84–0.98)	0.95 (0.87–1.03)
	P3	806/2292	56019/141442	0.89 (0.82–0.96)	0.92 (0.84–1.00)
	P4	816/2282	55834/141627	0.91 (0.84–0.98)	0.95 (0.87–1.03)
	P5	792/2306	56029/141432	0.87 (0.80–0.94)	0.90 (0.83–0.98)
	P6	764/2334	56079/141382	0.83 (0.76–0.90)	0.87 (0.80–0.95)
	P7	772/2326	56000/141461	0.84 (0.77–0.91)	0.88 (0.81–0.96)
32–36	B1	5850/16658	55136/142325	0.91 (0.88–0.94)	0.92 (0.89–0.95)
	P1	5900/16608	55507/141954	0.91 (0.88–0.94)	0.92 (0.89–0.95)
	P2	5937/16571	55770/141691	0.91 (0.88–0.94)	0.93 (0.90–0.96)
	P3	5911/16597	56019/141442	0.90 (0.87–0.93)	0.91 (0.88–0.94)
	P4	5966/16542	55834/141627	0.91 (0.89–0.94)	0.93 (0.90–0.96)

Gestational Weeks at Delivery	Month of Exposure[a]	Case (Preterm) (exposed/not-exposed)	Control (Term) (exposed/not-exposed)	Crude OR (95%CI)	Adjusted[b] OR (95%CI)
	P5	5976/16532	56029/141432	0.91 (0.88–0.94)	0.93 (0.90–0.96)
	P6	5871/16637	56079/141382	0.89 (0.86–0.92)	0.91 (0.88–0.93)
	P7	5921/16587	56000/141461	0.90 (0.87–0.93)	0.92 (0.89–0.95)
	P8	5782/16726	55662/141799	0.88 (0.85–0.91)	0.90 (0.87–0.93)

[a] B1=month before conception, P1–P8=each successive month from first to ninth month of pregnancy.

[b] Odds ratio adjusted for maternal age (years), race/ethnicity(non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other), education (less than high school, high school, more than high school),parity (1 or ≥2), prenatal care initiated by fifth month (yes vs no), payer source for care (Medi-Cal, private, or other).

Table 4

Risks (odds ratios) for any vs no gestational exposures (per month) for specific pesticide chemical groups among women of preterm cases and term controls. Shown are adjusted odds ratios for chemical groups where there were ≥5 cases exposed and for the exposure month closest to the time of delivery (e.g., for preterm cases 20–23 weeks at delivery the odds ratios shown are for month P5).

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
2,4 - Dichlorophenoxy acid or ester	20–23	P5	15/500	5792/191669	0.94 (0.54–1.64)
2,4 - Dichlorophenoxy acid or ester	24–27	P6	30/1762	5754/191707	0.60 (0.42–0.87)
2,4 - Dichlorophenoxy acid or ester	28–31	P7	63/3035	5683/191778	0.76 (0.59–0.97)
2,4 - Dichlorophenoxy acid or ester	32–36	P8	586/21922	5710/191751	0.92 (0.84–1.01)
2,6-Dinitroaniline	20–23	P5	15/500	8944/188517	0.65 (0.38–1.11)
2,6-Dinitroaniline	24–27	P6	66/1726	8657/188804	0.88 (0.68–1.13)
2,6-Dinitroaniline	28–31	P7	114/2984	8588/188873	0.89 (0.73–1.07)
2,6-Dinitroaniline	32–36	P8	909/21599	8442/189019	0.97 (0.90–1.04)
Alcohol/Ether	20–23	P5	12/503	6610/190851	0.70 (0.38–1.27)
Alcohol/Ether	24–27	P6	41/1751	6340/191121	0.72 (0.52–0.99)
Alcohol/Ether	28–31	P7	81/3017	6272/191189	0.86 (0.68–1.07)
Alcohol/Ether	32–36	P8	438/22070	6273/191188	0.63 (0.57–0.69)
Alkyl Phthalate	32–36	P8	11/22497	282/197179	0.33 (0.18–0.62)
Amide	24–27	P6	5/1787	1214/196247	0.51 (0.21–1.23)
Amide	28–31	P7	19/3079	1243/196218	1.13 (0.72–1.78)
Amide	32–36	P8	117/22391	1232/196229	0.83 (0.69–1.02)
Amine	28–31	P7	7/3091	698/196763	0.67 (0.32–1.41)
Amine	32–36	P8	46/22462	679/196782	0.62 (0.46–0.83)
Anthranilic diamide	24–27	P6	8/1784	547/196914	1.74 (0.86–3.52)
Anthranilic diamide	28–31	P7	11/3087	645/196816	1.25 (0.69–2.28)
Anthranilic diamide	32–36	P8	106/22402	675/196786	1.45 (1.17–1.78)
Antibiotic	32–36	P8	9/22499	44/197417	1.78 (0.84–3.80)
Aryloxyphenoxy propionic acid	28–31	P7	11/3087	301/197160	2.38 (1.26–4.48)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Aryloxyphenoxy propionic acid	32–36	P8	24/22484	296/197165	0.73 (0.48–1.12)
Avermectin	20–23	P5	11/504	5029/192432	0.83 (0.45–1.56)
Avermectin	24–27	P6	34/1758	5249/192212	0.77 (0.55–1.09)
Avermectin	28–31	P7	87/3011	5196/192265	1.14 (0.91–1.42)
Avermectin	32–36	P8	576/21932	5232/192229	0.97 (0.89–1.06)
Azole	20–23	P5	16/499	8873/188588	0.64 (0.38–1.09)
Azole	24–27	P6	54/1738	8914/188547	0.67 (0.51–0.89)
Azole	28–31	P7	128/2970	8554/188907	1.00 (0.84–1.20)
Azole	32–36	P8	945/21563	8588/188873	0.99 (0.92–1.06)
Benzoic acid	24–27	P6	6/1786	1453/196008	0.50 (0.22–1.11)
Benzoic acid	28–31	P7	20/3078	1425/196036	0.98 (0.63–1.52)
Benzoic acid	32–36	P8	125/22383	1425/196036	0.80 (0.66–0.96)
Bipyridylium	20–23	P5	23/492	9778/187683	0.90 (0.58–1.40)
Bipyridylium	24–27	P6	56/1736	9839/187622	0.65 (0.49–0.85)
Bipyridylium	28–31	P7	120/2978	9784/187677	0.83 (0.69–1.00)
Bipyridylium	32–36	P8	908/21600	9717/187744	0.84 (0.79–0.90)
Bis-Carbamate	32–36	P8	5/22503	52/197409	0.82 (0.33–2.07)
Botanical	20–23	P5	6/509	3408/194053	0.71 (0.32–1.58)
Botanical	24–27	P6	19/1773	3393/194068	0.61 (0.38–0.97)
Botanical	28–31	P7	54/3044	3315/194146	1.06 (0.80–1.40)
Botanical	32–36	P8	341/22167	3304/194157	0.91 (0.81–1.02)
Chloroacetanilide	24–27	P6	6/1786	953/196508	0.64 (0.27–1.55)
Chloroacetanilide	28–31	P7	13/3085	904/196557	0.92 (0.52–1.62)
Chloroacetanilide	32–36	P8	83/22425	890/196571	0.83 (0.66–1.05)
Copper compound	20–23	P5	21/494	11732/185729	0.71 (0.45–1.11)
Copper compound	24–27	P6	80/1712	11537/185924	0.80 (0.63–1.00)
Copper compound	28–31	P7	137/2961	11510/185951	0.78 (0.65–0.93)
Copper compound	32–36	P8	1158/21350	11486/185975	0.90 (0.84–0.96)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Cyclohexenone derivative	24–27	P6	6/1786	1357/196104	0.43 (0.18–1.05)
Cyclohexenone derivative	28–31	P7	17/3081	1335/196126	0.83 (0.51–1.36)
Cyclohexenone derivative	32–36	P8	120/22388	1375/196086	0.76 (0.63–0.92)
Diacylhydrazine	20–23	P5	6/509	2801/194660	0.88 (0.39–1.98)
Diacylhydrazine	24–27	P6	22/1770	2906/194555	0.88 (0.57–1.35)
Diacylhydrazine	28–31	P7	47/3051	2901/194560	1.11 (0.83–1.49)
Diacylhydrazine	32–36	P8	357/22151	2907/194554	1.12 (1.00–1.25)
Dicarboximide	20–23	P5	7/508	4047/193414	0.63 (0.28–1.41)
Dicarboximide	24–27	P6	18/1774	4085/193376	0.47 (0.29–0.77)
Dicarboximide	28–31	P7	44/3054	3868/193593	0.77 (0.57–1.04)
Dicarboximide	32–36	P8	316/22192	3825/193636	0.72 (0.63–0.81)
Dithiocarbamate-ETU	20–23	P5	13/502	4509/192952	1.21 (0.70–2.11)
Dithiocarbamate-ETU	24–27	P6	31/1761	4364/193097	0.80 (0.56–1.16)
Dithiocarbamate-ETU	28–31	P7	54/3044	4214/193247	0.85 (0.64–1.12)
Dithiocarbamate-ETU	32–36	P8	387/22121	4290/193171	0.79 (0.71–0.88)
Dithiocarbamate-MITC	24–27	P6	7/1785	1116/196345	0.78 (0.37–1.64)
Dithiocarbamate-MITC	28–31	P7	19/3079	1135/196326	1.18 (0.74–1.88)
Dithiocarbamate-MITC	32–36	P8	109/22399	1142/196319	0.85 (0.69–1.05)
Endothall	32–36	P8	16/22492	226/197235	0.67 (0.40–1.12)
Glyco Ether	32–36	P8	18/22490	205/197256	0.81 (0.50–1.32)
Glycol	20–23	P5	8/507	3276/194185	0.92 (0.44–1.94)
Glycol	24–27	P6	21/1771	3201/194260	0.75 (0.48–1.17)
Glycol	28–31	P7	54/3044	3219/194242	1.16 (0.88–1.52)
Glycol	32–36	P8	210/22298	3308/194153	0.57 (0.50–0.66)
Halogenated organic	24–27	P6	11/1781	2054/195407	0.65 (0.36–1.17)
Halogenated organic	28–31	P7	17/3081	1965/195496	0.58 (0.35–0.94)
Halogenated organic	32–36	P8	158/22350	1939/195522	0.73 (0.61–0.86)
Hydroxybenzonitrile	24–27	P6	7/1785	1186/196275	0.72 (0.34–1.52)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Hydroxybenzonitrile	28–31	P7	11/3087	1210/196251	0.65 (0.36–1.18)
Hydroxybenzonitrile	32–36	P8	116/22392	1117/196344	0.93 (0.76–1.13)
Imidazolinone	28–31	P7	6/3092	606/196855	0.69 (0.31–1.54)
Imidazolinone	32–36	P8	79/22429	664/196797	1.09 (0.86–1.38)
Insect growth regulator (Chitin)	20–23	P5	6/509	1433/196028	1.72 (0.77–3.86)
Insect growth regulator (Chitin)	24–27	P6	5/1787	1444/196017	0.42 (0.17–1.00)
Insect growth regulator (Chitin)	28–31	P7	20/3078	1477/195984	0.85 (0.54–1.36)
Insect growth regulator (Chitin)	32–36	P8	169/22339	1496/195965	1.01 (0.85–1.18)
Monochlorophenoxy acid or ester	24–27	P6	11/1781	1518/195943	0.89 (0.49–1.62)
Monochlorophenoxy acid or ester	28–31	P7	18/3080	1515/195946	0.85 (0.54–1.36)
Monochlorophenoxy acid or ester	32–36	P8	133/22375	1506/195955	0.78 (0.65–0.93)
N-Methyl Carbamate	20–23	P5	8/507	5496/191965	0.58 (0.29–1.17)
N-Methyl Carbamate	24–27	P6	39/1753	5436/192025	0.81 (0.59–1.12)
N-Methyl Carbamate	28–31	P7	80/3018	5428/192033	0.96 (0.76–1.20)
N-Methyl Carbamate	32–36	P8	526/21982	5382/192079	0.87 (0.79–0.95)
Naphthalene acetic acid derivative	32–36	P8	6/22502	45/197416	1.22 (0.52–2.87)
Neonicotinoid	20–23	P5	8/507	5141/192320	0.47 (0.21–1.06)
Neonicotinoid	24–27	P6	36/1756	5197/192264	0.77 (0.55–1.08)
Neonicotinoid	28–31	P7	83/3015	5342/192119	1.05 (0.84–1.32)
Neonicotinoid	32–36	P8	596/21912	5317/192144	1.01 (0.92–1.10)
Organoarsenic	32–36	P8	22/22486	310/197151	0.64 (0.42–0.99)
Organochlorine	24–27	P6	9/1783	1326/196135	0.80 (0.42–1.55)
Organochlorine	28–31	P7	18/3080	1310/196151	0.92 (0.58–1.47)
Organochlorine	32–36	P8	108/22400	1309/196152	0.74 (0.61–0.90)
Organophosphate	20–23	P5	41/474	16712/180749	0.91 (0.65–1.28)
Organophosphate	24–27	P6	123/1669	16763/180698	0.86 (0.71–1.03)
Organophosphate	28–31	P7	217/2881	16993/180468	0.86 (0.75–0.99)
Organophosphate	32–36	P8	1622/20886	17033/180428	0.85 (0.80–0.89)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Petroleum derivative-Aromatic	20–23	P5	31/484	11522/185939	1.02 (0.70–1.50)
Petroleum derivative-Aromatic	24–27	P6	84/1708	11398/186063	0.87 (0.70–1.08)
Petroleum derivative-Aromatic	28–31	P7	148/2950	11373/186088	0.90 (0.76–1.06)
Petroleum derivative-Aromatic	32–36	P8	1073/21435	11470/185991	0.83 (0.78–0.89)
Phosphine	24–27	P6	5/1787	997/196464	0.64 (0.26–1.53)
Phosphine	28–31	P7	8/3090	986/196475	0.51 (0.24–1.08)
Phosphine	32–36	P8	87/22421	974/196487	0.82 (0.66–1.03)
Phosphonoglycine	20–23	P5	53/462	25745/171716	0.79 (0.59–1.06)
Phosphonoglycine	24–27	P6	158/1634	25816/171645	0.68 (0.58–0.81)
Phosphonoglycine	28–31	P7	309/2789	25733/171728	0.78 (0.69–0.88)
Phosphonoglycine	32–36	P8	2612/19896	25416/172045	0.91 (0.87–0.95)
Piperonyl	32–36	P8	48/22460	465/196996	0.94 (0.69–1.28)
Polyalkyloxy Compound	20–23	P5	31/484	12148/185313	1.05 (0.73–1.53)
Polyalkyloxy Compound	24–27	P6	72/1720	11826/185635	0.68 (0.54–0.87)
Polyalkyloxy Compound	28–31	P7	154/2944	11677/185784	0.86 (0.73–1.02)
Polyalkyloxy Compound	32–36	P8	840/21668	11641/185820	0.64 (0.59–0.69)
Pyrethroid	20–23	P5	27/488	12509/184952	0.79 (0.52–1.19)
Pyrethroid	24–27	P6	91/1701	12452/185009	0.83 (0.66–1.03)
Pyrethroid	28–31	P7	161/2937	12582/184879	0.88 (0.75–1.03)
Pyrethroid	32–36	P8	1295/21213	12541/184920	0.91 (0.86–0.97)
Pyridazinone	20–23	P5	7/508	2053/195408	1.44 (0.68–3.05)
Pyridazinone	24–27	P6	6/1786	1994/195467	0.36 (0.16–0.81)
Pyridazinone	28–31	P7	22/3076	2012/195449	0.74 (0.48–1.14)
Pyridazinone	32–36	P8	148/22360	2029/195432	0.66 (0.56–0.78)
Quaternary Ammonium Compound	24–27	P6	13/1779	1522/195939	0.93 (0.53–1.65)
Quaternary Ammonium Compound	28–31	P7	22/3076	1560/195901	0.94 (0.62–1.44)
Quaternary Ammonium Compound	32–36	P8	164/22344	1570/195891	0.92 (0.78–1.08)
Silicone	20–23	P5	13/502	4358/193103	1.28 (0.74–2.23)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Silicone	24–27	P6	34/1758	4322/193139	0.88 (0.62–1.25)
Silicone	28–31	P7	61/3037	4297/193164	0.92 (0.71–1.20)
Silicone	32–36	P8	305/22203	4358/193103	0.62 (0.55–0.70)
Spinosyn	20–23	P5	8/507	4160/193301	0.78 (0.39–1.58)
Spinosyn	24–27	P6	44/1748	4304/193157	1.13 (0.83–1.55)
Spinosyn	28–31	P7	63/3035	4307/193154	1.01 (0.78–1.30)
Spinosyn	32–36	P8	503/22005	4287/193174	1.05 (0.95–1.15)
Streptomycin	32–36	P8	36/22472	473/196988	0.69 (0.49–0.98)
Strobin	20–23	P5	13/502	6184/191277	0.81 (0.46–1.44)
Strobin	24–27	P6	48/1744	6165/191296	0.86 (0.64–1.16)
Strobin	28–31	P7	90/3008	6140/191321	1.00 (0.80–1.24)
Strobin	32–36	P8	617/21891	6117/191344	0.89 (0.82–0.98)
Sulfonylurea	20–23	P5	5/510	1365/196096	1.59 (0.66–3.85)
Sulfonylurea	24–27	P6	7/1785	1468/195993	0.58 (0.27–1.21)
Sulfonylurea	28–31	P7	21/3077	1363/196098	1.07 (0.70–1.66)
Sulfonylurea	32–36	P8	145/22363	1346/196115	0.96 (0.80–1.14)
Thiocarbamate	24–27	P6	5/1787	756/196705	0.82 (0.34–1.97)
Thiocarbamate	28–31	P7	15/3083	761/196700	1.36 (0.80–2.30)
Thiocarbamate	32–36	P8	55/22453	776/196685	0.66 (0.50–0.87)
Thiophanate, benzimidazole precursor	28–31	P7	5/3093	761/196700	0.48 (0.20–1.15)
Thiophanate, benzimidazole precursor	32–36	P8	61/22447	783/196678	0.70 (0.53–0.91)
Thiophthalimide	28–31	P7	12/3086	1259/196202	0.69 (0.39–1.22)
Thiophthalimide	32–36	P8	100/22408	1203/196258	0.76 (0.62–0.94)
Triazine	20–23	P5	12/503	6948/190513	0.73 (0.41–1.29)
Triazine	24–27	P6	38/1754	6676/190785	0.65 (0.47–0.91)
Triazine	28–31	P7	87/3011	6831/190630	0.87 (0.70–1.08)
Triazine	32–36	P8	632/21876	6626/190835	0.86 (0.79–0.93)
Urea	20–23	P5	8/507	5284/192177	0.61 (0.31–1.24)

Chemical Class	Gestation Weeks at Delivery	Month of Exposure[a]	Case Preterm (exp/not-exp)	Control Term (exp/not-exp)	Adjusted OR[b] (95%CI)
Urea	24–27	P6	31/1761	5243/192218	0.66 (0.46–0.96)
Urea	28–31	P7	71/3027	5201/192260	0.92 (0.72–1.17)
Urea	32–36	P8	507/22001	5139/192322	0.88 (0.80–0.96)
Xylylalanine	24–27	P6	10/1782	1664/195797	0.74 (0.40–1.38)
Xylylalanine	28–31	P7	26/3072	1597/195864	1.01 (0.67–1.54)
Xylylalanine	32–36	P8	147/22361	1591/195870	0.81 (0.68–0.97)
Zinc,inorganic	24–27	P6	6/1786	984/196477	0.74 (0.33–1.65)
Zinc,inorganic	28–31	P7	8/3090	981/196480	0.43 (0.19–0.97)
Zinc,inorganic	32–36	P8	80/22428	971/196490	0.75 (0.60–0.95)

[a]B1=month before conception, P1–P8=each successive month from first to ninth month of pregnancy.

[b]Odds ratio adjusted for maternal age (years), race/ethnicity(non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other), education (less than high school, high school, more than high school), parity (1 or ≥2), prenatal care initiated by fifth month (yes vs no), payer source for care (Medi-Cal, private, or other).

Table 5

Adjusted Odds Ratios (ORs) for sums of specific classifications of pesticide exposures and preterm birth.

	20–23 weeks (Exposure month=P5)		24–27 weeks (Exposure month=P6)		28–31 weeks (Exposure month=P7)		32–36 weeks (Exposure month=P8)	
	Case/Control	OR (95%CI)[a]	Case/Control	OR (95%CI)[a]	Case/Control	OR (95%CI)[a]	Case/Control	OR (95%CI)[a]
No. of chemical groups with any exposure[b]								
0	393/142670	Reference	1384/142691	Reference	2343/142786	Reference	16871/143068	Reference
1–2	49/22574	0.80 (0.58–1.09)	192/22771	0.89 (0.76–1.04)	332/22811	0.92 (0.81–1.03)	2523/22572	0.96 (0.92–1.00)
3–5	46/18168	1.01 (0.74–1.38)	137/18121	0.83 (0.69–0.99)	261/18185	0.92 (0.81–1.05)	1868/18122	0.90 (0.85–0.95)
>5	27/14049	0.68 (0.45–1.03)	79/13878	0.61 (0.48–0.77)	162/13679	0.78 (0.67–0.92)	1246/13699	0.79 (0.75–0.84)
Continuous	515/197461	0.97 (0.93–1.01)	1792/197461	0.95 (0.92–0.97)	3098/197461	0.98 (0.96–0.99)	22508/197461	0.97 (0.97–0.98)
No. of endocrine disruptors with any exposure								
0	428/159266	Reference	1508/159413	Reference	2604/159562	Reference	18768/159666	Reference
1	42/17198	0.95 (0.69–1.32)	154/17351	0.98 (0.83–1.17)	222/17196	0.82 (0.71–0.95)	1798/17083	0.92 (0.87–0.96)
2	25/9561	1.02 (0.68–1.55)	68/9470	0.78 (0.61–1.01)	128/9490	0.86 (0.72–1.04)	974/9532	0.88 (0.82–0.95)
>2	20/11436	0.61 (0.37–0.99)	62/11227	0.61 (0.47–0.79)	144/11213	0.86 (0.72–1.02)	968/11180	0.76 (0.71–0.81)
Continuous	515/197461	0.93 (0.84–1.02)	1792/197461	0.90 (0.85–0.95)	3098/197461	0.95 (0.92–0.99)	22508/197461	0.94 (0.92–0.95)
No. of Prop. 65 reproductive toxicants with any exposure								
0	485/180295	Reference	1705/179906	Reference	2864/180147	Reference	20857/180276	Reference
1	23/13352	0.64 (0.41–1.00)	67/13588	0.56 (0.44–0.71)	167/13513	0.80 (0.68–0.94)	1316/13311	0.87 (0.82–0.92)
>1	7/3814	0.76 (0.36–1.60)	20/3967	0.58 (0.38–0.91)	67/3801	1.18 (0.92–1.52)	335/3874	0.76 (0.68–0.86)
Continuous	515/197461	0.77 (0.58–1.02)	1792/197461	0.69 (0.58–0.81)	3098/197461	0.97 (0.88–1.07)	22508/197461	0.88 (0.85–0.92)
No. of reproductive or developmental toxicants with any exposure								
0	397/144777	Reference	1403/144662	Reference	2371/144756	Reference	17083/145090	Reference
1–2	54/24235	0.85 (0.63–1.14)	204/24504	0.89 (0.77–1.04)	346/24455	0.89 (0.79–1.00)	2586/24139	0.93 (0.89–0.97)
3–4	41/13611	1.18 (0.85–1.63)	102/13451	0.83 (0.67–1.02)	194/13420	0.93 (0.80–1.08)	1432/13459	0.92 (0.87–0.98)
>4	23/14838	0.57 (0.36–0.88)	83/14844	0.61 (0.48–0.76)	187/14830	0.83 (0.71–0.97)	1407/14773	0.83 (0.78–0.88)
Continuous	515/197461	0.95 (0.91–1.00)	1792/197461	0.94 (0.92–0.97)	3098/197461	0.98 (0.96–1.00)	22508/197461	0.98 (0.97–0.99)

[a]Odds ratio adjusted for maternal age (years), race/ethnicity (non-Hispanic white, U.S.-born Hispanic, foreign-born Hispanic, other), education (less than high school, high school, more than high school), parity (1 or ≥2), prenatal care initiated by fifth month (yes vs no), payer source for care (Medi-Cal, private, or other).

[b] This categorization reflects the total number of chemical groups (total possible=67) that an individual was co