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Online Material: Methods

(1) California Pesticide Use Registry (PUR) data: additional information on mandatory reported substances

California's pesticide use reporting program is recognized as the most comprehensive in the world. In 1990, California became the first state to require full reporting of agricultural pesticide use in response to demands for more realistic and comprehensive pesticide use data. Under the program, all agricultural pesticide use must be reported monthly. According to the California Department of Pesticide Registration the California -PUR reporting requirements include pesticide applications to parks, golf courses, cemeteries, rangeland, pastures, and along roadside and railroad rights-of-way. In addition, all postharvest pesticide treatments of agricultural commodities must be reported along with all pesticide treatments in poultry and fish production as well as some livestock applications. The primary exceptions to the reporting requirements are home-and-garden use and most industrial and institutional uses. Regulation California Department of Pesticide Use Reports. Online http://www.cdpr.ca.gov/docs/pur/purmain.htm accessed 5/01/2018.

eTable 1. Classification by application

Substance	Application
Glyphosate	Broad spectrum systemic herbicide
Chlorpyrifos	Insecticide
Diazinon	Insecticide; acaricide
Acephate	Insecticide; foliar
Malathion	Insecticide
Permethrin	Insecticide
Bifenthrin	Insecticide
Methyl bromide	Fumigant; insecticide
Imidacloprid	Insecticide
Avermectin	Anthelmintic; insecticide
Myclobutanil	Fungicide

eTable 2a. Correlation matrix for the pregnancy period continuous exposures (lbs/acre, spearman coefficients)

	Glypho-sates	Chlorpy-rifos	Diazinon	Acephate	Mala-thion	Perme-thrin	Bifen-thrin	Methyl bromide	Imida-clorprid	Aver-mectin	Myclo-butanil
Glyphosates	1.00	0.58	0.29	0.13	0.25	0.33	0.16	0.22	0.38	0.44	0.44
Chlorpyrifos	0.58	1.00	0.23	0.19	0.27	0.28	0.21	0.19	0.32	0.44	0.36
Diazinon	0.29	0.23	1.00	0.08	0.09	0.14	0.00	0.23	0.16	0.06	0.32
Acephate	0.13	0.19	0.08	1.00	0.13	0.14	0.18	0.07	0.20	0.23	0.13
Malathion	0.25	0.27	0.09	0.13	1.00	0.18	0.08	0.08	0.19	0.24	0.15
Permethrin	0.33	0.28	0.14	0.14	0.18	1.00	0.16	0.16	0.20	0.32	0.26
Bifenthrin	0.16	0.21	0.00	0.18	0.08	0.16	1.00	0.01	0.21	0.35	0.13
Methyl bromide	0.22	0.19	0.23	0.07	0.08	0.16	0.01	1.00	0.10	0.06	0.13
Imidacloprid	0.38	0.32	0.16	0.20	0.19	0.20	0.21	0.10	1.00	0.46	0.42
Avermectin	0.44	0.44	0.06	0.23	0.24	0.32	0.35	0.06	0.46	1.00	0.34
Myclobutanil	0.44	0.36	0.32	0.13	0.15	0.26	0.13	0.13	0.42	0.34	1.00

eTable 2b. Correlation matrix for the pregnancy period binary exposures (ever/never, tetrachoric coefficients)

	Glypho-sates	Chlorpy-rifos	Diazinon	Acephate	Mala-thion	Perme-thrin	Bifen-thrin	Methyl bromide	Imida-clorprid	Aver-mectin	Myclo-butanil
Glyphosates	1.00	0.87	0.71	0.48	0.65	0.73	0.51	0.68	0.79	0.80	0.82
Chlorpyrifos	0.87	1.00	0.59	0.45	0.60	0.60	0.48	0.58	0.62	0.73	0.64
Diazinon	0.71	0.59	1.00	0.24	0.36	0.38	0.11	0.58	0.46	0.36	0.63
Acephate	0.48	0.45	0.24	1.00	0.33	0.33	0.33	0.20	0.35	0.46	0.30
Malathion	0.65	0.60	0.36	0.33	1.00	0.39	0.21	0.35	0.35	0.47	0.36
Permethrin	0.73	0.60	0.38	0.33	0.39	1.00	0.41	0.39	0.39	0.58	0.48
Bifenthrin	0.51	0.48	0.11	0.33	0.21	0.41	1.00	0.11	0.32	0.57	0.27
Methyl bromide	0.68	0.58	0.58	0.20	0.35	0.39	0.11	1.00	0.33	0.37	0.49
Imidacloprid	0.79	0.62	0.46	0.35	0.35	0.39	0.32	0.33	1.00	0.64	0.68
Avermectin	0.80	0.73	0.36	0.46	0.47	0.58	0.57	0.37	0.64	1.00	0.53
Myclobutanil	0.82	0.64	0.63	0.30	0.36	0.48	0.27	0.49	0.68	0.53	1.00

eTable 2c. Correlations between exposures in developmental periods (lbs/acre, spearman coefficients)

Chemical	Pregnancy vs pre-pregnancy	Pregnancy vs first year of life
Glyphosates	0.76	0.87
Chlorpyrifos	0.55	0.82
Diazinon	0.46	0.65
Acephate	0.37	0.51
Malathion	0.30	0.49
Permethrin	0.48	0.68
Bifenthrin	0.31	0.55
Methyl bromide	0.43	0.58
Imidacloprid	0.44	0.71
Avermectin	0.31	0.77
Myclobutanil	0.42	0.73

eTable 2d. Correlations between exposures in developmental periods (ever/never, tetrachoric correlation)

Chemical	Pregnancy vs pre-pregnancy	Pregnancy vs first year of life
Glyphosates	0.91	0.95
Chlorpyrifos	0.78	0.91
Diazinon	0.72	0.84
Acephate	0.70	0.78
Malathion	0.56	0.72
Permethrin	0.73	0.84
Bifenthrin	0.59	0.77
Methyl bromide	0.69	0.79
Imidacloprid	0.67	0.84
Avermectin	0.58	0.88
Myclobutanil	0.66	0.85

eTable 3. Odds ratios (95% CIs) for all ASD and ASD with ID comorbidity in relation to 3-month pre-pregnancy exposure

	All ASD				ASD with ID			
	OR[1]	95% CI	OR[2]	95% CI	OR[1]	95% CI	OR[2]	95% CI
Glyphosates	1.08	(1.00, 1.17)	1.07	(0.98, 1.18)	1.22	(0.99, 1.49)	1.19	(0.94, 1.52)
Chlorpyrifos	1.01	(0.94, 1.10)	0.94	(0.86, 1.04)	0.99	(0.82, 1.21)	0.81	(0.64, 1.03)
Diazinon	0.98	(0.88, 1.09)	0.95	(0.84, 1.07)	1.13	(0.88, 1.45)	1.01	(0.77, 1.33)
Acephate	1.12	(0.95, 1.31)	1.07	(0.91, 1.27)	1.54	(1.11, 2.13)	1.47	(1.04, 2.09)
Malathion	1.01	(0.89, 1.15)	0.97	(0.84, 1.11)	0.83	(0.59, 1.17)	0.73	(0.51, 1.05)
Permethrin	1.12	(1.02, 1.24)	1.10	(0.98, 1.22)	1.37	(1.09, 1.71)	1.30	(1.01, 1.67)
Bifenthrin	1.14	(1.01, 1.28)	1.10	(0.97, 1.26)	1.33	(0.99, 1.79)	1.27	(0.91, 1.76)
Methyl bromide	1.16	(1.04, 1.30)	1.15	(1.02, 1.29)	1.18	(0.91, 1.53)	1.09	(0.83, 1.45)
Imidacloprid	1.03	(0.94, 1.13)	0.99	(0.89, 1.10)	1.01	(0.80, 1.27)	0.84	(0.64, 1.09)
Avermectin	1.08	(0.99, 1.18)	1.04	(0.93, 1.16)	1.13	(0.90, 1.40)	1.03	(0.78, 1.36)
Myclobutanil	0.99	(0.90, 1.08)	0.94	(0.85, 1.05)	1.23	(0.99, 1.52)	1.17	(0.91, 1.51)

[1] Logistic regression; adjusted for year of birth, sex, maternal race/ethnicity, maternal age, maternal education, NOx (CALINE4); pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period.

[2] Logistic regression; adjusted for all in model #1; pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period with all considered pesticides in the model.

eTable 4. Exposure (ever vs never) in different developmental periods, among controls in percent

	Pre-pregnancy only	Pregnancy only	First year of life only	Pre-pregnancy and pregnancy only	Pre-pregnancy and the first year of life only	Pregnancy and the first year of life only	All three periods
Glyphosates	0.5%	3.2%	2.7%	1.4%	1.1%	11.8%	59.0%
Chlorpyrifos	1.2%	3.3%	5.4%	1.5%	2.9%	18.6%	35.7%
Diazinon	2.0%	4.8%	6.0%	1.7%	2.5%	9.6%	9.9%
Acephate	1.4%	3.5%	5.5%	1.0%	1.1%	4.4%	2.6%
Malathion	1.8%	5.6%	9.3%	1.4%	2.3%	9.3%	4.3%
Permethrin	1.5%	4.8%	7.6%	1.6%	2.6%	11.9%	12.1%
Bifenthrin	1.4%	4.3%	9.6%	1.2%	2.5%	10.4%	4.7%
Methyl bromide	1.8%	5.5%	7.5%	1.5%	2.1%	8.7%	7.1%
Imidacloprid	1.6%	4.8%	9.3%	1.3%	3.2%	17.8%	17.1%
Avermectin	1.1%	3.3%	8.2%	1.0%	4.3%	25.2%	19.1%
Myclobutanil	1.7%	5.1%	8.0%	1.4%	3.2%	18.7%	17.8%

eTable 5. Odds ratios (95% CIs) for ASD *without* ID comorbidity and exposure to pesticides for pregnancy and first year of life exposures in logistic regression models

	Pregnancy				First year of life			
Pesticide	OR[1]	95% CI	OR[2]	95% CI	OR[1]	95% CI	OR[2]	95% CI
Glyphosates	1.13	(1.03, 1.25)	1.11	(0.98, 1.27)	1.10	(1.00, 1.22)	1.14	(1.00, 1.30)
Chlorpyrifos	1.11	(1.02, 1.21)	1.07	(0.95, 1.20)	1.07	(0.98, 1.17)	1.04	(0.92, 1.17)
Diazinon	1.05	(0.96, 1.16)	1.06	(0.95, 1.18)	0.96	(0.87, 1.06)	0.93	(0.84, 1.05)
Acephate	1.06	(0.93, 1.21)	1.03	(0.90, 1.18)	0.96	(0.85, 1.09)	0.93	(0.82, 1.06)
Malathion	1.11	(1.00, 1.22)	1.07	(0.96, 1.20)	1.09	(0.99, 1.19)	1.08	(0.97, 1.20)
Permethrin	1.04	(0.95, 1.14)	0.98	(0.89, 1.09)	1.04	(0.96, 1.14)	1.01	(0.92, 1.12)
Bifenthrin	1.01	(0.92, 1.12)	0.96	(0.86, 1.07)	1.06	(0.96, 1.16)	1.03	(0.93, 1.14)
Methyl bromide	0.98	(0.88, 1.08)	0.91	(0.82, 1.02)	1.04	(0.95, 1.15)	1.03	(0.92, 1.15)
Imidacloprid	0.93	(0.85, 1.01)	0.83	(0.75, 0.92)	0.94	(0.86, 1.02)	0.88	(0.79, 0.98)
Avermectin	1.14	(1.05, 1.24)	1.16	(1.04, 1.30)	1.06	(0.98, 1.16)	1.06	(0.94, 1.19)
Myclobutanil	0.99	(0.91, 1.08)	0.96	(0.87, 1.06)	0.97	(0.89, 1.05)	0.94	(0.84, 1.04)

[1] Logistic regression; adjusted for year of birth, sex, maternal race/ethnicity, maternal age, maternal education, NOx (CALINE4); pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period.

[2] Logistic regression; adjusted for all in model #1; pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period with all considered pesticides in the model.

eTable 6a. Odds ratios (95% CIs) for all ASD and exposure to pesticides for pregnancy and first year of life exposures in 2,500m radius

	Pregnancy				First year of life			
Pesticide	OR[1]	95% CI	OR[2]	95% CI	OR[1]	95% CI	OR[2]	95% CI
Glyphosates	1.21	(1.10, 1.34)	1.20	(1.05, 1.38)	1.17	(1.07, 1.29)	1.21	(1.06, 1.39)
Chlorpyrifos	1.12	(1.03, 1.22)	0.98	(0.88, 1.10)	1.11	(1.02, 1.21)	1.02	(0.90, 1.15)
Diazinon	1.14	(1.05, 1.24)	1.12	(1.01, 1.23)	1.10	(1.01, 1.19)	1.06	(0.96, 1.17)
Acephate	1.12	(1.01, 1.25)	1.08	(0.97, 1.21)	0.99	(0.90, 1.10)	0.95	(0.86, 1.06)
Malathion	1.13	(1.04, 1.23)	1.08	(0.98, 1.18)	1.11	(1.02, 1.20)	1.06	(0.97, 1.16)
Permethrin	1.10	(1.02, 1.19)	1.03	(0.94, 1.12)	1.11	(1.03, 1.20)	1.07	(0.97, 1.17)
Bifenthrin	1.07	(0.98, 1.17)	1.01	(0.92, 1.11)	1.10	(1.02, 1.19)	1.06	(0.97, 1.17)
Methyl bromide	1.05	(0.97, 1.15)	0.97	(0.88, 1.07)	1.13	(1.04, 1.23)	1.09	(0.99, 1.20)
Imidacloprid	0.94	(0.87, 1.02)	0.81	(0.74, 0.89)	0.95	(0.88, 1.03)	0.85	(0.77, 0.94)
Avermectin	1.14	(1.05, 1.23)	1.10	(0.99, 1.22)	1.06	(0.97, 1.15)	0.96	(0.86, 1.08)
Myclobutanil	1.05	(0.98, 1.14)	0.99	(0.90, 1.09)	1.01	(0.94, 1.09)	0.93	(0.84, 1.03)

[1] Logistic regression; adjusted for year of birth, sex, maternal race/ethnicity, maternal age, maternal education, NOx (derived from CALINE4); pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period.

[2] Logistic regression; adjusted for all in model #1; pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period with all considered pesticides in the model.

eTable 6b. Odds ratios (95% CIs) for ASD with ID comorbidity and exposure to pesticides for pregnancy and first year of life exposures in in 2,500m radius

	Pregnancy				First year of life			
Pesticide	OR[1]	95% CI	OR[2]	95% CI	OR[1]	95% CI	OR[2]	95% CI
Glyphosates	1.46	(1.12, 1.89)	1.22	(0.86, 1.73)	1.57	(1.20, 2.05)	1.36	(0.94, 1.95)
Chlorpyrifos	1.39	(1.12, 1.72)	1.13	(0.84, 1.52)	1.39	(1.11, 1.74)	1.06	(0.77, 1.46)
Diazinon	1.38	(1.13, 1.69)	1.23	(0.97, 1.56)	1.43	(1.17, 1.74)	1.26	(0.99, 1.60)
Acephate	1.26	(0.98, 1.61)	1.14	(0.88, 1.47)	1.22	(0.96, 1.54)	1.07	(0.84, 1.38)
Malathion	1.23	(1.00, 1.51)	1.04	(0.83, 1.30)	1.26	(1.03, 1.53)	1.05	(0.84, 1.31)
Permethrin	1.52	(1.25, 1.84)	1.40	(1.12, 1.75)	1.49	(1.23, 1.80)	1.31	(1.04, 1.64)
Bifenthrin	1.23	(1.00, 1.53)	1.12	(0.89, 1.41)	1.44	(1.18, 1.76)	1.34	(1.07, 1.68)
Methyl bromide	1.31	(1.07, 1.61)	1.11	(0.88, 1.40)	1.31	(1.07, 1.60)	1.09	(0.86, 1.37)
Imidacloprid	0.92	(0.76, 1.12)	0.72	(0.58, 0.90)	1.07	(0.88, 1.30)	0.84	(0.67, 1.07)
Avermectin	1.13	(0.93, 1.38)	0.87	(0.68, 1.12)	1.08	(0.88, 1.32)	0.69	(0.53, 0.90)
Myclobutanil	1.20	(0.99, 1.45)	0.98	(0.77, 1.25)	1.31	(1.07, 1.59)	1.04	(0.81, 1.34)

[1] Logistic regression; adjusted for year of birth, sex, maternal race/ethnicity, maternal age, maternal education, NOx (CALINE4); pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period.

[2] Logistic regression; adjusted for all in model #1; pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period with all considered pesticides in the model.

eTable 7. Odds ratios (95% CIs) for ASD (all) and exposure to pesticides for pregnancy and first year of life exposures in logistic regression models stratified by males/females

	Pregnancy				First year of life			
	OR[1]	95% CI	OR[2]	95% CI	OR[1]	95% CI	OR[2]	95% CI
Pesticide	Males							
Glyphosates	1.14	(1.03, 1.26)	1.11	(0.97, 1.27)	1.12	(1.01, 1.23)	1.15	(1.00, 1.31)
Chlorpyrifos	1.12	(1.03, 1.22)	1.07	(0.95, 1.21)	1.07	(0.98, 1.17)	1.02	(0.90, 1.16)
Diazinon	1.10	(1.00, 1.22)	1.09	(0.98, 1.23)	1.00	(0.91, 1.11)	0.96	(0.86, 1.08)
Acephate	1.12	(0.98, 1.28)	1.10	(0.96, 1.26)	1.02	(0.90, 1.16)	0.99	(0.87, 1.13)
Malathion	1.10	(0.99, 1.22)	1.04	(0.93, 1.16)	1.12	(1.02, 1.23)	1.10	(0.99, 1.22)
Permethrin	1.12	(1.02, 1.23)	1.07	(0.97, 1.19)	1.10	(1.00, 1.20)	1.08	(0.97, 1.20)
Bifenthrin	1.00	(0.90, 1.11)	0.94	(0.84, 1.05)	1.04	(0.94, 1.14)	0.99	(0.89, 1.10)
Methyl bromide	1.02	(0.92, 1.13)	0.94	(0.84, 1.05)	1.08	(0.98, 1.20)	1.06	(0.95, 1.19)
Imidacloprid	0.92	(0.84, 1.00)	0.81	(0.73, 0.90)	0.92	(0.85, 1.01)	0.85	(0.76, 0.95)
Avermectin	1.11	(1.01, 1.21)	1.09	(0.97, 1.21)	1.04	(0.95, 1.13)	0.99	(0.88, 1.12)
Myclobutanil	1.02	(0.94, 1.11)	0.98	(0.88, 1.09)	0.99	(0.91, 1.08)	0.97	(0.87, 1.08)
	Females							
Glyphosates	1.27	(1.02, 1.58)	1.19	(0.90, 1.59)	1.34	(1.08, 1.66)	1.27	(0.95, 1.71)
Chlorpyrifos	1.20	(1.00, 1.44)	1.06	(0.83, 1.37)	1.26	(1.04, 1.52)	1.09	(0.84, 1.42)
Diazinon	1.12	(0.91, 1.38)	1.04	(0.82, 1.32)	1.20	(0.98, 1.47)	1.16	(0.92, 1.47)
Acephate	0.95	(0.71, 1.28)	0.87	(0.64, 1.18)	0.91	(0.69, 1.20)	0.81	(0.60, 1.07)
Malathion	1.16	(0.94, 1.44)	1.10	(0.87, 1.39)	1.06	(0.86, 1.30)	0.96	(0.77, 1.20)
Permethrin	1.04	(0.85, 1.26)	0.91	(0.73, 1.13)	1.10	(0.92, 1.33)	0.94	(0.75, 1.16)
Bifenthrin	1.15	(0.93, 1.42)	1.08	(0.86, 1.36)	1.36	(1.13, 1.65)	1.33	(1.07, 1.65)
Methyl bromide	1.08	(0.87, 1.35)	0.98	(0.77, 1.25)	1.08	(0.88, 1.33)	0.97	(0.77, 1.21)
Imidacloprid	0.96	(0.80, 1.16)	0.80	(0.64, 1.00)	1.05	(0.88, 1.26)	0.91	(0.73, 1.14)
Avermectin	1.21	(1.01, 1.46)	1.19	(0.94, 1.50)	1.22	(1.01, 1.47)	1.07	(0.83, 1.37)
Myclobutanil	1.11	(0.93, 1.33)	1.05	(0.84, 1.31)	1.06	(0.89, 1.27)	0.89	(0.71, 1.12)

[1] Logistic regression adjusted for year of birth, maternal race/ethnicity, maternal age, maternal education, NOx (CALINE4); pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period.

[2] Logistic regression; adjusted for all in model #1; pesticide exposure defined as “ever vs. never” to specific substance in considered developmental period with all considered pesticides in the model.