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# **Supplemental Material**

## High Pesticide Exposure Events and Olfactory Impairment among U.S. Farmers

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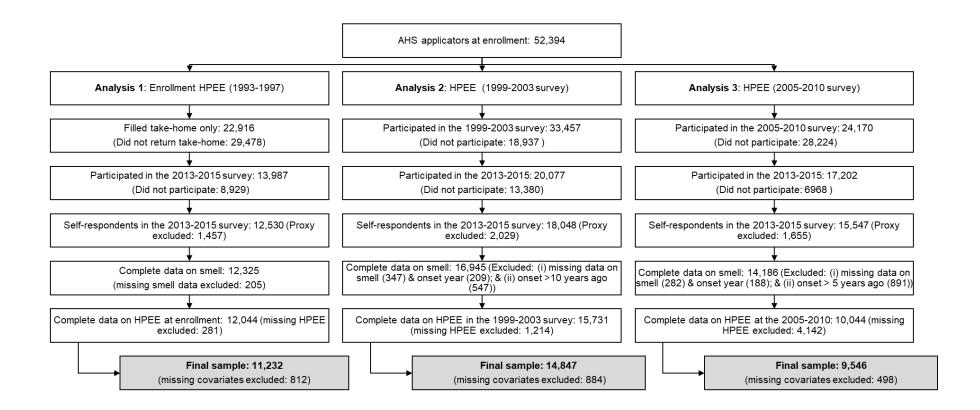
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### Supplemental methods: Details on inverse probability weighting

Of the 22916 participants who filled out the take-home questionnaire at enrollment, only about 61% participated in the third follow-up survey (2013-2015). Therefore, we examined associations between HPEE variables and OI using inverse probability weighting to account for the loss to follow-up in order to make inferences about all eligible farmers who returned the take-home questionnaire. Table S2 presents the characteristics of full cohort taking take-home questionnaire, those who participated in the third follow-up survey (2013-2015), and those who did not participate in 2013-2015. Participants with certain enrollment characteristics - older people (aged > 65 years), current smokers, those who did not graduate high school, those from North Carolina, those with selfreported diabetes and heart disease - were more likely not to participate in 2013-2015. Other enrollment characteristics - those who reported consuming alcohol in the past year, those reporting head injury, married applicators, and those who reported experiencing HPEE – were more likely to participate in 2013-2015. For estimation of inverse probability weights, first, we used logistic regression analyses to estimate probabilities of overall participation in 2013-2015 (a) conditional on exposure and baseline adjustment covariates (age, sex, education, smoking, state of residence, marital status, head injury, alcohol consumption, and pair-wise interaction between exposure and covariates) (the denominator of the stabilized weights); and (b) conditional only on exposure (the numerator of the stabilized weights). Finally, we estimated stabilized weights as the ratio of conditional probabilities and applied to logistic regression model examining an HPEE variable in relation to OI. We also evaluated other covariates including self-reported diabetes and heart disease at enrollment as predictors of loss-to-follow up in 2013-2015. Since the results from the analysis that used information on diabetes and heart disease were similar to that did not use such information, but because of missing data on these additional covariates, we present results based on the set of covariates that was used for confounding adjustment. The mean and standard deviation of the weights ranged from 1.00 (0.15) to 1.01 (0.22). Details on distribution of weights are presented in Table S4.

Figure S1: Sample selection for analysis of HPEE in relation to Olfactory impairment



Note:

Analysis 1: Self-reported olfactory impairment (OI) in 2013-2015 in association with a history of any high pesticide exposure event (HPEE) at enrollment (1993-1997)

Analysis 2: Self-reported olfactory impairment (OI) in association with high pesticide exposure events (HPEE) that occurred between enrollment (1993-1997) and the 1999-2003 survey (for OI first noticed within 10y of the 2013-2015 survey)

Analysis 3: Self-reported olfactory impairment (OI) in association with HPEE that occurred between the 1999-2003 and 2005-2010 surveys (for OI first noticed within 5y of the 2013-2015 survey)

Table S1: AHS survey questions on high pesticide exposure events and olfactory impairment

Questions on high pesticide exposure events asked in a take-home questionnaire at enrollmer (1993-1997)	nt
<ul> <li>25. Have you ever had an incident or experience while using <i>any</i> type of <i>PESTICIDE</i> which caused you <i>unusually high</i> personal exposure?</li> <li>○ No [GO TO QUESTION 30]</li> <li>○ Yes</li> </ul>	
26. What was the name of the product you were using during your highest exposure incident or experience?	
(Pesticides listed in questions 10 to 24 may assist you in remembering or spelling, if needed.)	
<ul> <li>27. During which decade did this pesticide incident occur?</li> <li>the 1990s</li> <li>the 1980s</li> <li>the 1970s</li> <li>the 1960s</li> <li>the 1950s</li> <li>the 1940s</li> </ul>	
<ul> <li>28. Which part(s) of your body were exposed to the pesticide? (Mark all that apply.)</li> <li>Head and/or face</li> <li>Arms</li> <li>Hands</li> <li>Chest/back/abdomen</li> <li>Groin area</li> <li>Legs</li> <li>Feet</li> <li>Lungs and respiratory tract (from breathing fumes)</li> <li>Digestive tract (from ingesting/swallowing)</li> </ul>	
<ul> <li>29. How soon after this pesticide incident were you able to wash (with soap and water) your exposed body part(s)?</li> <li>Cless than 30 minutes</li> <li>30-59 minutes</li> <li>1-3 hours</li> <li>4-6 hours</li> <li>7-9 hours</li> <li>More than 9 hours after the incident</li> </ul>	

Questions on high pesticide exposure events asked in the first follow-up (1999-2003)

	38d.	(During (Reference Year), did you <u>normally</u> use this type of glove when <u>applying</u> ) fungicides?
		1. YesDK
		2. NoRef
		3. Did not use
39.	Since	(year of enrollment), did you have any incidents with fertilizers, herbicides or other pesticides that caused you an unusually high personal
	exposi	
		1. YesREF [Go to Q41]
		0. Na [Go to Q41]DK [Go to Q41]
	39a.	How many of the exposure incidents have you had since (enrollment date)?
		DKREF
	39b.	Were any of the incidents during (last calendar year)?
		1. YesREF [Go to Q41]
		0. No [Go to Q41]DK [Go to Q41]
	39c.	Descending the must recent in sident, what was the name of the chamical year wave spaced to?
	<b>39</b> C.	Regarding the most recent incident, what was the name of the chemical you were exposed to? SELECT ONLY ONE PESTICIDE. IF MORE THAN ONE, MAKE REMARK.
		SEECT ONET ONE LESTICIEE. IT MORE THAN ONE, MARE REMARK.
		DKREF
	39d.	(Regarding the most recent incident,) what parts of your body were exposed?
		READ RESPONSES. MARK ALL THAT APPLY. WHEN COMPLETE PRESS ENTER.
		1. Head[Go to Q39e]       5. Feet[Go to Q39e]         2. Face (eyes, nose, mouth)[Go to Q39e]       6. Lungs (from breathing)[Go to Q39e]
		2. Face (eyes, hose, hour)[Go to Q39e]       0. Earlings (from oreaning)[Go to Q39e]         3. Torso, arms, legs [Go to Q39e]       7. Digestive tract (from swallowing)[Go to Q39e]
		4. Hands [Go to Q39e] 8. Something else
		DK [Go to Q39e]
		REF [Go to Q39e]
		39d1. What part was this?
		fill inDKREF
39	e. (R	tegarding the most recent incident,) what pesticide or fertilizer-related job were you doing when the exposure occurred?
		1. Mixing[Go to Q39g]       4. Cleaning/maintenance/repair of equipment[Go to Q39g]
		2. Loading[Go to Q39g]   5. Cleaning up a spill[Go to Q39g]
		3. Applying[Go to Q39f] 6. Something else
		DK[Go to Q39g]
		REF[Go to Q39g]
	39	e1. What was this?
		fill inDKREF
		[ALL RESPONSES Go to Q39g]
39	f. W	hat application method were you using?
	1	broadcast from farm vehicle[Go to Q39g]
		hand spray gun or wand[Go to Q39g]
		backpack sprayer[Go to Q39g]
		banded sprayer[Go to Q39g]
	5.	gas canister[Go to Q39g]
		mist blower or fogger[Go to Q39g]
		pre-applied to seed[Go to Q39g]
		greenhouse sprayer (only in any greenhouse applications)[Go to Q39g]
		airblast[Go to Q39g] ), applied dried pellets[Go to Q39g]
		. power, knapsack or air sprayer or duster[Go to Q39g]
		hand treatment such as pour-ons, hand wipes, oral paste or boluses[Go to Q39g]
		. injection[Go to Q39g]
		animal self-application method, like rubbing devise, dust bags, ear tabs, rope wicks or in feed additives[Go to Q39g]
		i. something else
		_DK[Go to Q39g]
	_	_REF[Go to Q39g]
		<b>39f1</b> . What was this?
		5711. What was this:
		fill inDKREF

39h. How soon after the incident did you wash off or change clothes?	
1. <30 minutes	
2. 30-59 minutes 3. 1-3 hours	
4. 4-6 hours	
5. 7-9 hours 6. >9 hours after the incident	
6. >9 nours after the incident DK	
40. Did this incident result in a health care visit?	
1. YesDK [Go to Q41]	
0. No [Go to Q41]REF [Go to Q41]	
40a. Were you hospitalized?	
1. YesDK 0. NoREF	
Questions on high pesticide exposure events asked in the second follow-up (2005-2010)	
SECTION 6. HIGH PESTICIDE EXPOSURE EVENTS	
O6 1) Since ADSD Vees Off activity how one had any insidents a will determine the time of the time	
Q6.1) Since ^DSP.YearOfLastInterview, have you had any incidents or spills that resulted in an unusually high exposure to pesticides from contact with your skin, from breathing fumes, or dust, or from accidental ingestion?	
0. NO (Skip to Section 7)	
1. YES	
8. REF (Skip to Section 7)	
9. DK (Skip to Section 7)	
Q6.2) Regarding the most recent incident, what was the name of the pesticide you were using?	
<display applicator="" for="" list="" names="" of="" pesticide="" reported="" this=""></display>	
99998. REF (Skip to Q6.3)	
99999. DK (Skip to Q6.3)	
BOX Q6.2: If "other" not listed, skip to Q6.3.	
Q6.2_OS) [Regarding the most recent incident, what was the name of the pesticide you were using?]	
OTHER, SPECIFY:	
Q6.3) Did this incident result in medical treatment or hospitalization?	
0. NO	
0. NO 1. YES	
0. NO 1. YES 8. REF	
0. NO 1. YES	
0. NO 1. YES 8. REF 9. DK	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015)	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell?	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? • Yes	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? • Yes • No	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? • Yes • No When did you start losing your sense of smell?	
<ul> <li>0. NO <ol> <li>YES</li> <li>REF</li> <li>DK</li> </ol> </li> <li>Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? <ul> <li>Yes</li> <li>No</li> </ul> </li> <li>When did you start losing your sense of smell? <ul> <li>Less than 1 year ago</li> </ul> </li> </ul>	
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<ul> <li>0. NO <ol> <li>YES</li> <li>REF</li> <li>DK</li> </ol> </li> <li>Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? <ul> <li>Yes</li> <li>No</li> </ul> </li> <li>When did you start losing your sense of smell? <ul> <li>Less than 1 year ago</li> <li>1 to 5 years ago</li> <li>5 to 10 years ago</li> </ul> </li> </ul>	
0. NO 1. YES 8. REF 9. DK Questions on olfactory impairment asked in the third follow-up (2013-2015) Do you suffer from a loss of sense of smell or a significantly decreased sense of smell? • Yes • No When did you start losing your sense of smell? • Less than 1 year ago • 1 to 5 years ago	

	All those returning take-	Did not participate	Participated in	Included in main	P-
	home questionnaire, n (%) (n=22916)	in (2013-2015), n (%) (n=8929)	(2013-2015), n (%) (n=13987)	analysis with complete exposure, outcome, and covariate data, n (%) (n=11232)	value <sup>a</sup>
Age at enrollment (years)					<0.0001
≤45	9657 (42.1)	3714 (41.6)	5943 (42.5)	5347 (47.6)	
46-55	5244 (22.9)	1585 (17.8)	3659 (26.2)	3055 (27.2)	
56-65	5059 (22.1)	1812 (20.3)	3247 (23.2)	2318 (20.6)	
>65	2956 (12.9)	1818 (20.4)	1138 (8.1)	512 (4.6)	
Sex					0.5012
Women	556 (2.4)	209 (2.3)	347 (2.5)	286 (2.5)	
Men	22360 (97.6)	8720 (97.7)	13640 (97.5)	10946 (97.5)	
Race <sup>c</sup>					<0.0001
Others	427 (1.9)	253 (2.9)	174 (1.3)	101 (0.9)	
White	21980 (98.1)	8399 (97.1)	13581 (98.7)	11122 (99.1)	
Missing	509	277	232	9	
State					<0.0001
Iowa	14810 (64.6)	5065 (56.7)	9745 (69.7)	8231 (73.3)	
North Carolina	8106 (35.4)	3864 (43.3)	4242 (30.3)	3001 (26.7)	
Marital status					<0.0001
Never married	2365 (10.4)	1055 (11.9)	1310 (9.4)	1155 (10.3)	
Married/Living as married	19220 (84.3)	7237 (81.7)	11983 (86)	9560 (85.1)	
Divorced/Widowed	1209 (5.3)	570 (6.4)	639 (4.6)	517 (4.6)	
Missing	122	67	55	0	
Education					<0.0001
High school or lower	12647 (58)	5317 (63.5)	7330 (54.5)	5798 (51.6)	
1–3 years beyond high	5173 (23.7)	1822 (21.8)	3351 (24.9)	2954 (26.3)	
College graduate or more	4001 (18.3)	1236 (14.8)	2765 (20.6)	2480 (22.1)	
Missing	1095	554	541	0	

Table S2: Characteristics of full cohort taking take-home questionnaire, those who participated in the third follow-up (2013-2015), and those who did not participate in the third follow-up (2013-2015)

Smoking					<0.0001
Never smoker	11974 (53.3)	4255 (49.4)	7719 (55.7)	6484 (57.7)	
Former smoker	7575 (33.7)	2980 (34.6)	4595 (33.1)	3564 (31.7)	
Current smoker	2922 (13)	1370 (15.9)	1552 (11.2)	1184 (10.5)	
Missing	445	324	121	0	
Snuff use on a regular basis for six	months or longer				0.6182
No	21950 (95.8)	8560 (95.9)	13390 (95.7)	10712 (95.4)	
Yes	966 (4.2)	369 (4.1)	597 (4.3)	520 (4.6)	
Alcohol drinking during the past					
12 months					<0.0001
No	7869 (36.3)	3289 (39.6)	4580 (34.2)	3627 (32.3)	
Yes	13813 (63.7)	5010 (60.4)	8803 (65.8)	7605 (67.7)	
Missing	1234	630	604	0	
Ever diagnosed with head					
injury requiring medical					0.000
attention	10700 (07 0)	7711 (00 7)	12010 (07.2)	0764 (96 0)	0.002
No	19729 (87.8)	7711 (88.7)	12018 (87.3)	9764 (86.9)	
Yes	2738 (12.2)	986 (11.3)	1752 (12.7)	1468 (13.1)	
Missing	449	232	217	0	
Cumulative days of any					<0.0001
pesticide use (days) Quartile 1: 0 to 64	6535 (28.5)	2812 (31.5)	3723 (26.6)	2872 (25.6)	<0.0001
Quartile $2: > 64$ to $225$	7181 (31.4)	2651 (29.7)	4530 (32.4)	3728 (33.2)	
Quartile 2: > $64 10 225$ Quartile 3: > 225 to 457	4660 (20.4)	1704 (19.1)	2956 (21.1)	2454 (21.8)	
	( )	( )	( )	( )	
Quartile 4: > 457	4514 (19.7)	1746 (19.6)	2768 (19.8)	2178 (19.4)	
Missing	26	16	10	0	
Change of sense of smell of					
taste during the past 12 months		7000 (00 0)	40740 (00 E)	40404 (02.0)	0.1083
No	20628 (93.3)	7880 (92.9)	12748 (93.5)	10421 (93.8)	
Yes	1489 (6.7)	600 (7.1)	889 (6.5)	689 (6.2)	
Missing	799	449	250	122	
Parkinson's disease					<0.0001

No	22483 (98.7)	8778 (99.2)	13705 (98.3)	11092 (99)	
Yes	307 (1.3)	72 (0.8)	235 (1.7)	115 (1)	
Missing	126	79	47	25	
Ever diagnosed with Diabetes (sug	ar) (other than while				
pregnant)					<0.0001
No	21583 (96.1)	8219 (94.6)	13364 (97.1)	10962 (97.8)	
Yes	876 (3.9)	470 (5.4)	406 (2.9)	247 (2.2)	
Missing	457	240	217	23	
Ever diagnosed with Heart disease					<0.0001
No	20004 (93.6)	7418 (91.1)	12586 (95.1)	10680 (96.2)	
Yes	1375 (6.4)	728 (8.9)	647 (4.9)	423 (3.8)	
Missing	1537	783	754	129	
Any HPEEs					<0.0001
No	19051 (85.8)	7587 (88.3)	11464 (84.2)	9387 (83.6)	
Yes	3156 (14.2)	1003 (11.7)	2153 (15.8)	1845 (16.4)	
Missing	709	339	370	0	
The decade highest exposure					
HPEE occurred					<0.0001
No HPEE	19051 (87)	7587 (89.4)	11464 (85.6)	9387 (84.9)	
1990s	502 (2.3)	193 (2.3)	309 (2.3)	287 (2.6)	
1980s	1126 (5.1)	344 (4.1)	782 (5.8)	694 (6.3)	
1970s	788 (3.6)	225 (2.7)	563 (4.2)	497 (4.5)	
1960s or before	420 (1.9)	141 (1.7)	279 (2.1)	197 (1.8)	
Missing	1029	439	590	170	
Time delay between the highest					
exposure HPEE and washing					0.0004
with soap and water No HPEE	19051 (86.3)	7587 (88.8)	11464 (84.7)	0207 (01)	<0.0001
	( )	( <i>y</i>	( <i>y</i>	9387 (84)	
<30 min	1315 (6)	410 (4.8)	905 (6.7)	783 (7)	
30-59	520 (2.4)	180 (2.1)	340 (2.5)	295 (2.6)	
1-3 hours	624 (2.8)	199 (2.3)	425 (3.1)	357 (3.2)	

4-6 hours	370 (1.7)	104 (1.2)	266 (2)	234 (2.1)	
>6 hours	200 (0.9)	65 (0.8)	135 (1)	115 (1)	
Missing	836	384	452	61	
Exposure route (highest exposure HPEE)					<0.0001
No HPEE	19051 (86)	7587 (88.6)	11464 (84.4)	9387 (83.8)	<0.0001
Respiratory or digestive tract	1152 (5.2)	362 (4.2)	790 (5.8)	664 (5.9)	
Dermal only	1943 (8.8)	619 (7.2)	1324 (9.8)	1154 (10.3)	
Missing	770	361	409	27	

<sup>a</sup>P-value for difference in characteristics between those who participated in 2013-2015 and those who did not

Table S3: Sensitivity analyses on HPEEs reported at enrollment (1993-1997) in relation to self-reported OI in 2013-2015 – adjusting for cumulative days of use of any pesticides and excluding Parkinson's disease patients

	Analysis 1 (n=11,232)		Analysis 2 (n=11,117)			
	No OI, n (%)	OI, n (%)	OR (95% CI)	No OI, n (%)	Ol, n (%)	OR (95% CI)
Any HPEEs						
No	8458 (84.2)	929 (78.3)	Ref	8422 (84.2)	866 (77.7)	Ref
Yes	1588 (15.8)	257 (21.7)	1.42 (1.22, 1.66)	1581 (15.8)	248 (22.3)	1.46 (1.24, 1.7)
Details about the highest HPEE						
The decade it occurred						
No HPEE	8458 (85.4)	929 (80.5)	Ref	8422 (85.4)	866 (80)	Ref
1990s	262 (2.6)	25 (2.2)	1.04 (0.68, 1.59)	261 (2.6)	25 (2.3)	1.09 (0.72, 1.67)
1980s	598 (6)	96 (8.3)	1.61 (1.27, 2.03)	597 (6.1)	95 (8.8)	1.67 (1.32, 2.11)
1970s	428 (4.3)	69 (6)	1.29 (0.99, 1.69)	425 (4.3)	62 (5.7)	1.24 (0.93, 1.64)
1960s or before	162 (1.6)	35 (3)	1.35 (0.92, 1.97)	162 (1.6)	34 (3.1)	1.40 (0.95, 2.06)
Missing	138	32		136	32	
Time delay between the HPEE and	I washing with	soap and wa	iter			
No HPEE	8458 (84.7)	929 (78.7)	Ref	8422 (84.7)	866 (78.2)	Ref
<30 min	687 (6.9)	96 (8.1)	1.33 (1.06, 1.68)	683 (6.9)	93 (8.4)	1.37 (1.09, 1.73)
30-59	256 (2.6)	39 (3.3)	1.32 (0.93, 1.88)	254 (2.6)	35 (3.2)	1.26 (0.88, 1.82)
1-3 hours	308 (3.1)	49 (4.2)	1.33 (0.97, 1.82)	307 (3.1)	49 (4.4)	1.42 (1.03, 1.94)
4-6 hours	188 (1.9)	46 (3.9)	1.96 (1.4, 2.74)	188 (1.9)	44 (4)	1.98 (1.4, 2.79)
>6 hours	94 (0.9)	21 (1.8)	1.81 (1.12, 2.94)	94 (0.9)	21 (1.9)	1.9 (1.17, 3.08)
Missing	55	6		55	6	
Exposure route <sup>a</sup>						
No HPEE	8458 (84.4)	929 (78.5)	Ref	8422 (84.4)	866 (77.9)	Ref
Respiratory/ digestive tract	564 (5.6)	100 (8.5)	1.46 (1.16, 1.83)	561 (5.6)	98 (8.8)	1.52 (1.2, 1.91)
Dermal only	1000 (10)	154 (13)	1.41 (1.17, 1.71)	996 (10)	147 (13.2)	1.43 (1.18, 1.73)
Missing	24	3		24	3	

Abbreviations: HPEE: high pesticide exposure event; OI: olfactory impairment. All models included age, sex, state, education, marital status, smoking status, alcohol consumption, and head injury. Analysis 1 further adjusted for cumulative days of any pesticide use; analysis 2 adjusted for cumulative days of any pesticide use and excluded PD patients

<sup>a</sup> Participants with a history of HPEE were classified as having respiratory or gastrointestinal tract exposure if they reported that they breathed fumes or ingested or swallowed the pesticide during the HPEE event, regardless of whether they might also have had dermal exposure. Participants were classified as having only dermal exposure if they reported exposure of the head and/or face, arms, hands, cheek/back/abdomen, groin area, legs, or feet, but did not report breathing fumes or ingesting/swallowing the pesticide

Analysis 1 (n=10,421) Analysis 2 Mean (SD); (Min, OR (95% CI) No OI, n (%) OI, n (%) OR (95% CI) No OI, n (%) Ol, n (%) Max)<sup>a</sup> Any HPEEs 805 (79.5) Ref 929 (78.3) Ref 7988 (84.9) 8458 (84.2) 1.00(0.15);No Yes 207 (20.5) 1588 (15.8) (0.75, 1.93)1421 (15.1) 1.46 (1.24, 1.73) 257 (21.7) 1.48 (1.27, 1.73) Details about the highest HPEE The decade it occurred No HPEE 7988 (86) 805 (81.5) Ref 8458 (85.4) 929 (80.5) Ref 1.01 (0.22); 1990s 240 (2.6) 21 (2.1) 1.07 (0.68, 1.69) 262 (2.6) 25 (2.2) 1.16 (0.74, 1.82) (0.71, 15.52)1980s 541 (5.8) 77 (7.8) 1.60 (1.24, 2.07) 598 (6) 96 (8.3) 1.64 (1.30, 2.07) 69 (6) 1970s 374 (4) 56 (5.7) 1.37 (1.02, 1.84) 428 (4.3) 1.34 (1.03, 1.75) 1960s or before 29 (2.9) 1.43 (0.95, 2.16) 35 (3) 1.34 (0.91, 1.99) 145 (1.6) 162 (1.6) 32 Missing 24 121 138 Time delay between the HPEE and washing with soap and water 1.01 (0.16); Ref No HPEE 7988 (85.4) 805 (79.9) Ref 8458 (84.7) 929 (78.7) 612 (6.5) 82 (8.1) 1.47 (1.15, 1.88) 687 (6.9) 96 (8.1) 1.40 (1.11, 1.77) (0.71, 3.65) <30 min 30-59 29 (2.9) 1.27 (0.85, 1.89) 256 (2.6) 39 (3.3) 226 (2.4) 1.31 (0.93, 1.85) 280 (3) 37 (3.7) 1.23 (0.86, 1.75) 308 (3.1) 49 (4.2) 1.40 (1.01, 1.92) 1-3 hours 36 (3.6) 1.98 (1.36, 2.87) 188 (1.9) 4-6 hours 166 (1.8) 46 (3.9) 2.10 (1.50, 2.95) 86 (0.9) 18 (1.8) 1.96 (1.17, 3.3) 94 (0.9) 21 (1.8) >6 hours 1.75 (1.06, 2.88) 51 55 6 Missing 5 Exposure route<sup>b</sup> No HPEE 7988 (85.1) Ref Ref 1.00 (0.15); 805 (79.8) 8458 (84.4) 929 (78.5) Respiratory/ 492 (5.2) 70 (6.9) 1.34 (1.03, 1.75) 564 (5.6) 100 (8.5) 1.52 (1.21, 1.91) (0.76, 1.94)digestive tract Dermal only 906 (9.7) 134 (13.3) 1.54 (1.26, 1.88) 1000 (10) 154 (13) 1.47 (1.22, 1.78) Missing 23 3 24 3

Table S4: Sensitivity analyses on HPEEs reported at enrollment (1993-1997) in relation to self-reported OI in 2013-2015 – excluded farmers who reported taste or smell changes at enrollment and using inverse probability weights

Abbreviations: HPEE: high pesticide exposure event; OI: olfactory impairment. All models included age, sex, state, education, marital status, smoking status, alcohol consumption, and head injury. Analyses 1 excluded farmers who reported taste or smell changes at enrollment; and analyses 2 used inverse probability weighing to account for potential loss to follow-up <sup>a</sup>Distribution of inverse probability weights

<sup>b</sup> Participants with a history of HPEE were classified as having respiratory or gastrointestinal tract exposure if they reported that they breathed fumes or ingested or swallowed the pesticide during the HPEE event, regardless of whether they might also have had dermal exposure. Participants were classified as having only dermal exposure if they reported exposure of the head and/or face, arms, hands, cheek/back/abdomen, groin area, legs, or feet, but did not report breathing fumes or ingesting/swallowing the pesticide

Table S5: Adjusted odds ratios (95% CI) for self-reported olfactory impairment (OI) in 2013–2015 in association with highest exposure high pesticide exposure event (HPEE) at enrollment (1993–1997) defined by time delay between the HPEE and washing with soap and water, stratified by exposure route, relative to OI in farmers without any history of HPEE at enrollment

Respiratory or digestive tract <sup>c</sup>	No OI, n (%)	OI, n (%)	OR (95% CI)
No HPEE	8458 (94.1)	929 (90.5)	Ref
<30 min	159 (1.8)	30 (2.9)	1.82 (1.21, 2.72)
30-59	86 (1)	14 (1.4)	1.35 (0.76, 2.40)
1-3 hours	140 (1.6)	20 (1.9)	1.16 (0.72, 1.87)
4-6 hours	83 (0.9)	21 (2)	2.07 (1.26, 3.39)
> 6 hours	62 (0.7)	13 (1.3)	1.79 (0.98, 3.30)
Missing <sup>b</sup>	34	2	
Dermal only <sup>c</sup>			
No HPEE	8458 (89.5)	929 (85.9)	Ref
<30 min	522 (5.5)	65 (6)	1.26 (0.96, 1.65)
30-59	169 (1.8)	25 (2.3)	1.42 (0.93, 2.18)
1-3 hours	167 (1.8)	29 (2.7)	1.58 (1.05, 2.37)
4-6 hours	104 (1.1)	25 (2.3)	2.09 (1.34, 3.27)
> 6 hours	32 (0.3)	8 (0.7)	2.12 (0.96, 4.66)
Missing <sup>b</sup>	6	2	
Missing information on exposure	<b>,</b> <sup>b</sup>		27

Abbreviations: HPEE: high pesticide exposure event; OI: olfactory impairment; OR: odds ratio; CI: confidence interval

<sup>a</sup> Adjusted for age (continuous variable), sex, state, education, marital status, smoking status, alcohol consumption, and head injury <sup>b</sup> Numbers with missing data among those who reported an HPEE

<sup>c</sup> Participants with a history of HPEE were classified as having respiratory or gastrointestinal tract exposure if they reported that they breathed fumes or ingested or swallowed the pesticide during the HPEE event, regardless of whether they might also have had dermal exposure. Participants were classified as having only dermal exposure if they reported exposure of the head and/or face, arms, hands, cheek/back/abdomen, groin area, legs, or feet, but did not report breathing fumes or ingesting/swallowing the pesticide