

Association between organophosphates and hay fever (NHANES 2005–2006): cross-sectional study

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Document version

Version	Alterations
01	Initial version

1 ABBREVIATIONS

- CI: confidence interval
- NHANES: National Health and Nutrition Examination Survey
- OP: Organophosphate
- OR: odds ratio
- SD: standard deviation

2 CONTEXT

This analysis is based on the 2005–2006 cohort of the NHANES study (Curtin, 2012), which is a nation-wide representative sample for the US population.

2.1 Objectives

To evaluate the association between exposure to organophosphates and hay fever in the US population.

3 METHODS

The data procedures, design and analysis methods used in this report are fully described in the annex document **SAP-2023-033-CM-v01**.

This analysis was performed using statistical software R version 4.3.0.

4 RESULTS

4.1 Study population and follow up

After the cleaning procedures the final sample included in the analysis had N = 2756 participants representing a population of 267,353,268.

Participant characteristics are shown in Table 1. The epidemiological profile can be summarized as participants having an average age of 39 years, and 51% were female. Whites were the majority with 69% of the sample.

An estimated total of 28,681,160 people had hay fever in the last 12 months (95% CI: 23,948,127 to 33,414,193 people). This translates to a prevalence of 10.8% (95% CI: 9.0% to 12.5%). Prevalences stratified by OP can be seen in the Appendix (Figure A2).

Table 1 Demographic characteristics of the participants, exposure to OP and occurrence of hay fever.

Characteristic	N ¹	N = 267,353,268
Age (years), Mean (SD)	267,353,268	39 (21)
Gender, n (%)	267,353,268	
Male		130,272,501 (49%)
Female		137,080,767 (51%)
Ethnicity, n (%)	267,353,268	
Non-Hispanic White		183,272,611 (69%)
Non-Hispanic Black		32,605,907 (12%)
Mexican American		23,895,586 (8.9%)
Other Hispanic		10,743,190 (4.0%)
Other Race - Including Multi-Racial		16,835,974 (6.3%)
Doctor told have hay fever, n (%)	266,354,668	28,681,159.9 (10.8%)

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Characteristic	N ¹	N = 267,353,268
(Missing)		998,599
Dimethylphosphate, n (%)	261,877,943	165,925,002.3 (63.4%)
(Missing)		5,475,325
Diethylphosphate, n (%)	261,877,943	181,644,463.1 (69.4%)
(Missing)		5,475,325
Dimethylthiophosphate, n (%)	261,638,434	76,945,352.4 (29.4%)
(Missing)		5,714,834
Diethylthiophosphate, n (%)	261,859,922	188,479,199.4 (72.0%)
(Missing)		5,493,346
Dimethyldithiophosphate, n (%)	261,877,943	212,389,421.6 (81.1%)
(Missing)		5,475,325
Diethyldithiophosphate, n (%)	238,981,398	237,933,405.0 (99.6%)
(Missing)		28,371,870

¹N not Missing

4.2 Effect of organophosphates in hay fever

A total of N = 2410 complete cases were available in the sample for analysis, representing a population of N = 237,725,268 inhabitants.

The base OR for the sample was OR = 0.15, that represents the basal chance of someone having hay fever without exposure to any OP, and reference categories for other variables (male, white and before adding the cumulative effect of age).

Out of the six OP evaluated, only one was associated with hay fever (Table 2). After adjusting for age, sex and ethnicity, participants exposed to Diethylphosphate had an increased risk of also reporting a positive diagnosis of hay fever with an OR of 1.88 (95% CI 1.16, 3.04; p=0.010).

Table 2 Effect of organophosphates in hay fever.

Characteristic	OR ¹	95% CI ¹	p-value
Dimethylphosphate	1.00	0.65 to 1.54	0.995
Diethylphosphate	1.88	1.16 to 3.04	0.010
Dimethylthiophosphate	0.96	0.61 to 1.52	0.867
Diethylthiophosphate	1.13	0.72 to 1.77	0.607
Dimethyldithiophosphate	0.63	0.38 to 1.03	0.068
Diethyldithiophosphate	0.35	0.03 to 3.78	0.387
Age (years)	1.01	1.01 to 1.02	<0.001
Gender			
Male	—	—	
Female	1.69	1.15 to 2.49	0.008
Ethnicity			
Non-Hispanic White	—	—	

Characteristic	OR ¹	95% CI ¹	p-value
Non-Hispanic Black	0.55	0.36 to 0.84	0.005
Mexican American	0.22	0.12 to 0.40	<0.001
Other Hispanic	0.33	0.07 to 1.51	0.154
Other Race - Including Multi-Racial	0.83	0.35 to 1.94	0.662

¹OR = Odds Ratio, CI = Confidence Interval

From a descriptive perspective, some OP appear less likely to be present with a hay fever diagnosis. Those include Dimethyldithiophosphate with an OR of 0.63 (95% CI 0.38, 1.03; $p=0.068$) and Diethyldithiophosphate with an OR of 0.35 (95% CI 0.03, 3.78; $p=0.387$), but those effects were not strong enough to be significant. Given the large power of the NHANES sample the null hypothesis cannot be rejected.

5 OBSERVATIONS AND LIMITATIONS

Assumptions about the exposures

The data for the exposure to OP originated in laboratory assays, which ensure the validity of those measurements. On the other hand those exposures measure a single event during the two-years period used here.

For the purpose of interpretation of the results of this analysis it is assumed that participants make frequent use of those insecticides, thus having chronic exposure to these compounds. This assumption could imply a risk of information bias if many participants had a single event of exposure coinciding with the data collection by NHANES staff. The assumption can be interpreted as the number of participants in the sample having only such acute exposures being small or negligible.

Recommended reporting guideline

The adoption of the EQUATOR network (<http://www.equator-network.org/>) reporting guidelines have seen increasing adoption by scientific journals. All observational studies are recommended to be reported following the STROBE guideline (von Elm et al, 2014).

6 CONCLUSIONS

After adjusting for age, sex and ethnicity, participants exposed to Diethylphosphate had an increased risk of also reporting a positive diagnosis of hay fever.

7 REFERENCES

- **SAP-2023-033-CM-v01** – Analytical Plan for Association between organophosphates and hay fever (NHANES 2005–2006): cross-sectional study
- Curtin LR, Mohadjer L, Dohrmann S, et al. The National Health and Nutrition Examination Survey: Sample design, 1999–2006. National Center for Health Statistics. Vital Health Stat 2(155). 2012.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg. 2014 Dec;12(12):1495-9 (<https://doi.org/10.1016/j.ijsu.2014.07.013>).

8 APPENDIX

8.1 Exploratory data analysis

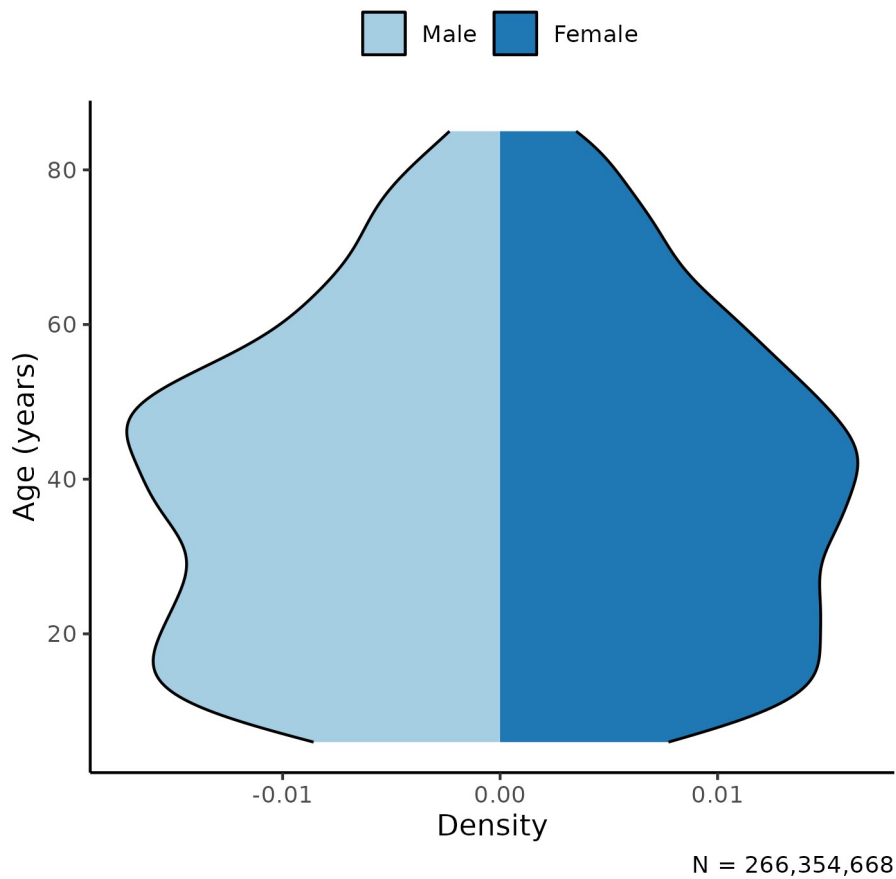
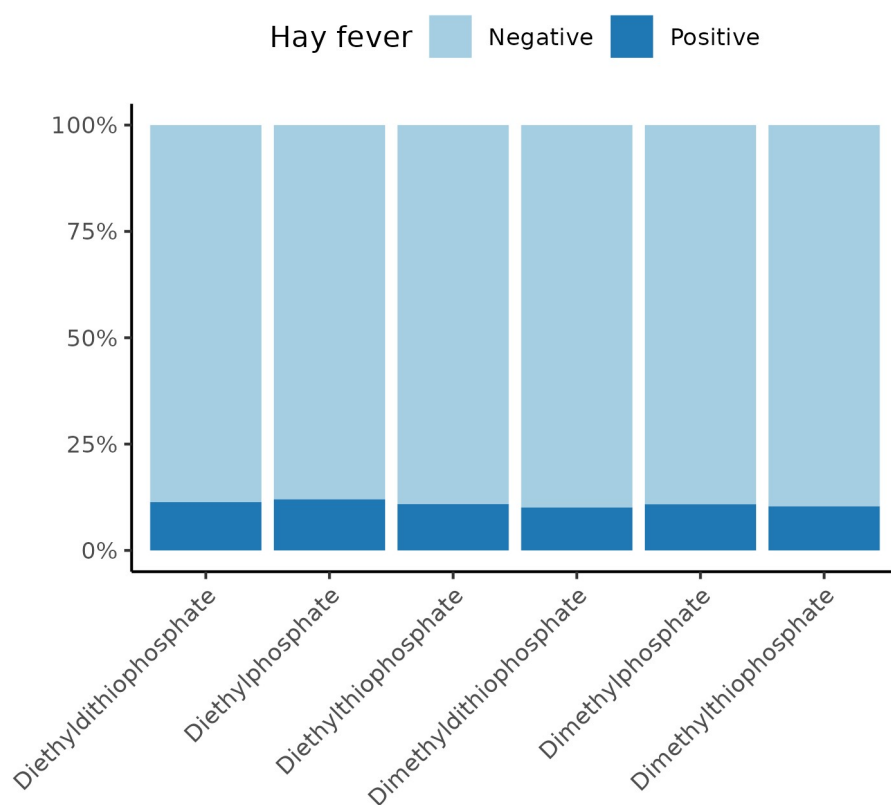


Figure A1 Distribution of age in the study population.

Statistical Analysis Report (SAR)



N = 266,354,668

Figure A2 Prevalence of hay fever by organophosphates.

8.2 Availability

All documents from this consultation were included in the consultant's Portfolio.

The portfolio is available at:

<https://philsf-biostat.github.io/SAR-2023-033-CM/>

8.3 Analytical dataset

Table A1 shows the structure of the analytical dataset.

Table A1 Analytical dataset structure

id	outcome	WTSC2YR	SDMVSTRA	RIDAGEYR	RIAGENDR	RIDRETH1	URDOP1LC	URDOP2LC	URDOP3LC	URDOP4LC	URDOP5LC	URDOP6LC
1												
2												
3												
...												
N												

Due to confidentiality the data-set used in this analysis cannot be shared online in the public version of this report.