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ORGANOPHOSPHATE PESTICIDE EXPOSURE AND RISK OF SARS-CoV-2 INFECTION

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Abstract

Several studies have reported immune modulation by organophosphate (OP) pesticides, but the relationship between OP exposure and SARS-CoV-2 infection is yet to be studied. We used two different measures of OP pesticide exposure (urinary biomarkers (N=154) and residential proximity to OP applications (N=292)) to examine the association of early-childhood and lifetime exposure to OPs and risk of infection of SARS-CoV-2 using antibody data. Our study population consisted of young adults (ages 18 to 21 years) from the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study, a longitudinal cohort of families from a California agricultural region. Urinary biomarkers reflected exposure from *in utero* to age 5 years. Residential proximity reflected exposures between in utero and age 16 years. SARS-CoV-2 antibodies in blood samples collected between June 2022 and January 2023 were detected via two enzyme linked immunosorbent assays, each designed to bind to different SARS-CoV-2 antigens. We performed logistic regression for each measure of pesticide exposure, adjusting for covariates from demographic data and self-reported questionnaire data. We found increased odds of SARS-CoV-2 infection among participants with higher urinary biomarkers of OPs *in utero* (OR=1.94, 95% CI: 0.71, 5,58) and from age 0–5 (OR=1.90, 95% CI: 0.54, 6.95).

Keywords

Organophosphate pesticides; SARS-CoV-2; immune system; long-term exposure

1. INTRODUCTION

The COVID-19 pandemic has provided some evidence that exposure to chemicals in the environment may impact SARS-CoV-2 infection and disease outcome.[1–9] Several studies have found associations between increased exposure to air pollution and risk of disease or death from SARS-CoV-2, potentially due to impaired function of immune cells and increased inflammation.[2–5] For example, a study of traffic-related air pollution across Los Angeles county neighborhoods found that regions with higher levels of NO_2 were associated with higher COVID-19 incidence and mortality.[2] Large-scale studies in the United States and England validated this relationship, in addition to observing associations with ozone

(O_3) and fine particulate matter (PM2.5).[3,4] A study based in Queens, NY, found an increase in transmission of the SARS-CoV-2 virus in areas with high levels of O_3.[5] Other environmental pollutants have also been linked to immune dysregulation and increased risk of SARS-CoV-2 infection. Higher serum concentrations of certain toxic metals have been associated with increased risk of SARS-CoV-2 infection and greater severity of disease.[6] Per- and polyfluoroalkyl substances (PFAS) have been associated with COVID-19 risk in some studies[7] but not others.[8] A prospective cohort study in Barcelona, Spain found that biomarker levels of the pesticide, DDE, and the metals, lithium, and gold, were associated with increased risk of COVID-19 and SARS-CoV-2 infection.[9] Until now, no studies have examined the role of exposure to current-use pesticides on risk of SARS-CoV-2 infection.

Organophosphate (OP) pesticides are synthetic compounds that function as insecticides primarily by inhibition of acetylcholinesterase, an enzyme important for neurotransmitter function.[10] Epidemiologic and toxicologic evidence suggests that OP pesticides may contribute to immune suppression and susceptibility to infectious diseases.[11] Examples of direct and indirect immunotoxic effects include alteration of cytokine levels in response to infection, alteration of lymphocytic cholinergic signaling, impairment of T-cell function, and effects on antibody production/levels.[11] Each of these are important for immune regulation, and their modulation can increase susceptibility to infectious diseases. Developing fetuses and children may be particularly susceptible to the effects of exposure to OPs, as exposure has been linked to impaired immune function, causing increased frequency of infections that could persist into adulthood.[12] OPs have been found to interact with key components of the immune system that play a role in SARS-CoV-2 infection *in vitro*,[1,13–17] including angiotensin converting enzyme-2 (ACE-2) receptor, which is a key component in the cell entry mechanism of SARS coronaviruses, including SARS-CoV-2.[14,15]

In the previous decade, OP pesticides accounted for 10% of the insecticides used, though they are applied to 65% of insecticide-treated crops in the United States.[18] The general population is not typically exposed to high levels of OP pesticides, but farmworkers are among those with the highest exposure.[19,20] In addition to direct exposure during field work, OP particulates can be carried home on clothing and may be a source of exposure for other members of farmworker families.[21] Diet is also an important source of exposure.[22,23]

People of color, especially those living in low-income areas like farmworker communities, have faced greater incidence and severity of COVID-19 infection.[24–27] This trend aligns with disparities seen in other diseases, both acute and chronic, due to living and work conditions and other socioeconomic factors.[24] Among other potential reasons for this trend, we aimed to test the hypothesis that early life and chronic OP exposure increased risk of infection. We examined whether exposure to OPs *in utero* and in childhood increased risk of SARS-CoV-2 infection among young adults living in a California agricultural community.

2. METHODS

2.1 Participants

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study is a longitudinal cohort study examining the role of pesticides and other

environmental exposures on the health and development of children in a farmworker community. The cohort consists of mother-child dyads living in the Salinas Valley of California, an intensively farmed region that produces most of the salad crops and berries in the United States. Participants enrolled as children in the cohort are now young adults. All were born between 2000 and 2002 to mothers who received prenatal care in the Salinas Valley, qualified for low-income health insurance during pregnancy, spoke either Spanish or English, and were at least 18 years old when their CHAMACOS child was born. Initial recruitment has been described in detail elsewhere [28] Briefly, approximately half the current young adult cohort was enrolled prior to birth (i.e., their mothers were enrolled during pregnancy); these are referred to as CHAM1 youth. The remainder were enrolled at age 9 years old (CHAM2). The CHAM1 portion of the cohort completed study visits twice during pregnancy, at or soon after delivery, and at ages 6 months and 1, 2, 3.5, 5, and 7 years prior to enrollment of the CHAM2 cohort. Starting at age 9 years, both CHAM1 and CHAM2 cohorts completed study visits at 9, 10.5, 12, 14, 16, and 18 years, plus collection of COVID-specific data in years 2021–2022 (described below). Informed written consent was obtained from all participants and the study was approved by the UC Berkeley Office for the Protection of Human Subjects.

2.2 Pesticide exposure assessment.

Pesticide exposure was assessed in two ways: using urinary biomarkers for CHAM1 participants and residential proximity to agricultural OP applications for both CHAM1 and CHAM2 participants.[29]

Dialkyl phosphate (DAP) metabolites were measured in the urine of CHAM1 mothers collected twice during pregnancy (at approximately 13- and 26-weeks gestation) and in the urine of CHAM1 children collected five times during early childhood (at 6 months and 1, 2, 3.5, 5 years).[30] DAPs are non-specific metabolites of OP pesticides to which 80% of all OPs devolve. DAPs were analyzed at the Centers for Disease Control and Prevention (CDC) according to methods described previously.[31] Six DAP metabolites were assessed: dimethylphosphate, dimethylthiophosphate, dimethyldithiophosphate, diethylphosphate, diethylthiophosphate, and diethyldithiophosphate. We imputed metabolite levels below the limit of detection using random imputation based on a log-normal probability distribution using maximum likelihood estimation.[32] Urinary creatinine was assessed separately using a commercially available diagnostic enzyme method (Vitros CREA slides, Ortho Clinical Diagnostics, Raritan, NJ).[30] For each timepoint, total DAPs were calculated as the sum of the six DAP metabolites, expressed as nmol per gram creatinine (nmol/g) to account for urinary dilution. For analyses, a simple average of the two total DAP measurements from mothers during pregnancy was calculated to reflect prenatal exposure. The area under the curve (AUC) for total DAP measurements from the child at ages 6 months – 5 years was calculated to reflect early childhood exposures.[33]

Participants' residential histories were linked with California Pesticide Use Reporting (PUR) data used to estimate CHAM1 and CHAM2 participants' ambient exposure to OP pesticides applied to local agricultural fields. The PUR database includes the amount (in kilograms) of active ingredient applied and application date and location within a 1.6-square km section,

with data available from 2000 through 2017 when this analysis was conducted. Residential history was ascertained using the address recorded at each study visit and parent report of all previous residences at the age 16-year study visit. All residential addresses were geocoded and time-stamped to reflect their span of residence. Participants who did not have historical address data for at least a 10-year span were excluded from 0-to-16-year PUR analyses. The residential history data were combined with PUR data to estimate each participant's cumulative ambient exposure to OP pesticides during three different exposure windows: pregnancy, 0–5 years, and 0–16 years. [34] We examined OP pesticides that were applied within 1km of residence for at least 50% of participants and had at least 30,000 pounds applied annually in the Salinas Valley. These included the following pesticides: acephate, chlorpyrifos, diazinon, malathion, oxydemeton methyl, bensulide, naled, methidathion, disulfoton and dimethoate. Participants' ambient exposure to each pesticide was expressed as kilograms applied within 1 km of the home per year (kg/year), and their overall PUR OP exposure value per developmental period of interest was calculated as the sum of their exposure to the ten specific pesticides measured during that developmental period.

2.3 COVID-19 specific data collection.

Between June 2021 and January 2022, when CHAMACOS young adults ranged in age from 18 to 21 years old, all CHAMACOS mothers and young adult children who were active in the cohort (i.e., had participated at 16-year or 18-year visits) were invited to complete a COVID-specific questionnaire and to provide a dry blood spot (DBS) sample for assessment of SARS-CoV-2 antibodies.

Separate versions of COVID-specific questionnaires were designed for mothers and young adult children. For mothers, questionnaires were administered by phone in the mother's language of choice (usually Spanish). Mothers were asked to report on several household factors, including household density (i.e., number of people divided by number of rooms in the home), family poverty status (based on family income and number of people supported)[35], and whether any children under age 5 lived in the household. Parent-reported values were used because the large majority of young adults lived with their parents during the pandemic, and parents tended to be more knowledgeable about household finances. The young adult version of the questionnaire was designed for self-administration on a phone or tablet computer and was available in English only. Young adults were asked to report on health and occupational factors, including the timing of any previous known SARS-CoV-2 infections, their COVID-19 vaccination status (participants with at least one dose were considered "vaccinated"), and their occupational status and environment (indoor or outdoor work) during the pandemic. Of 571 young adults participating in the CHAMACOS cohort at age 18, 412 completed the COVID-specific questionnaire between June 2021 and January 2022, and 320 provided blood samples for antibody testing. Participants who provided blood samples were similar to those who only answered the COVID-specific questionnaire, except that those who provided a blood sample were more likely to be living with their parents.

For the majority of participants, blood spots were obtained via finger prick using a sterilized lancet and collected on a filter paper collection card (TropBio). For a minority, blood was collected via venipuncture (collected for use in a separate study), and several drops of blood

from the butterfly tubing were transferred to a collection card by the licensed phlebotomist. Collection cards were left to air dry for 3–15 hours before packaging and transfer to UC Berkeley for antibody analysis.

Supernatant eluted from dried blood spot (DBS) cards were tested for both anti-spike (S) and nucleocapsid (N) antibodies to SARS-CoV-2, using enzyme-linked immunosorbent assays (ELISAs) as described in Wong et al.[36] The S antibody response is a specific marker of SARS-CoV-2 infection, but is present both in individuals who have been infected naturally and those who have been vaccinated against SARS-CoV-2 using SARS-CoV-2 S-targeted vaccines. The N antibody response occurs following natural infection but is not present in individuals vaccinated against SARS-CoV-2 S protein. For the purposes of this analysis, SARS-CoV-2 infection was defined based on a combination of measured antibody status and self-reported vaccination and COVID infection history status. Among unvaccinated participants, those positive for S antibodies were considered to have been infected with SARS-CoV-2 (N=53). Among vaccinated participants, those positive for both S and N antibodies were considered to have been infected (N=89). In addition, six participants who did not test positive based on the above criteria were considered to have been infected due to a self-reported history of having tested positive for COVID, under the assumption that the test was correct but anti-SARS-CoV-2 antibodies had waned.

2.4 Data Analysis

Individuals eligible for inclusion in this analysis were young adult participants with SARS-CoV-2 antibody status measured in DBS samples as well as having usable measurements of past OP pesticide exposure (N=320).

OP pesticide exposure was modelled using five separate variables, each modelled continuously: PUR-based ambient exposure estimates for the prenatal period, ages 0–5 years, and ages 0–16 years (kg used within 1 km of the home/year); and urinary DAP metabolite measurements for the prenatal period and from ages 0–5 years (nmol/g creatinine). Sample sizes differ by exposure variable as follows: PUR prenatal (N=292), PUR 0–5 years (N=240), PUR 0–16 years (N=274), DAPs prenatal (N=143), and DAPs 0–5 years (N=117). For multivariate analyses, all OP exposure variables were log-transformed to the log10 scale to reduce influence of outliers. The dependent variable, history of SARS-CoV-2 infection, was modelled as a binary variable (positive/negative).

Logistic regression models were used to estimate the change in the odds of SARS-CoV-2 infection per 10-fold increase in each OP pesticide exposure modelled separately. Covariates were selected based on a directed acyclic graph (DAG). All models adjusted for housing density, poverty status, living with a child under age 5 years, having lived with someone infected with SARS-CoV-2, occupational setting during the COVID-19 pandemic, body mass index (BMI), and maternal education level. Covariates were categorized as shown in Table 1. In sensitivity analyses, PUR-based and DAP exposure markers from the same time periods (prenatal and age 0–5 years) were included together in the same models. We also conducted sensitivity analyses considering the six people who were antibody-negative but reported a positive past Covid test as negative for SARS-CoV-2 infection. All statistical analyses were conducted using R 3.6.3.

3. RESULTS

The study population was largely Latino (97.6%) and ranged in age from 19–21 years, with 43.1% of participants below the poverty line and 48.0% living in crowded housing conditions (>1 person per room) (Table 1). Overall, 64.6% had received at least one dose of a COVID-19 vaccine.

We identified 148 (49.8%) past SARS-CoV-2 infections out of 192 vaccinated and 105 unvaccinated individuals. We found that 131 people were positive for both S and N antibodies (vaccinated n = 89, unvaccinated n = 42); all were considered previously infected. We found that 101 vaccinated people and 11 unvaccinated people were positive for S antibodies only; of these, only the unvaccinated people were considered to have been previously infected.

Table 2 shows the pesticide exposure levels of the participants as measured by 1) the amount of OPs applied within 1 km of the home and 2) DAP concentrations measured in maternal and child urine.

We found that each 10-fold increase in DAP concentrations during pregnancy and during the first 5 years of life was associated with an almost doubling of odds of SARS-CoV-2 infection, although these findings were not statistically significant (Table 3). Conversely, each 10-fold increase in OP pesticide used within 1 km of the home between birth and age 16 years was marginally associated with a 50% decrease in the odds of SARS-CoV-2 infection. Associations between childhood DAP concentrations and odds of infection did not change meaningfully when residential OP exposure or prenatal DAP exposure were added into the model (not shown). Of the covariates, only living with someone with a known infection was significantly associated with risk of SARS-CoV-2 infection (not shown).

4. DISCUSSION

Unlike what has been previously reported for traffic-related air pollution and other environmental toxicants, our analysis did not find a clear relationship between prenatal or lifetime exposure to OP pesticides and odds of SARS-CoV-2 infection among young adults in a California farmworker community. We found an almost doubling of risk associated with DAP urinary concentrations of the mother during pregnancy and the child during early life; however models were limited by small sample size and these findings were not statistically significant. We also saw a marginal protective association with OP use around the home between ages 0–16 years.

We found the test positivity for SARS-CoV-2 was 48.6% in our study population, which was higher than for California as a whole from June 2021 to January 2022, when the total number of cases was about one third of the population, much higher than the number of cases found in the East Bay COVID-19 study which used the same DBS ELISA method.[37,38] This trend is consistent with a previous study conducted in this community that found a higher test-positive rate in the farmworker population in Monterey County in comparison to non-farmworkers.[39] Another study of farmworkers in this area found numerous risk factors associated with COVID-19 cases, including lower education level,

speaking an indigenous language, working in the fields, exposure to COVID-19 cases, living in crowded housing, having young children or unrelated roommates, and having a high BMI or diabetes.[40] Many of these conditions were controlled for in our analysis. Our use of a combination of self-reported data and antibody data allowed us to identify individuals who may not have known they were previously infected, as well as identify people who had previously tested positive but whose antibodies had become undetectable by our antibody test.

Substantial epidemiologic and toxicologic evidence suggests that pesticides, including organophosphates (OPs) such as chlorpyrifos and malathion, can impact immunologic suppression and increase susceptibility to infectious diseases. [41–43] Studies have found associations between OP exposure and immune system-related negative health outcomes, such as increased risk of developing arthritis.[44] Long-term exposure to OPs have been shown to interact with the immune system on several levels, including increasing levels of the inflammatory cytokine interleukin-6 (IL-6)[1] which could have implications on the upregulation of the ACE-2 receptor, the cell surface protein used by SARS-CoV-2 for viral entry into the.[15] Increased levels of the ACE-2 receptor in epithelial cells would allow for greater chance of infection and proliferation of the SARS-CoV-2 virus if upregulated by IL-6 via OP exposure. An *in vitro* study showed that OPs have a similar effect on upregulation of the ACE-2 receptor on cells, and together, IL-6 and OP co-exposure led to increased epithelial cell apoptosis when exposed to SARS-CoV-2, suggesting a potential relationship between OPs and the molecular pathway of SARS-CoV-2.[1] These findings raised the hypothesis that OP exposure could also play a role in risk of SARS-CoV-2 infection in a population with high OP exposure and high disease risk, like farmworker communities. Our study provided us the opportunity to examine this mechanism *in vivo*, providing some evidence that OP exposure *in utero* and up to age 16 increased risk of SARS-CoV-2 infection at age 19–21.

Our study's access to lifetime pesticide exposure data and the ability to test antibodies to directly infer SARS-CoV-2 infection provided a unique opportunity to conduct this analysis. No other known studies like this have been published to date. We used two complementary methods of measuring pesticide exposure over multiple timepoints throughout the participants' lifetimes. Despite the strengths of our study, a limitation is the relatively small sample size. We lacked power to detect an association with risk of SARS-CoV-2 infection, though the effect estimates associated with early life urinary DAP levels were almost doubled. We also did not account for genetic variability in paraoxonase (PON1), an enzyme that catalyzes hydrolysis of OP metabolites and impacts and individual's susceptibility to OPs.[45] Future studies examining the effects of OPs on populations should take PON1 activity and genotype into consideration. Additionally, although we were able to examine pesticide exposure for many timepoints, we did not have the ability to examine concurrent exposure at the time of infection.

During the height of the pandemic, farmworkers were especially at risk for COVID-19 due to their status as essential workers, requiring them to continue to go to their workplace while many other Americans were able to shelter in place. Despite working outdoors, they often ride on crowded buses to their workplace, work in close proximity to one another, and are

much more likely to live in poor-quality, overcrowded housing. [40] Though there were efforts to secure millions of face masks and develop mass vaccination clinics for this population, farmworkers had poorer access to preventive measures in large part because they are more likely to be undocumented and uninsured, limiting healthcare services afforded to them.[46,47] These factors can contribute to increased risk of poor health outcomes, including respiratory infection.

In conclusion, early-childhood and long-term OP exposure were not significantly associated with increased risk of infection of SARS-CoV-2 in our study, although the small study size limited power to detect an association. Future research examining this relationship should explore how concurrent and/or acute exposure to OPs may affect risk of infection, as *in vitro* studies suggest potential interactions between OPs and mechanisms of the immune system associated with SARS-CoV-2 pathogenesis.

REFERENCES

1. Mondal A et al. Environmental organophosphate co-exposure in pre-existing systemic inflammation can Increase susceptibility to SARS-COV-2 infection in human lung epithelial cells. The FASEB Journal 35, (2021).
2. Lipsitt J et al. Spatial analysis of COVID-19 and traffic-related air pollution in Los Angeles. Environ Int 153, 106531 (2021). [PubMed: 33812043]
3. Liang D et al. Urban Air Pollution May Enhance COVID-19 Case-Fatality and Mortality Rates in the United States. Innovation (Camb) 1, 100047 (2020). [PubMed: 32984861]
4. Travaglio M et al. Links between air pollution and COVID-19 in England. Environ Pollut 268, 115859 (2021). [PubMed: 33120349]
5. Adhikari A & Yin J Short-Term Effects of Ambient Ozone, PM2.5, and Meteorological Factors on COVID-19 Confirmed Cases and Deaths in Queens, New York. International Journal of Environmental Research and Public Health 17, 4047 (2020). [PubMed: 32517125]
6. Domingo JL & Marquès M The effects of some essential and toxic metals/metalloids in COVID-19: A review. Food Chem Toxicol 152, 112161 (2021). [PubMed: 33794307]
7. Nielsen C & Jöud A Susceptibility to COVID-19 after High Exposure to Perfluoroalkyl Substances from Contaminated Drinking Water: An Ecological Study from Ronneby, Sweden. Environ Res 18(20), 10702 (2021).
8. Pumarega J et al. Prepandemic personal concentrations of per- and polyfluoroalkyl substances (PFAS) and other pollutants: Specific and combined effects on the incidence of COVID-19 disease and SARS-CoV-2 infection. Environ Res 237, 116965 (2023). [PubMed: 37652221]
9. Porta M et al. Individual blood concentrations of persistent organic pollutants and chemical elements, and COVID-19: A prospective cohort study in Barcelona. Environ Res 223, 115419 (2023). [PubMed: 36740154]
10. Trang A & Khandhar PB Physiology, Acetylcholinesterase. in StatPearls (StatPearls Publishing, 2022).
11. Rajak P et al. Immunotoxic role of organophosphates: An unseen risk escalating SARS-CoV-2 pathogenicity. Food Chem Toxicol 149, 112007 (2021). [PubMed: 33493637]
12. Raanan R et al. Early-life exposure to organophosphate pesticides and pediatric respiratory symptoms in the CHAMACOS cohort. Environ Health Perspect 123, 179–185 (2015). [PubMed: 25369257]
13. Simpson RJ, Hammacher A, Smith DK, Matthews JM & Ward LD Interleukin-6: structure-function relationships. Protein Sci 6, 929–955 (1997). [PubMed: 9144766]
14. Hamming I et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 203(2), 631–637 (2004) [PubMed: 15141377]

15. Beyerstedt S, Casaro EB & Rangel ÉB COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection. Eur J Clin Microbiol Infect Dis 40, 905–919 (2021). [PubMed: 33389262]
16. Bhaskar S et al. Cytokine Storm in COVID-19-Immunopathological Mechanisms, Clinical Considerations, and Therapeutic Approaches: The REPROGRAM Consortium Position Paper. Front Immunol 11, 1648 (2020). [PubMed: 32754159]
17. Zanza C et al. Cytokine Storm in COVID-19: Immunopathogenesis and Therapy. Medicina 58, (2022).
18. Miodovnik A Prenatal Exposure to Industrial Chemicals and Pesticides and Effects on Neurodevelopment. in Encyclopedia of Environmental Health (Second Edition) (ed. Nriagu J.) 342–352 (Elsevier, 2019). doi:10.1016/B978-0-12-409548-9.11008-5.
19. García-García CR et al. Occupational pesticide exposure and adverse health effects at the clinical, hematological and biochemical level. Life Sci 145, 274–283 (2016). [PubMed: 26475762]
20. Huen K et al. Organophosphate pesticide levels in blood and urine of women and newborns living in an agricultural community. Environmental research 117, 8 (2012). [PubMed: 22683313]
21. Bradman A et al. Pesticide exposures to children from California's Central Valley: results of a pilot study. J Expo Anal Environ Epidemiol 7, 217–234 (1997). [PubMed: 9185013]
22. Hyland C et al. Organic diet intervention significantly reduces urinary pesticide levels in U.S. children and adults. in Environmental Research 171 568–575 (2019). [PubMed: 30765100]
23. Bradman A et al. Effect of Organic Diet Intervention on Pesticide Exposures in Young Children Living in Low-Income Urban and Agricultural Communities. Environ Health Perspect 123, 1086–1093 (2015). [PubMed: 25861095]
24. Matthew O, Monaghan PF & Luque JS The Novel Coronavirus and Undocumented Farmworkers in the United States. New Solut 31, 9–15 (2021). [PubMed: 33517834]
25. Gu T et al. Characteristics Associated With Racial/Ethnic Disparities in COVID-19 Outcomes in an Academic Health Care System. JAMA Netw Open 3, e2025197 (2020). [PubMed: 33084902]
26. Tai DBG, Shah A, Doubeni CA, Sia IG & Wieland ML The Disproportionate Impact of COVID-19 on Racial and Ethnic Minorities in the United States. Clin Infect Dis 72, 703–706 (2021). [PubMed: 32562416]
27. Lusk JL & Chandra R Farmer and farm worker illnesses and deaths from COVID-19 and impacts on agricultural output. PLOS ONE 16, e0250621 (2021). [PubMed: 33909685]
28. Hyland C et al. Associations between pesticide mixtures applied near home during pregnancy and early childhood with adolescent behavioral and emotional problems in the CHAMACOS study. Environmental Epidemiology, 5, (2021).
29. Pesticide Use Reporting (PUR). California Department of Pesticide Regulation https://www.cdpr.ca.gov/docs/pur/purmain.htm.
30. Bradman A et al. Organophosphate urinary metabolite levels during pregnancy and after delivery in women living in an agricultural community. Environmental Health Perspective 113, 1802–1807 (2005).
31. Bravo R et al. Quantitation of dialkyl phosphate metabolites of organophosphate pesticides in human urine using GC-MS-MS with isotopic internal standards. J Anal Toxicol 26, 245–252 (2005).
32. Lubin JH, Colt JS, Camann D, et al. Epidemiologic evaluation of measurement data in the presence of detection limits. Environ Health Perspect. 112(17), 1691–6 (2004). [PubMed: 15579415]
33. Sagiv SK et al. Prenatal and Childhood Exposure to Organophosphate Pesticides and Behavior Problems in Adolescents and Young Adults in the CHAMACOS Study. Environmental Health Perspective 131, (2023).
34. California Irrigation Management Information System. California Department of Water Resources https://cimis.water.ca.gov/.
35. Current Population Survey. U.S. Bureau of the Census https://www.census.gov/data/tables/time-series/demo/income-poverty/historical-poverty-thresholds.html.
36. Wong MP et al. Development and Implementation of Dried Blood Spot-Based COVID-19 Serological Assays for Epidemiologic Studies. Microbiology Spectrum 10, (2022).

37. Tracking COVID-19 in California. https://covid19.ca.gov/state-dashboard/.
38. Adams C et al. Health inequities in SARS-CoV-2 infection, seroprevalence, and COVID-19 vaccination: Results from the East Bay COVID-19 study. PLOS Glob Public Health 2(8), (2022).
39. Lewnard JA et al. Prevalence and Clinical Profile of Severe Acute Respiratory Syndrome Coronavirus 2 Infection among Farmworkers, California, USA, June–November 2020. Emerging Infectious Diseases 27, 1330 (2021). [PubMed: 33657340]
40. Mora AM et al. Risk Factors Associated With SARS-CoV-2 Infection Among Farmworkers in Monterey County, California. JAMA Network Open 4, e2124116 (2021). [PubMed: 34524438]
41. Chen D, Zhang Z, Yao H, Cao Y, Xing H, Xu S. Pro- and anti-inflammatory cytokine expression in immune organs of the common carp exposed to atrazine and chlorpyrifos. Pestic Biochem Physiol 114, 8–15 (2014). [PubMed: 25175644]
42. Corsini E, Sokooti M, Galli CL, Moretto A, Colosio C. Pesticide induced immunotoxicity in humans: A comprehensive review of the existing evidence. Toxicology 307, 123–135 (2013). [PubMed: 23116691]
43. Mokarizadeh A, Faryabi MR, Rezvanfar MA, Abdollahi M. A comprehensive review of pesticides and the immune dysregulation: Mechanisms, evidence and consequences. Toxicol Mech Methods 25(4), 258–278 (2015). [PubMed: 25757504]
44. Koureas M, Rachiotis G, Tsakalof A & Hadjichristodoulou C Increased Frequency of Rheumatoid Arthritis and Allergic Rhinitis among Pesticide Sprayers and Associations with Pesticide Use. Int J Environ Res Public Health 14, 865 (2017). [PubMed: 28763046]
45. Costa LG et al. C. Paraoxonase 1 (PON1) as a Genetic Determinant of Susceptibility to Organophosphate Toxicity. Toxicology 307, 115–122 (2013). [PubMed: 22884923]
46. Sandhu NK, Strochlic R, Getz C, Diringer J & Brown PM Health Insurance coverage for Farmworkers in California After the Introduction of the Affordable Care Act: A Mixed-methods Study. Med Care 61, 431–437 (2022). [PubMed: 36729756]
47. COVID 19. Grower Shipper Association of California https://www.growershipper.com/our-work-covid-19.htm.

Table 1 –

Demographic characteristics of study population, CHAMACOS Study, June 2021 – January 2022 (n = 320)

Characteristic	n (%)
Sex	
Male	139 (43.4)
Female	181 (56.6)
Age	
19	143 (44.7)
20	149 (46.6)
21	28 (8.8)
Ethnicity	
White	3 (1.0)
Latino	306 (97.8)
Other	4 (1.3)
Living with parents?	
Yes	281 (87.8)
No	39 (12.2)
Housing density category (people/room)	
<= 0.5	14 (4.4)
0.51 – 1.00	146 (46.1)
1.01 – 1.50	57 (18.0)
>1.51	100 (31.6)
Living in same home as someone infected with SARS-CoV-2	
No/don’t know	212 (66.4)
Yes	107 (33.5)
Living with children <5 years	
Yes	79 (27.0)
No	214 (73.0)
Family poverty status (at age 18 years)	
Below poverty line	135 (44.3)
At or above poverty line	170 (55.7)
Maternal education category	
<= 6^{th} grade	137 (42.8)
7–12^{th} grade	109 (34.1)
>= High school graduate	74 (23.1)
Work location	
Unemployed	113 (40.1)
Works indoors (may also work outdoors)	141 (50.0)
Works outdoors only	28 (9.9)
Body Mass Index (BMI)	
Underweight (<18.5 kg/m^2)	18 (5.8)

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Characteristic	**n (%)**
Normal (18.5–24.9 kg/m^2)	107 (34.4)
Overweight (25–29.9 kg/m^2)	92 (19.6)
Obese (>=30 kg/m^2)	94 (30.2)
Received at least one dose of COVID-19 vaccine	
Yes	192 (64.6)
No	105 (35.4)
History of SARS-CoV-2 infection (based on antibody testing)	
Yes	148 (49.8)
No	149 (50.2)

Table 2 –

Organophosphate pesticide exposure, CHAMACOS Study

	N	Mean ± SD	Percentile			Max
			25th	50th	75th	
OP use in 1 km around home (kg/year)						
Pregnancy	292	233.3 ± 363.8	31.5	121.7	291.9	2774.2
Age 0 – 5 years	240	254.9 ± 283.3	49.7	142.6	390.2	1649.1
Age 0–16 years	274	143.3 ± 149.9	45.1	85.4	194.9	987.7
Urinary DAP metabolites (nmol/g creatinine):						
Pregnancy[*]	143	356.8 ± 520.7	101.4	182.5	404.6	4628.3
Age 0 – 5 years[**]	117	2769.9 ± 3085.4	835.7	1654.9	3222.5	18926.5

[*] Average of up to 2 measures

[**] Area under the curve of up to 5 measures

Table 3 –

Adjusted[1] odds of SARS-CoV-2 infection associated with OP pesticide exposure

	n	Odds ratio	(95% CI)	p-value
OP use near home (PUR):				
Pregnancy	292	1.20	(0.77, 1.90)	0.42
0 – 5 years	240	0.83	(0.46, 1.51)	0.54
0 – 16 years	274	0.53	(0.26, 1.06)	0.07
DAPs:		1.94	(0.71, 5.58)	0.20
Pregnancy (average)	143			
0 – 5 years (AUC)	154	1.90	(0.54, 6.95)	0.32

[1]Models adjusted for housing density, whether participants were living with someone under 5 years of age or infected with SARS-CoV-2, poverty status, maternal education level, occupation setting, and body mass index.