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Serum per- and polyfluoroalkyl substances (PFAS) concentrations and anti-spike SARS-CoV-2 IgG levels following COVID-19 vaccination: A cross-sectional study in three communities with elevated PFAS exposure

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are associated with reduced vaccine immune response, though most observational studies have found no link to COVID-19 vaccine response. Residents of North Carolina's Cape Fear River Basin have elevated serum PFAS levels. We investigated the cross-sectional association between serum PFAS and anti-Spike SARS-CoV-2 IgG (anti-S IgG) levels among COVID-19-vaccinated adults (N = 330) from three communities of the GenX Exposure Study with elevated PFAS. Eligibility criteria included no prior COVID-19 diagnosis and receipt of ≥2 COVID-19 vaccinations, the most recent within 180 days of data collection (June–November 2021). Serum PFAS (liquid chromatography-high resolution mass spectrometry) and anti-S IgG (AdviseDx SARS-CoV-2 IgG II Assay) were measured. For five PFAS with >85 % sample detection, we built general linear models of log-transformed PFAS and anti-S IgG for each community, adjusting for age, sex, and days since last vaccination. Most participants were mid-aged, female, and White. COVID-19 vaccination patterns (i.e., doses, manufacturer) and anti-S IgG levels varied by community. Modest positive and negative estimates of PFAS−anti-S IgG relationships were observed across communities and PFAS. One community (Lower Cape Fear River region) had the largest, and only statistically significant, estimate: 0.31 % (95 % CI: 0.07 %–0.56 %) increase in anti-S IgG per 1 % increase in PFHpS (PFAS with lowest median concentration). We observed no consistent evidence linking higher serum PFAS to lower COVID-19 vaccine response, aligning with prior studies. Assessing PFAS exposure and COVID-19 vaccine response in observational studies is challenging. Longitudinal studies with serial antibody measurements, and vaccine type considerations, might provide additional insight.

1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are a large class of synthetic chemicals manufactured for diverse applications, including consumer products (e.g., outdoor gear, furniture cookware) and fire-fighting foams (Sunderland et al., 2019). When PFAS are released into the environment from chemical manufacturing locations and industrial sites, they can contaminate drinking water near and far from the release location. A main pathway of PFAS exposure is ingestion of contaminated drinking water (Haug et al., 2011). PFAS contamination of North Carolina's (NC's) Cape Fear River was initially documented in 2007 (Nakayama et al., 2007). Subsequently, it was demonstrated that people who consumed drinking water sourced from the Cape Fear River had higher serum concentrations of all historically used PFAS (e.g., perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA)) compared to the U.S. general population (Kotlarz et al., 2020). Similarly, a fluorochemical facility near Fayetteville, NC (Fayetteville Works Plant) emitted PFAS into the air which contaminated the private well waters of nearby residents and discharged PFAS directing into the Cape Fear River, contributing to downriver PFAS drinking water

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contamination (Kotlarz et al., 2024). The GenX Exposure Study was initiated to address the concerns of these communities about the health impacts of PFAS contamination and to characterize exposure to GenX and other PFAS in these populations (Kotlarz et al., 2020; North Carolina State University).

PFAS exposure has been linked to adverse health outcomes, including immunosuppression. In epidemiologic studies, exposure to PFAS prenatally and during childhood has consistently been associated with disruptions in immune response, including lower vaccine-induced antibody concentrations (Rappazzo et al., 2017). Fewer studies have explored the impact of PFAS on immunotoxicity among adults (Chang et al., 2016; National Toxicology Program, 2016; Kielsen et al., 2016). In 2022, the National Academies of Sciences, Engineering, and Medicine Committee on the Guidance on PFAS Testing and Health Outcomes reported finding sufficient evidence of an association between PFAS and decreased vaccine antibody response in children and adults (Committee on the Guidance on, 2022).

With the COVID-19 pandemic came an opportunity to further characterize the potential impact of elevated serum PFAS concentrations on vaccine immune response. At the pandemic's start, SARS-CoV-2 was a novel virus circulating in an immunologically naïve population. However, even early in the pandemic, some populations were beginning to develop a level of immunity through infection and immunization, particularly as rapid development and distribution of COVID-19 vaccines was underway (Pingali et al., 2021). SARS-CoV-2 exposures and vaccine interventions were heterogenous across geographies due to a confluence of factors. For example, widely varied lockdown policies and practices and vaccine roll-out timing influenced SARS-CoV-2 spread within localities (Allcot et al., 2020; Zhao et al., 2021; Dooling et al., 2020, 2021; Do and Frank, 2021). Complicated distribution channels facilitated regional differences in COVID-19 vaccine availability by manufacturer (i.e., Johnson & Johnson, Pfizer, Moderna), type (i.e., viral vector, mRNA), and primary regimen (i.e., single dose, two dose series with booster) (Dooling et al., 2020, 2021; Tradigo et al., 2023; Hall et al., 2024). The resulting immune responses and durations of protection were further affected by an individual's underlying health status and COVID-19 history (Bobrovitz et al., 2023; Serra López-Matencio et al., 2023). Although published studies have reported a range of findings, largely suggestive of no association between serum PFAS levels and COVID-19 vaccine response (Bailey et al., 2023; Hollister et al., 2023; Andersson et al., 2023; Porter et al., 2022), additional studies of PFAS and SARS-CoV-2 antibody response conducted in different PFAS-exposed populations and at different pandemic timepoints are warranted.

As part of the GenX Exposure Study, biological samples and questionnaire data were collected during 2021 from study participants to explore the potential health effects of PFAS, including the impact on immune response to COVID-19 vaccine. Using these data, we evaluated the potential association between serum PFAS concentrations and anti-Spike SARS-CoV-2 IgG (anti-S IgG) serum levels following COVID-19 vaccination. Specifically, we hypothesized that elevated serum PFAS concentrations were associated with lower anti-S IgG serum levels following COVID-19 vaccination. This analysis is based on data collected at GenX Exposure Study events held in the latter half of 2021, following the wide availability of COVID-19 vaccines for adults in the U.S. in Spring 2021. (U.S. Department of Defense).

2. Materials and methods

Study population: This cross-sectional analysis was conducted using questionnaire data and biological specimens from adult GenX Exposure Study participants enrolled June 2021–November 2021, including participants from the following three communities: the Lower Cape Fear River region (LCFRR) of NC's New Hanover and Brunswick counties; the private well community around the Fayetteville Works Plant south of Fayetteville, NC; and the town of Pittsboro, NC. Eligible participants for the GenX Exposure Study were ≥6 years of age, not pregnant, HIV negative, and hepatitis C virus negative. Residency requirements varied by region. In LCFRR and Pittsboro, participants had to have been served by municipal drinking water for at least one 1 year. In the Fayetteville private well community (FPWC), participants had to have lived at an address where the drinking water well was on the list of wells tested for PFAS under order of the NC Department of Environmental Quality. Up to four individuals per household could participate. Additional details of the GenX Exposure Study data collection methods and biological specimen collection and processing methods can be found elsewhere (Kotlarz et al., 2020).

For this cross-sectional analysis, GenX Exposure Study participants who met the following criteria at the time of the study visit were included: 1) ≥ 18 years of age; 2) recipient of at least two COVID-19 vaccinations, with the most recent COVID-19 vaccination received ≤180 days prior; and 3) no history of COVID-19 diagnosis by a healthcare provider (Marziano et al., 2023). We restricted the study population for analysis, as described, to account for known waning immunity following initial vaccination (Menegale et al., 2023), and to minimize confounding by vulnerable life stage (e.g., early childhood) (Committee on the Guidance on, 2022), and neutralizing antibody production as a result of natural infection (Marziano et al., 2023; Muecksch et al., 2021).

Data collection: At data collection events in each community, participants completed a self-administered questionnaire that gathered information on demographic factors (e.g., age, race and ethnicity, sex) and medical history, including autoimmune conditions (i.e., inflammatory bowel disease, systemic lupus erythematosus, multiple sclerosis, Sjögren's syndrome, rheumatoid arthritis) and corticosteroid use in the past 6 months. COVID-19-related information included self-reported vaccination history and self-reported healthcare provider COVID-19 diagnosis. COVID-19 vaccination manufacturer options available in the questionnaire included Pfizer, Moderna, and Johnson & Johnson, in addition to other/unknown manufacturer. In 2021–2022, the primary regimen for the Pfizer product (Pfizer-BioNTech COVID-19 Vaccine) and for the Moderna COVID-19 Vaccine, both mRNA vaccines, was a two dose series followed by a booster dose (U.S. Food and Drug Administration, 2021; Moderna, U.S., 2022). The primary regimen for the Johnson & Johnson product (Janssen COVID-19 Vaccine), a viral vector vaccine, was a single dose. (U.S. Food and Drug Administration, 2023) Therefore, a consequence of restricting the study population to those with at least two COVID-19 vaccinations in this analysis is that participants who received the Johnson & Johnson for their primary series were not included, unless they additionally received at least one dose of a Pfizer or Moderna product.

Non-fasting venous blood samples were collected in red top tubes from participants and allowed to clot at room temperature for up to 1 h before centrifugation and separation of the serum (Kotlarz et al., 2020). Serum samples were transported on dry ice to the Clinical Laboratory Improvement Amendments (CLIA)-approved outpatient laboratory in the East Carolina Heart Institute (ECHI) at ECU Health (Greenville, NC) and subsequently stored at −80° Celsius until PFAS and anti-S IgG testing were performed.

PFAS analysis was conducted at the Molecular Education, Technology and Research Innovation Center (METRIC) at NC State University using a previously published method (Kotlarz et al., 2020; Enders et al., 2022). This method analyzes for a suite of 44 PFAS including chemicals unique to the Cape Fear River Basin. Serum PFAS measurements were conducted using liquid chromatography-high resolution mass spectrometry and reported as nanograms per milliliter (ng/mL). Each serum sample was analyzed using a Thermo Vanquish ultra-performance liquid chromatograph coupled to a Thermo Orbitrap Fusion mass spectrometer.

Serum concentrations of antibodies against SARS-CoV-2 were measured at the ECHI at ECU Health using the anti-S AdviseDx SARS-CoV-2 IgG II Assay (Abbott, Chicago, IL) on the Abbott Architect machine. This binding antibody detection test measures IgG antibodies to

the receptor binding domain of the S1 subunit of the spike (S) protein of SARS-CoV-2; these antibodies are generated as part of the human adaptive immune response following vaccination or natural infection (Abbott; Bradley et al., 2021). The anti-S AdviseDx SARS-CoV-2 IgG II Assay is a semi-quantitative assay with a qualitative interpretation due to cut offs of the negative and positive levels of IgG antibody detection. Semi-quantitative values were reported as arbitrary units (AU) per mL with a manufacturer's suggested cutoff of 50 AU/mL (Abbott). Of note, SARS-CoV-2 antibody testing is not used to diagnosis current SARS-CoV-2 infection, and SARS-CoV-2 antibody levels are not necessarily indicative of the presence or degree of immunity to COVID-19 (Abbott; Centers for Disease Control and Prevention, 2024).

We created a variable, "Days since most recent vaccination" by calculating the difference in days between the date of the participant's study visit and the date of the participant's most recent COVID-19 vaccination. As COVID-19 vaccination dates were available by month and year only, the first day of the month was assumed. If a subsequent vaccination was reported to have occurred the same month and year as a prior vaccination, the date of the subsequent vaccination was assumed based on the manufacturer of that vaccine (i.e., 21 days for Pfizer, 28 days for Moderna).

Statistical analyses. For each of the three GenX Exposure Study communities (i.e., LCFRR, FPWC, Pittsboro) individually, general linear models were used to examine associations between anti-S IgG levels (dependent variable) and each of the following five serum PFAS concentrations, individually (independent variables): PFOS, PFOA, perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), and perfluoroheptane sulfonic acid (PFHpS). These five PFAS were selected for analysis, as they were the only measured PFAS detected in >85 % of samples across all three GenX Exposure Study communities. The Gen X Exposure Study was not designed to evaluate PFAS exposure and immune response to a novel vaccine against a pandemic pathogen. Therefore, considering the likely presence of unmeasured COVID-19-related confounders (e.g., vaccine availability and uptake) that were unique to each of the three communities, we conducted analyses for each community separately. Additionally, for LCFRR only, general linear models were also used to examine the associations between anti-S IgG levels and each of the following two serum PFAS concentrations, individually: perfluoro-3,5,7,9,11-pentaoxadodecanoic acid (PFO5DoA) and perfluoro-2-{[perfluoro-3-(perfluoroethoxy)-2-proanyl]oxy} ethanesulfonic acid (also known as Nafion by-product 2). These two PFAS, unique to the Fayetteville Works Plant, were detected in >70 % of LCFRR participant samples included in this study.

For all analyses, PFAS values below the level of detection were re-expressed as the method reporting limit divided by the square root of two. We assessed correlations among PFAS using Spearman correlation coefficients. Anti-S IgG and PFAS distributions were normalized using a natural log transformation and modeled as continuous variables.

We created a directed acyclic graph (DAG) using DAGitty (Textor et al., 2017) to identify the minimally sufficient adjustment set of confounding variables for estimating the causal effect of PFAS concentration on COVID-19 vaccine response in this study (Supplemental Fig. 1). (Greenland et al., 1999) The identified adjustment set using the DAG included age and sex; in addition to these two covariates, we adjusted for the number of days since most recent COVID-19 vaccination in the final analyses (Agency for Toxic Substances and Disease Registry, 2022). Through additional analyses, we also explored adding a fourth covariate (total number of COVID-19 vaccinations received (i.e., two or three)) to the adjustment set. However, as inclusion of this fourth covariate did not meaningfully impact the adjusted estimates, we ultimately used the three covariate adjustment set of age, sex, and days since most recent COVID-19 vaccination (see supplementary material). Days since most recent vaccination and participant age at the time of data collection were modeled as continuous variables. Each variable in the adjustment set met the criteria outlined by VanderWeele for confounder selection, namely, a cause of the exposure or of the outcome or both, and not an instrumental variable (VanderWeele, 2019).

The reported estimates, with 95 % confidence intervals (CIs), from each individual PFAS regression model represent the percent change in anti-S IgG levels for every 1 % increase in PFAS level. By way of example, a beta of 0.15 is interpreted as follows: For every 1 % increase in PFAS, anti-S IgG increased by an estimated 0.15 %, while holding all other covariates constant in adjusted models. All analyses were conducted in SAS 9.1.4 (Cary, NC).

All participants provided written informed consent to participate. All phases of the study were conducted in compliance with the NC State University Institutional Review Board. This study was conducted under the NC State University Institutional Review Board approval #12229.

3. Results

Of the 374 adult GenX Exposure Study participants from whom data were collected June 2021–November 2021 and had been vaccinated against COVID-19 ≤ 180 days prior to their study visit, 355 (95 %) reported having received at least two COVID-19 vaccinations in total (Fig. 1). Of these 355 participants, 334 (94 %) had no history of COVID-19 diagnosis. SARS-CoV-2 anti-S IgG levels were not detectable in four (1 %) of these 334 participants. Therefore, the final dataset for this analysis included 330 participants across the three communities, as follows: LCFRR (N = 93), FPWC (N = 139), and Pittsboro (N = 98).

LCFRR participants' median age was 55 years (25th – 75th percentiles: 45–66 years), slightly lower than, but comparable to, participants from FPWC (64 years (55–70 years)) and Pittsboro (61 years (44–72 years)) (Table 1). Across all three communities, the participant distributions by sex, race, and presence of autoimmune conditions were similar. Considering all 330 participants, most were female (58 % (N = 192)), White (86 % (N = 285)) and had no history of an autoimmune condition (84 % (N = 278)).

Participant distributions of COVID-19-related variables varied by community. All but one FPWC participant and 57 % (N = 53) of LCFRR participants reported receiving exactly two COVID-19 vaccinations, while 80 % (N = 78) of Pittsboro participants reported receiving three COVID-19 vaccinations (Table 1). Although most LCFRR and Pittsboro participants reported receiving the Pfizer vaccine most recently (79 % (N = 73) and 50 % (N = 49), respectively), 60 % (N = 84) of FPWC participants reported receiving an "other or unknown" vaccine most recently. The community with the highest median (25th – 75th percentiles) anti-S IgG serum level was Pittsboro (17867 AU/mL (5571–50163 AU/mL)), followed by LCFRR (3378 AU/mL (1233–12055 AU/mL) and FPWC (1942 AU/mL (814 − 4954 AU/mL)).

Regarding the five PFAS (i.e., PFOS, PFHxS, PFOA, PFNA, PFHpS) for which data were available from all participants, detection in serum samples ranged from 87 % for PFHpS to ≥97 % for PFOS, PFHxS, and PFOA (Table 2). These five PFAS were moderately to highly correlated, with Spearman correlation coefficients ranging from 0.37 (PFOA and PFHpS in FPWC) to 0.80 (PFOS and PFNA in LCFRR) (Supplemental Table 1). In each community, the PFAS with the highest median participant serum concentration was PFOS. The median (25th – 75th percentiles) PFOS serum concentrations were most elevated in Pittsboro (9.03 ng/mL (5.38 − 13.38 ng/mL)), followed by FPWC (7.50 ng/mL (4.65 − 11.0 ng/mL)) and LCFRR (6.86 ng/mL (3.68 − 12.29 ng/mL)) (Table 2). Compared to LCFRR and FPWC participants, Pittsboro participants had the highest median serum concentrations of all five PFAS. Though, among LCFRR participants the median (25th – 75th percentiles) serum concentrations of PFOA, PFNA, and PFHpS (2.52 ng/mL (1.59 − 4.29 ng/mL), 0.70 ng/mL (0.40 − 1.09 ng/mL), and 0.44 ng/mL (0.13 − 0.74 ng/mL), respectively) were slightly higher than those of PFOA, PFNA, and PFHpS among FPWC participants (2.43 ng/mL (1.46 − 3.45 ng/mL), 0.59 ng/mL (0.35 − 0.89 ng/mL), and 0.43 ng/mL (0.19 − 0.73 ng/mL), respectively).

Regarding PFO5DoA and Nafion byproduct 2, two PFAS found frequently in the LCFRR community only, detection in serum samples

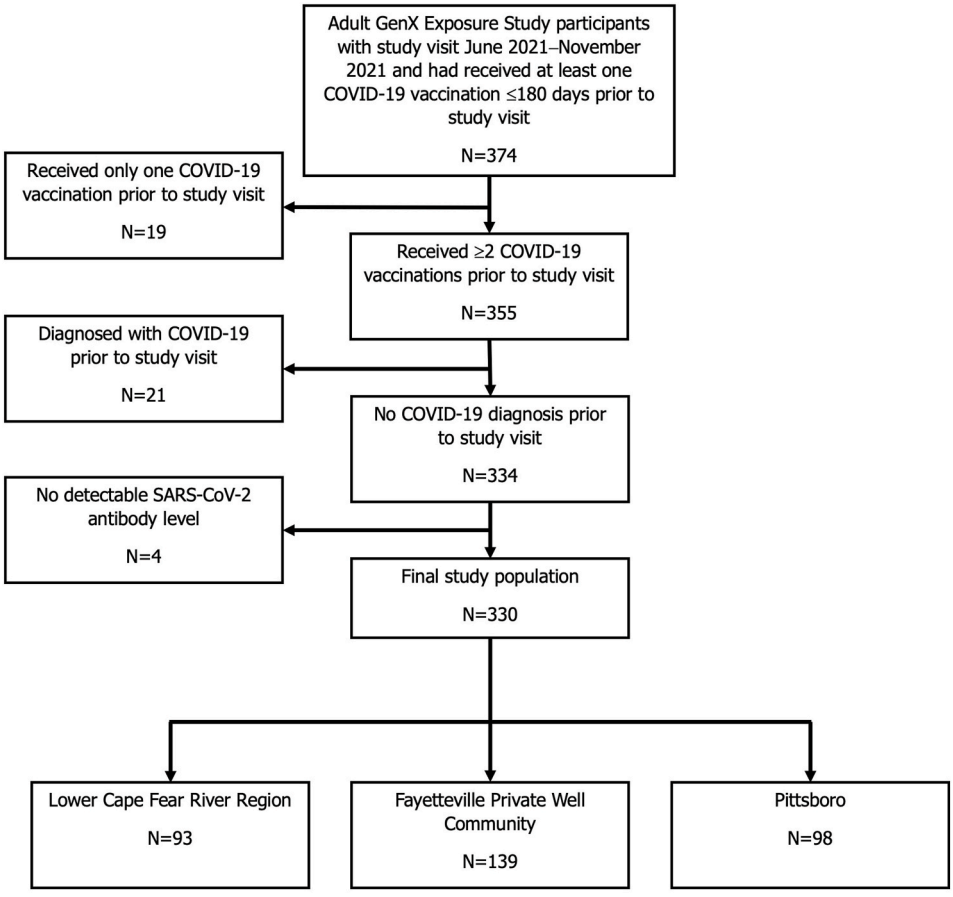

Fig. 1. Derivation of study population from adult GenX Exposure Study participants with a study visit June 2021–November 2021.

was 79 % and 71 %, respectively (Table 2). The Spearman correlation coefficient of 0.80 for PFO5DoA and Nafion byproduct 2 was higher than any individual correlations to the other five PFAS, which ranged from 0.50 (Nafion byproduct 2 and PFHpS) to 0.71 (Nafion byproduct 2 and PFNA) (Supplemental Table 2). Among the median (25th – 75th percentiles) serum concentrations of the seven PFAS measured in LCFRR participant samples, PFO5DoA (3.08 ng/mL (0.65 – 7.53 ng/mL)) was the second highest, following PFOS (6.86 ng/mL (3.68 – 12.29 ng/mL)), while Nafion byproduct 2 (0.17 ng/mL (0.06 – 0.32 ng/mL)) was the lowest (Table 2).

We observed no consistent evidence linking higher serum PFAS to lower COVID-19 vaccine response in any of the three communities. Modest positive and negative estimates of the PFAS–anti-S IgG relationship were observed across communities and by PFAS in unadjusted and adjusted models (Table 3). However, across all three communities the furthest from null – and only statistically significant – estimate was for PFHpS and anti-S IgG levels in LCFRR; specifically, for each 1 % increase in PFHpS among LCFRR participants, anti-S IgG increased by 0.31 % (95 % CI (0.07 % – 0.56 %)), while modeled confounders (i.e., participants' age, sex, and time since most recent COVID-19 vaccination) were held constant. Across the adjusted models, the largest percent decrease in anti-S IgG levels for each 1 % increase in a PFAS was for PFHpS in Pittsboro (−0.16 % (−0.38 % – 0.07 %)). In LCFRR, we observed negative, or inverse, relationships between serum PFO5DoA and Nafion byproduct 2 concentrations, individually, and anti-S IgG levels using adjusted models (Table 3).

Compared to estimates obtained using models adjusted for age, sex, and days since most recent COVID-19 vaccination (Table 3), estimates obtained using models adjusted for age, sex, days since most recent COVID-19 vaccination, and total number of COVID-19 vaccinations received did not differ in directionality or status of statistical significance and were of similar magnitude (Supplementary Table 3).

4. Discussion

Among GenX Exposure Study participants, recruited from three communities (i.e., LCFRR, FPWC, Pittsboro) with elevated PFAS exposure and heterogeneity between timing of COVID-19 vaccination and anti-S IgG level measurement, we observed a mix of positive and negative relationships in cross-sectional analysis between five different PFAS (i.e., PFOS, PFOA, PFHxS, PFNA, PFHpS) and anti-S levels following COVID-19 vaccination. The highest absolute – and only statistically significant – change (percent increase) in anti-S IgG was for PFHpS in LCFRR (0.31 % (0.07 % – 0.56 %). Of note, among the PFAS in this study PFHpS had the lowest median concentration and a relatively narrow interquartile range. Other relationships observed with adjusted models were inconsistent (i.e., some positive, some negative) across the three communities and the five PFAS, were modest overall, and were not statistically significant. Similarly, among LCFRR participants, the relationships between PFO5DoA and Nafion byproduct 2, individually, and anti-S levels following COVID-19 vaccination were negative, modest, and not statistically significant. Considering the recognized association between PFAS and immunotoxicity in children and adults (Rappazzo et al., 2017; Chang et al., 2016; National Toxicology Program, 2016; Kielsen et al., 2016; Committee on the Guidance on, 2022), a negative association between serum PFAS concentrations and COVID-19 vaccine immune response was hypothesized. However, other published studies have largely reported no association, as described in detail below.

Three observational studies of PFAS and immune response, conducted early in the pandemic (e.g., 2020–2022) in adult and adolescent populations with known PFAS exposure, included repeated measures of

Table 1
Self-reported demographic-, COVID-19-, and other health-related characteristics of adult GenX Exposure Study participants meeting analysis criteria[a], by North Carolina study community, 2021 (N = 330).

Characteristic	Lower Cape Fear River Region (N = 93)	Fayetteville Private Well Community (N = 139)	Pittsboro (N = 98)
Age (years) (median (25th; 75th percentile))	55 (45; 66)	64 (55; 70)	61 (44; 72)
Sex at birth (N (%))			
Female	66 (71)	73 (53)	53 (54)
Male	27 (29)	66 (47)	45 (46)
Race (N (%))			
White	81 (87)	115 (83)	89 (91)
Other Race or Multi-racial	12 (13)	24 (17)	9 (9)
Presence of autoimmune condition(s)[b] (N (%))	17 (18)	20 (14)	15 (15)
Corticosteroid use in past 6 months (N (%))	16 (17)	21 (15)	18 (18)
Number of COVID-19 vaccinations received (N (%))			
Two	53 (57)	138 (99)	20 (20)
Three	40 (43)	1 (1)	78 (80)
Manufacturer of most recent COVID-19 vaccination (N (%))			
Moderna	19 (20)	21 (15)	47 (48)
Pfizer	73 (79)	34 (25)	49 (50)
Other or unknown vaccine	1 (1)	84 (60)	2 (2)
Days since most recent COVID-19 vaccination (median (25th; 75th percentile))	137 (44; 176)	121 (86; 146)	44 (43; 74)
Anti-S SARS-CoV-2 IgG serum level (AU/mL) (median (25th; 75th percentile))	3378 (1233; 12055)	1942 (814; 4954)	17867 (5571; 50163)
Natural log of serum anti-S SARS-CoV-2 IgG (AU/mL) (median (25th; 75th percentile))	8.1 (7.1; 9.4)	7.6 (6.7; 8.5)	9.8 (8.6; 10.8)

Arbitrary units (AU).

[a] To be included in this analysis, adult GenX Exposure Study participants 1) must not have been diagnosed with COVID-19 any time before their study visit, and 2) must have received at least two COVID-19 vaccinations (as self-reported), with the most recent received ≤180 days before the study visit.

[b] Inflammatory bowel disease, ulcerative colitis, Crohn's disease, systemic lupus erythematosus, multiple sclerosis, Sjogren's syndrome, rheumatoid arthritis.

COVID-19 vaccine response and reported inconsistent findings. Porter et al. analyzed data from 3M employees and retirees (N = 415) who were vaccinated before enrollment or between enrollment and a 5–6 week follow-up, and within 180 days of vaccination. PFAS were measured at enrollment (April and May of 2021); anti-S IgG and neutralizing antibodies were measured at enrollment and again 5–6 weeks later (Porter et al., 2022). PFOS, PFOA, PFHxS, and PFNA serum concentrations were comparable to those of our study participants. Participants were categorized by antigenic stimulus group based on history of COVID-19 infection, vaccination manufacturer, and number of doses. Across all groups, the median days since antigenic stimulus ranged from 18 to 68, lower than the median (25th − 75th percentiles) days since antigenic stimulus in two of our study communities (LCFRR and FCWR) but similar to Pittsboro. In models adjusted for antigenic stimulus group, age, and other confounders, Porter et al. reported a modest inverse (i.e., negative), but not statistically significant, relationship between anti-S IgG and interquartile difference in serum concentrations of PFOS, PFOA, PFHxS, and PFNA; results were similar for neutralizing antibodies. In a study by Bailey et al., 226 participants from the Michigan PFAS Exposure and Health Study received a standard two-dose COVID-19 vaccination series; immune response was measured on four occasions (pre-vaccination, pre-second vaccination, 1–2 months and 2–3 months after second vaccination). Neither individual PFAS levels, measured at first vaccination, or PFAS mixtures were associated with anti-S IgG (Bailey et al.). Though the median (25th – 75th percentiles) PFOS concentration (9.09 ng/mL (5.25–21.79 ng/mL)) was slightly higher compared to our study participants, concentrations of other PFAS were comparable. Finally, Andersson et al.'s Swedish study, which included 367 participants with known PFAS exposure, assessed the association between anti-S IgG levels (before vaccination, and 5-weeks and 6-months after the two-dose course) and PFAS exposure at each of the following points: 1) current (at first COVID-19 vaccination), 2) historical (2014–2016), and 3) prenatal (determined, when possible, using each participant's mother's home address during pregnancy) (Andersson et al., 2023). This Swedish cohort had much higher median concentrations of PFOS (36 ng/mL) and PFHxS (34 ng/mL) at first COVID-19 vaccination, compared to our study participants, though other PFAS common to both studies were similar. Andersson et al. reported that PFAS exposure did not negatively affect COVID-19 vaccine responses up to 6 months after vaccination.

Three other observational studies of PFAS and SARS-CoV-2 immune response, conducted early in the pandemic and in populations with no known PFAS exposure, have also been published. Beginning in July 2020, Hollister et al. followed a cohort (N = 860), recruited from existing healthcare, emergency response, and essential worker study cohorts in the U.S. Southwest, for 12 months post-vaccination. Participants for this study were randomly selected from among study cohort members who 1) had received two doses of Pfizer-BioNTech, two doses of Moderna mRNA-1273, or one dose of the Johnson & Johnson/Janssen COVID-19 Vaccine; and 2) had no history of SARS-CoV-2 infection at vaccination. They measured binding to the SARS-CoV-2 Spike protein receptor binding domain and to the S2 subunit domain shortly after the primary vaccination series (two-dose or one-dose primary series) and then every 3-months for up to a year. Median PFOS, PFHxS, PFOA, and

Table 2
Serum PFAS concentrations (ng/mL) of adult GenX Exposure Study participants meeting analysis criteria[a], by North Carolina study community, 2021 (N = 330).

	Lower Cape Fear River Region (N = 93)		Fayetteville Private Well Community (N = 139)		Pittsboro (N = 98)	
PFAS[b]	N (%) detect	Median (25th; 75th percentiles)	N (%) detect	Median (25th; 75th percentiles)	N (%) detect	Median (25th; 75th percentiles)
PFOS	93 (100)	6.86 (3.68; 12.29)	139 (100)	7.50 (4.65; 11.0)	98 (100)	9.03 (5.38; 13.38)
PFHxS	90 (97)	2.08 (1.20; 3.17)	138 (99)	2.48 (1.51; 4.00)	97 (99)	2.99 (1.65; 4.09)
PFOA	93 (100)	2.52 (1.59; 4.29)	136 (98)	2.43 (1.46; 3.45)	98 (100)	4.13 (2.43; 6.90)
PFNA	87 (94)	0.70 (0.40; 1.09)	134 (96)	0.59 (0.35; 0.89)	97 (99)	0.93 (0.62; 1.40)
PFHpS	81 (87)	0.44 (0.13; 0.74)	121 (87)	0.43 (0.19; 0.73)	85 (87)	0.50 (0.23; 0.85)
PFO5DoA	73 (79)	3.08 (0.65; 7.53)	.	.	.	.
Nafion byproduct 2	71 (76)	0.17 (0.06; 0.32)	.	.	.	.

Nanograms per milliliter (ng/mL), perfluorooctane sulfonic acid (PFOS), perfluorohexane sulfonic acid (PFHxS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluoroheptane sulfonic acid (PFHpS), perfluorooctanoic acid (PFOA), perfluoro-3,5,7,9,11-pentaoxadodecanoic acid (PFO5DoA), perfluoro-2-{[perfluoro-3-(perfluoroethoxy)-2-proanyl]oxy}ethanesulfonic acid (also known as Nafion by-product 2).

[a] To be included in this analysis, adult GenX Exposure Study participants 1) must not have been diagnosed with COVID-19 any time before their study visit, and 2) must have received at least two COVID-19 vaccinations (as self-reported), with the most recent received ≤180 days before the study visit.

[b] Values less than the level of detection were re-expressed as PFAS concentration divided by the square root of 2.

Table 3
Regression estimates for serum PFAS[a] and anti-S SARS-CoV-2 serum IgG levels[b] among adult GenX Exposure Study participants meeting analysis criteria[c], by North Carolina study community, 2021 (N = 330).

	Lower Cape Fear River Region (N = 93) Estimate[d] (95 % CI)	Fayetteville Private Well Community (N = 139) Estimate[d] (95 % CI)	Pittsboro (N = 98) Estimate[d] (95 % CI)
PFOS			
Unadjusted model	0.43 (0.06, 0.80)	0.04 (−0.28, 0.36)	0.55 (0.08, 1.0)
Adjusted model	0.15 (−0.27, 0.56)	0.23 (−0.10, 0.56)	0.16 (−0.28, 0.61)
PFHxS			
Unadjusted model	0.20 (−0.09, 0.50)	−0.10 (−0.40, 0.19)	0.23 (−0.16, 0.63)
Adjusted model	0.04 (−0.25, 0.34)	−0.03 (−0.33, 0.27)	−0.07 (−0.42, 0.28)
PFOA			
Unadjusted model	0.28 (−0.14, 0.70)	−0.13 (−0.41, 0.14)	0.31 (−0.12, 0.73)
Adjusted model	−0.10 (−0.55, 0.36)	−0.08 (−0.35, 0.19)	0.12 (−0.25, 0.49)
PFNA			
Unadjusted model	0.25 (−0.05, 0.55)	0.06 (−0.23, 0.35)	0.26 (−0.20, 0.72)
Adjusted model	0.06 (−0.25, 0.36)	0.20 (−0.09, 0.49)	0.13 (−0.28, 0.53)
PFHpS			
Unadjusted model	0.29 (0.06, 0.52)	−0.15 (−0.34, 0.05)	0.02 (−0.24, 0.28)
Adjusted model	0.31 (0.07, 0.56)	−0.10 (−0.29, 0.10)	−0.16 (−0.38, 0.07)
PFO5DoA			
Unadjusted model	0.04 (−0.10, 0.18)	.	.
Adjusted model	−0.02 (−0.15, 0.11)	.	.
Nafion byproduct 2			
Unadjusted model	0.02 (−0.23, 0.27)	.	.
Adjusted model	−0.12 (−0.36, 0.12)	.	.

CI: confidence interval; Adjusted model: adjusted for age, sex, and days since most recent COVID-19 vaccination.

[a] Modeled as the natural log of serum PFAS level (nanograms per milliliter).

[b] Modeled as the natural log of SARS-CoV-2 serum IgG level (arbitrary units per milliliter).

[c] To be included in this analysis, adult GenX Exposure Study participants 1) must not have been diagnosed with COVID-19 any time before their study visit, and 2) must have received at least two COVID-19 vaccinations (as self-reported), with the most recent received ≤180 days before the study visit.

[d] Estimate represents the percent change in SARS-CoV-2 IgG serum level for every 1 % increase in the PFAS level, holding all other variables constant, as applicable.

PFNA concentrations, measured in the first sample collected after vaccination, were lower among these participants than our study participants (Hollister et al., 2023). No statistically significant relationship was present between PFAS and peak antibody response after vaccination or between PFAS and antibody-level changes over time after vaccination. In contrast, Kaur et al.'s cross-sectional study beginning in April 2020 reported an inverse relationship of PFAS concentrations and anti-S IgG levels, measured at enrollment, in a cohort of 72 pregnant SARS-CoV-2 anti-S IgG positive women in New York City (Kaur et al., 2023). This cohort included COVID-19-vaccinated and -unvaccinated individuals with a history of SARS-CoV-2 infection. The inverse relationship did not change when the seven vaccinated participants were excluded in sensitivity analysis. Median serum PFAS (PFOS, PFHxS, PFOA, PFNA, PFHpS) concentrations in this cohort were lower than in our study participants. Results of Hollister et al. and Kaur et al. further suggest that, even in populations with no known PFAS exposure, an association between elevated PFAS and reduced COVID-19 vaccine immune response is not consistently apparent. Finally, Timmerman et al. reported no association between serum PFAS concentrations and spike IgG antibody concentrations after SARS-CoV-2 mRNA vaccinations from 2021 in an adult cohort in Denmark (Timmermann et al., 2024). However, those authors also noted that at higher PFAS concentrations, the increase in immune response following the third (booster) vaccination, compared to the response following the second vaccination, was consistently lower.

Studies of PFAS exposure and vaccines against other infectious diseases (i.e., not COVID-19) have characterized initial and longer-term immune response through timed antibody measurements. For example, in the Faroe Islands where frequent seafood consumption has been linked to elevated serum perfluorinated compound (e.g., PFOA, PFOS, PFHxS) concentrations, Grandjean et al. examined tetanus and diphtheria vaccine immune response at age 5 years (pre-booster and 4 weeks post-booster) and at age 7 years in 587 participants (Grandjean et al., 2012). Perfluorinated compound concentrations at age 5 years were negatively associated with the antibody levels at age 5 years (pre-booster and post-booster) and at age 7 years. Among 411 adults with known PFAS exposure in mid-Ohio and West Virginia, Looker et al. measured antibody levels before influenza vaccination and 21 days post-vaccination and reported that elevated PFOA, measured at time of vaccination, was associated with reduced influenza vaccine antibody titer rise (Looker et al., 2014). Stein et al.'s study of 78 healthy adults with no known PFAS exposure explored immune response to intranasal influenza vaccine by measuring antibody response pre-vaccination, 3 days post-vaccination, and 30 days post-vaccination. Their findings did not support an association between higher PFAS concentrations, measured at the first study visit, and reduced immune response to the intranasal vaccine (Stein et al., 2016). Similar to these studies, the COVID-19 vaccine studies described above from Bailey et al. Andersson et al., and Timmerman et al. benefitted from timed SARS-CoV-2 antibody measurements following vaccination, for example assessment of initial immune response (e.g., 1–2 months post-vaccination) and follow-up (e.g., 2–3 months or 6 months post-vaccination). This reduced the heterogeneity in the number of days between vaccination and anti-S IgG measurement which was present in Porter et al. (2022) and in our study.

With the COVID-19 pandemic, mRNA vaccines reached a large global presence (Fleck, 2024). Prior studies, excluding COVID-19 vaccine studies, examining associations between PFAS exposure and vaccine immune response have considered other (non-mRNA) vaccine types. For example, Grandjean et al. involved tetanus and diphtheria toxoid vaccines, Looker et al. explored inactivated trivalent influenza vaccine, and Stein et al. studied intranasal live attenuate influenza vaccine (Grandjean et al., 2012; Looker et al., 2014; Stein et al., 2016). Additional studies exploring the impact of PFAS exposure on mRNA vaccine immune response are needed, particularly as mRNA vaccinations against other infectious diseases (e.g., seasonal influenza) become available (Ananworanich et al., 2024). In our study, some participants, notably 60 % of those from FPWC, reported most recently receiving a COVID-19 vaccine from an unknown (or non-Pfizer, non-Moderna) manufacturer. Possibly, some of these participants received a Johnson & Johnson vaccine (a vector vaccine) but mistakenly selected unknown/other vaccine on the data collection instrument, instead of the available Johnson & Johnson vaccine option. Never-the-less, our study was not designed to explore differences between immune response to COVID-19 mRNA vaccines and non-mRNA vaccines. This could be an area for future work, depending on the volume of published data or availability of other historical data related to Johnson & Johnson COVID-19 vaccine immune response.

Many questions about PFAS exposure and immunotoxicity remain unanswered (Starling, 2023). Although the COVID-19 pandemic facilitated a unique opportunity to further investigate this health issue, several challenging factors were at play. During early stages of the

pandemic, many populations were naïve to SARS-CoV-2 while others were beginning to develop immunity through infection and vaccination. Lockdowns and the need for essential workers (e.g., healthcare workers) resulted in unbalanced SARS-CoV-2 exposures and COVID-19 vaccinations across populations (Do and Frank, 2021). As restrictions loosened and exposures increased, vaccines became more widely available. However, the timing of vaccine roll-out and distribution by manufacturer varied geographicly (Dooling et al., 2020, 2021; Do and Frank, 2021). Effectiveness of the COVID-19 vaccine, like other vaccines, can be influenced by host-related (e.g., age, prior infection) and pathogen-related (e.g., circulating viral variants) factors (Marziano et al., 2023; Menegale et al., 2023; Centers for Disease Control and Prevention (U .S.), 2023). Furthermore, even among populations with no known PFAS exposure, primary vaccination with an original two-dose mRNA COVID-19 vaccine produced a robust antibody responses to S protein, but waning antibody levels by 6-months post-vaccination (Kato et al., 2022; Ikezaki et al., 2022; Naaber et al., 2021). Recognizing these factors, we aimed to address potential confounding in our analysis through restriction of the study population, stratified analysis by community, and considered inclusion of measured confounding variables in adjusted models. Despite these efforts, the observed relationships could be due to uncontrolled confounding or other unrecognized biases. Notably, observational studies of COVID-19 vaccine response remain challenging to conduct, interpret, and compare.

COVID-19 vaccination rates across our study's three communities differed. Many Pittsboro participants were enrolled in COVID-19 vaccine trials, leading to higher vaccination rates in this community. Additionally, the data collection event in the Pittsboro community, which occurred in November of 2021, was the last of the three communities in this study. This provided more opportunity for Pittsboro participants to receive multiple vaccines before sample collection. Although the anti-S IgG levels of our participants were comparable to those reported in other study populations, the Pittsboro community had the highest anti-S IgG levels in our study (Đaković et al., 2022; Sugiyama et al., 2022). In all three communities, PFAS levels were higher than contemporary U.S. national levels from the National Health and Nutrition Examination Survey, though Pittsboro participants had the highest median PFAS concentrations (Kotlarz et al., 2020; Kotlarz et al., 2024). The interquartile range for all PFAS overlapped among the three communities; however, our study included a wide range of exposure values across the communities.

A main limitation of this study was the lack of specificity in time between COVID-19 vaccination and anti-S IgG measurement, mitigating our ability to more fully characterize the influence of PFAS exposure on vaccine response. Another important limitation was the cross-sectional study design; studies with repeated antibody level measurements can better elucidate changes in response to vaccine. While the cross-sectional design was not optimal to explore this issue, given the public health importance and unique timing of the study during the summer and fall of 2021, our analysis remains a valuable contribution. Given the relatively small number of participants included in this study, we were unable to fully explore potential confounding by vaccine manufacturer or reasonably assess effect measure modification by race and ethnicity (Swilley-Martinez et al., 2023). Finally, we did not explicitly explore PFAS mixtures. Future observational studies of PFAS exposure and vaccine immune response should include serial measurements of serum IgG against vaccine and PFAS concentrations, ideally over an extended time; routine data collection on health status changes (e.g., new medications or diagnoses of relevance); and exploration of the impact of PFAS mixtures on results.

Several other aspects of this study are worthy of mention. Although COVID-19 vaccination dates were self-reported, at the time of data collection most study participants referred to their COVID-19 vaccination cards when providing this information to the study team. Undiagnosed or asymptomatic SARS-CoV-2 infection could have occurred in participants; however, it is difficult to assess how this could impact results. Although not a limitation, it is important to note that, like all SARS-CoV-2 antibody tests available at the time that participant samples were processed, the anti-S AdviseDx SARS-CoV-2 IgG II Assay (Abbott, Chicago, IL) was not specifically authorized to assess immunity in vaccinated people.

Our results align with evidence from most published studies. Elevated PFAS are not consistently associated with reduced COVID-19 vaccine response in cross-sectional studies (or those with repeated measures) of general population adults. Our results also highlight the challenges of observational studies of the relationship between PFAS and vaccine antibody response. Future studies should consider how duration and timing of PFAS exposure could influence vaccine antibody response over longer time periods and further explore how vaccine type (e.g., mRNA) could modify associations. This information is relevant not only for populations currently affected by high PFAS exposures but also for similar populations identified moving forward.

CRediT authorship contribution statement

Sarah Rhea: Writing – original draft, Methodology, Formal analysis. **David Collier:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Michael Cuffney:** Writing – review & editing, Validation, Project administration, Investigation, Formal analysis, Data curation. **C. Suzanne Lea:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Nadine Kotlarz:** Writing – review & editing, Methodology, Investigation, Formal analysis, Data curation. **Jane A. Hoppin:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare they have nothing to disclose.

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Glossary:

anti-S IgG	anti-Spike SARS-CoV-2 IgG
AU	arbitrary units
CIs	confidence intervals
DAG	directed acyclic graph
ECHI	East Carolina Heart Institute
FPWC	Fayetteville private well community
LCFRR	Lower Cape Fear River region
METRIC	Molecular Education, Technology and Research Innovation Center
Nafion by-product 2	perfluoro-2-{[perfluoro-3-(perfluoroethoxy)-2-proanyl]oxy}ethanesulfonic acid
PFAS	per- and polyfluoroalkyl substances

PFHpS perfluoroheptane sulfonic acid
PFHxS perfluorohexane sulfonic acid
PFNA perfluorononanoic acid
PFOA perfluorooctanoic acid
PFOS perfluorooctane sulfonic acid
PFO5DoA perfluoro-3,5,7,9,11-pentaoxadodecanoic acid

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2026.114755.

References

Abbott. AdviseDx SARS-CoV-2 IgG II. https://www.fda.gov/media/146372/download. (Accessed 12 September 2024).

Agency for Toxic Substances and Disease Registry, 2022. PFAS Exposure Assessments Final Report: Findings Across 10 Exposure Assessment Sites. US Department of Health & Human Services. https://www.atsdr.cdc.gov/pfas/docs/PFAS-EA-Final-Report-508.pdf. (Accessed 13 August 2024).

Allcot, H., Boxell, L., Conway, J.C., Ferguson, B.A., Gentzkow, M., Goldman, B., 2020. What Explains Temporal and Geographic Variation in the Early US Coronavirus Pandemic? National Bureau of Economic Research. https://www.nber.org/system/files/working_papers/w27965/w27965.pdf. (Accessed 27 August 2025).

Ananworanich, J., Lee, I.T., Ensz, D., et al., 2024. Safety and immunogenicity of mRNA-1010, an investigational seasonal influenza vaccine, in healthy adults: final results from a phase 1/2 randomized trial. J. Infect. Dis. https://doi.org/10.1093/infdis/jiae329. Published online June 27:jiae329.

Andersson, A.G., Lundgren, A., Xu, Y., et al., 2023. High exposure to perfluoroalkyl substances and antibody responses to SARS-CoV-2 mRNA Vaccine—An observational study in adults from ronneby, Sweden. Environ. Health Perspect. 131 (8), 087007. https://doi.org/10.1289/EHP11847.

Bailey, J.M., Wang, L., McDonald, J.M., et al., 2023. Immune response to COVID-19 vaccination in a population with a history of elevated exposure to per- and polyfluoroalkyl substances (PFAS) through drinking water. J. Expo. Sci. Environ. Epidemiol. https://doi.org/10.1038/s41370-023-00564-8.

Bobrovitz, N., Ware, H., Ma, X., et al., 2023. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. Lancet Infect. Dis. 23 (5), 556–567. https://doi.org/10.1016/S1473-3099(22)00801-5.

Bradley, B.T., Bryan, A., Fink, S.L., et al., 2021. Anti-SARS-CoV-2 antibody levels measured by the AdviseDx SARS-CoV-2 assay are concordant with previously available serologic assays but are not fully predictive of sterilizing immunity. In: Caliendo, A.M. (Ed.), J Clin Microbiol, vol. 59. https://doi.org/10.1128/JCM.00989-21, 9):e00989-21.

Centers for Disease Control & Prevention, 2024. Overview of testing for SARS-CoV-2 for healthcare providers. https://www.cdc.gov/covid/hcp/clinical-care/overview-testing-sars-cov-2.html#:~:text=Antibody%20testing%20is%20primarily%20used%20for%20public,(nucleocapsid%20or%20spike%20protein)%20of%20the%20virus. (Accessed 12 January 2026).

Centers for Disease Control and Prevention (U.S.), 2023. COVID-19 vaccine effectiveness trials. Vaccine effectiveness trials. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/effectiveness/how-they-work.html. (Accessed 20 February 2024).

Chang, E.T., Adami, H.O., Boffetta, P., Wedner, H.J., Mandel, J.S., 2016. A critical review of perfluorooctanoate and perfluorooctanesulfonate exposure and immunological health conditions in humans. Crit. Rev. Toxicol. 46 (4), 279–331. https://doi.org/10.3109/10408444.2015.1122573.

Committee on the Guidance on PFAS Testing and Health Outcomes, Board on Environmental Studies and Toxicology, Board on Population Health and Public Health Practice, Division on Earth and Life Studies, Health and Medicine Division, National Academies of Sciences, Engineering, and Medicine. *Guidance on PFAS Exposure, Testing, and Clinical Follow-Up*, 2022. National Academies Press, 26156. https://doi.org/10.17226/26156.

Đaković, R.O., Bodulić, K., Zember, S., et al., 2022. Decline of Anti-SARS-CoV-2 IgG antibody levels 6 months after complete BNT162b2 vaccination in healthcare workers to levels observed following the first vaccine dose. Vaccines (Basel) 10 (2), 153. https://doi.org/10.3390/vaccines10020153.

Do, D.P., Frank, R.U.S., 2021. Frontline workers and COVID-19 inequities. Prev. Med. 153, 106833. https://doi.org/10.1016/j.ypmed.2021.106833.

Dooling, K., McClung, N., Chamberland, M., et al., 2020. The advisory committee on immunization practices' interim recommendation for allocating initial supplies of COVID-19 vaccine — united States, 2020. MMWR Morb. Mortal. Wkly. Rep. 69 (49), 1857–1859. https://doi.org/10.15585/mmwr.mm6949e1.

Dooling, K., Marin, M., Wallace, M., et al., 2021. The advisory committee on immunization practices' updated interim recommendation for allocation of COVID-19 vaccine - united States, December 2020. Morb. Mortal. Wkly. Rep. 69 (5152), 1657–1660. https://doi.org/10.15585/mmwr.mm695152e2.

Enders, J.R., Weed, R.A., Griffith, E.H., Muddiman, D.C., 2022. Development and validation of a high resolving power absolute quantitative per- and polyfluoroalkyl substances method incorporating skyline data processing. Rapid Commun. Mass Spectrom. 36 (11), e9295. https://doi.org/10.1002/rcm.9295.

U.S. Food and Drug Administration, 2023. Fact sheet for healthcare providers administering vaccine: emergency use authorization of the Janssen COVID-19 vaccine to prevent COVID-19. In: . https://www.fda.gov/media/146304/download (Accessed 18 September 2024).

Fleck, K., 2024. mRNA vaccines: not just for COVID soon? Medscape. https://www.medscape.com/viewarticle/promising-mrna-vaccines-new-therapies-infections-cancer-and-2024a10008gs (Accessed 20 September 2024).

Grandjean, P., Andersen, E.W., Budtz-Jørgensen, E., et al., 2012. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. JAMA 307 (4), 391–397. https://doi.org/10.1001/jama.2011.2034.

Greenland, S., Pearl, J., Robins, J.M., 1999. Causal Diagrams for Epidemiologic Research. Epidemiology. 10 (1), 37–48.

Hall, E., Mahon, B.E., Peacock, G., 2024. The U.S. COVID-19 vaccination program: a look back and future directions. Vaccine 42, 125628. https://doi.org/10.1016/j.vaccine.2024.01.053.

Haug, L.S., Huber, S., Becher, G., Thomsen, C., 2011. Characterisation of human exposure pathways to perfluorinated compounds — comparing exposure estimates with biomarkers of exposure. Environ. Int. 37 (4), 687–693. https://doi.org/10.1016/j.envint.2011.01.011.

Hollister, J., Caban-Martinez, A.J., Ellingson, K.D., et al., 2023. Serum per- and polyfluoroalkyl substance concentrations and longitudinal change in post-infection and post-vaccination SARS-CoV-2 antibodies. Environ. Res. 239, 117297. https://doi.org/10.1016/j.envres.2023.117297.

Ikezaki, H., Nomura, H., Shimono, N., 2022. Dynamics of Anti-Spike IgG antibody level after the second BNT162b2 COVID-19 vaccination in health care workers. J. Infect. Chemother. 28 (6), 802–805. https://doi.org/10.1016/j.jiac.2022.02.024.

Kato, H., Miyakawa, K., Ohtake, N., et al., 2022. Vaccine-induced humoral response against SARS-CoV-2 dramatically declined but cellular immunity possibly remained at 6 months post BNT162b2 vaccination. Vaccine 40 (19), 2652–2655. https://doi.org/10.1016/j.vaccine.2022.03.057.

Kaur, K., Lesseur, C., Chen, L., et al., 2023. Cross-sectional associations of maternal PFAS exposure on SARS-CoV-2 IgG antibody levels during pregnancy. Environ. Res. 219, 115067. https://doi.org/10.1016/j.envres.2022.115067.

Kielsen, K., Shamim, Z., Ryder, L.P., et al., 2016. Antibody response to booster vaccination with tetanus and diphtheria in adults exposed to perfluorinated alkylates. J. Immunot. 13 (2), 270–273. https://doi.org/10.3109/1547691X.2015.1067259.

Kotlarz, N., Guillette, T., Critchley, C., et al., 2024. Per- and polyfluoroalkyl ether acids in well water and blood serum from private well users residing by a fluorochemical facility near Fayetteville, North Carolina. J. Expo. Sci. Environ. Epidemiol. 34 (1), 97–107. https://doi.org/10.1038/s41370-023-00626-x.

Kotlarz, N., McCord, J., Collier, D., et al., 2020. Measurement of novel, drinking water-associated PFAS in blood from adults and children in Wilmington, North Carolina. Environ. Health Perspect. 128 (7), 077005. https://doi.org/10.1289/EHP6837.

Looker, C., Luster, M.I., Calafat, A.M., et al., 2014. Influenza vaccine response in adults exposed to perfluorooctanoate and perfluorooctanesulfonate. Toxicol. Sci. 138 (1), 76–88. https://doi.org/10.1093/toxsci/kft269.

Marziano, V., Guzzetta, G., Menegale, F., et al., 2023. Estimating SARS-CoV-2 infections and associated changes in COVID-19 severity and fatality. Influenza Resp. Viruses 17 (8), e13181. https://doi.org/10.1111/irv.13181.

Menegale, F., Manica, M., Zardini, A., et al., 2023. Evaluation of waning of SARS-CoV-2 vaccine–induced immunity: a systematic review and meta-analysis. JAMA Netw. Open 6 (5), e2310650. https://doi.org/10.1001/jamanetworkopen.2023.10650.

Moderna, U.S., 2022. Vaccine Information Fact Sheet for Recipients and Caregivers About Spikevax (COVID-19 Vaccine, mRNA), Moderna Covid-19 Vaccine, and Moderna COVID-19 Vaccine, Bivalent (Original And Omicron Ba.4/Ba.5) to Prevent COVID-19. https://www.fda.gov/media/144638/download# (Accessed 18 September 2024).

Muecksch, F., Wise, H., Batchelor, B., et al., 2021. Longitudinal serological analysis and neutralizing antibody levels in coronavirus disease 2019 convalescent patients. J. Infect. Dis. 223 (3), 389–398. https://doi.org/10.1093/infdis/jiaa659.

Naaber, P., Tserel, L., Kangro, K., et al., 2021. Dynamics of antibody response to BNT162b2 vaccine after six months: a longitudinal prospective study. Lancet Reg. Health - Europe 10, 100208. https://doi.org/10.1016/j.lanepe.2021.100208.

Nakayama, S., Strynar, M.J., Helfant, L., Egeghy, P., Ye, X., Lindstrom, A.B., 2007. Perfluorinated compounds in the cape fear drainage basin in North Carolina. Environ. Sci. Technol. 41 (15), 5271–5276. https://doi.org/10.1021/es070792y.

National Toxicology Program, 2016. NTP monograph on immunotoxicity associated with exposure to perfluorooctanoic acid or perfluorooctane sulfonate. Natl. Insitut. Environ. Sci. U.S. Department of Health and Human Services; https://ntp.niehs.nih.gov/sites/default/files/ntp/ohat/pfoa_pfos/pfoa_pfosmonograph_508.pdf.

North Carolina State University. The GenX exposure study. GenX Exposure Study. Accessed September 5, 2023. https://genxstudy.ncsu.edu.

Pingali, C., Meghani, M., Razzaghi, H., et al., 2021. COVID-19 vaccination coverage among insured persons aged ≥16 years, by race/ethnicity and other selected characteristics — eight integrated health care organizations, United States, December 14, 2020–May 15, 2021. MMWR Morb. Mortal. Wkly. Rep. 70 (28), 985–990. https://doi.org/10.15585/mmwr.mm7028a1.

Porter, A.K., Kleinschmidt, S.E., Andres, K.L., et al., 2022. Antibody response to COVID-19 vaccines among workers with a wide range of exposure to per- and polyfluoroalkyl substances. Environ. Int. 169, 107537. https://doi.org/10.1016/j.envint.2022.107537.

Rappazzo, K., Coffman, E., Hines, E., 2017. Exposure to perfluorinated alkyl substances and health outcomes in children: a systematic review of the epidemiologic literature. IJERPH 14 (7), 691. https://doi.org/10.3390/ijerph14070691.

Serra López-Matencio, J.M., Vicente-Rabaneda, E.F., Alañón, E., Aranguren Oyarzabal, A., Martínez Fleta, P., Castañeda, S., 2023. COVID-19 vaccination and immunosuppressive therapy in immune-mediated inflammatory diseases. Vaccines 11 (12), 1813. https://doi.org/10.3390/vaccines11121813.

Starling, A.P., 2023. Invited perspective: per- and polyfluoroalkyl substances and impaired antibody response to vaccination—who is affected? Environ. Health Perspect. 131 (8), 081304. https://doi.org/10.1289/EHP12971.

Stein, C.R., Ge, Y., Wolff, M.S., et al., 2016. Perfluoroalkyl substance serum concentrations and immune response to FluMist vaccination among healthy adults. Environ. Res. 149, 171–178. https://doi.org/10.1016/j.envres.2016.05.020.

Sugiyama, A., Kurisu, A., Nagashima, S., et al., 2022. Seroepidemiological study of factors affecting anti-spike IgG antibody titers after a two-dose mRNA COVID-19 vaccination in 3744 healthy Japanese volunteers. Sci. Rep. 12 (1), 16294. https://doi.org/10.1038/s41598-022-20747-x.

Sunderland, E.M., Hu, X.C., Dassuncao, C., Tokranov, A.K., Wagner, C.C., Allen, J.G., 2019. A review of the pathways of human exposure to poly- and perfluoroalkyl substances (PFASs) and present understanding of health effects. J. Expo. Sci. Environ. Epidemiol. 29 (2), 131–147. https://doi.org/10.1038/s41370-018-0094-1.

Swilley-Martinez, M.E., Coles, S.A., Miller, V.E., et al., 2023. "We adjusted for race": now what? A systematic review of utilization and reporting of race in *American Journal of Epidemiology* and *Epidemiology* , 2020–2021. Epidemiol. Rev. 45 (1), 15–31. https://doi.org/10.1093/epirev/mxad010.

Textor, J., Van Der Zander, B., Gilthorpe, M.S., Liśkiewicz, M., Ellison, G.T.H., 2017. Robust causal inference using directed acyclic graphs: the R package 'dagitty.'. Int. J. Epidemiol. https://doi.org/10.1093/ije/dyw341. Published online January 15: dyw341.

Timmermann, A., Johansen, I.S., Tolstrup, M., et al., 2024. Antibody response to SARS-CoV-2 mRNA vaccination in Danish adults exposed to perfluoroalkyl substances (PFASs): the ENFORCE study. Environ. Res. 263, 120039. https://doi.org/10.1016/j.envres.2024.120039.

Tradigo, G., Das, J.K., Vizza, P., Roy, S., Guzzi, P.H., Veltri, P., 2023. Strategies and trends in COVID-19 vaccination delivery: what we learn and what we may use for the future. Vaccines 11 (9), 1496. https://doi.org/10.3390/vaccines11091496.

U.S. Department of Defense. Coronavirus timeline. Coronavirus timeline. https://www.defense.gov/Spotlights/Coronavirus-DOD-Response/Timeline/. (Accessed 17 January 2024).

U.S. Food and Drug Administration, 2021. Pfizer-BioNTech COVID-19 vaccine EUA letter of authorization. Published online May 10. https://www.fda.gov/media/144412/download. (Accessed 18 September 2024).

VanderWeele, T.J., 2019. Principles of confounder selection. Eur. J. Epidemiol. 34 (3), 211–219. https://doi.org/10.1007/s10654-019-00494-6.

Zhao, M., Holtz, D., Aral, S., 2021. Interdependent program evaluation: geographic and social spillovers in COVID-19 closures and reopenings in the United States. Sci. Adv. 7 (31). https://doi.org/10.1126/sciadv.abe7733 eabe7733.