# Pease Study Report

## Design, Methods and Cohort Description

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# Contents

## Background/Introduction

Per- and polyfluoroalkyl substances (PFAS) are a family of chemicals used in industrial applications and consumer products. The most commonly studied PFAS are perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS). The next most commonly studied are perfluorohexane sulfonic acid (PFHxS), and perfluorononanoic acid (PFNA) (ATSDR, 2017; Wang 2017).

The scientific evidence linking PFAS exposures with adverse health effects is rapidly growing but is inconsistent for a variety of reasons, including differences concerning exposure levels, methods of ascertaining diseases, and effect biomarkers measured. For some health endpoints, only limited studies of PFAS exposure currently exist. Nevertheless, studies have found associations with changes in lipids (Li 2020, Steenland 2009; Zeng 2015, Mora 2018), levels of uric acid (Arrebola 2019, Steenland 2010), thyroid and sex hormones (Wen 2013, Preston 2020; Wang 2021, Lopez-Espinosa 2016, Preston 2018), liver function (Sen 2022, Darrow 2016, Mora 2018), and immune function (Grandjean 2012, 2017), as well as reduced birth weight (Shoaff 2018, Bach 2015, Verner 2015), developmental effects (Ernst 2019, Lopez-Espinosa 2011) and some cancers (Barry 2013, Bartell 2021, Messmer 2022, Shearer 2020, Steenland 2020). Additionally, in children, there is some evidence that PFAS exposures might be associated with attention deficit hyperactivity disorder (ADHD) (Stein 2011, Liew 2015, Ode 2014, Hoffman 2010, Skogheim 2021), conduct and coordination problems (Oulhote 2016; Fei 2011), and executive function deficits (Harris 2021, Vuong 2016).

Most studies of the health effects from PFAS exposures have focused on PFOA and PFOS; PFHxS, perfluorononanoic acid (PFNA) and other PFAS have only been assessed sparingly (ATSDR 2017a). These include studies that evaluated data from the National Health and Nutrition Examination Survey (NHANES), occupational studies, studies of West Virginia and Ohio residents and workers exposed to PFOA from a chemical plant (the “C8” studies), and national surveys conducted in other countries where exposures to PFAS were found mostly from consumption of food and beverages in PFAS-contaminated packaging. While the C8 studies provided extensive and high-quality information on PFOA by studying a large cohort of highly exposed workers and residents (60,000+ people) living in the vicinity of the production facility, they did not address the full range of other PFAS and exposures routes. Except for the C8 studies, there is scant information on the health effects of exposures to PFAS-contaminated drinking water (Li 2020, Xu 2021). Because of these gaps, there is a need for more epidemiological research on the health effects of PFAS exposures.

PFOS, PFOA, PFHxS, and other PFAS are constituents in aqueous film-forming foam (AFFF), used to extinguish flammable liquid fires. Since the 1970s, military bases in the U.S. have used AFFF with PFAS constituents for firefighting training as well as to extinguish fires. At some military bases, such as the Pease Air Force Base in Portsmouth, NH, AFFF use has resulted in the migration of PFAS through soils to groundwater and/or surface water sources of drinking water for the base and/or surrounding communities (ATSDR 2017a). The base closed in 1991 and was redeveloped as a business and aviation industrial park known as the Pease International Tradeport (“Pease”). Three on-site wells provided drinking water to Pease, one of which was found to be contaminated with PFAS at

concentrations measured in 2014 as high as 2.4 µg/L for PFOS and 0.35 µg/L for PFOA, well above EPA advisory concentrations at the time (0.2 µg/L for PFOS and 0.4 µg/L for PFOA (NH DHHS 2016, US EPA 2009)). In 2016, EPA established a lifetime health advisory for combined concentrations of PFOA and PFOS of 0.07 µg/L, and in 2022, EPA proposed new health advisory concentrations for PFOS and PFOA of $4 \times 10^{-6}$ and $2 \times 10^{-5}$ µg/L, respectively (US EPA 2016, 2022).

In response to the affected community members' request for clinical testing following their consumption of PFAS-contaminated water and to obtain a direct measurement of individuals' PFAS exposure, the New Hampshire Department of Health and Human Services (NH DHHS) initiated the New Hampshire Biomonitoring Program in 2015. From 2015-2017, the New Hampshire Biomonitoring Program obtained blood specimens for PFAS analyses from 1,836 participants. This included about 370 children who attended daycare at Pease and had potential exposure to the PFAS-contaminated drinking water. The results from the blood testing program indicated that the exposed population had serum concentrations of PFOS and PFHxS that were about two to three times higher than the U.S. population based on data from NHANES 2013-2014 and from other epidemiological studies in the United States (NH DHHS 2016). A feasibility study completed by ATSDR in 2017 concluded that a multi-site PFAS study was necessary for sufficient sample size to evaluate important health endpoints in children and adults such as thyroid, liver, and immune function and autoimmune diseases (ATSDR 2017a).

The current research study (hereafter referred to as the "Pease Study") is a first site and a proof-of-concept for the Multi-Site PFAS Health Study, (*Human health effects of drinking water exposures to per- and poly-fluoroalkyl substances (PFAS): A multi-site cross-sectional study*; hereafter, the "Multi-site Study"). The Pease Study has the main goals of evaluating 1) the methods and procedures in the study protocol to identify any issues that need to be addressed before implementing a multi-site study; and 2) the associations between specific health effects and serum PFAS concentrations among those exposed to PFAS-contaminated drinking water at Pease. The objective of this report is to describe methods, present PFAS exposure concentrations, and present descriptive data on health outcomes that were self-reported in the questionnaire and those reported by participants' health care providers. Statistical analyses of PFAS data for associations with Pease health outcomes will be the topic of future presentations at the Pease community meeting, scientific conferences, as well as other publications.

Data collected from the Multi-site Study will be combined with data from the Pease Study with a goal of having a large enough sample size to effectively evaluate health outcomes of interest. In addition to fulfilling the main research goals above, the Pease Study is also a response to a strong call from the Portsmouth community for a study examining the potential health effects of the PFAS-contaminated drinking water at Pease. Assessing exposure data from the Pease Study and the New Hampshire Biomonitoring Program will also allow researchers the opportunity to explore possible changes in PFAS serum concentrations over time as well as provide an additional time point closer to when exposure was reduced.

The protocol for the Pease Study has undergone external peer review and was reviewed and approved by the Centers for Disease Control and Prevention (CDC) Institutional

Review Board (ICDC protocol number 7061) under CDC's Federal wide Assurance (FWA) No. 00001413 and by the Office of Management and Budget (OMB control number 0923-0061).

# Methods

## *Recruitment*

Based on sample size calculations during the feasibility assessment, this cross-sectional study aimed to enroll a convenience sample of at least 350 children (ages 4–17 years) and 1,000 adults (aged ≥18 years) with community exposure to PFAS. The study also aimed to enroll approximately 175 referent children (ages 4–17 years) and 100 adults (aged ≥18 years) from the Portsmouth area who were not exposed to PFAS contaminated drinking water at Pease and did not have a history of occupational exposure to PFAS.
Recruitment was divided into waves to prioritize the enrollment of target populations. The first wave included adults and children who participated in the New Hampshire Biomonitoring Program between 2015 and 2017. To protect confidential information, the NH DHHS mailed an invitation letter to each participant of the NH Biomonitoring Program to announce the Pease Study and request consent to share their contact information with the Pease Study investigators starting in September 2019. Participants who consented to have their contact information shared were asked to mail back a signed copy of their consent form to NH DHHS. Consented participants were then contacted to be screened by the Pease Study team or were provided with the study call center's phone number. Participants of the NH DHHS Biomonitoring Program were eligible if they met the criteria for the exposed group as listed in Table 1. In December 2019, NH DHHS sent a follow up invitation letter to those that did not respond to the invitation letter sent in October 2019.

**Table 1. Pease Study Eligibility Criteria**

| Adults who drank contaminated water at Pease (Exposed) | Adults who did not drink contaminated water at Pease (Referent) | Children who drank contaminated water at Pease (Exposed) | Children who did not drink contaminated water at Pease (Referent) |
|---|---|---|---|
| **Inclusion Criteria**:<br>1. Aged ≥18 years at enrollment (Oct 2019 – Dec 2021).<br>2. Resided or worked in areas served by PFAS-contaminated drinking water caused by AFFF use.<br>3. Exposure to drinking water at Pease occurred between January 2004 and May 2014<br>Note: Females who were pregnant were eligible to enroll.<br>**Exclusion Criteria:** | **Inclusion Criteria**:<br>Aged ≥18 years at enrollment (Oct 2019-Dec 2021).<br>Unexposed to contaminated drinking water at Pease.<br>**Exclusion Criteria:**<br>1. Prisoners, including those under house arrest.<br>Ever employed as a firefighter, ever participated in fire training exercises using AFFF foam, or ever employed at industrial | **Inclusion Criteria:**<br>Inclusion Criteria:<br>1. Aged 4 – 17 years at enrollment (Oct 2019-Dec 2021)<br>2. Resided or attended day care in areas served by PFAS-contaminated drinking water caused by AFFF use or were exposed in utero or during breastfeeding when the mother consumed contaminated drinking water.<br>3. Exposure to drinking water at Pease occurred between 2004 and May 2014. | **Inclusion Criteria:**<br>Inclusion Criteria:<br>1. Aged 4 – 17 years at enrollment (Oct 2019 – Dec 2021)<br>2. Unexposed to contaminated drinking water at Pease.<br>**Exclusion Criteria:**<br>1. Prisoners, including those under house arrest.<br>2. Children whose birth mothers were ever employed as a firefighter, ever participated in fire training exercises using |

| Adults who drank contaminated water at Pease (Exposed) | Adults who did not drink contaminated water at Pease (Referent) | Children who drank contaminated water at Pease (Exposed) | Children who did not drink contaminated water at Pease (Referent) |
|---|---|---|---|
| 1. Prisoners, including those under house arrest.<br>2. Ever employed as a firefighter, ever participated in fire training exercises using AFFF foam, or ever employed at industrial facilities that used PFAS in the manufacturing process | facilities that used PFAS in the manufacturing process. | Note: Females who were pregnant were eligible to enroll.<br><br>**Exclusion Criteria:**<br>1. Prisoners, including those under house arrest.<br>2. Children whose birth mothers were ever employed as a firefighter, ever participated in fire training exercises using AFFF foam, or were ever employed at industrial facilities that used PFAS in the manufacturing process | AFFF foam, or were ever employed at industrial facilities that used PFAS in the manufacturing process. |

To shortly summarize, the following adults and children were eligible to participate:

- Adults aged 18 years or older who worked or attended school at Pease International Tradeport at any time from January 2004 to May 2014, or
- Who lived in Newington, NH, at any time from January 2004 to the present and used a private well with documented PFAS contamination.
- Children aged 4 through 17 years who received parent or guardian study participation permission and who attended daycare at Pease International Tradeport at any time from 2004 to May 2014, or
- Were born to and/or breastfed by a mother who met the adult eligibility criteria were eligible.

When Wave 1 enrollment began to decline, the second phase of recruitment opened allowing for enrollment to those that did not participate in the 2015 NH DHHS Biomonitoring Program but met eligibility criteria for either the exposed or referent groups as outlined in Table 1. This round of recruitment consisted of widespread outreach to the community surrounding Pease. A specific area of focus was given to the towns that had the highest number of participants in the NH DHHS Biomonitoring Program. Outreach included activities such as, but not limited to, media interviews with community members and leaders on local news stations and in newspapers, yard signs and flyers placed throughout the community, social media posts, promotion at local events, and outreach to

local schools. Similar to Wave 1 recruitment, interested community members were either provided with the study phone number to call or were encouraged to provide their phone number for study staff to contact them for screening. At some events, study staff were available to screen individuals for eligibility at the time of initial contact.

### *Data Collection Overview*

Interested community members were asked a series of screening questions over the phone or in person to determine if they or their child would be eligible to participate in the Pease Study. Eligible participants were then scheduled to attend a study visit at a central study office where they were consented, provided body and blood pressure measurements, provided their urine sample and fasting blood sample, and completed a questionnaire. For child participants, it was preferred to have the child's birth mother, when possible, complete screening and the questionnaire for the child as the questionnaire included questions about the child's birth mother which may determine potential in *utero* exposure. Child participants were scheduled for a secondary appointment where neurobehavioral tests were administered to the child. The parent or guardian was also asked to fill out neurobehavioral questionnaire regarding the child at that appointment.

Enrollment for the study began in November 2019. All data collection was paused in March 2020 due to the coronavirus disease 2019 (COVID-19) pandemic; recruitment resumed in October 2020 after IRB and OMB review and approval of a detailed restart plan. Upon study restart, data collection procedures were modified to limit the amount of time the participant needed to spend in the office. As a result, trained staff obtained verbal consent and administered questionnaires via telephone. Prior to entering the study office, all participants were screened for COVID-19 symptoms. Participants' written consent was collected at the in-office appointment along with body and blood pressure measurements, urine sample, and a fasting blood sample. Enrollment closed in December 2021.

Each study activity is further described in the following sections.

### *Informed Consent Process*

The informed consent included a description of study procedures, risks and benefits of participation and of measures to protect participant data including a Privacy Act Statement and Certificate of Confidentiality (CoC; Section 301(d) of the Public Health Service Act). Study staff emphasized the voluntary nature of participation and answered any questions the participant, or parent of the child participant, had prior to obtaining signatures. The participants consented specifically to collection of data from the questionnaire; obtaining fasting blood specimens for analyses of PFAS, clinical tests and effect biomarkers; and collection of a morning void urine sample. Consent also requested permission to archive any residual blood and urine specimens for future analyses of PFAS and/or effect biomarkers.

### *Urine Collection*

Participants were asked to bring a first morning void urine sample to their study visit using

the urine collection kit provided prior to their appointment. Participants were instructed to keep their urine samples in a refrigerator until the study visit appointment, at which point study staff immediately placed them on ice. If the participant did not bring their urine sample, they were asked to provide a urine sample in the study office. Study staff recorded if the sample was a first morning void. Urine samples were transferred to a -80°C freezer and shipped to the CDC Biorepository for long term storage for potential future analysis. The CDC Biorepository is the main facility for long term storage of collected biological samples across all CDC Centers and Agencies (CDC Biorepository | CDC).

### *Body and Blood Pressure Measurements*

Study staff collected participant's height in inches using a wall mounted measuring tape and weight in pounds using a digital floor scale. Waist and hip circumference were measured using standard procedures. Study staff then collected participant's resting blood pressure using a digital blood pressure monitor. Three blood pressure measurements were taken and averaged because of biological and observer variability. If possible, study staff alternated arms for each blood pressure reading.

### *Blood Sample Processing and Laboratory Methods*

Participants were requested to fast for 8 hours prior to the study visit appointment. Prior to attempting to collect a blood sample from a participant, study staff administered a blood draw screening questionnaire for conditions that excluded the participant from the blood draw (i.e., hemophilia, skin condition, or chemotherapy in the past 4 weeks), and asked the participant about certain factors that would affect the blood draw such as diabetes, blood thinning medications, and fasting status. A trained study phlebotomist would then attempt to draw up to 30 ml of blood from a child participant and up to 40 ml of blood from an adult participant using standard venipuncture techniques. If a participant was unable to provide the desired volume of blood, a smaller amount was drawn and documented.

The study staff aliquoted blood and serum specimens for analysis by centralized laboratories – Division of Laboratory Sciences (DLS) within CDC's National Center for Environmental Health (NCEH), LabCorp, and the State University of New York (SUNY) Medical University – for the analyses of PFAS and clinical tests of interest specified in the study protocol. (Additional reserve serum and whole blood specimens were aliquoted for potential future testing and long-term storage at the CDC's Biorepository.

### *PFAS Testing*

The Pease Study analyzed PFAS in fasting serum using methods developed at a CDC NCEH laboratory (Kuklenyik 2015; Kato 2018). For the current analyses, the PFAS analytes included linear and the sum of branched isomers of PFOA, linear and the sum of PFOS, and PFHxS,2-(N-methyl-perfluorooctane sulfonamido) acetic acid (MeFOSAA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA). The lab excluded three PFAS analytes from the analytical list of those measure in the 2017-2018 NHANES: 9-Chlorohexadecafluoro-3-oxanonane-1-sulfonic acid,

Adona (ammonium salt of 4,8-dioxa-3H-perfluorononanoic acid), and GenX (ammonium salt of 2,3,3,3-tetrafluoro-2-(1,1,2,2,3,3,3-heptafluoropropoxy)-propanoic acid (HFPO-DA). These analytes' reference ranges were all below the limit of detection (CDC 2021) and were therefore not measured in the Pease Study samples.

Following collection, staff stored serum samples at -80°C freezers in PFAS-free cryovials and shipped them on dry ice to CDC for PFAS analysis. Analytical methods for the PFAS samples were the same as those used in NHANES 2017-2018 cycle and have been described previously (CDC, 2021; Kato 2018). Briefly, the laboratory used on-line solid- phase extraction coupled with isotope dilution high-performance liquid chromatography- tandem mass spectrometry to quantify concentrations of nine PFAS listed above. The laboratory ensured accuracy and reliability by analyzing low and high-concentration quality control materials, analytical standards, and reagent and serum blanks along with the study samples (Kato et al., 2011a). The limit of detection (LOD) was 0.1 ng/mL for all PFAS measured; for statistical analyses we replaced values below LOD with LOD/√2 (Hornung and Reed, 1990).

### *Clinical Testing*

For clinical analyses conducted at LabCorp, aliquots were provided to LabCorp daily and shipped to assigned laboratories within LabCorp for testing. For clinical analyses conducted at SUNY, aliquots were stored in the -80°C freezer and shipped to the lab for testing in October 2021, December 2021, and January 2022. Table 2 provides an overview on the clinical tests that were conducted at each of the labs. We determined the clinical tests to be performed considering literature-reported and potential associations with PFAS exposure and limited blood volumes available for testing.

**Table 2. Clinical Analyses Conducted on Pease Study Blood and Serum Samples**

| Clinical Biomarker | Laboratory | Population Tested |
|---|---|---|
| Lipid Panel with Non-HDL Cholesterol | LabCorp | Adults and Children |
| Uric Acid | LabCorp | Adults and Children |
| Creatinine | LabCorp | Adults and Children |
| Thyroid Profile II, Comprehensive | LabCorp | Adults and Children |
| Thyroxine (T4) Free, Direct, Serum | LabCorp | Adults and Children |
| Thyroid Antibodies | LabCorp | Adults and Children |
| Testosterone, Total, Serum | LabCorp | Adults and Children |
| Estradiol (E2), Sensitive (LC/MS) | LabCorp | Adults and Children |
| Sex Hormone Binding Globulin, Serum | LabCorp | Adults and Children |
| FSH, Serum | LabCorp | Adults and Children |
| Insulin-Like Growth Factor 1 (IGF-1) | LabCorp | Adults and Children |
| Hepatic Function Panel | LabCorp | Adults and Children |
| GGT | LabCorp | Adults and Children |
| Glucose | LabCorp | Adults and Children |
| Insulin | LabCorp | Adults and Children |
| C-peptide | LabCorp | Adults and Children |
| Glutamic Acid Decarboxylase Autoantibody (Anti-GAD) | LabCorp | Adults and Children |
| C-Reactive Protein | LabCorp | Adults |
| Rheumatoid Arthritis (RA) Factor | LabCorp | Adults |

| | | |
|---|---|---|
| Antinuclear Antibodies (ANA), by IFA | LabCorp | Adults |
| CBC w/ Diff and Platelet | LabCorp | Adults |
| Pro-Insulin | LabCorp | Adults |
| IA-2 Autoantibodies (Endocrine Sciences) | LabCorp | Adults |
| Tetanus/Diphtheria Antibody Profile | LabCorp | Children |

| Clinical Biomarker | Laboratory | Population Tested |
|---|---|---|
| MMR Antibodies | LabCorp | Children |
| Interleukin-2 (IL-2) | SUNY | Adults |
| Interleukin-4 (IL-4) | SUNY | Adults |
| Interleukin-6 (IL-6) | SUNY | Adults |
| Interleukin-8 (IL-8) | SUNY | Adults |
| Interleukin-10 (IL-10) | SUNY | Adults |
| Tumor Necrosis Factor-Alpha | SUNY | Adults |
| Plasminogen Activator Inhibitor 1 (PAI-1) Activity | SUNY | Adults |
| Adiponectin | SUNY | Adults |
| Leptin | SUNY | Adults |
| Resistin | SUNY | Adults |
| Cytokeratin-18 (M60, M35) | SUNY | Adults and Children |
| IgA, IgE, IgG, IgM, Serum, Quantitative | SUNY | Adults and Children |
| Glycated hemoglobin (HgvA1c) | SUNY | Adults and Children |

## *Questionnaire*

### *Child Questionnaire*

For child participants, the questionnaire obtained demographic information (e.g., education and primary occupation of parents or legal guardians), medical history of the birth mother and child, any recent medications the child has taken, the birth mother's reproductive history (including maternal age at birth of the participating child) and any occupational exposures the birth mother may have had to PFAS. The questionnaire asked about the dates the child's birth mother worked at Pease, her water consumption (including bottled water) while at Pease, the dates the child attended daycare at Pease and the child's water consumption (including use of water for formula, juices, bottled water use, etc.) while attending a daycare center at Pease. Given the focus on collecting data related to the birth mother, we administered the questionnaire to the birth mother whenever possible.

Information was requested on the child's vaccination history (to assist in evaluation of vaccines antibodies, to be reported elsewhere) and whether the child regularly exercises, and children 13 years and older were asked about current smoking habits (and the number of cigarettes/day) or alcohol consumption (and the number of drinks/week). Parents of child participants were also asked information on the child's history of potential exposure to modifiers such as blood transfusions and blood donations. For females, the questionnaire asked when the child first began to menstruate. Specific questions addressing health outcomes of interest were also included. Similarly, the questionnaire asked if the child had learning or behavioral problems.

### *Adult Questionnaire*

For adult participants, the questionnaire obtained demographic information, occupational history, medical history, reproductive history, smoking history, information on alcohol use, family medical history and any recent medications the participant has taken. Medical conditions of particular interest included kidney disease, liver disease, cardiovascular disease, hypertension, thyroid disease, diabetes, autoimmune diseases, osteoporosis, osteoarthritis, pregnancy-induced hypertension, and endometriosis. For each reported disease or condition, the date of diagnosis was collected. The questionnaire asked for the dates the participant worked at Pease and water consumption habits (including bottled water use) while working at Pease. Information concerning conditions that might affect PFAS serum concentrations such as date of menopause and menstrual cycle information for female participants, blood transfusions, and blood donations was also collected. The health outcome of interest were selected based on ATSDR evaluation of results and endpoints from previous epidemiological and toxicological PFAS studies, need for follow up or additional information, and in vitro/in vivo activity (Human health effects of drinking water exposures to per- and poly-fluoroalkyl substances (PFAS): A multi-site cross-sectional study Protocol (cdc.gov).

### *Neurobehavioral Testing*

Prior to scheduling an appointment for neurobehavioral testing (Table 3), study staff asked parents/guardians a series of questions to assess eligibility and to confirm that the child would be able to sit for 1-1.5 hours to complete the testing. Participants with the following reported conditions were not eligible due to the research nature of this testing: intellectual disabilities (e.g., IQ less than 70), cerebral palsy, traumatic brain injury or concussion lasting greater than 1-hour, legal blindness, severe hearing loss not corrected with hearing aid, or mutism. Three children were found ineligible. If the participant was eligible, the study staff scheduled a follow-up appointment at the central study office for the neurobehavioral testing.

On the day of testing, parents/guardians were asked additional screening questions to confirm that the child would be eligible for testing that day. Participants were not eligible for testing if the parent/guardian reported a new diagnosis of any conditions that would make the child ineligible for testing, as asked during initial neurobehavioral screening or if the parent/guardian reported that they did not think the child could sit for 1-1.5 hours for the testing that day (none were deemed unable to sit for testing). Participants were then administered the neurobehavioral battery of tests listed in Table 3. The accompanying parent/guardian was asked to complete the Behavior Rating Inventory of Executive Function and Strengths and Difficulties Questionnaires about their child.

**Table 3. Neurobehavioral Test Battery for Child Participants**

| Neurobehavioral Test | Domain | Age (years) | Group Administered to |
|---|---|---|---|
| Wechsler Abbreviated Scale of Intelligence – 2nd Edition (WASI – II) | Two Subtest Form (FSIQ) | 6 – 17 | Child |
| A Developmental Neuropsychological Assessment – 2nd edition (NEPSY – II) subtests | Comprehension of Instructions* (receptive language, trouble following multi-step commands) | 5 – 16 | Child |
| | Speeded Naming* (expressive language, processing speed) | 5 – 16 | Child |
| | Narrative Memory* (comprehension, verbal memory) | 5 – 16 | Child |
| | Design Copying (visuospatial processing) | 5– 16 | Child |
| | Affect Recognition (social perception) | 5 – 16 | Child |
| | Statue (inhibitory control) | 5 – 6 | Child |
| | Word Generation (expressive language, executive control) | 5 – 16 | Child |
| Conners Kiddie Continuous Performance Test, 2nd Edition (Conners K-CPT 2) | Inattentiveness, Impulsivity, Sustained Attention, Vigilance | 5 – 7 | Child |
| Conners Continuous Performance Test 3rd edition (CPT 3) | Inattentiveness, Impulsivity, Sustained Attention, Vigilance | 8 – 17 | Child |
| Strengths and Difficulties Questionnaire© (SDQ©) | Double-sided form with impact supplement (behavioral problems) | 5 – 17 | Parent about Child |
| Behavior Rating Inventory of Executive Function® (BRIEF®) | Executive Function | 6 – 17 | Parent about Child |
| Behavior Rating Inventory of Executive Function® – Preschool Version (BRIEF®-P) | Executive Function – Preschool | 5 | Parent about Child |

### *Medical and School Record Abstraction*

If certain health conditions were reported in the questionnaire, study staff attempted to verify them with the participant's reported primary medical provider. Study staff sent requests to the reported primary medical provider to complete an abstraction form for the participant. Medical providers were asked to indicate if the participant had certain health conditions and the year of diagnosis. Completed abstraction forms were returned to the study staff and entered into the centralized database. Health conditions that were self-reported and verified by medical records are listed in later in Tables 6a and 6b.

If certain learning and behavioral conditions among children were reported in the questionnaire, study staff attempted to verify these conditions with the participant's reported school. Study staff sent requests to the reported school to complete an abstraction form. School officials were asked (1) to indicate if the participant had certain learning and behavioral conditions and (2) to provide relevant information from the participant's individualized education program (IEP), the IEP evaluation report ("Full

Individual Evaluation" or "FIE"), and if available, the Independent Educational Evaluation. Completed abstraction forms were returned to the study staff and entered into the centralized database.

### *Statistical Methods*

Numbers and percents were reported for descriptive demographic, water, and health outcomes variables. Geometric means and 95% confidence intervals were used to describe PFAS serum concentrations. We used the "survey" package in R to calculate the geometric means of NHANES 2017-2018 survey data with the provided sample weights. We subset the age and sex categories only after we used the "svydesign" function in the package including all survey participants. Geometric means were calculated with "svymean" function (NHANES Survey Methods and Analytic Guidelines (cdc.gov). Differences in PFAS serum concentrations between Pease and NHANES were assessed with a Welch two sample t-test. Corresponding p-values were listed in tables as appropriate. Consistent with NHANES guidelines, non-detects in our study data were assigned a value equal to the limit of detection (LOD) divided by the square root of 2. All analyses were performed in SAS 9.4 (Cary, IN) and R [version 2.002; Vienna, Austria]. The outlines of statistical analyses for Pease and Multi-site studies contrasting PFAS and health outcomes are not covered in this report and can be found on the ATSDR website (Human health effects of drinking water exposures to per- and poly-fluoroalkyl substances (PFAS): A multi-site cross-sectional study Protocol (cdc.gov); pease-feasibility-assessment-november-2017-508.pdf (cdc.gov).

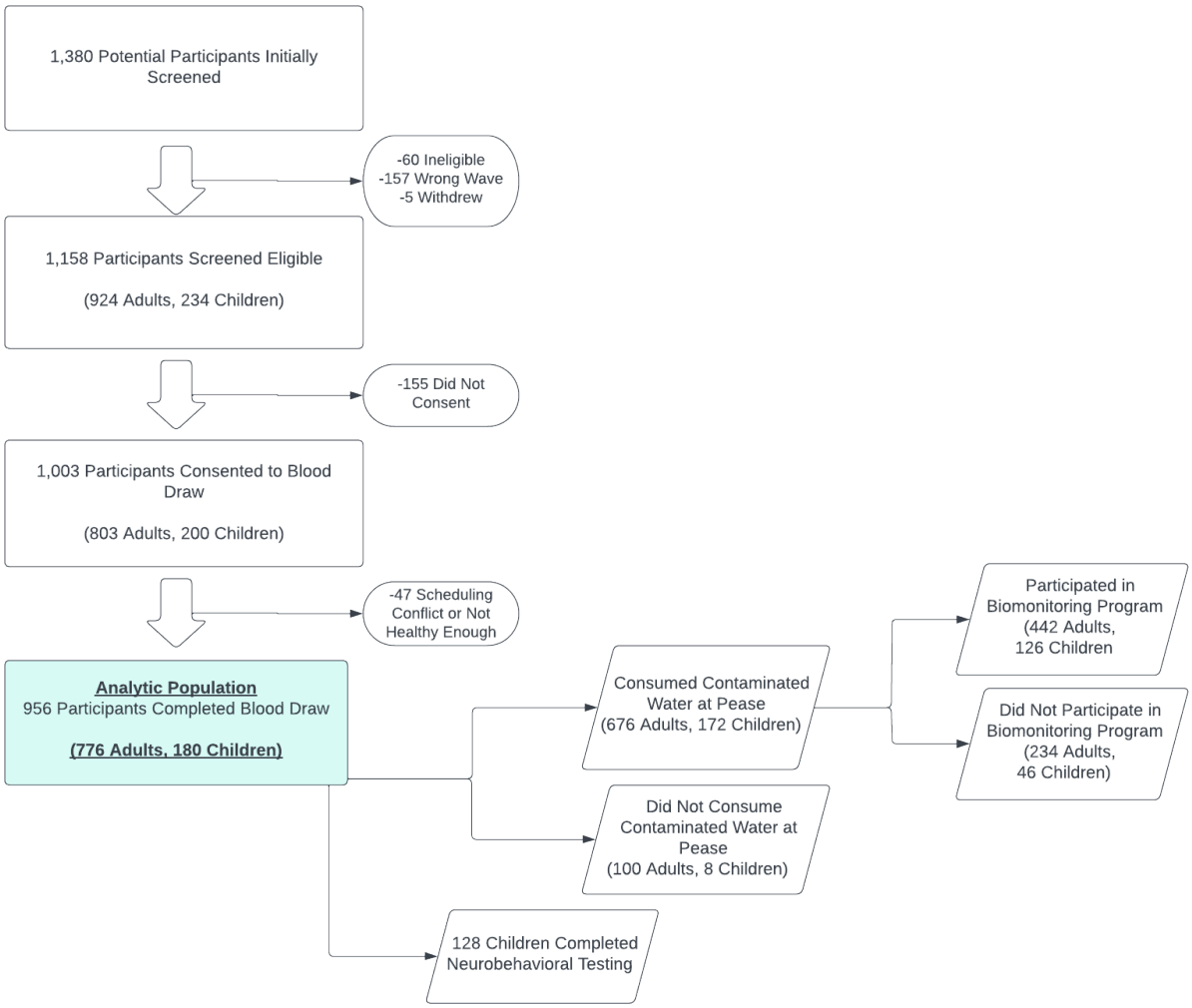
# Results

## *Cohort Recruitment*

The Pease Study screened 1,158 eligible community members from November 2019 to March 2020 and October 2020 to December 2021 (924 adults, 234 children). Approximately 87% (n=1,013; 812 adults, 201 children) of these eligible community members were consented into the study and completed at least the questionnaire. Seven hundred seventy-six adults and 180 children completed all core study activities, which is defined as completing the questionnaire and providing a blood sample. They are considered the analytic population for the remaining analyses. One hundred twenty-eight (71%) children also completed neurobehavioral testing. Figure 1 provides an overview of the number of participants who completed each study activity, as well as the number of children who completed neurobehavioral testing.

During the initial screening (Oct-Dec 2019), the study enrollment was open only to wave 1 participants who were part of the NH Biomonitoring Program. Afterwards, the enrollment was open to all three waves.

**Figure 1. Screening and Completion of Study Activities**




## *Demographic Characteristics and Exposure Assessment*

Demographic characteristics of the analytic population are outlined in Table 4. Among adults, the majority were between 40 and 59 years of age (n=412, 53.1%), White (n=748, 96.4%)) and non-Hispanic (n=769, 99.1%). Most reported having at least a high school education (n=773, 99.6%) and lived in households earning middle to upper income (n=589, 75.9%). Nearly all adult participants reported having health insurance over the previous 12 months (n=776, 99.9%).

Among children, most were between the ages of 6 and 11 years (n=112, 62.2%), White (n=172, 95.6%) and non-Hispanic (n=179, 99.4%). Most children lived in middle to upper income households (n=156, 86.7%) and all had health insurance for the previous 12 months.

Overall, the analytic population was representative of the Portsmouth area (U.S. Census Bureau, 2020). Twenty percent of the analytic population (n=191, 140 adults, 51 children) reported the Portsmouth public water system as their home tap water source. All but 8

children attended daycare at Pease and 80 children (44%) have mothers that participated in this study due to prior exposure at Pease.

**Table 4. Community Cohort Demographics in the Pease Adult and Child Analytic Population**

| Adults (n=776) | | Children (n=180) | |
|---|---|---|---|
| **Category** | **n (%)** | **Category** | **n (%)** |
| **Sex** | | | |
| Male | 366 (47.2) | | 101 (56.1) |
| Female | 410 (52.8) | | 79 (43.9) |
| **Age (years)** | | | |
| 18-39 | 117 (15.1) | 4-5 | 11 (6.1) |
| 40-59 | 412 (53.1) | 6-11 | 112 (62.2) |
| 60+ | 247 (31.8) | 12-17 | 57 (31.7) |
| **Hispanic or Latino** | | | |
| Yes | 7 (0.9) | | 1 (0.6) |
| No | 769 (99.1) | | 179 (99.4) |
| **Race** | | | |
| White | 748 (96.4) | | 172 (95.6) |
| Other[a] | 20 (2.6) | | 8 (4.4) |
| **Highest Level of Education** | | | |
| High School or Equivalent (GED) | 58 (7.5) | Preschool or Kindergarten | 20 (11.1) |
| Some University/College | 119 (15.3) | Grades 1 to 5 | 106 (58.8) |
| Technical or Trade School | 28 (3.6) | Grades 6 to 11 | 54 (30) |
| University/College Graduate | 365 (47) | | |
| Graduate School or higher | 206 (26.5) | | |
| **Household Income[b]** | | | |
| < $25,000 | 17 (2.2) | | 0 (0) |
| $25,000 to $69,999 | 126 (16.2) | | 11 (6.1) |
| $70,000 to $149,999 | 338 (43.6) | | 61 (33.9) |
| More than 150,000 | 251 (32.3) | | 95 (52.8) |
| Missing | 44 (5.7) | | 13 (7.2) |
| **Health Insurance for the Last 12 Months** | | | |
| Yes | 775 (99.9) | | 180 (100) |
| No | 1 (0.1) | | 0 (0) |
| **Home Tap Water Source** | | | |
| Pease International Tradeport public water system | 1 (0.1) | | 0 (0) |
| Other Portsmouth public water system | 140 (18) | | 51 (28.3) |
| Newington | 1 (0.1) | | 0 (0) |
| Private well not in Pease International Tradeport area | 272 (35.1) | | 56 (31.1) |
| Other[c] | 362 (46.6) | | 73 (40.6) |

[a]Includes American Indian or Alaska Native, Asian, Black or African American, and Multiracial. Each of these groups contained fewer than 10 individuals.

[b]Household income for the child population is represented by the income for the household as earned by their parents.

[c]Other represents home tap water source from areas outside of Pease and Portsmouth area.

Among the analytic population, 848 (88.7%; 676 adults, 172 children) reported working at or attending childcare at the Pease International Tradeport or Pease Air Force Base or lived in a home near the Pease facilities that were served by a PFAS-contaminated private well between 2004 and May 2014. These participants were considered exposed to PFAS contaminated drinking water. Of those in the exposed group, 568 (67.0%; 442 adults, 126 children) also participated in the New Hampshire Biomonitoring Program. The Pease Study also enrolled 108 referent participants (100 adults, 8 children) who were never exposed to PFAS contaminated drinking water from Pease. Figure 2 illustrates the breakdown of the analytic population by exposure status.

Figure 2a-d compares NHANES 2017-2018 and the Pease cohort by age groups and sex for PFOS, PFOA, PFHxS, and PFNA. Boxplots depicts median (middle line) and 25$^{th}$ (bottom line) and 75$^{th}$ (top line) quartile. Circle depicts arithmetic mean. The upper whisker shows the largest value within 1.5 times the interquartile range above the 75$^{th}$ percentile and the lower whisker shows the smallest value within 1.5 times the interquartile range below the 25$^{th}$ percentile. The youngest age group (4-17 years) have higher serum concentrations of PFOS, PFOA, and PFHxS for boys and girls than their counterparts in NHANES 2017-2018 of the same age range. PFHxS concentrations exhibit the largest differences between NHANES and Pease where Pease individuals have higher concentrations. For both NHANES 2017-2018 and the Pease cohort we observe higher serum concentrations of PFOS, PFOA, PFNA, and PFHxS for males when compared to females for adults. Sex differences are no longer apparent for the oldest age group (>60 years) for all PFAS analytes within cohorts, except for PFOS where males remain higher at older ages. Pease PFAS concentrations typically overlap with NHANES PFAS concentrations for PFOS among adults except in the oldest age group (>60 years) which is higher for NHANES participants. PFNA did not differ between Pease and NHANES for the oldest age group (>60 years). The results in this paragraph are visual comparisons of medians/geometric, interquartile ranges, and overall ranges are provided for age and sex groups. Statistical testing for differences is provided later in Tables 8a and 8b.

**Figure 2a-b. PFOS and PFOA Concentrations (µg/L) Comparisons Between Pease Study and NHANES 2017 – 2018**

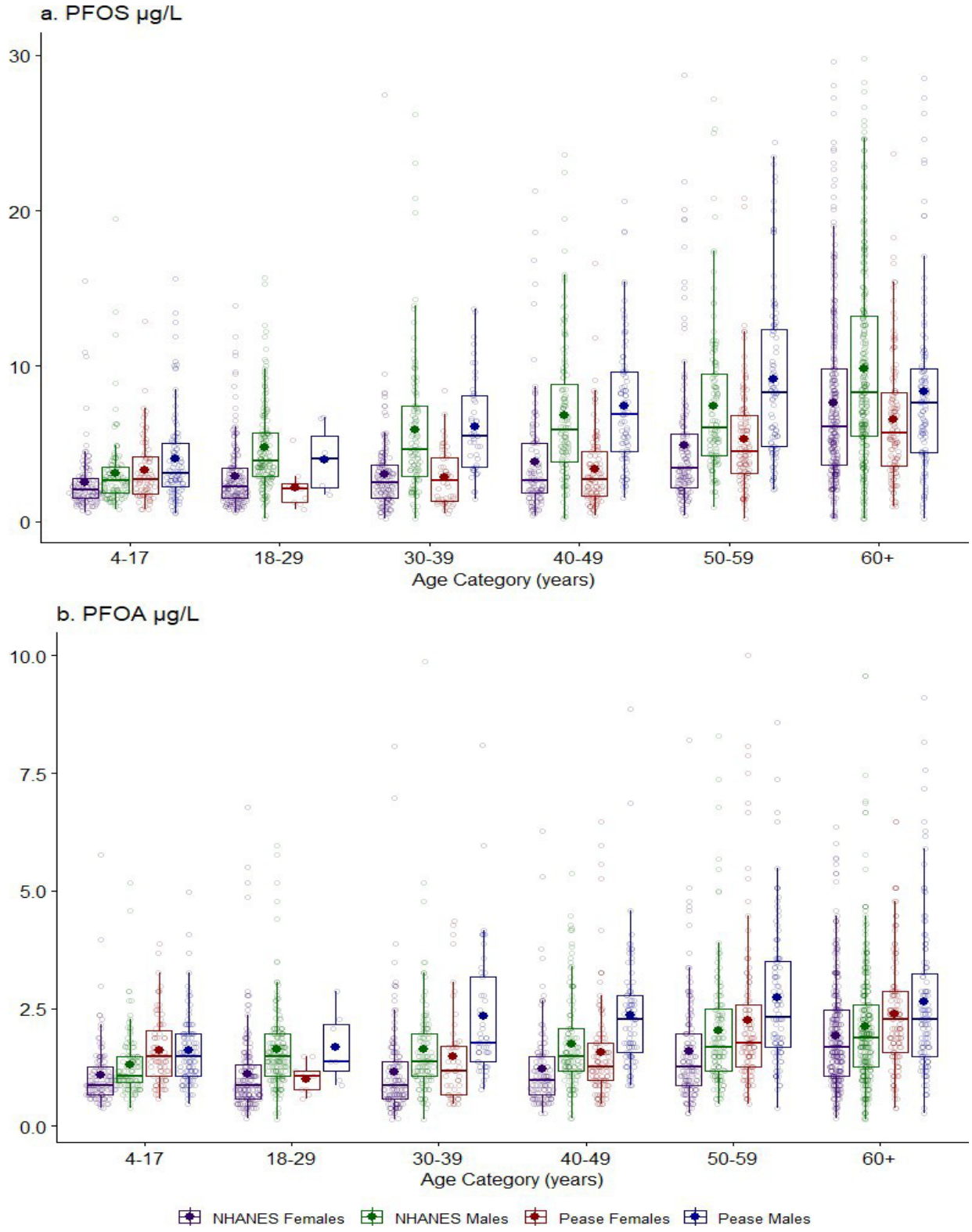
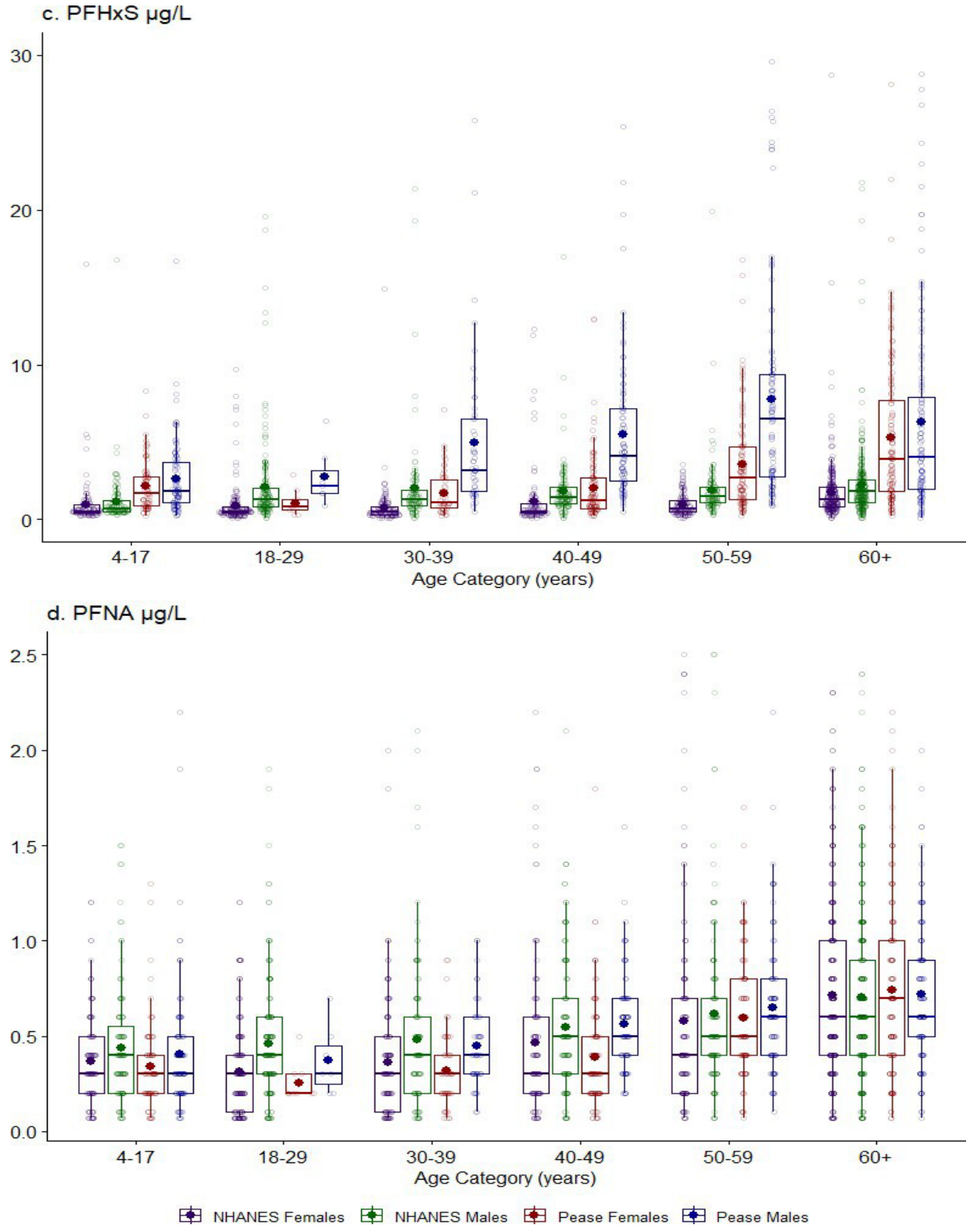


**Figure 2c-d. PFHxS and PFNA Concentrations (µg/L) Comparisons Between Pease Study and NHANES 2017 – 2018**



Tables 5a and 5b outline the water consumption characteristics and frequency of potential exposure modifiers of the analytic population. Most adult participants (n=685, 88.3%%) reported spending no time at the Pease Air Force Base before it closed in 1991. The majority of participants (675 adults, 87%) indicated spending one or more years on Pease after base closure (International Tradeport) before the contaminated well was shut down in June 2014. Eighty percent (n=144) of the child participants attended daycare at Pease. 136 (94.4%) of these children attended before June 2014.

Over half of the adult participants (n=486, 62.6%) had ever donated blood. Only 4.2% of all participants (n=40; 36 adults, 4 children) reported ever receiving a blood transfusion. No children had ever donated blood.

**Table 5a. Water Consumption and Exposure Modifiers among Pease Study Adults (n=776)**

| | Total Adults n (%) |
|---|---|
| **Current Water Consumption at Home (cups per day) (n=776)** | |
| 0-3 | 253 (32.6) |
| 4-7 | 297 (38.3) |
| 8+ | 226 (29.1) |
| **Water Consumption at Base (before 6/1/91) (cups per day) (n=89)** | |
| 0-3 | 19 (21.3) |
| 4-7 | 36 (40.4) |
| 8+ | 34 (38.2) |
| **Time Spent on Base (before 6/1/91) (years) (n=776)** | |
| None | 685 (88.3) |
| <1 | 3 (0.4) |
| 1-4 | 43 (5.5) |
| 5-9 | 24 (3.1) |
| 10-19 | 18 (2.3) |
| 20+ | 3 (0.4) |
| **Water Consumption at Tradeport before June 2014 (cups per day) (n=655)** | |
| 0-3 | 224 (34.2) |
| 4-7 | 273 (41.7) |
| 8+ | 158 (24.1) |
| **Time Spent on Tradeport before June 2014 (years) (n=776)** | |
| None | 101 (13.0) |
| <1 | 39 (5.0) |
| 1-4 | 173 (22.3) |
| 5-9 | 233 (30.0) |
| 10-19 | 202 (26.0) |
| 20+ | 28 (3.6) |
| **Water Consumption at Tradeport after June 2014 (cups per day) (n=511)** | |
| 0-3 | 266 (52.1) |
| 4-7 | 156 (30.5) |
| 8+ | 89 (17.4) |
| **Time Spent on Tradeport after June 2014 (years) (n=776)** | |
| None | 260 (33.5) |
| <1 | 44 (5.7) |
| 1-4 | 130 (16.8) |
| 5-9 | 342 (44.1) |
| **Daycare Attendance (under 35 only) (n=52)** | |
| Yes | 9 (17.3) |
| No | 43 (82.7) |
| **Water Consumption at Daycare before June 2014 (cups per day) (n=7)** | |
| 0-3 | 3 (42.9) |
| 4-7 | 4 (57.1) |

| | Total Adults n (%) |
|---|---|
| 8+ | 0 (0.0) |
| **Time Spent at Daycare before June 2014 (years) (n=52)** | |
| None | 43 (82.7) |
| <1 | 0 (0.0) |
| 1-4 | 7 (13.5) |
| 5+ | 2 (3.8) |
| **Time since Last on Pease (years) (n=721)** | |
| None | 328 (45.5) |
| <1 | 36 (5.0) |
| 1-4 | 130 (18.0) |
| 5-9 | 185 (25.7) |
| 10-19 | 10 (1.4) |
| 20+ | 32 (4.4) |
| **Ever had Blood Transfusion (n=776)** | |
| Yes | 36 (4.6) |
| No | 736 (94.9) |
| Missing | 4 (0.5) |
| **Number of Blood Transfusions (n=36)** | |
| 1 | 23 (63.9) |
| 2 | 7 (19.4) |
| 3 | 3 (8.3) |
| 4+ | 2 (5.6) |
| Missing | 1 (2.8) |
| **Ever Donated Blood (n=776)** | |
| Yes | 486 (62.6) |
| No | 286 (36.9) |
| Missing | 4 (0.5) |
| **Number of Blood Donations (n=486)** | |
| 1-10 | 327 (67.3) |
| 11-20 | 83 (17.1) |
| 21-30 | 33 (6.8) |
| 31-40 | 12 (2.5) |
| 41-50 | 7 (1.4) |
| 50+ | 17 (3.5) |
| Missing | 7 (1.4) |
| **Average Yearly Blood Donations in Last 10 Years (n=776)** | |
| 0 | 325 (41.9) |
| 1 | 73 (9.4) |
| 2 | 36 (4.6) |
| 3 | 19 (2.5) |
| 4 | 16 (2.1) |
| 5 | 6 (0.8) |
| 6 | 5 (0.6) |
| 7 | 1 (0.1) |

| | Total Adults n (%) |
|---|---|
| Missing | 295 (38.0) |

**Table 5b. Water Consumption and Exposure Modifiers among Pease Child Analytic Population (n=180)**

| | Total Children n (%) |
|---|---|
| **Current Water Consumption at Home (cups per day) (n=180)** | |
| 0-3 | 85 (47.2) |
| 4-7 | 75 (41.7) |
| 8+ | 20 (11.1) |
| **Daycare Attendance (n=180)** | |
| Yes | 144 (80.0) |
| No | 36 (20.0) |
| **Water Consumption at Daycare before June 2014 (cups per day) (n=127)** | |
| 0-3 | 58 (45.7) |
| 4-7 | 60 (47.2) |
| 8+ | 9 (7.1) |
| **Time Spent at Daycare before June 2014 (years) (n=180)** | |
| None | 44 (24.4) |
| <1 | 11 (6.1) |
| 1-4 | 110 (61.1) |
| 5+ | 15 (8.3) |
| **Water Consumption at Daycare after June 2014 (cups per day) (n=78)** | |
| 0-3 | 51 (65.4) |
| 4-7 | 26 (33.3) |
| 8+ | 1 (1.3) |
| **Time Spent at Daycare after June 2014 (years) (n=180)** | |
| None | 96 (53.3) |
| <1 | 25 (13.9) |
| 1-4 | 54 (30.0) |
| 5+ | 5 (2.8) |
| **Time since Last on Pease (years) (n=144)** | |
| None | 0 (0.0) |
| <1 | 4 (2.8) |
| 1-4 | 47 (32.6) |
| 5-9 | 93 (64.6) |
| 10-19 | 0 (0) |
| 20+ | 0 (0) |
| **Ever had Blood Transfusion (n=180)** | |
| Yes | 4 (2.2) |
| No | 176 (97.8) |
| Missing | 0 (0.0) |
| **Number of Blood Transfusions (n=4)** | |

| | Total Children n (%) |
|---|---|
| 1 | 4 (100) |
| **Ever Donated Blood (n=180)** | |
| Yes | 0 (0.0) |
| No | 180 (100) |
| Missing | 0 (0.0) |

## Reported Health Conditions

Most participants (80.2%; 653 adults, 114 children) self-reported at least one health condition in the questionnaire. Of these participants, 77.2% (n=738; 625 adults, 113 children) consented to medical records abstraction, and 601 (523 adults [67.4%], 78 children [43.3%]) records were returned by participants' medical providers. Frequencies of self-reported health conditions of interest are presented in Tables 6a and 6b. Among adults, the most reported conditions were allergies (n=373, 48.1%), followed by high cholesterol (n=258, 33.2%) and high blood pressure (n=216, 27.8%). Allergies (n=64, 35.6%), atopic dermatitis (n=30, 16.7%), attention deficit hyperactivity disorder (ADHD) or attention deficit disorder (ADD) (n=27, 15.0%), and learning and behavioral problems besides ADD/ADHD and autism (n=30, 16.7%) were the most reported conditions for children.

Table 6a. Frequency and Percent of Self-reported Health Outcomes in the Adult Pease Study Analytic Population (n=776)

| Health Outcomes | Total | Medically Verified |
|---|---|---|
| | n (%) | n (%) |
| High Cholesterol | 258 (33.2) | 211 (81.4) |
| High Blood Pressure | 216 (27.8) | 163 (75.5) |
| Heart Disease | 32 (4.1) | 20 (62.5) |
| Diabetes | 60 (7.7) | 52 (86.7) |
| Liver Disease | 15 (1.9) | 7 (46.7) |
| Kidney Disease | 19 (2.4) | 9 (47.4) |
| Thyroid Disease | 76 (9.8) | 57 (75.0) |
| Osteoarthritis | 88 (11.3) | 37 (42.0) |
| Osteoporosis | 58 (7.5) | 41 (70.7) |
| Rheumatoid Arthritis | 15 (1.9) | 3 (20.0) |
| Ulcerative Colitis | 13 (1.7) | 5 (46.2) |
| Lupus | 2 (0.3) | 0 (0.0) |
| Multiple Sclerosis | 7 (0.9) | 4 (57.1) |
| Parkinson's Disease | 0 (0) | n/a* |
| Celiac Disease | 8 (1.0) | 3 (37.5) |
| Crohn's Disease | 4 (0.5) | 3 (75.0) |
| Scleroderma | 3 (0.4) | 0 (0.0) |
| Atopic Dermatitis | 109 (14.0) | 25 (22.9) |
| Allergies | 373 (48.1) | 165 (44.2) |
| Asthma | 113 (14.6) | 66 (58.4) |
| Chronic Bronchitis | 19 (2.4) | n/a** |
| Emphysema | 6 (0.8) | n/a** |
| Fibromyalgia | 12 (1.5) | 1 (8.3) |
| Infertility | 40 (5.2) | 2 (5.0) |
| Endometriosis | 33 (4.3) | 7 (21.2) |

*n/a, not applicable
**Verification was not sought for chronic bronchitis or emphysema

**Table 6b. Frequency and Percent of Self-reported Health Outcomes in the Child Pease Study Analytic Population (n=180)**

| Health Outcomes | Total | Medically Verified |
|---|---|---|
| | n (%) | n (%) |
| High Cholesterol | 2 (1.1) | 0 (0.0) |
| Diabetes | 0 (0) | n/a* |
| Thyroid Disease | 0 (0) | n/a* |
| Lupus | 0 (0) | n/a* |
| Celiac Disease | 1 (0.6) | 1 (100.0) |
| Crohn's Disease | 1 (0.6) | 0 (0.0) |
| Scleroderma | 0 (0) | n/a* |
| Atopic Dermatitis | 30 (16.7) | 6 (20.0) |
| Allergies | 64 (35.6) | 35 (54.7) |
| Asthma | 21 (11.7) | 14 (66.7) |
| Chronic stuffy/runny nose (rhinitis/sinusitis) | 8 (4.4) | 2 (25.0) |
| Delayed puberty | 1 (0.6) | 0 (0.0) |
| Obesity | 2 (1.1) | 1 (50.0) |
| Attention deficit hyperactivity disorder (ADHD) or attention deficit disorder (ADD) | 27 (15.0) | 23 (85.2) |
| Autism | 4 (2.2) | 3 (75.0) |
| Other learning or behavioral problems | 30 (16.7) | 6 (20.0) |

*n/a, not applicable

## *Serum PFAS Concentration Measurements*

Table 7 shows the PFAS testing panel with corresponding limits of detection (LOD) and number of samples tested for each analyte. Most samples had detectable concentrations of PFAS; however, only 1.3% and 44.4% of samples were above the LOD for Sb-PFOA and MeFOSAA, respectively.

**Table 7. Per- and Polyfluoroalkyl Substance Testing Panel and Corresponding Limits of Detection**

| PFAS Name | PFAS Abbreviation | Limits of Detection (LOD) (µg/L) | Number of Samples Tested | Number > LOD n (%) |
|---|---|---|---|---|
| Perfluorooctanoic acid | PFOA | | | |
| Branch perfluorooctanoic acid isomers | Sb-PFOA | 0.1 | 956 | 12 (1.3) |
| n-perfluorooctanoic acid | n-PFOA | 0.1 | 956 | 956 (100) |
| Perfluorooctanoic sulfonic acid | PFOS | | | |
| Perfluoromethylheptane sulfonic acid isomers | Sm-PFOS | 0.1 | 956 | 954 (99.8) |
| n-perfluorooctane sulfonic acid | n-PFOS | 0.1 | 956 | 955 (99.9) |
| Perfluorohexane sulfonic acid | PFHxS | 0.1 | 956 | 956 (100) |
| Perfluorononanoic acid | PFNA | 0.1 | 956 | 932 (97.5) |
| Perfluorodecanoic acid | PFDA | 0.1 | 956 | 871 (91.1) |
| Perfluoroundecanoic acid | PFUnDA | 0.1 | 956 | 687 (71.9) |
| 2-(N-methyl-perfluorooctane sulfonamido) acetic acid | MeFOSAA | 0.1 | 956 | 424 (44.4) |

LOD: limits of detection; PFAS: per- and polyfluoroalkyl substance.

Serum PFAS concentrations for the population that consumed contaminated water at Pease, which will be referred to as exposed (n=848), are presented in Tables 8a and 8b. Differences between Pease exposed averages and NHANES2017-2018 averages were assessed with a Welch two sample t-test. For exposed adults, serum PFAS concentrations were significantly different from NHANES 2017-2018 concentrations for all analytes. PFOS (GM 5.04, CI: 4.74, 5.35), PFOA (GM 1.93, 95% CI: 1.85, 2.03), PFNA (GM 0.48, 95% CI: 0.45, 0.50), PFHxS (GM 3.21, 95% CI: 2.97, 3.48), and PFUnDA (GM 0.15, 95% CI: 0.15, 0.16) concentrations were all significantly higher among exposed Pease participants than NHANES, while MeFOSAA (GM 0.10, 95% CI: 0.10, 0.11) and PFDA (GM 0.19, 95% CI: 0.18, 0.20) were significantly lower. When compared to concentrations measured among adults in the New Hampshire Biomonitoring Program, concentrations of PFOS, PFOA, PFNA, and PFHxS were lower among adult Pease participants.

Among exposed child participants, PFOS (GM 3.06, 95% CI: 2.78, 3.38), PFOA (GM 1.47, 95% CI: 1.38, 1.57), and PFHxS (GM 1.82, 95% CI: 1.61, 2.05) concentrations were significantly higher when compared to NHANES 2017-2018. There was no significant difference in PFNA (GM 0.31, 95% CI: 0.28, 0.34), PFDA (GM 0.14, 95% CI: 0.13, 0.15), PFUnDA (GM 0.09, 95% CI: 0.08, 0.10), or MeFOSAA (GM 0.11, 95% CI: 0.10, 0.12) between child participants of Pease and NHANES.

Tables 9a and 9b include comparisons of serum PFAS concentrations between Pease participants and NHANES 2017-2018 participants by sex for adult and child cohorts, respectively. Among adult males, serum concentrations of PFOS (GM 6.93, 95% CI: 6.42, 7.48), PFOA (GM 2.28, 95% CI: 2.13, 2.43), PFNA (GM 0.54, 95% CI: 0.50, 0.57), PFHxS (GM 4.75, 95% CI: 4.27, 5.27), and PFUnDA (GM 0.15, 95% CI: 0.14, 0.16) were significantly higher for Pease participants and MeFOSAA (GM 0.11, 95% CI: 0.10, 0.12) was significantly lower than in NHANES 2017-2018. Among female adults, serum concentrations of PFOA (GM 1.68, 95% CI: 1.57, 1.79), PFNA (GM 0.43, 95% CI: 0.40, 0.46), PFHxS (GM 2.28, 95% CI: 2.05, 2.53), and PFUnDA (GM 0.16, 95% CI: 0.15, 0.17) were significantly higher in Pease and PFDA (GM 0.18, 95% CI: 0.17, 0.20) and MeFOSAA (GM 0.10, 95% CI: 0.10, 0.11) were significantly lower when compared to NHANES 2017-2018. For children, Pease participants had significantly higher serum concentrations of PFOS, PFOA, and PFHxS for both males and females. There was no statistical difference for PFNA, PFDA, PFUnDA, and MeFOSAA among both males and females between Pease Study and NHANES. When comparing the subset of Pease Study participants who also participated in the New Hampshire Biomonitoring Program, concentrations of all PFAS analytes were lower in the Pease Study testing.

**Table 8a. Per- and Polyfluoroalkyl Substance Serum Concentrations in Adult Pease Study Participants in 2019-2021 Compared with NHANES 2017-2018 and New Hampshire (NH) Biomonitoring Program.**

| PFAS | Pease Exposed 2019-2021[a] | | Pease Referent 2019-2021[a] | | NHANES 2017-18 | | | NH Biomonitoring Program (2015-2017)[b] | |
|---|---|---|---|---|---|---|---|---|---|
| | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | p-value for Difference (Pease Exposed v. NHANES 2017-2018)[c] | n | Geometric Mean (95% CI) |
| PFOS (µg/L) | 676 | 5.04 (4.74, 5.35) | 100 | 3.97 (3.47, 4.54) | 1700 | 4.45 (4.10, 4.83) | **0.035** | 1181 | 8.9 (8.5, 9.3) |
| PFOA (µg/L) | 676 | 1.93 (1.85, 2.03) | 100 | 1.70 (1.52, 1.90) | 1700 | 1.45 (1.35, 1.56) | **<0.001** | 1181 | 3.0 (2.9, 3.2) |
| PFNA (µg/L) | 676 | 0.48 (0.45, 0.50) | 100 | 0.51 (0.46, 0.57) | 1700 | 0.41 (0.37, 0.47) | **<0.001** | 1181 | 0.7 (0.7, 0.7) |
| PFHxS (µg/L) | 676 | 3.21 (2.97, 3.48) | 100 | 1.79 (1.50, 2.15) | 1700 | 1.11 (1.02, 1.21) | **<0.001** | 1181 | 4.3 (4.1, 4.6) |
| PFDA (µg/L) | 676 | 0.19 (0.18, 0.20) | 100 | 0.19 (0.17, 0.21) | 1700 | 0.20 (0.18, 0.21) | **0.027** | - | - |
| PFUnDA (µg/L) | 676 | 0.15 (0.15, 0.16) | 100 | 0.16 (0.14, 0.18) | 1700 | 0.13 (0.12, 0.14) | **<0.001** | - | - |
| MeFOSAA (µg/L) | 676 | 0.10 (0.10, 0.11) | 100 | 0.13 (0.11, 0.14) | 1700 | 0.13 (0.12, 0.14) | **<0.001** | - | - |

[a]Exposed - Pease participants who consume contaminated water, Referent - Pease participants who did not consume contaminated water.
[b] includes results from adult participants (n ≥20 years) from Daly et al., 2018.
[c]Bolded values are considered to be statistically significantly different at an alpha of 0.05**.**

**Table 8b. Per- and Polyfluoroalkyl Substance Serum Concentrations in Child Pease Study Participants in 2019-2021 Compared with NHANES 2017-2018**

| PFAS | Pease Exposed 2019-2021[a] | | Pease Referent 2019-2021 [a] | | NHANES 2017-2018 | | |
|---|---|---|---|---|---|---|---|
| | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | p-value for Difference (Pease Exposed v. NHANES 2017-2018)[b] |
| PFOS (µg/L) | 172 | 3.06 (2.78, 3.38) | 8 | 2.00 (1.61, 2.05) | 229 | 2.53 (2.18, 2.93) | **<0.001** |
| PFOA (µg/L) | 172 | 1.47 (1.38, 1.57) | 8 | 1.38 (1.02, 1.85) | 229 | 1.13 (1.04, 1.22) | **<0.001** |
| PFNA (µg/L) | 172 | 0.31 (0.28, 0.34) | 8 | 0.20 (0.10, 0.39) | 229 | 0.37 (0.30, 0.46) | 0.539 |
| PFHxS (µg/L) | 172 | 1.82 (1.61, 2.05) | 8 | 1.10 (0.69, 1.76) | 229 | 0.80 (0.70, 0.90) | **<0.001** |
| PFDA (µg/L) | 172 | 0.14 (0.13, 0.15) | 8 | 0.12 (0.08, 0.19) | 229 | 0.15 (0.13, 0.17) | 0.988 |
| PFUnDA (µg/L) | 172 | 0.09 (0.08, 0.10) | 8 | 0.11 (0.07, 0.17) | 229 | 0.10 (0.09, 0.10) | 0.156 |
| MeFOSAA (µg/L) | 172 | 0.11 (0.10, 0.12) | 8 | 0.09 (0.06, 0.12) | 229 | 0.14 (0.13, 0.15) | 0.091 |

[a]Exposed - Pease participants who consume contaminated water, Referent - Pease participants who did not consume contaminated water.

[b]Bolded values are considered to be statistically significantly different at an alpha of 0.05.

**Table 9a. Per- and Polyfluoroalkyl Substance Serum Concentrations in Adult Pease Study Participants in 2019-21 Compared with NHANES 2017-2018 by Sex**

| PFAS | Sex | Pease Exposed 2019-2021[a] | | Pease Referent 2019-2021[a] | | NHANES 2017-2018 | | p-value for Difference (Pease Exposed v. NHANES 2017-2018)[b] |
|---|---|---|---|---|---|---|---|---|
| | | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | |
| PFOS (µg/L) | Male | 316 | 6.93 (6.42, 7.48) | 50 | 5.09 (4.31, 6.02) | 837 | 5.72 (5.18, 6.30) | **0.002** |
| | Female | 360 | 3.81 (3.51, 4.12) | 50 | 3.09 (2.56, 3.74) | 863 | 3.53 (3.18, 3.91) | 0.445 |
| PFOA (µg/L) | Male | 316 | 2.28 (2.13, 2.43) | 50 | 1.91 (1.67, 2.17) | 837 | 1.65 (1.55, 1.77) | **<0.001** |
| | Female | 360 | 1.68 (1.57, 1.79) | 50 | 1.52 (1.27, 1.82) | 863 | 1.28 (1.18, 1.39) | **<0.001** |
| PFNA (µg/L) | Male | 316 | 0.54 (0.50, 0.57) | 50 | 0.54 (0.48, 0.61) | 837 | 0.45 (0.41, 0.49) | **<0.001** |
| | Female | 360 | 0.43 (0.40, 0.46) | 50 | 0.48 (0.40, 0.58) | 863 | 0.39 (0.33, 0.46) | **0.035** |
| PFHxS (µg/L) | Male | 316 | 4.75 (4.27, 5.27) | 50 | 2.45 (1.96, 3.08) | 837 | 1.55 (1.39, 1.74) | **<0.001** |
| | Female | 360 | 2.28 (2.05, 2.53) | 50 | 1.31 (1.01, 1.70) | 863 | 0.81 (0.75, 0.88) | **<0.001** |
| PFDA (µg/L) | Male | 316 | 0.20 (0.19, 0.21) | 50 | 0.18 (0.16, 0.21) | 837 | 0.19 (0.18, 0.21) | 0.650 |
| | Female | 360 | 0.18 (0.17, 0.20) | 50 | 0.20 (0.17, 0.24) | 863 | 0.20 (0.18, 0.22) | **0.013** |
| PFUnDA (µg/L) | Male | 316 | 0.15 (0.14, 0.16) | 50 | 0.14 (0.12, 0.16) | 837 | 0.12 (0.12, 0.13) | **0.005** |
| | Female | 360 | 0.16 (0.15, 0.17) | 50 | 0.18 (0.15, 0.21) | 863 | 0.13 (0.12, 0.15) | **0.028** |
| MeFOSAA (µg/L) | Male | 316 | 0.11 (0.10, 0.12) | 50 | 0.13 (0.11, 0.16) | 837 | 0.13 (0.12, 0.15) | **<0.001** |
| | Female | 360 | 0.10 (0.10, 0.11) | 50 | 0.12 (0.10, 0.15) | 863 | 0.13 (0.12, 0.14) | **<0.001** |

[a]Exposed - Pease participants who consume contaminated water, Referent - Pease participants who did not consume contaminated water.
[b]Bolded values are considered to be statistically significantly different at an alpha of 0.05.

**Table 9b. Summary of Per- and Polyfluoroalkyl Substance Serum Concentrations in Child Pease Study Participants in 2019-21 Compared with NHANES 2017-2018 by Sex***

| PFAS | Sex | Pease Exposed 2019-2021[a] | | Pease Referent 2019-2021[a] | | NHANES 2017-18[c] | | p-value for Difference (Pease Exposed v. NHANES 2017-2018)[b] |
|---|---|---|---|---|---|---|---|---|
| | | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | |
| PFOS (µg/L) | Male | 97 | 3.26 (2.84, 3.74) | 4 | 2.39 (1.42, 4.01) | 115 | 2.72 (2.43, 3.04) | **0.022** |
| | Female | 75 | 2.83 (2.47, 3.24) | 4 | 1.68 (1.23, 2.29) | 114 | 2.35 (1.92, 2.86) | **<0.001** |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| PFOA (µg/L) | Male | 97 | 1.46 (1.34, 1.60) | 4 | 1.42 (0.78, 2.60) | 115 | 1.18 (1.06, 1.31) | **<0.001** |
| | Female | 75 | 1.47 (1.33, 1.64) | 4 | 1.34 (0.72, 2.46) | 114 | 1.08 (0.95, 1.22) | **<0.001** |
| PFNA (µg/L) | Male | 97 | 0.33 (0.29, 0.37) | 4 | 0.27 (0.06, 1.17) | 115 | 0.39 (0.32, 0.47) | 0.507 |
| | Female | 75 | 0.29 (0.25, 0.33) | 4 | 0.14 (0.05, 0.41) | 114 | 0.35 (0.26, 0.48) | 0.706 |
| PFHxS (µg/L) | Male | 97 | 1.91 (1.61, 2.27) | 4 | 1.33 (0.54, 3.26) | 115 | 0.91 (0.76, 1.07) | **<0.001** |
| | Female | 75 | 1.70 (1.43, 2.02) | 4 | 0.92 (0.37, 2.25) | 114 | 0.70 (0.60, 0.81) | **<0.001** |
| PFDA (µg/L) | Male | 97 | 0.15 (0.13, 0.16) | 4 | 0.15 (0.07, 0.35) | 115 | 0.15 (0.13, 0.17) | 0.619 |
| | Female | 75 | 0.13 (0.12, 0.15) | 4 | 0.10 (0.05, 0.22) | 114 | 0.15 (0.13, 0.18) | 0.519 |
| PFUnDA (µg/L) | Male | 97 | 0.09 (0.09, 0.10) | 4 | 0.14 (0.05, 0.41) | 115 | 0.09 (0.08, 0.10) | 0.775 |
| | Female | 75 | 0.09 (0.08, 0.09) | 4 | 0.08 (0.06, 0.10) | 114 | 0.10 (0.09, 0.11) | **0.019** |
| MeFOSAA (µg/L) | Male | 97 | 0.11 (0.10, 0.12) | 4 | 0.10 (0.05, 0.22) | 115 | 0.14 (0.12, 0.15) | 0.089 |
| | Female | 75 | 0.11 (0.09, 0.12) | 4 | 0.08 (0.06, 0.10) | 114 | 0.14 (0.12, 0.16) | 0.469 |

[a]Exposed - Pease participants who consume contaminated water, Referent - Pease participants who did not consume contaminated water.
[b]Bolded values are considered to be statistically significantly different at an alpha of 0.05.
[c]Pease data includes children 4-17 years. NHANES data includes children 12-17 years.

# Discussion

This cross-sectional study aimed to assess methods and procedures prior to ATSDR implementing a multi-site study of PFAS-contaminated drinking water. This study demonstrates that the protocol was feasible, and that the order and administration of certain study activities could be adjusted, if needed. Our modified procedures in response to the COVID-19 pandemic included participant screening for COVID-19 symptoms prior to entering study office, obtaining verbal consent over the phone followed by signed consent at the office visit, administering the questionnaire over the phone to reduce participant time spent in the study office, adjusting in-person appointment schedules to limit the number of individuals in the study office at any given time, and requiring masks and face shields during the administration of neurobehavioral tests.

The objective of the present report was to provide description of the cohort and the data collected including demographic information, patterns of water consumption, concentrations of PFAS compared with national averages and previous NH Biomonitoring Program, and descriptive information on reported and verified health outcomes. A core aim of the Pease Study was to evaluate the associations between specific health effects and serum PFAS concentrations among those exposed to PFAS-contaminated drinking water at Pease; these analyses are underway, and results will be presented at future community meeting(s) and in peer-reviewed publications.

The descriptive analyses in this report found that adults and children in this study had significantly higher concentrations of PFOS, PFOA, PFNA, and PFHxS and significantly lower concentrations of MeFOSAA compared to NHANES 2017-2018. Additionally, PFUnDA concentrations were significantly higher among Pease Study adults; this association was not observed in Pease children. When comparing the Pease Study results to the 2015-2017 NH Biomonitoring Program results, Pease Study exposed participants had lower concentrations of all PFAS analytes. When comparing the subset of Pease Study participants who also participated in the NH Biomonitoring Program, these trends remained. A possible explanation for these lower concentrations is the expected breakdown of the chemicals in the body over time (Olsen 2007a). The contaminated drinking water exposure occurred prior to the wellbeing shut down in 2014. After PFAS enter the human body, some PFAS can remain there for a long time—sometimes years. Most studies estimate a half-life of PFHxS between 4.7 and 8.5 years, although some have estimated half-lives as long as 35 years (ATSDR 2021a). Most half-life estimates for PFOS are between 3.3 and 7.4 years, with a maximum of 27 years (ATSDR 2021a). For PFOA, most studies estimate the half-life between 2.1 and 3.9 years with a maximum of 10.1 years (ATSDR 2021a).

The Pease Study has several strengths. First, the study focused on drinking water exposures to PFAS. Few studies have evaluated PFAS drinking water exposures. In particular, the contamination was from a specific source, i.e., the use of AFFF at the Pease Air Force Base. Second, the large size of the adult cohort provides additional information on PFAS serum concentrations in this community. While the cohort of children was smaller than the adult cohort, it also expands the PFAS exposure profile and adds a number of participants' characteristics related to exposure not collected in the NH Biomonitoring Program. Third, the availability of the NH Biomonitoring Program data meant that two points in time for serum PFAS concentrations (in particular, a sample close in time to when the Haven well was in operation) were available for some of the cohort. Lastly, the same lab conducted the serum analyses for various analytes for this study and NHANES.

Despite a number of strengths, we encountered several limitations that affected our ability to meet the desired enrollment targets. The study office had to temporarily close in March 2020 due

to the COVID-19 pandemic. After the study office reopened in October 2020, despite increased efforts to engage the community and extensive measures to protect the health of the staff and study participants, community members were hesitant to enroll and complete study activities that required an in-person visit to the study office. Further, the office was located on the Pease which we anticipated would help to facilitate recruitment and enrollment. However, during the pandemic when many people transitioned to a work-from-home environment, a visit to the study office was no longer convenient for many. Wave three (referent) enrollment suffered greatly from the COVID pandemic especially for children.

Additionally, the protocol was designed to recruit participants in waves, with the focus at the start being on past NH Biomonitoring Program participants. To educate the community about the study we held a community meeting where, at the end, we collected contact information for those interested in participating. Interested individuals who noted that they participated in the NH Biomonitoring Program were followed up with soon after the event to be screened for eligibility and scheduled for a Pease study visit. Because we limited our focus and did not screen community members that did not participate in the NH Biomonitoring Program during the first wave of recruitment, we likely lost potential participants who did not call our study line or return our outreach attempts once we opened the study to all eligible community members later. Despite low enrollment of participants who did not consume contaminated water at Pease, the statistical analysis will be unaffected due to the measured serum concentrations of PFAS being used as the indicator of exposure magnitude.

To support the Pease Study and assist us in our recruitment efforts, the NH DHHS mailed multiple letters to biomonitoring participants requesting consent for their information to be shared. This process was necessary because participants of the NH Biomonitoring Program (2015-2017) were not consented for contact regarding future studies. The plans for ATSDR's Pease Study only became public in 2018-2019. For those who responded, NH DHHS securely transferred their contact information to the Pease Study staff who then followed up with additional outreach. Of the 1,836 biomonitoring participants, only 652 interested participants (498 adults, 154 children) contacted the Pease Study and were screened as eligible. 568 (442 adults, 126 children) individuals enrolled in the Pease Study, completed the questionnaire, and provided a blood sample. It is possible that direct contact with the more than 1,000 known exposed individuals would have increased our ability to meet the original target sample size of 350 children and 1,000 adults.

This study contributes important information to the broader understanding of serum concentrations of PFAS in a community impacted by contaminated drinking water. As the study instruments asked participants about the water consumption 20 and 30 year prior in their place of employment, we cannot exclude the possibility of participants' error in self-reporting or remembering those behaviors. A potential of exposure misclassification in estimating historically reconstructed concentrations could occur. But the recall bias would only be an issue if those with certain disease(s) had recalled their water consumption differently, or when those exposed recall (report) their health outcomes differently. Neither is relevant to this report since it does not compare exposures with health outcomes. The report here is simply presenting, solely for descriptive purposes, the frequency of self-reported water consumption and time spent on base. Given the length of time that has passed, there may be errors in the self-reporting of water consumption and time spent on base, but this would not have any impact on the key comparisons in this paper, i.e., comparisons between the PFAS serum concentrations of those who did or did not drink the Pease water and NHANES.

Regarding reporting health outcomes, it is unlikely that that those with higher PFAS serum concentrations would report health outcomes differently than those with lower PFAS serum concentrations. Moreover, the same health outcomes are also reported (verified) by health care providers minimizing the possibility of this bias even further. In addition, response bias would not occur when comparing measured PFAS serum concentrations with the effect biomarkers.

For a subset of individuals who participated in both the NH Biomonitoring Program and the Pease Study, more analyses can be conducted to understand how their individual serum concentrations have changed over an approximate 8-year period. While the Pease Study demonstrated the feasibility of the study protocol, the limitations affecting the ability to meet enrollment targets provided important lessons learned prior to embarking on the Multi-site Study. Combining Pease Study data with data from a Multi-site Study will provide ATSDR with larger sample sizes to evaluate associations between PFAS exposures and important health outcomes.

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