U.S. Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry



Housekeeping before we begin

- This meeting is being recorded
- Chat and Q/A are disabled due to the large number of participants and Microsoft Teams constraints
- Despite the ability to raise your hand virtually, we are unable to take questions or comments from participants during this meeting
- For questions about the PFAS Multi-site Study, please email <u>mss@cdc.gov</u>
- For individual health/medical questions about PFAS, please email <u>atsdrmedicalofficer@cdc.gov</u>
- For media inquiries, please email <u>envhealthmedia@cdc.gov</u>



PFAS Multi-site Study (MSS)

Virtual Open House

Presented by ATSDR and Site Teams



Topics for tonight's meeting



Introduction to the study and results from the first research paper

Presented by: Marian Pavuk, MD, PhD



How are the MSS data being analyzed?

Presented by: Tamarra James-Todd, MPH, PhD



Preliminary results from MSS researchers on PFAS and health outcomes

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ATSDR MSS Overview

- First major study to look at multiple PFAS at sites across the nation with different exposure levels
- The MSS was authorized through the National Defense Authorization Acts of 2018 and 2019 to provide information to communities about the health effects of PFAS exposure
- Expands on the pilot health study conducted near Portsmouth, NH (<u>Pease Study</u>)
- Study findings will inform all communities in the
 U.S. with PFAS drinking water exposures



What are PFAS?

- Per and polyfluoroalkyl substances (PFAS) are a large group of manufactured chemicals used in industry and consumer products worldwide since the 1940s
- Most commonly studied PFAS:
 - Perfluorooctanoic acid (PFOA)
 - Perfluorooctane sulfonic acid (PFOS)
- Other studied PFAS in MSS:
 - Perfluorohexane sulfonic acid (PFHxS)
 - Perfluorononanoic acid (PFNA)
 - Perfluorodecanoic acid (PFDA)
 - Perfluoroundecanoic acid (PFUnDA)
 - N-methylperfluorooctanesulfonamidoacetic acid (MeFOSAA)

ENVIRONMENTAL IMPACT

Drinking water contamination sources include emissions from manufacturing facilities and the use of firefighting foams at military bases and airports.

PFOA and PFOS are no longer produced in the U.S. (other PFAS may still be produced in the U.S.) but remain in the environment for years and are still used and manufactured in other countries.

PFAS contamination of drinking water is widespread, affecting at least 83-105 million residents in the United States.









Goals of MSS

The MSS investigates the relationship between PFAS exposure and health outcomes across differing populations, expanding our understanding of PFAS and their risks to our health.



Intended Insights:

- Relationship between PFAS exposures and health outcomes
- What specific health effects may be associated with PFAS exposure
- Information on health endpoints and PFAS levels in the blood of participants
- Research on PFAS, individually and in mixtures
- Historical reconstruction will help better understand the effects of long-term exposures over time
- Results of the study are generalizable to all populations affected by PFAS contaminated drinking water

Eligibility for the Multi-site Study

Eligible

- Adults aged 18 years or older and children aged 4 through 17
- Live or have lived in areas with PFAS-contaminated drinking water
- People exposed to PFAS in-utero or during breastfeeding

Not Eligible

- People exposed more than 15 years before the study began
- People exposed to PFAS through their work (firefighters, workers in chemical/industrial plants that use PFAS)

Data Collected from Study Participants

Trained staff and phlebotomists collected biospecimens and conducted clinical assessments of participants including:



Resting blood pressure



Fasting serum sample



Waist and hip circumference



Height



Whole blood sample



Neurobehavioral tests (for children aged 5-17)



Weight



First morning urine void samples

We used summary statistics, including geometric means and 95% confidence intervals (95% CIs), to describe demographic characteristics and PFAS serum concentrations.

MSS Methods Paper

Environment International 202 (2025) 109589



Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint



Full length article

Multi-site study of communities with PFAS-contaminated drinking water: Methods, demographics, and PFAS serum concentrations

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Study publication

M Pavuk et al. 2025. Multi-site study of communities with PFAS-contaminated drinking water: Methods, demographics, and PFAS serum concentrations. *Environment International*.

doi: https://doi.org/10.1016/j.envint.2025.109589



Scan with your phone for the research paper

MSS Recruitment Phase (2019-2023)

ATSDR and cooperative agreement partners (listed below) recruited participants for the study across eight states and 11 different communities:

- University at Albany and New York State Department of Health
- University of California Irvine
- **Colorado School of Public Health**
- Michigan Department of Health and Human Services

- RTI and Pennsylvania
 Department of Health
- Rutgers School of Public Health
- **Silent Spring Institute**
- **CDC/ATSDR** (through the Pease Study)

Despite unexpected recruitment delays and ongoing challenges due to the COVID-19 pandemic, ATSDR and cooperative agreement partners successfully recruited the following cohort for the study:

Site	Adults	Children
California	518	51
Colorado	925	141
Massachusetts	689	90
Michigan	422	27
New Jersey	776	88
New York	468	44
Pennsylvania	1,252	89
New Hampshire (Pease Study)	776	180
TOTAL	5,826	710

Key Demographic Characteristics



The average ages were 54 years for adult participants and 11 years for children.



 60% of adult participants were female, whereas 48% of child participants were female.



 Over 77% of adult participants reported being non-Hispanic white.



 Over 80% of adult participants had more than a high school education.

Key Findings from Blood Test Results

- We found 4 PFAS (PFOS, PFOA, PFHxS, and PFNA) in over 96% of adults in the study.
 - The levels of these four PFAS varied among the 8 sites in the study (see following graphs).
 - These differences are because of differences in the type of contamination and historical levels of PFAS in drinking water.
- Three other PFAS were found in 30% to 55% of adult participants.



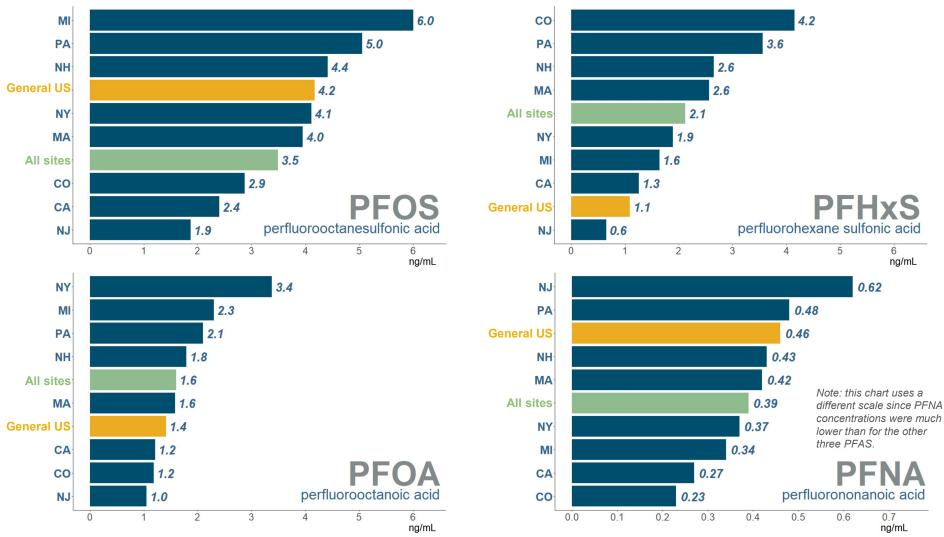
Key Findings from Blood Test Results

- Across all sites, adults in the study had higher average levels of PFHxS (2 times higher) and PFOA (>12% higher) than adults in the general population (both p-values <0.001).
- Children in the study had lower PFAS levels than adults in the study.
 - Compared to children in the general population, children in the study had higher levels of PFHxS (p<0.001).
- Premenopausal females (ages 12-49) had lower levels of most PFAS than males. In older adults, levels were similar between males and females.



Average PFAS Levels in Blood





The bar charts show the average (geometric mean) PFAS blood levels for adults across the different study sites (blue bars) compared to national levels. These averages are adjusted for the distributions of age and sex in the general US population. Gold bars show adults in the general U.S. population (2017-2020) in CDC's National Health and Nutrition Examination Survey (NHANES). Green bars represent all study sites combined.

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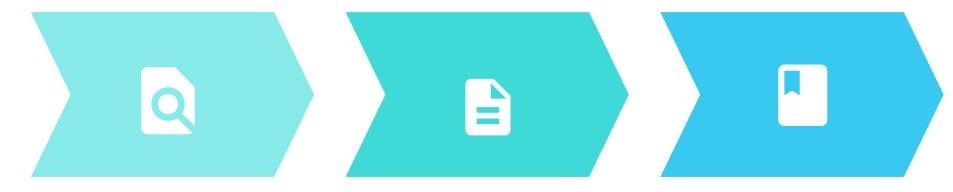
Preliminary results from MSS researchers on PFAS and health outcomes

Data analysis – Cleaning and preparation

(1) Review all information(data) collected across all 8 sites

(2) Develop new variables that can be used in analyses

(3) Document all variables in data dictionary



- Look at consistency
- Missing values
- Potential errors

- Examples include adding data together to get total exposure
- Makes it possible for researchers to find and understand needed variables for analysis

Data analysis - Making and reviewing a plan

(4) Write research question and hypothesis

(5) Write research analysis plan

(6) Review by Publications Committee





- Identify study population and variables
- Describe statistical methods



- Committee ensures appropriate design, methods, and variables are being used
- May ask for edits and re-review to ensure best science

- Review previous literature
- Identify research gaps
- Develop plausible hypothesis

Data analysis – Analyzing and presenting results

(7) Describe PFAS and health outcomes by community

(8) Calculate
 associations
 between PFAS
 and health

(9) Conduct sensitivity analyses

(10) Present results in graphs and figures



Look at PFAS levels by

site, age, and other

- 000 + x · ·
 - Examples include calculating associations between PFAS and diabetes or PFAS and thyroid disease



 Ask additional questions that help further explain data based on literature



 Use tables and figures to present results

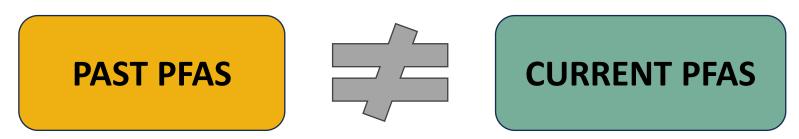
 Look at health outcomes by site, age, and other community descriptors

community descriptors

• Check for consistency in results

Data Analysis – PFAS in the past

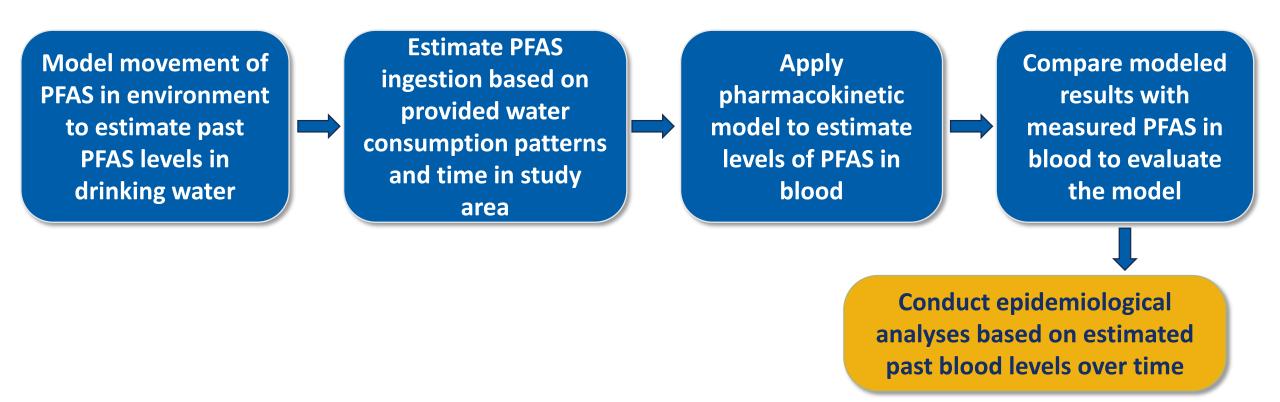
- There is a complicating factor to all analyses on PFAS and health.
- In all studied communities, exposure to PFAS from the drinking water was reduced or eliminated at the time the study took place.
- Once you reduce exposure, PFAS levels in the body decrease with time.



Levels of PFAS in MSS participants were likely different in the past from what can be measured today.

Reconstruction of historical PFAS blood levels

- Estimating PFAS blood levels over time will support future data analysis:
 - Allows for considering effects of cumulative exposures over time and exposures during specific developmental stages
 - Provides an estimate of exposure independent of measured blood concentrations



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Preliminary results from MSS researchers on PFAS and health outcomes

Updates on MSS and Health Outcome Manuscripts



Lipids (Marian Pavuk, MD, PhD)



Thyroid (Michael Bloom, PhD)



Diabetes (Anne Starling, PhD)



Blood Pressure (Yuting Wang, PhD, MPH)



Metabolic Syndrome (Abby Bline, PhD)



Heart Disease (Celina Phillipson, MS)

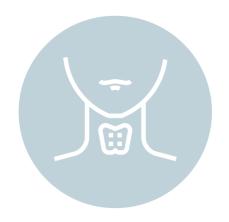


Obesity (Yerin Jung, PhD)

Updates on MSS and Health Outcome Manuscripts



Lipids (Marian Pavuk, MD, PhD)



Thyroid



Diabetes



Blood Pressure



Metabolic Syndrome



Heart Disease



Obesity

PFAS and Blood Lipid Levels Research: Background

Why are we studying blood lipids (cholesterol and triglycerides)?

- In the general population, higher cholesterol and triglyceride levels have been strongly linked to increased risk of heart disease and stroke.
- Earlier studies showed that exposure to some PFAS might change cholesterol and triglyceride levels in blood.
- Most of these studies looked at PFOA and PFOS;
 PFHxS, PFNA, and other PFAS are less studied.

What are we trying to learn about PFAS and blood lipids?

- Whether higher exposure to PFAS is associated with higher blood lipid levels.
- Whether certain PFAS appear to be more strongly associated with blood lipid levels.
- Whether our findings are consistent with PFAS being a cause of increased blood lipid levels.



PFAS and Blood Lipid Levels Research: Methods

How were the data evaluated?

- We measured seven PFAS in the blood samples provided by study participants.
- We measured different kinds of lipids in the blood samples:
 - Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein (HDL-C), non-HDL-C, and triglycerides (TG)
- We studied the relationship of level of each PFAS with the levels of the blood lipids.
- In our analysis, we considered other factors that could influence associations between PFAS and blood lipid levels including:
 - Age, sex, body mass index, race and ethnicity, cigarette and alcohol use, income, and education

Who is included in the lipids study?

- Adult participants (18 years and older)
- (Child and adolescent participants planned)



PFAS and Blood Lipid Levels Research: Initial Findings*

What have we found so far?

- Higher blood levels of PFOA, PFOS, PFNA, PFHxS, PFDA, and PFUnDA were associated with higher TC, LDL-C, HDL-C, and non-HDL-C.
- Higher levels of PFAS in the blood were not linked to higher triglycerides, as we saw either lower triglycerides or no apparent connection.
- Some PFAS appeared to have stronger associations with cholesterol levels than others.

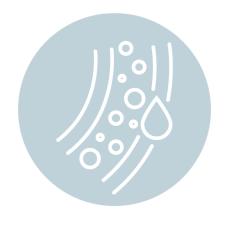
What are next steps for this research?

- Use estimates of past PFAS levels to study effects on current cholesterol levels.
- Study links between serum PFAS levels and cholesterol levels in children and adolescent study participants.



^{*} Results are preliminary and subject to change as analyses are finalized. No definitive conclusions have been made yet.

Updates on MSS and Health Outcome Manuscripts



Lipids



Thyroid (Michael Bloom, PhD)



Diabetes



Blood Pressure



Metabolic Syndrome



Heart Disease



Obesity

PFAS and Thyroid Research: Background

Why are we studying PFAS and thyroid effects?

- The thyroid gland regulates metabolism, growth and development, mood and reproduction.
- The thyroid gland synthesizes chemical messengers (hormones), including thyroxine (T4) and triiodothyronine (T3).
- Insufficient thyroid hormone can lead to hypothyroid disease (hypothyroidism).
- Excess thyroid hormone can lead to hyperthyroid disease (hyperthyroidism).
- Previous studies in animals and cells using high doses of PFAS and some human studies suggest that PFAS may affect the thyroid gland and thyroid hormones.

What are we trying to learn about PFAS and thyroid effects?

- Is exposure to PFAS associated with hypothyroid disease or hyperthyroid disease? Are specific PFAS more/less important?
- Is exposure to PFAS associated with changes in the levels of thyroid hormones in the blood?
- Are there specific groups of people that are more susceptible to thyroid effects from PFAS exposure?



PFAS and Thyroid Research: Methods

How were the data evaluated?

- PFAS were considered as predictors of thyroid disease and thyroid hormones as individual chemicals.
- PFAS was considered as a predictor of thyroid disease and of thyroid hormones as a single mixture of multiple chemicals.
- Differences in the associations were tested by study sites, gender, thyroid autoantibodies, and years since thyroid disease diagnosis.

Who was included in the thyroid study?

- 5771 Adults (≥ 18 years) in 2019-2023
- Residents of 8 communities with drinking water
 PFAS contamination
- Blood PFAS data and thyroid disease data (selfreported and/or medically-abstracted)



PFAS and Thyroid Research: Initial Findings*

What have we found so far?

- ~15% had hypothyroidism, and ~2% had hyperthyroidism.
- Overall population: higher levels of PFAS were mostly associated with a lower prevalence of hypothyroidism.
- Female population: higher PFHxS was associated with a higher prevalence of hypothyroidism.
- *Male population:* higher PFOS was associated with a higher prevalence of hyperthyroidism.

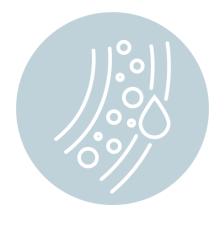
What are next steps for this research?

- Test the associations between PFAS and thyroid hormones.
- Test the associations between PFAS and thyroid autoantibodies.
- Determine if associations between PFAS and thyroid hormones can explain the associations we see between PFAS and thyroid disease.



^{*} Results are preliminary and subject to change as analyses are finalized. No definitive conclusions have been made yet.

Updates on MSS and Health Outcome Manuscripts







Thyroid



Diabetes (Anne Starling, PhD)



Blood Pressure







Heart Disease



Obesity

PFAS and Diabetes Research: Background

Why are we studying PFAS and diabetes?

- Some previous studies found that people with higher blood PFAS levels are more likely to develop type 2 diabetes.
- However, some other studies showed no association between PFAS and diabetes, or an inverse relationship.
- Few of the previous studies were conducted in populations with high levels of PFAS in their drinking water.

What are we trying to learn about PFAS and diabetes?

- For the seven PFAS that were widely detected among participants in the MSS, is there a positive relationship between PFAS levels and diabetes?
- Is there a relationship between PFAS levels in blood and blood markers of diabetes risk, such as glucose, insulin, and glycated hemoglobin (HbA1c)?



PFAS and Diabetes Research: Methods

How were the data evaluated?

- We used a common statistical method (logistic regression) to compare the frequency of diabetes diagnoses among participants with higher levels, compared to those with lower levels of each PFAS.
- We also looked at the relationship between each blood PFAS level and fasting glucose, insulin, and HbA1c, using linear regression models.
- In our analyses, we accounted for other factors that could influence PFAS exposure and diabetes risk, including age, sex, race and ethnicity, socioeconomic status, smoking history, and body mass index.

Who is included in the diabetes study?

- The diabetes analysis included 5,753
 adults; 60% were women, and the average age
 was 56 years.
- We looked at blood markers of diabetes risk in 4,582 adults without diagnosed diabetes.



PFAS and Diabetes Research: Initial Findings*

What have we found so far?

- In the study population, about 12% of adults had diabetes. This is similar to the percentage of adults in the U.S. with diabetes.
- Diabetes was not more likely to be detected among participants with higher PFAS levels in their blood. In fact, for some PFAS, participants with higher blood PFAS levels were less likely to have diabetes.
- The relationship with blood markers of diabetes risk was different for each PFAS. For example, PFOA and PFOS were associated with lower HbA1c, but PFDA was associated with higher HbA1c.

What are next steps for this research?

- Study possible reasons for the inverse relationship between diabetes and certain PFAS. For example, this result may be related to the cross-sectional study design.
- Use estimated historic PFAS exposure to study the relationship between diabetes and estimated PFAS levels before the diagnosis.
- Children were not included in this analysis because there were so few cases of diabetes in children. However, we will analyze the relationship between PFAS and blood markers of diabetes risk in children.

^{*} Results are preliminary and subject to change as analyses are finalized. No definitive conclusions have been made yet.

Updates on MSS and Health Outcome Manuscripts







Thyroid



Diabetes



Blood Pressure (Yuting Wang, PhD, MPH)





Heart Disease



Obesity

PFAS and Blood Pressure Research: Background

Why are we studying PFAS and blood pressure?

- Exposure to PFAS has been associated with an increased risk of pregnancy-induced hypertension and preeclampsia.
- Some studies have found that certain PFAS are associated with increased blood pressure and hypertension risk, but others have not.
- Previous studies only analyzed PFAS one at a time, while few studies have assessed PFAS mixtures.
- Elevated blood pressure during early adulthood may increase the risk of future cardiovascular diseases.

What are we trying to learn about PFAS and blood pressure?

- Are higher levels of PFAS in blood (individually and as a mixture) associated with higher blood pressure?
- Do certain PFAS have stronger effects on blood pressure?
- Do the effects of PFAS on blood pressure vary based on age, sex, or body mass index (BMI)?



PFAS and Blood Pressure Research: Methods

How were the data evaluated?

- We measured 7 PFAS in blood samples from participants.
- We measured systolic and diastolic blood pressure in all participants.
- We studied relationships between each individual PFAS and blood pressure, as well as the sum of seven PFAS and PFAS mixtures.
- We studied relationships between each PFAS and blood pressure according to sex and to different ranges of age and BMI.

Who did we include in the blood pressure study?

- Adult participants (18+).
- We focused on people who were not taking medications to lower their blood pressure.
- We plan to study children and adolescents in the future.



PFAS and Blood Pressure Research: Initial Findings*

What have we found so far?

- Higher serum PFOS and PFHxS levels were associated with higher blood pressure.
- We found effects of PFAS were stronger on blood pressure in younger adults (18-29).
- We found effects of PFAS were stronger on blood pressure in adults in the middle range of BMI (25-29.9 kg/m²⁾.

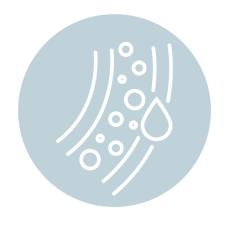
What are next steps for this research?

- Use historically reconstructed serum PFAS concentrations to better estimate effects of longterm PFAS exposures.
- Study the relationships between historically reconstructed serum PFAS and hypertension diagnosis.
- Study effects of PFAS on blood pressure in children and adolescents.



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Updates on MSS and Health Outcome Manuscripts







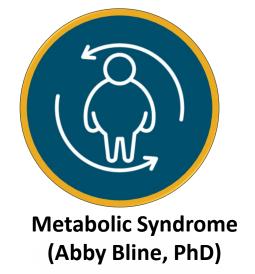
Thyroid



Diabetes



Blood Pressure







Obesity

PFAS and Metabolic Syndrome Research: Background

Why are we studying PFAS and metabolic syndrome?

- Metabolic syndrome increases risk of cardiovascular disease.
- MCP-1 and PAI-1 are substances our bodies make that often occur at higher levels in people with metabolic syndrome and can also increase risk of cardiovascular disease.
- Some studies have found associations between PFAS and metabolic syndrome, but others have not.
- Very few studies have looked at associations between PFAS and MCP-1 or PAI-1.

What are we trying to learn about PFAS and metabolic syndrome?

- Are people with higher levels of PFAS in their blood more likely to have metabolic syndrome than people with lower levels?
- Are higher levels of PFAS in blood associated with higher levels of MCP-1 or PAI-1 in blood?
- Do age or sex affect the relationships between PFAS and these outcomes?



PFAS and Metabolic Syndrome Research: Methods

How were the data evaluated?

- We used the waist size, HDL cholesterol, triglyceride, blood pressure, and blood glucose measurements collected during the study visit and medication use reported by participants to categorize people into two groups: those with metabolic syndrome and those without.
- We used statistics to study relationships between PFAS and whether people have metabolic syndrome when considering other things like a person's age.
- We used similar methods to study relationships between PFAS and MCP-1 or PAI-1.

Who is included in the metabolic syndrome study?

- Adults who were not pregnant, were fasting for their blood draw, and did not have type I diabetes were included.
- People who did not have serum PFAS
 measurements or measurements for
 metabolic syndrome categorization
 available were excluded.
- People who did not have MCP-1 or PAI-1 measurements were excluded from analyses of these outcomes.

PFAS and Metabolic Syndrome Research: Initial Findings*

What have we found so far?

- About 33% of the ~5,300 people included in our analysis had metabolic syndrome.
- People with higher PFOA and PFOS levels in blood were slightly less likely to have metabolic syndrome than people with lower levels of these PFAS.
- Higher PFOA and PFOS levels in blood were associated with higher levels of MCP-1 in blood.
- Higher PFOS and PFHxS levels in blood were associated with higher levels of PAI-1 in blood.

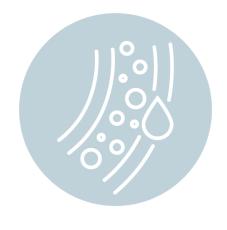
What are next steps for this research?

• Study whether estimated historical exposure to PFAS in blood is associated with metabolic syndrome.

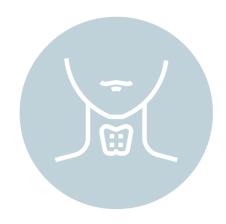


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Updates on MSS and Health Outcome Manuscripts







Thyroid



Diabetes



Blood Pressure





Heart Disease (Celina Phillipson, MS)



Obesity

PFAS and Heart Disease Research: Background

Why are we studying PFAS and heart disease?

- Heart disease is the leading cause of death in the United States 680,981 deaths in 2023.
- Studies have linked PFAS to an increase in cardiovascular diseases; however, other studies have found null or inverse associations.

What are we trying to learn about PFAS and heart disease?

- Whether people with higher levels of PFAS in their blood are more likely to report having heart disease.
- Are certain PFAS more strongly linked to heart disease, individually, or as mixtures?



PFAS and Heart Disease Research: Methods

How were the data evaluated?

- We measured PFAS in the blood.
- We collected heart disease diagnosis status from participants during questionnaire.
- We used logistic regression model to analyze the odds between those with and without heart disease looking at just PFAS - and then adjusting for or including other covariates: age, sex, race/ethnicity, education, income, smoking, alcohol, waist to hip ratio, and eGFR.

Who is included in the heart disease study?

 5,824 adult participants who answered questionnaires and had PFAS serum measurements



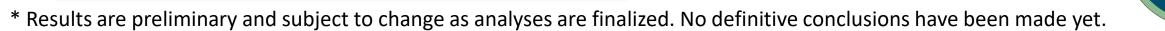
PFAS and Heart Disease Research: Initial Findings*

What have we found so far?

- 528 participants reported heart disease (9.1% prevalence).
- Most PFAS showed null associations to heart disease, except PFUnDA, which showed an inverse association.

What are next steps for this research?

- We will perform sensitivity analysis with medically validated cases.
- We will do mixture analysis to look at joint effects of PFAS exposure.
- We will use historically reconstructed PFAS serum levels to better estimate serum concentrations prior to heart disease diagnosis.



Updates on MSS and Health Outcome Manuscripts







Thyroid



Diabetes



Blood Pressure





Heart Disease



Obesity (Yerin Jung, PhD)

PFAS and Obesity Research: Background

Why are we studying PFAS and obesity?

- We found weight gain effects by PFAS exposure in lab studies.
- We found inconsistent findings in human studies.

What are we trying to learn about PFAS and obesity?

- Is a higher blood PFAS level associated with a higher risk of obesity?
- Are there differences in the associations between males and females?
- Does using different obesity measures lead to different conclusions?



PFAS and Obesity Research: Methods

How were the data evaluated?

- Measured blood PFAS concentrations
- Obesity indicators
 - Body mass index (BMI)
 - Waist circumference
 - Waist to hip ratio
 - Body roundness index (BRI)
- Regression model with potential cofounders
 - Age, sex, race/ethnicity, income, education

Who is included in the obesity study?

- Adults
 - With at least one PFAS measurement
 - With at least one obesity measurement
- Excluded
 - Current pregnant women
 - Ever diagnosed with chronic kidney diseases



PFAS and Obesity Research: Initial Findings*

What have we found so far?

- Participants with higher blood PFAS levels were less likely to be obese.
- Association between PFAS levels and obesity were similar for males and females.

What are next steps for this research?

- Mixture analysis to look at joint effects of PFAS exposure with obesity.
- Analyses to assess the association between PFAS and obesity in children.



^{*}Results are preliminary and subject to change as analyses are finalized. No definitive conclusions have been made yet.

MSS Next Steps

The MSS researchers are continuing to analyze these and other data to understand how exposures to PFAS may affect the health of adults and children.

Conclusions about cause-and-effect relationships are limited, especially in the analyses of chronic diseases, because we don't know what the blood PFAS levels were *before* the disease developed.

Our **historical modeling** will allow us to estimate the PFAS levels in tap water back to 2000, and this will provide some information about how high blood PFAS levels were in the past.

More research underway on:

- antibodies in children
- pregnancy complications
- neurobehavioral outcomes in children



Responses to questions submitted prior to the Open House





Closing Remarks

For questions about the PFAS Multi-site Study, please email mss@cdc.gov



For individual health/medical questions about PFAS, please email atsdrmedicalofficer@cdc.gov

For media inquiries, please email envhealthmedia@cdc.gov

https://www.atsdr.cdc.gov/pfas/health-studies/multi-site-study.html

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry.

