Exposure to Perfluorooctanoic Acid (PFOA) in Bennington and North Bennington, Vermont: Results of Blood Testing and Exposure Assessment

September 2017



Environmental Health

healthvermont.gov

Table of Contents

List of Figures and Tables
Executive Summary2
Background Information
Description of Vermont's PFOA Blood Testing and Exposure Assessment Study 4
PFOA Concentrations in Blood and Well Water5
Association Between PFOA Concentrations in Blood With Measures of Exposure to PFOA 7
Comparison of PFOA Concentration in Blood Across Subgroups
Comparison of PFOA Concentrations in Blood by Demographic Characteristics
Comparison of PFOA Concentrations in Blood by Work History
Comparison of PFOA Concentrations in Blood by Diet, Among Non-Workers
Comparison of PFOA Concentrations in Blood by Medication Use
Comparison of PFOA Concentrations in Blood by Lifestyle Factors
Comparison of PFOA Concentrations in Blood by Women's History and Blood Donation 13
Association Between PFOA Concentrations in Blood and Adverse Health Outcomes
Strengths and Limitations of This Exposure Assessment Study14
Conclusions and Recommendations15
Appendices16
Appendix A: Statistical Methodology16
Appendix B: Supplemental Data Tables

List of Figures and Tables

- Figure 1. Breakdown of Health Department blood testing and exposure assessment participants
- Figure 2. Distribution of PFOA blood results
- Figure 3. Distribution of water results
- Table 1. PFOA levels in blood (μ g/L) by demographic characteristics
- **Table 2.** PFOA levels in blood (μ g/L) by work history
- **Table 3.** PFOA levels in blood (μ g/L) by diet (among non-workers)
- Table 4. PFOA levels in blood (µg/L) by medication use
- Table 5. PFOA levels in blood (μ g/L) by smoking, alcohol, exercise and weight status
- **Table 6.** PFOA levels in blood (μ g/L) by women's history and blood donation

Executive Summary

In 2016, Perfluorooctanoic Acid (PFOA) was found in private drinking water wells in Bennington and North Bennington, Vermont near the former Chemfab property. The Vermont Department of Health did a study looking at blood testing results of people in the Bennington/North Bennington community and how they were exposed to PFOA. The study focused on the following three goals:

- 1. to better understand how people in the Bennington/North Bennington community were exposed to PFOA,
- 2. to make sure no additional actions were needed to stop continued exposure to PFOA, and
- 3. to provide community members with their PFOA blood level and how it compares to background levels in the U.S. population.

Conclusion and Recommendations

The study shows that concentrations of PFOA in blood were linked to concentrations of PFOA in drinking water, which indicates drinking water from contaminated wells was the main way people were exposed to PFOA.

The Health Department recommends people in the Bennington/North Bennington community:

- NOT use water with PFOA concentrations above 20 parts per trillion for drinking, preparing food, cooking, brushing teeth, watering gardens or any other way of taking in water
- Contact their health care provider if they are worried about their health related to their PFOA exposure

The Health Department will update health care providers in the area if there is any new information about PFOA and health.

Background Information

Perfluorooctanoic Acid (PFOA) in Vermont

In early 2016, PFOA-contaminated municipal water wells were discovered in Hoosick Falls, New York. Following this discovery, residents of North Bennington, Vermont raised concerns about the former Chemfab property, which had applied non-stick coatings to fiberglass fabrics from 1970 to 2002. In 2016, the Vermont Department of Environmental Conservation began testing private drinking water wells near the former Chemfab facility for PFOA. The concentrations of PFOA ranged from non-detectable levels to nearly 3,000 parts per trillion. This discovery prompted an investigation by the Health Department, with support from the Southwestern Vermont Medical Center, beginning in April 2016.

What is PFOA?

PFOA is a manufactured chemical that is often used to make household and commercial products that resist heat and chemical reactions, and repel oil, stains, grease and water. PFOA does not break down easily and therefore can stay in the environment and in the body for a long time.

Why is PFOA contamination a health concern?

Prior studies, such as those conducted by the C8 Science Panel in the Mid-Ohio Valley, have shown an association between PFOA in blood and the following adverse health outcomes:

- High cholesterol
- Ulcerative colitis
- Thyroid disease
- Kidney cancer
- Testicular cancer
- High blood pressure during pregnancy

The associations found in these studies are not proof of a cause-and-effect relationship between exposure to PFOA and the above adverse health outcomes. More research is needed before scientists will be able to determine whether there is a definitive cause-and-effect relationship between PFOA and any adverse health outcomes—such as the cause-and-effect relationship between smoking and lung cancer. However, the Health Department does not require such definitive causal relationships to be established in order to take action to protect public health.

Description of Vermont's PFOA Blood Testing and Exposure Assessment Study

Exposure Assessment Description

Each participant in the exposure assessment study was asked to provide a blood sample and complete a questionnaire. The questionnaire was adapted from the questionnaire distributed by New York State to the residents of Hoosick Falls, and focused on sources of PFOA exposure and associated health outcomes that had been identified in previous studies, such as those conducted by the C8 Panel. The purpose of collecting the questionnaire data was to better understand the relationship between consumption of PFOA-contaminated drinking water, the level of PFOA in an individual's blood, and potential adverse health outcomes. Additionally, the Health Department wanted to verify that the consumption of contaminated drinking water was the primary source of exposure to PFOA, and that there was not another, unaccounted for source of exposure in the Bennington area.

Participants were asked a series of questions regarding potential sources of exposure to water contaminated with PFOA, including number of eight-ounce glasses consumed daily of: unfiltered water, filtered water, and bottled water. Participants were also asked to identify other potential sources of exposure to PFOA, such as the consumption of various foods (milk, meat, or eggs) from animals raised in the sampling area, fish caught within the sampling area, or fruits and vegetables grown in the sampling area. Lastly, participants were asked to identify whether they have ever worked or lived at the former Chemfab facility, which was converted to residential, multi-unit housing in after the Chemfab/Saint-Gobain plant closed in 2002 (yes or no). Participants were asked to self-report if they had ever been diagnosed with high cholesterol, chronic kidney disease, increased uric acid levels, altered liver enzymes, ulcerative colitis, pregnancy-induced hypertension, and kidney or testicular cancer.

Who was eligible to have their blood tested?

Individuals were eligible for blood testing if:

- 1. the Vermont Department of Environmental Conservation (DEC) tested their well water for PFOA, or
- 2. they lived in a home in the past 8 years that was tested by DEC, or
- 3. they live or lived, work or worked at the Chemfab/Saint Gobain site.

There were 477 blood samples collected as part of the Health Department's blood testing and exposure assessment.

<u>Study Participants</u>

The results of 472 individuals were included in the following analysis. The blood samples of five individuals were not included for various reasons, e.g. not completing the questionnaire. The final group of participants included 65 who were occupationally exposed to PFOA and 407 who were non-occupationally exposed.

Figure 1 illustrates the breakdown of study participants.

Figure 1. Breakdown of Health Department blood testing and exposure assessment participants



PFOA Concentrations in Blood and Well Water

PFOA Concentrations in Blood

The Bennington/North Bennington exposure assessment analysis included 472 PFOA blood results. The results ranged from 0.3 to 1125.6 μ g/L. The geometric mean (a type of average) of these results was 10.1 μ g/L compared to a geometric mean of 2.1 μ g/L for the entire U.S. population. The 95th percentile was 157.8 μ g/L compared to 5.7 μ g/L for the entire U.S. population.

Figure 2 illustrates the distribution of these blood test results.

Figure 2. Distribution of PFOA blood results



Note: The double black line (||) signifies a change in the PFOA concentration interval width in order to present all of the results on one chart—the range of test results represented in the bar on the far right is greater than the others presented. There is no clinical significance to this distinction.

PFOA Concentrations in Well Water

Drinking water samples were taken from various locations in the Bennington/North Bennington area. There were 345 water samples matched to the blood samples of current residents. When multiple water samples had been taken for a particular household, the maximum concentration was used in this analysis. Of the 345 samples, the geometric mean of PFOA concentrations in well water was 81.4 μ g/L, and 291 drinking water results had levels of PFOA that were higher than the Health Department's drinking water health advisory level of 20 parts per trillion.

Figure 3 illustrates the distribution of the water results for the 345 current residents.





Note: A result value of ND means that PFOA was not detected.

Association Between PFOA Concentrations in Blood With Measures of Exposure to PFOA

PFOA concentrations in blood were compared to different measures of exposure to PFOA to assess which factors may have influenced the concentration of PFOA in the bodies of study participants. The strength of the association between PFOA in blood and the measures of exposure was assessed using Spearman's rank correlation. The statistical significance of the correlation is reported as the p-value. A description of all the statistical methods used in this analysis can be found in <u>Appendix A</u>.

Results of blood testing showed that PFOA levels in blood were strongly correlated with PFOA levels in well water (Spearman's rank correlation coefficient = 0.62). The higher the concentration of PFOA in a person's drinking water, the higher the level of PFOA in their blood. Adding further support to this finding, the association with PFOA in blood remained strong (Spearman's rank correlation coefficient = 0.65) when the amount of water an individual drank and how long they drank it for was considered. In other words, the more contaminated water an individual drank and the longer they drank it for, the higher the level of PFOA in their blood.

PFOA levels in blood were weakly correlated with the number of years at current residence (Spearman's rank correlation coefficient = 0.12). Study participants who lived at their current residence longer generally had slighly higher levels of PFOA in their blood. However, it should

be noted that current PFOA concentrations in water may not be equal to historic PFOA concentrations for all years of residence.

PFOA levels in blood were weakly and negatively correlated with the number of glasses of filtered water consumed per day (Spearman's rank correlation coefficient = -0.13). This means that study participants who consumed more filtered water generally had slightly lower PFOA concentrations in blood. This is to be expected, as appropriate filters remove PFOA from water.

PFOA levels in blood were not correlated with the number of glasses of unfiltered water consumed per day at the residence. This means there was no association between consumption of unfiltered water at home and an individual's blood PFOA level. This may be due to individuals being unsure of how much water they consume in a given day. PFOA levels in blood were also not correlated with the number of glasses of bottled water consumed per day. This is to be expected, as presumably, bottled water does not contain PFOA.

Comparison of PFOA Concentration in Blood Across Subgroups

For the purposes of these comparisons, a subgroup was made up of participants who had different demographic or exposure characteristics (e.g. men versus women, workers versus residents, etc.). The comparisons were made using non-parametric statistical methods due to the distribution of the PFOA blood results. The specific tests used were the Wilcoxon rank-sum test (to compare two subgroups) and the Kruskal-Wallis test (to compare three or more subgroups). A more detailed description of these statistical methods can be found in <u>Appendix A</u>.

All the tables in this section of the report include a column entitled "n," which indicates the number of participants in each subgroup. The "geometric mean" column indicates the geometric mean (a type of average) of the blood PFOA concentration for each subgroup. The "p-value" column provides an indication of whether the difference in blood PFOA concentration between the subgroups is statistically significant. For the purposes of this report, a p-value of ≤0.05 was considered to indicate that the PFOA concentrations in blood in one group were significantly different from the PFOA concentrations of the other group.

Comparison of PFOA Concentrations in Blood by Demographic Characteristics

Study results showed higher PFOA blood levels in men compared to women. These data are consistent with other studies, including PFOA biomonitoring in Minnesota and New York. The difference between women and men could be due to sex-specific physiological differences, different occupational histories, consumer product use, or PFOA clearance rates—the time it takes for PFOA to leave the body. Studies have shown that PFOA can leave women's bodies through menstruation, childbirth and breastfeeding. Higher levels of PFOA in blood were seen among women ages 60 and over than among women ages 18 to 59. This may due to less PFOA leaving older women's bodies through menstruation following menopause.

	n	Geometric mean	p-value
All participants	472	10.1	N/A
Age groups			
Adults	412	10.7	
Children	60	7.0	p=0.07
Adults			
Male	189	13.0	
Female	213	8.8	p<0.01
Males by age group			
Males, age 18-39 years	30	7.4	
Males, age 40-59 years	75	14.4	
Males, age 60 years and older	81	14.4	p=0.10
Females by age group (3 categories)			
Females, age 18-39 years	39	4.0	
Females, age 40-59 years	89	8.4	
Females, age 60 years and older	83	13.0	p<0.001
Females by age group (2 categories)			
Females, age 18-59 years	128	6.9	
Females, age 60 years and older	83	13.0	p<0.01
Children			
Boys	22	6.5	
Girls	38	7.2	p=0.61
Boys by age group			
Boys, age 12 years and under	13	6.3	
Boys, age 13-17 years	9	6.8	p=0.84
Girls by age group			
Girls, age 12 years and under	20	8.0	
Girls, age 13-17 years	18	6.5	p=0.31
Race/ethnicity			
White	407	10.5	
Other	65	7.9	p=0.16
Household income			
Less than \$40,000	93	8.9	
\$40,000 to less than \$90,000	112	10.8	
\$90,000 or more	72	9.0	
Don't know/refused	120	12.6	p=0.40
Highest level of education (adults only)			
High school or less	122	12.6	
Some college	86	11.7	
College graduate	170	8.6	
Don't know/refused	34	14.0	p=0.11

Table 1. PFOA levels in blood (μ g/L) by demographic characteristics

Comparison of PFOA Concentrations in Blood by Work History

As expected, individuals who worked directly with PFOA had statistically higher PFOA levels (geometric mean = 59 μ g/L) in their blood compared to those who did not work directly with PFOA (geometric mean = 9.6 μ g/L).

Average PFOA blood levels in other populations that worked with PFOA were higher than in the Bennington and North Bennington communities. For example, in a study of workers in Decatur, Alabama, participants had an average level of PFOA in blood of 1130 μ g/L. Levels were likely lower among the Bennington and North Bennington worker group, in part, because most of these workers stopped working with PFOA in 2002 or earlier.

	n	Geometric mean	p-value
Potential sources of exposure to PFOA			
Worked directly with PFOA	24	59.0	
Worked indirectly with PFOA prior to 2003	41	10.7	
Worked or lived at Chemfab building after 2002	16	2.8	
Currently live in a home that was tested	351	10.6	
Formerly lived in a home that was tested	27	4.5	
Other	13	2.7	N/A
Work directly with PFOA at job?			
Yes	24	59.0	
No	388	9.6	p<0.001
Ever served in the military?			
Yes	45	13.3	
No	362	10.4	p=0.22
Ever served as a professional/volunteer firefighter?			
Yes	21	10.5	
No	383	10.7	p=0.95
Ever work at power plant?			
Yes	7	8.4	
No	405	10.7	p=0.38
Ever work in wire manufacturing?			
Yes	8	19.6	
No	404	10.6	p=0.20
Ever work in electronics manufacturing?	-		
Yes	20	15.0	
No	392	10.5	p=0.22
Ever work with fluorocarbons?		20.5	
Yes	44	30.5	
No	368	9.4	p<0.001
Ever work in rubber or plastics industry?	10	24.6	
Yes	16	21.6	0.05
NO	396	10.4	p=0.05
Ever work with fire-fighting foam?	11	10.2	
Yes	11	10.2	- 0.04
	401	10.7	p=0.84

Table 2. PFOA levels in blood (μ g/L) by work history

Comparison of PFOA Concentrations in Blood by Diet, Among Non-Workers

Preliminary results showed an association between people who frequently ate fruits and vegetables grown within the sampling area and PFOA in blood. However, this association was only present among those who also consumed contaminated water with high levels of PFOA and was not present among those who consumed water with low levels of PFOA. In other words, consuming contaminated drinking water likely was responsible for the original association. Please see <u>Appendix B</u> (Supplemental Table 1) for these data.

	n	Geometric mean	p-value
Fruit/vegetable grown within sampling area			
Daily/Weekly	165	11.8	
Monthly/Never	215	8.3	p=0.04
Milk from animals raised within sampling area			
Yes	19	16.7	
No	236	10.0	p=0.15
Meat from animals raised within sampling area			
Yes	42	7.4	
No	232	10.5	p=0.11
Fish caught within sampling area			
Yes	24	7.8	
No	284	10.3	p=0.30
Eggs from animals raised within sampling area			
Yes	105	12.2	
No	169	9.5	p=0.22

Table 3. PFOA levels in blood (μ g/L) by diet (among non-workers)

Comparison of PFOA Concentrations in Blood by Medication Use

Statistically significant differences in blood PFOA concentrations were seen among those who reported taking blood pressure or cholesterol-lowering medication. These individuals had a higher geometric mean level of blood PFOA than those who did not report taking such medications.

Table 4. PFOA levels in blood (μ g/L) by medication use

	n	Geometric mean	p-value
Cholesterol-lowering medication			
Yes	90	18.1	
No	372	8.9	p<0.001
Blood pressure-lowering medication			
Yes	115	16.2	
No	350	8.9	p<0.001
Thyroid medication			
Yes	44	11.9	
No	416	9.9	p=0.71

Comparison of PFOA Concentrations in Blood by Lifestyle Factors

The results indicate that PFOA concentrations in blood were not statistically different based on lifestyle factors.

Table 5. PFOA levels in blood (µg/L) by sinoking, alconol, exercise and weight stati	Table 5.	PFOA levels i	n blood (µg/l	L) by smoking,	alcohol, exe	ercise and wei	ight status
---	----------	---------------	---------------	----------------	--------------	----------------	-------------

	n	Geometric mean	p-value
Have you smoked 100 cigarettes in your lifetime?			
Yes	169	12.4	
No	222	9.3	p=0.06
Do you currently smoke?			
Yes	39	15.5	
No	364	10.2	p=0.12
How many drinks do you have in an average			
None	184	11.0	
1 to 3 drinks a week	122	9.3	
4 or more drinks a week	89	13.0	p=0.15
Hours spent doing strenuous exercise			
Less than 3 hours	215	11.3	
3 or more hours	156	9.6	p=0.24
BMI Categories			
Underweight/normal	144	9.2	
Overweight	141	12.9	
Obese	127	10.4	p=0.20

Comparison of PFOA Concentrations in Blood by Women's History and Blood Donation

The results indicate that PFOA concentrations in blood were not statistically different based on number of children, history of breastfeeding, or blood/plasma donation.

	n	Geometric mean	p-value
Women's History			
How many children have you had?			
0	<6	Suppressed	
1	34	9.8	
2	63	9.4	
3 or more	55	10.2	p=0.52
Breastfed at least one child?			
Yes	89	9.5	
No	17	9.4	p=0.76
Blood Donation			
Donate blood or plasma?			
Yes	31	8.5	
No	370	10.8	p=0.17

Table 6. PFOA levels in blood (μ g/L) by women's history and blood donation

Note: The Health Department does not report findings (suppresses) when there are less than 6 individuals in a given category. This is to protect confidential health information.

Association Between PFOA Concentrations in Blood and Adverse Health Outcomes

Potential associations between blood PFOA concentration and adverse health outcomes were assessed among adults only. Logistic regression modeling was used, which is a statistical method that can be used to estimate the probability of a given outcome using one or more predictor variables. Further information about this statistical method, how the models were built, and how to interpret the results can be found in <u>Appendix A</u>. The unadjusted (crude) associations between blood PFOA concentration and the various health outcomes can be found in <u>Appendix B</u> (Supplemental Table 2). The associations between blood PFOA concentration and lifetime smoking can be found in <u>Appendix B</u> (Supplemental Table 3).

The results of this exposure assessment **indicated an association** between PFOA concentrations in blood and the following conditions:

- High cholesterol
- Hypertension during pregnancy

The results of this exposure assessment **did not indicate that there is an association** between PFOA concentrations in blood and the following conditions in this population:

- Chronic kidney disease
- Increased uric acid levels
- Altered liver enzymes
- Fatty liver disease
- Hypothyroidism
- Hyperthyroidism
- Ulcerative colitis

Due to sample size, an association between less common health outcomes (such as some of those listed above) and exposure to PFOA, was unlikely to have been detected in this study. The fact that no association was detected with these health outcomes in the Bennington/North Bennington community does not rule out the possibility that an association exists.

The Health Department does not report findings when there are less than 6 individuals with a given health outcome. This is to protect confidential health information, as well as to avoid calculating potentially unstable rates due to small numbers. Due to the limited sample size, we were unable to evaluate the association between PFOA concentrations in blood and the following conditions:

- Testicular cancer
- Kidney cancer

Strengths and Limitations of This Exposure Assessment Study

As with all epidemiologic studies, this exposure assessment is subject to several limitations. First, the Bennington/North Bennington investigation was limited by a small sample size when compared to other PFOA exposure assessment studies. This impacted the Health Department's ability to assess associations between blood PFOA concentration and certain, rare health outcomes.

Additionally, this study was cross-sectional in nature, meaning that it was a "snapshot" of exposure and outcome at one point in time. It does not consider what blood PFOA

concentrations may have been in the past, or health outcomes that participants may develop in the future. Most importantly, it does not allow for temporality to be established between exposure and outcome. With this type of study, it is impossible to determine whether exposure to PFOA occurred before or after health outcomes developed. Therefore, with this type of study, it is impossible to say whether or not exposure to PFOA definitively caused a given health outcome.

Information about exposure to PFOA and various health outcomes was self-reported, and the Health Department did not validate the information via other sources (e.g. medical records).

Lastly, the study population was composed of those who were willing to have their blood tested and share their personal information. The Health Department does not know how many other people were eligible and chose not to participate. Therefore, volunteer/selection bias may be present.

There are several strengths to this study that should also be considered. Response rate for the survey was incredibly high. Only a handful of the 477 surveys that were distributed were not returned. Blood samples were collected for all participants and water samples were collected for all participants who never worked or resided at the former Chemfab building. This allowed for accurate quantification of the concentration of PFOA in both blood and water at the individual level.

Conclusions and Recommendations

Drinking water from contaminated wells was the main, non-occupational source of exposure to PFOA in the Bennington/North Bennington community. The Health Department would have been concerned that there was another undetected and unaddressed exposure pathway if this association between blood PFOA concentration and PFOA concentration in drinking water had not been found.

The Health Department recommends that water with PFOA above 20 parts per trillion NOT be used for drinking, preparing food, cooking, brushing teeth, watering gardens, or any other manner of ingestion. The Health Department recommends that anyone who has concerns about their health related to their exposure to PFOA consult with their health care provider. If new information regarding PFOA and health emerges, the Health Department will update health care providers in the area.

Appendices

Appendix A: Statistical Methodology

Spearman's Rank Correlation

Spearman's rank correlation is the non-parametric version of the commonly used Pearson product-moment correlation. This means that it can be used when data is not normally distributed, and it would be inappropriate to use the Pearson product-moment method. Similar to a Pearson product-moment correlation, Spearman's rank correlation measures the strength and direction of an association between two variables.

A Spearman's rank correlation coefficient of zero indicates that there is no association between the two variables. A Spearman's rank correlation coefficient of 1 indicates that the two variables are perfectly positively correlated (all the data points would fall on the trendline), and that as one variable increases, so does the other. A Spearman's rank correlation coefficient of negative 1 indicates that the two variables are perfectly negatively correlated (all the data points would fall on the trendline), and that as one variable increases, the other decreases.

<u>p-values</u>

In statistics, p-values are used to assess whether the difference seen between two (or more) groups is a true difference or due to chance. These p-values represent the likelihood that an association was found when none truly exists. The smaller the p-value, the stronger the statistical significance of the association, and the more likely there is a true difference between groups. Generally speaking, a p-value of 0.05 is considered to be "statistically significant." As p-values get smaller, for example a p-value of 0.01 or 0.0001, the difference between groups is considered to be more and more significant.

When to Use a Non-Parametric Statistical Test

The decision to use parametric or non-parametric statistics is based upon whether the variables meet the assumptions (rules for appropriate choice) for a statistical test. One of the assumptions for performing a parametric test (e.g. an independent samples t-test or an Analysis of Variance (ANOVA) test) is that the outcome variable is normally distributed (evenly distributed above and below the average). In contrast, non-parametric statistical tests do not make these types of assumptions. In the case of this exposure assessment, the PFOA concentrations in blood were not "normally" distributed. There were far more low concentrations and fewer high concentrations, so the assumption of normality was not met. Therefore, non-parametric statistics were used to compare the mean PFOA concentrations in blood by the different sub-groups.

Wilcoxon Rank-Sum Test

To compare the mean PFOA concentrations in blood across two groups (e.g. adults as compared to children), p-values were generated using a Wilcoxon rank-sum test (the non-parametric equivalent to the independent samples t-test). Instead of comparing mean values, like the independent samples t-test, the Wilcoxon rank-sum compares the order in which the observations from two samples fall when ranked from lowest to highest. This allows the test to assess for statistically significant differences (in this case, of blood PFOA concentration) between two groups, without being affected by the distribution of the data.

Kruskal-Wallis Test

To compare mean PFOA concentrations in blood across three or more groups (e.g. having a BMI considered underweight/normal, a BMI considered overweight, or a BMI considered obese), p-values were generated using a Kruskal-Wallis test (the non-parametric equivalent to an ANOVA test). Rather than comparing the mean values of three or more groups, like the ANOVA test, the Kruskal-Wallis test compares the ranks of three or more groups. This allows the test to assess for a statistically significant difference (in this case, of blood PFOA concentration) between any of the three or more groups.

It is important to remember that a statistically significant p-value generated by a Kruskal-Wallis test is indicative of a difference between any two of the three or more groups. This test does not allow you to identify which two groups are different from each other, or whether all of the groups you are considering are different from each other.

Logistic Regression

Logistic regression is a statistical method used to determine the probability or odds of an outcome occurring. Outcomes modeled in this way must be binary, which means that there are only two alternatives (either you have high cholesterol or you do not). In a logistic regression model, changes in the odds of a given outcome are assessed based on the values of one or more predictor variables. For example, a person's age, smoking status, and weight could be included in a logistic regression model assessing the odds of developing lung cancer.

For this study, two types of logistic regression models were built for each health outcome. The first model, known as a crude model, assessed the odds of each health outcome using only blood PFOA concentration as a predictor variable. These results are presented in Appendix B, Supplemental Table 2. The second model, known as an adjusted model, attempted to control for other variables that may have also influenced likelihood of developing the various health outcomes (confounding variables).

Potential confounders were assessed by adding each variable to the model one at a time. If the crude odds ratio changed by more than 10%, then the variable was considered for adjustment in the final model. Previous studies, biological plausibility, and the 10% change in estimate rule, were considered in determining which confounders to include in the final adjusted model for

each outcome. The final model for each health outcome was adjusted for age and lifetime smoking. These results are presented in Appendix B, Supplemental Table 3.

Odds Ratio Interpretation

An odds ratio is a statistical term that describes the association between an exposure and an outcome. It represents the odds that an outcome will occur given a particular exposure. For example, an odds ratio could be used to describe the odds of getting lung cancer, given exposure to smoking cigarettes.

In the case of this PFOA exposure assessment study, the associated odds of the adverse health outcome increased or decreased by the amount shown in the odds ratio when the PFOA blood concentration increased 10-fold. An odds ratio of 1 indicates no change, an odds ratio of 2 indicates a doubling of the odds of a given outcome, and an odds ratio of 0.5 indicates a halving of the odds of a given outcome.

<u>95% Confidence Interval</u>

The 95% confidence interval is used to estimate the precision of an odds ratio. The narrower a 95% confidence interval is, the more precise the odds ratio estimate. For example, a 95% confidence interval of 1.1 to 1.2 indicates a more precise odds ratio estimate than a 95% confidence interval of 1.1 to 10.0. An odds ratio estimate is considered to be statistically significant if the 95% confidence interval does not contain the "null" value of 1.0. For example, a 95% confidence interval of 0.8 to 1.3 would not be considered statistically significant.

Appendix B: Supplemental Data Tables

Supplemental Table 1. PFOA levels in blood by fruit/vegetable intake, stratified by maximum PFOA level above or below 20 parts per trillion (ppt)

	n	Geometric mean	p-value
Maximum PFOA in Water ≤ 20 ppt			
Fruit/vegetable grown within sampling area			
Daily/weekly	36	3.0	
Monthly/never	58	3.3	p=0.69
Maximum PFOA in Water > 20 ppt			
Fruit/vegetable grown within sampling area			
Daily/weekly	129	17.3	
Monthly/never	157	11.7	p=0.01

Supplemental Table 2. Crude associations between PFOA levels in blood (for each $1-\log_{10} \mu g/L$ increase) with various outcomes

Outcome	n with outcome	n without outcome	Crude OR (95% Cl)
High Cholesterol	118	286	1.8 (1.3, 2.5)
Chronic Kidney Disease	8	392	0.6 (0.2, 1.9)
Increased Uric Acid Levels	21	374	1.3 (0.7, 2.4)
Altered Liver Enzymes	20	377	1.1 (0.6, 2.2)
Fatty Liver Disease	16	382	0.9 (0.4, 1.8)
Hypothyroidism	46	353	1.1 (0.7, 1.8)
Hyperthyroidism	8	391	0.6 (0.2, 1.9)
Ulcerative Colitis	14	383	1.2 (0.6, 2.7)
Preeclampsia (pregnant women)	15	128	2.0 (0.9, 4.3)

Supplemental Table 3. Adjusted associations between PFOA levels in blood (for each $1-\log_{10} \mu g/L$ increase) with various health outcomes

Outcome	n with outcome	n without outcome	Adjusted OR (95% CI)
High Cholesterol	112	269	1.4 (1.1, 2.1)
Chronic Kidney Disease	8	370	0.4 (0.1, 1.3)
Increased Uric Acid Levels	20	353	1.1 (0.5, 2.2)
Altered Liver Enzymes	20	355	1.0 (0.4, 1.9)
Fatty Liver Disease	14	362	0.7 (0.3, 1.7)
Hypothyroidism	44	334	1.0 (0.6, 1.7)
Hyperthyroidism	7	370	0.5 (0.1, 1.8)
Ulcerative Colitis	10	365	1.4 (0.5, 3.5)
Preeclampsia (pregnant women)	13	126	6.2 (1.9, 20.3)

Abbreviations: CI, confidence interval; OR, odds ratio; n, number of participants