The PFAS Health Study

Cross-sectional Survey and Blood Serum Study Research Protocol

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1. Project summary

Rationale

The Per- and Poly-Fluoroalkyl Substances (PFAS) Health Study: Phase II will investigate the exposure to and potential health effects of PFAS in areas of known contamination in the communities of Williamtown in New South Wales, Oakey in Queensland, and Katherine in the Northern Territory, Australia. In particular, this study will concentrate on the main chemical components of the firefighting foams used on Australian Defence facilities, which are perfluorohexane sulfonic acid (PFHxS), perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS).

Objectives

The primary goal of the study is to measure blood serum concentrations of PFAS in people who have ever lived or worked in the PFAS Investigation and Management Areas of Williamtown, Oakey and Katherine, and compare them to otherwise similar comparison (non-exposed) populations. In addition, the study will identify and characterise the health outcomes and health concerns of the exposed and comparison populations.

Methods

The cross-sectional survey will measure participants' health conditions and concerns and potential exposure to PFAS. The blood serum study will measure participants' blood serum samples for eight PFAS and two disease biomarkers, total cholesterol and uric acid.

Study Population

The exposed population will include past and present residents of and workers of the PFAS Investigation and Management Areas in the Williamtown, Oakey and Katherine townships. The comparison population will be random samples of residents in three similar Australian townships, each matched by demographic characteristics to one of the three towns under investigation.

Timeframe

The cross-sectional survey and blood serum study will commence in September 2018 with the final report due in June 2020.

Expected outcomes

We expect the study to produce knowledge that will assist community members in understanding the impact on their health, if any, of living in a PFAS Investigation and Management Area, and assist policy makers in responding to PFAS contamination issues.

2. General information

Protocol title

The PFAS Health Study: Cross-sectional Survey and Blood Serum Study Research Protocols

Protocol date

20 March 2019

Project funding

The Australian Government Department of Health[1] has commissioned the Australian National University to undertake the PFAS Health Study.

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3. Rationale and background information

Per- and polyfluoroalkyl substances (PFAS) are a diverse family of fluorinated organic chemicals that have been produced commercially since the 1950s. [1] PFAS have a carbon backbone with one or more fluorine substitutions and functional end groups which provide specific properties. [2] The carbon-fluorine bond is extremely strong, [3] giving PFAS high chemical, thermal and biological stability. The fluorinated carbon tail is hydrophobic and oleophobic, while the functional end group is hydrophilic, resulting in substances with highly effective surface tension-lowering properties. Perfluoroalkylacids have all hydrogen atoms substituted with fluorine, while polyfluoroalkylacids have one or more but not all hydrogen atoms substituted with fluorine.

Due to their stability and hydrophobic and lipophilic properties, PFAS have been used in a wide variety of consumer products, including surface treatments for textiles, non-stick coatings for cookware, grease-repellent food packaging and paints; and in industrial applications, such as in the metal plating industry, in hydraulic fluids and as key ingredients in aqueous film forming foams (AFFF). The AFFF have been used extensively as flame-retardants for firefighting, particularly in aviation settings. The extensive use of these chemicals and their persistence has led to concerns about environmental and human health impacts. The general population is exposed to background levels of PFAS through food consumption, drinking water and house dust. [4-6] The extensive use, distribution, manufacture and disposal of PFAS chemicals, and their effects on wildlife and humans, [7-12] have resulted in substantial scientific investigation, community concern and publicity. Since the early 2000s, major manufacturers have phased out production of key long-chain PFAS compounds, although it is likely that substantial production of PFAS still occurs in low- and middle-income countries. [2, 13, 14]

Concerns over the potential for PFAS to adversely affect human health arise from their ease of absorption into and distribution through the body, and their prolonged half-life in humans. PFAS can be detected in blood serum samples from the general human population. [9, 15, 16] The most widely studied PFAS chemicals are perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid also known as perfluorooctanesulfonate (PFOS). People in communities with high levels of PFOS and/or PFOA in their drinking water have been found to have serum PFOA and PFOS concentrations above those reported for the general population. [17-19] PFAS may be passed to infants through breastmilk, [20] and prenatal exposure to PFAS can occur through the placenta. [21]

PFOA and PFOS bind to serum proteins, especially albumin, with high affinity. [22-24] PFAS are absorbed into the blood stream via digestive and gas-exchange pathways. Generally, PFAS tend to accumulate in tissues with a large blood supply, including the liver, kidneys and lungs. [25]

Information from animal studies, which generally use high oral doses of PFAS, have indicated potential effects on pre- and postnatal development and the liver and immune system. Importantly, there are considerable differences in the toxicokinetics of PFAS in different animal species and humans, and the half-life of PFAS in some animals is much shorter than in humans. [26] The biological half-life in human serum varies with the type of PFAS, with estimates of 3.8 years for PFOA, 5.4 years for PFOS and 8.5 years for perfluorohexane sulfonate (PFHxS). [27] Studies in the United States have shown substantial declines in PFAS concentrations since the early 2000s, when industries began phasing-out production of PFAS chemicals. [28]

The toxicity of PFAS in humans is poorly understood, although PFAS with longer carbon chains are thought to be more toxic than those with shorter carbon chains. [26, 29] There have been a range of proposed mechanisms for possible adverse health effects of PFAS, many of which relate to endocrine disruption potentially affecting male and female reproduction and thyroid function. [30, 31] Human health research into PFAS has focused on: reduced foetal growth and development, decreased fertility and reproductive hormone levels, increased cholesterol levels, immunological effects and cancer.

3.1. PFAS reference populations

Several studies have reported PFAS blood concentration ranges that can be used to make inferences about blood concentrations of PFAS in Australians. Broadly speaking, these can be divided between studies reporting on PFAS values within populations not known as having been exposed to unusually high environmental levels of PFAS, and populations being investigated following a potential or confirmed exposure to high levels of PFAS. The latter can be subdivided into populations that have been exposed to PFAS predominantly through environmental contamination (exposed community cohorts), and populations exposed through their occupation (occupational cohorts).

The studies below include large numbers of study participants and represent potential reference populations for Australian studies of PFAS.

3.2. Populations with background PFAS exposure

CDC Fourth national report on human exposure to environmental chemicals, March 2018 – survey years 2013-4 [32]

This report presents biomonitoring measurements collected as part of the National Health and Nutrition Examination Survey (NHANES). The aim of NHANES is to collect data on the health and nutritional status of the U.S. population over time. NHANES collects information about a wide range of health-related behaviours, and includes physical examinations and collection of clinical samples for laboratory tests. Beginning in 1999, NHANES became a continuous survey, sampling the U.S. population annually and releasing the data in 2-year cycles. The study involves stratified multistage cluster sampling to select a representative sample of the civilian, noninstitutionalized population in the United States based on age, gender, and race/ethnicity. This is not a cohort study design, as different people are sampled for each wave of the survey.

The updated tables from March 2018, present U.S. nationally representative biomonitoring data. The data used originate in volume one (data tables for chemicals measured in the general U.S. population) and refer to the survey years 2013–14. See Table 1 (Appendix 1) for PFOS values. Similar data is also available for these survey years for additional PFAS chemicals: PFOA, PFNA, PFHxS, PFHpA, PFDA and PFBS.

Decline in perfluorooctane sulfonate and perfluorooctanoate serum concentrations in an Australian population from 2002 to 2011 [15]

This study reported temporal trends of PFAS concentrations in human blood in Australia between 2002 and 2011. Pooled human sera from South East Queensland were obtained from de-identified surplus pathology samples. This represented samples from those seeking health care and obtaining pathology testing, and so are not necessarily fully representative of background population levels. A total of 9775 samples in 158 pools were analysed for PFAS.

The most recent results from 2010/11, representing a total of 24 pools of human serum, or 2400 individual samples, is outlined in Table 2 (Appendix 1).

3.3. Populations exposed to PFAS through environmental contamination

The C8 Health Project: design, methods and participants [33]

The C8 Health Project was created, authorized, and funded as part of the settlement agreement reached in the case of Jack W. Leach, et al. v. E.I. du Pont de Nemours & Company. [34] The settlement stemmed from the perfluorooctanoic acid (PFOA, or C8) contamination of drinking water in six water districts in two states close to the DuPont Washington Works facility near Parkersburg, West Virginia. The study included 69,030 participants enrolled over a 13-month

period in 2005/6. Extensive data were collected, including demographic data and determination of serum concentrations of 10 perfluorocarbons. The C8 study presents the largest known population study of community perfluorocarbon exposure.

See Table 3 (Appendix 1) for serum perfluorocarbon concentrations. Similar data are also available by age group.

3.4. PFAS in Williamtown, Oakey, and Katherine

In recent years, historical firefighting activities on Australian Defence Force (ADF) Bases have been linked to environmental PFAS contamination in nearby areas of Williamtown in New South Wales (NSW), Oakey in Queensland (Qld) and Katherine in the Northern Territory (NT). Use of AFFF containing PFAS as the main components have been associated with elevated PFAS concentrations in ground water, soil, and biota. [35-37] Members of these communities have probably been exposed to PFAS through the ingestion and use of contaminated bore water, with exposure occurring from the 1970s onwards. Bioaccumulation of PFAS in the food chain has led to concerns about the consumption of home grown produce and animal products from the local farming regions (including livestock raised on contaminated land), and fish and crustaceans sourced from local rivers and waterways. In 2004, the ADF began phasing out the use of AFFF concentrates that contained PFOS and PFOA as active ingredients, switching to alternative chemicals with similar properties. [38] These often have a different fluorination that makes them less persistent. [38] The chemicals in the formerly used long-chain fluorinated foams (≥C7) are likely to persist in the environment, particularly in ground water, sediment and soil, of locally contaminated areas. [38]

3.5. The PFAS Health Study

The public health significance of PFAS exposure is unclear. Risk assessments of contaminated areas have evaluated likely exposure but have been unable to quantify associated health risks due to lack of consistent evidence about the health outcomes from exposure. To date, there have been no well-designed epidemiological studies examining health effects of PFAS in Australia, as the affected communities are often small and the levels of exposure highly variable.

The PFAS Health Study has five main components, over two phases. During Phase I a systematic review was conducted to examine the health effects of PFAS in humans as reported in published literature. Phase II includes an epidemiological study of the PFAS contamination in three Australian communities, Williamtown (NSW), Oakey (Qld) and Katherine (NT). This phase comprises four component studies:

i. Component 1 – Focus group study

A focus group study to determine the concerns that individuals living in the vicinity of Williamtown, Oakey and Katherine have in relation to exposure to PFAS and their health.

ii. Component 2 – Cross-sectional survey

A cross sectional survey to investigate the exposure and risk factors for high serum PFAS levels, including sociodemographic (e.g. age, sex, location) and other factors (e.g. duration of residence in the area, water source), and associations of high serum PFAS levels with common symptoms, signs and diagnosed illnesses in the Williamtown, Oakey and Katherine communities.

iii. Component 3 – Blood serum study

A blood serum study to define the serum concentrations (mean and range) of PFAS in Williamtown, Oakey and Katherine residents living in the PFAS Investigation and Management Areas and to compare the levels to those of people residing in non-contaminated areas.

Component 2 and Component 3 will be undertaken in combination.

iv. Component 4 – Data linkage study

A data linkage study to examine whether sex-specific age-adjusted rates of diseases potentially associated with PFAS are higher among people who have lived in the Williamtown, Oakey and Katherine PFAS Investigation and Management Areas, compared to those living outside the Investigation and Management Areas and in the general Australian population.

4. Study goals and objectives for the cross-sectional survey and blood serum study (Components 2 and 3)

This document outlines the protocol for Components 2 and 3 of the PFAS Health Study. Component 1 (focus group discussions) has been completed. Component 4 (data linkage study) will commence in the coming months and will have its own separate research protocol.

4.1. Goals

The primary goal of this component of the study will be to measure blood serum concentrations of PFAS in people who have ever lived or worked in the PFAS Investigation and Management Areas of Williamtown, Oakey and Katherine, and compare them to those in an otherwise similar non-exposed, comparison population. In addition, the study will identify the population characteristics and exposure-related factors and characterise the health concerns and health outcomes of people who have ever lived or worked in PFAS Investigation and Management Areas, compare them to an appropriate comparison population and relate them to individually measured blood PFAS concentrations.

4.2. Research questions

1. What are the main potential sources of exposure to PFAS through occupation, food, waters, or other factors in Williamtown (NSW), Oakey (Qld) and Katherine (NT)?
2. What are the main concerns regarding health problems associated with living or working in the PFAS Investigation and Management Areas in Williamtown, Oakey and Katherine?
3. What are the main self-reported health outcomes associated with living in or working in the PFAS Investigation and Management Areas in Williamtown, Oakey and Katherine?
4. What are the current levels of psychological distress and how do these relate to PFAS blood results and location of residence or work?
5. What are the main risk factors for higher than background level serum PFAS concentration regarding sociodemographic and other factors?
6. Does the geographic distribution of blood PFAS levels correlate with known zones of contamination of groundwater and soil?
7. What are the mean serum concentrations of PFAS in Williamtown, Oakey and Katherine residents and how do these levels compare to those of people residing in non-contaminated areas?
8. How do serum concentrations vary by location and demographic factors, such as age, sex and length of residence, in the townships of Williamtown, Oakey and Katherine?

9. How do serum concentrations of PFAS in Williamtown, Oakey and Katherine residents correlate with other blood markers of disease risk, such as cholesterol and kidney function?

5. Study design

5.1. Study design

This epidemiological study will be a cross-sectional design.

5.2. Study population

The research population for the PFAS Health Study will include both exposed and non-exposed populations. The exposed population will include two groups:

E.1. Current residents of the PFAS Investigation and Management Areas in the Williamtown, Oakey and Katherine townships; and

E.2. Those who are not current residents of the PFAS Investigation and Management Areas but are eligible to participate in the Commonwealth Department of Health Voluntary Blood Testing Program (VBTP)[1] for PFAS; these are individuals who have previously lived or worked in the PFAS Investigation and Management Areas, or currently or previously potentially been exposed to PFAS chemicals while working within the PFAS Investigation and Management Areas, including the Royal Australian Air Force (RAAF) Base at Williamtown, the Army Aviation Centre (AAC) at Oakey or the RAAF Base at Katherine.

The PFAS Investigation and Management Areas have been determined by the Australian Government Department of Defence in Oakey and Katherine and the NSW Environmental Protection Authority (EPA) in Williamtown based on environmental sampling and are outlined in Attachment 1.

We propose the following comparison (non-exposed) population for each of the three exposed populations:

C.1. Individuals currently living in three Australian townships, which are similar demographically to Williamtown, Oakey and Katherine, frequency matched to residents of the corresponding Investigation and Management Areas by demographic characteristics (for example age, sex, urban/rural location, Aboriginal or Torres Strait

[1] Under the Voluntary Blood Testing Program (VBTP), the Australian Government offers a free blood test for Per- and Poly-fluoroalkyl Substances (PFAS) to people who live or work, or who have lived or worked, in the RAAF Base Williamtown, NSW, Army Aviation Centre Oakey, Qld and RAAF Base Tindal, NT Investigation and Management Areas and who have potentially been exposed to PFAS. The VBTP will run concurrently with the PFAS Health Study and will run until 30 June 2019.

Islander status and socioeconomic status); this will provide populations that are similar to the exposed populations in terms of sociodemographic characteristics. They may differ in other local environmental hazards or other health related characteristics, which we will document.

5.3. Sampling frame

All individuals who participated in the VBTP for PFAS were invited at the time of blood testing to participate in the ANU PFAS Health Study (Northern Territory Department of Health and Menzies School of Health Research Human Research Ethics Committees (NTDoHMSHR HREC) protocol number 2018-3130 and ANU Human Research Ethics Committees (ANU HREC) protocol number 2016/707). Consenting VBTP participants who are current residents of the PFAS Investigation or Management Areas will make up the first sampling frame, exposed population E.1. Past residents of the Investigation and Management Areas, or current or past workers in, but not residents of, the Investigation and Management Areas who are consenting VBTP participants will make up the second sampling frame, exposed population E.2. Potential participants for the exposed populations (E.1 and E.2) who are eligible but have not participated in the VBTP for PFAS will be eligible to participate in Component 2 of the ANU PFAS Health Study only.

Potential participants for the comparison population (C.1) will be identified through the Australian Government Department of Human Services Medicare database. All Australian citizens and permanent residents are eligible for registration with Medicare. Comparison group individuals will be randomly selected from these sex and age strata to reflect the exposed population distribution and enable adequate numbers for subgroup analyses. This probability sampling will enable estimation of sampling weights to adjust analyses to appropriate population estimates. Depending on the final estimated exposed population size and study participation rates, we will attempt to obtain a ratio of comparison to exposed participants of 1:1.

5.4. Inclusion and exclusion criteria

Individuals are eligible for inclusion in Component 2 of the PFAS Health Study (cross-sectional survey) if:

a) They are current residents of the PFAS Investigation and Management Areas in the Williamtown, Oakey and Katherine townships (exposed population E.1); or
b) They are not current residents of the PFAS Investigation and Management Areas in Williamtown, Oakey and Katherine, but are eligible to participate in the VBTP for PFAS (for example Defence employees or past residents) (exposed population E.2); or

c) They are current residents of a comparison area and are registered with Medicare (comparison population C.1).

a) Individuals are eligible for inclusion in Component 3 of the PFAS Health Study (blood serum study) if: They are current residents of the PFAS Investigation and Management Areas in Williamtown, Oakey and Katherine and have participated in the VBTP for PFAS (exposed population E.1); or

b) They are not current residents of the PFAS Investigation and Management Areas in Williamtown, Oakey and Katherine, but have participated in the VBTP (for example Defence employees or past residents) (exposed population E.2); or

c) They are current residents of a comparison area and are registered with Medicare (comparison population C.1).

5.5. Recruitment

All participants in the VBTP who have given consent to participation in the ANU PFAS Health Study (exposed populations E.1 and E.2) will be contacted directly by the ANU PFAS study team and mailed a recruitment package for Component 2 of the PFAS Health Study (cross-sectional survey): Letter of Invitation from the ANU (Attachment 2), Participant Information Sheet (Attachment 4), consent form (Attachments 6 and 7), cross-sectional survey (Attachments 8 and 10), a link to the study website where individuals can complete the consent form and study questionnaire/s online. The Participant Information Sheet requests individuals interested in participating in the study to return their consent form and questionnaire in the pre-paid envelope provided, or to complete them online. For individuals aged under 16 years of age, the letters and invitation package will be addressed to the child's parent or guardian. A reminder letter will be mailed to all participants by the ANU PFAS study team two weeks following the initial invitation (Attachment 15).

Individuals who are eligible but have not participated in the VBTP for PFAS (exposed populations E.1 and E.2) will need to contact the ANU PFAS study team to receive a recruitment package for Component 2 of the PFAS Health Study (cross-sectional survey): Participant Information Sheet (Attachment 4), consent form (Attachments 6 and 7), cross-sectional survey (Attachments 8 and 10), a link to the study website where individuals can complete the consent form and study questionnaire/s online. Individuals will not receive a letter of invitation from the ANU if they have not participated in the VBTP for PFAS. Targeted advertising campaigns in the Williamtown, Oakey and Katherine townships will communicate this recruitment pathway to potential participants.

Individuals randomly selected from the Medicare database (comparison population C.1) will be contacted by the Department of Human Services, on behalf of the ANU study team, and invited to participate in Component 2 and 3 of the PFAS Health Study (cross-sectional survey and blood

serum study). The comparison group (C.1) will receive an invitation package including a Letter of Invitation (Attachment 3), Participant Information Sheet (Attachment 5), consent form (Attachments 6 and 7), cross-sectional survey (Attachments 8 and 10), a link to the study website where individuals can complete the consent form and study questionnaire/s online and a pathology request form for PFAS and biomarker blood testing (Attachment 12). The ANU study team will not receive personal information of the individuals sampled through the Medicare database unless they consent to participate in the study. Medicare will, however, provide tabular data on the matching characteristics of the samples selected so that the extent of response bias can be assessed. For individuals aged under 16 years of age, the letters and invitation package will be addressed to the child's parent or guardian. A reminder letter will be mailed to all participants by the Department of Human Services on behalf of the ANU study team two weeks following the initial invitation (Attachment 15).

A pilot study will be undertaken using a mail-out to 100 individuals in each of the PFAS Investigation and Management Areas and 100 individuals in each of the comparison populations to estimate participation rates (which will help inform final numbers to be sampled) and identify any unanticipated problems in the recruitment process and study methods.

5.6. Withdrawal procedure

Participants can withdraw from the study at any time by contacting the ANU study team at the email address or telephone number provided in the Participant Information Sheet or by writing to the study team at the address provided on correspondence. At this time their survey data and blood test results will be removed from the database and their blood sample will be destroyed.

Potential participants of the blood serum study will be withdrawn from the study if the blood sample cannot be collected, by a qualified medical professional, on the third attempt for adults or the second attempt for children.

5.7. Expected duration

The cross-sectional survey and blood serum study are expected to take 21 months to complete, from September 2018 to June 2020. Blood testing for the exposed population under the VBTP commenced in November 2016 and will cease on April 30 2019. The cross-sectional survey for the exposed population is expected to commence in early 2019. Blood testing for the comparison population is expected to commence in early 2019 and will occur in conjunction with the cross-sectional survey.

6. Methodology

6.1. Cross-sectional survey

The cross-sectional survey has been developed based on literature and findings from the PFAS Health Study Focus Group Study conducted between January and August 2018 with current residents and workers of the Williamtown, Oakey and Katherine PFAS Investigation and Management Areas. The survey questions were drawn from national and international surveys conducted in communities affected by PFAS contamination or the general population, as well as to further explore and quantify themes that arose during focus group discussion.

The survey will be primarily delivered using paper questionnaires addressed and sent to each participant's residential address with the invitation package. The ANU study team will send the questionnaire to all participants of the VBTP for PFAS. On behalf of the ANU, the Department of Human Services will send the questionnaire to all individuals selected by random sampling from the comparison population (C.1). Participants will be offered the option of completing the survey via an included paper copy or online. A website for online completion of the questionnaire will be made accessible to all individuals selected for inclusion in the study. The first page of the online and paper survey will outline the nature of the survey, the risks of participation, and the options for non-completion and include a statement of consent for collection of information. The ANU study team will provide support to participants with enquiries about completion of the survey through a toll-free telephone service staffed during business hours.

The cross-sectional survey will be produced by an external survey company chosen by the ANU study team. A formal tender process will inform this decision. The survey company will sign a Deed of Confidentiality with the ANU. All participants will receive a pre-paid envelope to return the cross-sectional survey to the external survey company for scanning and verification. The external survey company will administer and verify the online version of the survey. The ANU study team will complete the analysis of survey responses.

The questionnaire has been tested among study team members to ensure that it is functional and easily understood. Prior to release of the cross-sectional survey to the exposed and comparison populations, it will be pre-tested with members of the PFAS Health Study Community Reference Panel, which includes community representatives from each of the three PFAS Investigation and Management Areas. As previously outlined, the survey will also be piloted in the comparison populations. Results from the pilot study will be used to amend the recruitment process and/or the survey content as appropriate.

The draft cross-sectional surveys and data dictionary are available in Attachments 8–11. For the purpose of the cross-sectional survey, participants under 16 years old will be defined as children. A parent or guardian will complete the child version of the cross-sectional survey (Attachment 10) on behalf of exposed and comparison group children recruited in the study.

i. Exposure measurement

Participants will be asked a filtering question at the outset of the survey to identify whether they have ever lived or worked in an Investigation Area. Participant self-reporting will contribute to estimates of PFAS exposure. Residential exposure will include questions about residential address history, length of occupancy, type of property (apartment, house or rural property) and type of water supply on their property (town water, rainwater, bore water or other). Comparison group participants will not answer questions related to residential history since they have been selected from populations without a specific source of environmental PFAS exposure. Occupational exposure questions will ask about knowledge of personal occupational exposure to PFAS, AFFF, and their frequency of exposure, while community exposure will ask about recreational exposure to AFFF.

The survey will measure a participant's ingestion of and dermal contact with water sources that are potentially contaminated through questions on town water and bore water, including ingestion behaviours, use of water on properties and recreational use. The survey will measure ingestion of food sources grown in or harvested from PFAS contaminated water through consumption of locally grown produce. Questions include consumption on vegetables and fruit, meat, poultry and eggs, and locally caught seafood from Williamtown or Katherine water bodies.

ii. Health outcome and concerns measurement

Questions on health diagnoses have been adapted from the Biomonitoring Project to Assess Body Burden of Perfluorinated Chemicals, the Air Services Fire Fighting Questionnaire and the National Health Survey Australia 2014–2015. These questions explore general level of physical and mental health, various disease diagnoses (cancer, autoimmune, thyroid and many others), female health and fertility.

Questions on health concerns and mental wellbeing include the Physical Symptoms (PHQ-15), Distress Questionnaire-5 (DQ5), Kessler 10, Patient Health Questionnaire-2 (PHQ-2), Generalised Anxiety Disorder scale (GAD-2) and items derived from results of the focus group discussions in community. These questions enquire about general health and mood over the last 30 days, health seeking behaviour, changes in health and behaviour since finding out about the PFAS contamination and if participation in the VBTP for PFAS was helpful. The child specific survey

includes questions from the Strengths and Difficulties Questionnaire which has questions about physical symptoms, interactions with others, behaviour and attentiveness.

iii. Demographic characteristics

Demographic characteristics (age, sex, Indigenous status, marital status, country of birth, language spoken at home, educational attainment, occupation, household income) and lifestyle questions, such as smoking, alcohol consumption and exercise questions, have been adapted from the Australian Bureau of Statistics, 45 and Up Study and the Air Services Fire Fighting Questionnaire.

6.2. Blood serum study

i. Pathology test

Exposed participants have received information about accessing PFAS blood testing through the VBTP from the Commonwealth Department of Health. A free blood test and two free general practice consultations are available to VBTP invitees—one prior to the blood test, and one following the blood test. This is to ensure that patients are adequately informed of the limitations of the blood test and have their follow-up questions addressed.

Following the general practice consultation, exposed participants are given a pathology request form for the VBTP (Attachment 13). The pathology request form includes a section for the individual to consent to their blood sample and result being transferred to the ANU to be included in the epidemiological study and to consent to the study team contacting them in the future. To have their blood test result included in the study the patient needs to sign the relevant section on the pathology request form. All participants who agree to blood tests under the VBTP are referred to Sonic Healthcare by their General Practitioner. Participants should take their completed Statutory Declaration and PFAS pathology request forms to a Sonic Healthcare Pathology Collection Centre.

Randomly sampled comparison group participants will receive a Participant Information Sheet and consent form for the blood serum study and a pathology request form for a PFAS blood test through Sonic Healthcare Pathology in the invitation package from the Department of Human Services, on behalf of the ANU. This information will be sent to their residential address alongside the Letter of Invitation for the study and the cross-sectional survey. Comparison group participants will not be required to request a blood test through their General Practitioner as the population is expected to have background levels of PFAS in their blood. A doctor from the PFAS Health Study team will be listed as the referring doctor for all comparison group participants and will provide over the phone consultations for enquiries about the PFAS blood testing from

participants. Participants will be asked to take their completed ANU PFAS pathology request forms to a Sonic Healthcare Pathology Collection Centre. Information on Sonic Healthcare Pathology Collection Centre in participants' local area will be sent with the Letter of Invitation for the study, the cross-sectional survey and the blood serum study information.

ii. Blood collection

Each blood sample will be collected in a single BD vacutainer SST tube for the PFAS blood serum measurement. These have been tested and shown to cause no interference in the analysis. The sample will be stored and transported at 2–8°C prior to analysis.

iii. PFAS blood serum measurement

Serum samples will be analysed for eight PFAS: PFOA, PFOS, PFHxS, perfluorobutane sulphonate (PFBS), perfluorohexanoic acid (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), 6:2 fluorotelomer sulphonate (62FTS).

Samples will be prepared for Liquid Chromatography-Mass Spectrometry/Mass Spectrometry (LC-MS/MS) by solvent extraction, protein precipitation, sonication and filtration. The analytes of interest are measured roughly in the range of 0.2–100 ng/mL with some variation depending on the specific compound. All tests will be subject to quality control and calibration.

iv. Biomarker blood serum measurements

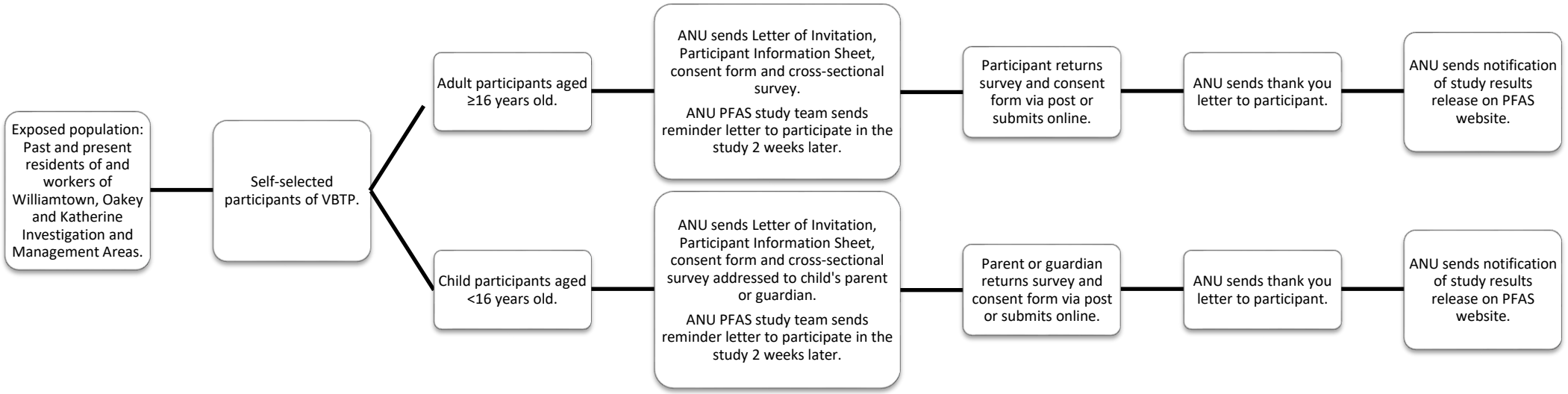
Blood serum samples from exposed group participants that have already been collected via the VBTP will be re-sampled for total cholesterol and uric acid levels retrospectively, following storage at the ANU. Specimens collected prospectively from comparison group participants will include testing for total cholesterol and uric acid in addition to blood PFAS levels. Samples will undergo routine biochemistry testing. All tests are subject to quality control and calibration.

v. Specimen storage

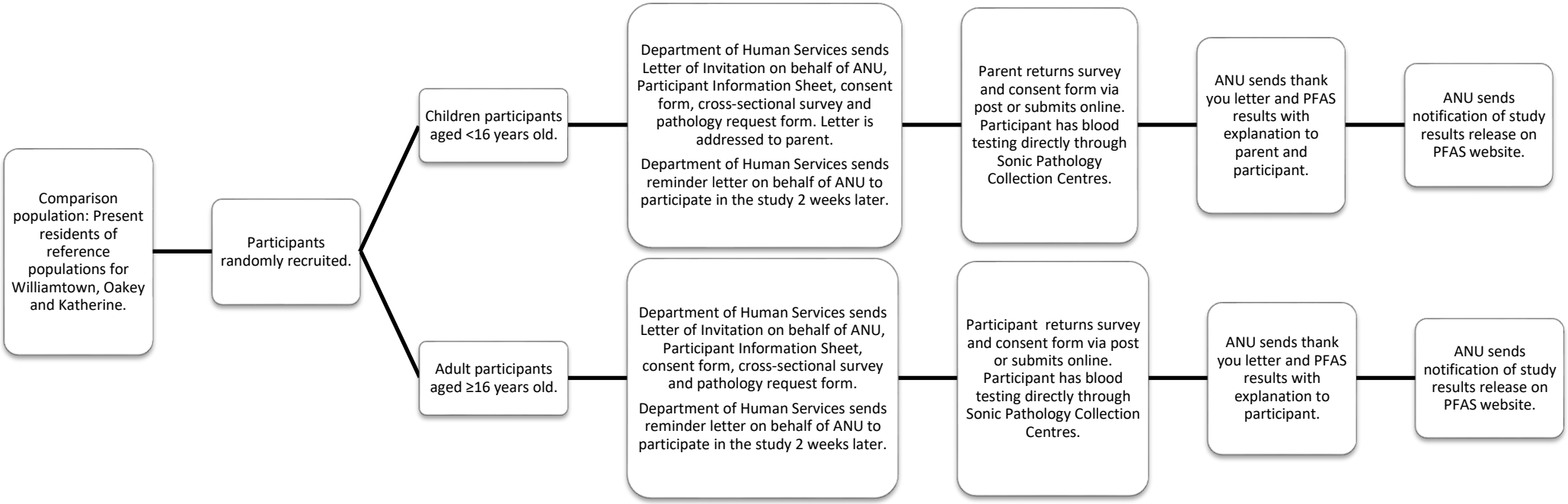
Following testing, Sonic Healthcare Pathology will ship all blood serum samples to the ANU for storage with the participants' consent. One sample provided in a 2mL aliquot tube per participant will be required for storage. A minimum volume of 1mL will be provided to allow for duplicate analysis. Each blood sample will be clearly labelled with the date of collection, time of collection, ID number, initials of the participant and the pathology barcode. The details written on each blood sample will be compared to the details provided on the participant's pathology request form. The blood samples will be stored upright in 9x9 cryogenic boxes in a freezer set to –80 degrees Celsius.

6.3. Graphic outline of the study

i. Exposed population



ii. Comparison population



7. Safety considerations

The main safety considerations for participants anticipated via conduct of this study include pain and discomfort experienced during blood collection, follow-up of abnormal results (discussed below), and distress surrounded the PFAS blood test result.

In order to minimise discomfort or pain from blood collection, the contract with Sonic Healthcare Pathology will require that all bloods will be collected by qualified phlebotomists. Unsuccessful collection attempts will be limited to three for adults, and two for children. If the phlebotomist is unsuccessful after this number of attempts, the blood testing component will be abandoned or deferred, depending on the wishes of the participant. Children will be offered an EMLA™ topical anaesthetic patch by the phlebotomist at the time of collection, funded by the study, to be applied 15–30 minutes prior to blood collection to minimise pain.

Participants in exposed areas who experience distress as a result of participating in this study will be referred to appropriate mental health and counselling services. Patients in unexposed areas will receive their results as outlined at point 8.3, below. Participants with further questions or concerns about their results will initially be offered the opportunity of an individual telephone discussion of their results with a doctor on the PFAS Health Study team. For those participants with additional health concerns or who are experiencing significant distress, they will be referred to their General Practitioner via a direct call from the study team to the GP with the patient's permission.

An adverse event register will be maintained by the study team to collate any reports from participants of concerns or adverse events. This will be reviewed by the study team on a weekly basis. Any emerging patterns will be addressed as a matter of urgency.

8. Follow-up

8.1. PFAS blood test results

There are no accepted reference ranges for blood PFAS concentrations in humans. Currently, all Australian blood serum measurements are reported against the 95th percentiles for PFOA and PFOS from the 2011–2012 Australian population.[40] Age and sex specific PFOA and PFOS concentrations that are less than their 95th percentiles are considered to be consistent with background exposure in the general population of that specific sex- and age-group, while PFOA and PFOS concentrations ≥95th percentile are suggestive of previous exposure to PFAS at levels higher than the general population of the specific sex- and age-group. Several additional fluoroalkyl substances are also measured through the Sonic Healthcare Pathology PFAS panel. These included PFHxS, PFBS, 62FTS, PFHxA, PFHpA, PFNA and PFDA. The toxicology of these compounds in humans is not well studied, and only tested and reported by Sonic Healthcare Pathology for research purposes.

Table 4. Estimated 95th percentile for the Australian population, 2011–2012. [40]

Compound	Age group	ng/mL
PFOS	0–4 years	13
	5–15 years	18
	16–30 years	20
	31–45 years	25
	46–60 years	29
	61+ years	37
PFOA	0–4 years	9
	5–15 years	8
	16–30 years	8
	31–45 years	8
	46–60 years	8
	61+ years	10

8.2. Reporting of results to exposed participants

Under the VBTP, individual blood test results will be reported to the requesting General Practitioner within 7–10 days through the practice's usual channel for receiving pathology results. Each individual receives post-test counselling for their PFAS results via their General Practitioner; this includes an explanation of the results, including the limitations of PFAS blood testing in individuals. Those tested may also be referred to mental health and support services if required.

8.3. Reporting of results to comparison group participants

A doctor on the PFAS Health Study team will be the referring doctor for the comparison group participants. Participants will be sent a letter (Attachment 15) to their residential address reporting their individual results against the Australian 95th percentiles for PFAS, and to the reference range for total cholesterol and uric acid. Participants with abnormal cholesterol and uric acid results will be informed in the letter that these results are outside the reference range and that they should follow up with their regular GP. Any results that require urgent follow-up will be contacted by telephone by a study team medical practitioner. Comparison group participants who have additional concerns about any of their results on receipt of the letter will be encouraged to contact the study team doctor by telephone or their General Practitioner to discuss their concerns.

9. Data management and statistical analysis

9.1. Data management

Data checking for incorrect/unusual values and outliers, investigation of missing values, assessment of distributions and exploratory data analysis will be undertaken of all variables, using frequency tables for categorical variables and frequency tables (where relevant), summary statistics and histograms for continuous variables. We will consider combining categories with small numbers of observations and undertaking transformation or categorisation of non-normally distributed variables.

i. Data storage

Confidential information about participants will be stored on secure, password-protected networks at the ANU and only made available to approved members of the study team. Any external parties working on the project will have signed confidentiality agreements. Data will be stored for a minimum of five years on secure servers at the ANU following completion of the study.

9.2. Statistical Methods

i. Statistical Analysis

All analyses will be undertaken separately for Williamtown, Oakey and Katherine communities, and will be adjusted for the sampling scheme, including correlation of outcomes within households, where appropriate. Separate analyses will able be undertaken for each of the nine PFAS measures. Most analyses will be undertaken separately by broad age strata, and some analyses will be sex specific (for example fertility/reproductive outcomes).

Depending on the study objective, PFAS values will be considered in one of four different formats:

- As a continuous outcome variable, potentially log- or other transformed (Research Questions 6, 7, and 8);
- As an exposure variable, using quantiles of PFAS, with the particular type of quantile (e.g. quintile, quartile, etc.) to be determined based on the distribution of PFAS level and the samples size (to ensure an appropriate number of observations in each quantile) (Research Questions 2, 3 and 4); and
- Dichotomised into high versus not high, based on whether or not measures are greater than the age-specific 95th percentile of the Australian population norms and considered as an outcome (Research Question 5).

If there are adequate numbers of participants in the VBTP who are not current residents of the PFAS Investigation and Management Areas (exposure group E.2) these will be treated as a separate exposure group in relevant analyses; if numbers are small then analyses will be undertaken combining the two exposure groups, with sensitivity analyses excluding the VBTP-only participants.

Analyses for Research Questions 6–8, which consider PFAS exposure as the outcome variable, will involve presentation of mean PFAS with 95% Confidence Intervals (CIs) for groups/subgroups of interest, undertaking t-tests or a non-parametric equivalent to compare PFAS across subgroups and multivariable linear regression to examine the relationship between characteristics of interest (e.g. age; sex; exposure group) and PFAS blood level, adjusted for relevant covariates/potential confounders. For Research Questions 2–4, the number and percentage for categorical outcomes of interest, or mean and standard deviation (or median and quartiles as appropriate) for continuous outcomes will be reported for exposed and comparison groups, comparison of outcomes between groups using the Chi-square test, t-test, or a non-parametric equivalent, and multiple regression (linear or logistic as appropriate) will be undertaken to examine the relationship between outcomes (self-reported health outcomes and concerns, including psychological distress) and exposures, adjusted for relevant covariates. Analyses for Research Question 10 will involve obtaining correlation coefficients followed by multiple linear regression to examine the relationship between PFAS level and blood biomarkers of disease risk (unadjusted and adjusted for relevant covariates). To address Research Question 5, participants will be classified as having high versus not high PFAS, based on reference values for their sex and age group; this new measure will then be considered as an outcome, with potential risk factors compared between those with and without high PFAS using bivariable analyses and multiple logistic regression.

Covariates to be included in the analyses will be informed by biological and clinical conceptual frameworks, and may vary for different outcomes.

Primary analysis will be a complete case analysis, with sensitivity analyses using multiple imputation to account for missing data, if considered appropriate.

ii. Sample Size and Statistical Power

The sample size will be limited by the number of individuals in the community Investigation and Management Areas, which is anticipated to be approximately 1,500 for Williamtown and 4,500 for Oakey. For the Katherine Investigation Area the site encompasses a much larger population of around 10,000. All exposed individuals in Williamtown Oakey, and Katherine who have participated in the VBTP will be invited to participate. If consent rates among comparison individuals is low, we can increase the number approached to participate in the study. The pilot

study will provide estimates of consent rates which will be used to finalise the sampling strategy. Assuming a consent rate of 75% in the exposed group, and using 3 broadly similar sized age groups, with a smaller number aged <16 years, we could expect approximately 250–350 exposed individuals for subgroups of interest.

The sampling scheme will involve clustered (correlated) data and will potentially require weighting to ensure that the sample correctly reflects the population of interest. This sampling strategy will increase the standard errors for estimates, thus reducing the 'effective' sample size. While the amount by which the sample size is impacted is unknown, a design effect of 1.2 is suggested. This means that the actual samples size should be divided by 1.2 to allow for the effect of the sampling scheme. For example, if the actual sample size is 350, the PFAS sampling design means that there will be the same precision and power as a sample of 350/1.2 ~= 300; for an actual sample of 250, the effective sample size is ~200.

For an effective sample size of 300, the 95% CI will be within ± 0.12 standard deviations for a mean and ± 5–6% for a proportion (depending on the prevalence). For an effective sample size of 200, the precision will be ± 0.14 standard deviations for a mean and ± 5–7% for a proportion.

For an (effective) sample size of 300 participants per group (600 in total), the study will have 80% power for a 5% significance level to detect a difference in means of approximately 0.23 standard deviations and a difference in proportions of 10–12% for binary variables.

For an (effective) sample size of 200 participants per group (400 in total), the study will have 80% power for a 5% significance level to detect a difference in means of approximately 0.28 standard deviations and differences in proportions of 10–14%. If PFAS is categorised into quartiles, the study will be able to detect differences, between highest and lowest quartiles, of 0.32 standard deviations and 12–16% for an overall effective sample size of 600; and 0.4 standard deviations and 15–20% for an overall effective sample size of 400.

9.3. Limitations

This study has a number of limitations due to its observational nature and the fact that it incorporates the existing VBTP for PFAS. The people who have already participated in the VBTP have self-selected; therefore there is a potential for selection bias between this group and those in the comparison population who will be randomly selected. In addition, people who in the exposed group are more likely to consent to participate in this study due to their high interest in the health effects of PFAS. We anticipate low response rates from the comparison population due to the request for a blood test and their potentially lower interest in the health effects of PFAS. Finally, there will be an element of survivor bias when judging the health effects of PFAS as participants need to be alive and well to be included in this component of the study. We will

conduct a data linkage study (Component 4) in the future which will consider mortality and disease incidence.

10. Quality assurance

10.1. Research protocol review

The ANU is proactive and responsible in its approach to risk management. The Research Office within the College of Health and Medicine oversees all population health research within ANU. The Research Office oversees the application of research proposals and financial accountability for the conduct of research. The ANU has human and animal research ethics committees that function in accordance with National Health and Medical Research Council guidance. The Research Office ensures that all funded research is approved by the appropriate ethics committee and complies with University policies.

The study will have ethics approval from the Human Research Ethics Committee at the ANU and all other relevant committees. These Committees will ensure that research is conducted according to the National Health and Medical Research Council's National Statement on Ethical Conduct in Human Research.

10.2. Pathology testing

All pathology tests conducted by Sonic Healthcare Pathology are subject to quality control and calibration. All Sonic laboratories in Australia are accredited by the National Association of testing Authorities (NATA), Australia. Sonic Healthcare Pathology is the only NATA-accredited laboratory that performs PFAS testing in Australia.

11. Expected outcomes of the study

The expected outcome of the study is to be able to describe the self-reported health conditions experienced by past and present residents and workers in the three PFAS Investigation and Management Areas, and to compare their frequency with that of those who do not live in an exposed community. In addition, it is expected that potential factors associated with high blood PFAS level (such as age and sex) will be identified. This information will assist community members in understanding the impact of living in a PFAS Investigation and Management Area on their health and assist policy makers in responding to the ongoing issue of PFAS contamination. This study is the first of its kind in Australia and will add to the body of international literature around the effects of environmental PFAS exposure on human health.

12. Dissemination of results

The results from each component of the PFAS Health Study will be detailed in a report provided to the Australian Government Department of Health. The study team will also prepare articles for publication in peer-reviewed journals. All reports and publications will acknowledge funding from the Department of Health and input from the community and other experts. Authorship of peer reviewed articles will be determined in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals produced and endorsed by the International Committee of Medical Journal Editors, specifically those considerations set out under heading IIA 'Ethical Considerations in the Conduct and Reporting of Research: Authorship and Contributorship'.

The final report for each component of the study will be made publicly available via the study webpage. In addition to the final report, study results will be summarised in a format suitable for lay-people. This will be made available on the study website and sent via email to study participants who have indicated that they would like to receive a copy and have provided their email address on the survey form. Additionally, the study team will hold face-to-face community consultations in each of the three communities, including Aboriginal communities where appropriate, to present the findings of each report.

13. Duration of the project

The cross-sectional survey and blood serum study are expected to take 21 months to complete, from September 2018 to June 2020.

14. Project management

The PFAS Health Study team includes eight co-investigators, six associate investigators, one PhD Candidate and three research assistants. Co-investigators and associate investigators provide expertise in the fields of PFAS toxicology, environmental epidemiology, biostatistics, Aboriginal community engagement and geospatial analysis. Experts will oversee the execution and analysis of the research, while research officers will manage daily administration of the project.

15. Ethics

The PFAS Health Study blood serum study and cross-sectional survey will be submitted to the Northern Territory Department of Health/Menzies School of Health Research and ANU Human Research Ethics Committees for approval.

Additional ethical consideration must be given with the inclusion of children and Aboriginal persons in the study. For children we will be seeking a parent's or a guardian's informed consent to participate on the child's behalf (16 years of age or less). For all participants we will collect written informed consent to participate in the blood serum component separately from written informed consent to participate in the cross-sectional survey. For all participants, blood collection staff will not obtain a sample from a participant if they refuse to participate or if they show signs of distress during the collection process. Blood collection staff will also be advised to cease a collection attempt if they cannot collect the sample by the third attempt for adults and second attempt for children.

We have addressed six core values with reference to how the Aboriginal population will benefit or be impacted by the study:

1. Reciprocity Participation in the study can provide Aboriginal people with the opportunity to detail how and to what extent they have been exposed to PFAS. They will also be provided with an opportunity to discuss any health issues associated with the exposure. The study team is actively working with an Aboriginal Elder to provide advice on Aboriginal engagement. The study team will return to Katherine to present the outcomes of the cross-sectional survey and blood serum study reports to the Katherine community. Wurli-Wurlinjang Health Services and our Aboriginal advisors will be consulted regarding how best to deliver the results, so they are easily understandable and usable in the community, after the conclusion of the research.

2. Respect The PFAS Health Study team aims to develop respectful and sustainable relationships with the local Aboriginal communities. Researchers will ensure key Aboriginal community members are consulted before any material is published and made available to the public. Additionally, all published material will acknowledge Aboriginal communities and their contribution to the research.

3. Equality The Chief Investigator and a Co-Investigator presented the overall study design to the Board, CEO and Director of Medical Services at Wurli-Wurlinjang Health Service. The cross-sectional study will be open to all Aboriginal people in the Investigation and Management Areas, and participants of the survey will be encouraged to participate in the blood serum study either through the VBTP for PFAS, for those in the exposed communities, or through a collection facility organised for the comparison population. There is no individual benefit in participating and this is balanced against a minimal risk of harm, which is managed by the option to use the free 24

hour service Support Now 1300 096 257 and access to local support services. The PFAS Health Study team will also ensure that the research findings are presented to the community in a manner that is easily understood and usable in the community.

4. Responsibility If required, the PFAS Health Study team will work with Aboriginal consultants to help Aboriginal participants complete the survey. This may involve holding community sessions where Aboriginal participants receive help in completing an online or paper copy of the questionnaire.

5. Survival & Protection In partnering with Professor Adrian Miller, the Wurli-Wurlinjang Health Service and other Aboriginal consultants the PFAS Health Study team hopes to establish trust and credibility within the Katherine community. From a generational perspective PFAS contamination in Katherine, occurred in the past, but is now a concern in the present and future. The PFAS Health Study team acknowledges the impact PFAS might have on local Aboriginal communities, including their ongoing connection to country and any cultural activities.

6. Spirit & Integrity The study team will be guided by the Wurli-Wurlinjang Health Service and our Aboriginal consultant as to how best to conduct the survey. The blood serum collection will be conducted through Wurli-Wurlinjang Health Service.

15.1. Consent

Participants of comparison populations randomly sampled by the Department of Human Services will be asked to give consent for their participation in the cross-sectional survey and the blood serum study prior to initiation of survey completion and collection of blood for the pathology test. All self-selected participants of the VBTP for PFAS have previously given consent for participation in the blood serum study before collection of blood for the pathology test. Additional consent will be required for their participation in the cross-sectional survey component of the study, for data linkage between the survey and blood test results, for future testing of blood samples, and to be contacted in the future by the study team.

15.2. Privacy and confidentiality

Confidential information about participants will be stored on secure, password-protected networks at the ANU and only made available to approved members of the study team. Any external parties working on the project, including market research company staff and staff collecting data in the field, will sign a confidentiality agreement. Data will be stored for a minimum of five years on secure servers at the ANU following completion of the study.

All participants will be informed about the nature of the blood testing study, the risks of participation, and the options for non-completion and include a statement of consent for collection of the blood specimen, reporting of results, and storage of the blood serum. Following analysis of blood test specimens at Sonic Healthcare Pathology, blood samples will be shipped to the ANU and stored in numbered aliquot tubes in a secure freezer. Similarly, the details of the patient providing the blood specimens will be stored on a secure password protected University network. Received consent forms will also be stored in a secured filing cabinet, in a secured office building. Blood samples, will be retained for future research into PFAS, provided consent is given by participants. Any testing of blood samples for additional analytes will be subject to approval by the relevant Human Research Ethics Committees.

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17. Appendices and attachments

17.1. Appendix 1

Table 1. Geometric mean and selected percentiles of serum concentrations (in ng/mL) of PFOS for the U.S. population from the National Health and Nutrition Examination Survey (samples years 2013-4)

	Geometric mean (95% CI)	50th percentile (95% CI)	75th percentile (95% CI)	90th percentile (95% CI)	95th percentile (95% CI)	n
Total	4.99 (4.50-5.52)	5.20 (4.80-5.70)	8.70 (7.90-9.40)	13.9 (11.9-15.5)	18.5 (15.4-22.0)	2165
Age 12-19	3.54 (3.17-3.96)	3.60 (3.10-4.20)	5.20 (4.60-6.20)	7.80 (7.00-8.90)	9.30 (7.90-11.7)	401
20 and older	5.22 (4.70-5.81)	5.60 (5.10-6.00)	9.10 (8.20-10.2)	14.5 (12.9-16.1)	19.5 (15.8-23.0)	1764
Males	6.36 (5.62-7.20)	6.40 (5.70-7.30)	10.2 (8.70-11.5)	15.5 (13.2-19.8)	22.1 (16.7-26.9)	1031
Females	3.96 (3.60-4.35)	4.00 (3.60-4.60)	7.20 (6.40-7.70)	11.8 (9.70-13.6)	15.1 (13.9-17.3)	1134
Age 3-11 years	3.88 (3.53-4.27)	3.75 (3.44-4.17)	5.56 (4.83-6.33)	7.99 (7.02-9.53)	11.0 (9.03-12.4)	639
Age 3-5 years	3.38 (3.04-3.77)	3.41 (2.84-3.78)	4.78 (3.98-6.32)	7.18 (5.50-8.71)	8.82 (7.18-11.0)	181
Age 6-11 years	4.15 (3.76-4.58)	4.02 (3.54-4.45)	5.77 (5.10-6.43)	8.78 (6.75-11.8)	12.4 (9.32-14.1)	458
Males 3-11	4.07 (3.56-4.65)	4.13 (3.44-4.76)	6.19 (5.29-7.18)	8.78 (7.18-11.8)	11.8 (8.01-15.4)	343
Females 3-11	3.70 (3.38-4.06)	3.54 (3.24-3.96)	4.88 (4.45-5.70)	7.02 (6.33-8.71)	9.44 (7.17-12.0)	296

Table 2. Summary measurements of PFAS concentrations (ng/ml) from 2010/11, 24 pools of human blood serum, all ages and both sexes, Australia

	Minimum-maximum	Mean	Median
PFOS	4.4-17.4	10.2	9.4
PFOA	3.1-6.5	4.5	4.3
PFNA	0.6-0.9	0.7	0.8
PFHxS	1.4-5.4	3.3	3.3

Table 3. Population serum concentrations of seven perfluorocarbons (ng/mL) collected in the U.S. in 2005/6 for the C8 Health project

	Measure	PFOS	PFOA	PFNA	PFHxS	PFHxA	PFHpA	PFDA
Sex								
Female	Arithmetic Mean	20.7	68.8	1.5	4.3	1.4	1.2	0.8
	Median	17.6	23.6	1.3	2.7	1	0.8	0.7
	Geometric mean	17	27.9	1.3	2.8	1.1	1	0.7
	Standard deviation	14.1	190.6	0.8	6.2	1.1	1.2	0.4
Male	Arithmetic Mean	26	98.2	1.7	5.9	1.4	1.3	0.8
	Median	22.9	33.7	1.5	3.8	1	0.9	0.7
	Geometric mean	21.9	39.4	1.5	4	1.2	1	0.7
	Standard deviation	16.5	284.3	0.9	12.8	1.4	1.3	0.8
Both sexes	Arithmetic Mean	23.3	82.9	1.6	5.1	1.4	1.2	0.8
	Median	20.2	28.2	1.4	3.2	1	0.9	0.7
	Geometric mean	19.2	32.9	1.4	3.3	1.1	1	0.7
	Standard deviation	15.6	240.8	0.9	10	1.3	1.2	0.7

17.2. Attachment 1

Oakey, Williamtown and Katherine PFAS Investigation and Management Area Maps (Attachment 01 Oakey, Williamtown and Katherine PFAS Investigation and Management Area Maps).

17.3. Attachment 2

Letter of Invitation for exposed participants who have participated in the VBTP to be sent by the ANU study team (Attachment 02 Letter of Invitation (exposed population) PFAS Health Study).

17.4. Attachment 3

Letter of Invitation for comparison group participants to be sent by the Department of Human Services (Attachment 03 Letter of Invitation (comparison population) PFAS Health Study).

17.5. Attachment 4

Participant Information Sheet for exposed participants (Attachment 04 Participant Information Sheet (exposed population) PFAS Health Study).

17.6. Attachment 5

Participant Information Sheet for comparison group participants (Attachment 05 Participant Information Sheet (comparison population) PFAS Health Study).

17.7. Attachment 6

Consent form for adult (Attachment 06 Consent Form (adult) PFAS Health Study).

17.8. Attachment 7

Consent form for child (Attachment 07 Consent Form (child) PFAS Health Study).

17.9. Attachment 8

Draft cross-sectional survey adult (Attachment 08 Cross-sectional survey (adult) PFAS Health Study).

17.10. Attachment 9

Draft data dictionary adult (Attachment 09 Cross-sectional survey data dictionary (adult) PFAS Health Study).

17.11. Attachment 10

Draft cross-sectional survey child (Attachment 10 Cross-sectional survey (child) PFAS Health Study).

17.12. Attachment 11

Draft data dictionary child (Attachment 11 Cross-sectional survey data dictionary (child) PFAS Health Study).

17.13. Attachment 12

Sonic Healthcare Pathology request form for PFAS and biomarker blood testing Attachment 12 Sonic pathology request form (comparison population)).

17.14. Attachment 13

VBTP Pathology request form for blood testing (Attachment 13 VBTP pathology request form).

17.15. Attachment 14

Reminder letter for cross-sectional survey and blood testing (Attachment 14 Reminder letter PFAS Health Study).

17.16. Attachment 15

Comparison group participant results letter (Attachment 15 Results letter (comparison group) PFAS Health Study).