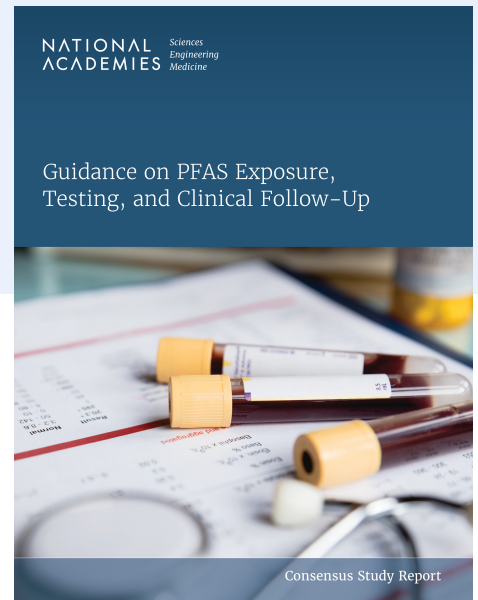


# Guidance on PFAS Exposure, Testing, and Clinical Follow-Up

Perfluoroalkyl and polyfluoroalkyl substances (PFAS) are a class of chemicals that includes over 12,000 different compounds, some of which are linked to health effects including certain cancers, thyroid dysfunction, small reductions in birth weight, and high cholesterol. PFAS are used in thousands of products, such as water and stain proof fabrics, non-stick cookware, and fire-fighting foams, because they have desirable chemical properties that repel oil and water, reduce friction, and resist temperature changes. PFAS compounds are often referred to as “forever chemicals” because they are resistant to degradation and when they do break down, the chemical products will include another PFAS.

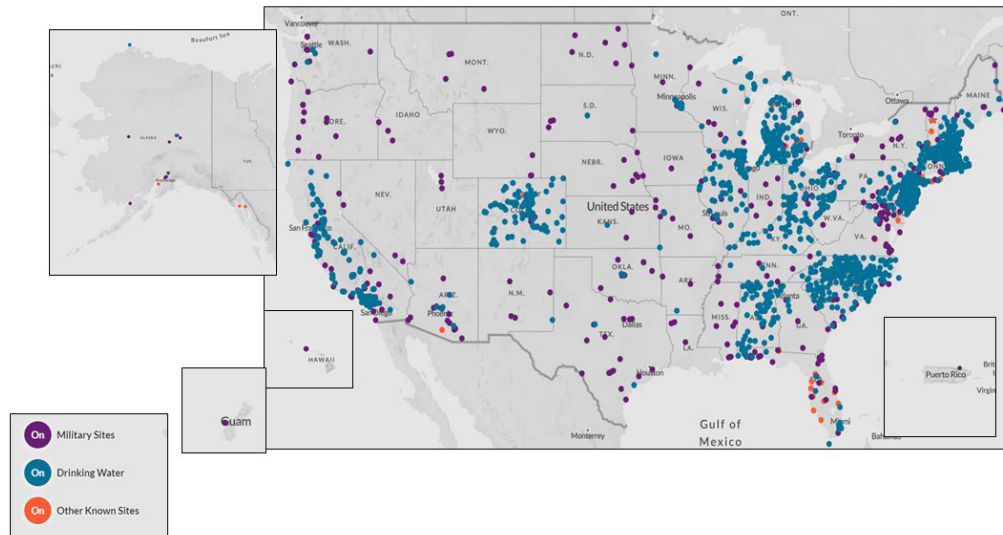
An estimated 2,854 U.S. locations (in all 50 states and two territories) have some level of PFAS contamination (Figure 1). Although not all of the contamination exceeds health advisories, the pervasiveness of the contamination is alarming. The people who live, work, and play in environments where PFAS contamination exceeds standards most often do not know how to protect themselves from the health risks of exposure. Some members of communities who have discovered their exposure exceeds health advisory levels are calling for a medical program that prevents, leads to early disease detection, or treats diseases related to the health risks they may face.

To help clinicians respond to patient concerns about PFAS exposure, the Agency for Toxic Substances Disease Registry (ATSDR) published guidance for clinicians that summarizes general information about PFAS and PFAS health studies and suggests answers to example patient questions. However, the ATSDR’s guidance does not provide specific recommendations on when to test for PFAS, how to interpret the results, or what clinical follow-up based on PFAS exposure might look like. Conducted at the request of ATSDR and the National Institute of Environmental Health Sciences (NIEHS), this report develops principles and recommendations for biological testing for PFAS exposure and



# PFAS Water Contamination

Estimated in 2,854 sites in 50 states and two territories



**FIGURE 1** PFAS Contamination Across the U.S. SOURCE: Environmental Working Group (EWG).

clinical evaluation for those exposed to help ATSDR update its guidance.

## POTENTIAL HEALTH EFFECTS OF PFAS

In order to determine the health effects of PFAS, the Committee conducted a literature review of studies that evaluated the effects of PFAS in humans. The committee's review focused on the PFAS compounds that are currently being measured in the National Health and Nutrition Examination Survey.<sup>1</sup> The Committee synthesized available evidence, including previous decisions from other authoritative bodies and more recent human studies, into four categories of "strength of evidence" used by other National Academies' committees: (1) Sufficient evidence of an association; (2) Limited suggestive evidence of an association; (3) Inadequate or insufficient evidence of an association; and (4) Limited suggestive evidence of no association. The Committee's conclusions are summarized in Table 1. Because most people are exposed to mixtures of PFAS, making it difficult to disentangle the specific effects

<sup>1</sup> PFAS compounds currently being measured in the National Health and Nutrition Examination Survey are perfluorooctanoic acid (PFOA), perfluorooctanesulfonic acid (PFOS), perfluorohexanesulfonic acid (PFHxS), perfluorononanoic acid (PFNA), Perfluorodecanoic acid (PFDA), Perfluoroundecanoic acid (PFuDA), and Methyl-perfluorooctane sulfonamide (MeFOSAA)

of each PFAS, the Committee provided one strength of evidence determination for all PFAS for each health effect.

## PFAS EXPOSURE REDUCTION





The primary exposure route to PFAS in non-occupational settings is likely ingestion. This may include drinking contaminated water and eating contaminated foods such as vegetables, fish, wildlife, meat, or dairy products from contaminated soil or water. PFAS are often used in food contact materials such as microwave popcorn bags or packaging of fast foods or processed foods. Exposure may also occur when dust containing PFAS is ingested. PFAS can transfer to the fetus during pregnancy, and in early life through feeding with formula made with contaminated water or through breastfeeding. Inhalation is the most common pathway in occupational settings, and is a route of exposure for people living near fluorochemical plants, or incinerators. Dermal exposure has not been well-studied but could be possible.

To advise patients who would like to reduce their exposure to PFAS, clinicians should: (1) talk with their patients to determine if and how they might be exposed to PFAS; (2) advise that those with occupational exposure

TABLE 1

## CATEGORY OF ASSOCIATION

HEALTH OUTCOMES WITH INCREASED RISK  
ASSOCIATE WITH PFAS EXPOSURE

 <p><b>Sufficient evidence of an association</b> Based on strong evidence, there is high confidence that there is an association between exposure to PFAS and the health outcome. It is unlikely that the association is due to chance or bias.</p>	<ul style="list-style-type: none"> <li>• Decreased antibody response (in adults and children)</li> <li>• Dyslipidemia (in adults and children)</li> <li>• Decreased infant and fetal growth</li> <li>• Increased risk of kidney cancer (in adults)</li> </ul>
 <p><b>Limited suggestive evidence of an association</b> Based on limited evidence, there is moderate confidence that there is an association between exposure to PFAS and the health outcome. It is possible that the association is due to chance or bias.</p>	<ul style="list-style-type: none"> <li>• Increased risk of breast cancer (in adults)</li> <li>• Liver enzyme alterations (in adults and children)</li> <li>• Increased risk of pregnancy-induced hypertension (gestational hypertension and preeclampsia)</li> <li>• Increased risk of testicular cancer (in adults)</li> <li>• Thyroid disease and dysfunction (in adults)</li> <li>• Increased risk of ulcerative colitis (in adults)</li> </ul>
 <p><b>Inadequate or Insufficient Evidence to Determine an Association</b> Based on inconsistent evidence, a lack of evidence, or evidence of insufficient quality, there is moderate confidence that there is an association between exposure to PFAS and the health outcome. No conclusion can be made about a potential association.</p>	<ul style="list-style-type: none"> <li>• Immune effects other than reduced antibody response, and ulcerative colitis; Cardiovascular outcomes other than dyslipidemia;</li> <li>• Developmental outcomes other than small reductions in birthweight</li> <li>• Cancers other than kidney, breast, and testicular; Reproductive effects other than hypertensive disorders of pregnancy; Endocrine disorders other than thyroid hormone levels; Hepatic effects other than liver enzyme levels; Respiratory effects; Hematological effects</li> <li>• Musculoskeletal effects, such as effects on bone mineral density; Renal effects, such as renal disease; Neurological effects</li> </ul>
 <p><b>Limited Suggestive Evidence of No Association</b> Based on at least limited evidence, there is at least moderate confidence that there is NO association between PFAS and the health outcome.</p>	<ul style="list-style-type: none"> <li>• No outcomes were identified.</li> </ul>

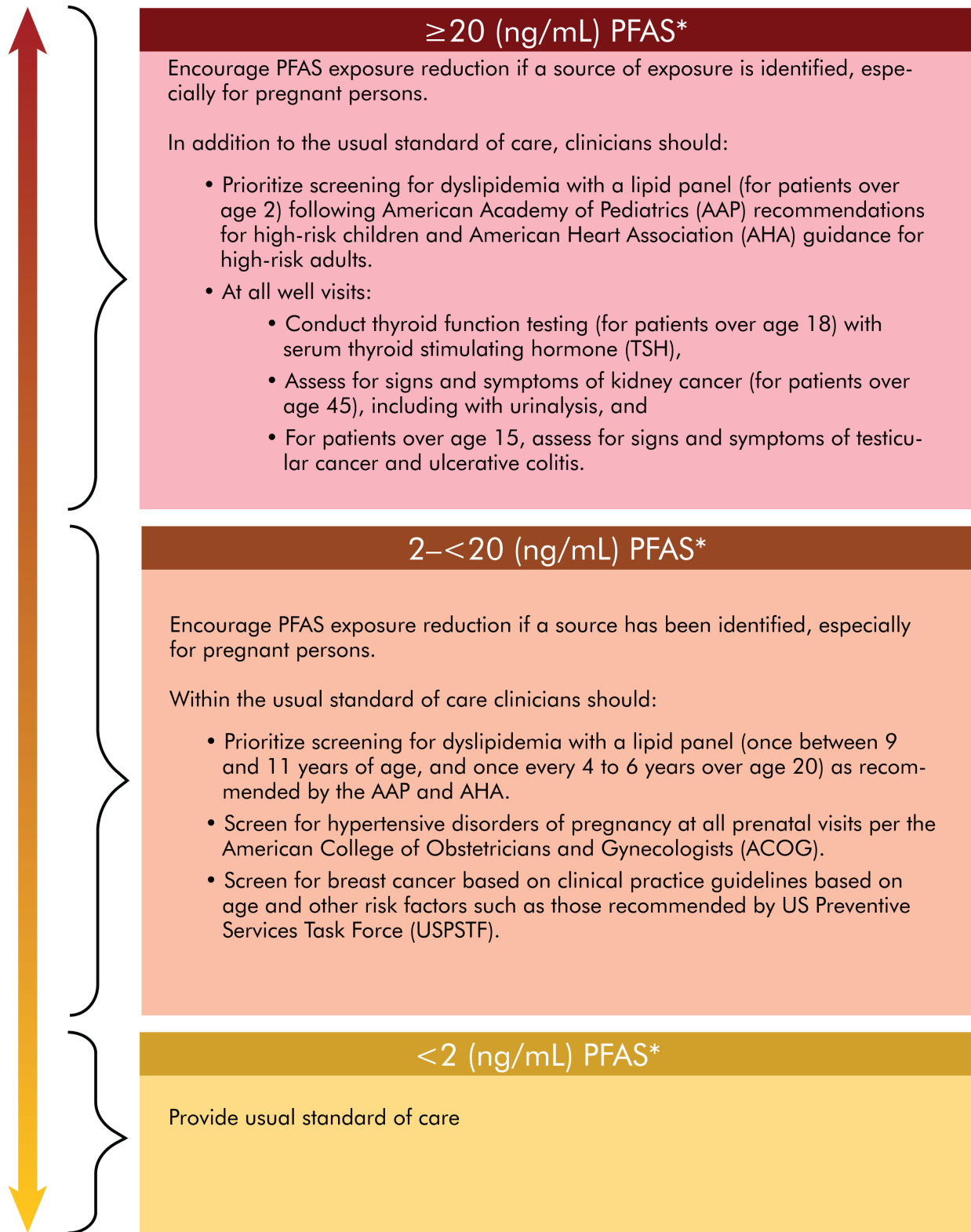
to PFAS consult with occupational health and safety professionals about reducing exposure; (3) advise individuals with elevated PFAS in their drinking water to filter their water; (4) advise patients living in areas of known PFAS contamination that PFAS can be present in fish, wildlife, meat, and dairy. Clinicians counseling parents of infants on PFAS exposure should discuss infant feeding and steps that can be taken to lower sources of exposure to PFAS.

#### PFAS TESTING AND LEVELS THAT CAN INFORM CLINICAL CARE

Report advises ATSDR to update its guidance to say, clinicians should offer PFAS blood testing to patients who are likely to have a history of elevated exposure to PFAS. PFAS testing has many potential benefits, such as empowering people to manage their own health, but it also carries some harms, such as stress or concern about the health effects of PFAS exposure. Decisions about PFAS testing require shared, informed decision making between patient and clinician. Clinicians should explain that exposure biomonitoring may provide important

information about an individual's exposure levels which might guide clinical follow-up. But PFAS testing measures exposure at the time of sample collection, and a person with low levels today may have had higher levels in the past. At the same time, this information cannot indicate or predict how likely it is that an individual will end up with a particular condition. Discussions about PFAS testing should always include information about how PFAS exposure occurs, potential health effects of PFAS, limitations of PFAS testing, and the benefits and harms of PFAS testing.

To determine PFAS levels in serum or plasma that could inform clinical care, the Committee considered publications from the Human Biomonitoring Commission in Germany and the European Food Safety Authority. These organizations determined guidance values that can be interpreted as levels below which health effects are unlikely to be observed, and levels above which effects have been observed in both the general population and more sensitive groups such



\* Simple additive sum of MeFOSAA, PFHxS, PFOA (linear and branched isomers), PFDA, PFUnDA, PFOS (linear and branched isomers), and PFNA in serum or plasma

FIGURE 2 Clinical guidance for follow-up with patients after PFAS testing.

as pregnant persons. Using the risk based values the committee found and assumptions of dose additivity, the committee determined that:

- Adverse health effects related to PFAS exposure are not expected at less than 2 nanograms per milliliter (ng/mL).
- There is a potential for adverse effects, especially in sensitive populations, between 2 and 20 ng/mL.
- There is an increased risk of adverse effects above 20 ng/mL.

Testing for PFAS, though expensive, offers an opportunity to identify people who may need to reduce PFAS exposure and who are at increased risk of certain health outcomes. Race, age, and other social and demographic characteristics already have disadvantaged many patients from accessing clinical preventive services, meaning that these groups may not be offered PFAS testing and the accompanying exposure reduction counseling. If testing primarily occurs among those with stable access to health care, there could be the unintended consequence of aggravating disparities in exposure to PFAS, a severe disadvantage of encouraging testing without a funded PFAS testing program with a national scope.

#### **PATIENT FOLLOW-UP FOR PFAS-ASSOCIATED HEALTH EFFECTS**

Most health effects or conditions found to be associated with PFAS exposure are already common in the general population and all have multiple known risk factors. The Committee's guidance for patient follow-up is summarized in Figure 2, which suggests that clinicians

engage in shared, informed decision making with their patients regarding follow-up care for PFAS-associated health endpoints. For patients with a PFAS level of 2 ng/mL to less than 20 ng/mL, clinicians should encourage the standard of care for conditions associated with PFAS. For a PFAS level of 20 ng/mL or greater, clinicians should screen for dyslipidemia following guidance for high risk individuals, thyroid dysfunction (for patients over 18), signs and symptoms of testicular cancer (for patients over 15) and ulcerative colitis, and signs and symptoms of kidney cancer with urinalysis (for patients over 45).

#### **NEXT STEPS TO GUIDE CLINICIANS AND PROTECT PUBLIC HEALTH**

ATSDR should revise its guidance to ensure consistency with the findings, conclusions, and recommendations in this report, and improve the writing, design, dissemination, and implementation of the guidance. Evidence of the health effects of PFAS should be updated every two years, and the clinical guidance should be updated at least every five years.

Public health requires the use of multifaceted approaches to emerging health issues. In environmental health—the subset of public health focused on environmental factors—mitigation of potential harms associated with chemical exposures is often complicated because there is no exposure surveillance system exists for most chemicals. The people and communities with high exposures to PFAS need to be identified. The recommendations in this report will be most protective of the public's health if they are part of a national effort toward increased biomonitoring, exposure surveillance, and clinicians' and public health professionals' education on environmental health issues.

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