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

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JULY 28 2022

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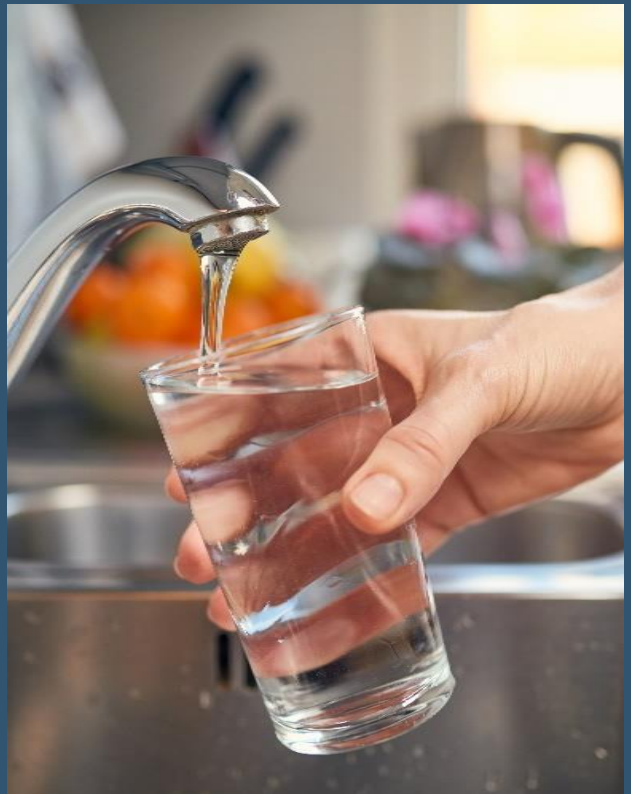
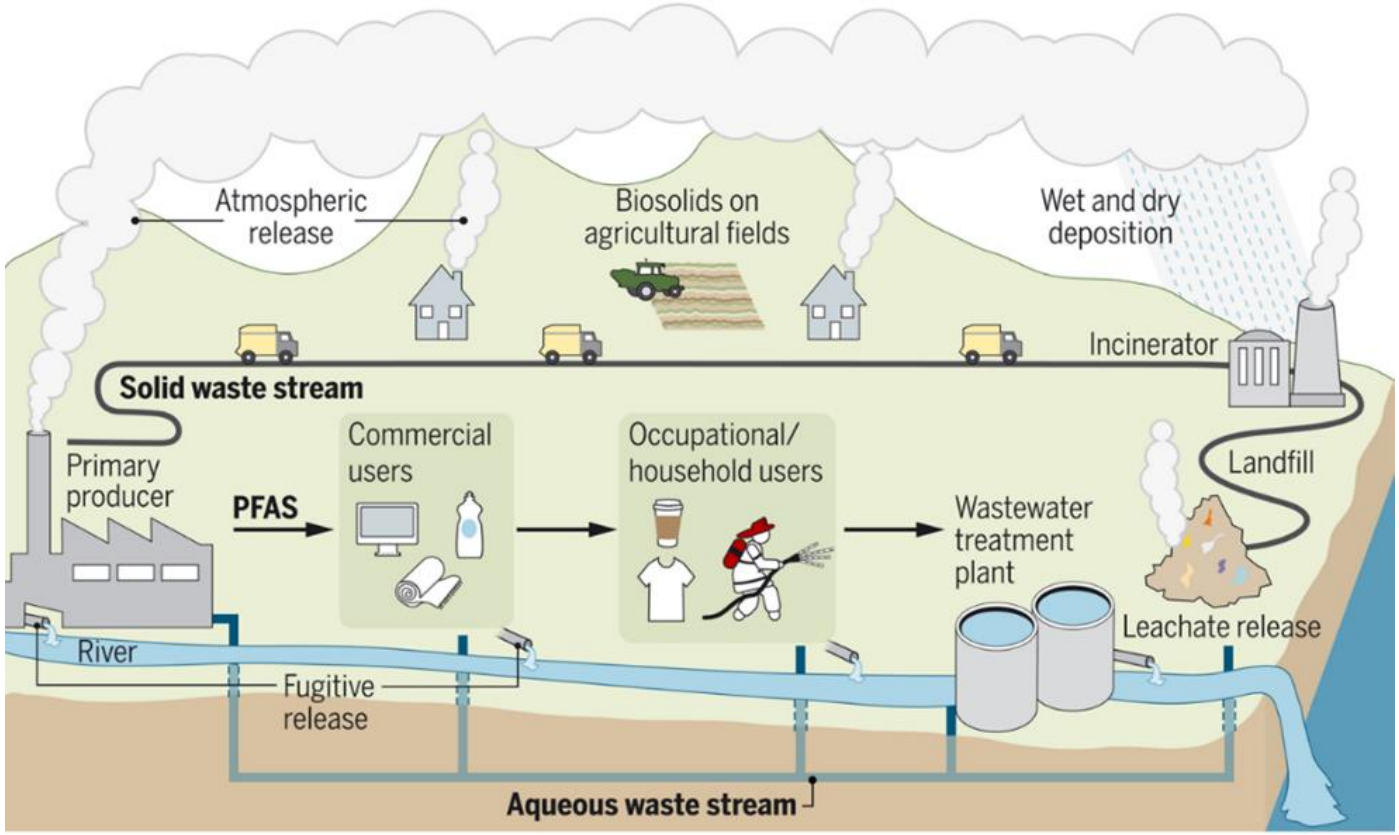
Introduction and Background



About PFAS (Per- and polyfluoroalkyl substances)

- A class of chemicals that includes over 12,000 different compounds.
- Used because they repel oil and water, resist heat, and reduce friction.
- Used in numerous industrial processes and consumer products since the 1940s
- Are known as “forever chemicals” because they resist degradation, and when they do break down, the chemical products will include another PFAS.

How PFAS Enter the Environment



SOURCE: Evich et al., 2022.

Some PFAS Milestones

1999 – Lawsuit filed against DuPont for contaminating a farm

2000 – 3M voluntarily stopped manufacturing several PFAS, PFOA, PFOS, PFHxS

2001 – Class action lawsuit filed for water contamination around Parkersburg, WV – Led to the C-8 Study and Medical Monitoring Panel

2012 – EPA passed a rule to monitor for several PFAS in drinking water

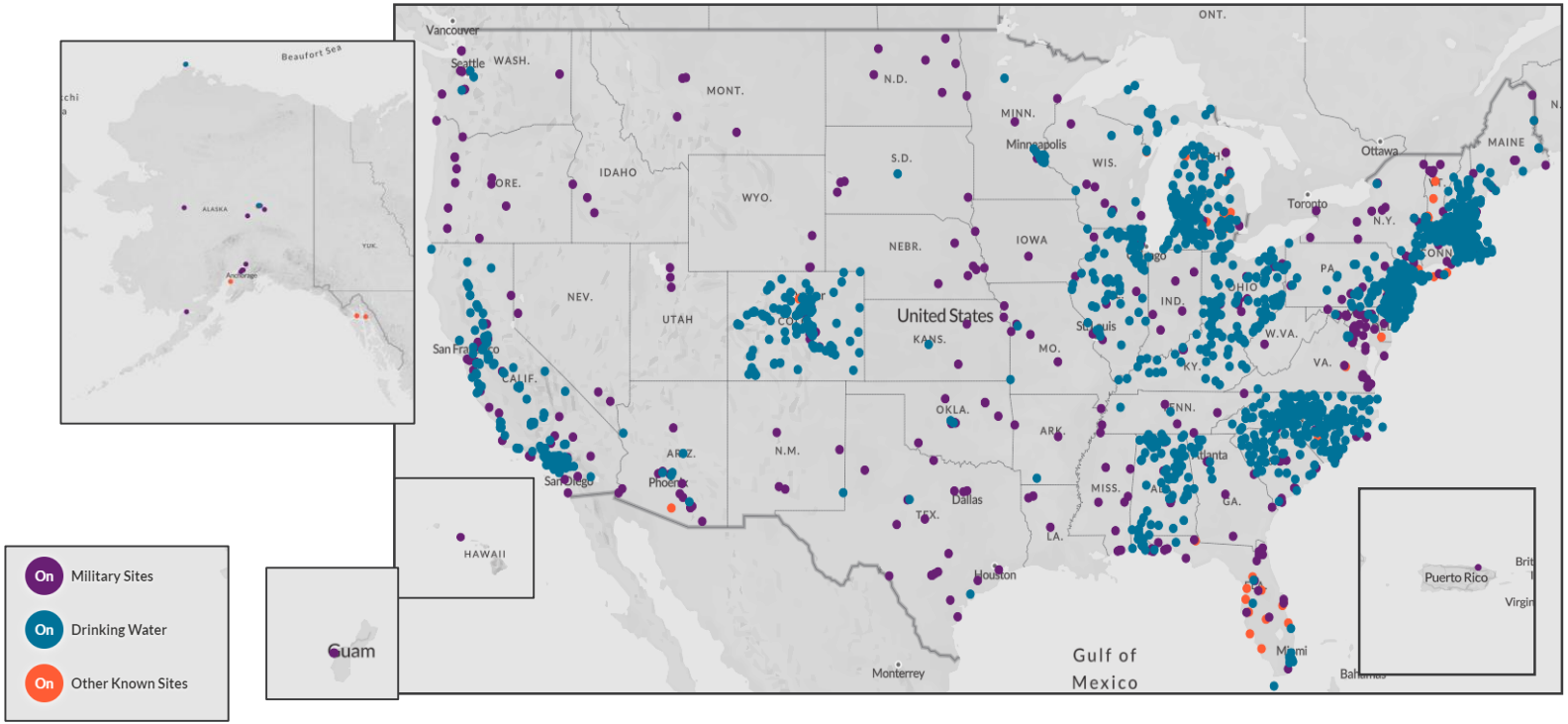
2016 – Many communities identified to have water over the EPA health advisory

How are people exposed to PFAS?

- Occupational exposures include work with fluorochemicals or as a firefighter
- Consumption of contaminated drinking water
- Consumption of contaminated food such as fish, wildlife, meat, and dairy products
- Individuals living near fluorochemical plants may also be exposed via inhalation of air emissions

PFAS Water Contamination

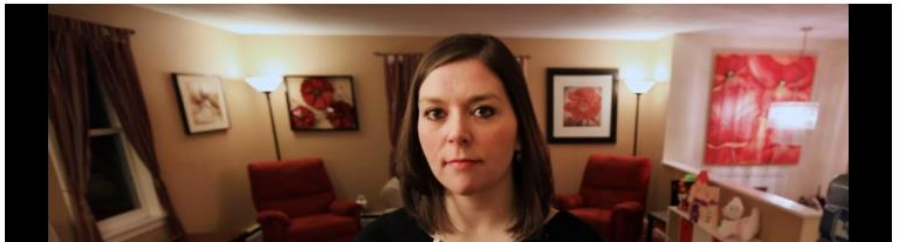
Estimated in 2,854 sites in 50 states and two territories



Source: Environmental Working Group, October 2021

PFAS-affected communities want data

Resident upset by delayed health testing on Pease water contaminant



EXPERT BLOG › ANNA READE

PFAS Blood Tests: Needed but Denied

Improved medical screening in PFAS-impacted communities to identify early disease

ehn.org/pfas-testing-2653577444.html

Isabella Raponi June 29, 2021

PFAS communities with water contamination "were exposed…without their consent, and now they have to fight tooth and nail to get a blood test result to know how much exposure they had? It just seems incredibly wrong […] We don't have all the answers yet, but not testing them is not the right answer." --

Andrea Amico, Testing for Pease, at National Academies PFAS Exposure Workshop in 2018

Statement of Task (Abbreviated)

- Review the human health literature for health effects of PFAS
- Develop principles for biological testing and clinical evaluation given substantial scientific uncertainty
- Characterize human exposure pathways and develop principles for exposure reduction
- Advice to update CDC ATSDR's clinical guidance and a strategy to keep it updated
- Provide recommendations on blood testing
- Provide recommendations on patient follow-up

What we were NOT asked to do

- Propose strategies for regulating PFAS
- Discuss strategies for clean-up, disposal, or removal of PFAS
- Suggest replacement chemicals for PFAS
- Propose or review PFAS drinking water standards
- Develop a PFAS Clinical Guidance for ATSDR
- Develop plans for payment of PFAS testing and clinical follow-up

Statement of Task challenges

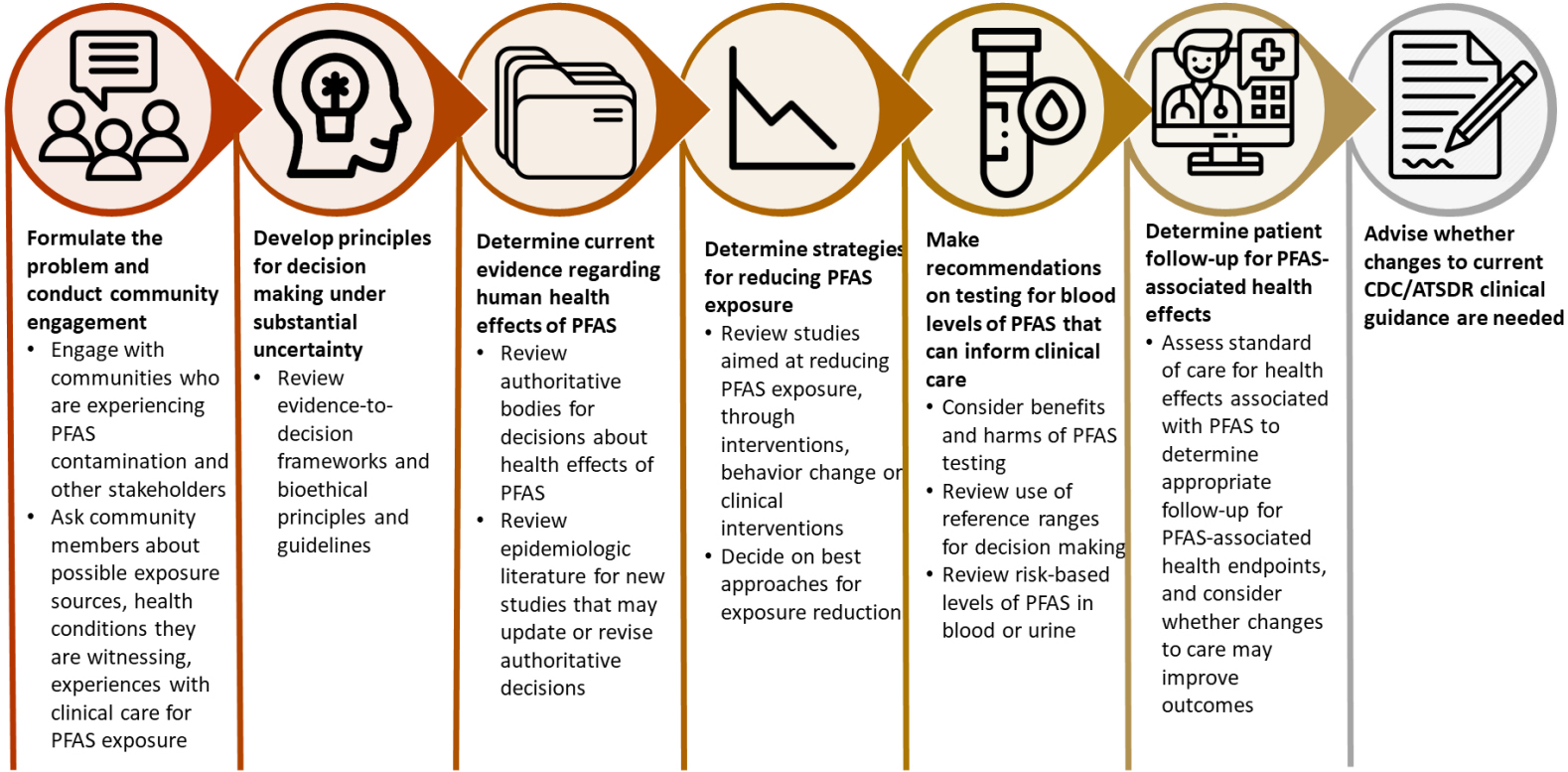
- Charge is unique from other environmental health reports because the focus is on reducing harms that may have occurred
- Estimated 12,000 PFAS and evaluated 7 of them, can the committee's recommendations apply to other PFAS?
- Everyone does not have equal ability to reduce sources of exposure or access to medical care, need to consider environmental justice and health equity.
- Need for effective communication to all impacted audiences, clinicians, communities, scientists, regulators.

Environmental Justice

- Pellow's Environmental Justice Framework accounts for the complexity of relationships and decisions that impact PFAS exposure and health.
  - How communities can mitigate their exposure and associated health risk is influenced not just in differences in exposure patterns but also sociohistorical processes, the complex roles of those involved, the effect of inequality on stakeholders, and agency of the individuals.
  - Need to consider structural factors beyond simply race, ethnicity, and socioeconomic status and to account for how individuals and communities are impacted by decisions made at local, state, and policy levels by government, industry, and health care professionals.

Committee’s approach

Committee's Approach



Problem Formulation: Community Engagement Plan for PFAS

Community Liaison Process

- Called for nominations, much like a committee
- Appointed 41 community liaisons, names and bios listed on the website
- Held a kick-off meeting to explain the study process, and the study statement of task
- Staff met regularly with community liaisons during the study data collection phase.
  - Liaisons suggested speakers, topics, and discussion questions for public meetings, provided documents or other data/information to staff, for committee's review.

Community Liaisons

Ms. Laurene Allen
Merrimack Citizens for Clean Water

Ms. Andrea Amico
Testing for Pease

Ms. Stel Bailey
Fight 4 Zero

Dr. Kyla Bennett
Public Employees for Environmental Responsibility (PEER)

Ms. Karen Blondel
Public Housing Civic Association

Dr. Phil Brown
Northeastern University

Dr. Alberto Caban-Martinez
University of Miami

Ms. Cheryl Cail
South Carolina Indian Affairs Commission/SC Idle No More

Dr. Courtney Carignan
Michigan State University

Ms. Tracy Carluccio
Delaware Riverkeeper Network

Ms. Charlotte Cisneros
Galveston Bay Foundation

Dr. Jamie DeWitt
East Carolina University

Ms. Emily Donovan
Clean Cape Fear

Dr. Alan Ducatman
unaffiliated

Mr. Patrick Elder
Military Poisons

Ms. Teresa Gerade
Don't Undermine Memphremagog's Purity (DUMP)

Ms. Hope Grosse
Buxmont Coalition for Safe Water

Ms. Loreen Hackett
PFOA Project New York

Ms. Ayesha Khan
Nantucket PFAS Action Group

Dr. Rainer Lohmann
University of Rhode Island

Ms. Samraa Luqman
Concerned Residents for South Dearborn (CRSD)

Ms. Beth Markesino
North Carolina Stop GenX in Our Water

Mr. Aaron Maruzzo
University of California, Berkeley

Ms. Tobyn McNaughton
unaffiliated

Ms. Kristen Mello
Westfield Residents Advocating For Themselves (WRAFT)

Ms. Pamela K. Miller
Alaska Community Action on Toxics (ACAT)

Dr. Elizabeth Neary
Wisconsin Environmental Health Network

Ms. Laura Olah
Citizens for Safe Water Around Badger (CSWAB.org)

Dr. Jacob Park
Castleton University

Ms. Sue Phelan
GreenCAPE

Ms. Andrea Rich
S.O.H2O

Ms. Dana Sargent
Cape Fear River Watch

Dr. Laurel Schaider
Silent Spring Institute

Mrs. Linda Shosie
Environmental Justice Task Force-Tucson

Mr. Lenny Siegel
Center for Public Environmental Oversight

Mr. Mike Watters
Grays Creek Residents United Against PFAS in our Wells & Rivers

Professor La'Meshia Whittington
North Carolina Black Alliance

Dr. Alan Woolf
Harvard Medical School/Boston Children's Hospital

Ms. Cathy Wusterbarth
Need Our Water (NOW)

Ms. Sandy Wynn-Stelt
unaffiliated

Approach: Health Effects of PFAS

- Task limits health effects to the seven PFAS measured in CDC's National Report on Human Exposure to Environmental Chemicals (MeFOSAA, PFHxS, PFOA, PFDA, PFUnDA, PFOS, and PFNA)
  - Other PFAS may cause harm
  - Most people are exposed to mixtures of PFAS
  - Committee provided one strength-of-evidence determination for all PFAS for each health effect
- Used authoritative reviews, systematic reviews and newer prospective epidemiologic studies to draw conclusions
- Animal evidence was not included in the committee's review of the literature but the committee considered animal studies discussed in ATSDR's Toxicological Profile for Perfluoroalkyls and systematic reviews considered by the committee.

Health Effects of PFAS Categories of Association

Category of Association	What Does it Mean?
+ + **Sufficient Evidence of an Association**	• 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.
+ **Limited or Suggestive Evidence of an Association**	• 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.
? **Inadequate or Insufficient Evidence to Determine an Association**	• Based on inconsistent evidence, a lack of evidence, or evidence of insufficient quality of an association between exposure to PFAS and the health outcome, no conclusion can be made about a potential association.
- **Limited or Suggestive Evidence of No Association**	• Based on at least limited evidence, there is at least moderate confidence that there is NO association between PFAS and the health outcome.

Findings, Conclusions, and Recommendations

Principles for Decision Making Under Uncertainty

- **Proportionality**: Decisions should balance plausible harms and benefits proportionally.
- **Justice**: Decisions should balance harms and benefits fairly across all individuals, promote health equity, and respect human rights.
- **Autonomy**: Decisions should incorporate informed decision-making by individuals and respect their values.
- **Feasibility**: Decisions should take account of resource availability, including follow-up services.
- **Adaptability**: Decisions should respond to new information about harms, benefits, and other relevant considerations (e.g., health equity and feasibility).

Health Effects of PFAS: Findings

- From the search of the literature the committee identified:
  - 8 Authoritative reviews
  - 26 Systematic reviews
  - 139 Prospective epidemiologic studies published since 2018 (when the literature search for the most recent authoritative review was completed)
- Several PFAS were noted to be associated with different health effects by authoritative bodies
- Effects studied span many different health effect categories

Health Effects of PFAS: Conclusions

Sufficient evidence of an association

- Decreased antibody response (in adults and children)
- Dyslipidemia (in adults and children)
- Decreased infant and fetal growth
- Increased risk of kidney cancer (in adults)

Limited suggestive evidence of an association

- Increased risk of breast cancer (in adults)
- Increased risk of testicular cancer (in adults)
- Liver enzyme alterations (in adults and children)
- Increased risk of pregnancy-induced hypertension (gestational hypertension and preeclampsia)
- Thyroid disease and dysfunction (in adults)
- Increased risk of ulcerative colitis (in adults)

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Recommendations – Exposure Reduction

Recommendation 4-1: Clinicians advising patients on PFAS exposure reduction should begin with a conversation aimed at first determining how they might be exposed to PFAS (sometimes called an environmental exposure assessment) and what exposures they are interested in reducing. This exposure assessment should include questions about current occupational exposures to PFAS (such as work with fluorochemicals or firefighting) and exposures to PFAS through the environment. Known environmental exposures to PFAS include living in a community with PFAS-contaminated drinking water, living near industries that use fluorochemicals, serving in the military, and consuming fish and game from areas with known or potential contamination.

Recommendation 4-2: If patients may be exposed occupationally, such as by working with fluorochemicals or as a firefighter, clinicians should consult with occupational health and safety professionals knowledgeable about the workplace practices to determine the most feasible ways to reduce that exposure.

Recommendations – Exposure Reduction

Recommendation 4-3: Clinicians should advise patients with elevated PFAS in their drinking water that they can filter their water to reduce their exposure. Drinking water filters are rated by NSF International, an independent organization that develops public health standards for products. The NSF database can be searched online for PFOA to find filters that reduce the PFAS in drinking water included in the committee's charge. Individuals who cannot filter their water can use another source of water for drinking.

Recommendation 4-4: In areas with known PFAS contamination, clinicians should advise patients that PFAS can be present in fish, wildlife, meat, and dairy products and direct them to any local consumption advisories.

Recommendation 4-5: Clinicians should direct patients interested in learning more about PFAS to authoritative sources of information on how PFAS exposure occurs and what mitigating actions they can take. Authoritative sources include the Pediatric Environmental Health Specialty Units (PEHSUs), the Agency for Toxic Substances and Disease Registry (ATSDR), and the U.S. Environmental Protection Agency (EPA).

Recommendations – Exposure Reduction

Recommendation 4-6: When clinicians are counseling parents of infants on PFAS exposure, they should discuss infant feeding and steps that can be taken to lower sources of PFAS exposure. The benefits of breastfeeding are well known; the American Academy of Pediatrics, the American Academy of Family Physicians, and the American College of Obstetricians and Gynecologists support and recommend breastfeeding for infants, with rare exceptions. Clinicians should explain that PFAS can pass through breast milk from a mother to her baby. PFAS may also be present in other foods, such as the water used to reconstitute formula and infant food, and potentially in packaged formula and baby food. It is not yet clear what types and levels of exposure to PFAS are of concern for child health and development.

Recommendation 4-7: Federal environmental health agencies should conduct research to evaluate PFAS transfer to and concentrations in breast milk and formula to generate data that can help parents and clinicians make shared, informed decisions about breastfeeding.

PFAS Testing and Concentrations to Inform Clinical Care of Exposed Patients: Findings

Potential Harms

- Fear of blood draw
- Small risk of injury or infection at draw site
- Difficulties in interpreting results
- Stress or concern about the health effects of exposure
- Clinical consequences from medical follow-up as a result of exposure
- Decreased property values resulting from identifying property contamination
- Social isolation

Potential Benefits

- Increased awareness of exposure so it can be reduced
- Empowerment of communities to respond to contamination
- Relief from the stress of not knowing one's exposure level
- Identification of the potential risk for health conditions associated with PFAS exposure, informing subsequent preventive care
- Help in monitoring whether efforts to reduce exposure are working through the conduct of baseline and follow-up tests

Harms and benefits of PFAS testing roughly equal and varies for each person

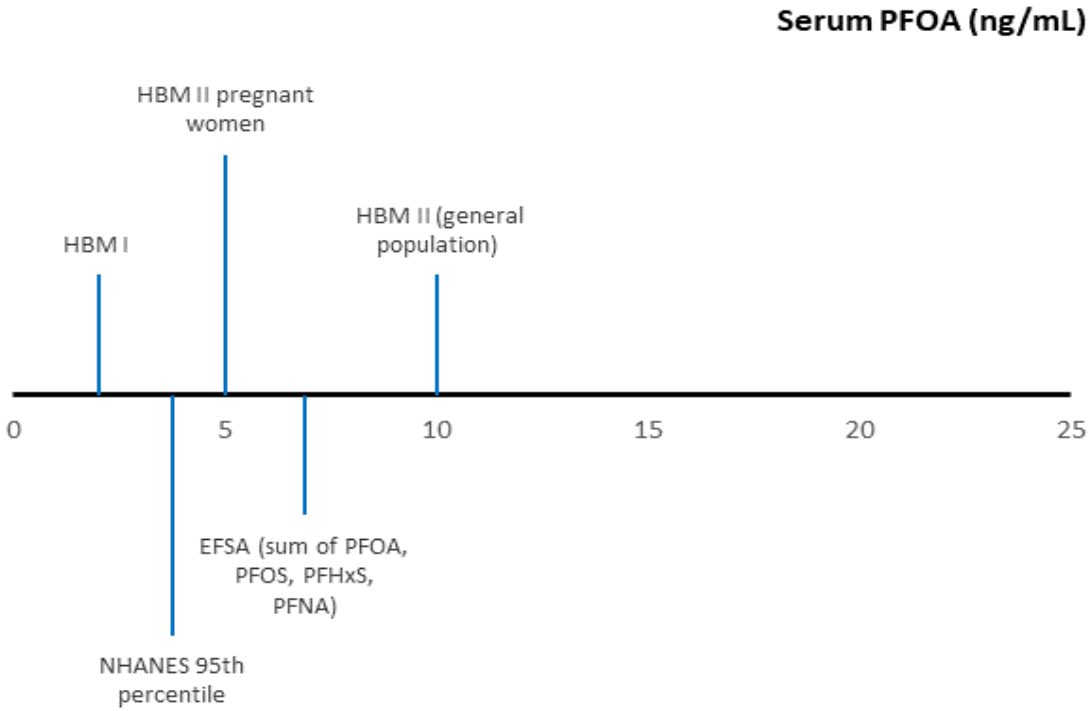
Committee Found Several Risk Levels

- **German Human Biomonitoring Commission** (HBM Commission) develops human biomonitoring (HBM) values for the interpretation of concentrations of environmental chemicals measured in biological samples.
    - HBM-I values are the concentrations below which effects are not expected
    - HBM-II values are the concentrations above which adverse health effects are possible
- **EFSA Point of Departure** is the modeled estimate of maternal exposure which would lead to negligible risk to a breastfed infant

Type of Risk-Based Levels	PFOS ng/ml	PFOA ng/ml	Sum of PFAS* ng/ml
HBM-I	5	2	
HBM-II	20	10	
HBM-II (women of childbearing age)	10	5	
EFSA Point of Departure (women of childbearing age)			6.9

* PFOA, PFOS, PFHxS and PFNA

Graph of Risk-Based & Reference-Based Levels: PFOA



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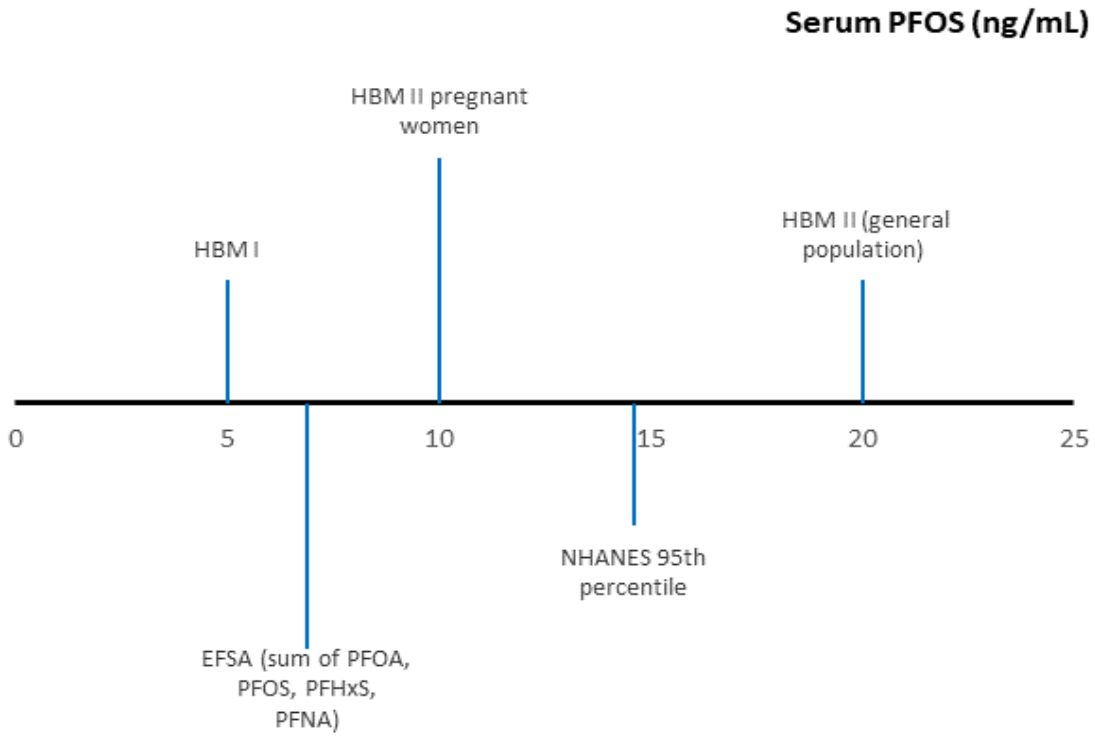
Graph of Risk-Based & Reference-Based Levels: PFOS



PFAS Testing and Concentrations that Can Inform Clinical Care Recommendations

- **Recommendation 5-1**: As communities with PFAS exposure are identified, government entities (e.g., Centers for Disease Control and Prevention [CDC]/Agency for Toxic Substances and Disease Registry [ATSDR], public health departments) should support clinicians with educational materials about PFAS testing so they can discuss testing with their patients.

- Educational materials should cover:
  - How people can be exposed to PFAS: Potential health effects of PFAS exposure and strategies for reducing exposure.
  - Limitations of PFAS blood testing: PFAS blood testing does not identify the sources of exposure or predict future health outcomes; it only assesses body burden at the time of sample collection. For example, a person with low blood levels today may have had higher levels in the past.
  - The benefits and harms of PFAS testing.

PFAS Testing and Concentrations that Can Inform Clinical Care Recommendations

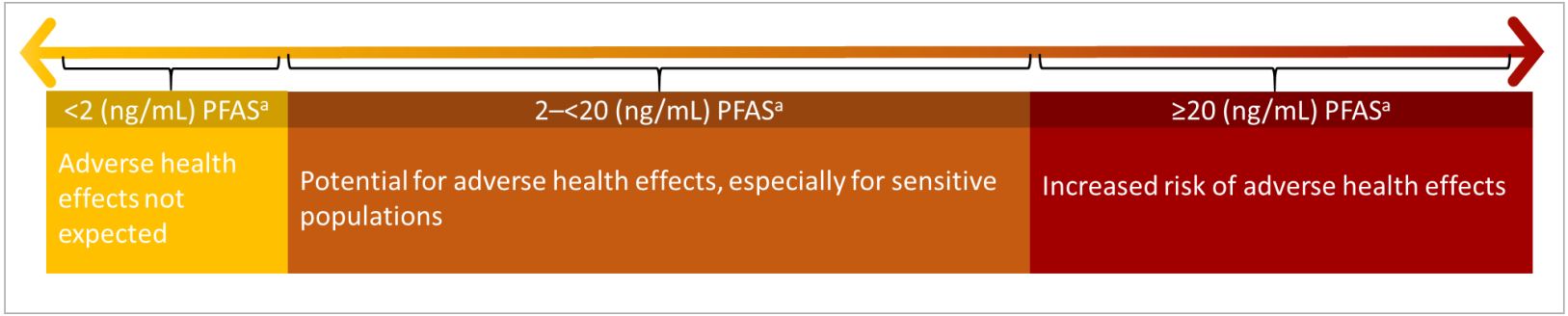
Recommendation 5-2: Clinicians should offer PFAS testing to patients likely to have a history of elevated exposure. In all discussions of PFAS testing, clinicians should describe the potential benefits and harms of the testing and the potential clinical consequences (such as additional follow-up), related social implications, and limitations of the testing so patient and clinician can make a shared, informed decision. Patients who are likely to have a history of elevated exposure to PFAS include those who have

- had occupational exposure to PFAS (such as those who have worked with fluorochemicals or served as a firefighter);
- lived in communities where environmental and public health authorities or academic researchers have documented PFAS contamination; or
- lived in areas where PFAS contamination may have occurred, such as near facilities that use or have used fluorochemicals, commercial airports, military bases, wastewater treatment plants, farms where sewage sludge may have been used, or landfills or incinerators that have received PFAS-containing waste.

PFAS Testing and Concentrations that Can Inform Clinical Care Recommendations

Recommendation 5-3: Clinicians should use serum or plasma concentrations of the sum of PFAS* to inform clinical care of exposed patients, using the following guidelines for interpretation:

- 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.



*Simple additive sum of MeFOSAA, PFHxS, PFOA (linear and branched isomers), PFDA, PFUnDA, PFOS (linear and branched isomers), and PFNA in serum or plasma. Caution is warranted when using capillary blood measurements as levels may differ from serum or plasma levels.

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PFAS Testing and Concentrations that Can Inform Clinical Care Recommendations

Recommendation 5-4: The National Health and Nutrition Examination Survey should begin collecting and sharing more data on children younger than 12 years of age and pregnant people to generate reference populations for those groups.

Guidance for Clinicians on Exposure Determination, PFAS Testing, and Clinical Follow-Up

Recommendation 6-1: Clinicians should treat patients with serum PFAS concentration **below 2 nanograms per milliliter (ng/mL)** with the usual standard of care.

Recommendation 6-2: For patients with serum PFAS concentration of **2 nanograms per milliliter (2 ng/mL) or higher and less than 20 ng/mL**, clinicians should encourage PFAS exposure reduction if a source of exposure is identified, especially for pregnant persons. Within the usual standard of care clinicians should:

- Prioritize screening for dyslipidemia with a lipid panel (once between 9 and 11 years of age, and once every 4 to 6 years over age 20) as recommended by the American Academy of Pediatrics (AAP) and American Heart Association (AHA).
- Screen for hypertensive disorders of pregnancy at all prenatal visits per the American College of Obstetricians and Gynecologists (ACOG).
- Screen for breast cancer based on clinical practice guidelines based on age and other risk factors such as those recommended by the U.S. Preventive Services Task Force (USPSTF).

Guidance for Clinicians on Exposure Determination, PFAS Testing, and Clinical Follow-Up

Recommendation 6-3: For patients with serum PFAS concentration of **20 nanograms per milliliter (ng/mL) or higher**, clinicians should encourage PFAS exposure reduction if a source of exposure is identified, especially for pregnant persons. In addition to the usual standard of care, clinicians should:

- Prioritize screening for dyslipidemia with a lipid panel (for patients over age 2) following American Academy of Pediatrics (AAP) guidelines for high-risk children and American Heart Association (AHA) guidance for high-risk adults.
- At all well visits:
  - conduct thyroid function testing (for patients over age 18) with serum thyroid stimulating hormone (TSH),
  - assess for signs and symptoms of kidney cancer (for patients over 45), including with urinalysis, and
  - for patients over 15, assess for signs and symptoms of testicular cancer and ulcerative colitis.

Revising the ATSDR Clinical Guidance

Recommendation 7-1: The Agency for Toxic Substances and Disease Registry (ATSDR) should update its PFAS clinical guidance to make it more succinct and accord with the review of PFAS-associated health effects, exposure reduction considerations, PFAS testing recommendations and interpretation, and recommendations for clinical follow-up presented in this report. When describing the health effects of PFAS, ATSDR should avoid using terms typically used to categorize toxicants, such as “endocrine disrupter” or “neurotoxin,” because they are vague and not necessarily clinically meaningful. When discussing the strength of the association between PFAS and a health outcome, ATSDR should use standard categories of association (such as sufficient evidence of an association, limited suggestive evidence of an association, inadequate or insufficient evidence of an association, and limited suggestive evidence of no association).

Revising the ATSDR Clinical Guidance

Recommendation 7-2: The Agency for Toxic Substances and Disease Registry (ATSDR) should incorporate a reader-centered approach when developing its guidance, with the knowledge that many different audiences will turn to its clinical guidance document to prepare for discussions with their clinicians. ATSDR should also solicit feedback on the guidance from a variety of stakeholders, such as community groups, practicing clinicians, and medical associations. In addition, ATSDR should encourage clinicians to use evidence-based organizational health literacy strategies to support shared, informed decision making; patient-centered care; cultural humility; and accessible language when communicating with patients about potential health risks.

Revising the ATSDR Clinical Guidance

Recommendation 7-3: The Agency for Toxic Substances and Disease Registry (ATSDR) should develop a process for updating its PFAS guidance that adheres to criteria for making guidelines trustworthy, such as being based on a thorough, transparent, unbiased review of the evidence and being developed by a knowledgeable panel of experts free from strong biases and conflicts of interest. A review of the evidence on the health effects of PFAS should be completed by an authoritative neutral party every 2 years, and the clinical guidance should be updated every 5 years or sooner if warranted by the evidence on the health effects of PFAS. Clinicians and members of communities with elevated PFAS exposure should be engaged to inform the problem and review updated guidance.

Suggested framework for updating the ATSDR's clinical guidance based on new evidence

Foundational Principles: Proportionality, Justice, Autonomy, Feasibility, Adaptability

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Implementing the Committees' Recommendations to Improve Public Health

Recommendation 8-1: Laboratories conducting PFAS testing of serum or plasma should report the results to state public health authorities, following the respective states' statutes and reporting regulations. This reporting would improve PFAS exposure surveillance; it could be linked with the Centers for Disease Control and Prevention's (CDC's) environmental public health tracking network and help build capacity for improvements in the state-based national biomonitoring network.

When I would go to the doctors and tell them about some of the exposures of over 50 chemicals that I was exposed to, the doctors would laugh and say no. Clearly, they didn't have any information about environmental components [of disease]. They made me feel small; they made me feel stupid and embarrassed even just asking the question.

Hope Grosse, Buxmont Coalition For Safer Water, April 7, 2021 Town Hall Testimony

Environmental Health Education

- Reports from the National Academies have called for improvements in environmental health education of clinicians
  - Addressing the Physician Shortage in Occupational and Environmental Medicine: Report of a Study (IOM 1991)
  - Environmental Medicine: Integrating a Missing Element into Medical Education (IOM 1995)
  - Nursing, Health, & the Environment Strengthening the Relationship to Improve the Public's Health (IOM 1995)

Continuing Education of Clinicians

- Numerous resources exist that may help improve education of practicing clinicians
  - Pediatric Environmental Health Specialty Units
  - Alliance of Nurses for Healthy Environments (ANHE)
  - Children's Environmental Health Network (CEHN)
  - American College of Occupational and Environmental Medicine (ACOEM)

Closing thoughts

- Environmental factors are important components of disease risks.
- A more comprehensive approach to evaluating environmental exposures is needed to understand the causes and contributors to chronic disease.
- Such an approach will ultimately depend on breaking down the barriers between environmental public health and the clinical care setting.
- Identifying environmental exposures, measuring exposure levels in patients and providing indicated medical follow-up is a critical frontier that could and should bring the two disciplines closer together to improve health of those in our communities.

Thank you for your attention

Questions comments?

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