Advising Patients in PFAS Exposed Communities: Clinician Perspective

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Goals:

Usual rules for Environmental Health Communications

Patient Concerns from Impacted Communities

Health Outcomes & What can Be Done

Problems/Opportunities for Improved Advising

(Clinical Discussion as Aerobic Sport)

PFAS History/Declarations (including "COI")

Past:

- WVU: Project Design Consultation and Web Health Communications for the "C8 Health Project" (circa 2005, n=69,030)
- Active Duty: Investigation of Testicular Cancer at two Naval Air Rework Facilities ("NARFs" late 1980s)
- Screening programs for government, industry, communities

NAVAIR Media

Present/Future:

- Participate with entities interested in medical screening in affected communities, both as science advisor volunteer and as paid consultant (2018)
- Ongoing peer review publication concerning PFAS and health

Rules of Environmental (Toxicity) Health Communications (simplified for time constraints)

Topics For Affected **communities**

- Discuss exposure
- Delineate: about background vs **community at risk**
- What is wanted:

Outcomes Fairly and Honestly, Degrees of Evidence, opportunities and pros/cons of intervention, acknowledgement that reasons for worry are real

- **Biomarkers**: exposure & outcome

For **Healthcare Providers**

Same as for Communities and, also…

- Are there biomarkers for early detection?
- If so, do they detect processes for which we have some useful intervention?

(Distinguish between the uses of biomarkers of exposure vs biomarkers of disease detection)

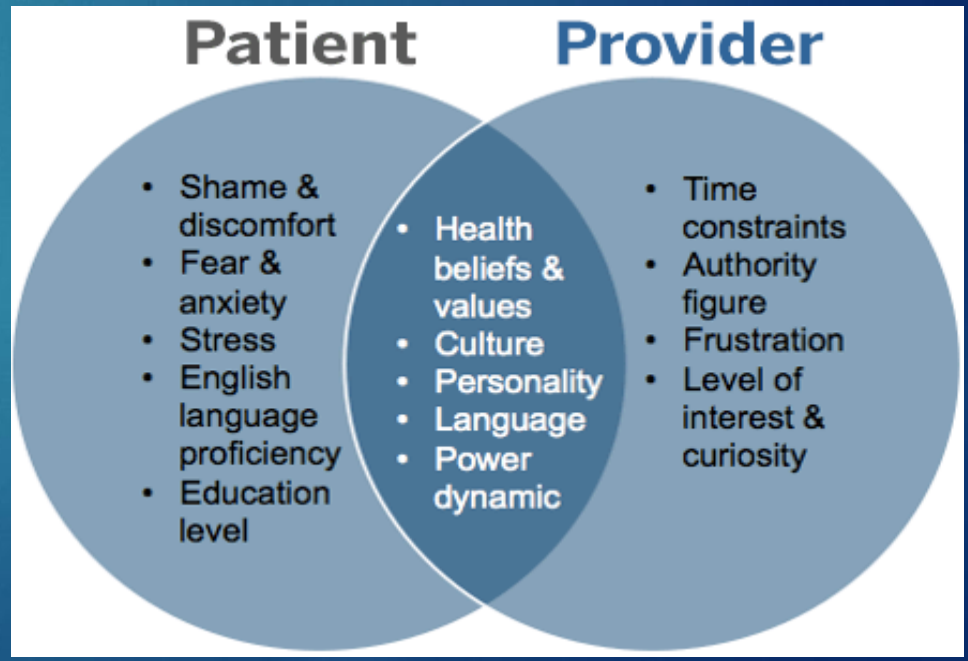
- And will the process have net benefits? (Screening should consider harms as well as benefits before undertaken).
- NB: Most of the considerations are clinical science, not feelings.

Keep in Mind: Official Communications To Clinicians Affect More than Screening*

AHRQ SOCIO ECOLOGICAL MODEL for Prevention

CLINICAL MODEL

*Water manager, well owner, insurers, officials with budgets……



ATSDR's Criteria for Screening: 60 FR 388839; 1995:

https://www.federalregister.gov/documents/1995/07/28/95-18578/atsdrs-final-criteria-for-determining-the-appropriateness-of-a-medical-monitoring-program-under

- Exposure
- Outcome
- Early Detection
- Benefits/Harms

"An exposure will be considered to be a sufficient level if there is ***documentation of an increased opportunity for exposure to a level that meets or exceeds some Reference Doses (RfDs) or that meets a level reported in the peer-reviewed*** *or sampling from the general area . . . .* ***Documentation of individual levels of exposure is not required."***

Office Implications for Biomarkers of Exposure

ATSDR's internal guidance: Environmental measures, Exposure models, and Population Biomarkers are all means to determine presence/absence of ***an exposed population*** (CFR 60:145; 1995. 38839-44)

Theory: A stated implication is that internal biomarkers are not needed for everyone in the contaminated community once the exposure population is defined. It is sufficient to identity the community and follow the health outcomes.

Experience: However, the message *"Better off not knowing ……."*

Is predictably not working

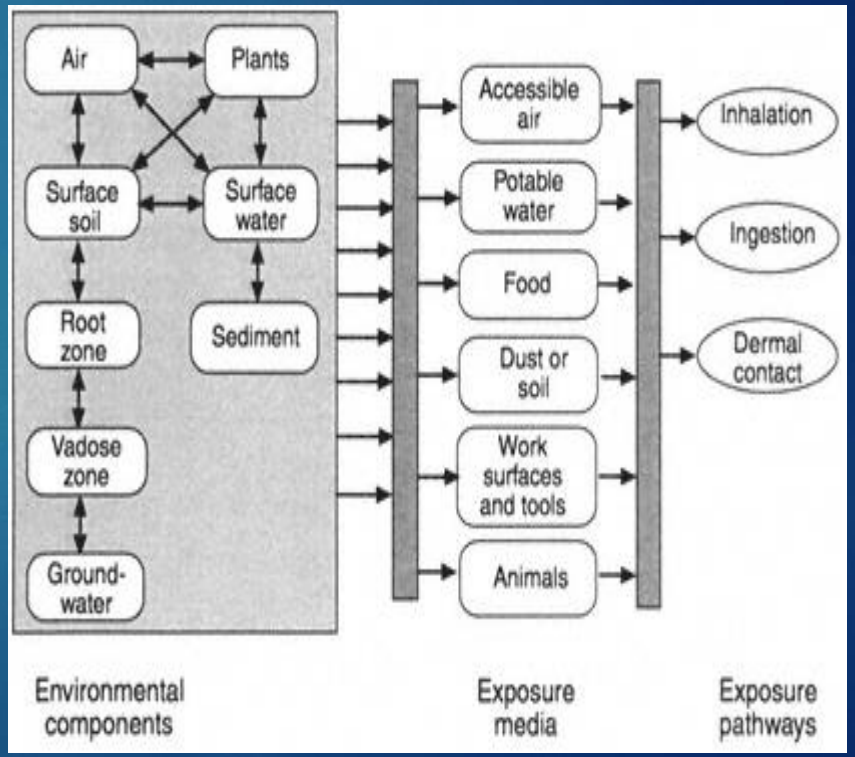
Currently, PFAS easier to measure for a group. Peer reviewed survey data – Internal Contamination Results are strongly appreciated

(One other consideration: "*Doc, how sure are that the filters are working.*")

Overlooked Exposure consideration - Who is the Communication for?** Contaminated Communities vs World at large

**Current PFAS guidance to communities and clinicians routinely fail to distinguish between the world with background exposures and highly contaminated communities. This problem is an ongoing source of exposure community patient frustration.

NAS press image



Common **Patient Concerns** (Exposure Community)

HEALTH OUTCOME(S)

- Cancer
- Infertility
- Transgenerational Exposure and Pregnancy Timing or Choosing to Breastfeed
- Human Development

  Birth Defects, Developmental Delays
- Stress (Property value, maintenance of filtration equipment, guilt concerning children or family)

Goals: 1° & 2° Prevention

- Our help for water sources and water filtration
- Breast Feeding and Pregnancy Timing: (Honest advice includes unknowns)
- **Decrease Risk, Screen for Exposure/Outcomes**
- **Remove Internal Contamination**

  (Yes, we can, but should we? Clinical trial underway in FFs)
- Give blood?
- Influence Entities Perceived as Unscientific/Uncaring

ATSDR framing for patient Health Outcomes

Early Detection, and Useful Intervention 60 FR 388839; 1995

There should be a scientific basis

for a ***reasonable***

association *between an exposure*

to a hazardous substance and a

specific ***adverse health effect***

(such as an illness or change in

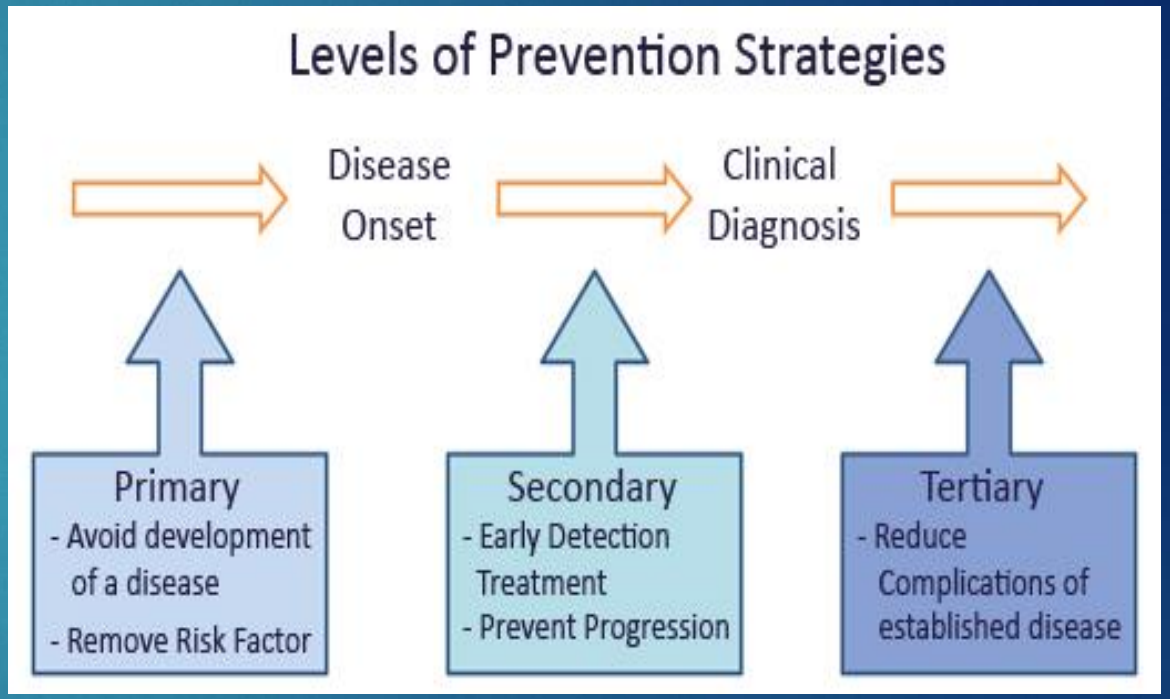
a biological marker or effect)*."*

- *"The monitoring should be directed at detecting adverse health effects that are consistent with the existing body of knowledge and* ***amenable to prevention or intervention measures."***
- *"In addition, the adverse health effects (disease process, illness, or biomarkers of effect) should be such that early detection and treatment or intervention affect the progress to symptomatic disease, improves the prognosis, ... quality of life .....or is amenable to primary prevention."*

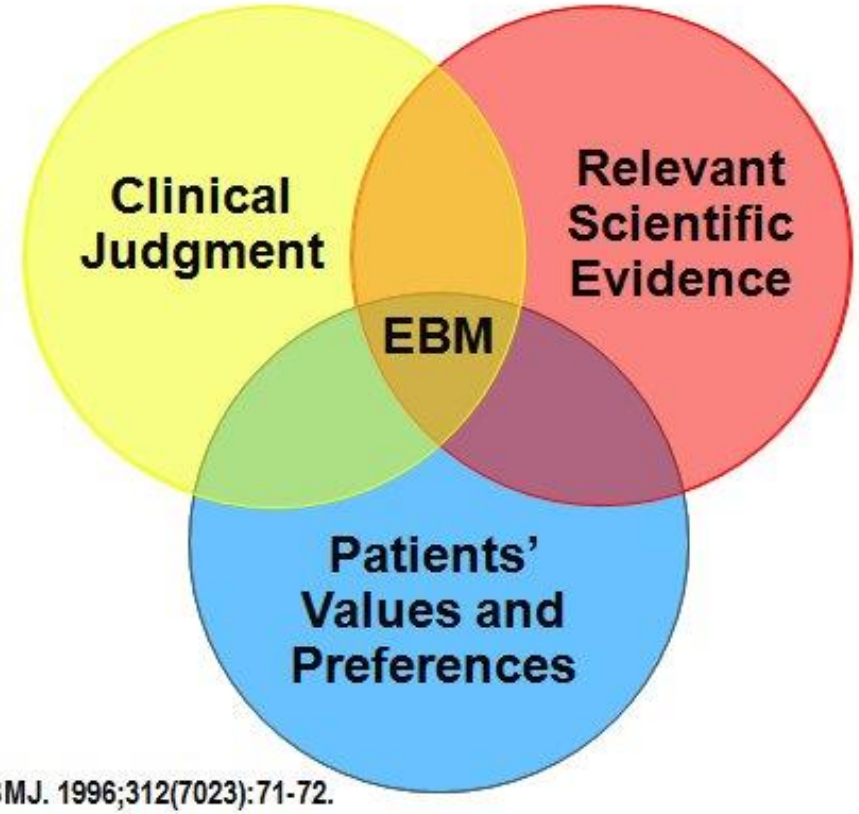
Implications for Clinical Preventive Services

- Primary, Secondary, and Tertiary Outcome mitigation are all part of the consideration
- Biomarkers of Disease Processes are a sufficient reason for the consideration.

Columbia University Primary Care Resources



What Is Evidence-Based Medicine?



Sackett DL, et al. BMJ. 1996;312(7023):71-72.

Implicit to the clinician-patient Discussion - improve Health Outcomes*

*Weighing the evidence from populations and experiments, the outcomes we know most about overlap with but are not identical to patient concerns

PFAS health outcomes evidence taxonomy: Dr/ Samet mentioned several (Bradford Hill and others)

Substantial

Multiple Populations and different study designs

Findings pertain to populations with a wide range of exposure (less focus on all high or all low)

Dose response

Unifying Experimental evidence such as histopathology and plausible pathways

Well Above Equipoise

Population Evidence but in fewer populations

Experimental: Mechanistic or histologic data available but less rich

Above or at Equipoise

Population evidence only, or a smaller number of studies.

More Conflicting outcomes in Strong studies

Less Indication of Mechanisms or Parallel findings in experimental settings.

Current Evidence: An updating personal task and the background basis of discussions

Strong Evidence

- Immunotoxicity
- Lipids /Sterol interference, Associated Codeable conditions and longitudinal diagnoses and medications
- Liver Functions and Steatosis
- Thyroid Alterations/Binding proteins
- Uric Acid - Hyperuricemia/Gout

>> Equipoise

- Breast Feeding, diminished capability
- Insulin Resistance
- Kidney Cancer
- Kidney Disease
- Osteoporosis
- Testicular Cancer
- Ulcerative Colitis
- Vaccine -Diminished uptake

≥ Equipoise

- Asthma, Allergy
- Cardiovascular (including thrombus)
- Diabetes
- Fecundity diminished (with physiology evidence for ovarian, testicular function and sperm morphology motility)
- Infections in early childhood
- Thyroid disease
- Developmental: Intrauterine Growth Retardation (IUGR), Preterm birth, & Pregnancy Induced Hypertension (PIH).

Population evidence informs the Discussion

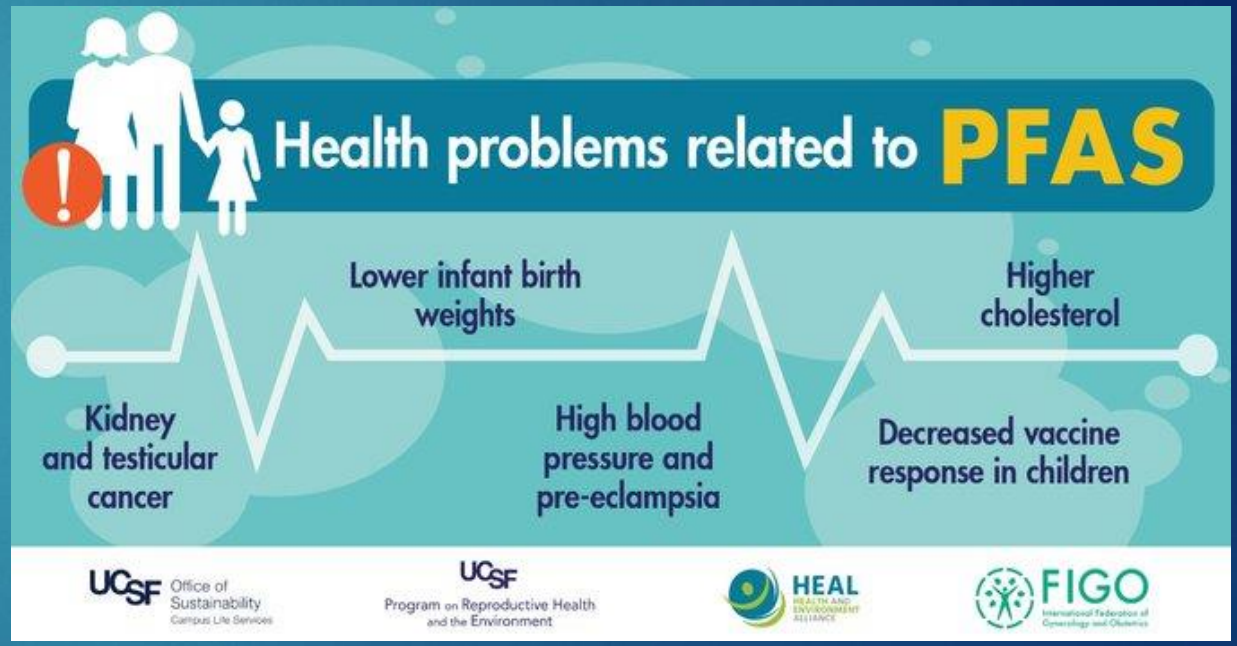
- Lipids* >>20 populations and many study designs, replicable dose response, longitudinal diagnoses and need for RX, estimate of Strength from meta-analysis, findings include children.
- Liver* functions (and case-control results from studies of patients undergoing liver workup for NAFLD) > 10 populations with multiple study designs, including children. A small clinical study indicates increased evidence of steatohepatitis (not just steatosis) in children. One study (of bariatric patients) did not find a positive association to stages of NAFLD.
- Uric acid* >7 populations, including children.
- Insulin resistance – Includes children. Increasing evidence, more conflicting studies than for the lipids, liver, and uric acid findings.

*These health outcomes include examples of occupational exposure populations

Bias & Outcomes

- Multiple study designs, reasonable consistency, high consistency in large populations with wide exposure range
- Noncausal Explanations not found in 15 years of increasingly intense research for lipid and liver outcomes

  Studies also point to systemic underestimation of outcomes associated with kidney disease due to complicated excretion mechanics, especially in albuminuria
- Multiple pathways in play from experimental data



The Science Panel Changed Thinking.
& Evidence continues. Clinician advice needs updating

- Kidney disease is an example:
- (But thyroid disease is

Looking more complex, and may

Involve subpopulations)

Clinical Synthesis: Experiment and Epi (vs "everything and anything"). Reading with a clinical eye.

Experimental

Bile acid disruption (mechanism),ROS, Fatty droplet and accumulation & hepatocyte enlargement (histology) , disruption of sterol binding proteins across species (pathway) across species, in PPAR-humanized models, and in cell lines (Armstrong and Guo, Das et al., Hamilton et al., Marques et al., Rowan Carrol et al., Salter et al., Schlezinger et al.)

Disruption of insulin signaling

Clinical concern?-

↑ Pattern recognition: *If a patient population was known to have this profile, would look for:*

- Lipid, liver, uric acid, (and insulin resistance) as clinical outcome areas

  (Steatosis is the first phase of NAFLD)

- Would also be concerned with increased risk of several comorbid susceptibilities (autoimmune, obesity, as well as early life exposure based on sterol pathways)

Patients who are/aren't concerned

- Not Concerned? (Usually not in the office or other PFAS communication.) The discussion does not need to be forced.
- Across a broad, high exposure population with a high participation rate, most concerned and appreciate their data.
- However, consider a clinical alert filter for emergencies

Random Survey-Perceived benefit to health of C8 Health Project results*

Very important	44.1%
Important	40.3%

Benefit to health outperformed personal benefit from settlement.

*Malone, Cig, et al. PMID 21092115.

Screening- “System level:” local participation and population level summary feedback

Missing

- There are likely complex reasons these are omitted from official guidance to clinicians, & there are public health and participation reasons to pay attention and return to principles.
- (The report back function is not intended as research, and not described at a research level)
- System level recommendations affect participation

ATSDR Recommended

- Local input, an advisory board, and Summary population feedback “program reports” are specifically mentioned in ATSDR guidance 60 FR 388839; 1995

  “ individuals screened……. diagnoses”

- The mechanisms for annual reporting require a degree of centralization not often included in real world situations.

Patient and Clinician Feedback: Lessons learned

- Communications are different for high exposure vs background
- Distinguish levels of evidence* (& Reasonably consider how the population and experimental data relate)
- Provide **Supportive** (rather than Dismissive) **Advice,*** consistent with reasons for patient concerns, and the literature concerning outcomes, and what we know about decreasing risk and building patient-provider success
- ATSDR was right in 1995: System level feedback and local participation matter

*If the official health communication goal of articulating doubt as if it applied equally to all outcomes was to decrease anxiety, it's not working.

Well intended perhaps, but Deemphasizing Prevention

To the Patient: “**If you are concerned**…….see your doctor. “

To Clinicians:

A. “The types of health problems that may be associated with PFAS are also caused by a variety of factors (lifestyle, environmental, social, genetic). It is possible that PFAS contributed to your health problems but there is no way to know if PFAS exposure has caused your illness or made it worse.

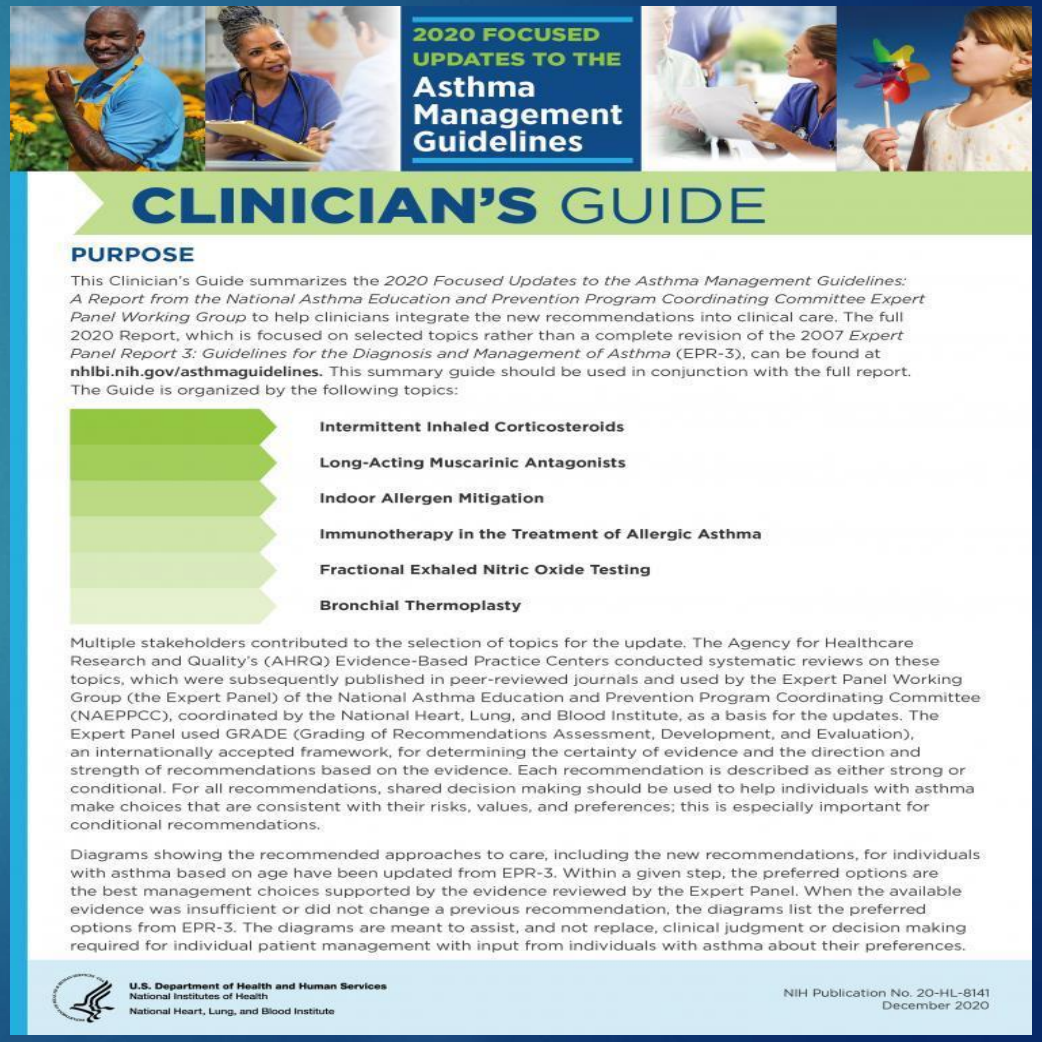
- *or*

B. Based on what we know at this time, there is no reason to think your health problem is associated with exposure to PFAS. Researchers continue to evaluate the potential health risks from PFAS so more may be known in the future .”

Analysis: Puzzling emphasis on Post Hoc Cause

Enabling

- Prevention, not Post Hoc Causation, is the common reason for a PFAS question
- Patients and doctors understand that a priori increased risk is only a piece of post hoc causation assignments.
- (If post hoc causation were the issue, the current guidance is still misaligned with societal judgments, including in consensus and adjudicated settings.) Advice if followed decreases clinician credibility.



2020 FOCUSED UPDATES TO THE Asthma Management Guidelines

CLINICIAN'S GUIDE

PURPOSE

This Clinician's Guide summarizes the *2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group* to help clinicians integrate the new recommendations into clinical care. The full 2020 Report, which is focused on selected topics rather than a complete revision of the 2007 *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma* (EPR-3), can be found at **nhlbi.nih.gov/asthmaguidelines.** This summary guide should be used in conjunction with the full report. The Guide is organized by the following topics:

- **Intermittent Inhaled Corticosteroids**
- **Long-Acting Muscarinic Antagonists**
- **Indoor Allergen Mitigation**
- **Immunotherapy in the Treatment of Allergic Asthma**
- **Fractional Exhaled Nitric Oxide Testing**
- **Bronchial Thermoplasty**

Multiple stakeholders contributed to the selection of topics for the update. The Agency for Healthcare Research and Quality's (AHRQ) Evidence-Based Practice Centers conducted systematic reviews on these topics, which were subsequently published in peer-reviewed journals and used by the Expert Panel Working Group (the Expert Panel) of the National Asthma Education and Prevention Program Coordinating Committee (NAEPPCC), coordinated by the National Heart, Lung, and Blood Institute, as a basis for the updates. The Expert Panel used GRADE (Grading of Recommendations Assessment, Development, and Evaluation), an internationally accepted framework, for determining the certainty of evidence and the direction and strength of recommendations based on the evidence. Each recommendation is described as either strong or conditional. For all recommendations, shared decision making should be used to help individuals with asthma make choices that are consistent with their risks, values, and preferences; this is especially important for conditional recommendations.

Diagrams showing the recommended approaches to care, including the new recommendations, for individuals with asthma based on age have been updated from EPR-3. Within a given step, the preferred options are the best management choices supported by the evidence reviewed by the Expert Panel. When the available evidence was insufficient or did not change a previous recommendation, the diagrams list the preferred options from EPR-3. The diagrams are meant to assist, and not replace, clinical judgment or decision making required for individual patient management with input from individuals with asthma about their preferences.

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

NIH Publication No. 20-HL-8141
December 2020

Early Detection: Doable for many outcomes. Clinical algorithms & Benefits vs Harms

Guidance to date amplifies uncertainty, is top-down, dismissive, not focused on prevention, and has predictable outcomes. Lets change that.

- Clinicians get algorithms
- Clinicians get increased risk
- Clinicians understand multiple comorbid risk factors, use them as teachable moments, and value patient-clinician partnerships.
- **Clinicians don't get time and need support**

Compare Benefits, Harms, Overlaps

PFAS : mostly mysterious to clinicians

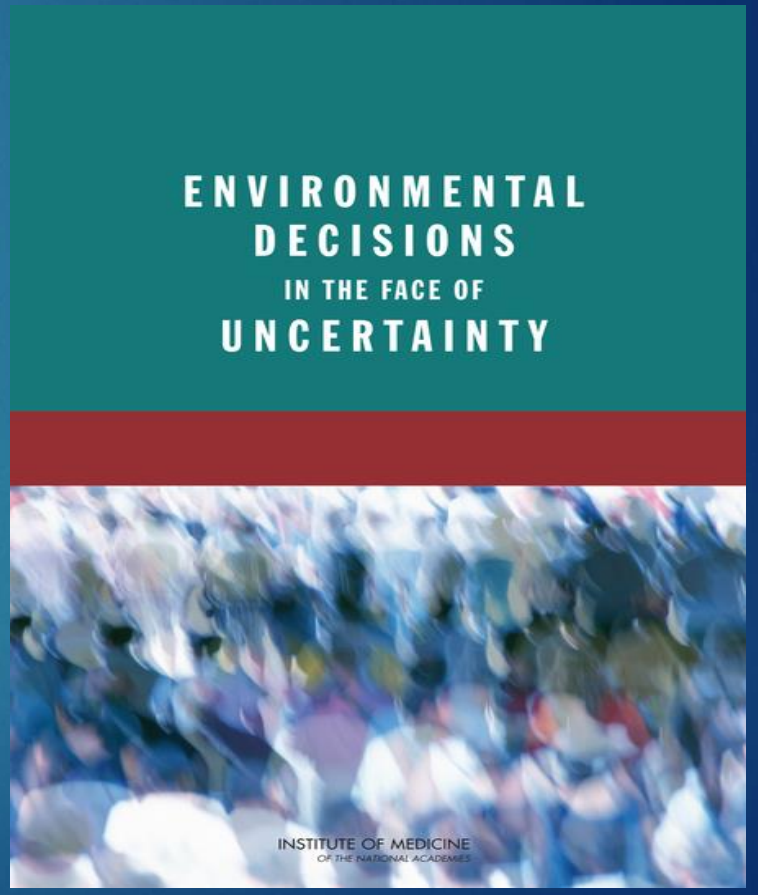
However, Evaluations of the outcomes are mostly familiar and rely on simple things.

Modern algorithms go beyond ancient lab cut-offs.

Handling Evidence Gaps, a 2-way street

Example: We default to recommend breast feeding in the highly exposed mother. AND, we can honestly admit absence of comparative evidence and confer about patient choice.

NAS/IOM



Templates for improvement

- The Association of State and Territorial Health Officials (ASTHO) has risk communications to patients and to clinicians. These address: the differences in PFAS, that different PFAS health outcomes have different weights of evidence. Most important, public health primary and secondary prevention interventions and shared (rather than top-down) decision making are emphasized. https://www.astho.org/PFAS/
- State of Connecticut on levels of evidence
- PFAS REACH (including Silent Spring Institute in association with Northeastern U and others) Has useful fact sheets on a PFAS Exchange including a detailed medical screening rubrics for patients and for clinicians. https://pfas-exchange.org/resources/ **It provides simple tests that clinicians understand**

The PFAS REACH Documents

https://wordpress.silentspring.org/wp-content/uploads/2021/06/PFAS-REACH-Medical-screening-guidance_PFAS-impacted-communities.pdf

- Linking the evidence of causation to screening approaches that clinicians already understand.
- Guidance for Adult patients
- Guidance for Pediatric patients

PFAS Exposure: Information for patients and guidance for clinicians to inform patient and clinician decision making

For people in PFAS-impacted communities

Laboratory tests

Clinical examinations

Counseling topics

Thank you for the invitation to learn with you

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- L: Straightforward message in US (State of Michigan)
- R: Community reaction to official messages in New South Wales