

# **Serum PFAS concentrations and testicular cancer among U.S. Air Force servicemen**

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# Disclaimer

Opinions, interpretations, conclusions, and recommendations are mine and are not to be construed as official or necessarily endorsed by the Department of Defense, Uniformed Services University of the Health Sciences, the Centers for Disease Control and Prevention, or the National Institutes of Health.

I have no conflicts of interest to disclose.

# Presentation Outline

- 1) Background on PFAS
- 2) Study Aims, Methods, Results
- 3) Summary and Next Steps

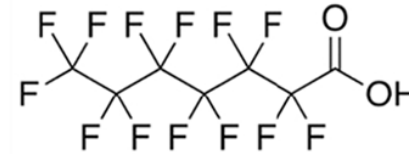
# Per- and Polyfluoroalkyl Substances (PFAS)

## ➤ Synthetic chemicals

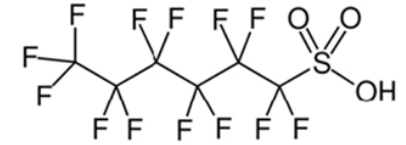
- multiple fluorine atoms attached to an alkyl chain

## ➤ Unique properties:

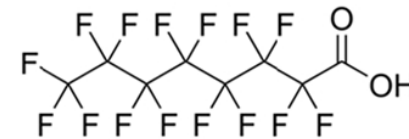
- impart oil and water repellency
- temperature resistance
- friction reduction



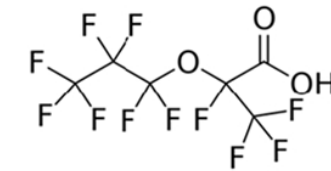
Perfluoroheptanoic acid (PFHpA)



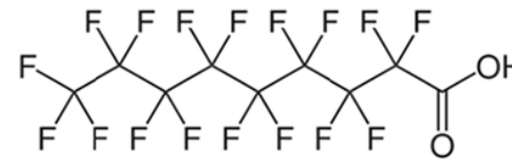
Perfluorohexane sulfonic acid (PFHxS)



Perfluorooctanoic acid (PFOA)



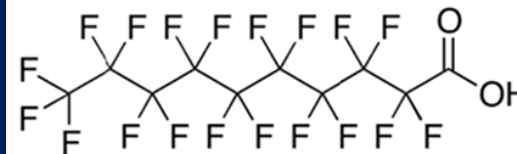
Hexafluoropropylene oxide dimer acid (HFPO-DA or GenX)



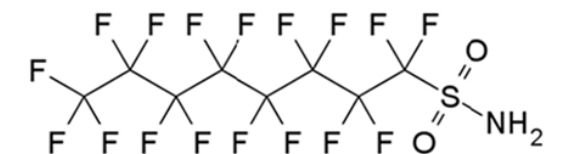
Perfluorononanoic acid (PFNA)



Perfluorooctane sulfonic acid (PFOS)



Perfluorodecanoic acid (PFDA)



Perfluorooctanesulfonamide (PFOSA)

# PFAS: History and Uses

- Invented in 1930s
- In 1940s, companies begin manufacturing PFAS for use in commercial products
- Used as non-stick coating for many commercial products:
  - Cookware
  - Textiles
  - Paper products (food wrappers)



# PFAS and Firefighting Foams

## ➤ Aqueous Film-Forming Foam (AFFF)

- Effective in extinguishing flammable liquid fires
- PFAS a key ingredient



## ➤ Military use of AFFF

- Used by DoD since 1970s
- Mostly AFFF formulations containing PFOS, PFHxS and, sometimes, PFOA



# Phaseout of PFOS

- 2003: 3M ceases production, sale of **PFOS**
  - Phaseout of PFOS-based AFFF (originally ~75% of DoD supplies)

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- 2016: DoD restricts use of PFOS-based AFFF and initiates water testing across all bases (Sullivan 2016)
  - 401 bases with known/suspected PFAS release
  - 90 bases with groundwater PFOS/PFOA concentrations > 70 ppt
  - 36 bases with drinking water PFOS/PFOA concentrations > 70 ppt



# Phaseout of PFOS

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- 2018: DoD begins conversion to AFFF with short-chain PFAS (low bioaccumulation risk) & exploring PFAS-free alternatives

# PFAS and the Environment

- Resistant to degradation; persist in the environment (“forever chemicals”)
- PFAS detectable in most Americans (Calafat et al. 2007)
  - Occupational exposures (e.g. PFAS production, firefighters)
  - Consumption of contaminated food and water
  - AFFF use at airports and military facilities an important source of PFAS in public water systems (Hu et al. 2016)



# PFAS – Suspected Health Effects

- Epidemiologic studies have suggested associations between PFAS exposures and several health outcomes:
  - Elevated total & LDL cholesterol
  - Pregnancy-induced hypertension
  - Immune effects
  - Thyroid disease
  - Cancer

# PFAS and Cancer

- In 2014, the World Health Organization's International Agency for Research (IARC) on Cancer classified **PFOA** as a **possible human carcinogen**
  - Evidence strongest for cancers of the kidney and testis
- Fewer studies have investigated other PFAS (mainly **PFOS**); evidence inconclusive

# Knowledge Gaps

- 1) What is the level of PFAS exposure among military personnel?
  - *How do they compare to the general population?*
  - *Are there service-related predictors of elevated exposure?*
- 2) Are PFAS exposures associated with cancer risk in this population?

# Nested Case-Control Study of Serum PFAS and Testicular Cancer in Air Force Servicemen

## ➤ Why Testicular Cancer?

- Most common cancer diagnosed among active-duty servicemen
- Previous evidence suggesting associations with PFOA

## ➤ Why Air Force Personnel?

- In 2016-2017 DoD testing of military drinking water systems, half of the bases with known or suspected PFOS/PFOA release were Air Force installations (Sullivan 2018)

# Study Design

## ➤ Source Population:

- Active-duty Air Force servicemen with serum banked in the **DoD Serum Repository** between 1988 and 2017

## ➤ Cases:

- **530 cases** of testicular cancer diagnosed during active duty (1990 - 2018)

## ➤ Controls:

- Individually matched to cases (1:1 ratio) on birth date, race/ethnicity, accession year, year(s) of sample collection

# Serum Selection

- For most subjects, 1 banked sample selected
- 2 samples per subject selected for **187** case-control pairs with cases diagnosed  $\geq 5$  years after earliest serum collection date
  - Sample 1 usually collected at start of service (*median 0.3 years of service*)
  - Sample 2 usually collected several years later (*median 5.8 years of service*)



# Serum PFAS Concentrations

- Measurements conducted at CDC using isotope-dilution tandem mass spectrometry
- Seven PFAS measured:
  - PFOS
  - PFOA
  - PFHxS
  - PFNA
  - MeFOSAA
  - PFDA
  - PFUnDA

# RESULTS

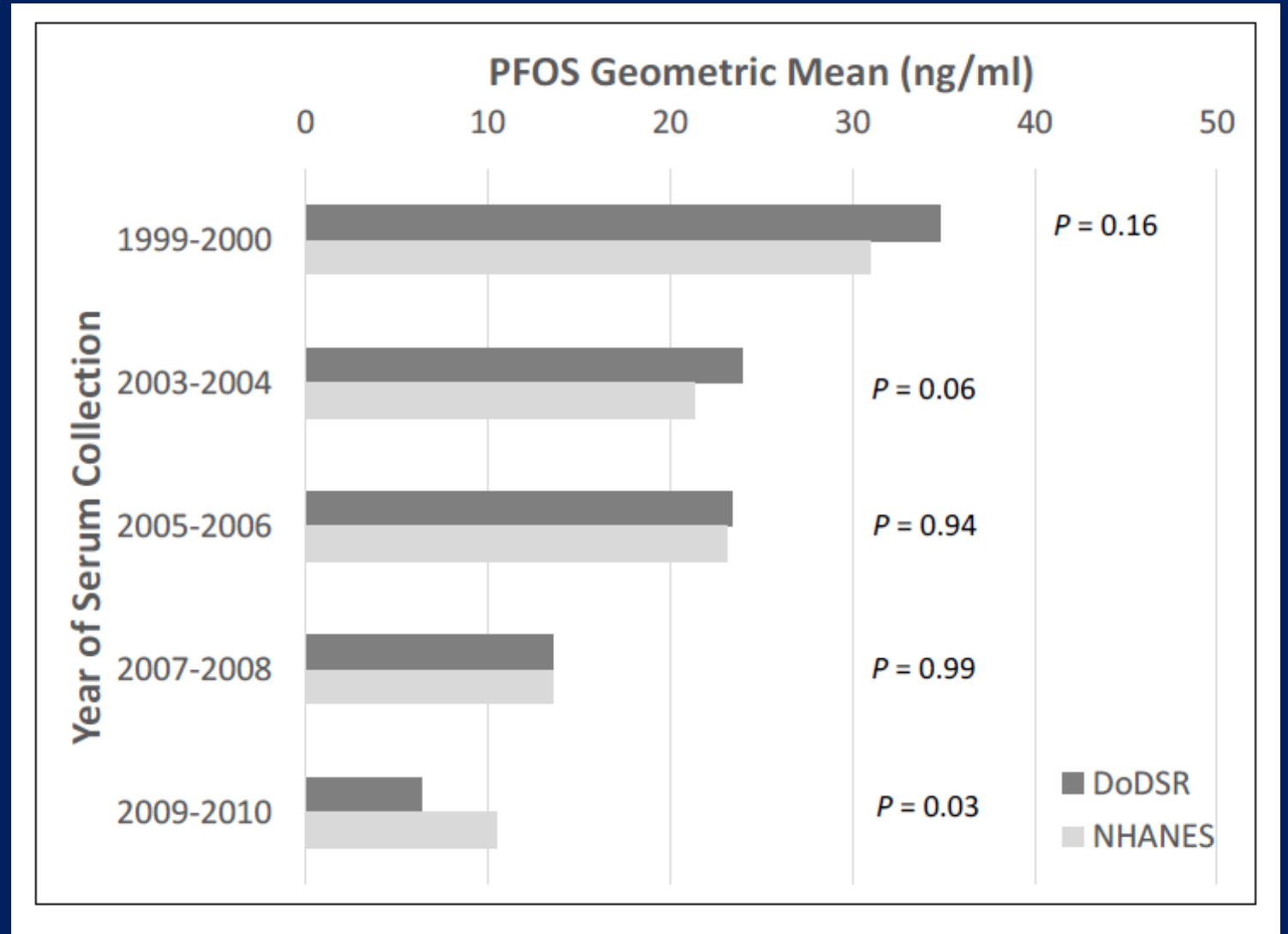
# Study Participant Characteristics

Characteristic	Cases	Controls	<i>P</i>
<b>Age at Case Diagnosis [n (%)]</b>			
<25	121 (23%)	121 (23%)	-
25-34	272 (51%)	272 (51%)	(matching factor)
35-39	137 (26%)	137 (26%)	
<b>Race and Ethnicity [n (%)]</b>			
Non-Hispanic White	422 (80%)	422 (80%)	-
Hispanic	57 (11%)	57 (11%)	(matching factor)
Non-Hispanic Black	13 (3%)	13 (3%)	
Asian	6 (1%)	6 (1%)	
Other / Unknown	27 (5%)	27 (5%)	
<b>Military Grade [n (%)]</b>			
Enlisted	410 (77%)	435 (82%)	0.06
Officer	120 (23%)	95 (18%)	

# PFAS: Controls vs. General Population

## PFOS

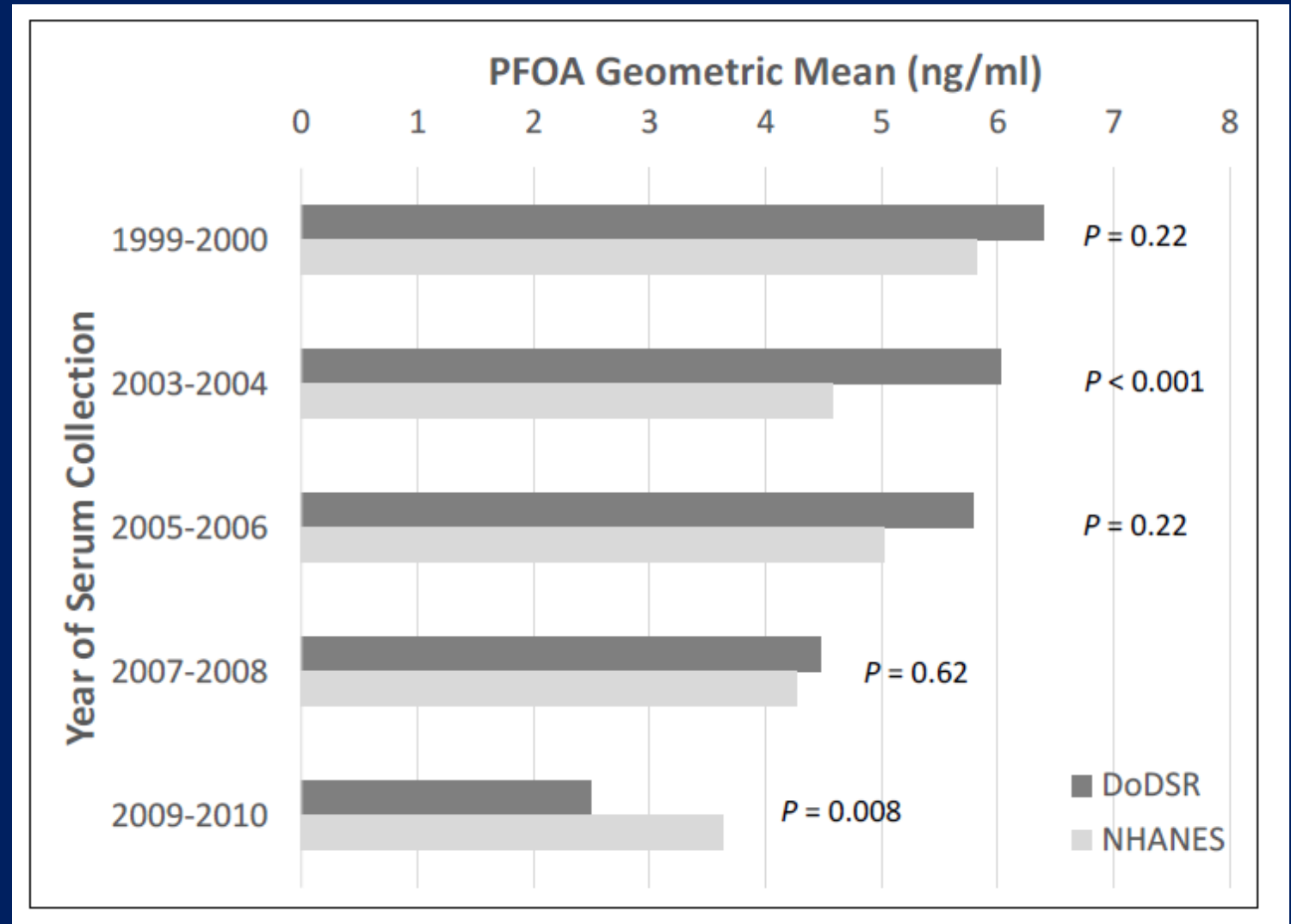
- Serum concentrations declined over time in both populations



# PFAS: Controls vs. General Population

## PFOA

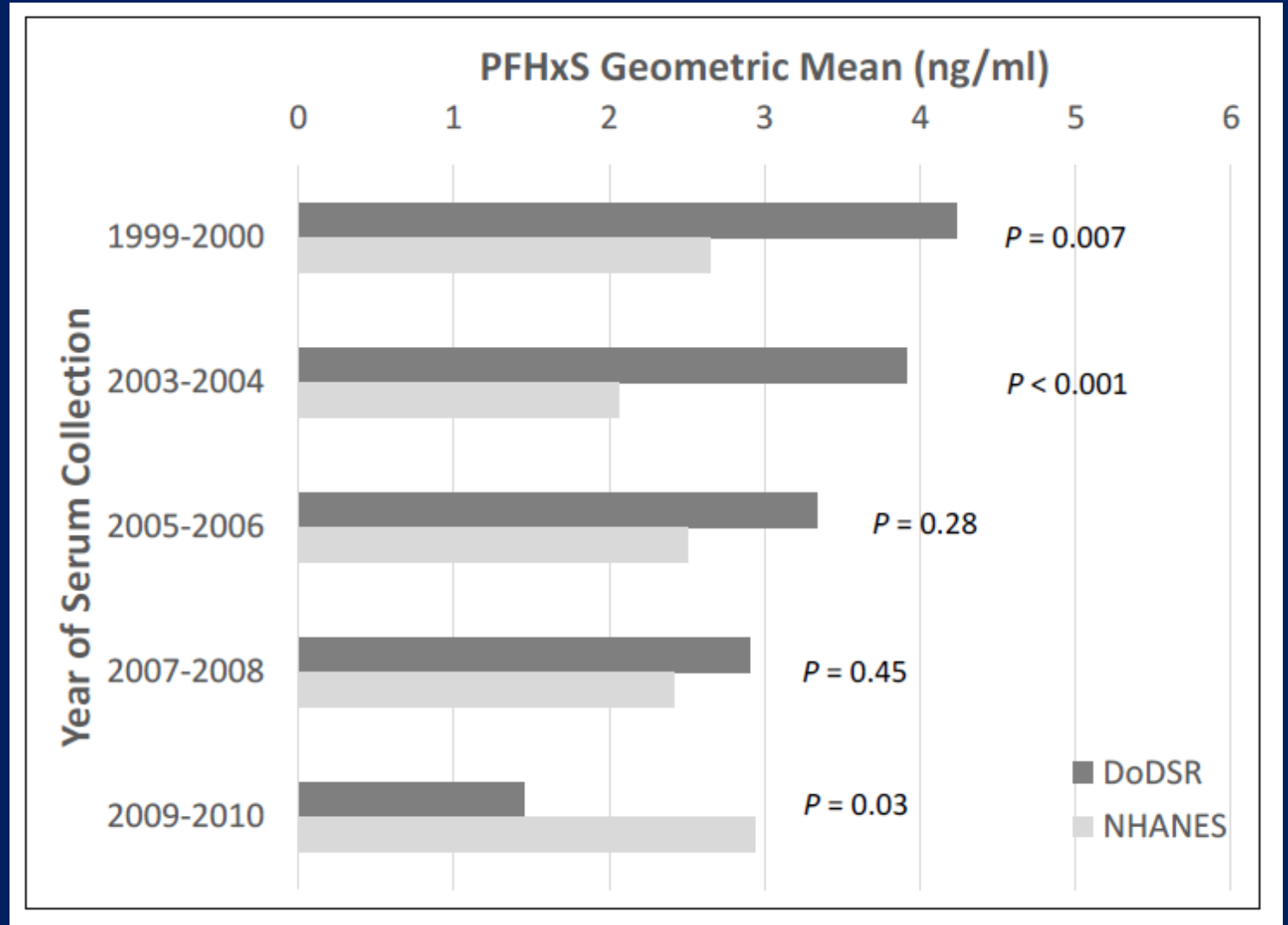
- Weaker decline over time



# PFAS: Controls vs. General Population

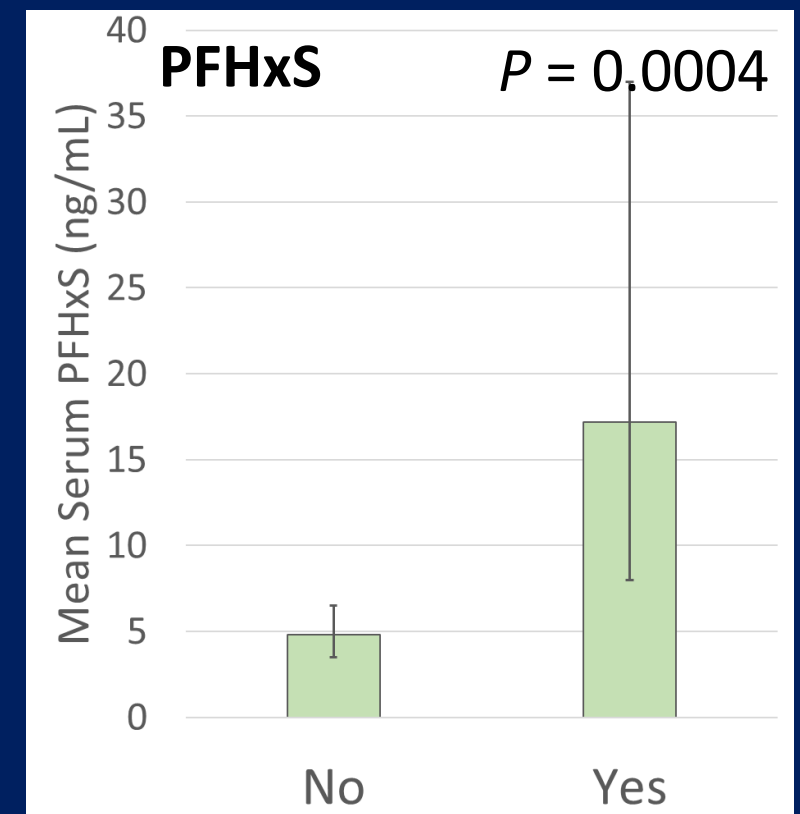
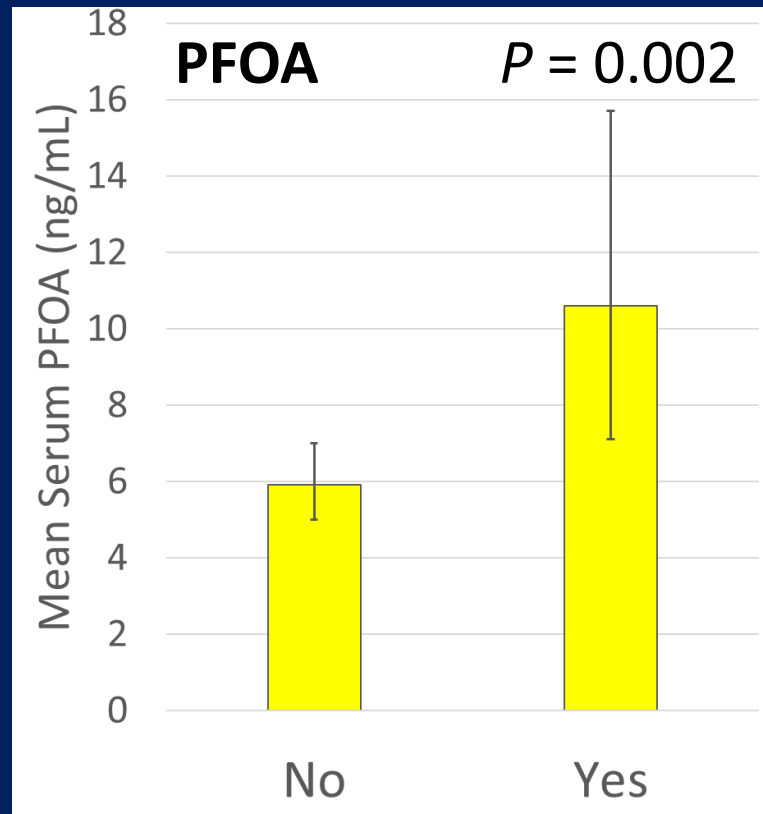
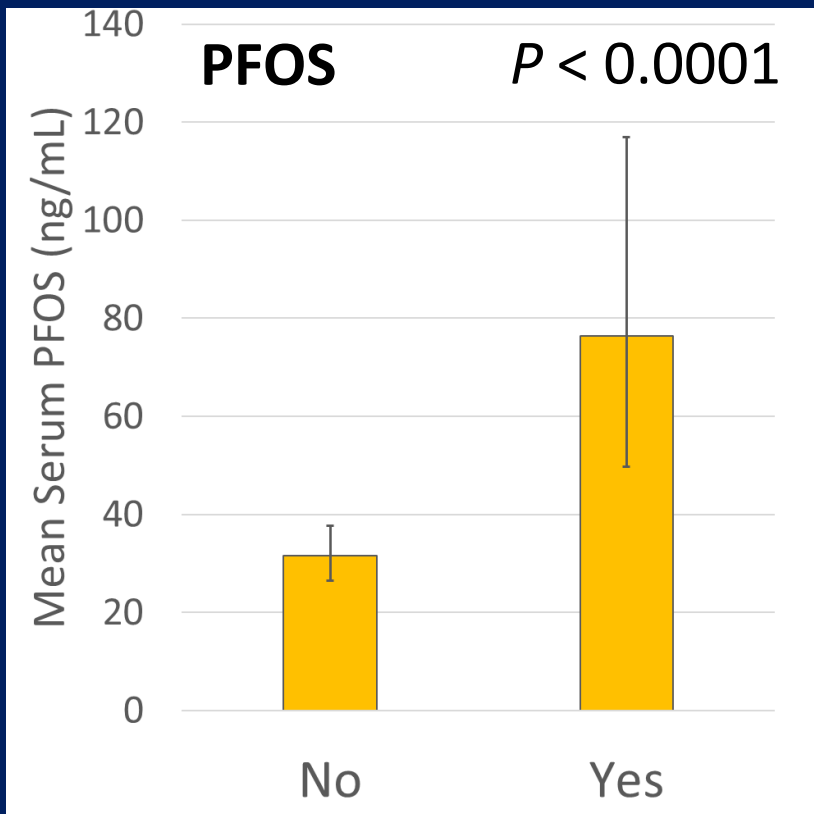
## PFHxS

- higher in study controls vs. NHANES (<2004); lower in 2009-2010



# Results: Service-Related Predictors of Serum PFAS

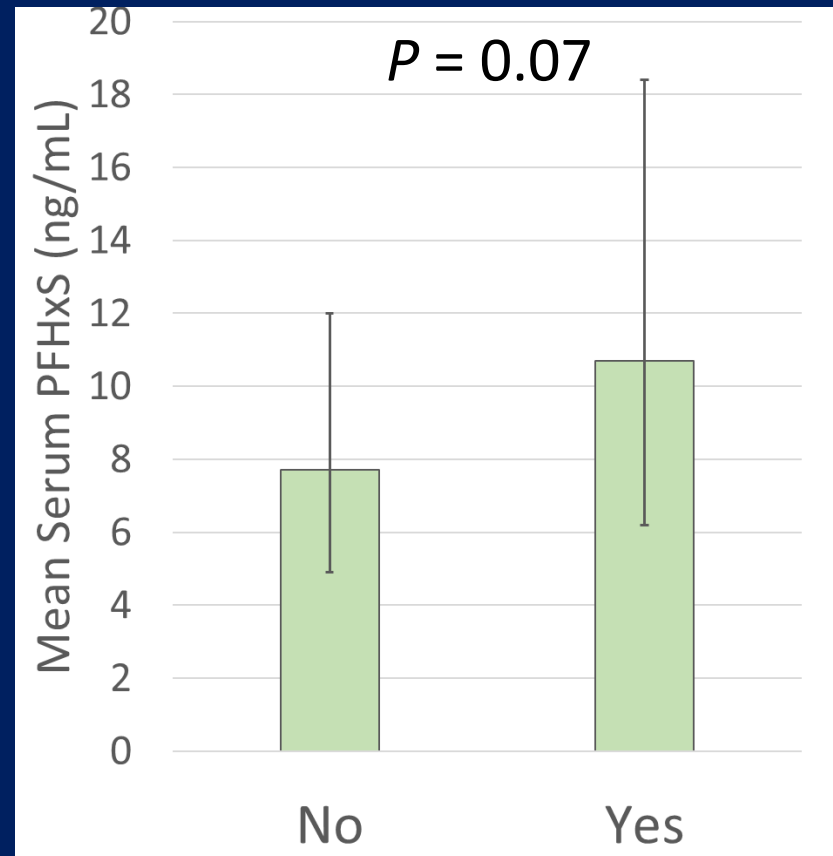
1) Military firefighting associated with elevated serum PFOS, PFOA, PFHxS



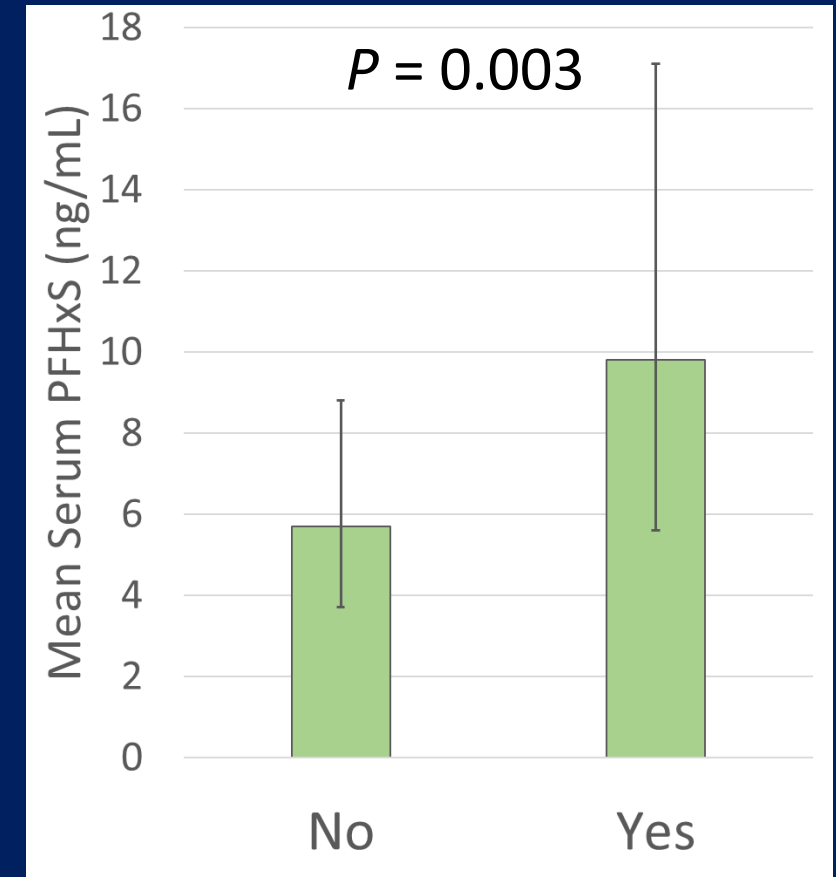
# Results: Service-Related Predictors of Serum PFAS

Service at an Air Force installation with drinking water PFOS/PFOA concentration > 70 ppt  
(Sullivan 2018)

PFHxS (First / Only Sample)



PFHxS (Second Sample)

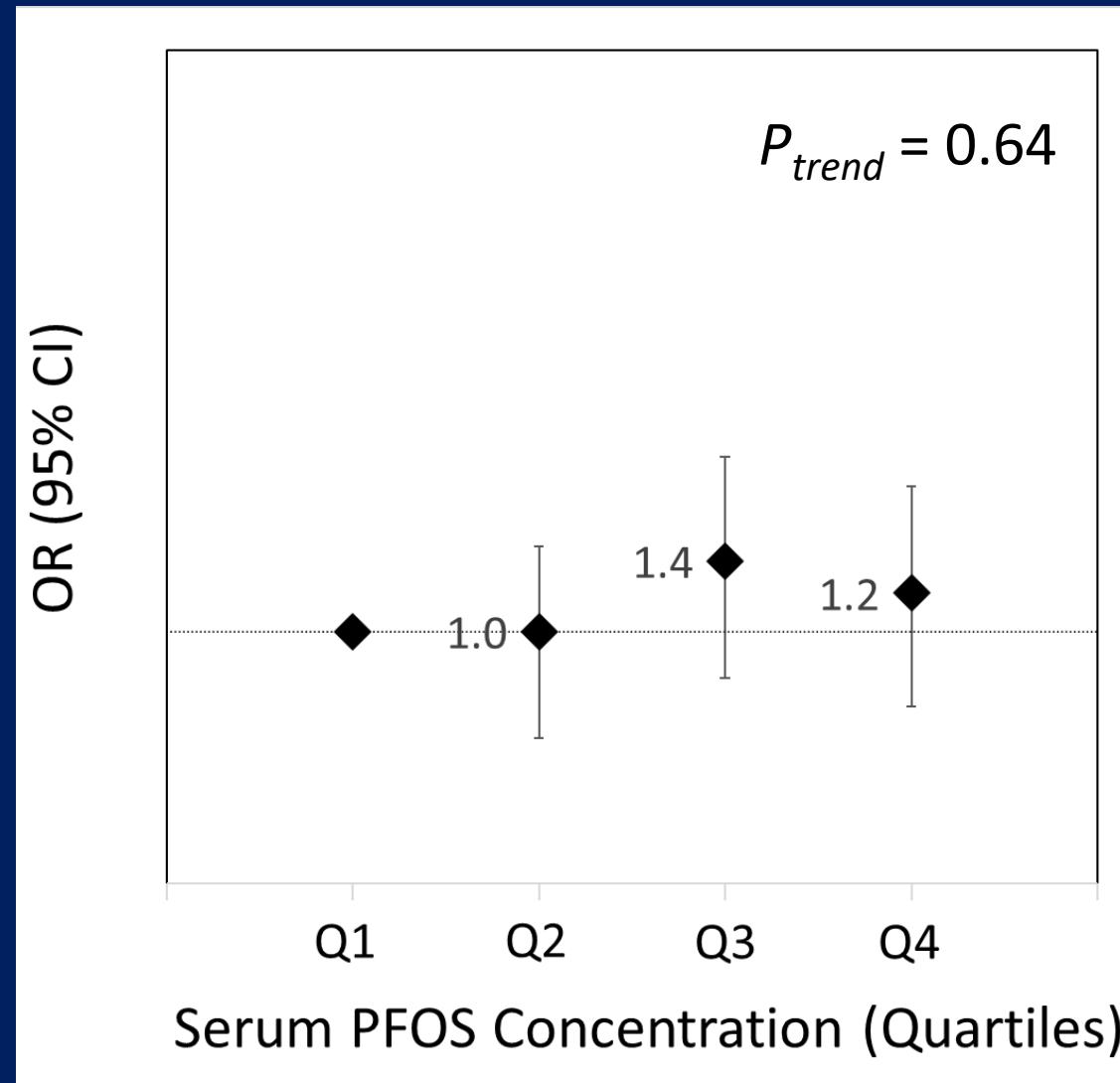




# Serum PFOS and Testicular Cancer

First / Only Sample  
(530 cases, 530  
controls)

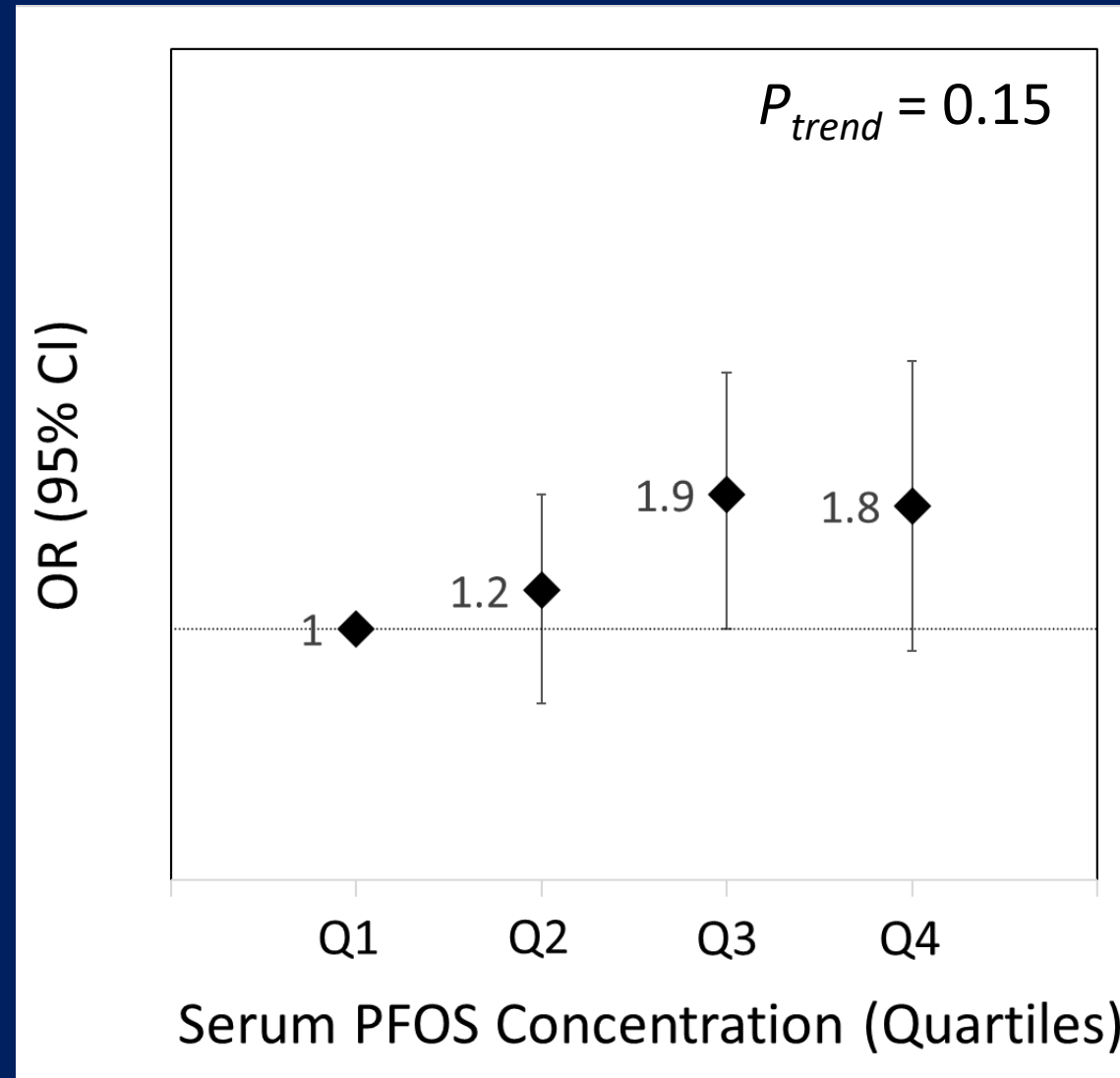
Odds ratios computed  
using conditional  
logistic regression  
adjusted for grade and  
# of overseas  
deployments



# Serum PFOS and Testicular Cancer

First / Only Sample  
(530 cases, 530  
controls)

Odds ratios computed  
using conditional  
logistic regression  
adjusted for grade  
and # of overseas  
deployments  
and **other PFAS**

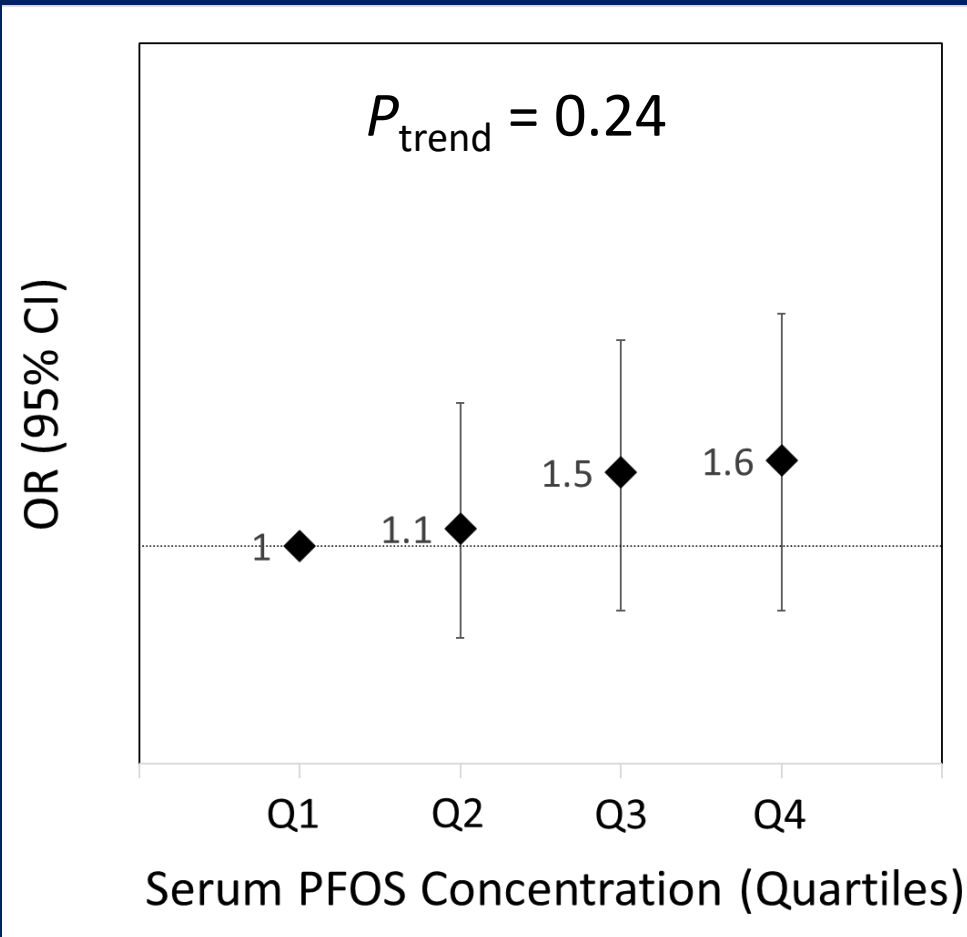


# Serum PFOS and Testicular Cancer

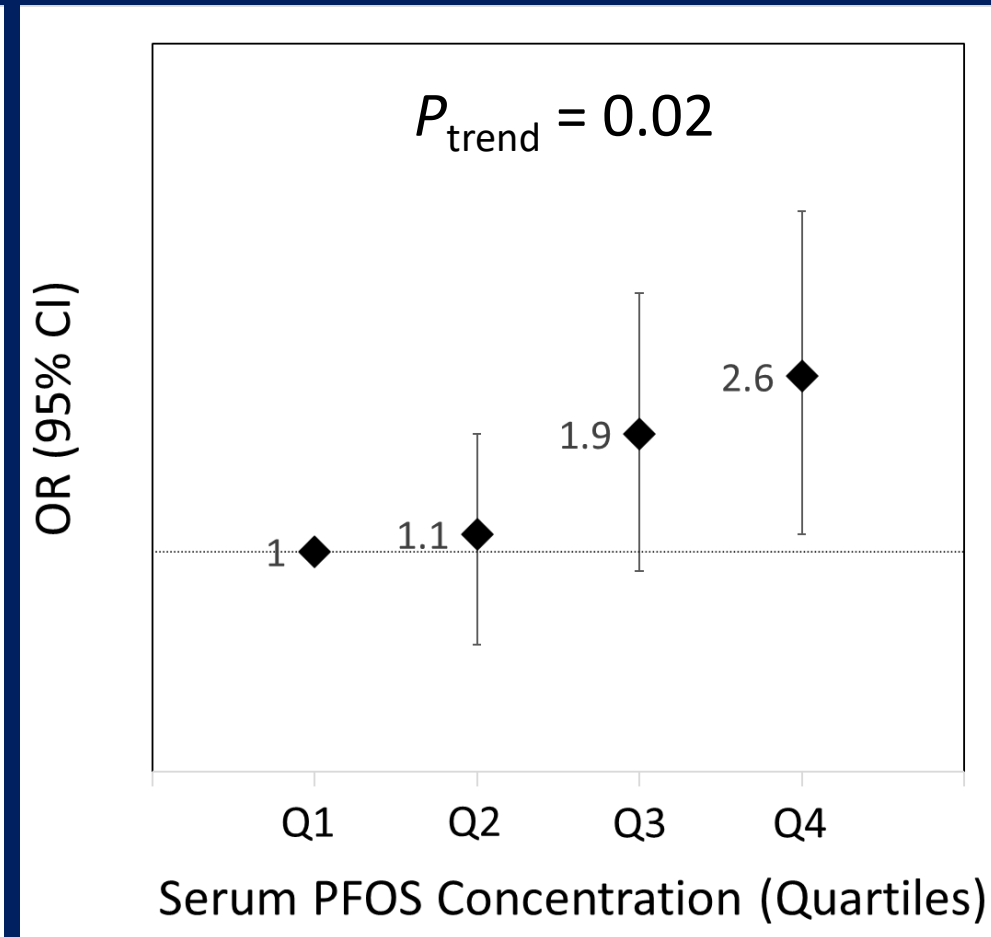
Participants with **two samples** (187 cases, 187 controls)

ORs adjusted for grade, # of deployments

First Sample

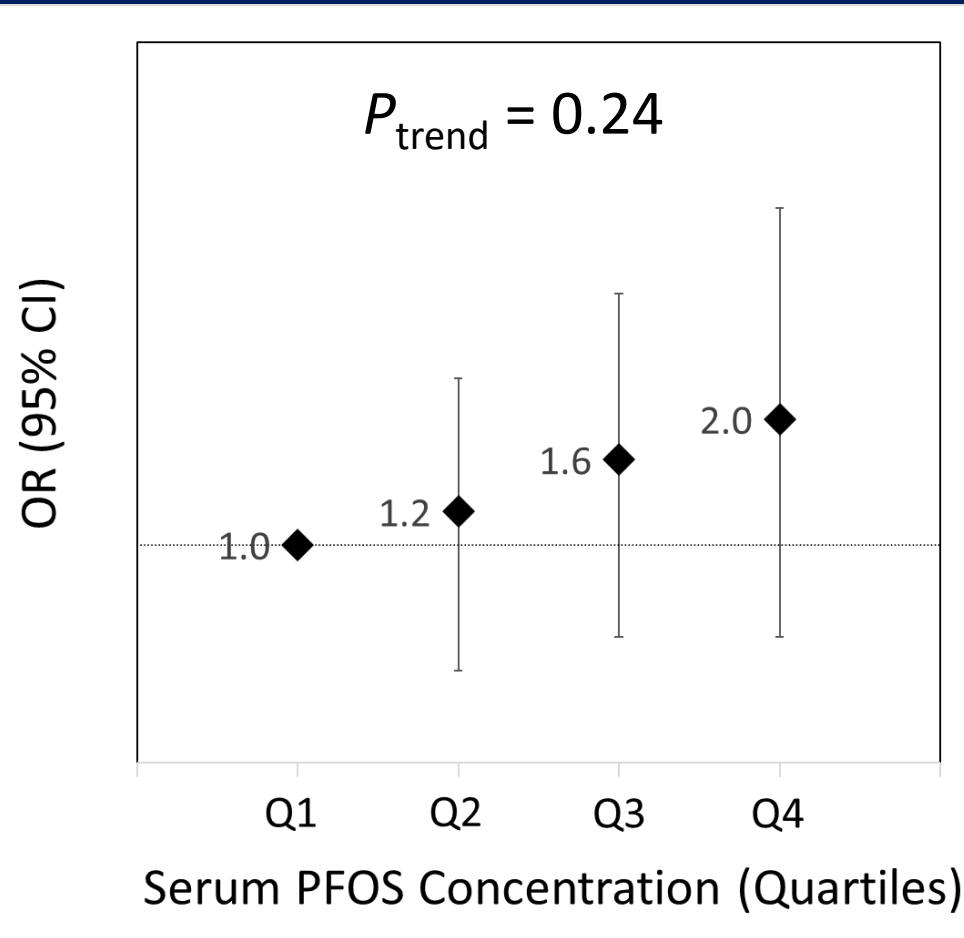


Second Sample

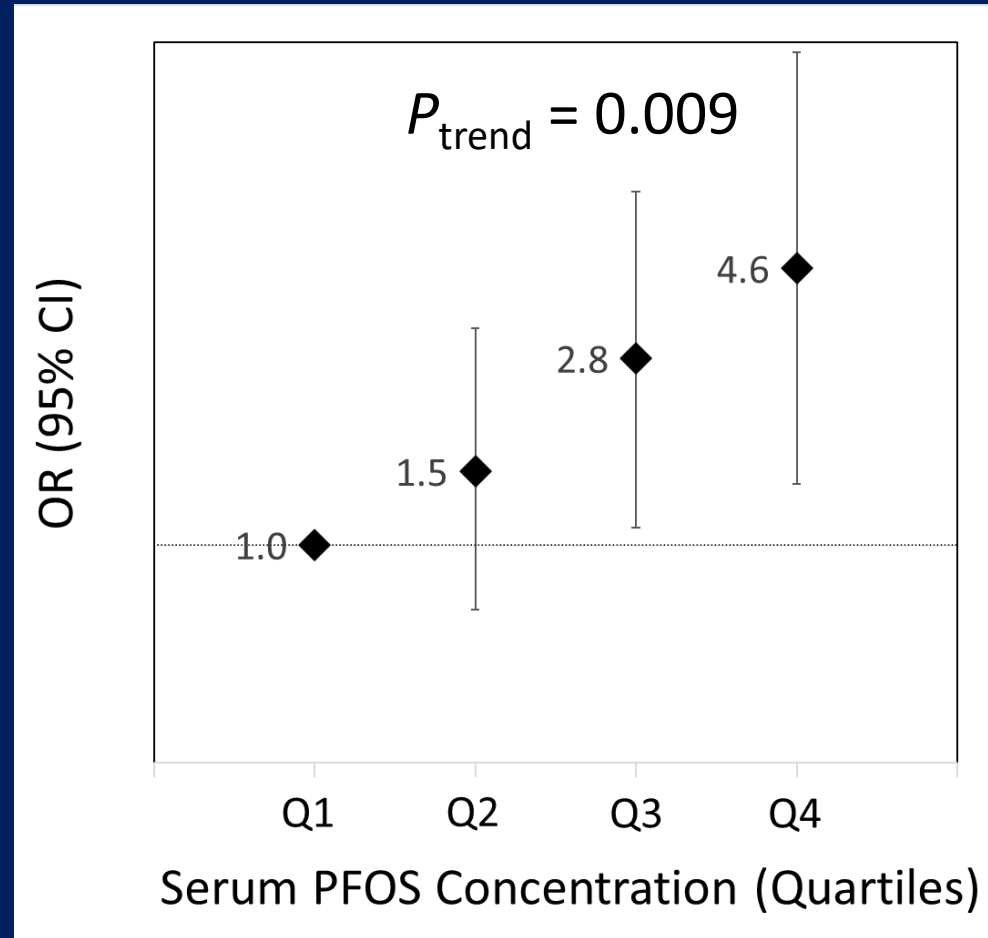


# Serum PFOS and Testicular Cancer

First Sample



Second Sample



Participants with **two samples** (187 cases, 187 controls)

ORs adjusted for grade, # of deployments and **other PFAS**

# Results for Other PFAS

- **PFOA**, PFHxS and other PFAS not associated with testicular cancer
- Serum PFNA inversely associated with testicular cancer
  - Association confined to cases diagnosed <5 years after serum collection

# Discussion: Key Findings

- 1) In early 2000s, higher serum PFHxS in servicemen vs. NHANES
- 2) Service-related predictors of elevated serum PFAS:
  - Fire protection occupation (PFOS, PFOA, PFHxS)
  - Service on base with drinking water PFOA/PFAS >70 ppt (PFHxS)
- 3) Elevated serum PFOS associated with increased risk of testicular cancer (and findings null for PFOA)

# Discussion: PFOS and Testicular Cancer

- First evidence associating PFOS levels and testicular cancer
- Hypothesized that endocrine-disrupting chemicals may contribute to the pathogenesis of testicular cancer (Toppari 2008)
- Experimental evidence of PFOS-induced male reproductive toxicity (summarized in Zeng et al. 2019)
  - **Adult mice:** reduced testis weight and sperm counts
  - **Adult rats:** testicular edema, degeneration of gonadotrophic cells
  - **Zebrafish:** gonad structural changes, decreased sperm counts

# Important Research Questions

- Are these findings replicable?
  - *Follow-up DoDSR study in other service branches under development*
- What is the PFAS serum burden among current DoD personnel?
- Are PFAS associated with other health conditions among military personnel and veterans?
- Are short-chain PFAS (now used in AFFFs) safe?



## **STUDY COLLABORATORS:**

### **USU**

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### **NCI**

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### **Air Force School of Aerospace Medicine**

Maj. Michael A. Lang

### **U.S. Air Force Medical Readiness Agency**

Maj. Paul D. Vu

## **ACKNOWLEDGMENTS:**

### **USU**

Ivy Hung

### **Armed Forces Health Surveillance Division**

Shauna Stahlman

Angelia Cost

## **FUNDING:**

This research was supported by:

- the Office of the Assistant Secretary of Defense for Health Affairs through the Peer-Reviewed Cancer Research Program (W81XWH-19-1-1044) and
- the Intramural Research Program of the National Cancer Institute, National Institutes of Health