



# The C8 Study: PFOA exposure, aims, methods and findings

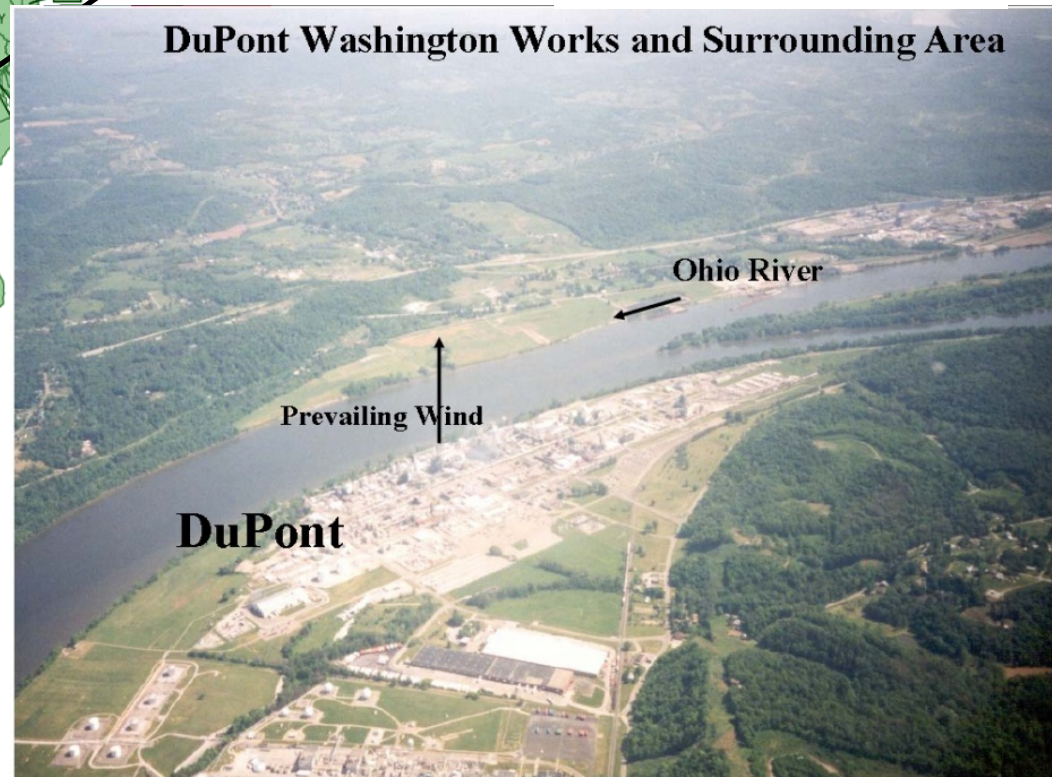
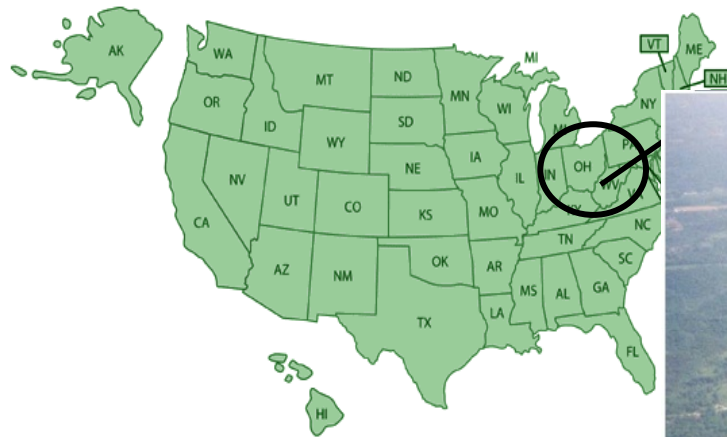
Tony Fletcher, PhD

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**PHE** - Environmental Epidemiology Group, Department of Climate Change, Centre for Radiation Chemicals and the Environment, Public Health England, Chilton, UK

# C8 Study area

- West Virginia/Ohio



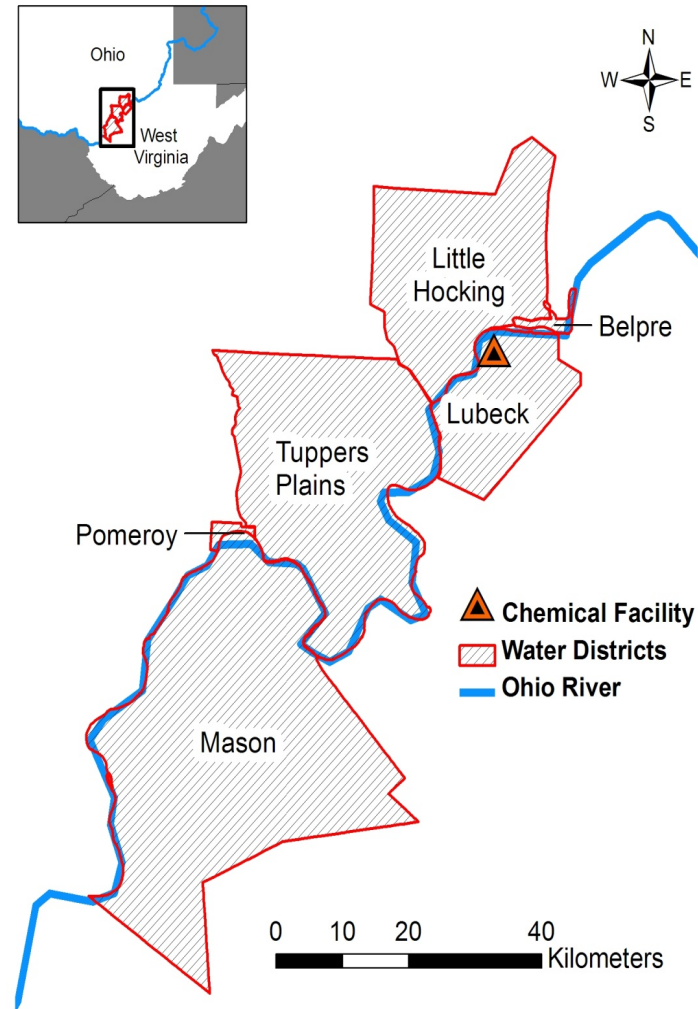
# PFOA at Dupont plant in West Virginia

- PFOA is a surfactant for polymerization of tetrafluoroethylene (TFE) to produce polytetrafluoroethylene, PTFE or Teflon.
- Teflon itself does not contain PFOA
- However PFOA was released from plant

- Dupont plant emitted/discharged PFOA from the late 1950s until recently, with a peak in the 1990s.
- Air emissions from plant wash down into groundwater; plant discharges into the Ohio River can enter groundwater.
- Detected at higher levels in water supplies near the Dupont Plant due to air emissions and river discharges
- Led to a class action court case against Dupont

# C8 study population in Mid Ohio, exposed to PFOA or “C8”

- PFOA-Detected at higher levels in water supplies in 6 districts near Dupont Plant due to emissions
- Phases of agreed settlement:
  1. Clean-up of supplies
  2. Biomonitoring survey
  3. “C8 Science Panel” set up



# First was set up “The C8 Health Project”

A “health and education project” to gather medical histories and information and blood samples from “class members” who have been exposed to C8/PFOA for at least one year.

It generated a large database of C8/PFOA levels in serum, clinical markers and questionnaire data.

# C8 Health Project

- Data assembled on 69,030 participants
- A special company was set up to survey population supplied in 6 water districts with (identified contamination)
- Health questionnaire (past medical history, occup history, reported diagnoses, smoking and drinking).
- Took blood to measure the chemical contaminant (PFOA) and a battery of over 50 assays.
- \$400 payment offered per person so achieved high take up.

# C8 Health Project survey 2005-6

included questionnaire data for 69030 people,  
blood samples, clinical markers and PFAS:  
10 perfluorochemicals measured.

Highest was **PFOA** (mean 82.9 ng/mL),  
then PFOS (mean 23.3)

Table 3. Continued

Ana/cov		Measure	PFHxA <sup>a</sup>	PFHxL <sup>b</sup>	PFHxS	PFHnLA <sup>a</sup>	PFHnLB <sup>b</sup>	PFOLA	PFOS	PFMA	PFOLA <sup>a</sup>	PFOLA <sup>b</sup>
Total population												
Female	Mean		0.8	1.4	4.3	0.6	1.2	68.8	20.7	1.5	0.5	0.8
	Median		0.5	1.0	2.7	0.3	0.8	23.6	17.6	1.3	0.3	0.7
	Geometric mean		0.5	1.1	2.8	0.4	1.0	27.9	17.0	1.3	0.4	0.7
	SD		1.0	1.1	6.2	0.8	1.2	190.6	14.1	0.8	0.4	0.4
Male	Mean		0.9	1.4	5.9	0.7	1.3	98.2	26.0	1.7	0.5	0.8
	Median		0.6	1.0	3.8	0.3	0.9	33.7	22.9	1.5	0.3	0.7
	Geometric mean		0.6	1.2	4.0	0.4	1.0	39.4	21.9	1.5	0.4	0.7
	SD		1.2	1.4	12.8	0.9	1.3	284.3	16.5	0.9	0.6	0.8
Total	Mean		0.9	1.4	5.1	0.6	1.2	82.9	23.3	1.6	0.5	0.8
	Median		0.5	1.0	3.2	0.3	0.9	28.2	20.2	1.4	0.3	0.7
	Geometric mean		0.6	1.1	3.3	0.4	1.0	32.9	19.2	1.4	0.4	0.7
	SD		1.1	1.3	10.0	0.9	1.2	240.8	15.6	0.9	0.5	0.7



# PFOA distribution and mean by age

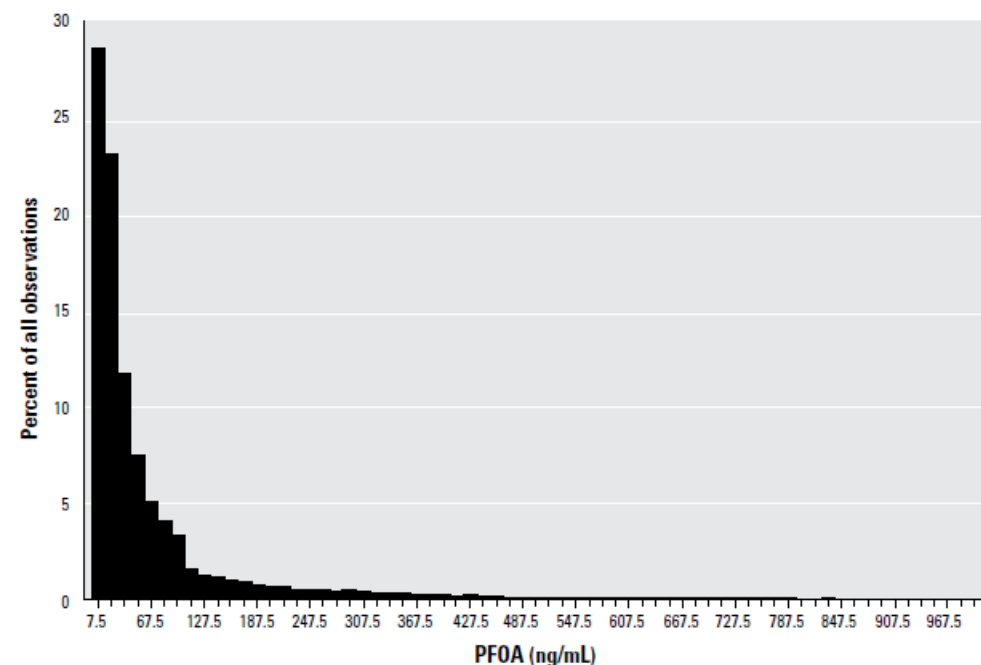
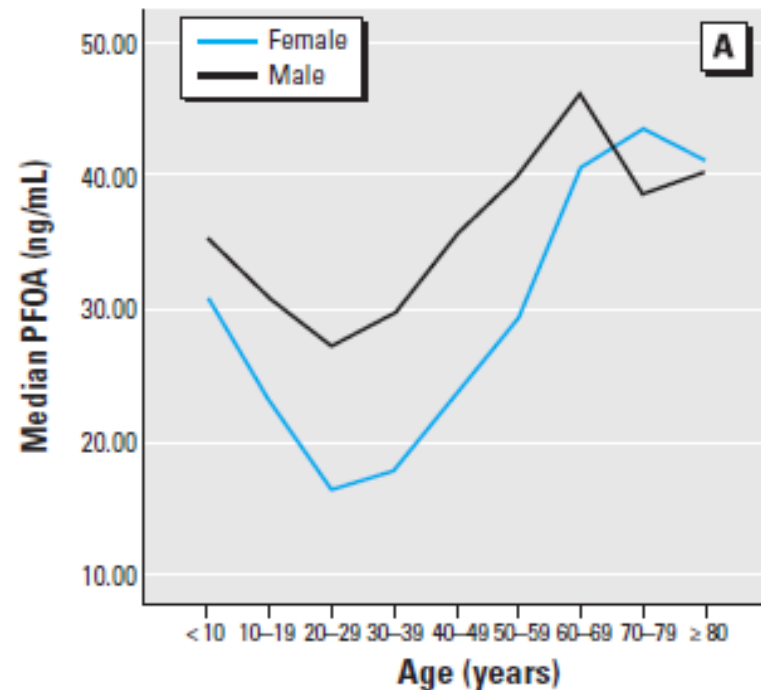
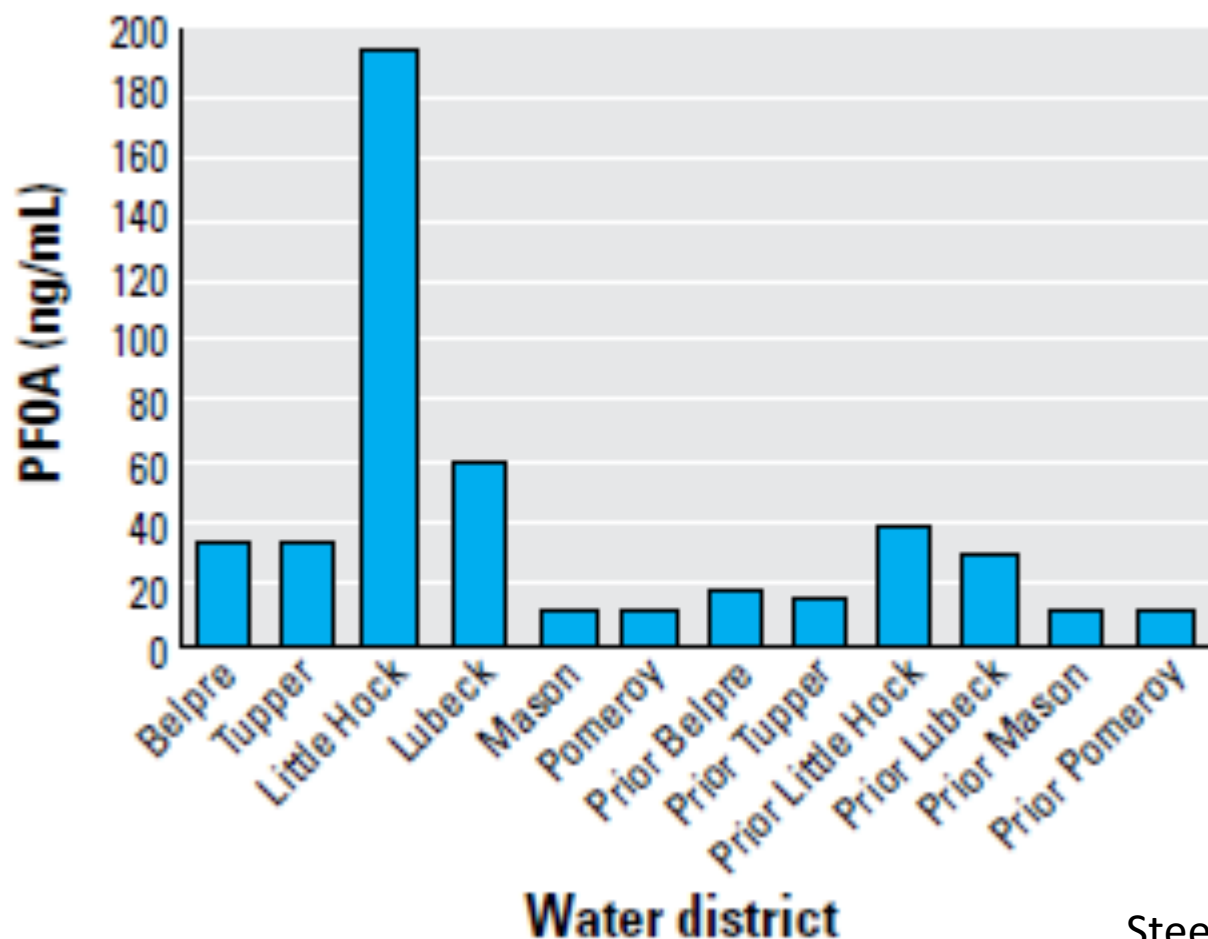


Figure 2. Distribution of PFOA (C8; 405 observations > 1,000 ng/mL not shown).



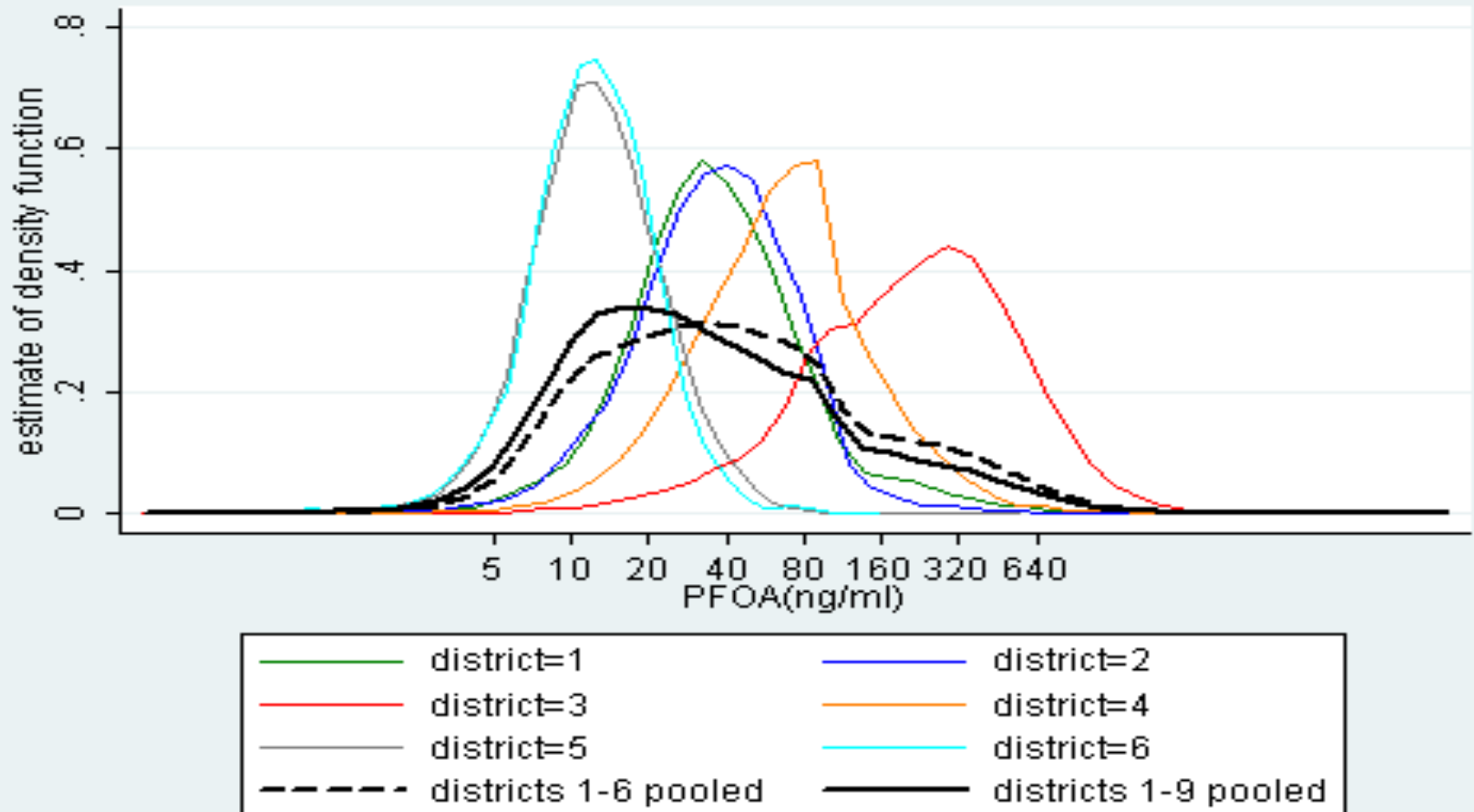
Frisbee et al 2009 EHP

# Average PFOA by water district



Steenland et al 2009 EHP

# PFOA levels. Large differences in contamination between water districts.



# C8 Health Project: range of clinical chemistry

- PFOA in blood
- Comprehensive Metabolic Panel (12),
- Lipid Panel,
- Thyroid Panel,
- Uric Acid,
- Phosphorus,
- LDH, SGPT, GGT, Iron, and CBC,
- Magnesium, Serum Folic Acid
- Carcinoembryonic Antigen (CEA)
- Alpha-Fetoprotein (AFP),
- SerumCancer Antigen (CA) 125,
- Serum Insulin Prolactin Estradiol
- Prostate-Specific Antigen (PSA),
- SerumInsulin-Like Growth Factor I (IGF-I)
- Testosterone,
- Cortisol
- Antinuclear Antibodies (ANA)
- Immunoglobulins (Quantitative, IgA, IgE, IgG, IgM),
- C-Reactive Protein

# The C8 Science Panel

- 3 person “Science Panel” created under the terms of the legal settlement after a class action vs. Dupont over PFOA
- We were selected by agreement between the two sides: Dupont and the Class Action: the “Settling Parties”
- Independent of the two sides, we had no prior opinions on the risks of PFOA
- Appointed by Wood County Court under the Settlement Agreement.
- Mission: to determine if PFOA is associated with any health effects

# The C8 Science Panel



- Tony Fletcher, London School of Hygiene and Tropical Medicine, London, England



- David Savitz, Brown University, Rhode Island



- Kyle Steenland, Emory University, Atlanta, Georgia

# C8 Science Panel Role

A) Plan and carry out epidemiological studies in exposed area

- B) Report to Court on whether PFOA linked to diseases:
- **“Given available scientific evidence, is it more probable than not that a connection is present between C8 (PFOA) exposure and human disease?”**
- *In the event of any probable links, a further phase was triggered: screening of those conditions for early detection and treatment*

# Science Panel Research Programme

Choice of endpoints to study based on toxicological and epidemiological data



# Science Panel Research Programme

Overall objective: to assess relationship of PFOA and several diseases and/or clinical parameters including:

- Cancer
- Heart Disease
- Low birth weight and pregnancy loss
- Thyroid, Liver and Immune dysfunction
- Clinical blood tests from PFOA Health Project (eg, cholesterol)
- Neurological development
- Several designs: reconstruction of exposure history, cross sectional studies, follow up studies, ecologic studies

# Projects:

1. Cross sectional study cholesterol, diabetes, uric acid
2. Cross sectional study cancer, immune and liver function
3. Cohort follow-up study of 40,000 adults
4. Cohort follow-up study of 6,000 workers
5. Reproductive outcomes women C8 Health Project\*
6. Reproductive outcomes women living near plant
7. Geographical (ecologic) study of cancer rates near plant
8. Neurobehavioral study of 320 children in C8 Health Project
9. Follow-up study immune function, 750 C8 Health Project
10. Half life study, 200 people, 5 years
11. Exposure study: estimate exposure over time

# Categories of Disease considered

Based on new epi, prior epi and tox literature

**Reproductive Health** (Preg Ind Hyper, Birth Defects, Miscarriage, Low Birth Weight)

**Autoimmune Disease** (Colitis, Lupus, Crohn's Disease, Diabetes Type 1, Multiple Sclerosis, Rheumatoid Arthritis)

**Thyroid Disease**

**Cancer** (Testes, Kidney, Pancreatic, Liver... 21 sites in total)

**Cardiovascular Disease** (High Cholesterol, BP, CAD, Stroke)

**Kidney Disease**

**Liver Disease**

**Respiratory Disease** (Asthma, COPD)

**Infectious Disease** (Resp., GI, Other)

**Neurological disease** (Children, PD)

**Diabetes** (Type 2)

**Osteoarthritis**

# Example of positive probable link: High Cholesterol

- Background: cholesterol positively associated with higher PFOA in 10 human studies, six statistically significant
- PFOA not lipophilic, binds with albumin
- Most prior studies cross-sectional, prohibiting causal inference
- Positive human association opposite to animal data, where association is inverse (at high dose)

# Science Panel Studies in mid Ohio valley: 3 for raised cholesterol

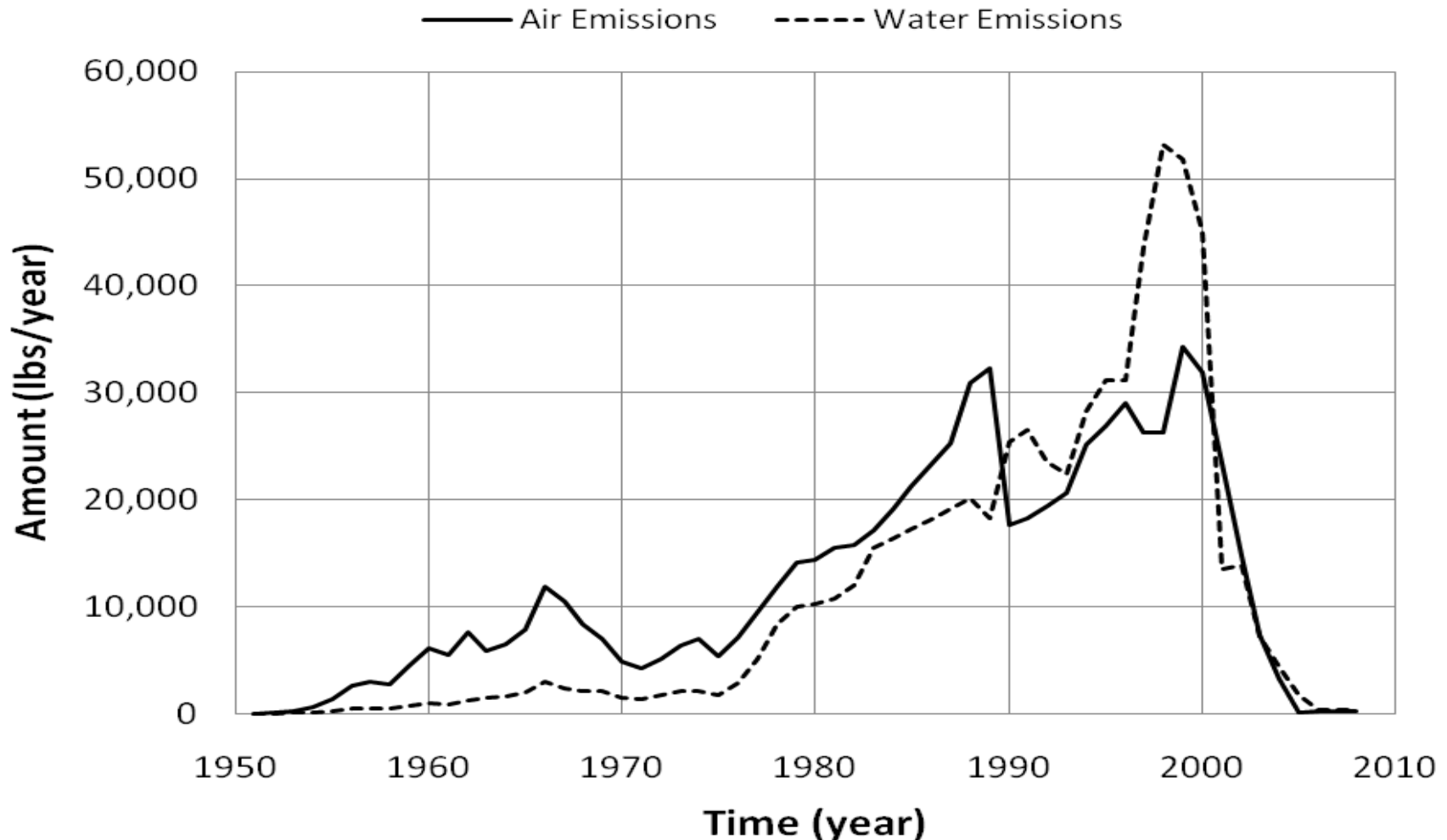
1. Cohort study of 32,000 adults
2. Cross sectional studies of adults and children
3. Longitudinal study of 560 adults with blood drawn in both 2005 and 2010

# Science Panel Cohort study

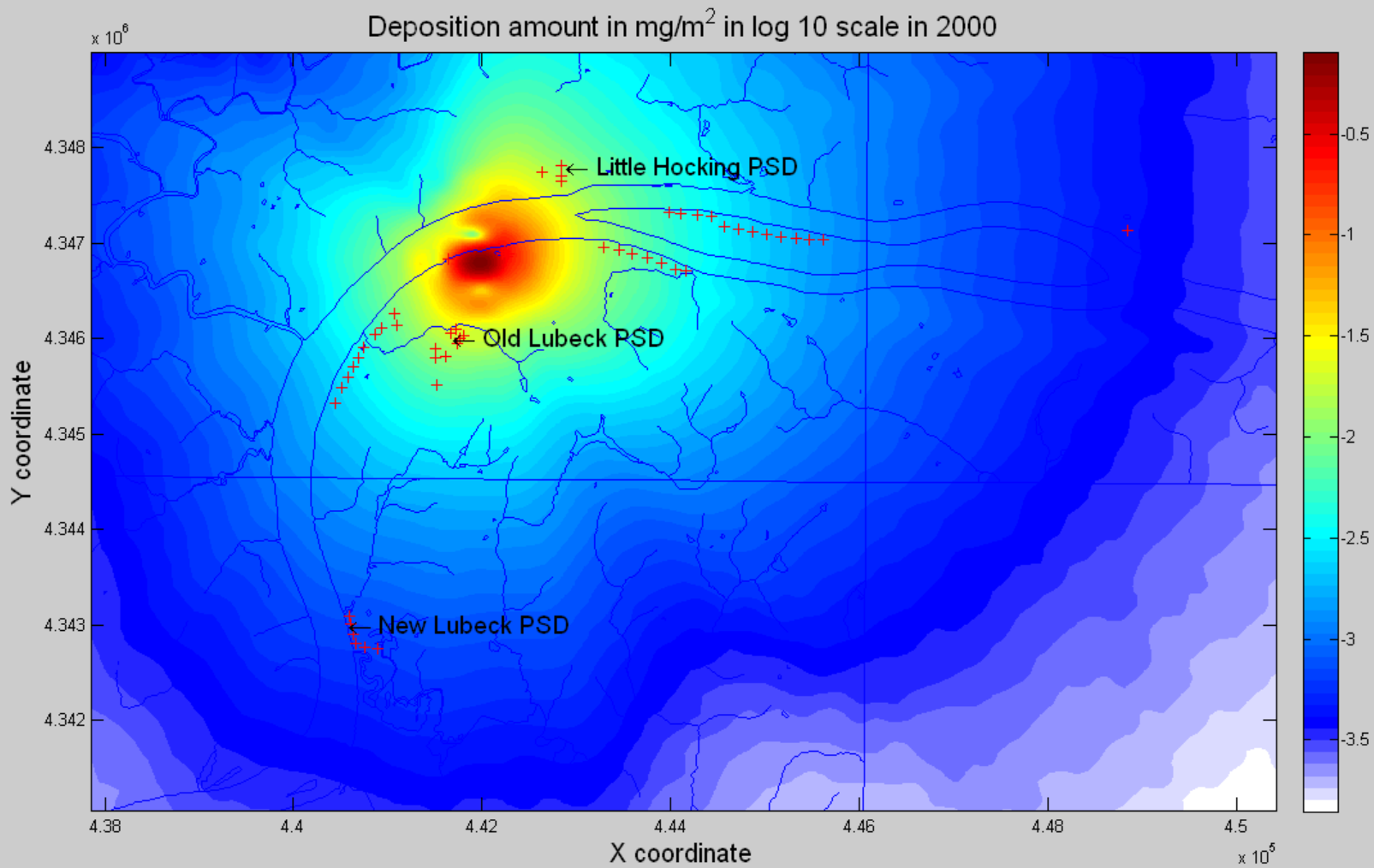
- Study population: 28,000 community adult residents and 4,000 workers at Dupont plant
- Interviewed twice in 2009-2011 to collect medical and residential history
- Lifetime exposure to PFOA modelled.
- Past diagnoses associated with modelled PFOA cumulated to year of diagnosis: Hazard Ratio from Cox regression

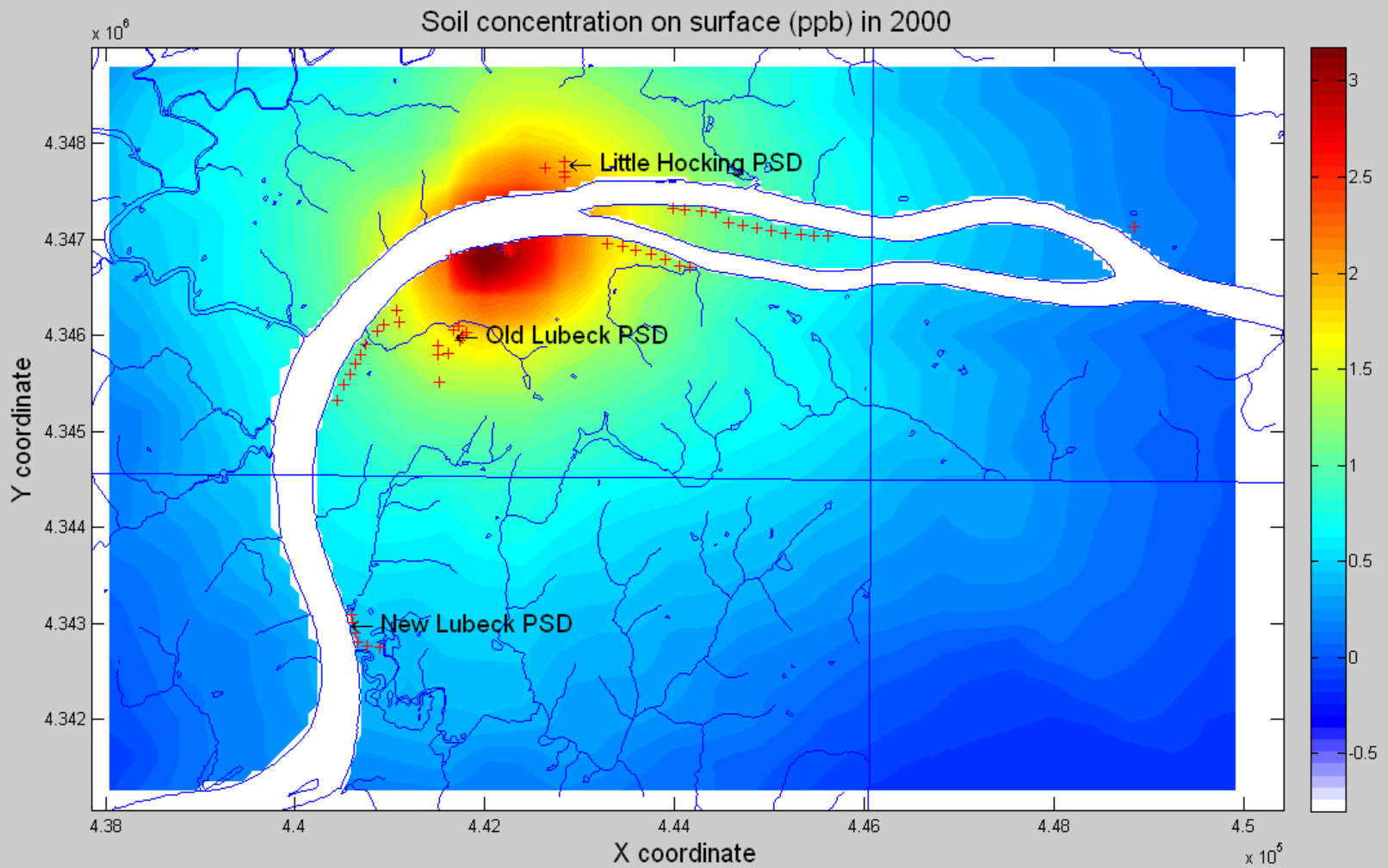
# Modelling exposure

# Plant emissions to air and river, 1950-2005

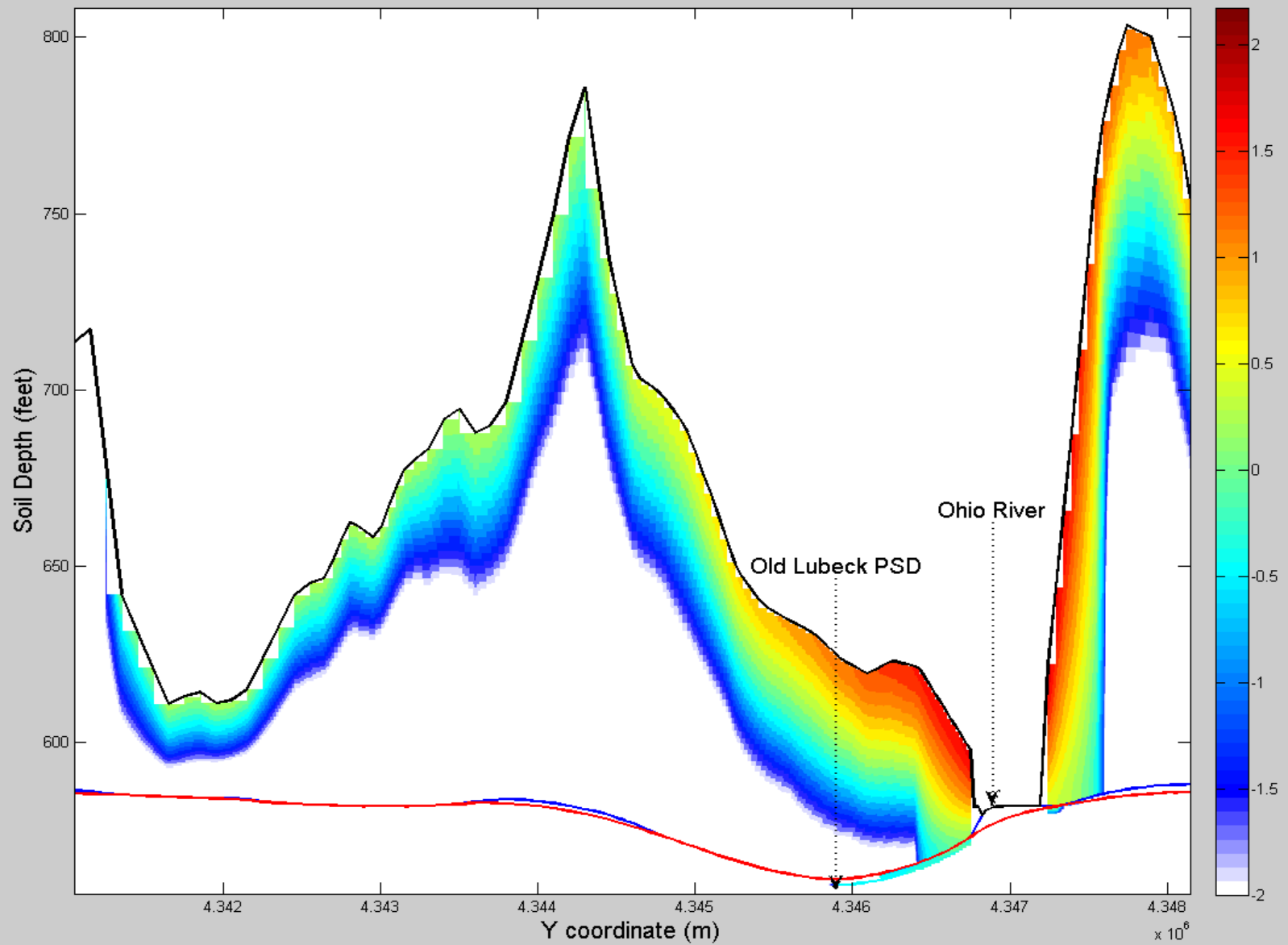


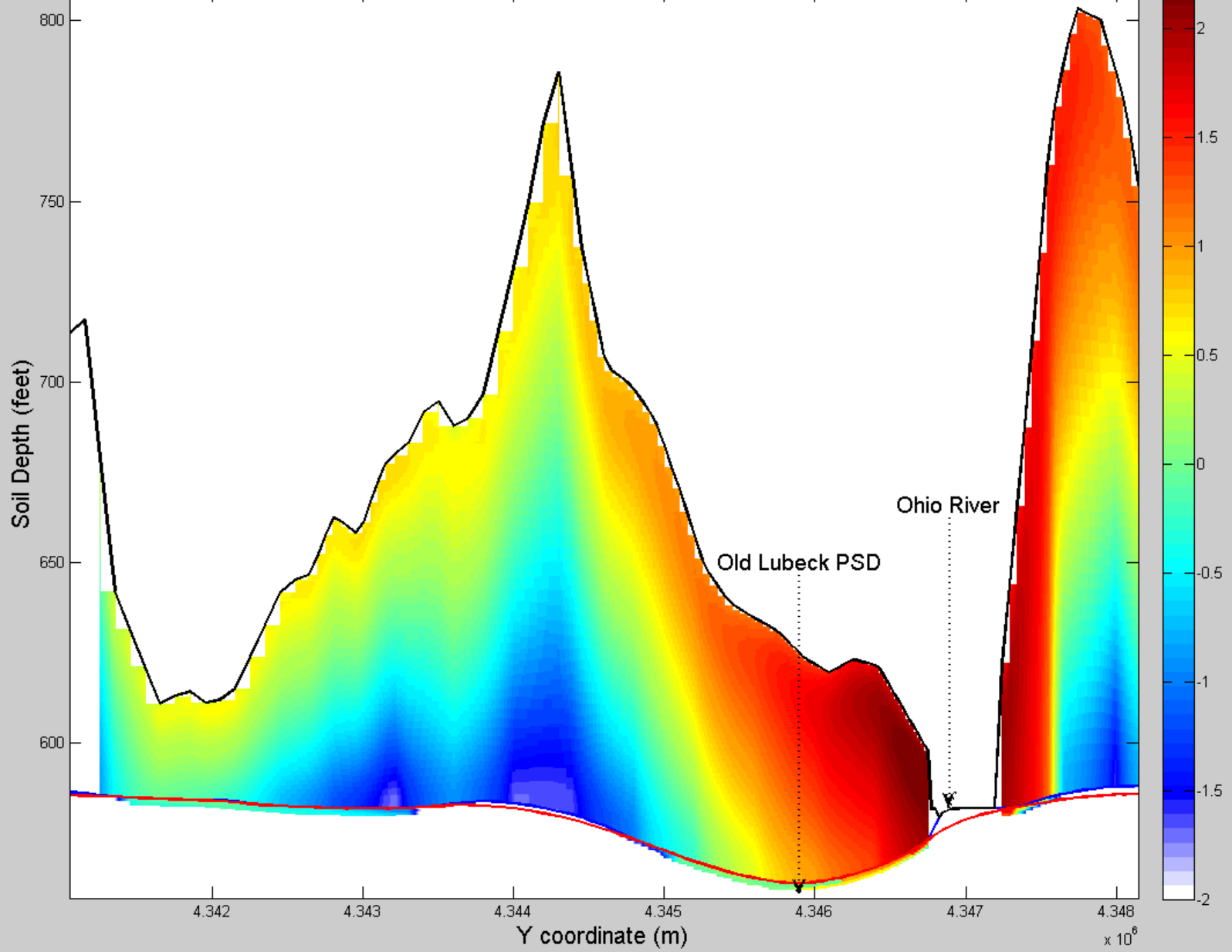




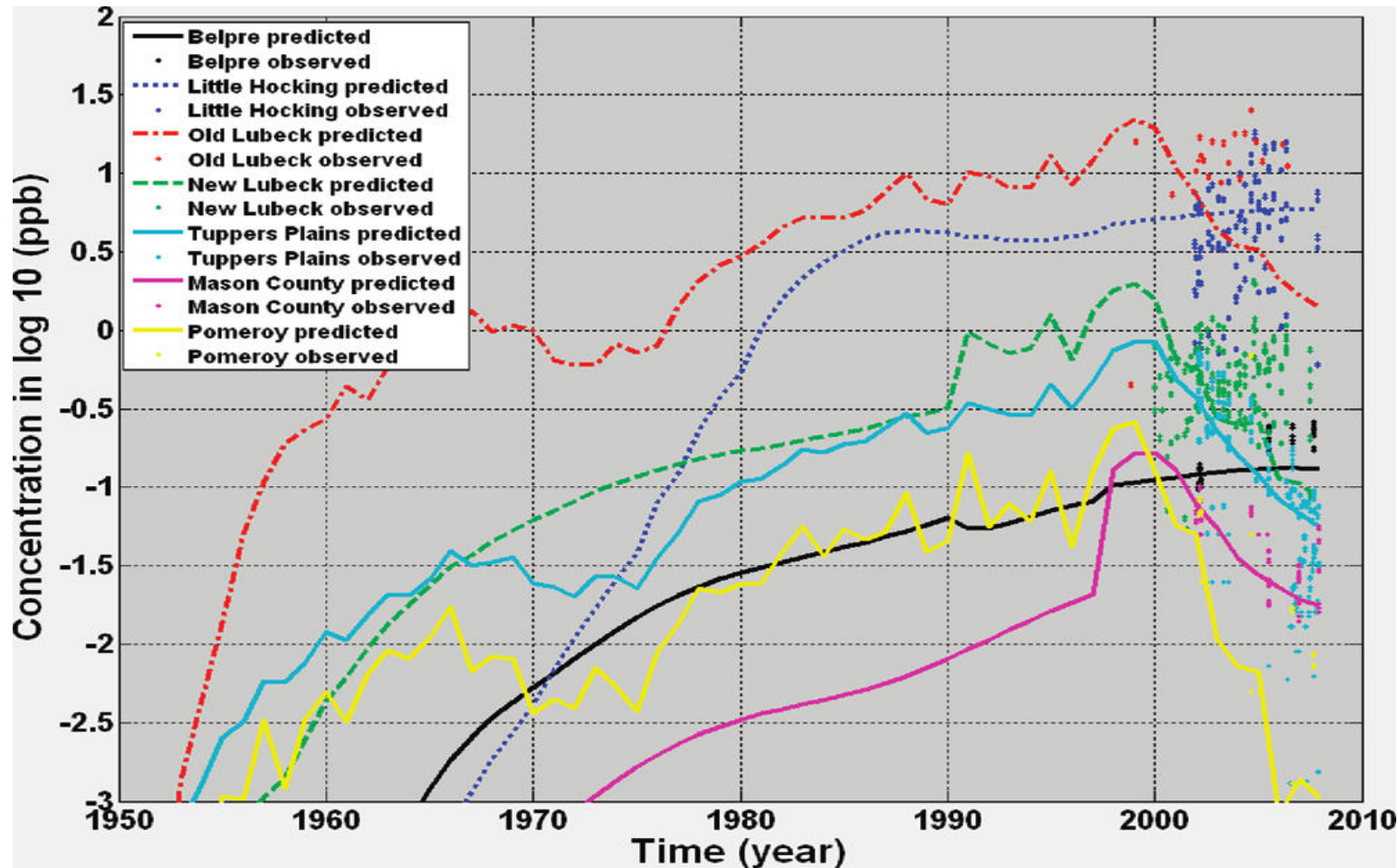


Subsurface soil concentration in lateral view (ppb) in log 10 scale in 1970

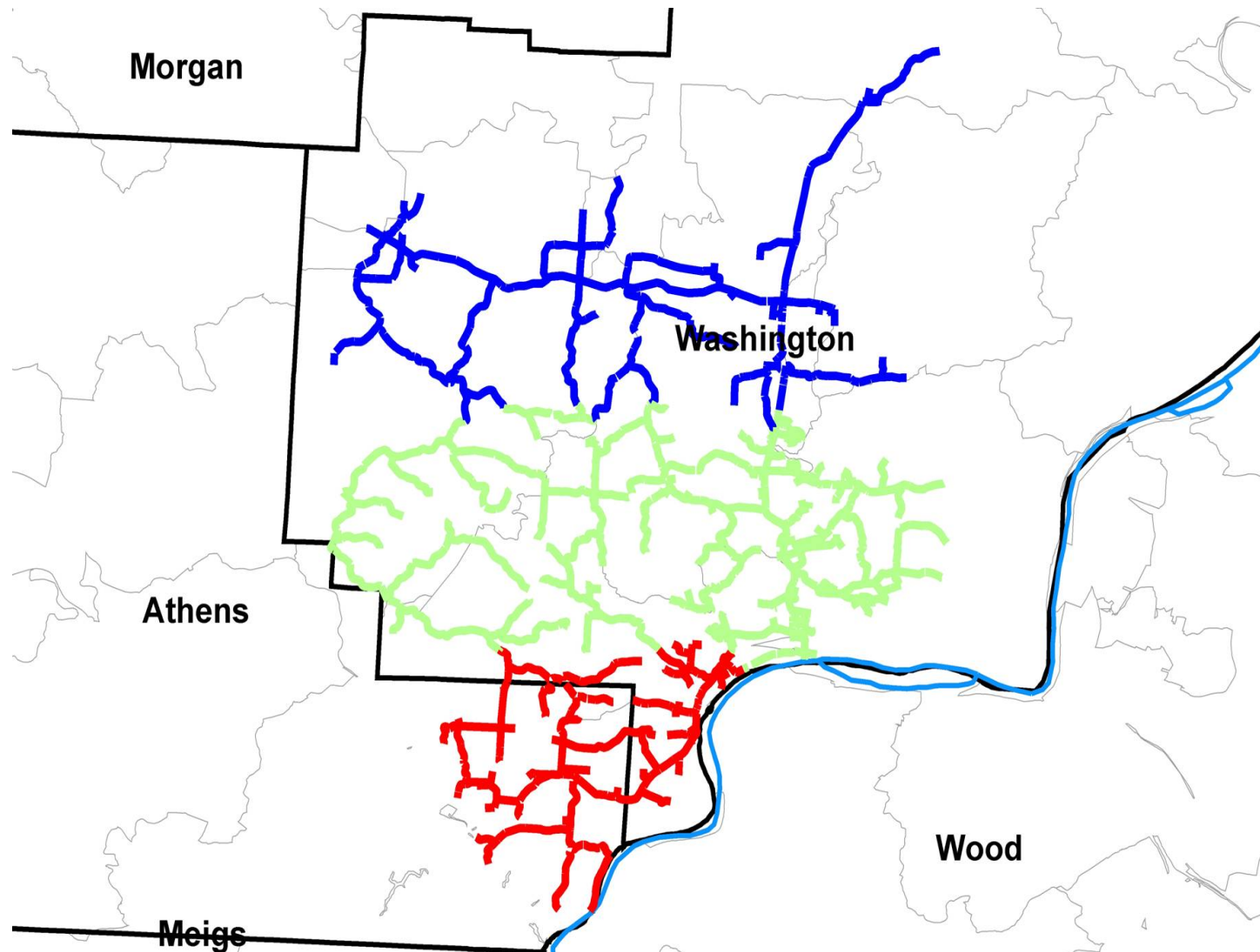


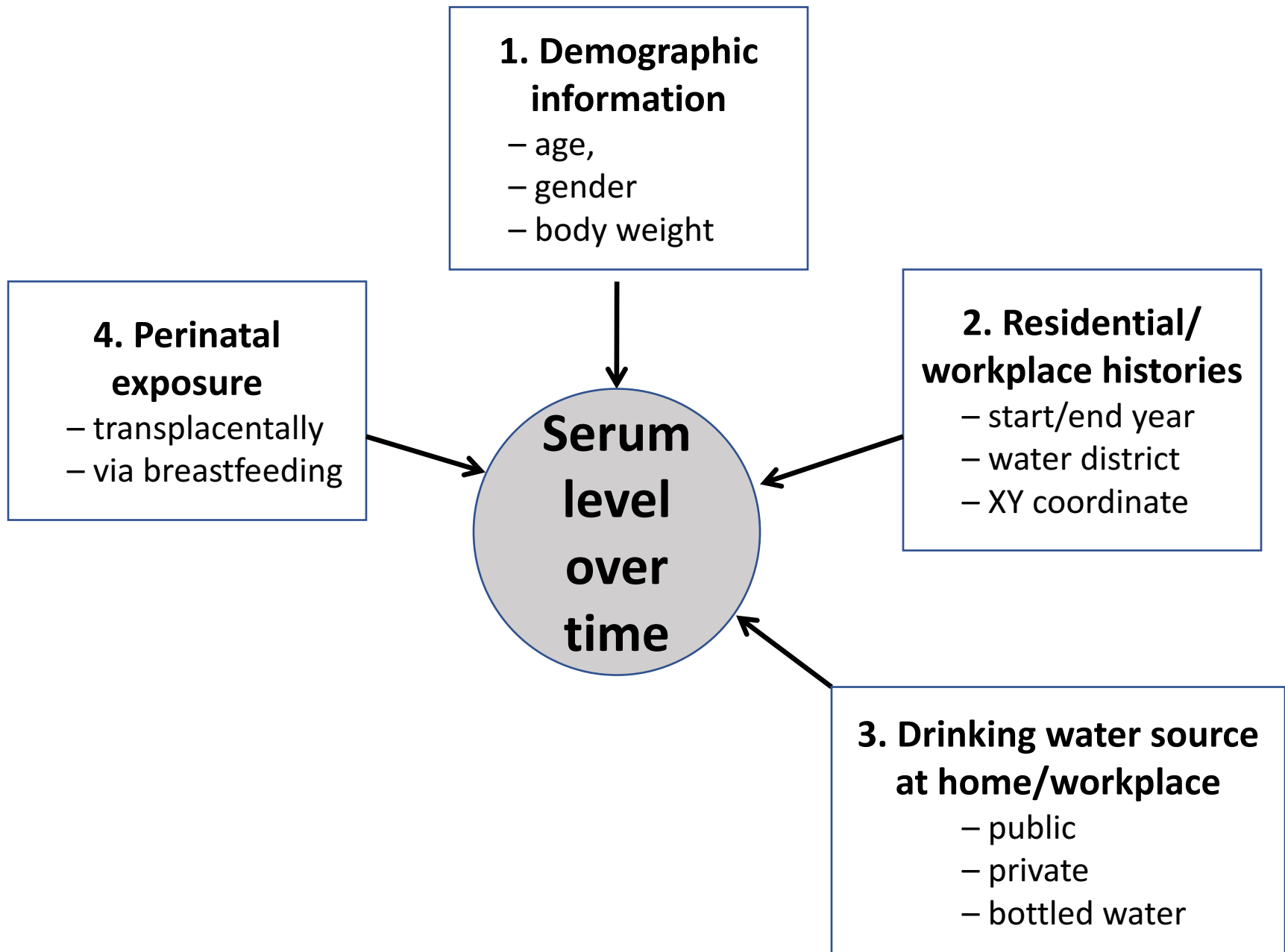


# Predicted water district well PFOA concentrations & recent observations

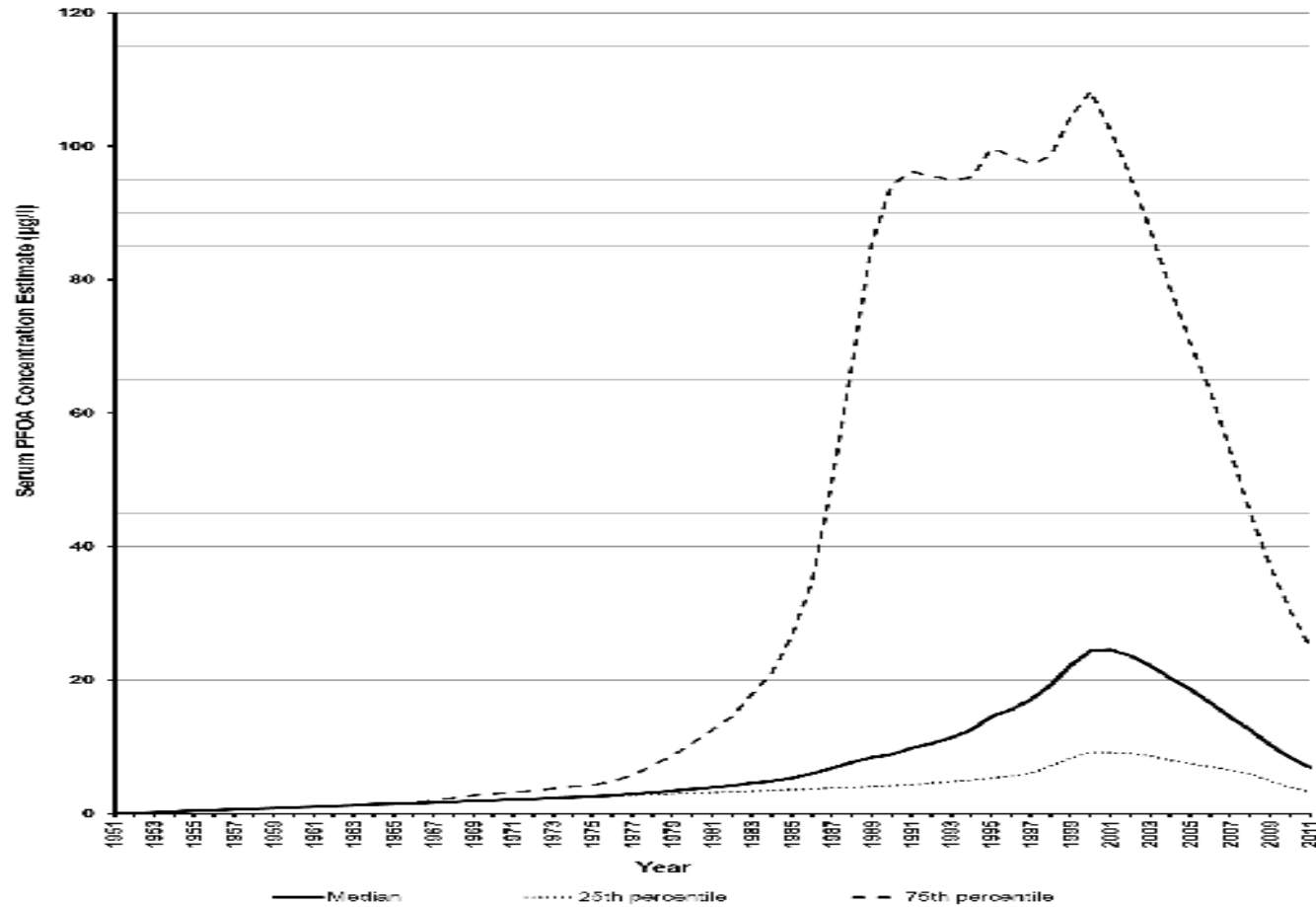


# Pipes added to district in stages



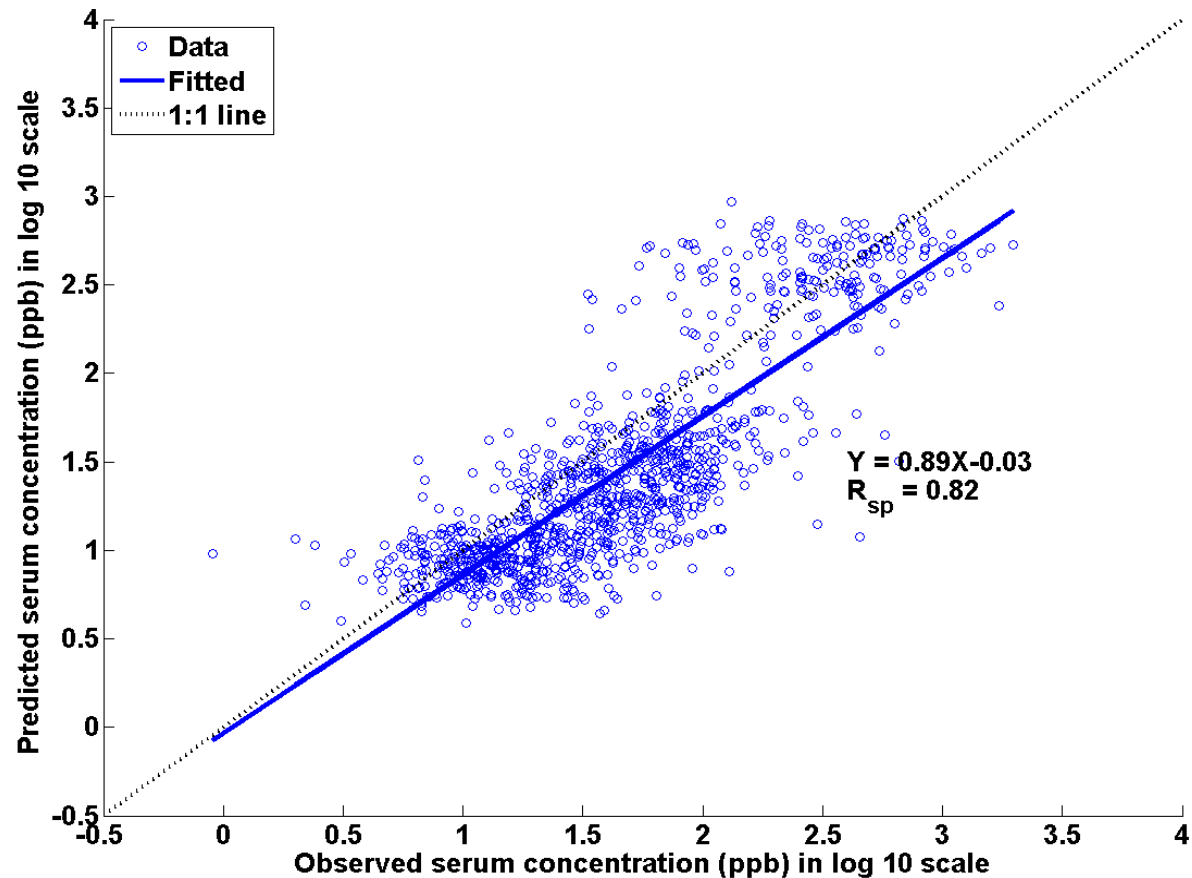


# Modelled serum levels over time



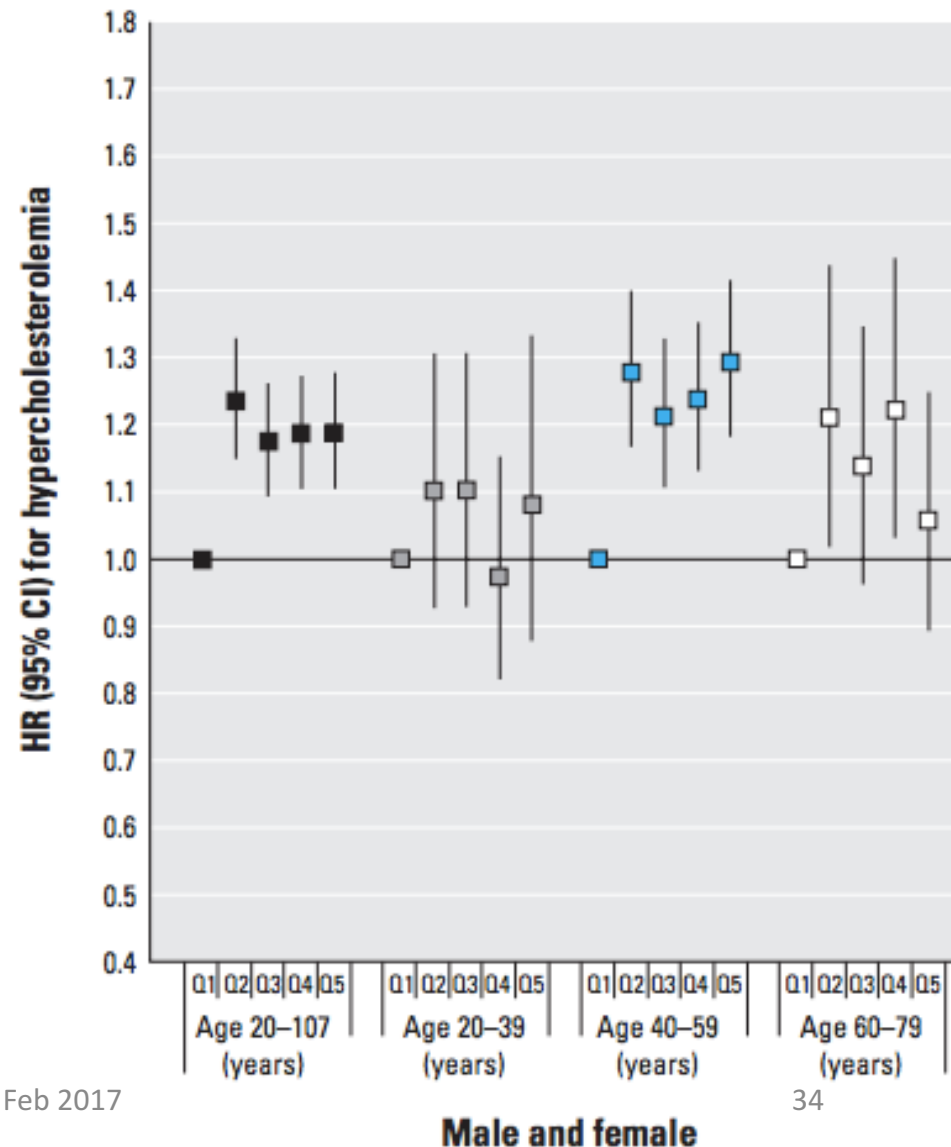


# Modelled vs measured PFOA serum concentrations at survey 2005-6



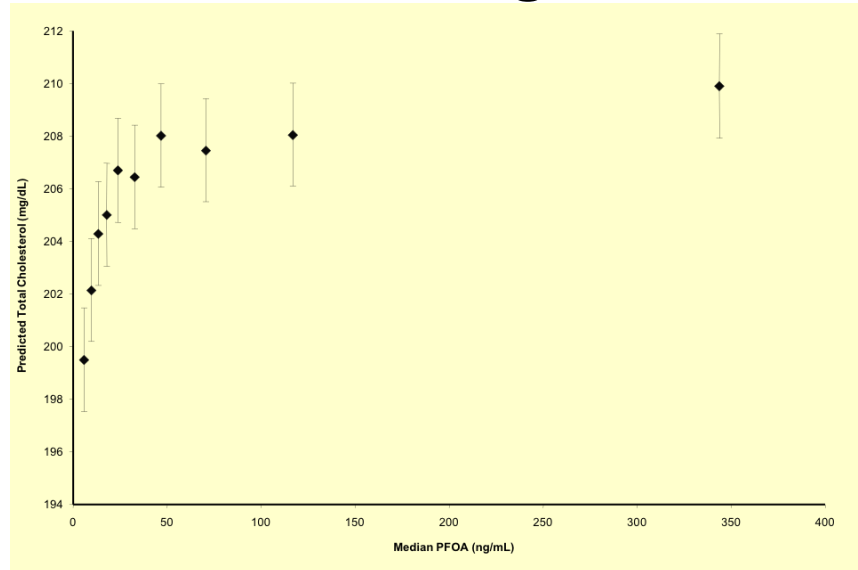
# Longitudinal study of doctor-diagnosed raised cholesterol

- Past diagnoses “high cholesterol with prescription medication” reported and associated with modelled PFOA at year of diagnosis: 9653 cases in population of 32000
- Risks shown by quintile of cumulative exposure



# Cross sectional data

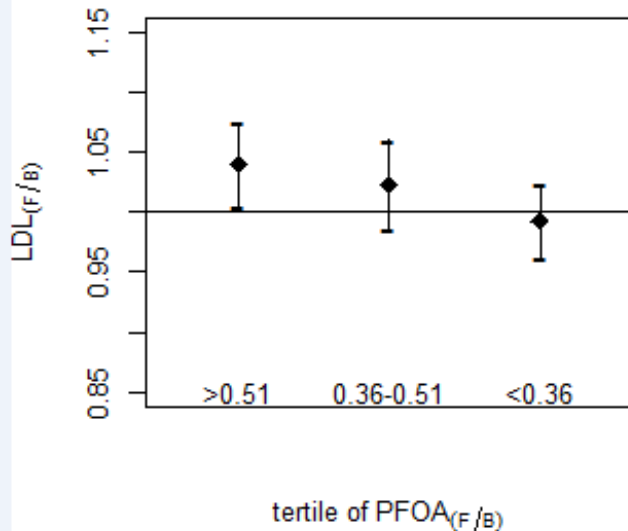
- Cross sectional analyses, 44000 adults, significant association between cholesterol and PFOA
- Logistic regression of high cholesterol (<240) significant trend with increasing PFOA



- LDL relationships steeper than total chol.
- Slope steeper at lower levels <40 ng/ml
- Consistent with multiple cross sectional studies

# Longitudinal study of lipids

- Lipid measures repeated 4 years after first survey  
n=560, most PFOA fell, by mean of ~50%
- Is change in LDL related to rate of change in serum level of PFOA?



Response	% change per halving of PFOA
(LDL) cholesterol	-3.58 (-1.47, -5.66)

# Probable link conclusion: cholesterol

Given the evidence from a variety of different study designs, it was concluded that there is a probable link between PFOA and diagnosed high cholesterol.

# Categories of Disease considered

Based on new epi, prior epi and tox literature

**Reproductive Health** (Preg Ind Hyper, Birth Defects, Miscarriage, Low Birth Weight)

**Autoimmune Disease** (Colitis, Lupus, Crohn's Disease, Diabetes Type 1, Multiple Sclerosis, Rheumatoid Arthritis)

**Thyroid Disease**

**Cancer** (Testes, Kidney, Pancreatic, Liver... 21 sites in total)

**Cardiovascular Disease** (High Cholesterol, BP, CAD, Stroke)

**Kidney Disease**

**Liver Disease**

**Respiratory Disease** (Asthma, COPD)

**Infectious Disease** (Resp., GI, Other)

**Neurological disease** (Children, PD)

**Diabetes** (Type 2)

**Osteoarthritis**

# Categories of Disease considered

6 positive probable links (out of 47)

**Reproductive Health** (**Preg Ind Hypertension/Preeclampsia**,  
Birth Defects, Miscarriage, Low Birth Weight)

**Autoimmune Disease** (**Ulcerative Colitis**, Lupus, Crohn's  
Disease, Diabetes Type 1, Multiple Sclerosis, Rheumatoid  
Arthritis)

**Thyroid Disease**

**Cancer** (**Testes, Kidney**, Pancreatic, Liver... 21 sites in total)

**Cardiovascular Disease** (**High Cholesterol**, BP, CAD, Stroke)

**Kidney Disease**

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**Respiratory Disease** (Asthma, COPD)

**Infectious Disease** (Resp., GI, Other)

**Neurological disease** (Children, PD)

**Diabetes** (Type 2)

**Osteoarthritis**

# Medical monitoring programme implemented

C-8 Medical Monitoring Program

[C-8MedicalMonitoringProgram.com](http://C-8MedicalMonitoringProgram.com)

WELCOME TO THE C-8 MEDICAL MONITORING PROGRAM WEBSITE



# The Columbus Dispatch

## DuPont to pay \$670 million to settle C8 lawsuits



 [BUY PHOTO](#)

 [HIDE CAPTION](#)

The Dupont Washington Works plant outside of Parkersburg, West Virginia, is where the c8 contamination in the area air and water began. [Dispatch file photo]

**Monday**

Posted Feb 13, 2017 at 8:31 AM

Updated Feb 13, 2017 at 11:59 AM

By [Earl Rinehart](#)

The Columbus Dispatch

[@esrinehart](#)

Venice Feb 2017

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# Thank you

- More info at
- [www.c8sciencepanel.org](http://www.c8sciencepanel.org)
- [tony.fletcher@lshtm.ac.uk](mailto:tony.fletcher@lshtm.ac.uk)