Epidemiology of PFOA and PFOS - new findings

Tony Fletcher, PhD

Department of Social and Environmental Health Research

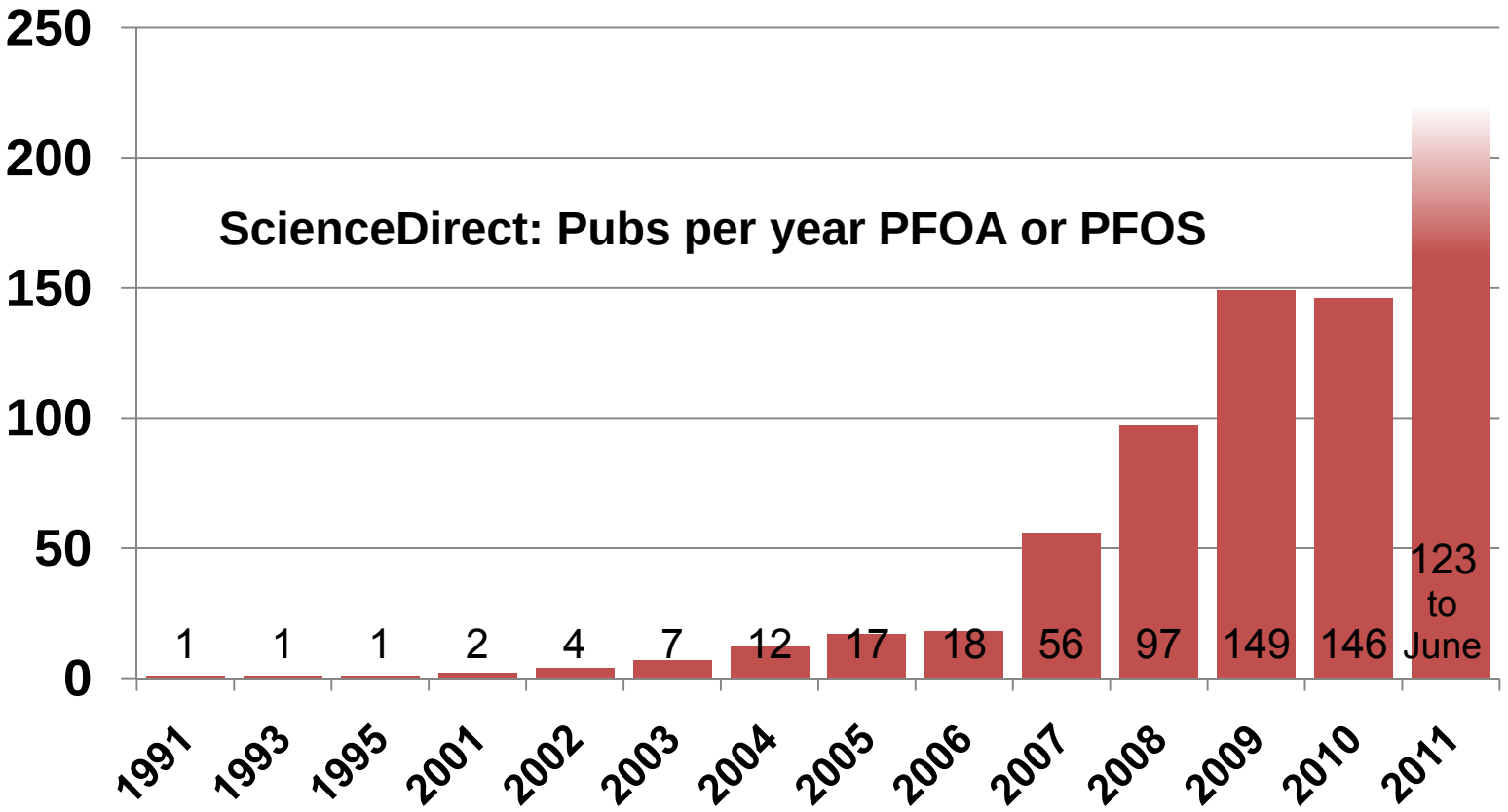
London School of Hygiene & Tropical Medicine

Outline

- Background to the West Virginia/Ohio PFOA study
- Exposure patterns
- First results
- Other literature on key outcomes
- Further results planned from our studies

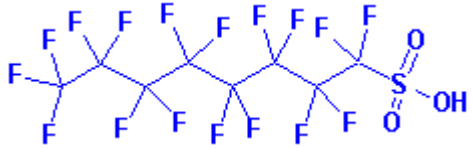
There has been a rapid rise in publications on exposure, toxicology and epidemiology of PFOA and PFOS

1199 pubs since 1983 on Pubmed by June 2011
643 pubs since 1991 on Science Direct

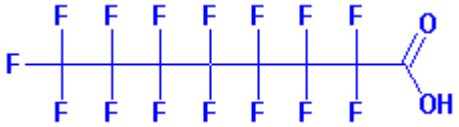


What are perfluoroalkyl acids?

- Synthetic fluorinated compounds used predominantly as surfactants (both water and oil resistant)
- Numerous consumer and industrial applications…cleanings, coatings, lubricants, fire-fighting foams, insecticides… PTFE manufacture
- C8 (PFOA and PFOS) compounds are most abundant



Perfluorooctane Sulfonate (PFOS)



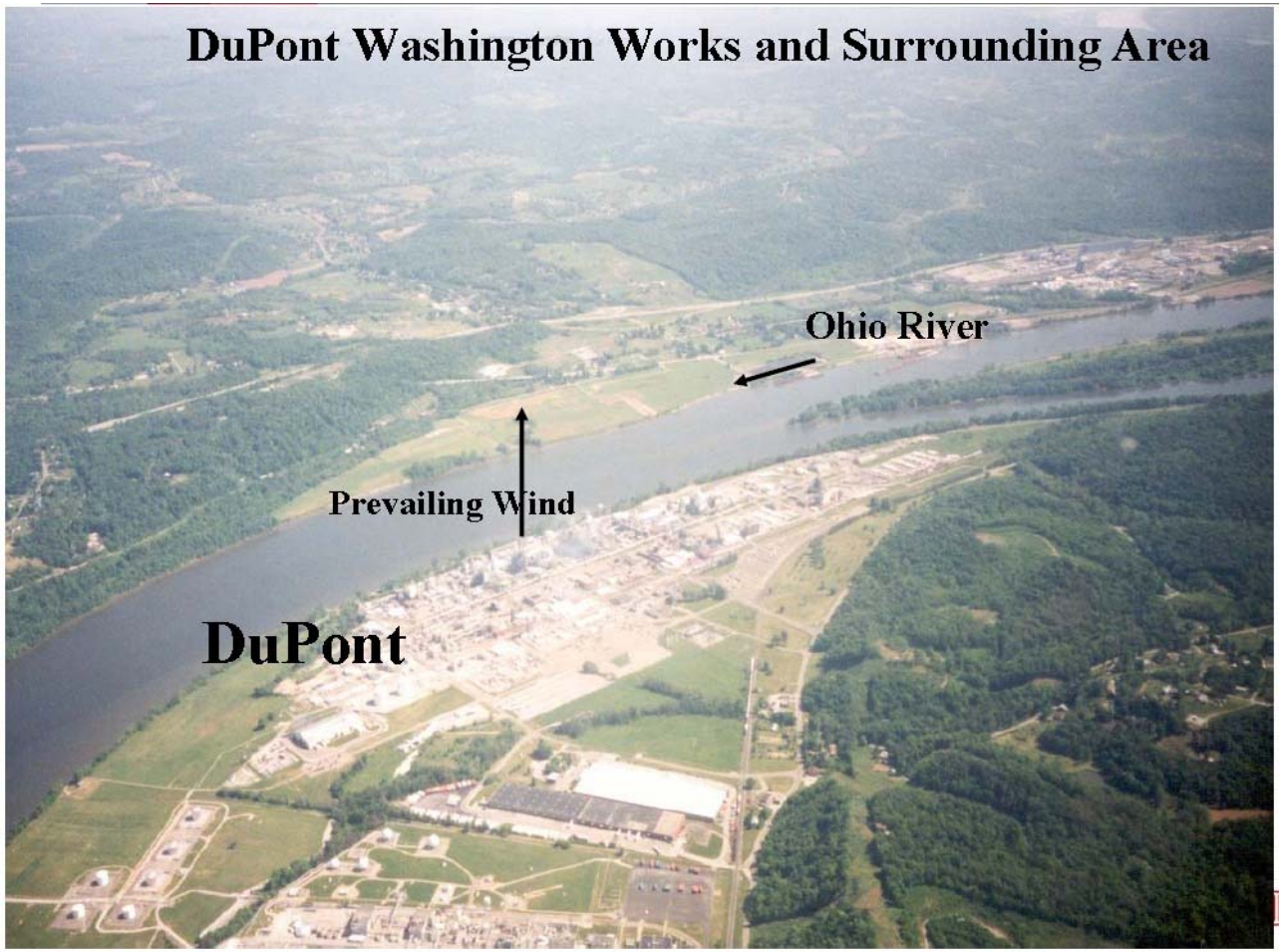
Perfluorooctanoic Acid (PFOA)

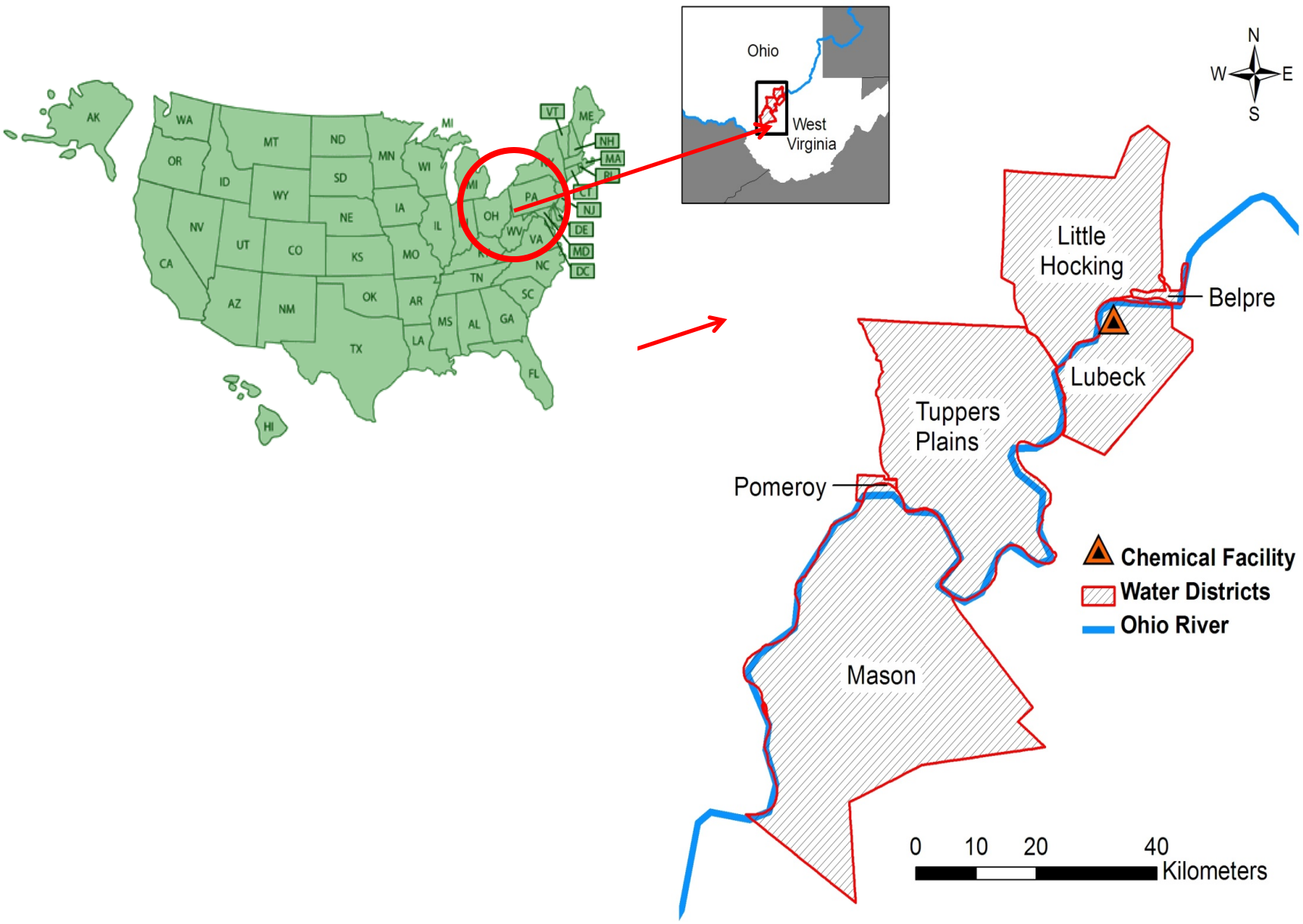
PFAA toxicity?

- Persistent, resistant, and pervasive in environment
- Reported adverse effects in animal models
  - Carcinogenicity – liver, pancreatic, and testicular
  - Developmental toxicity – survival, delays, and deficits
  - Hepatotoxicity – hypertrophy, altered lipid metabolism, peroxisome proliferation
  - Neurotoxicity – altered behavior, cell replication, and proteins
  - Immunotoxicity – suppression

NB: PPARα mechanism may account for interspecies differences

Background to the C8 Science Panel Study: PFOA emissions from a Teflon plant in West Virginia, USA




Ohio
West Virginia
N
W
E
S
Little Hocking
Belpre
Lubeck
Tuppers Plains
Pomeroy
Mason
Chemical Facility
Water Districts
Ohio River
0 10 20 40
Kilometers

PFOA in public water and private wells near Dupont Washington Works

After PFOA was detected at higher levels in water supplies near the Dupont Plant due to air emissions and river discharges, this led to a:

Class Action legal case against Dupont

Settlement mandated:

1. Installation of GAC filtration of water
2. **C8 Health Project**, a survey of exposure and clinical markers
3. **C8 Science Panel** to research and evaluate link of PFOA to disease

The C8 Science Panel

- **Members: Tony Fletcher, LSHTM; David Savitz, Brown Univ; Kyle Steenland, Emory Atlanta**

- We were selected by agreement between the two sides, the "Settling Parties" - Dupont and the Plaintiffs/Class Action; Independent of the two sides.
- **Roles**:

1. design and conduct a health study in the communities exposed to C8/PFOA.
2. evaluate the evidence to determine if there is a "**Probable Link**" between C8/PFOA exposure and any human disease
   - If so a screening programme will be set up

Data sources

- Data on history of plant emissions of PFOA into the air and river
- Biomonitoring data on PFAAs and clinical markers, and questionnaire responses in community – 69030 participants in the “C8 Health Project”
- Further follow up in the C8 Science Panel Study: with additional disease, interview and biomarker data in population samples

Science Panel Research Programme

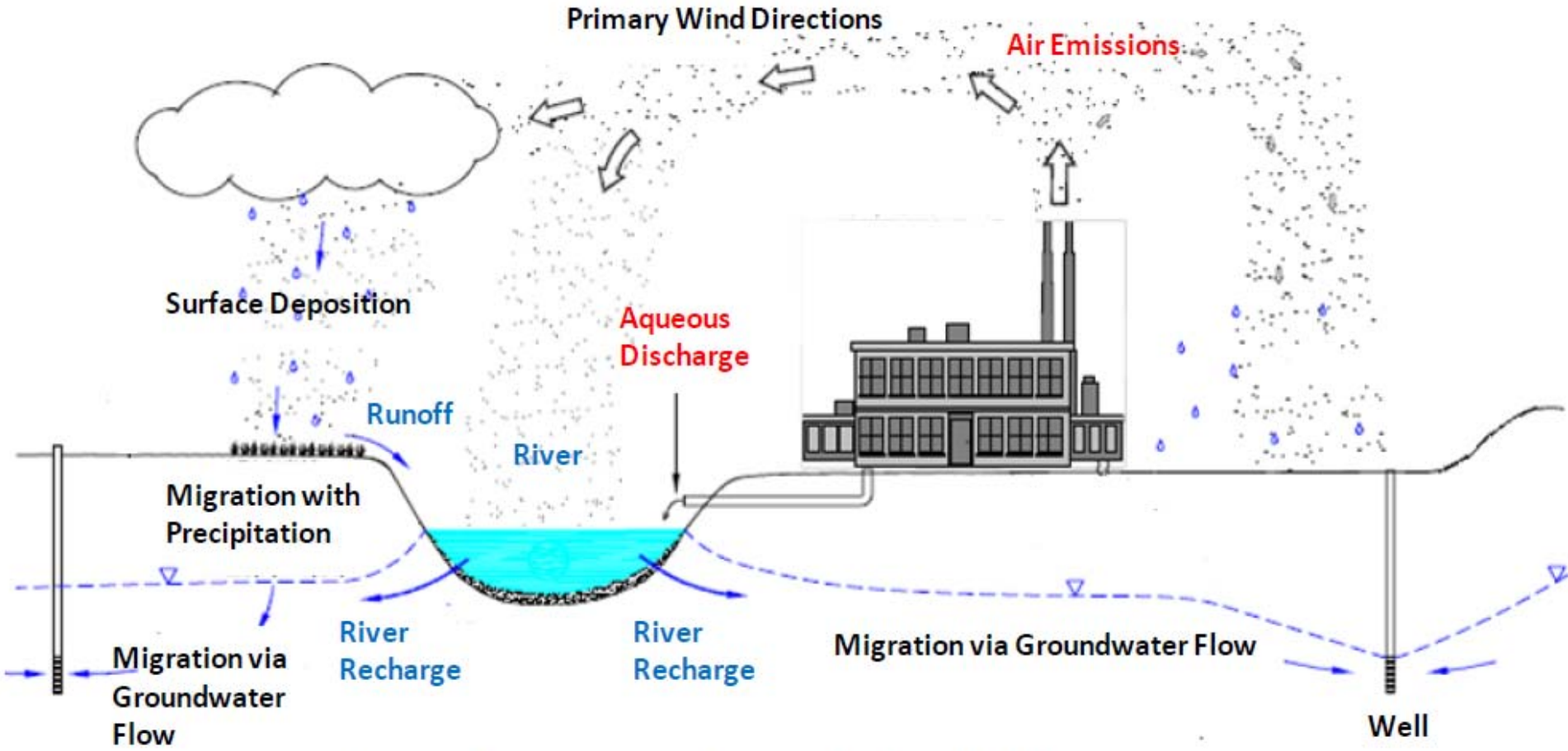
Overall objective: to assess relationship of PFOA and several diseases and clinical markers including:

- Cancer
- Cardiovascular Disease and lipids
- Reproductive outcome and endocrine disruption
- Thyroid, Liver and Immune dysfunction
- Neurological impairment

- Several designs: reconstruction of exposure history, cross sectional studies, follow up studies, ecologic studies – details on C8 Science panel website

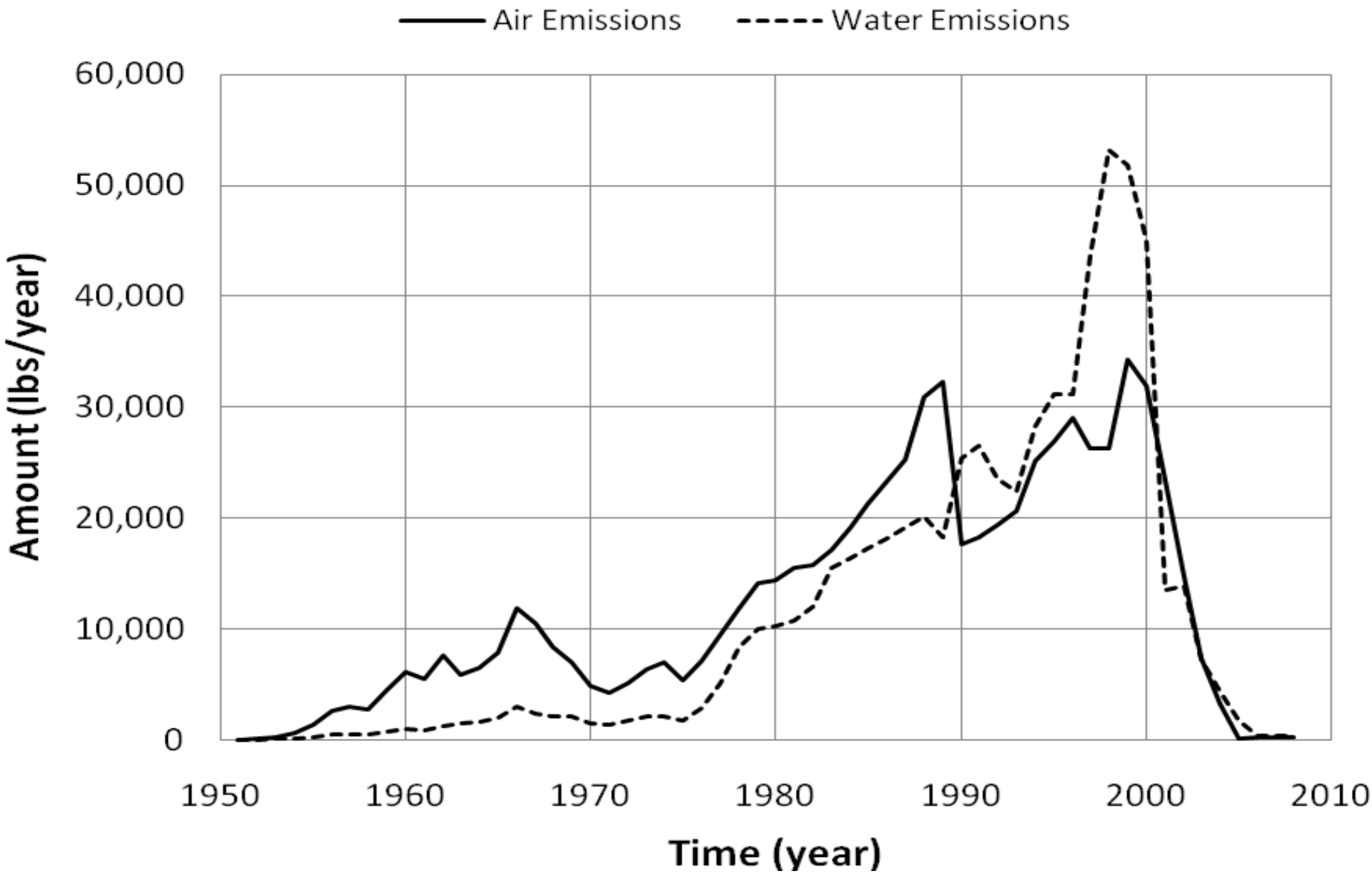
Exposure in the community

Schematic Transport Pathways



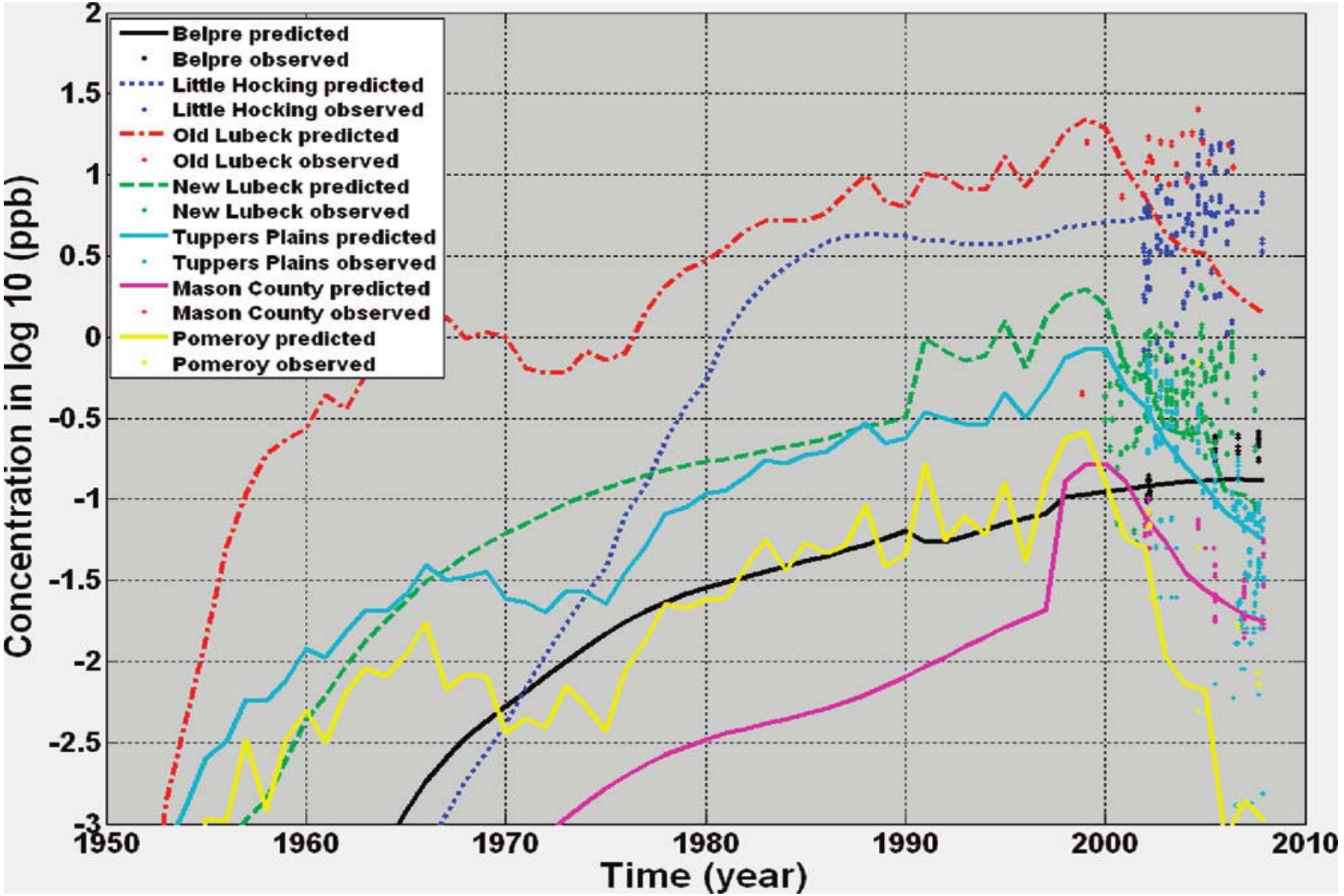
Source: Data Assessment Report, DuPont (2008)

Plant emissions to air and river, 1950-2005



[Shin et al ES&T 2011]

Predicted water district well PFOA concentrations & recent observations



[Shin et al ES&T 2011]

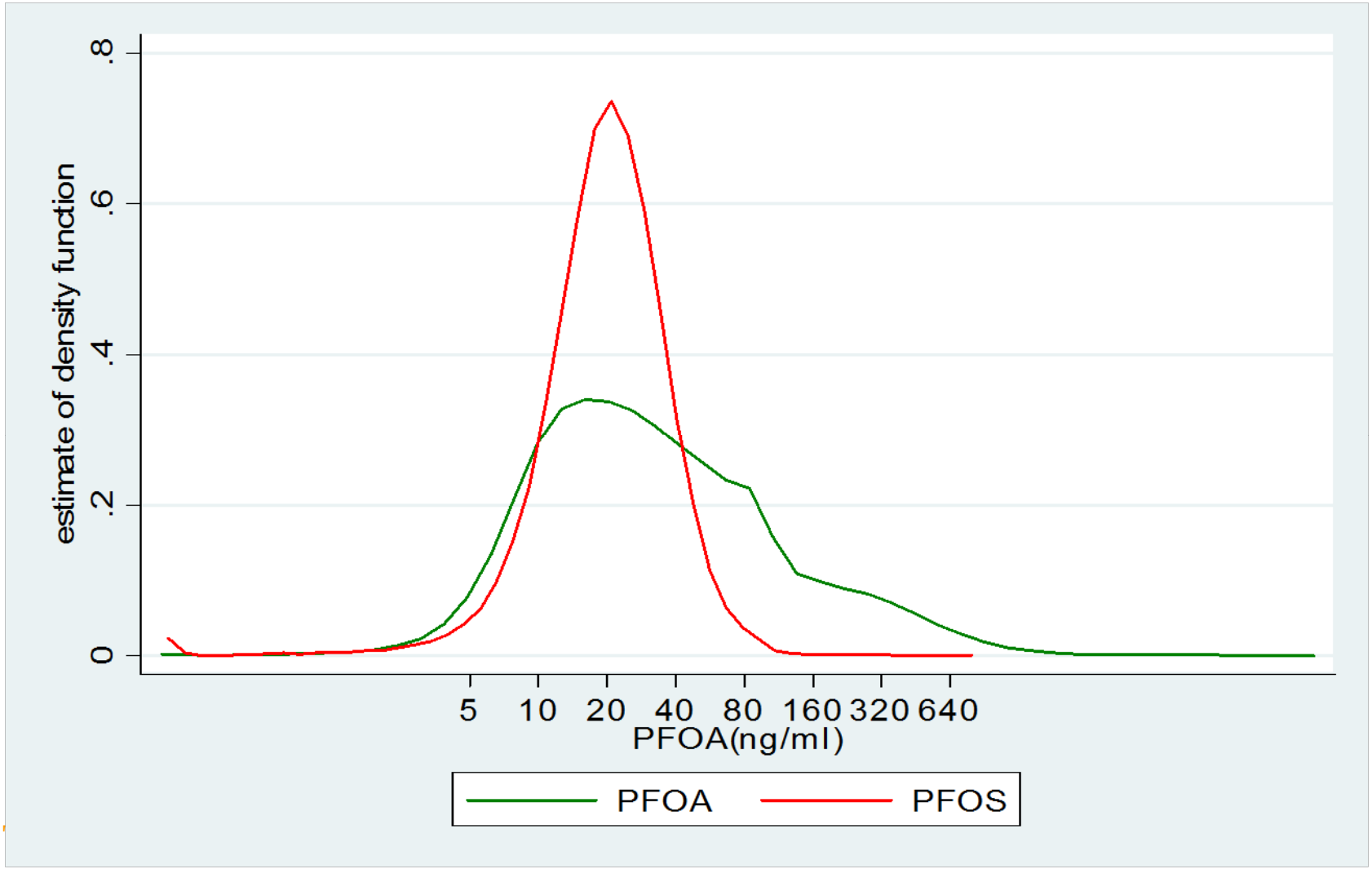
C8 health project data included biomarkers in blood and questionnaire data for 67000 people. 10 perfluorochemicals measured. Highest was PFOA (mean 82.9 ng/mL), *normal range 4-5*, then PFOS (mean 23.3)

Table 3. Continued

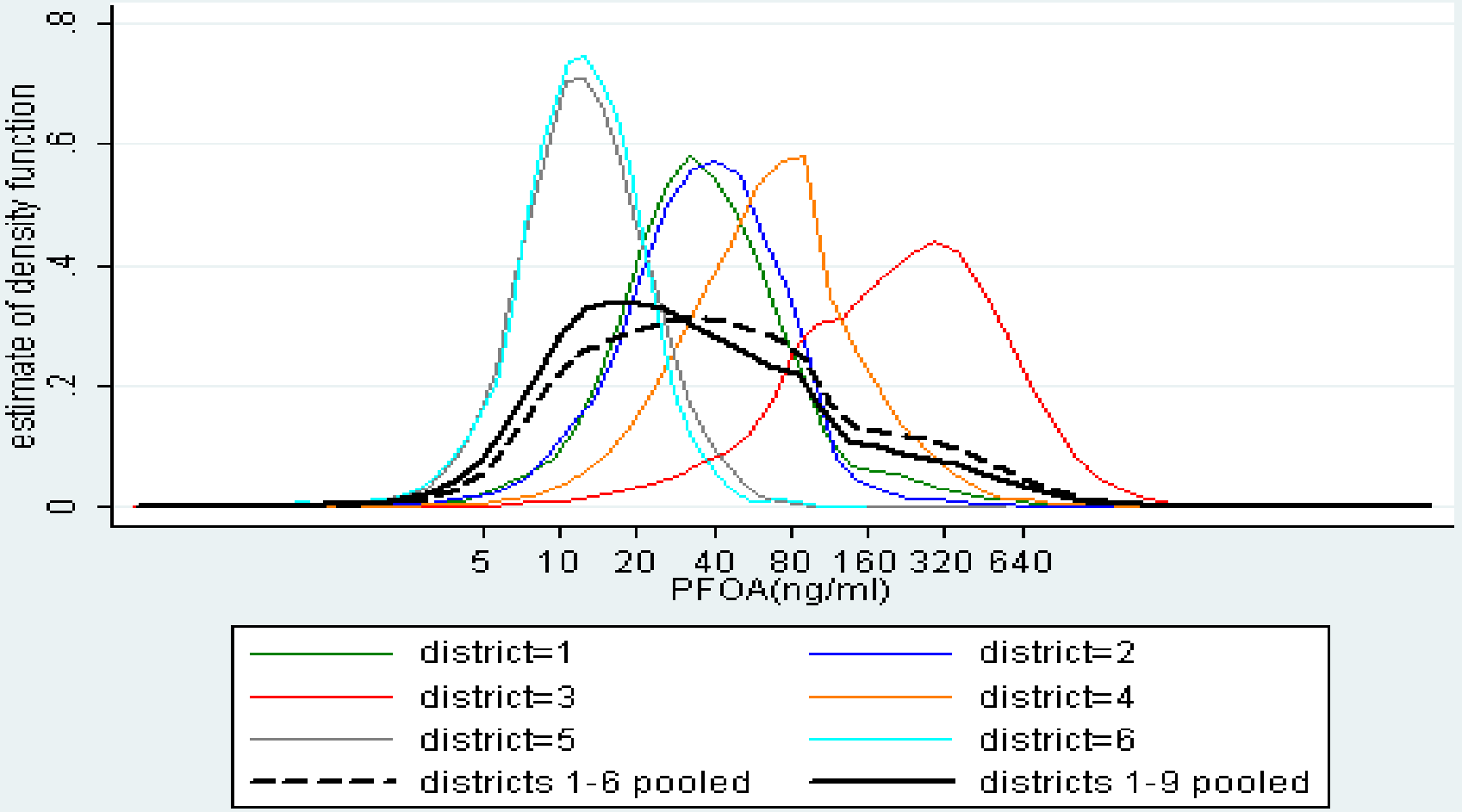
Age/sex	Measure	PFHxA[a]	PFHxA[b]	PFHS	PFHpA[a]	PFHpA[b]	PFOA	PFOS	PFNA	PFDA[a]	PFDA[b]
Total population											
Female	Mean	0.8	1.4	4.3	0.6	1.2	68.8	20.7	1.5	0.5	0.8
	Median	0.5	1.0	2.7	0.3	0.8	23.6	17.6	1.3	0.3	0.7
	Geometric mean	0.5	1.1	2.8	0.4	1.0	27.9	17.0	1.3	0.4	0.7
	SD	1.0	1.1	6.2	0.8	1.2	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

[Frisbee et al EHP 2009]

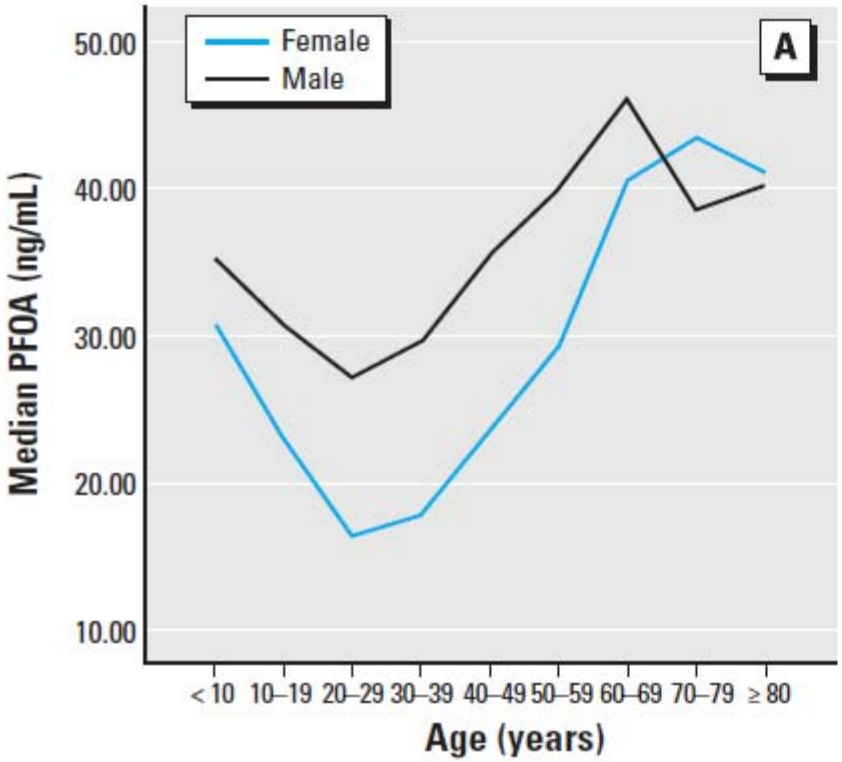
Distribution of PFOA and PFOS in serum, n=67000. Much higher than normal background though less than many occupational serum level

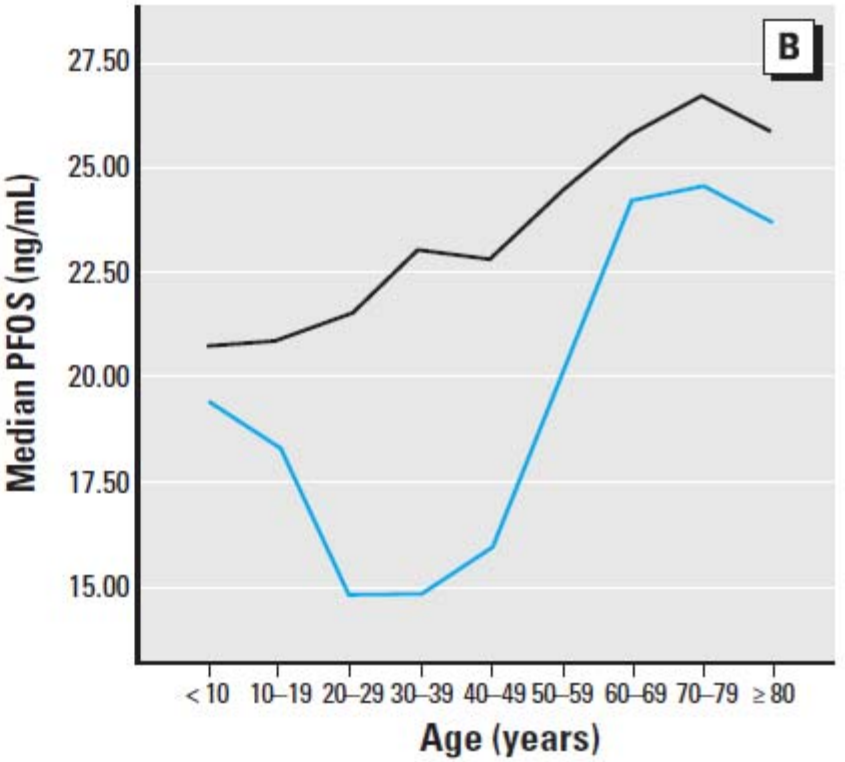


PFOA levels. Large differences in contamination between water districts.

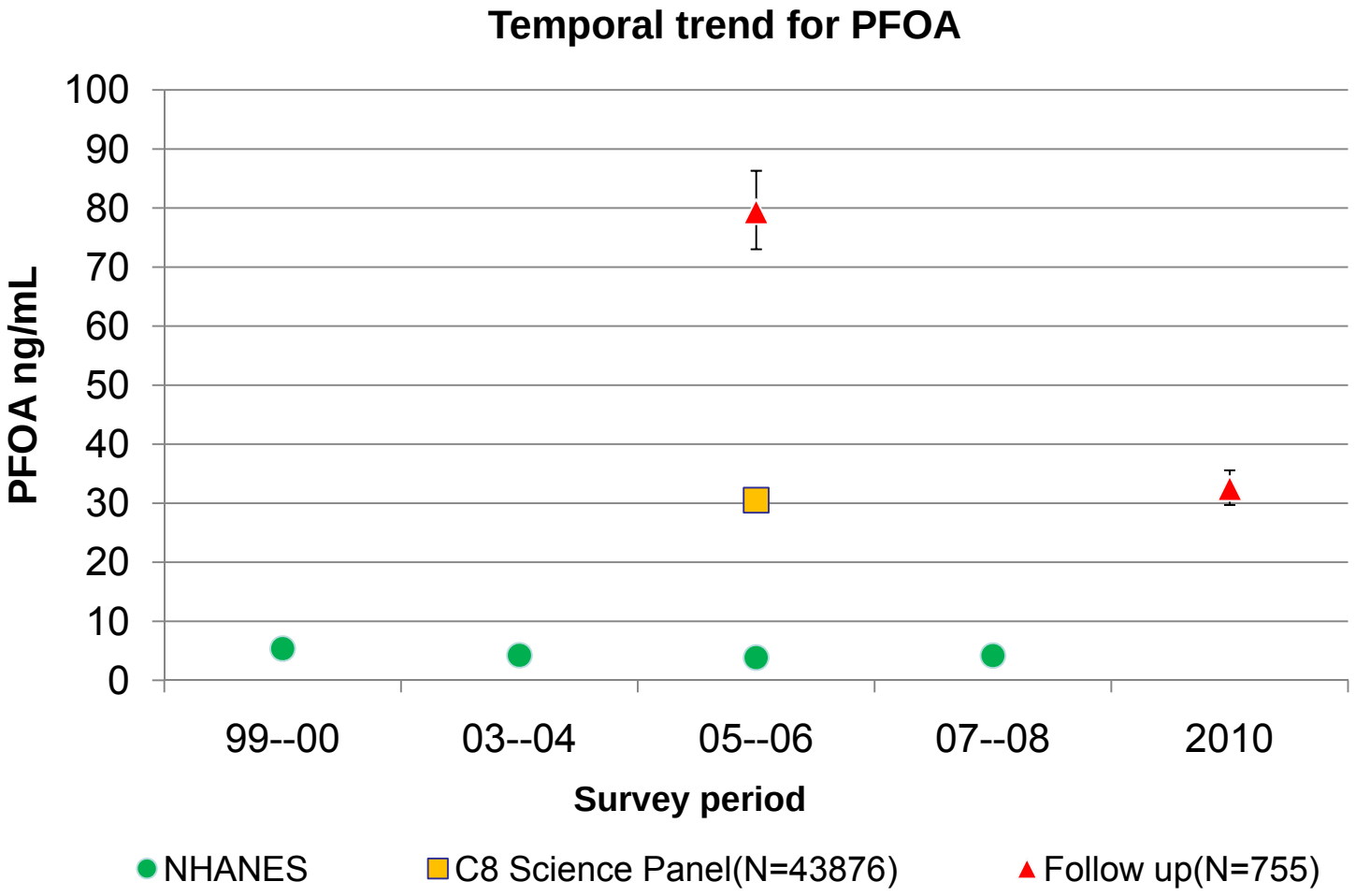


Other significant predictors: age, sex (males +35%), has private well (+12%), use bottled water for drinking (-6%), grow own vegetables (+11%), vegetarian (-10%), consumed alcohol in last 3 days (+7%), current smoker (+6%)



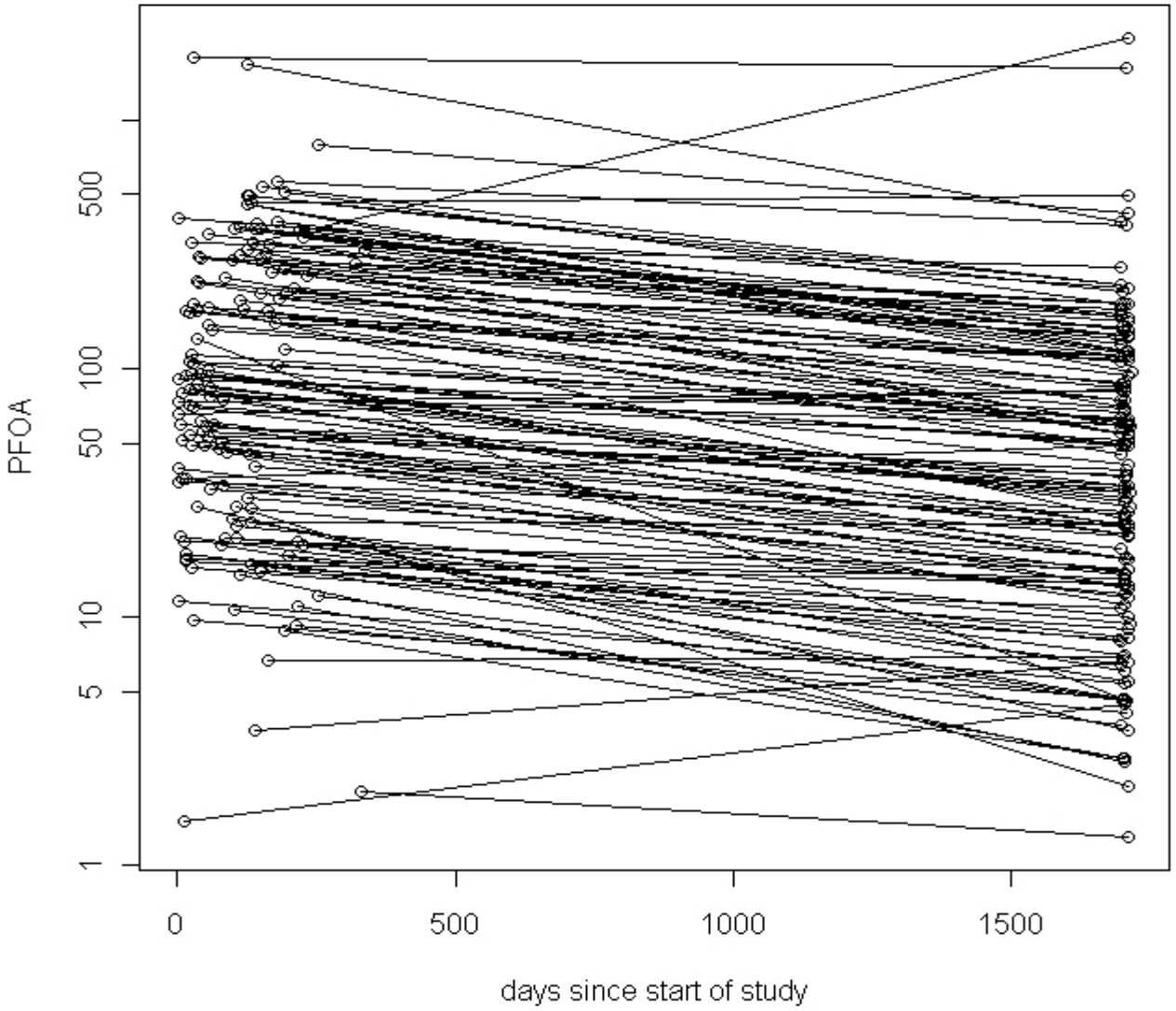


Serum PFOA is declining in population 2005 to 2010

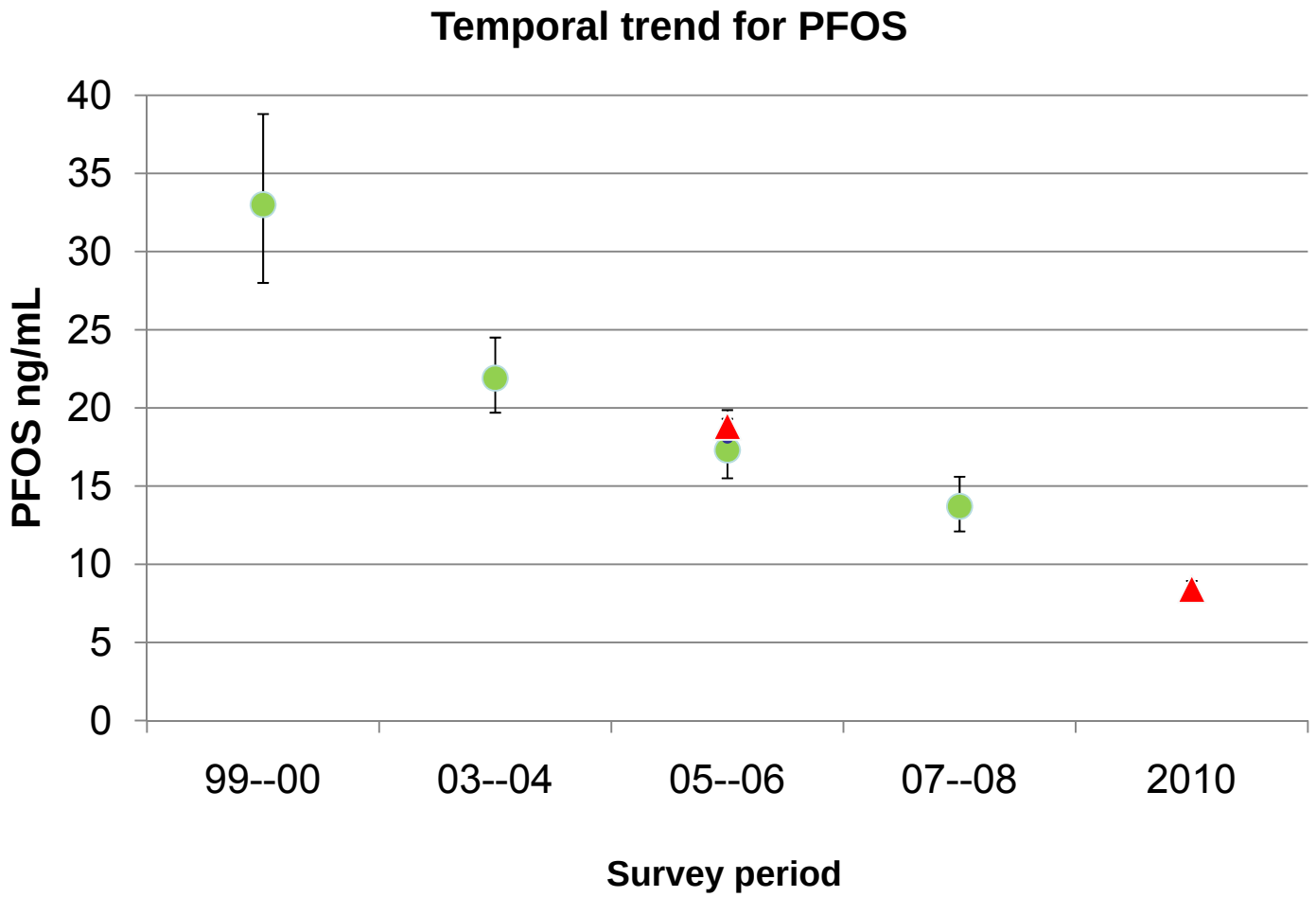


[Poster at conference]

PFOA Decline varies across population



Serum PFOS decline in population similar to US

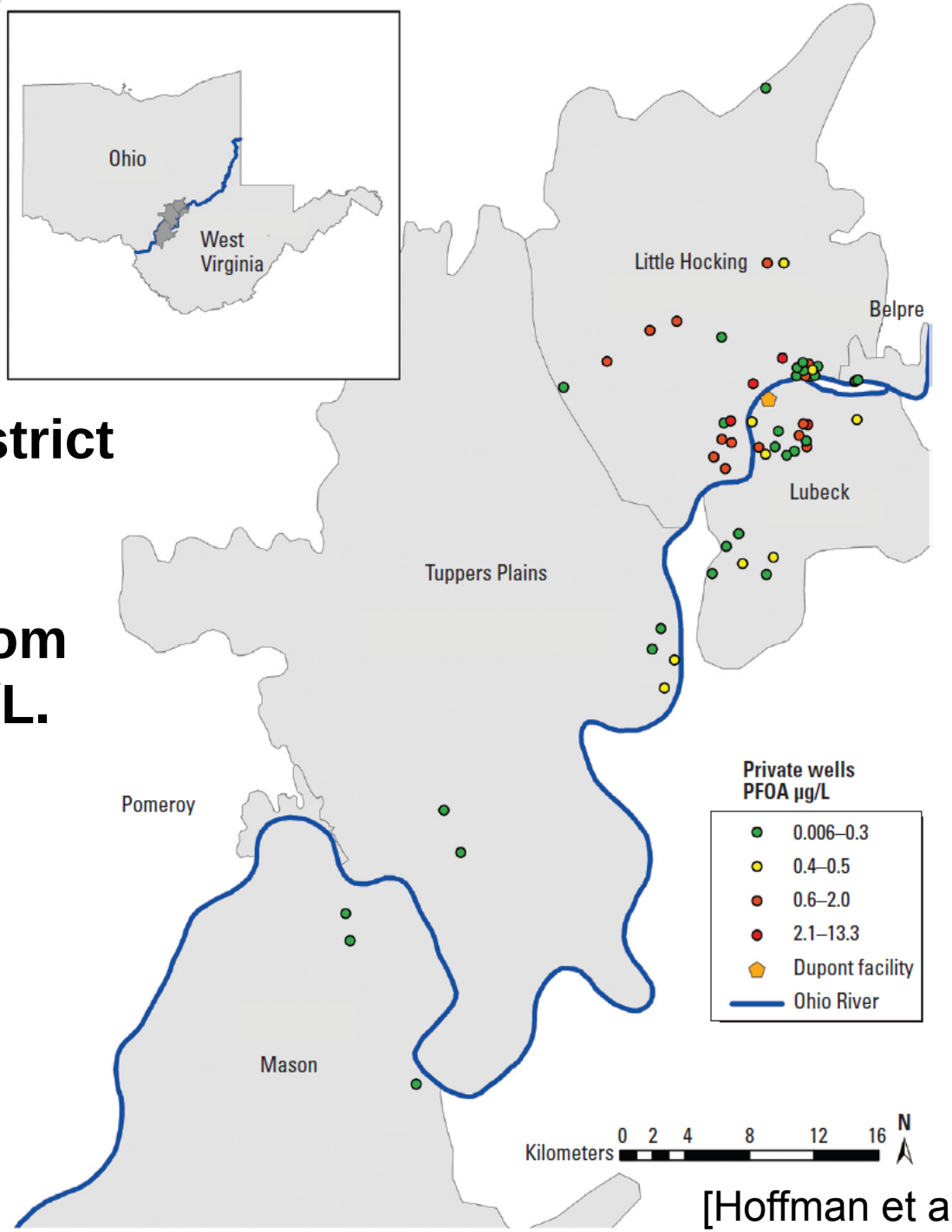


[Poster at conference]

Bioconcentration of PFOA from drinking water

Private wells with PFOA measurements >LOD in the 6 contaminated public Water District areas.

PFOA ranged from 0.006 to 13.3 µg/L.



Tony Fletcher / Perfoc

[Hoffman et al EHP 2011]

Mean Serum PFOA in 108 users of private contaminated wells for drinking water

Characteristic	*n* (%)	Median serum PFOA [µg/L (interquartile range)]	*p*-Value
Total population	108 (100)	75.7 (31.5–130.5)	
Male	51 (47.2)	82.2 (45.9–164.3)	0.10
Female	57 (52.8)	68.1 (21.0–115.5)	
Grow own vegetables			
No	64 (59.3)	50.7 (24.9–107.3)	< 0.001
Yes	44 (40.7)	91.2 (57.0–145.2)	
Employed at DuPont			
No	94 (87.0)	67.6 (72.2–102.4)	0.11
Yes	14 (13.0)	87.1 (27.4–145.1)	

[Hoffman et al EHP 2011]

Model predictors of serum PFOA in 108 users of private wells.
BCF: Mean biological concentration factor = 141.5 µg/L PFOA in serum per µg/L in drinking water

Table 3. Adjusted[a] robust regression model of serum PFOA.

Covariate	β-Coefficient (95% CI)
Intercept	7.4 (–9.8 to 24.4)
Well PFOA	141.5 (134.9 to 148.1)
Males	18.8 (–1.6 to 39.1)
Age > 65 years	–4.2 (–24.2 to 15.9)
Grow own vegetables	18.4 (–1.3 to 38.1)
Employed at DuPont	5.9 (–24.1 to 36.2)

[a]The inclusion of other covariates (body weight, bottled water consumption, cigarette smoking, and alcohol consumption) did not alter the main associations.

[Hoffman et al EHP 2011]

C8 Science Panel study – results so far cross sectional findings and PFOA

• Uric acid	+ve association
• Birth outcomes	null
• Diabetes	null
• Cholesterol	+ve association
• Age of puberty	delay for girls
• ADHD	null
• Immune markers	-ve for IgA, CRP

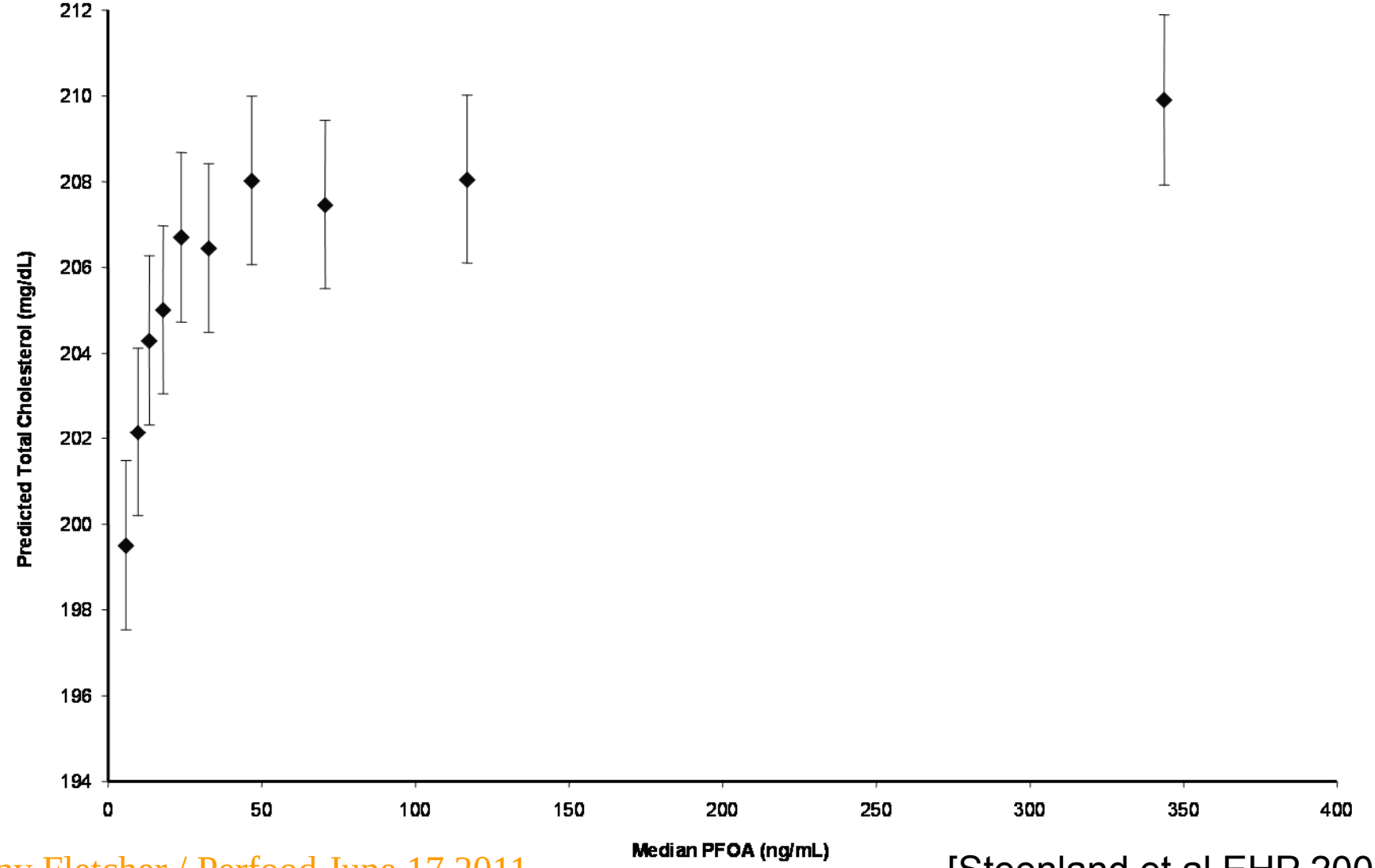
[www.c8sciencepanel.org/study_results.html]

Cholesterol and PFOA

- positively associated with higher PFOA in 10 human studies, six statistically significant
- PFOA not lipophilic, binds with albumin
- Most studies cross-sectional, prohibiting causal inference
- Positive human association opposite direction to animal data, where association is negative

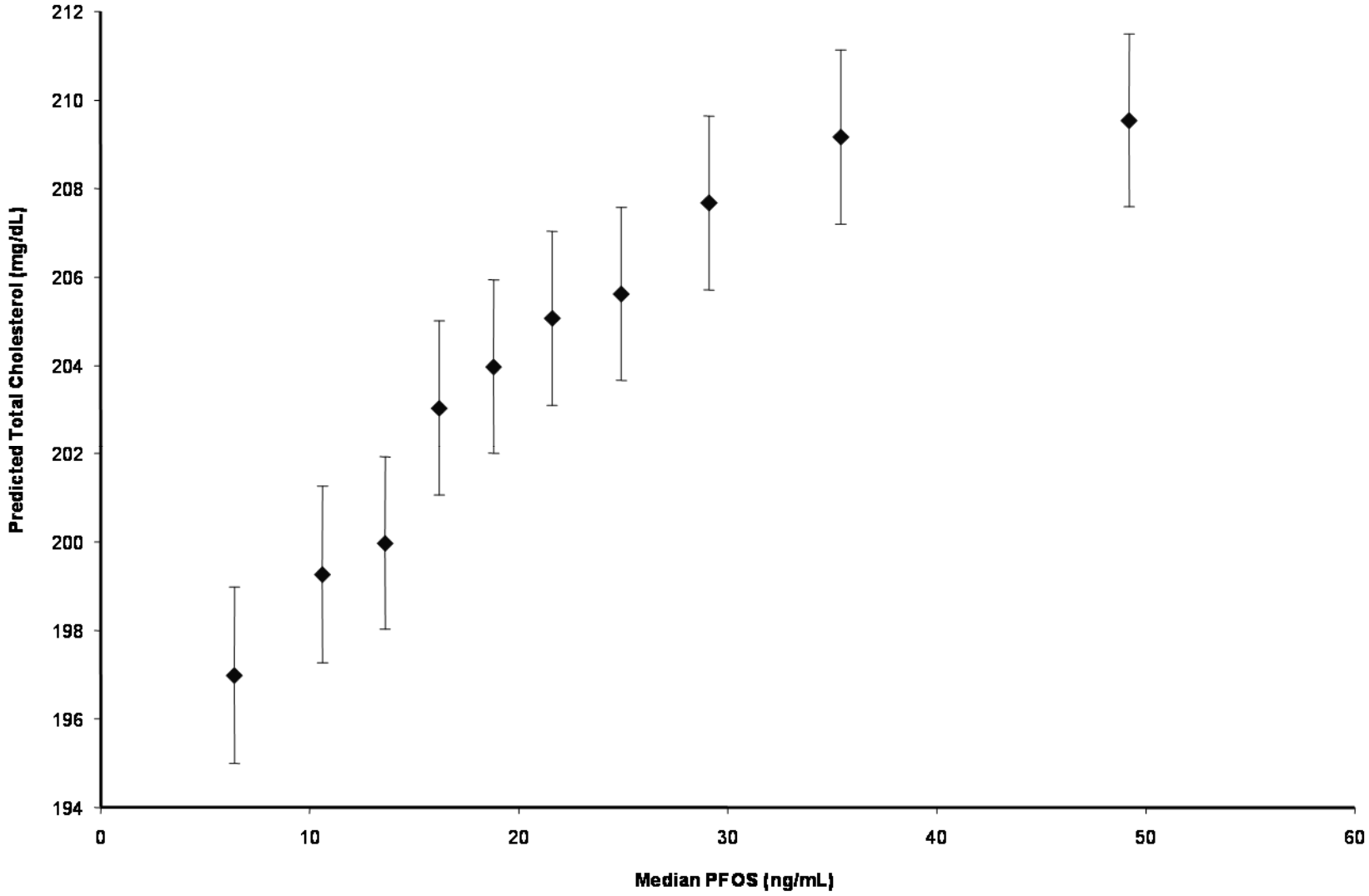
Author, year	Study Description	Number	Mean PFOA	Change in PFOA (ng/mL)	Change in cholesterol (mg/dL)	Slope (assumes linearity)
Olsen et al. 2000	Cross-sectional; workers	54	22,000	~ 22,000	~ 16	0.0007
Olsen et al. 2003	Longitudinal; workers	265	1,500	NA	NA	0.001
Emmett et al. 2006b	Cross-sectional;community; adults	860	354	4,000	22	0.006
Olsen and Zobel 2007	Cross-sectional; workers	371	2,210	NA	NA	0.001
Sakr et al. 2007a	Cross-sectional; workers	1,024	428	1,000	5	0.005
Sakr et al. 2009b	Longitudinal; workers	454	1,130	1,000	1	0.001
Costa et al. 2009	Longitudinal; workers	54	12,000	NA	NA	0.001
Frisbee et al. 2010	Cross-sectional;community; children	12,476	69	400	10	0.03
Nelson et al. 2010	Cross-sectional;community; adults	860	4	5	10	2
Steenland et al. 2009b	Cross-sectional;community; adults	46,294	80	340	11	0.03

Total cholesterol by PFOA decile in mid-Ohio valley adults. Adjusted, n=46,294



[Steenland et al EHP 2009]

Total cholesterol by PFOS decile in mid-Ohio valley adults. Adjusted, n=46,294



[Steenland et al EHP 2009]

Age of puberty

Endocrine Effects

- Estrogen and testosterone levels affected by PFOS and PFOA – in different directions in different species
- Both premature and delayed maturation observed in animals exposed to PFOS & PFOA

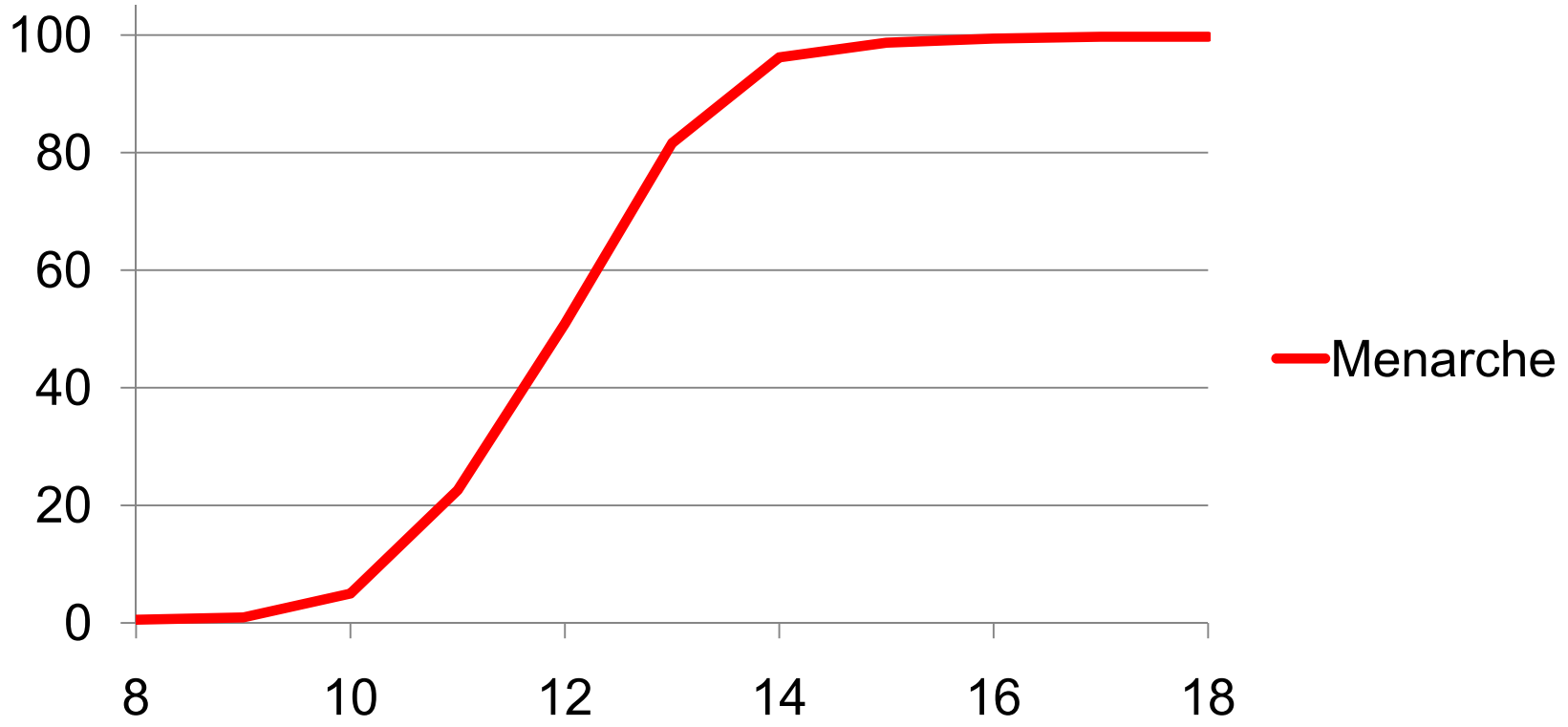
Study Population

- Age range 8-18 years
- 3076 Boys
- 2931 Girls
- with data from community survey on:
  - exact age at interview
  - valid C8 values
  - measured hormones
  - questionnaire data

[Lopez et al ES&T 2011]

Indicators of Puberty: Prevalence of “puberty” by age in girls

Menarche: Question on whether periods had started



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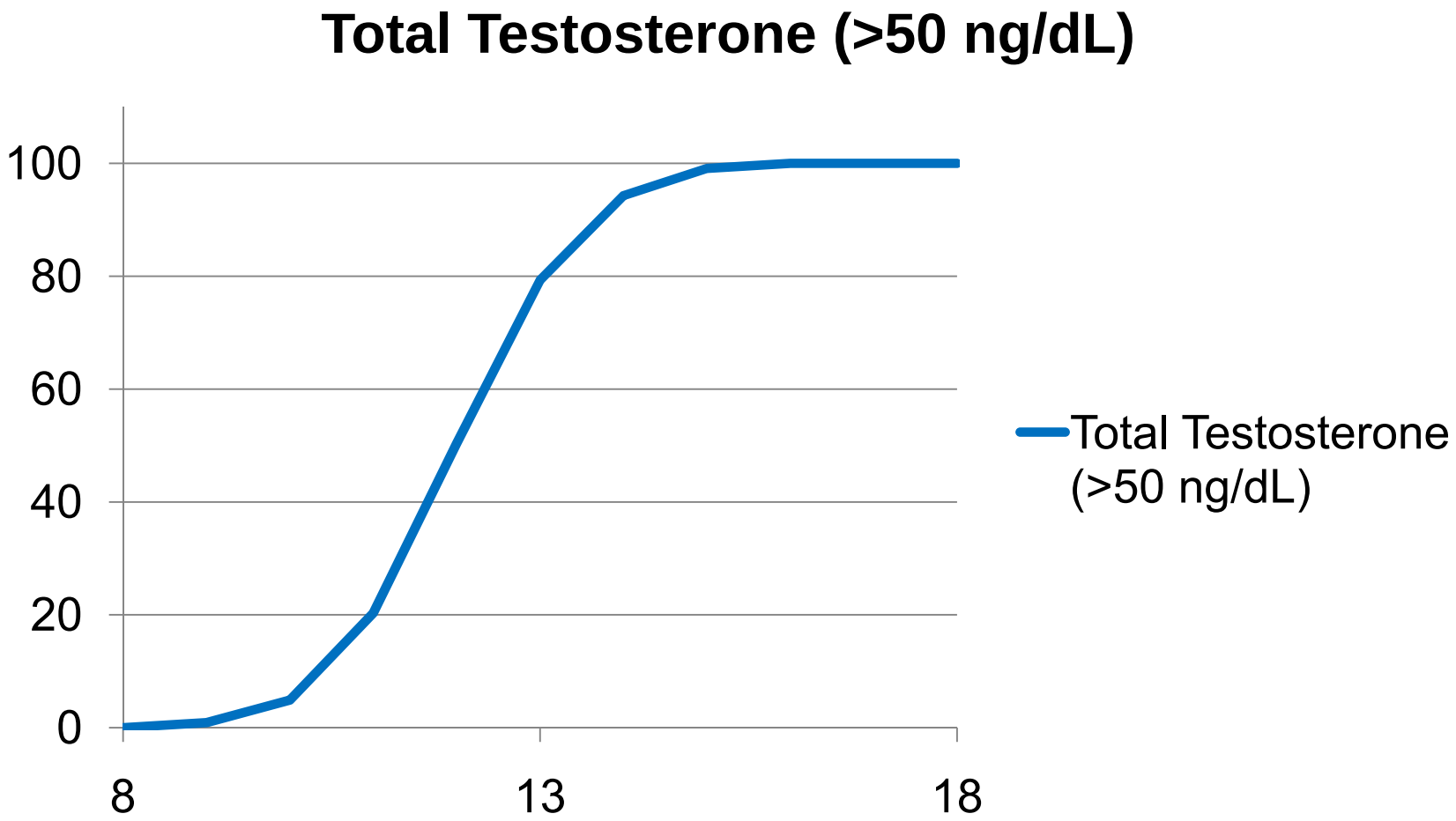
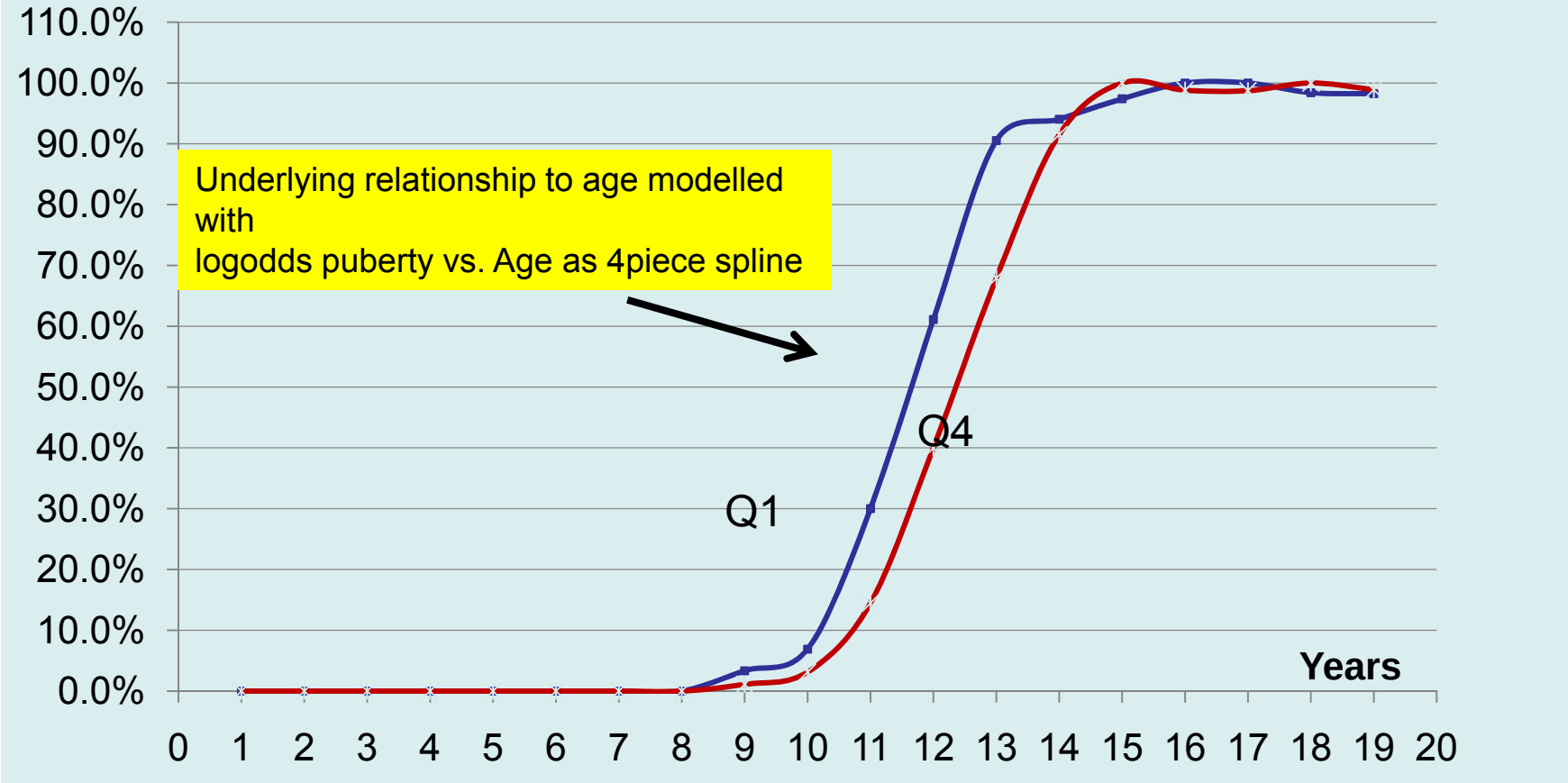
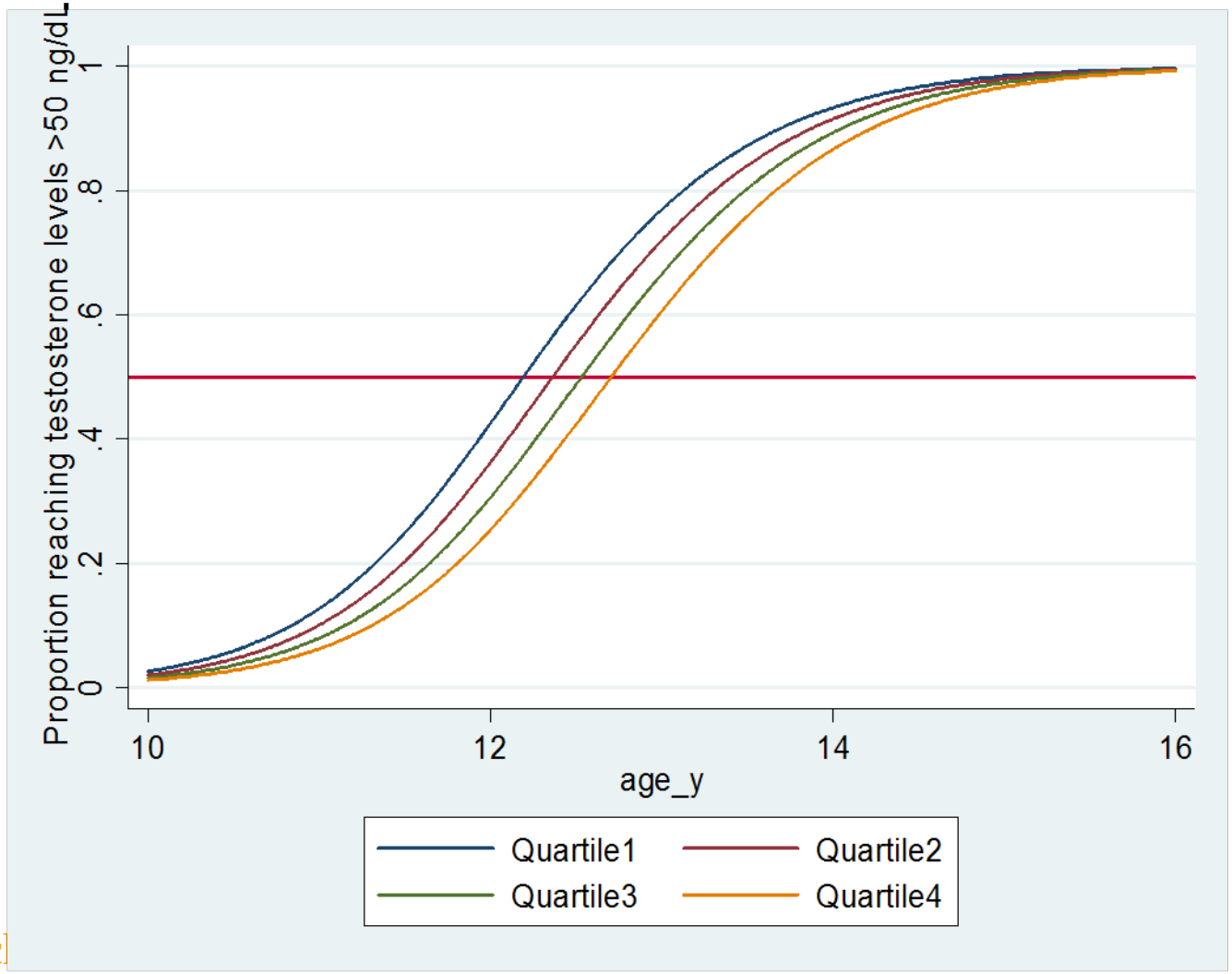


Puberty by age by PFOS quartile



Fitted cumulative frequency of reaching puberty (total testosterone >50ng/dL) by quartile of PFOS. Shift in median age is measure of delay in puberty



Boys: puberty OR & delay: PFOA or PFOS
Total testosterone

	Total testosterone PFOS			Total testosterone PFOA (PFOS in model)		
	OR	**95% CI**	**Days**	**OR**	**95% CI**	**Days**
Q2	0.74	0.46, 1.19	70	1.12	0.71, 1.75	-26
Q3	0.58	0.37, 0.90	131	1.16	0.73, 1.84	-35
Q4	0.46	0.29, 0.71	190	0.88	0.57, 1.37	31
logPFOS/ logPFOA	0.58	0.44, 0.77	130	0.91	0.80, 1.04	23

[Lopez et al ES&T 2011]

Girls: puberty OR & delay: PFOA or PFOS
Menarche

	Menarche PFOS			Menarche PFOA		
	OR	**95% CI**	**Days**	**OR**	**95% CI**	**Days**
Q2	0.72	0.47, 1.10	79	0.54	0.35, 0.84	142
Q3	0.55	0.35, 0.86	141	0.50	0.32, 0.77	163
Q4	0.55	0.35, 0.87	138	0.57	0.37, 0.89	130
logPFOS/ logPFOA	0.60	0.43, 0.83	120	0.83	0.73, 0.95	42

[Lopez et al ES&T 2011]

Conclusions

- Delay in puberty average 4-6 months in relation to interquartile shift in PFOS
- Evident for boys and girls (girls only for PFOA)
- But exposure estimated was at/after age of puberty so can not be sure of direction of causality
- Further work planned on linking age of puberty to measures of pre-pubertal and in-utero PFC exposure in this population

ADHD in children in relation to PFAS, n=10,546, aged 5-18

	ADHD Diagnosis			
	No.	Crude	Adjusted[a]	
Serum PFC, ng/mL	Cases	OR	OR	95% CI
PFOA				
Q1: 0.6 – <13.0	327	1.00	1.00	
Q2: 13.0 – <28.2	364	1.14	1.10	0.94, 1.30
Q3: 28.2 – <65.3	337	1.04	0.98	0.83, 1.15
Q4: 65.3 – 2070.6	275	0.83	0.76	0.64, 0.90
PFOS				
Q1: 0.25 – <14.8	299	1.00	1.00	
Q2:14.8 – <20.2	321	1.06	0.99	0.83, 1.17
Q3: 20.2 – <27.9	318	1.06	0.96	0.81, 1.14
Q4: 27.8 – 202.1	365	1.22	1.09	0.93, 1.29
PFHxS				
Q1: 0.25 – <2.9	258	1.00	1.00	
Q2: 2.9 – <5.2	304	1.32	1.27	1.06, 1.52
Q3: 5.2 – <10.1	364	1.49	1.43	1.21, 1.70
Q4: 10.1 – 276.4	377	1.59	1.53	1.29, 1.83

[Stein et al EHP 2011]

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REVIEW OPEN ACCESS

Epidemiologic Evidence on the Health Effects of Perfluorooctanoic Acid (PFOA)

Article

Kyle Steenland[1], Tony Fletcher[2], David A. Savitz[3]
1 Rollins School of Public Health, Emory University, Atlanta, Georgia, USA, **2** London School of Hygiene and Tropical Medicine, London, United Kingdom, **3** Mount Sinai School of Medicine, New York, New York, USA

Jump to
Abstract

CONCLUSIONS: Epidemiologic evidence remains limited, and to date data are insufficient to draw firm conclusions regarding the role of PFOA for any of the diseases of concern.

[Steenland et al EHP 2010]

Birthweight

- Seven studies of birthweight in relation to PFOA serum levels
- Two showed significantly lower birthweight with higher PFOA, two showed similar but not significant results, while three were negative.
- Most were done at low general population PFOA levels and causality cannot be deduced due to cross sectional design.

Fertility

- Two reports from Denmark (general population) indicate decreased fertility with higher PFOA or PFOS, and decreased semen count with higher PFOA

- One report from mid-Ohio valley showed no association with miscarriage and a modest association with pre-eclampsia, but is limited by small numbers

Heart disease

- Data sparse in humans
- One worker mortality study showed positive trends with PFOA with 10-year lag (p=0.06)
- Second worker mortality study showed no association

Cancer

- PFOA causes pancreatic, testicular, liver, and perhaps breast tumors in rodents, but is not genotoxic/mutagenic
- Human data sparse. Two worker cohort mortality studies show no consisted cancer excesses but numbers are small. A borderline-significant kidney cancer excess in one study.
- Danish population based study shows no strong trends at low general population exposure levels; prostate and pancreatic cancer show some positive but not significant trends.

C8 Science Panel study – results over next 12 months, mainly longitudinal results including:

- Cancer
- Heart disease
- Liver, Kidney,Thyroid disease
- Infections
- Birth outcomes
- Neurobehavioural function in children
- Kidney, liver and thyroid function
- Longitudinal changes in clinical markers
- Endocrine and other effects in relation to in utero exposure
- Immune and inflammatory markers
- Gene-PFOA interactions

Funding is acknowledged from the C8 Class Action Settlement Agreement between DuPont and Plaintiffs (Circuit Court of Wood County, West Virginia, 2004). Funds are administered by an agency that reports to the Court. The C8 Science Panel, this research and its conclusions are independent of either party to the lawsuit.

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Mike Luster
David Savitz
Kyle Steenland
Veronica Vieira

Thank you

see results on website:

www.c8sciencepanel.org