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Characterisation of human exposure pathways to perfluorinated compounds - comparing exposure estimates with biomarkers of exposure

6th POPs Network Conference

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Norwegian Institute of Public Health

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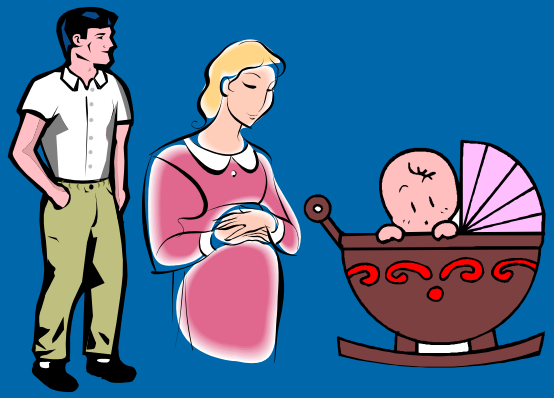
Outline



- Background
- Aim
- Studies and samples
- Results
- Future perspectives

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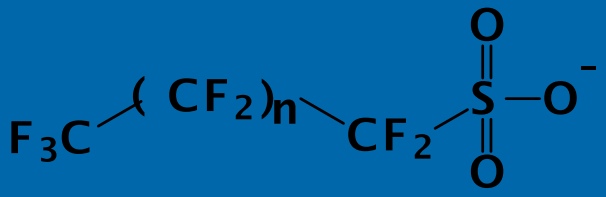
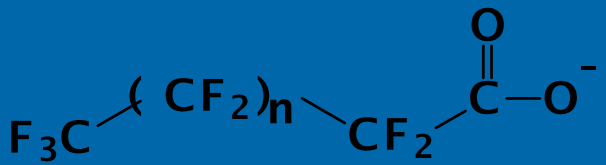
Perfluorinated compounds (PFC)

Perfluoroalkyl sulfonates (PFSAs)



Perfluoroalkyl carboxylates (PFCAs)



<u>Precursors of PFCs</u>

- Fluortelomer alcohols (FTOHs)
- Perfluoralkyl sulfonamides (FOSAs)
- Perfluoroalkyl sulfonamidoethanol (FOSEs)

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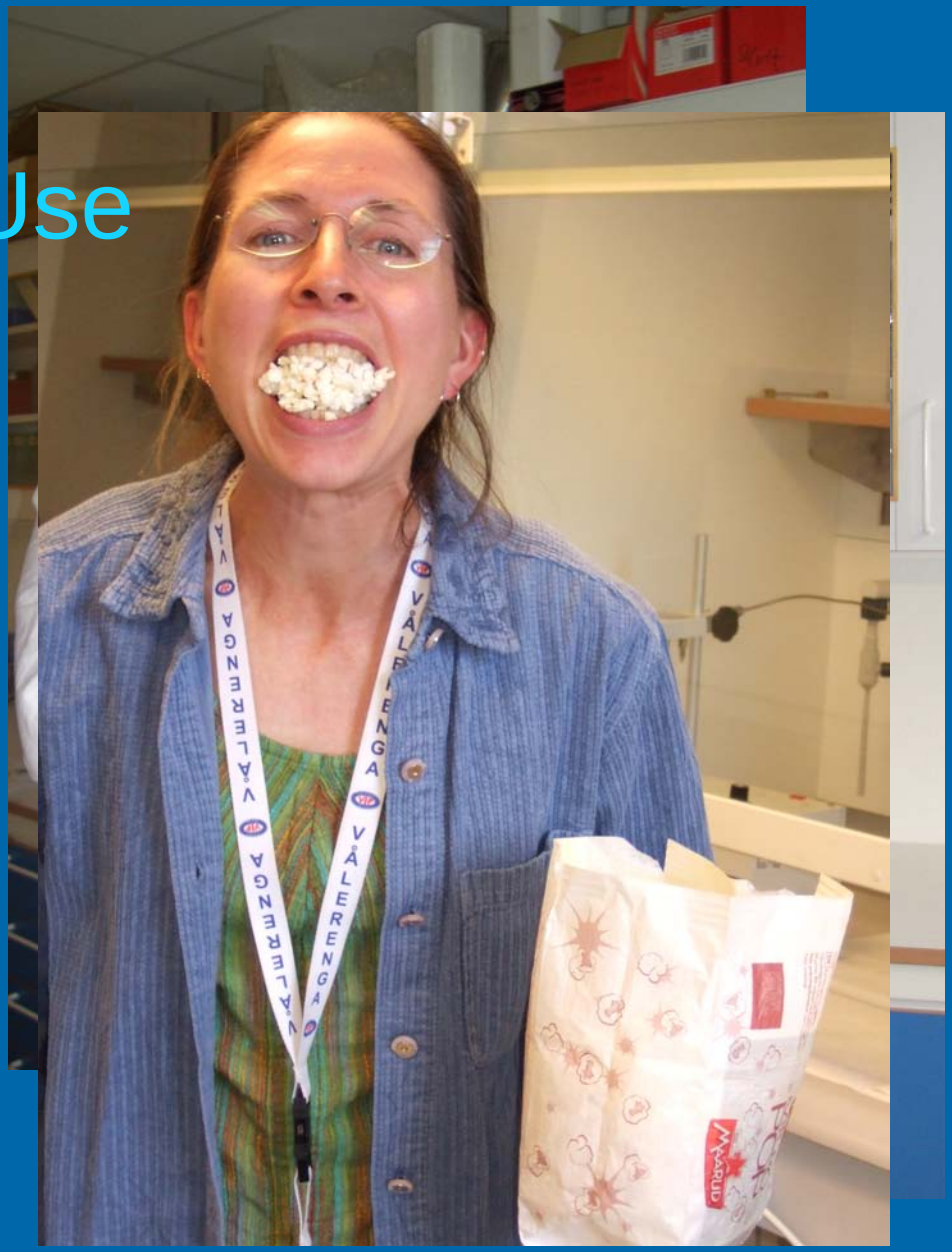
Use



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Toxicokinetics

- Readily absorbed (oral, inhalation)
- Associated to proteins (e.g. serum albumin)
- Highest concentrations in blood and liver
- Not metabolised
- Excreted primarily via urine
- Long elimination half-lives in humans (2-7 years)

PFCs have been found in human blood world-wide

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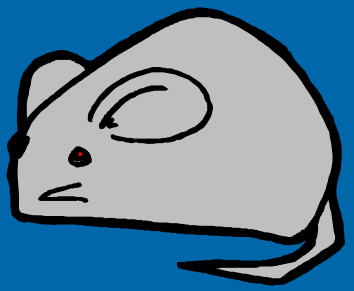
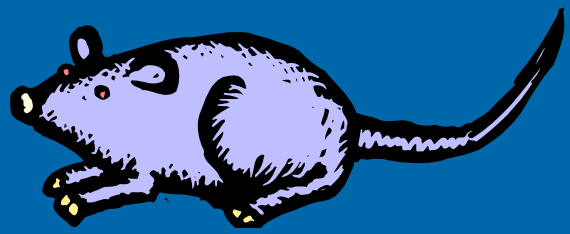
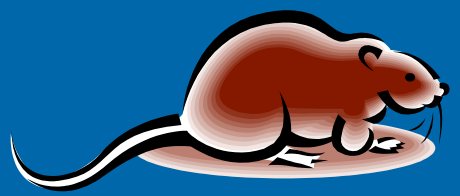
Toxicity – animal studies

- hepatotoxicity
- immunotoxicity
- developmental toxicity
- neonatal mortality
- hormonal effects







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Adverse health effects - in humans

- Several epidemiological studies conducted
- For example : diabetes, cardiovascular diseases, cholesterol level, thyroid function, immune function, liver and kidney function, reproductive and developmental outcomes
- Findings are not consistent
- Need for more studies!

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Do to their toxicokinetic properties and the observed adverse effects, PFCs are of concern

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Risk assessment

How frequent and to what extent are we exposed to PFCs?

Hazard identification

Dose-response determination

Exposure assessment

Risk characterisation

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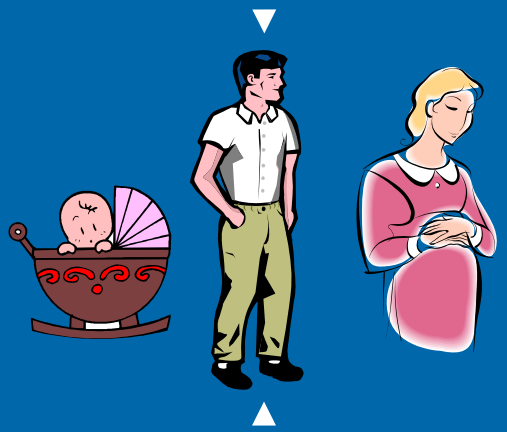
Exposure pathways to PFCs

Air

Breast milk

In utero



Diet

Dust

Dermal contact

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Exposure

PFOA

Precursors to PFOA

Metabolism of precursors of PFOA

Degradation in the environment

PFOA

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Exposure assessment - external dose

Exposure factors

- Measuring concentrations in delivering media, e.g. food and dust
- Combine with exposure factors (e.g. food consumption or inhalation rate)
- Calculate total intake

- Compare different exposure pathways
- Important for selecting appropriate actions

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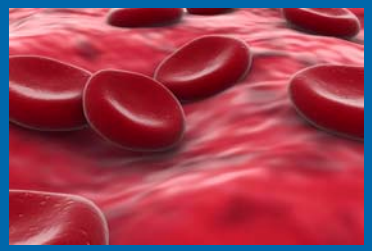
Exposure assessment - internal dose

- Measure chemicals in biological matrices such as blood, breast milk, urine (biomonitoring)
- Combine with knowledge on distribution in the body
- Calculate body burden (total amount in the body)

- Integrated exposure over time
- Take individual differences into consideration (e.g. age and gender)



Distribution

Half-life

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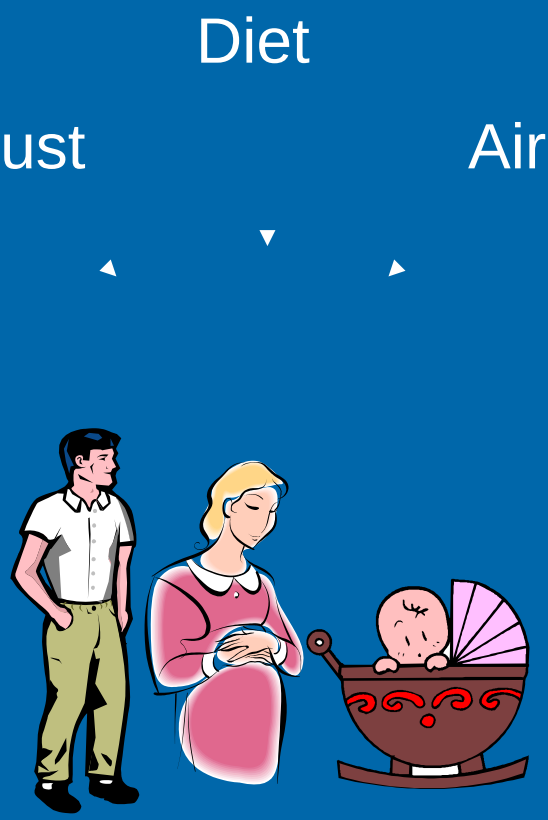
Principal objective

To characterise different human exposure pathways of PFCs by comparing estimates of exposure from diet, indoor air and house dust with biomarkers of exposure



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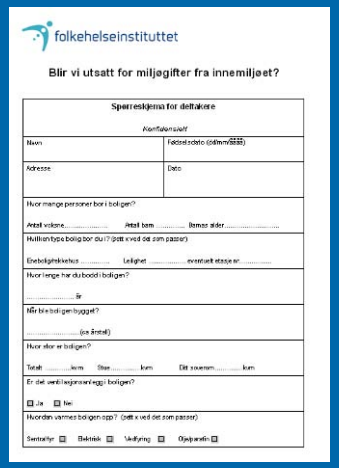
BROFLEX study

questionnaire


folkehelseinstituttet

Blir vi utsatt for miljøgifter fra innemiljøet?

Spørreskjema for deltakere

Kontrollspørsmål

Navn	Fødselsdato (ddmmyy)
Adresse	Dato

Hvor mange personer bor i boligen?

Antall voksne..... Antall barn ..... Barnas alder.....

Hvilken type bolig bor du i? (sett kryss på det som passer)

Enebolig/rekkehus ..... Leilighet ..... eventuelt etasje nr .....

Hvor lenge har du bodd i boligen?

..... år

Når ble boligen bygget?

..... (se Årstall)

Hvor stor er boligen?

Totalt ..... kvm Stue..... kvm Ditt soverom..... kvm

Er det ventilasjonsanlegg i boligen?

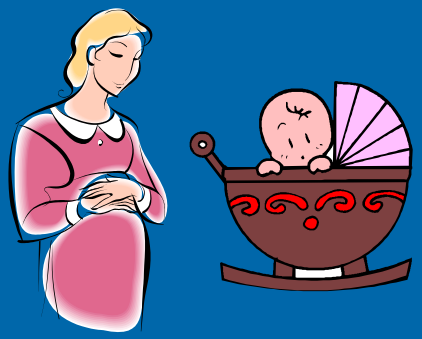
☐ Ja ☐ Nei

Hvordan varmes boligen opp? (sett x ved det som passer)

Sentralfyr ☐ Elektrisk ☐ Vedfyring ☐ Oljekjel/ovn ☐

dust

air

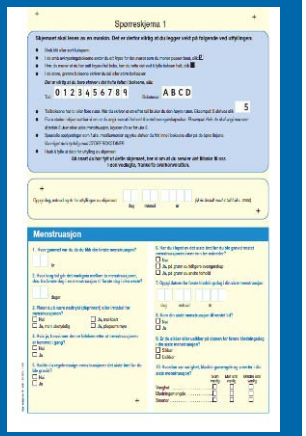


n = 41

beverages

food

questionnaire


Spørreskjema 1

Menstruasjon

blood

breast milk

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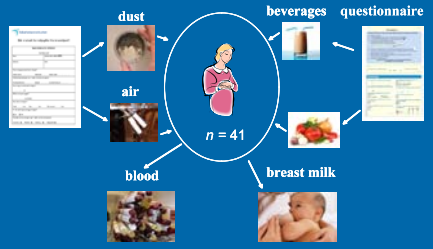
Studies

BROFLEX study



Time trends:

pools of serum, males, 40-50 years, 1977-2006

Levels in food:

pools, 21 types of food and beverages

Which food and predictors:

175 serum samples, FFQ

Levels in breast milk:

longitudinal samples, up to 12 months, 10 mothers

Levels in cord blood:

plasma from mother at birth and cord plasma, 123 pairs

Not part of my Thesis

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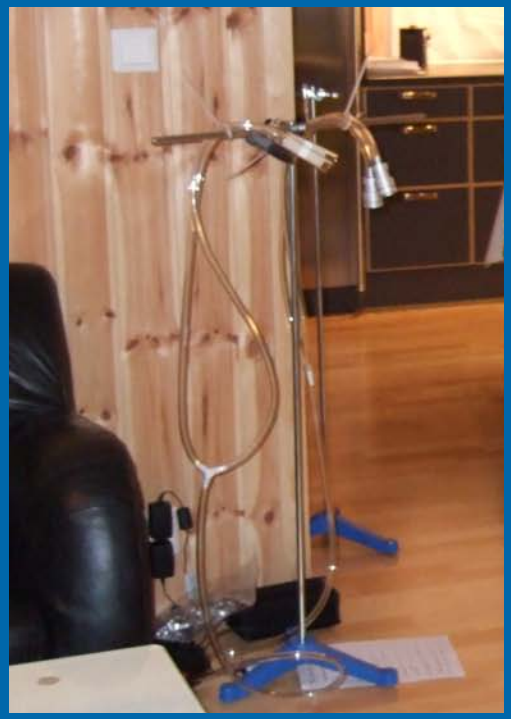

Sampling

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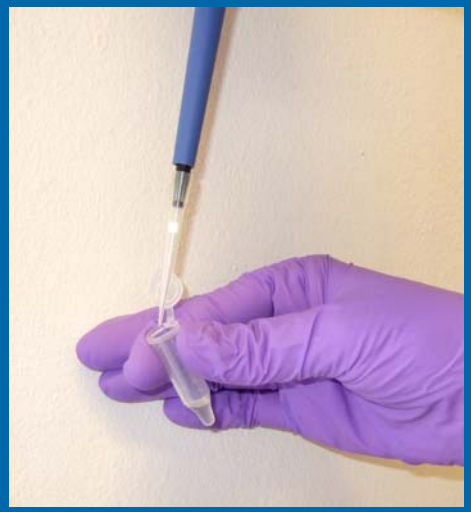
Methods for PFCs i plasma/serum and breast milk

blood/breast milk +

internal standard +

methanol/acetonitrile

mixing +
centrifugation +
dilution



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Column switching LC-MS/MS

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Summary of method validation

- High sensitivity
- High repeatability and accuracy
- Suitable for large sample series:
  - Low sample volume 150 - 200 µl
  - High capacity (100 samples per week)
  - Low operational costs

Haug et al., J. Chromatogr A. 1216 (2009), 385-393
Thomsen et al. Environ. Sci. Technol. 44 (2010), 9550-9556

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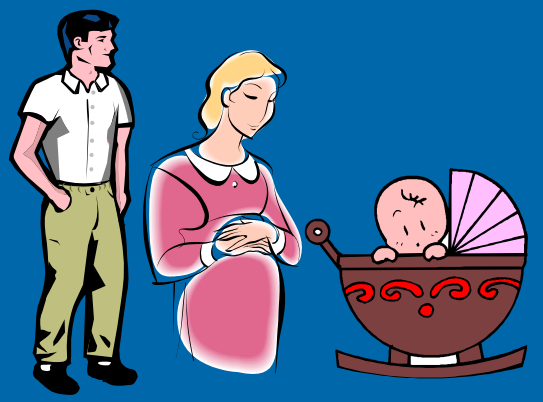
Results



- Internal dose
  - Levels in blood and breast milk
- External dose
  - Adults
  - 6 months old infants
- Comparison of external and internal doses
  - Associations
  - PK modeling

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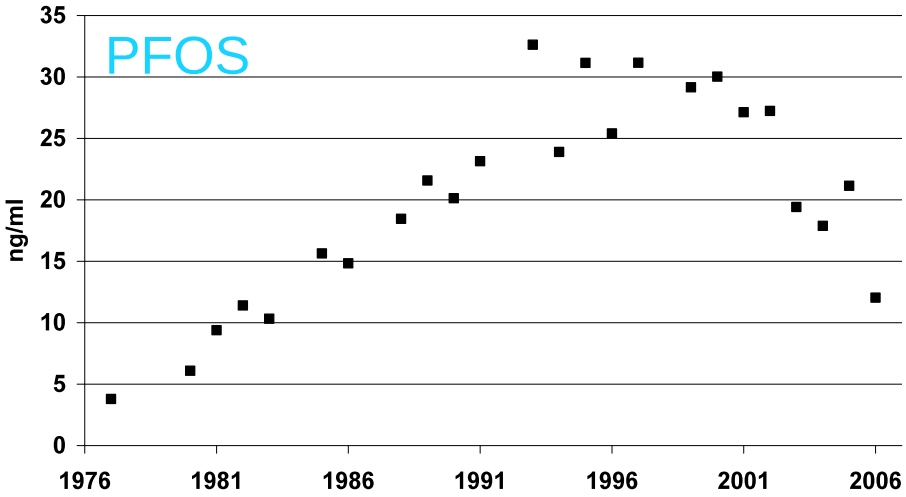
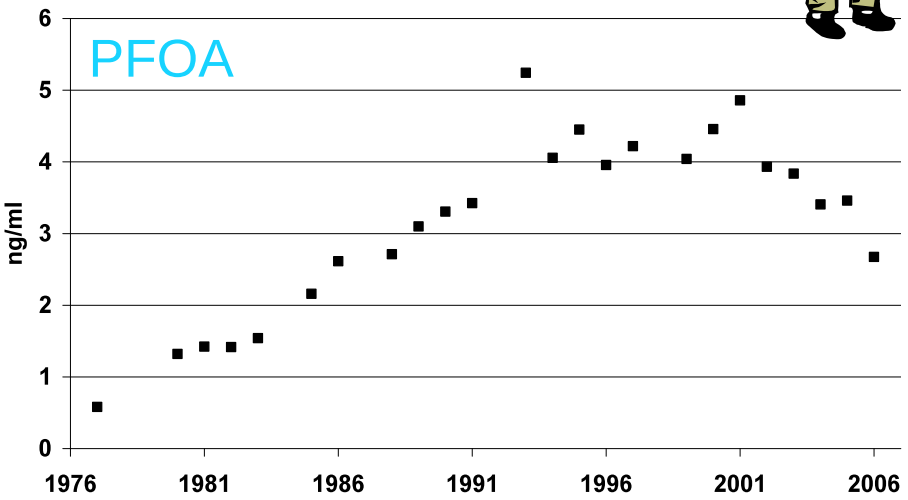
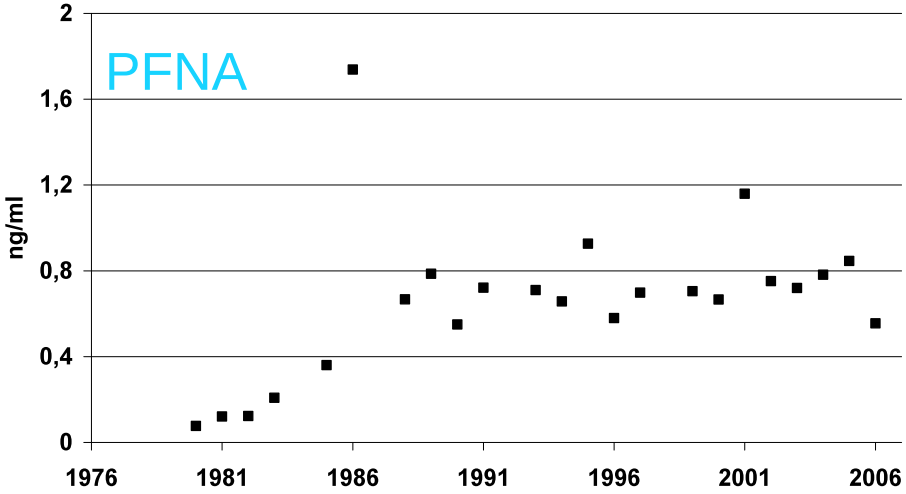
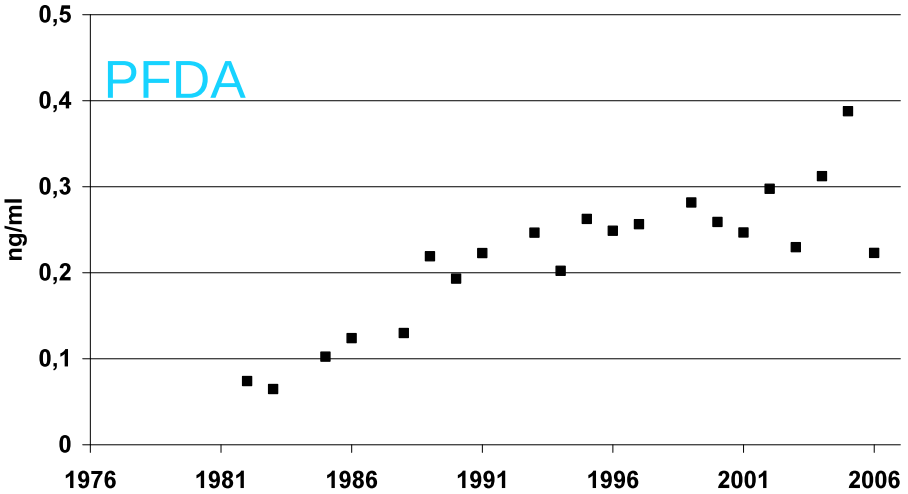
Time trends - blood









Haug et al. Environ. Sci. Technol. (2009) 43. 2131-2136

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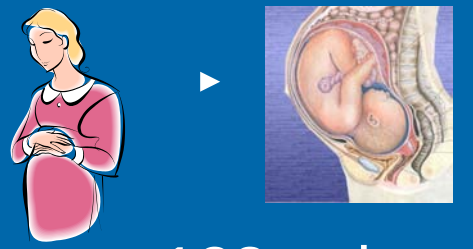
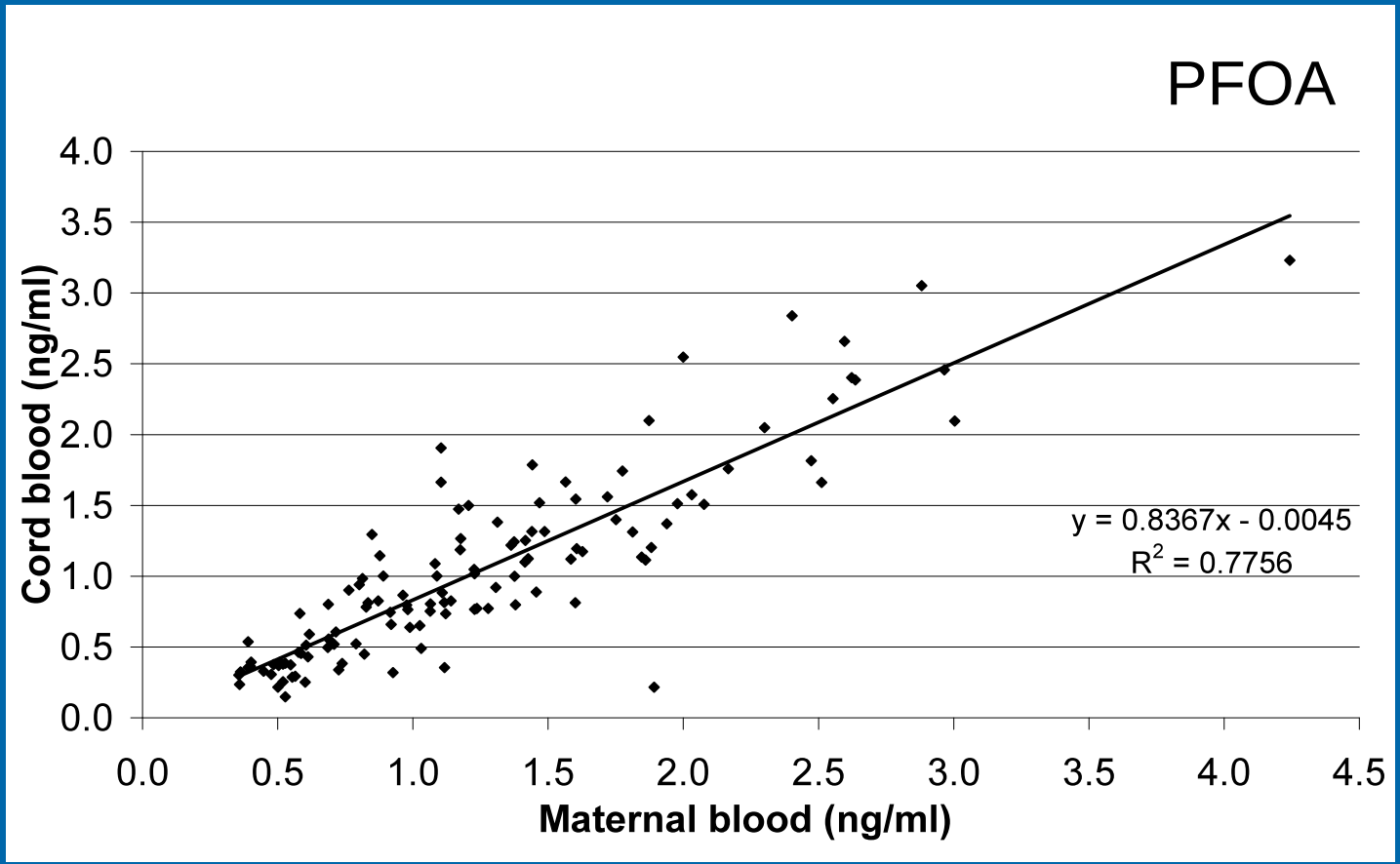


In *utero* exposure

n=123 pairs



Gutzkow et al. Int. J. Hyg. Environ. Health (2011), doi:10.1016/j.ijheh.2011.08.011.

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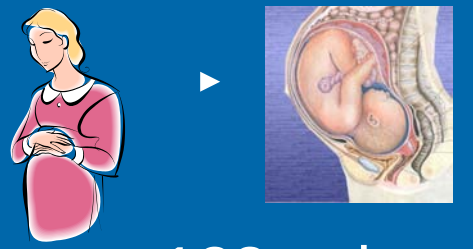

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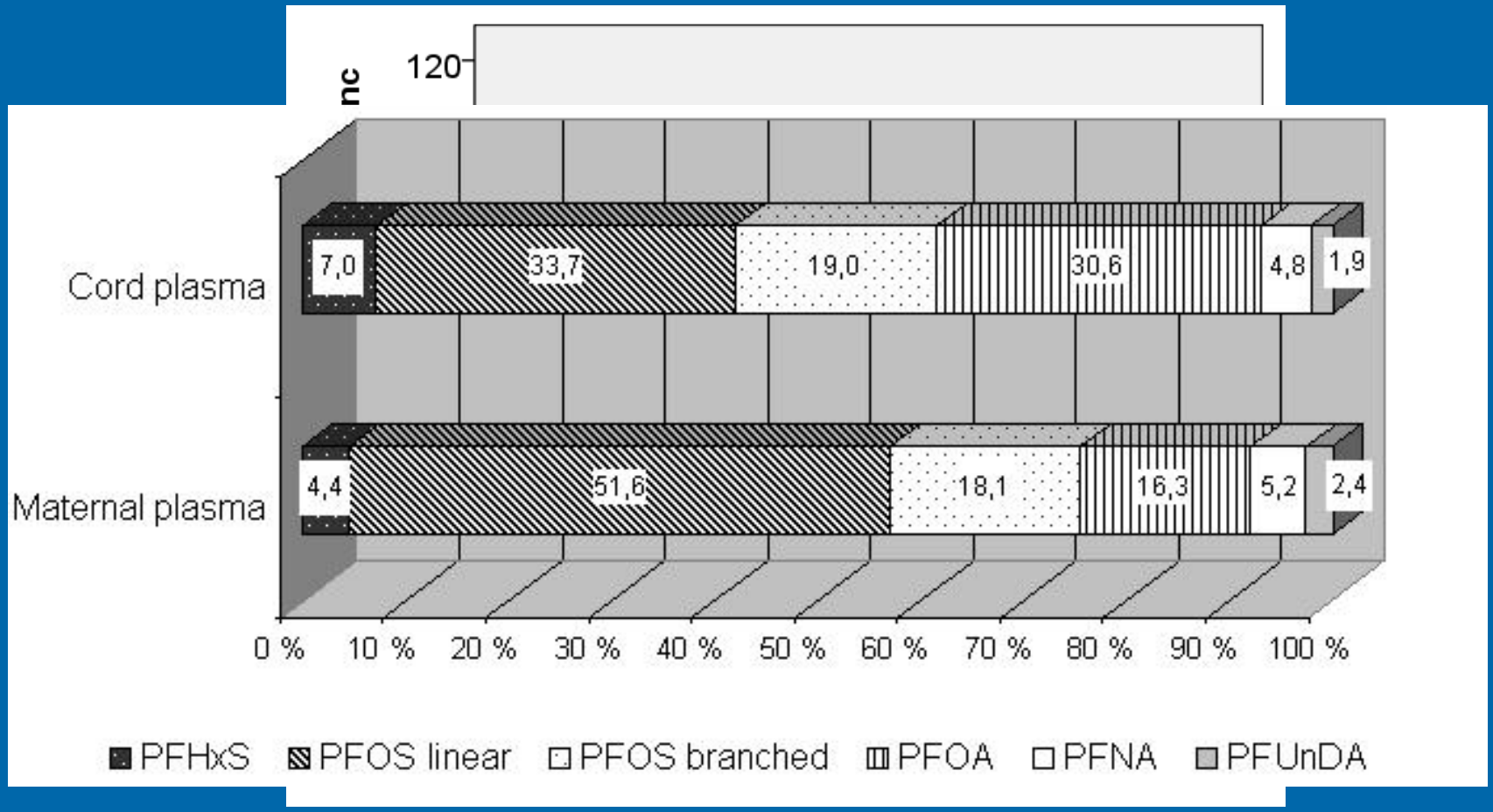

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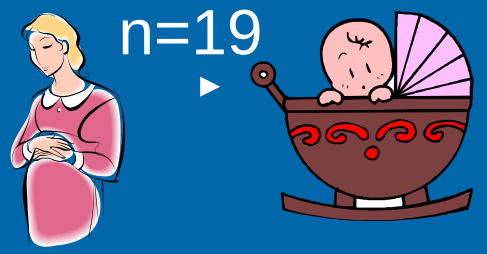
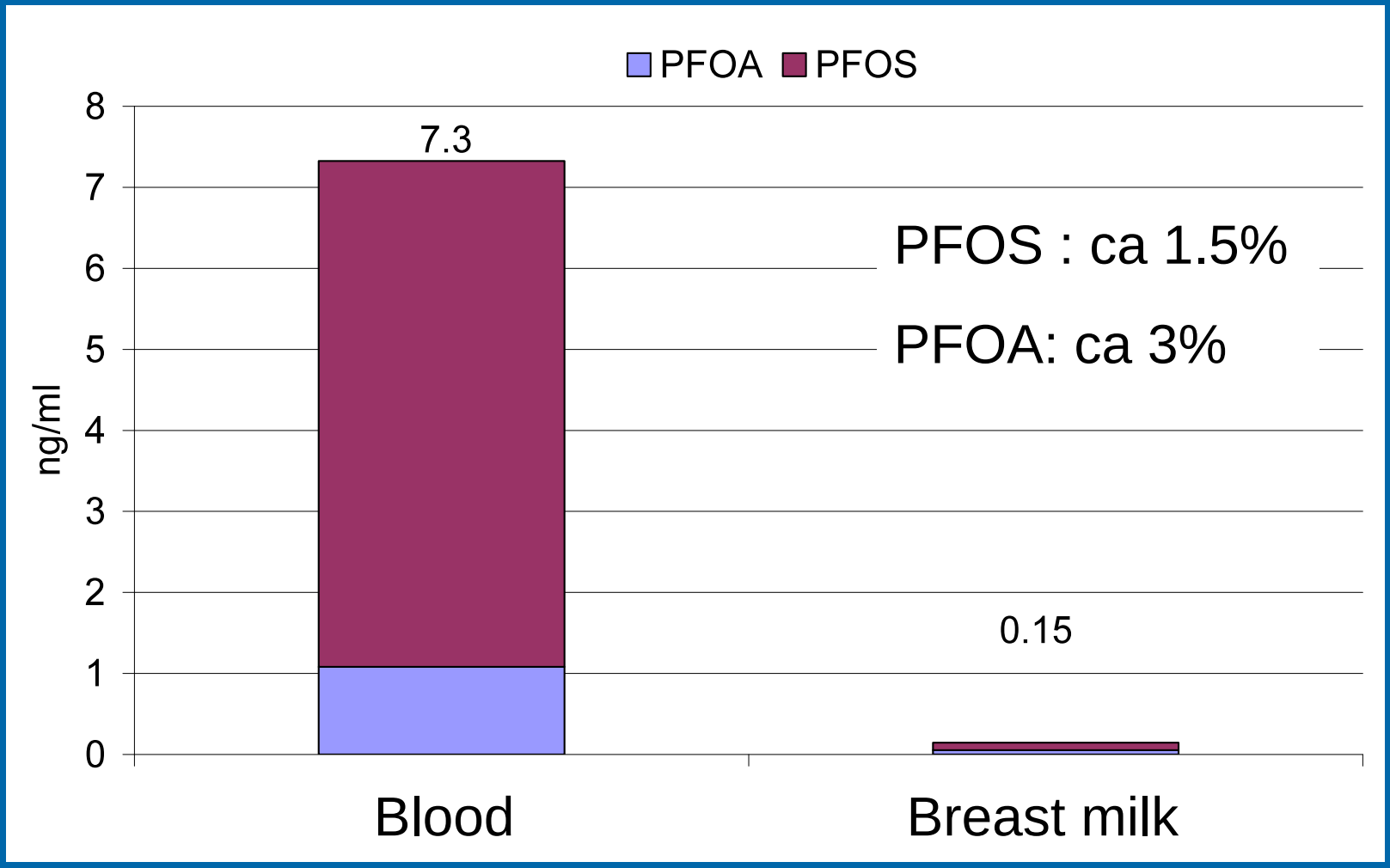


Blood vs breast milk



Haug et al. Environ. Int. (2011) 37, 687-693

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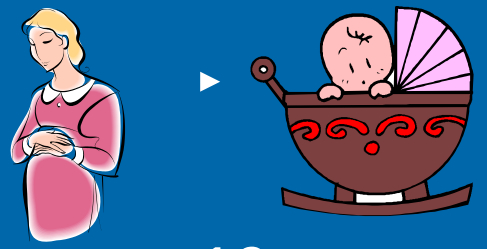
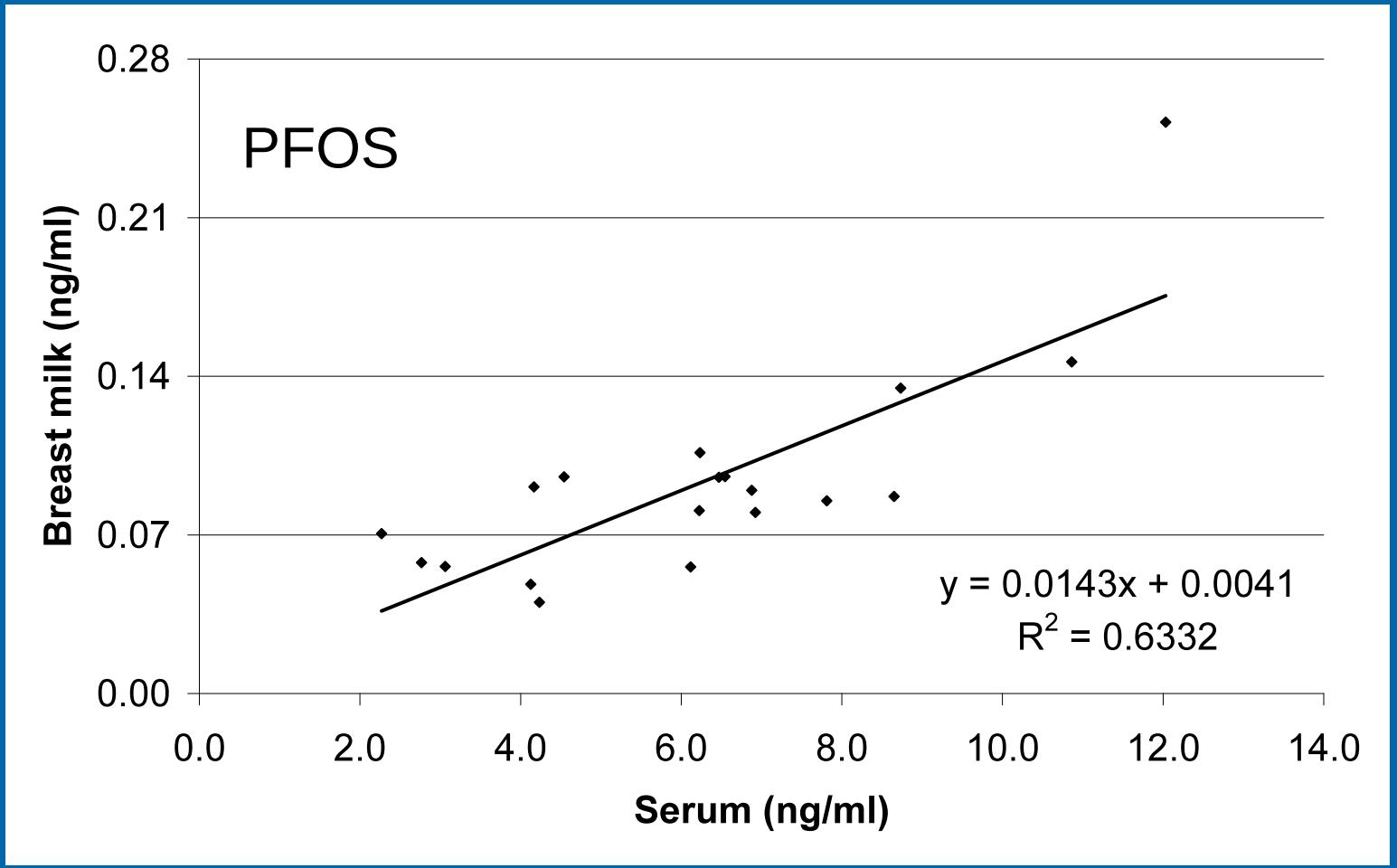
Blood vs breast milk



n=19



Haug et al. Environ. Int. (2011) 37, 687-693

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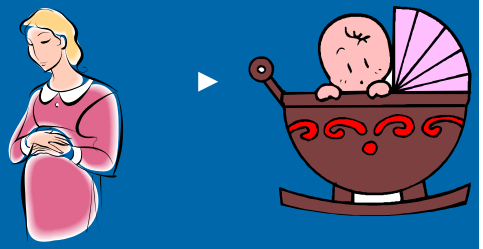
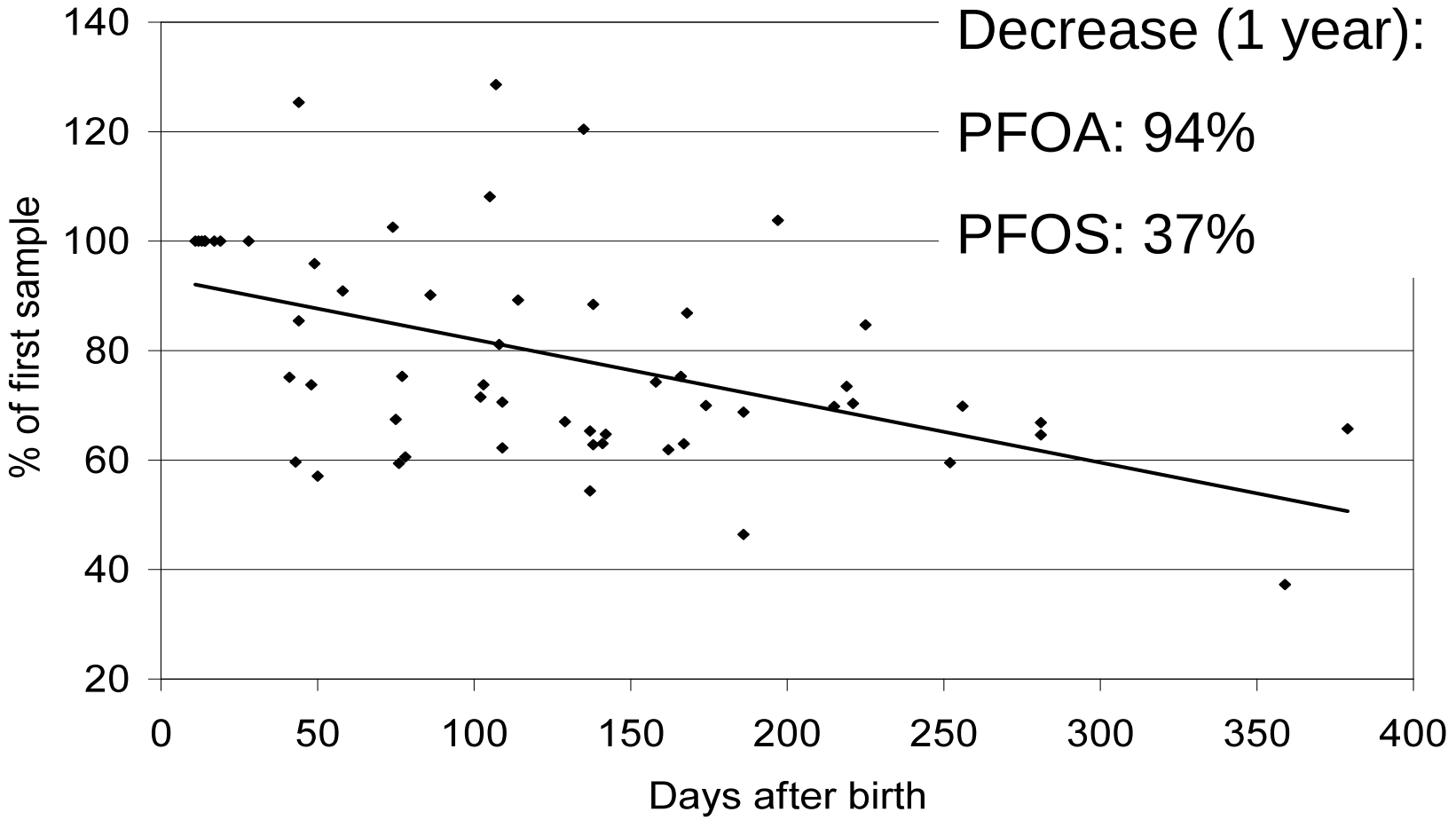
Breast feeding period





Thomsen et al. Environ. Sci. Technol. 44 (2010), 9550-9556

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Internal dose

- PFCs are found in blood
- PFCs are transferred to the fetus through the placenta
- PFCs are found in breast milk

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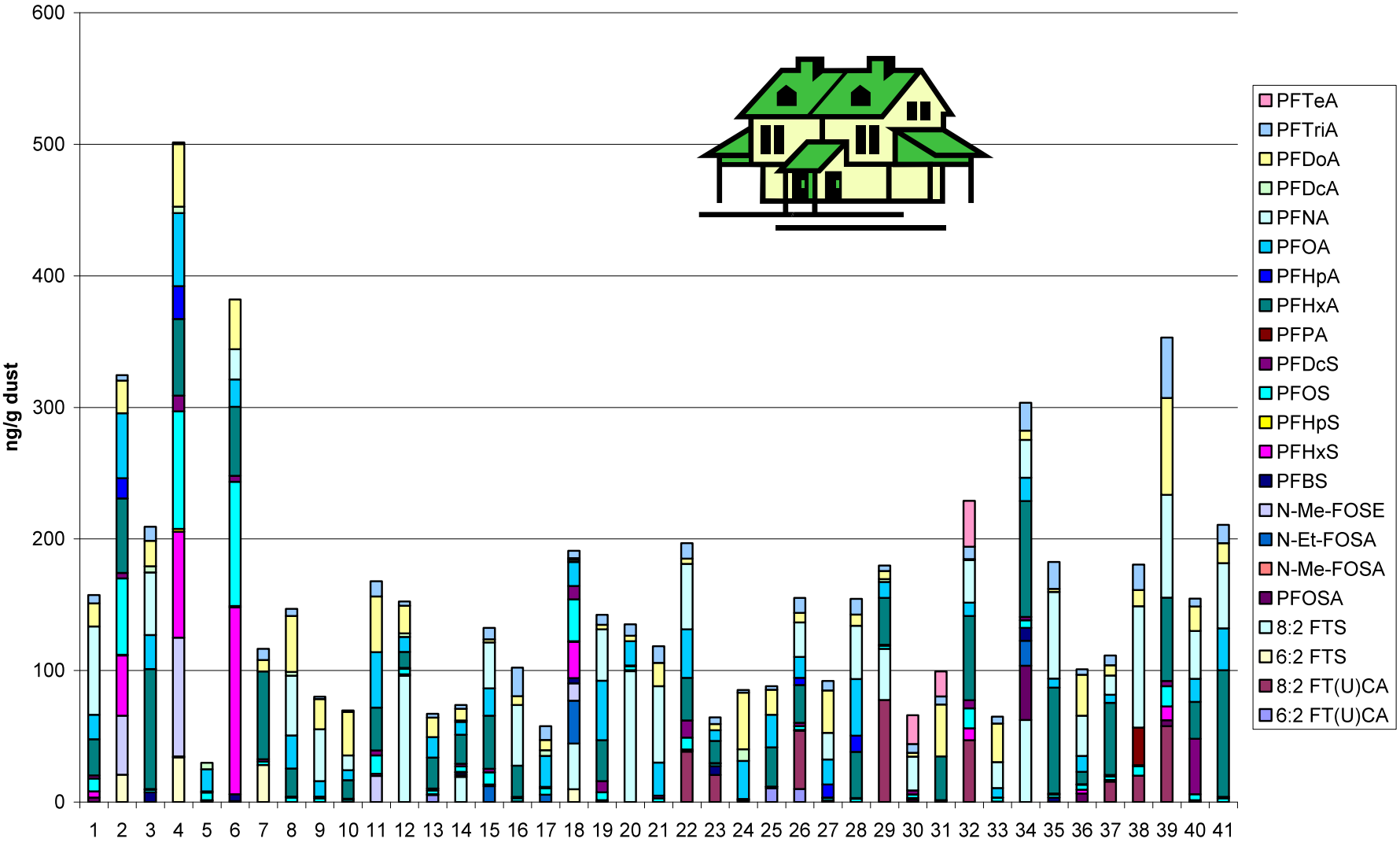
Levels in house dust



Haug et al. Environ. Sci. Technol. (2011), 45, 7991-7998

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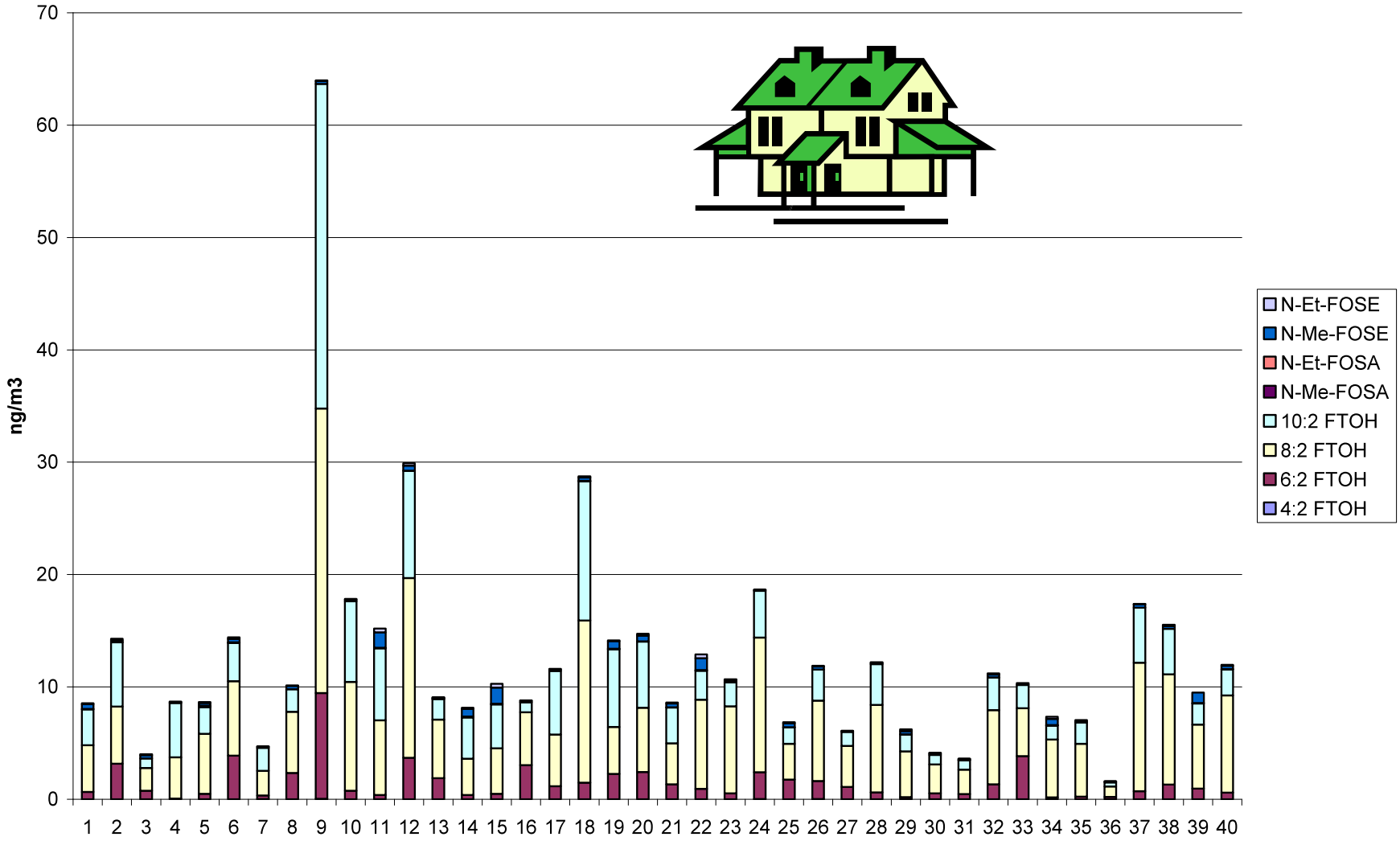
Levels in indoor air



Haug et al. Environ. Sci. Technol. (2011), 45, 7991-7998

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PFCs in indoor air vs house dust

- FOSA/FOSEs in air were significantly correlated to PFSAs in dust
- No significant correlations between FTOHs in air and PFCAs in dust

Haug et al. Environ. Sci. Technol. (2011), 45, 7991-7998

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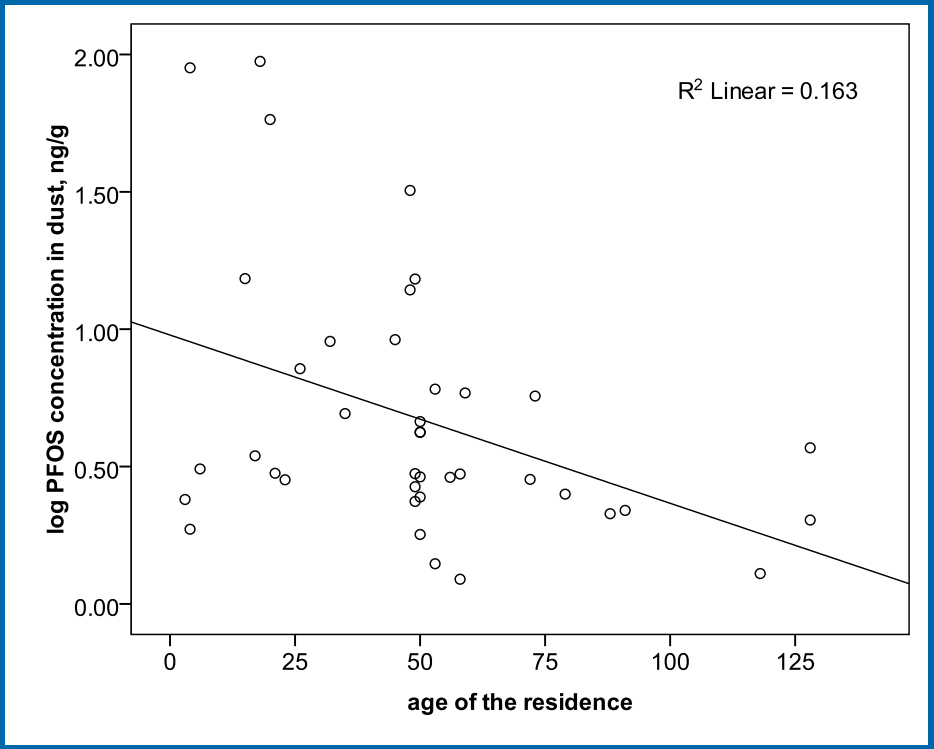
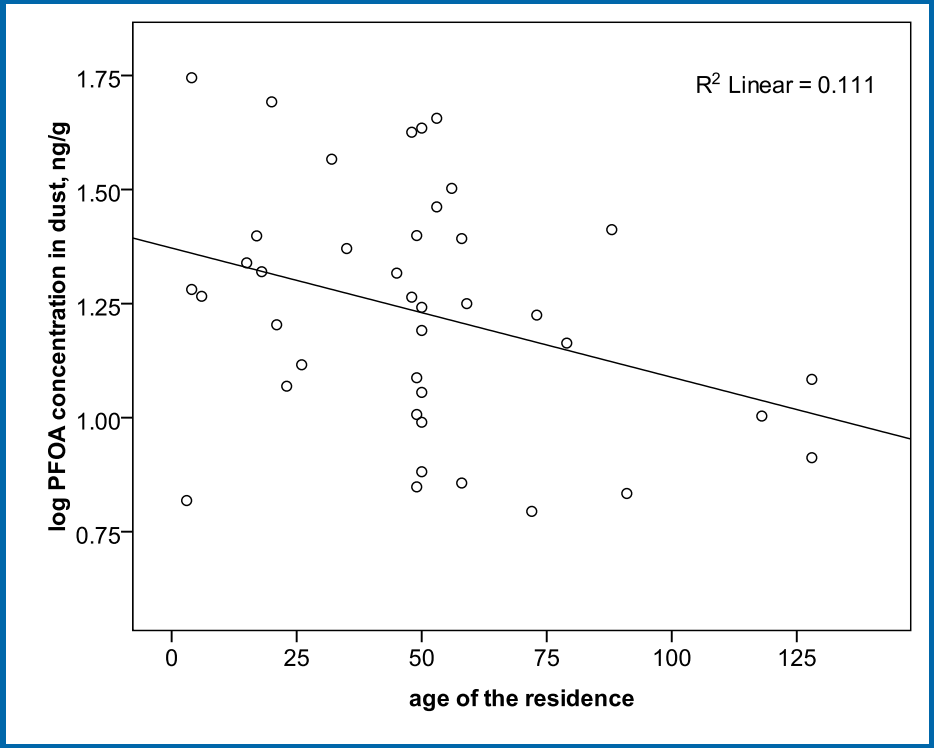
Predictors of PFCs in indoor air/house dust

PFOS



PFOA



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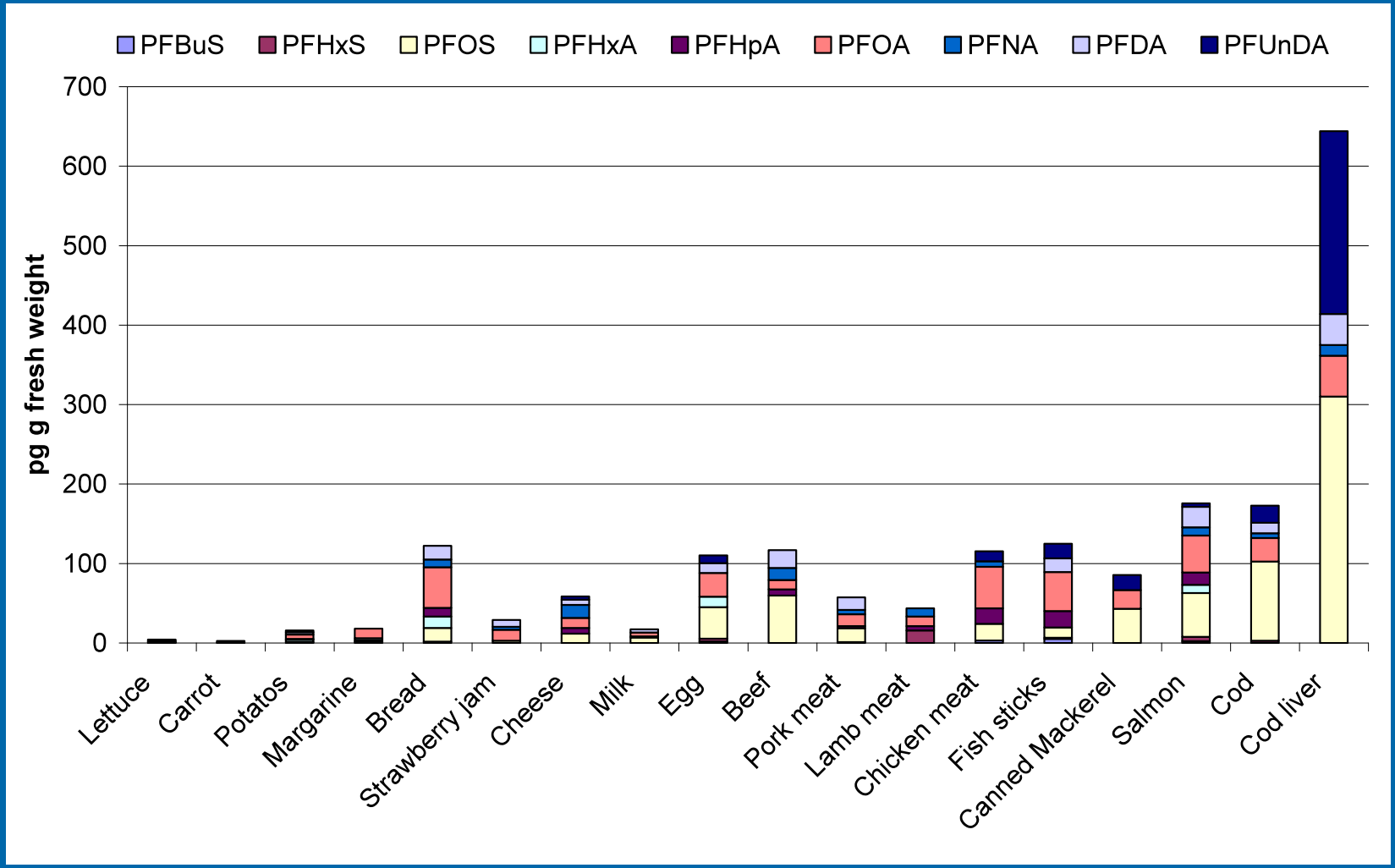
Levels in food and beverages



Haug et al. Chemosphere (2010) 80. 1137-1143

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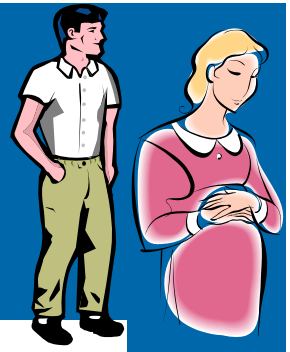
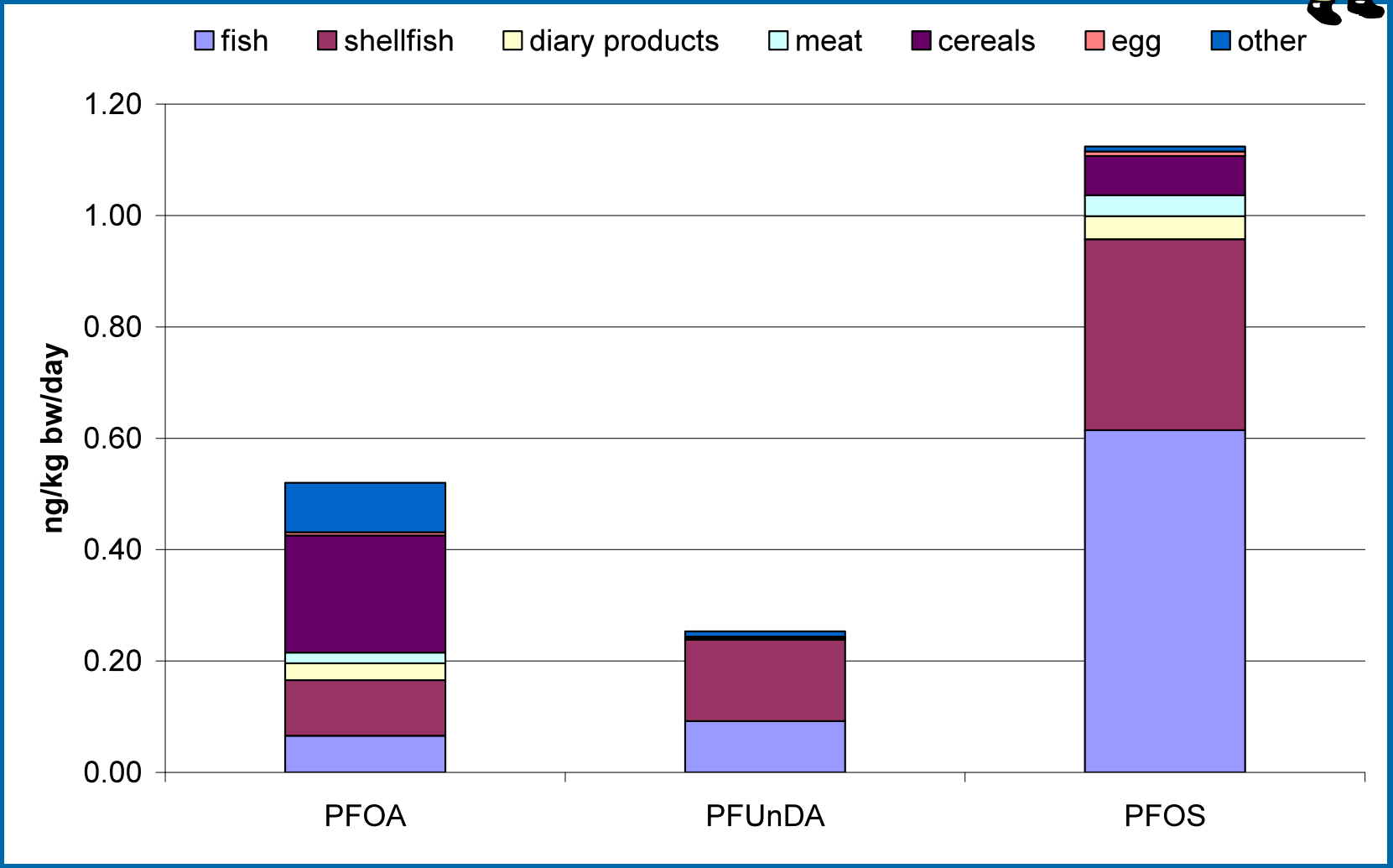
Intake of PFCs from the diet





Haug et al. Environ. Int. (2010) 36. 772-778.

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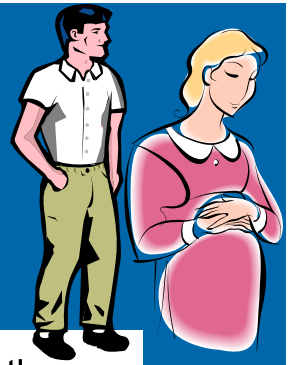
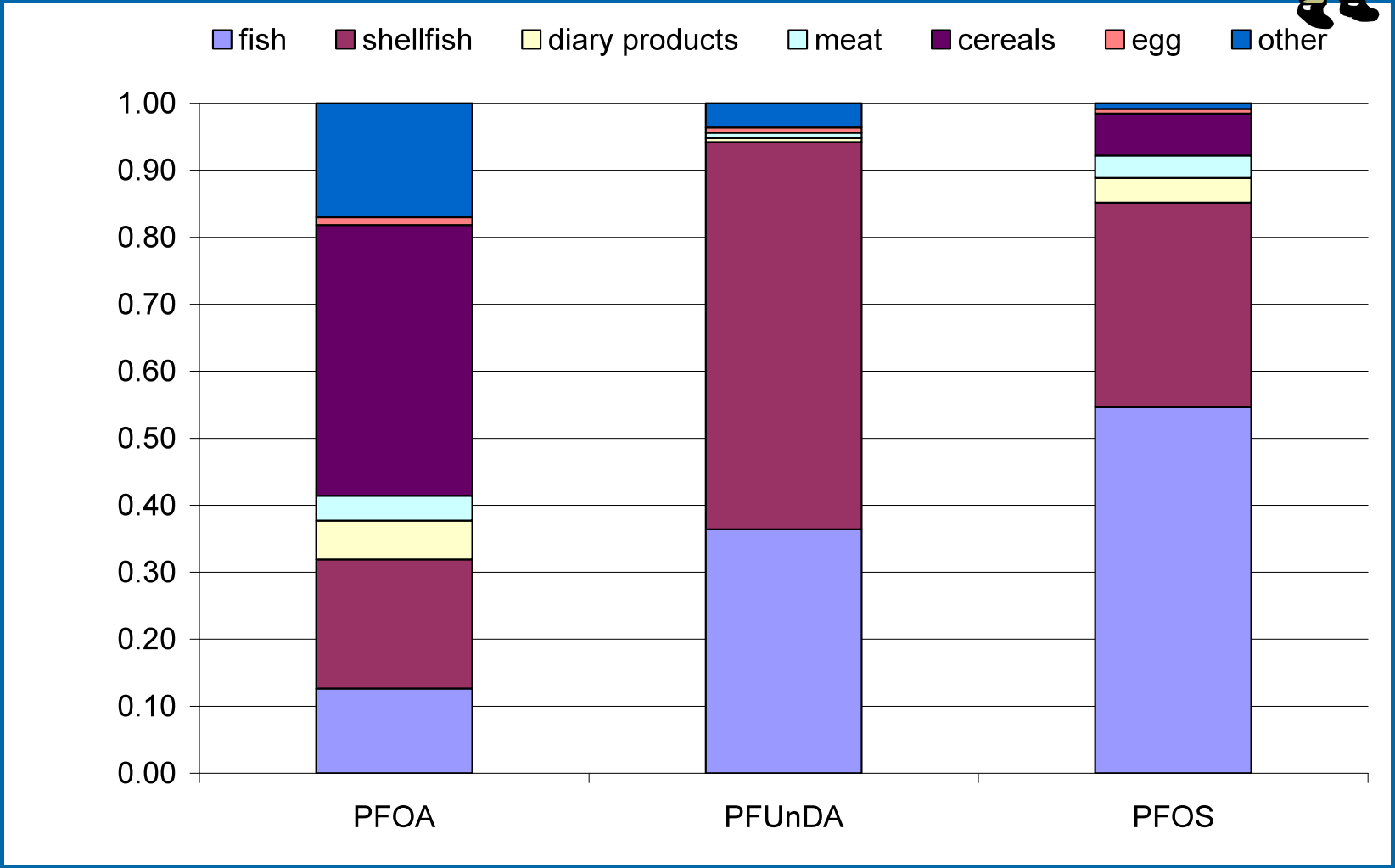
Intake of PFCs from the diet





Haug et al. Environ. Int. (2010) 36. 772-778.

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Intakes of PFOA/PFOS

- Absorption assumed to be 100%

- Food - questionnaire
- Drinking water - 1.41 L/day
- Dust – 50, 100 or 200 mg/day

PFOA/PFOS exposure

- Indoor air – 3 biotransformation factors for precursors
  - FTOHs to PFOA 0.02, 0.5 or 1.7%
  - FOSAs/FOSEs to PFOS 1, 20 or 100%
  - Inhalation rates of 13.3 m^3/day (adults), 6.8 m^3/day (infants)

- Consumption of breast milk assumed to be 700 mL/day

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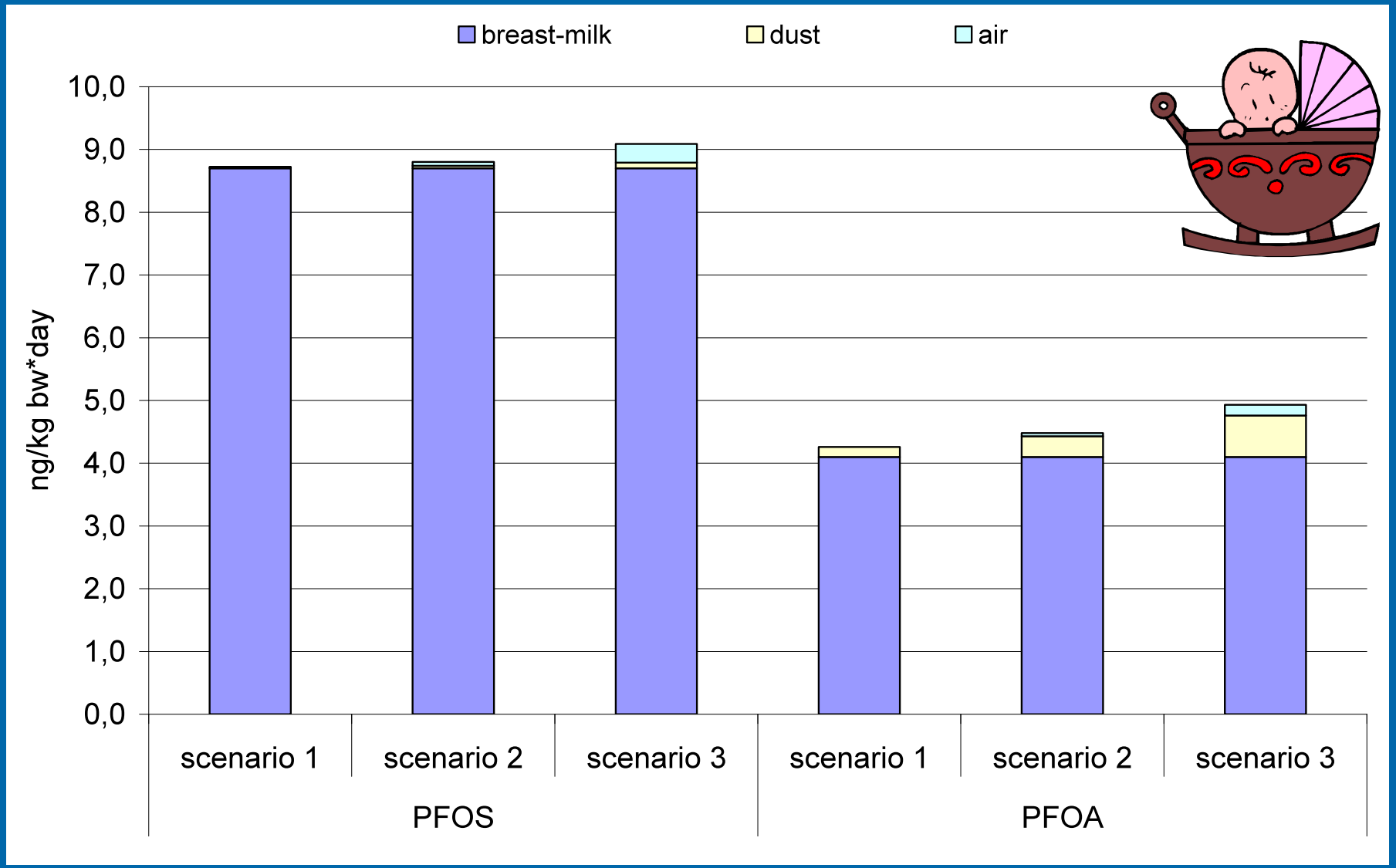
Median of intakes; infants



Haug et al. Environ. Int. (2011) 37, 687-693

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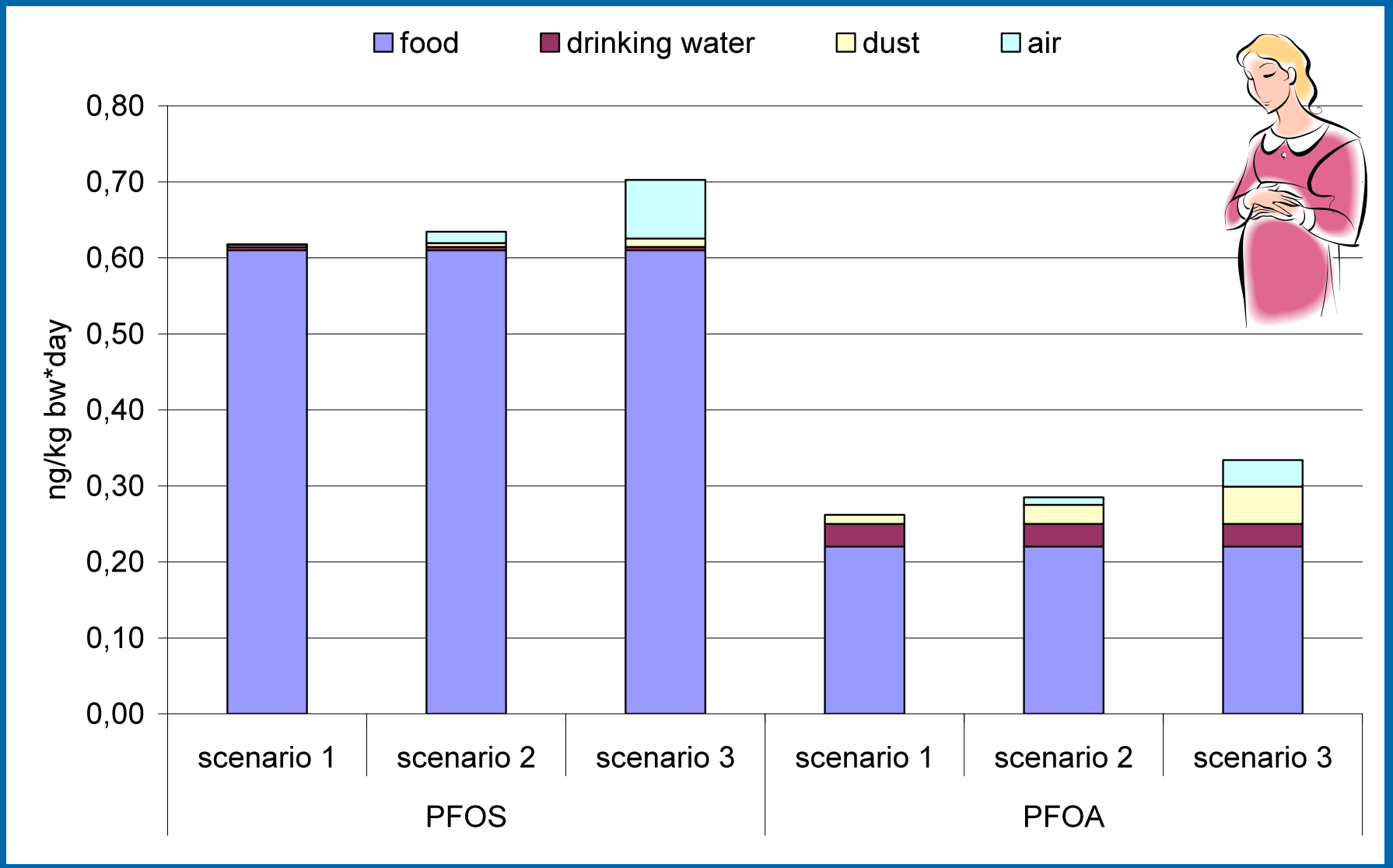
Median intakes; women



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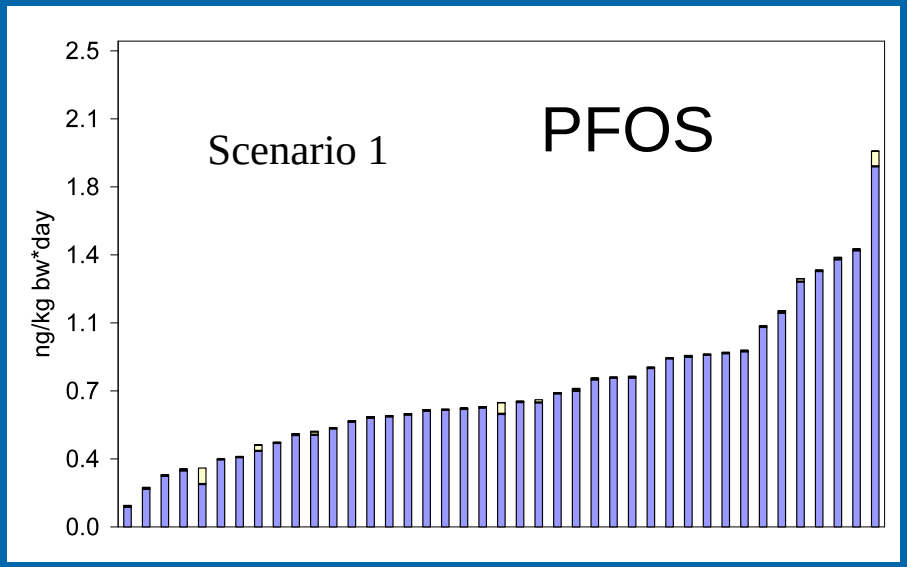
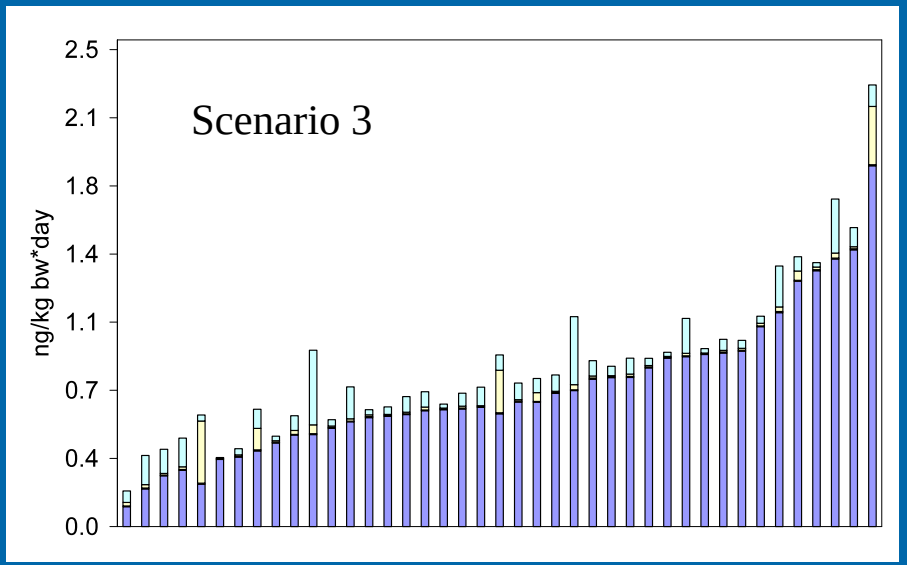
Individual intakes - women



air
dust
drinking water
food



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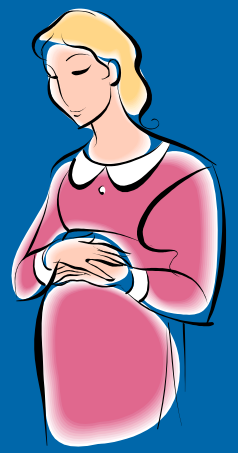
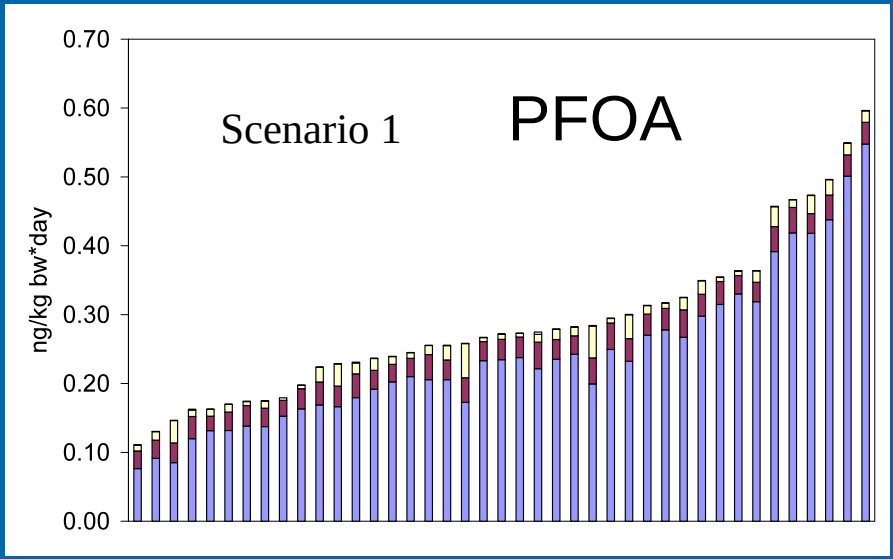
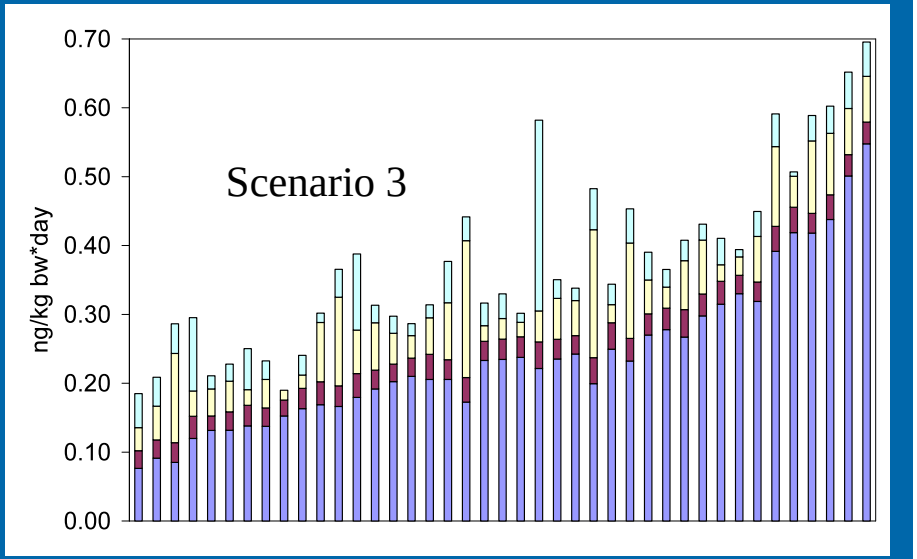
Individual intakes - women





air
dust
drinking water
food



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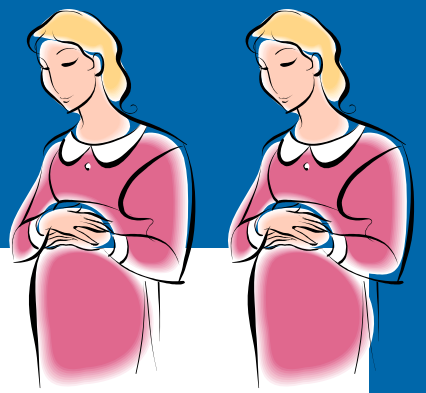

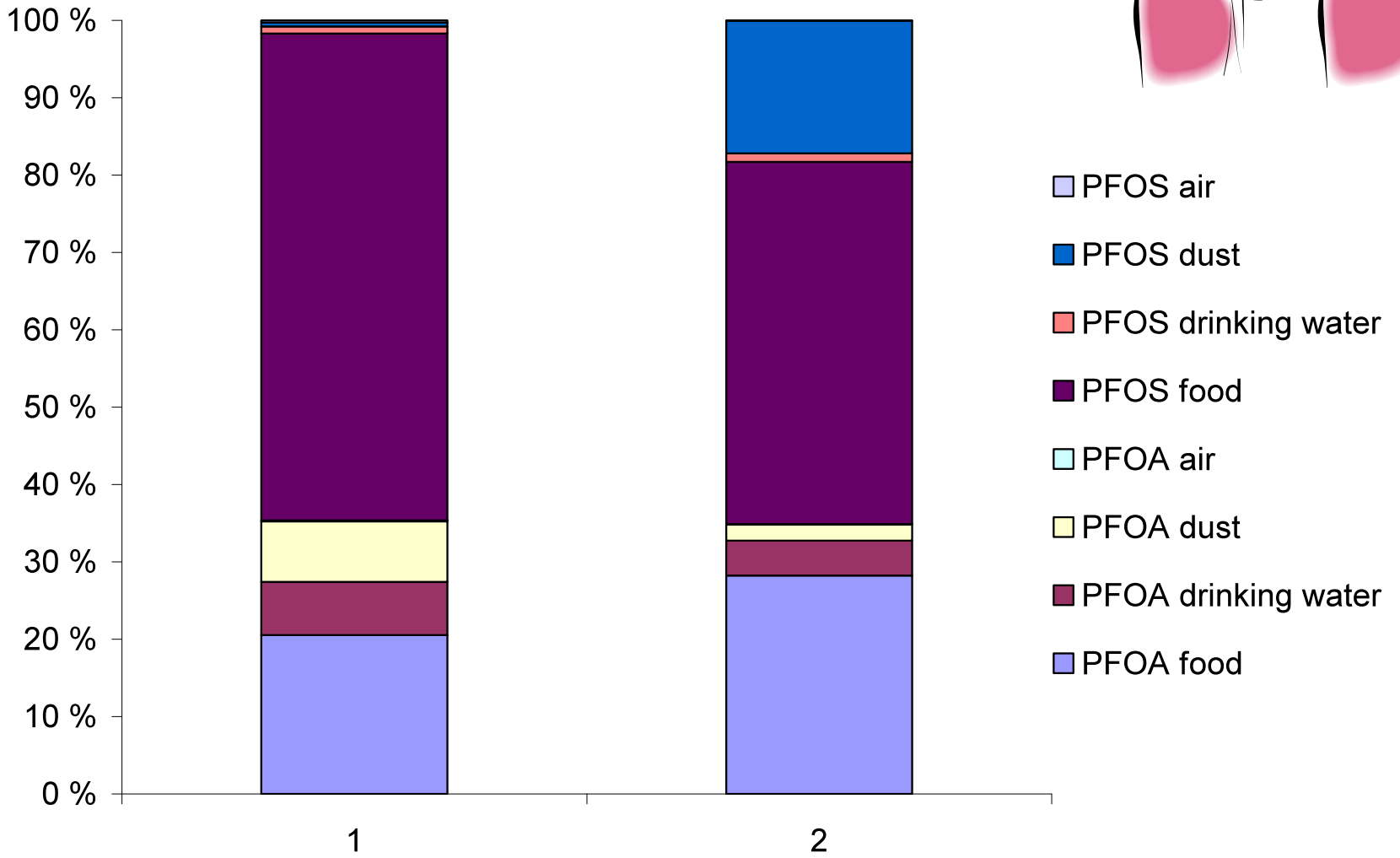

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External dose

Food is generally the major source of exposure for adults, however the relative importance of the indoor environment vary a lot and contribute considerably for several individuals

Breast milk is the major source of exposure for breast-fed infants

The major contributors to dietary intake were fish and shellfish

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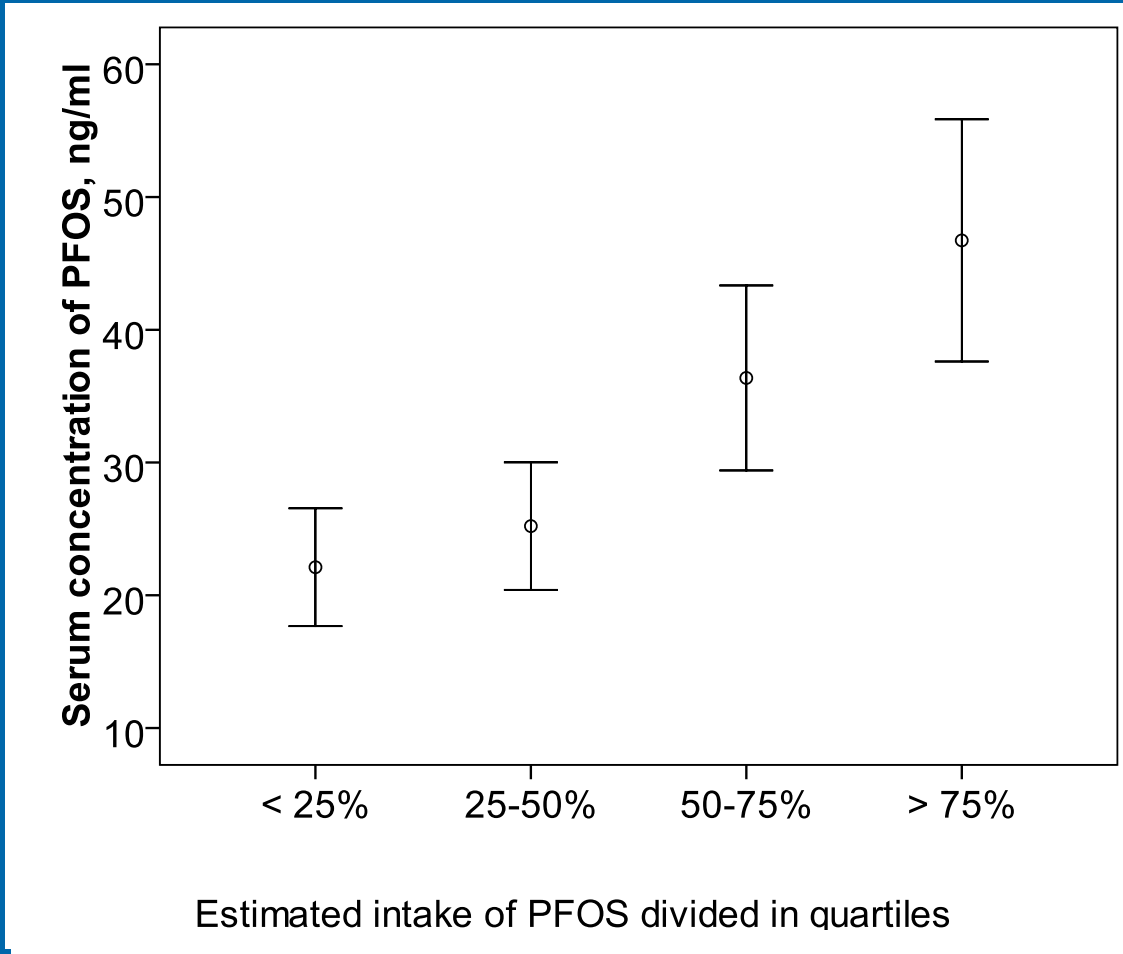
Internal vs external dose



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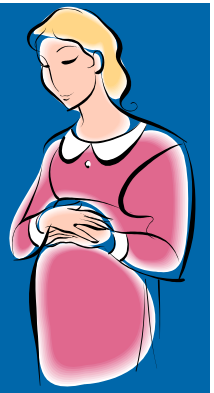
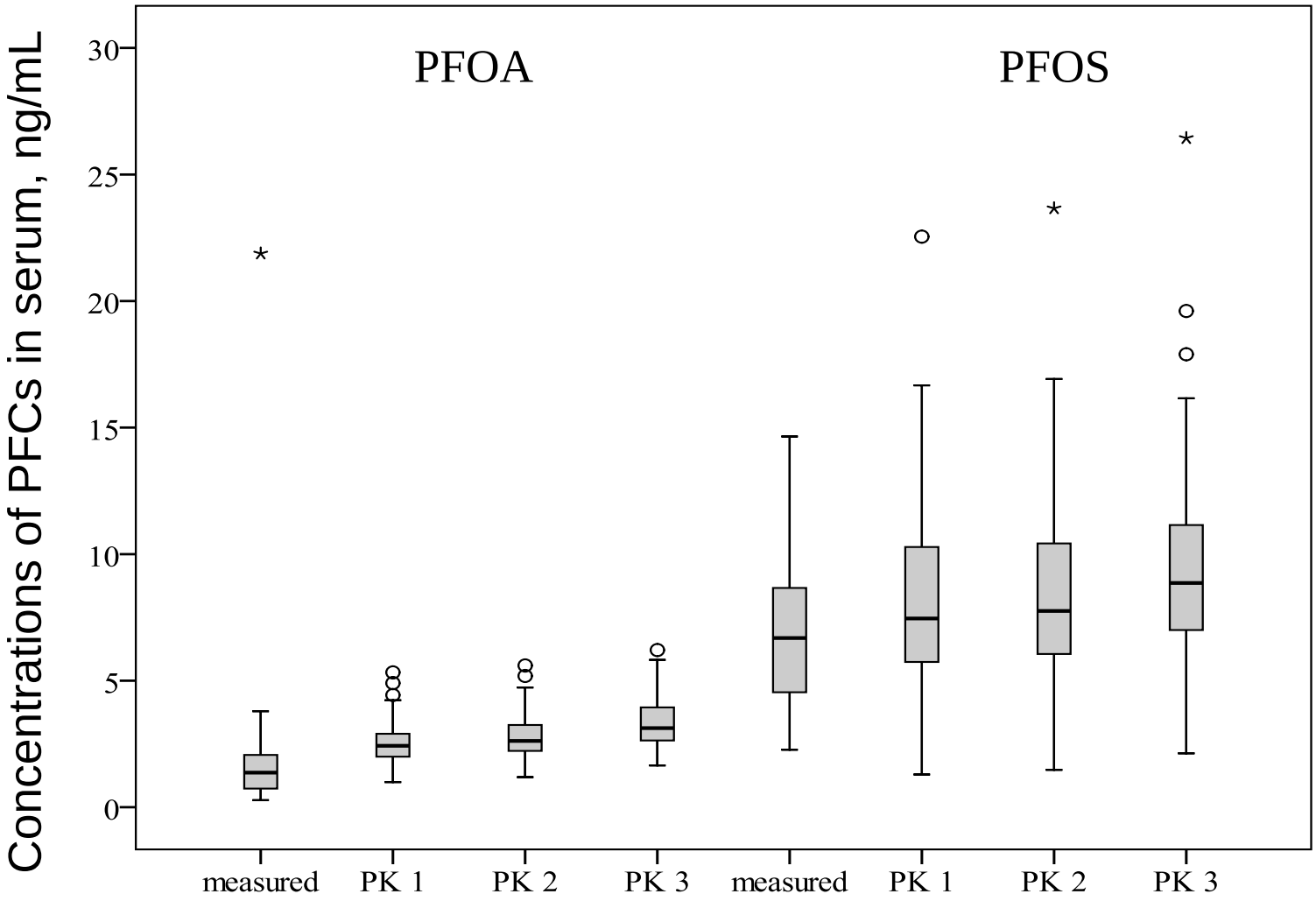
PK modelling





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Comparing internal and external dose

- Significant associations between intakes and blood levels were seen

- PK modelling showed that the intakes calculated are reasonable

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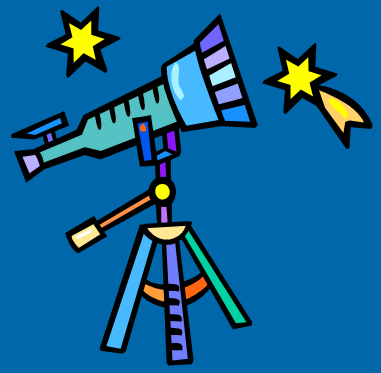

Future perspectives

- “New” compounds
- Larger studies and more environments
- Sampling strategy
- Products - environment
- Exposure factors
- Young children

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