

# Menneskers optag af UV-filtre fra tøj

**Hanne Frederiksen**

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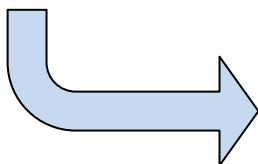
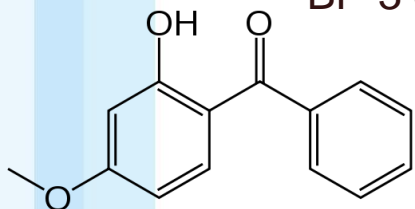
**Center for Hormonforstyrrende Stoffer, Informationsdag 31. Oktober 2017**

## UV-filtres hormonforstyrrende egenskaber

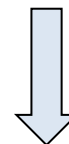
- Nogle UV-filtre har vist østrogene, anti-androgene og anti-thyroide egenskaber og påvirker i dyreforsøg udvikling af pubertet, skjoldbruskkirtel og reproduktive funktioner (Foster et al. 1983, Schlumpf et al. 2008, Krause et al. 2012, Kim og Choi 2014, Watanabe et al. 2015).
- Benzophenone-3 (BP-3) eksponering af zebrafisk ændre kønsratioen → færre hanner, flere hunner (Kinnberg et al. 2015).
- Præ- og perinatal eksponering af rotter viser anti-androgene effekter → nedsat antal spermatozytter hos afkom (Nakamura et al. 2015).
- In vitro-studier har vist, at nogle UV-filtre (bl.a. BP-3, 4-MBP, 4-MBC, 3-BC) kan aktivere den sædspecifikke CatSper-kanal (kationkanal i sædceller) og derved "snyde" sædcellerne til for tidlig at igangsætte den hyper-mobilitet, som er nødvendig for at befrugte ægget (Rehfeld et al. 2016, Schiffer et al. 2014)

# Human Biomonitoring

BP-3 og andre UV-filtre



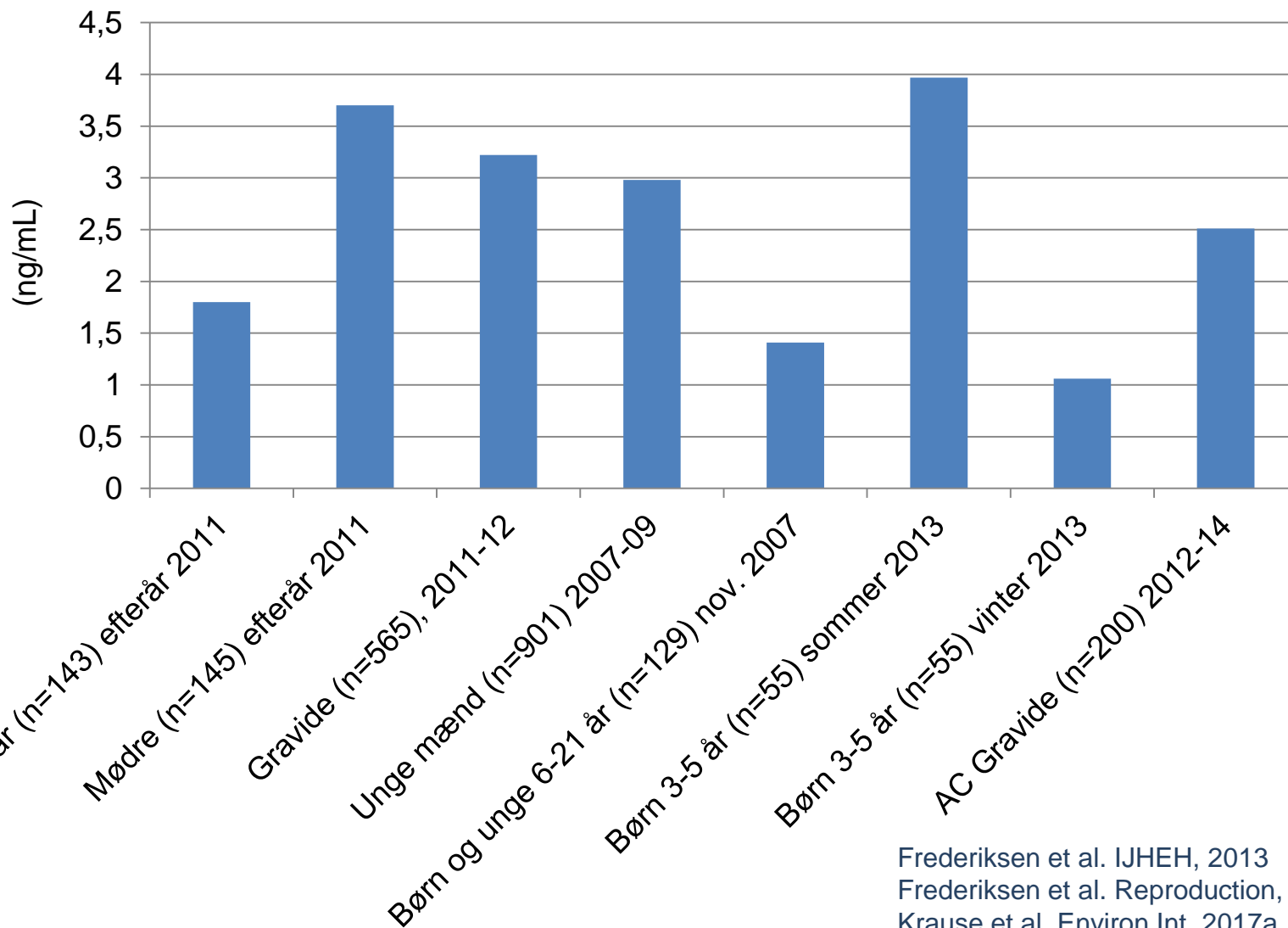
- Fedt (hjerne- og brystvæv)
- Sædvæske
- Fostervand
- Serum
- Urin



**BP-3 eller metabolitter (BP-1)**  
udskilles i urin (4-24 timer)

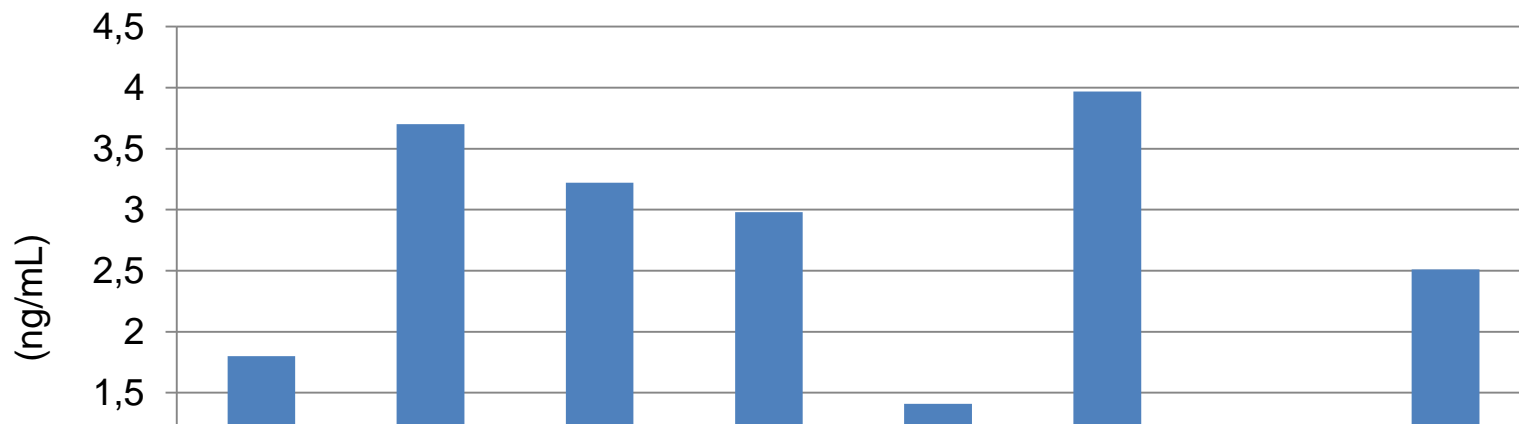


## BP-3 målt i danskeres urin



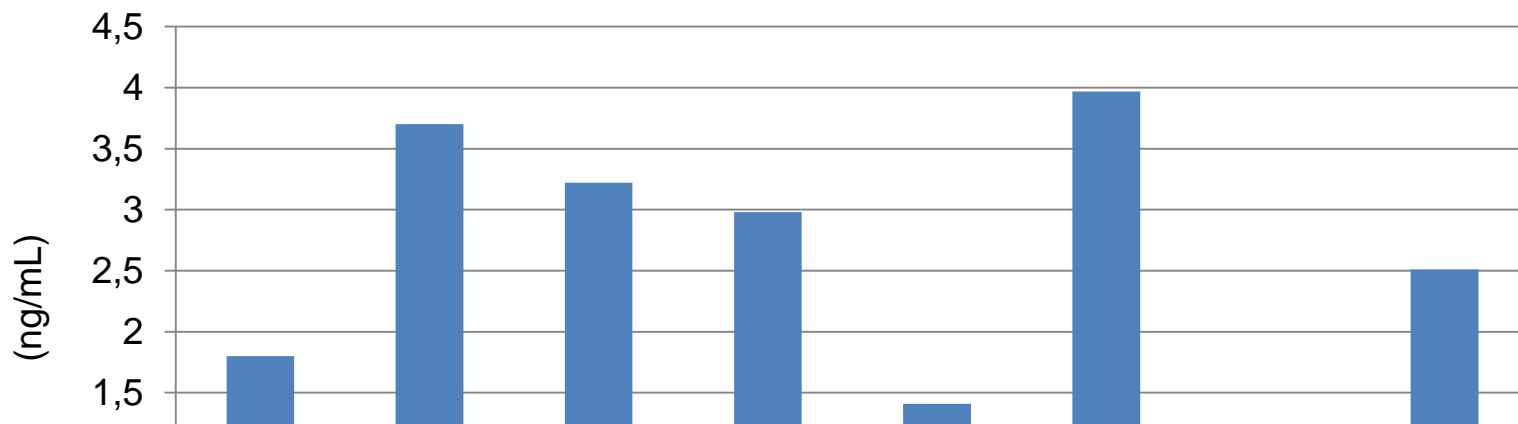
Frederiksen et al. IJHEH, 2013  
Frederiksen et al. Reproduction, 2014  
Krause et al. Environ Int, 2017a  
Krause et al. Environ Int, 2017b

## BP-3 målt i danskeres urin



**>95% af alle danskere eksponeres for BP-3**

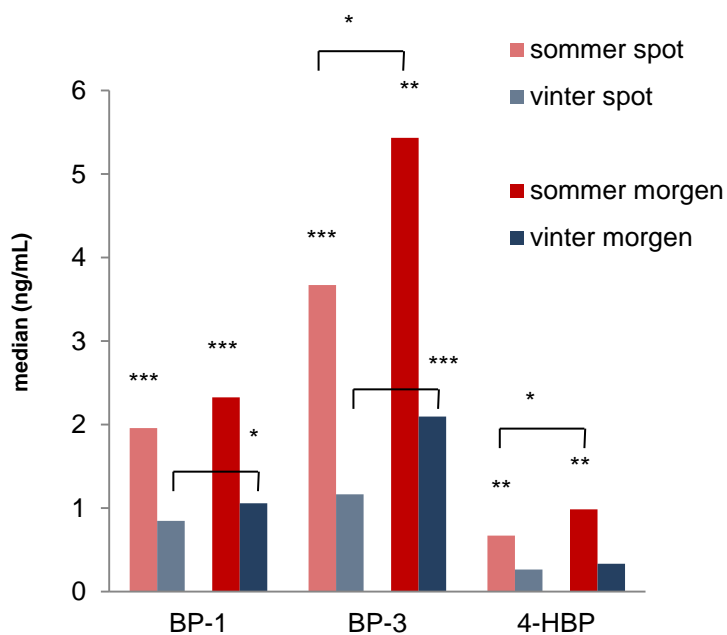
## BP-3 målt i danskeres urin



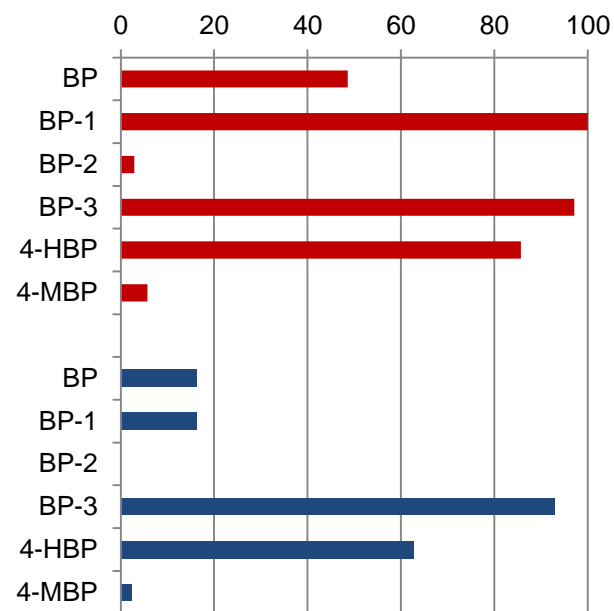
>95% af alle danskere eksponeres for BP-3

Børn 6-11 år (n=148) efterår 2011  
Mødre (n=145) efterår 2011  
Gravide (n=565), 2011-12  
Unge mænd (n=901) 2007-09  
Børn og unge 6-21 år (n=129) nov. 2007  
Børn 3-5 år (n=55) sommer 2013  
Børn 3-5 år (n=55) vinter 2013  
AC Gravide (n=200) 2012-14

# UV-filtre i danske børnehave-børn

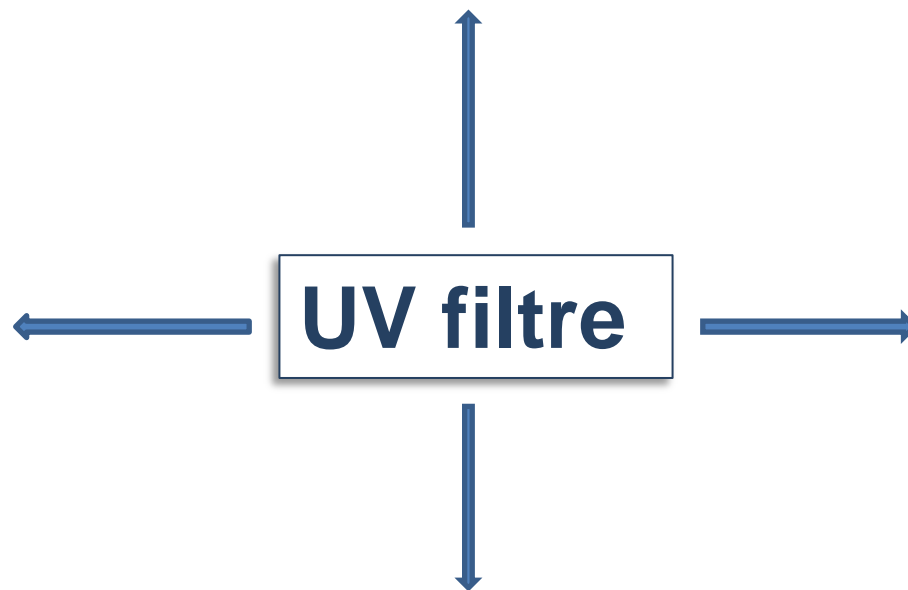


Procent børn med målbare UV-filterkoncentrationer



- Børn eksponeres for nogle UV-filtre året rundt
- Nogle UV-filtre bruges også som absorbere i forbrugerprodukter

## Kilder til eksponering



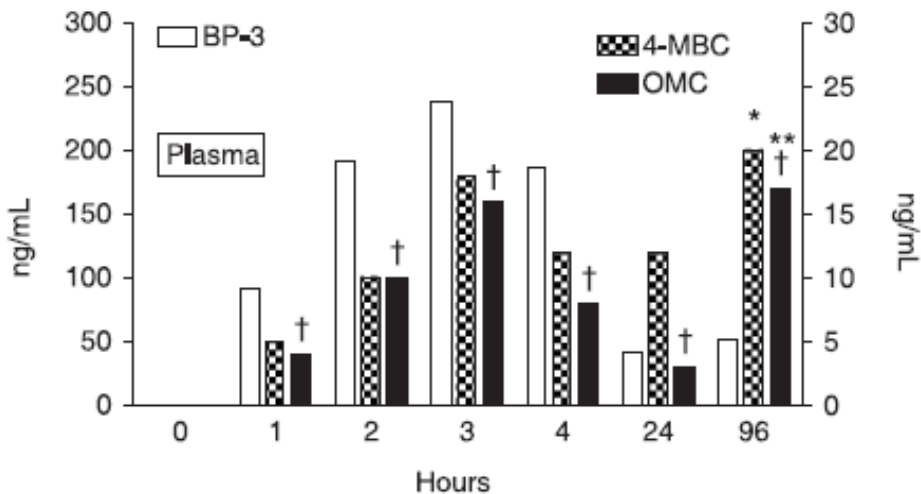
## Kemiske UV-filtre / absorbere optages gennem huden

- Smøring af hele kroppen,
- 2 mg creme per cm<sup>2</sup> hud
- Cremen indeholdt 10% (w/w) af hver tre UV-filtre:

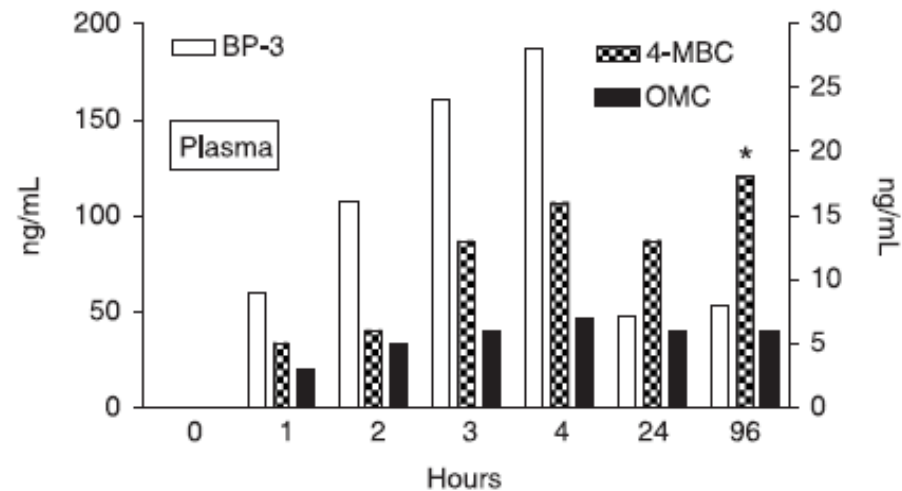
Benzophenone-3 (BP-3)  
 Octyl-methoxycinnamate (OMC)  
 3-(4-methylbenzylidene) camphor (4-MBC)



Mænd, N=15



Kvinder, N=17

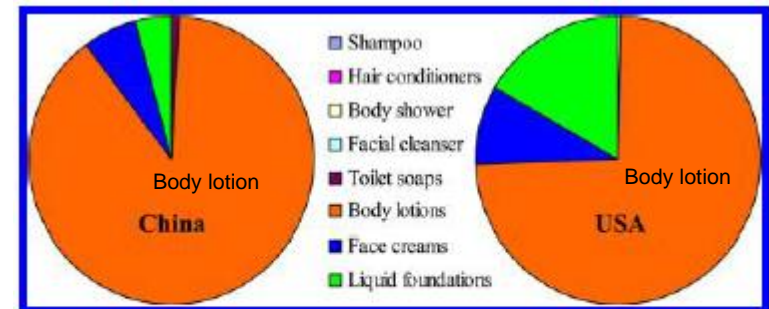
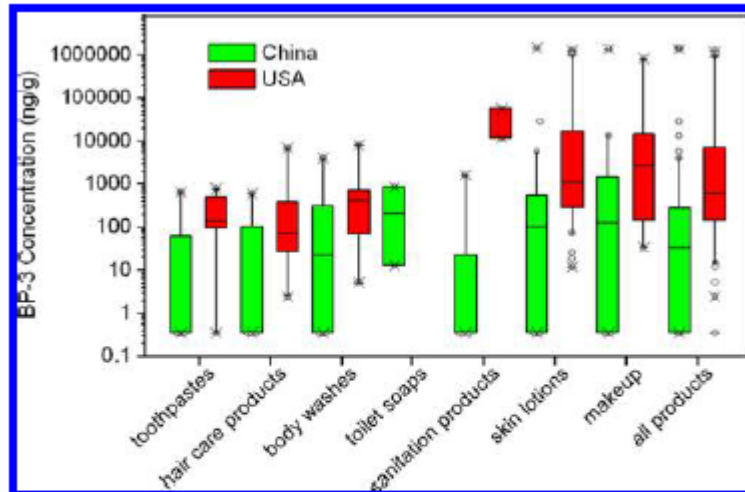


## BP-3 i plejeprodukter i Kina og USA (ikke solcremer)

**Table 1. Concentrations (ng/g Product Weight) and Detection Rates (%) of BP-3 in Personal Care Products from China and the United States<sup>a</sup>**

|                     | n   | GM   | fifth percentile | median | 95th percentile | range        | detection rate (%) |
|---------------------|-----|------|------------------|--------|-----------------|--------------|--------------------|
| toothpastes         | 17  | 10.0 | 0.354            | 43.6   | 679             | nd–786       | 58.8               |
| hair care products  | 32  | 20.5 | 0.354            | 42.5   | 886             | nd–6810      | 71.9               |
| Body shampoo        | 31  | 61.0 | 0.354            | 92.1   | 5440            | nd–8190      | 80.6               |
| toilet soaps        | 3   | 132  | 32.3             | 205    | 788             | 13.1–853     | 100                |
| sanitation products | 9   | 18.1 | 0.354            | 0.562  | 38 300          | nd–56 100    | 55.6               |
| Body lotion         | 107 | 548  | 0.354            | 530    | 973 000         | nd–1 480 000 | 88.8               |
| makeup              | 32  | 284  | 0.354            | 221    | 391 000         | nd–1 370 000 | 84.4               |
| China               | 117 | 20.1 | 0.354            | 32.7   | 3860            | nd–1 480 000 | 64.1               |
| USA                 | 114 | 1200 | 16.9             | 628    | 923 000         | nd–1 290 000 | 99.1               |
| all products        | 231 | 151  | 0.354            | 184    | 825 000         | nd–1 480 000 | 81.4               |

<sup>a</sup>GM = geometric mean; nd = not detected.



# Bisphenoler og benzophenoner i tekstiler og babytøj

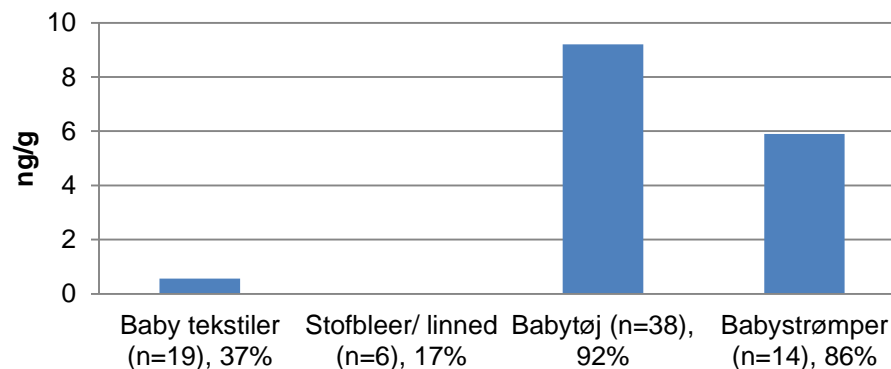
77 stykker tøj produceret i Sydøstasien og El Salvador

**Table 1. Overall Concentrations (ng/g) of Bisphenols, Benzophenones, Bisphenol A Diglycidyl Ether (BADGE), and Their Derivatives in Textiles (n = 77) Collected from Albany, New York, USA<sup>a</sup>**

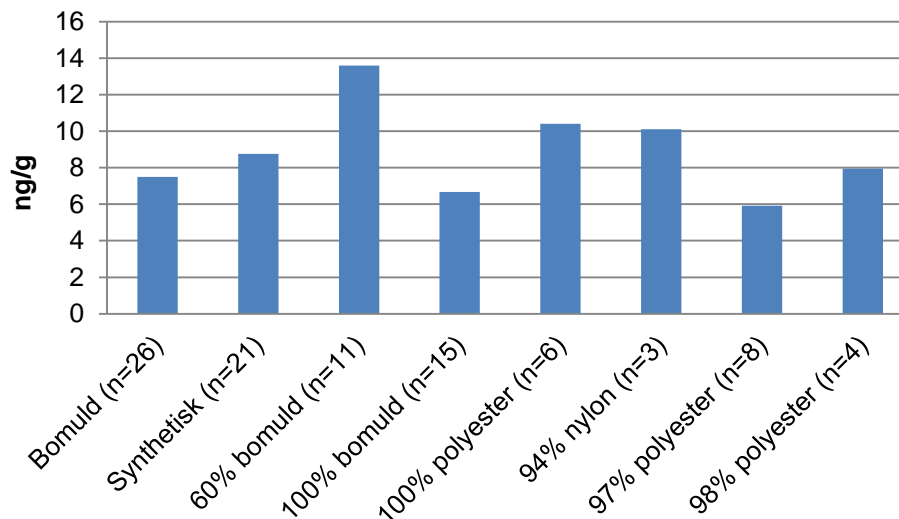
| n = 77                     | DR (%) | mean | SD   | median | range       |
|----------------------------|--------|------|------|--------|-------------|
| BPA                        | 82     | 366  | 1690 | 10.7   | <2.21–13300 |
| BPS                        | 53     | 15.0 | 58.9 | 1.02   | <0.74–394   |
| BPF                        | 5.2    | 6.70 | 25.3 | 0.32   | <14.7–194   |
| BPP                        | 5.2    | 0.23 | 0.99 | 0.004  | <0.74–7.96  |
| BP3                        | 70     | 11.3 | 19.9 | 5.94   | <2.21–157   |
| 4-OH-BP                    | 7.8    | 0.41 | 1.01 | 0.10   | <1.47–7.66  |
| BP1                        | 1.3    | n.a. | n.a. | n.a.   | <1.10–1.21  |
| BADGE·2H <sub>2</sub> O    | 22     | 1.92 | 2.84 | 0.82   | <1.47–13.1  |
| BADGE                      | 7.8    | 0.23 | 0.62 | 0.04   | <0.74–4.37  |
| BADGE·HCl·H <sub>2</sub> O | 16     | 7.32 | 11.9 | 2.88   | <1.47–62.9  |
| BFDGE                      | 29     | 13.6 | 27.2 | 2.44   | <1.47–132   |
| BFDGE·2H <sub>2</sub> O    | 1.3    | n.a. | n.a. | n.a.   | <3.68–79.0  |
| 3R-NOGE                    | 25     | 13.3 | 30.4 | 1.47   | <0.74–174   |
| 4R-NOGE                    | 12     | 1.77 | 3.54 | 0.64   | <2.94–27.2  |

<sup>a</sup>DR = detection rate; SD = standard deviation; n.a. = not available.

BP-3 i babytekstiler sorteret efter brug



BP-3 i babytekstiler sorteret efter materiale



## Kan BP-3 i tøj optages gennem huden?



**BP-3** kan måles i indendørs luft (Wan et al., 2015), er målt i nyt tøj (Xue et al., 2017) og forventes også at være i tøj, der er i brug.



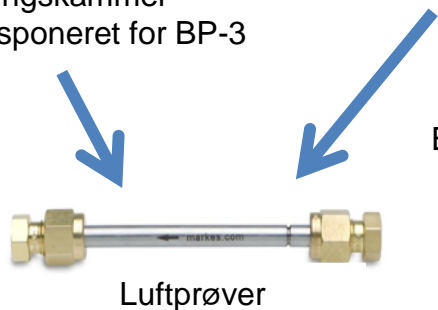
**Hypothese:** Dermal BP-3 optagelse fra tøj bidrager væsentligt til den samlede BP-3 eksponering.

## Studie design



3 timers  
personeksponering i  
et særligt  
eksponeringsrum

Forseglet prepareringskammer -  
Bomulds T-shirt eksponeret for BP-3  
gennem 32 dage



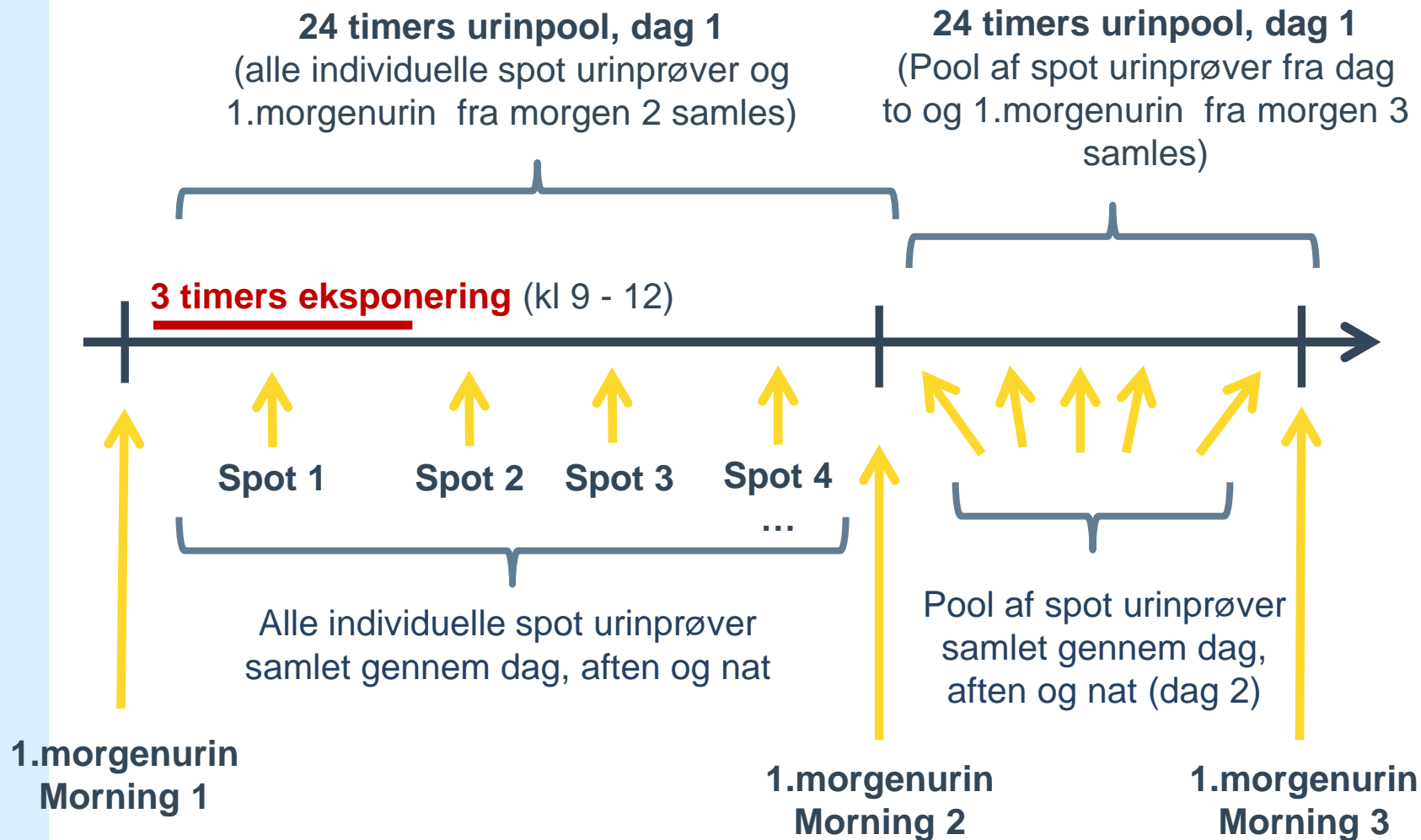
Blod



Urin



## Studie design



## Forsøgsdeltagere

|                          | Person 1 | Person 2 | Person 3 |
|--------------------------|----------|----------|----------|
| Alder (år)               | 27       | 36       | 51       |
| Vægt (kg)                | 73       | 71       | 84       |
| Højde (m)                | 1.8      | 1.8      | 1.84     |
| BMI (kg/m <sup>2</sup> ) | 22.5     | 21.9     | 24.8     |
| BSA (m <sup>2</sup> )    | 1.92     | 1.89     | 2.08     |

## Analyser

- Blod (serum) og urin: Turboflow væskekromatografi-tandem massespektrometri (LC-MS/MS)
- Luft: Termisk desorptions-gaskromatografi massespektrometri (TD-GC/MS)
- T-shirts: Ekstraktion og HPLC-UV

## Luftmålinger

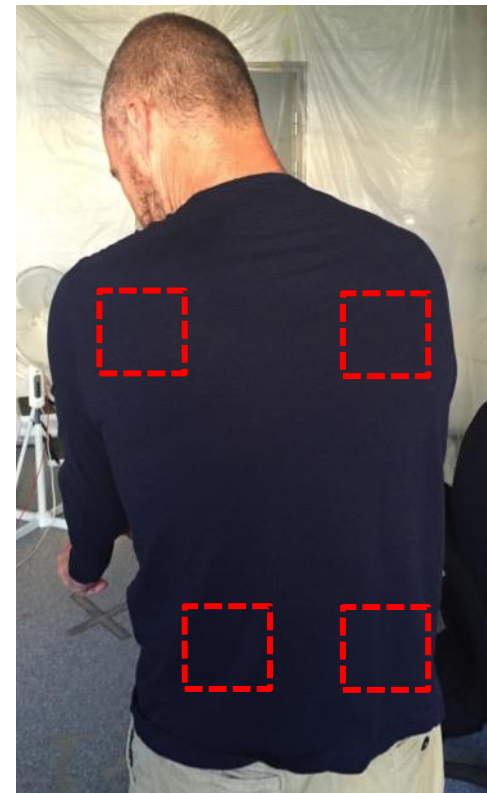
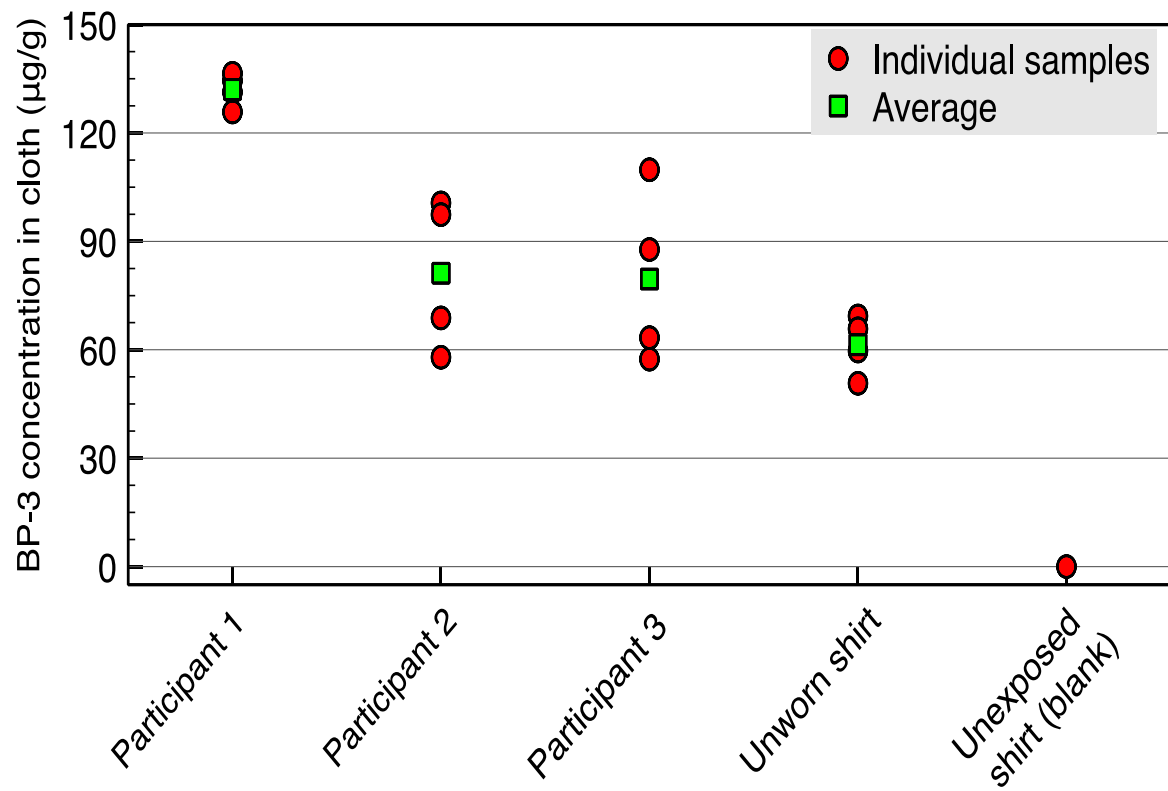


Forseglet prepareringskammer:  
Efter 32 dage var BP-3  
koncentrationen  
i kammeret =  $4,4 \text{ mg/m}^3$

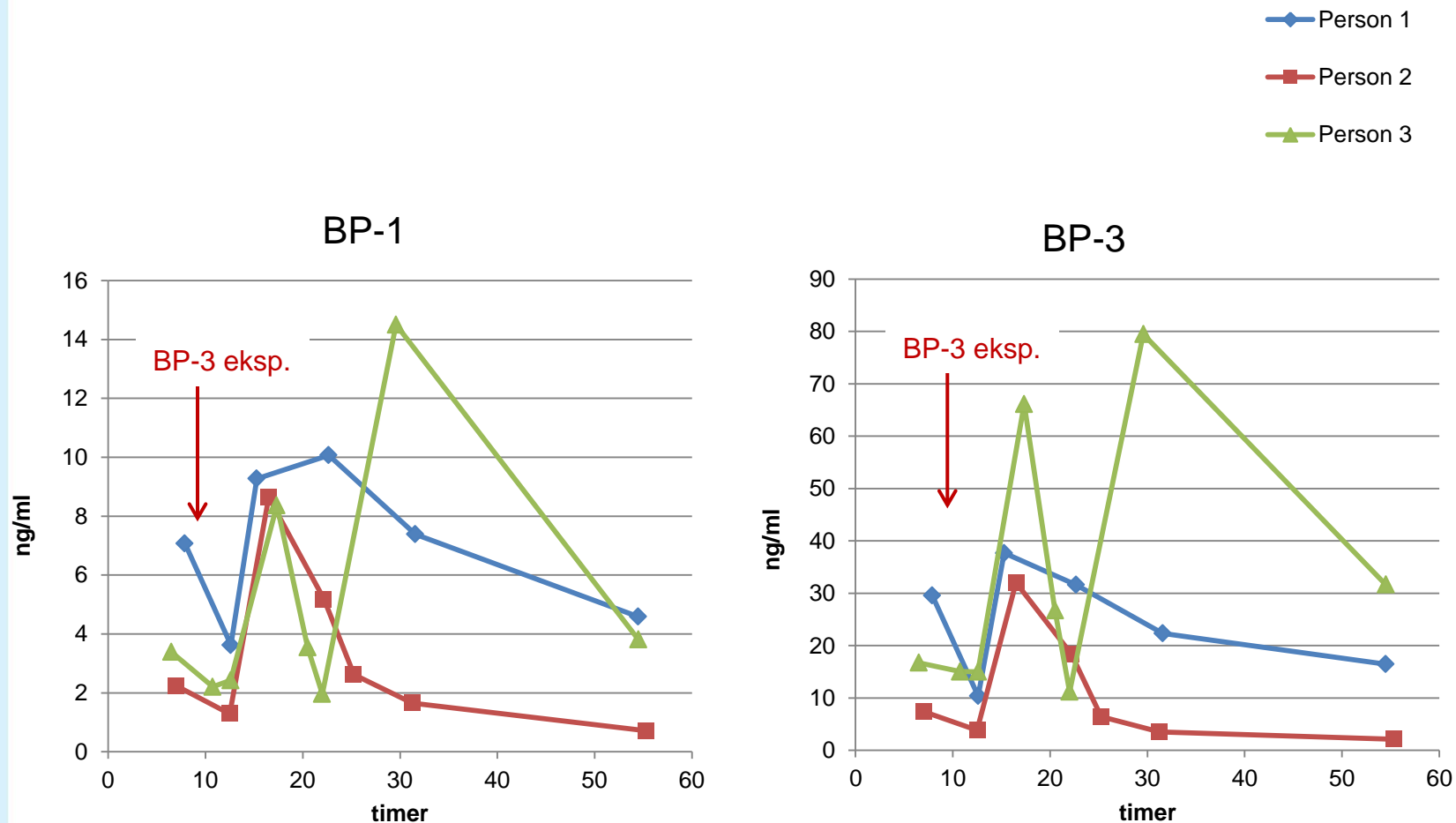


Eksponeringsrum:  
Luft nær vejtrækningszone  
BP-3 koncentration  $< \text{LOQ}$  ( $0,3 \text{ mg/m}^3$ )  
Indåndingsestimat  $< 0,3 \text{ mg}$

## BP-3 koncentration i T-shirts

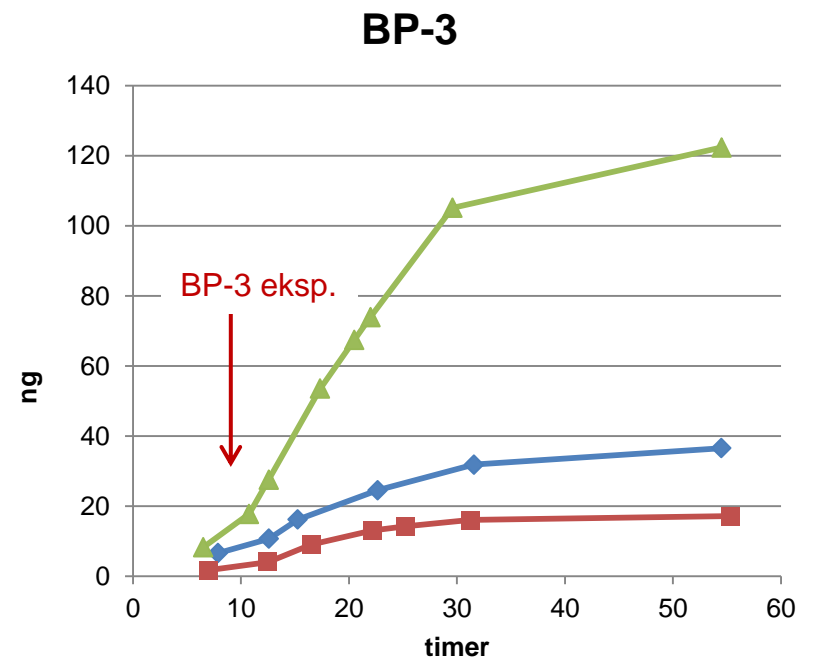
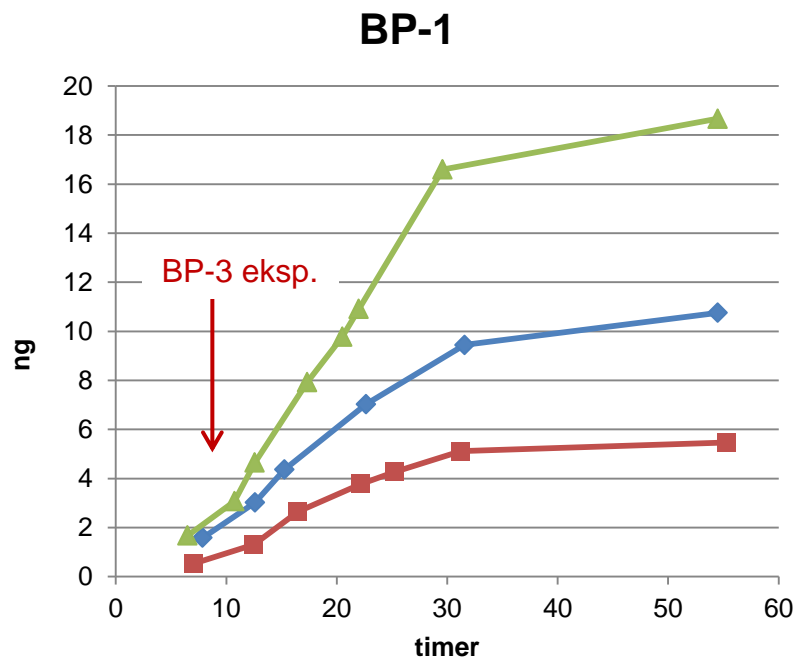


## BP-1 og BP-3 koncentration målt i urin

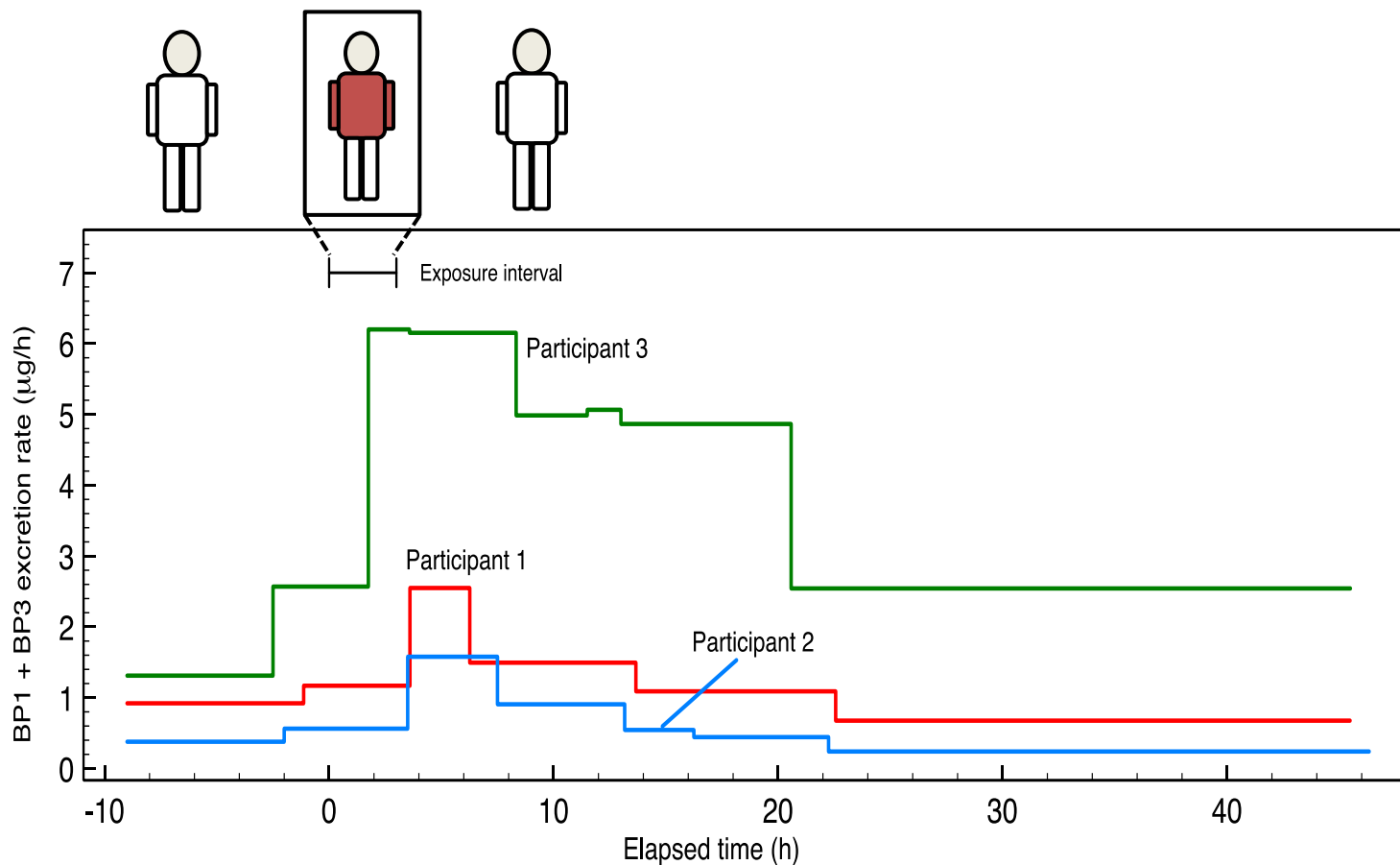


## Akkumuleret urinudskillelse

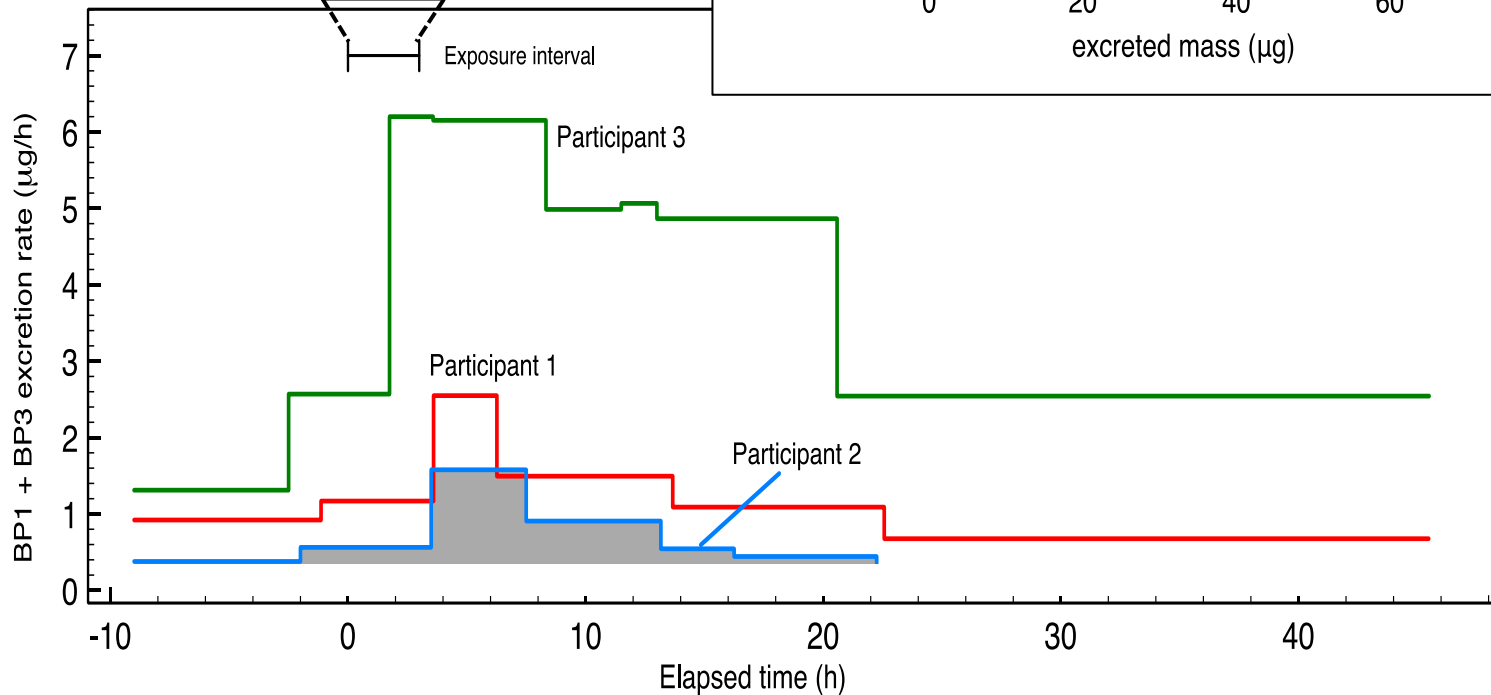
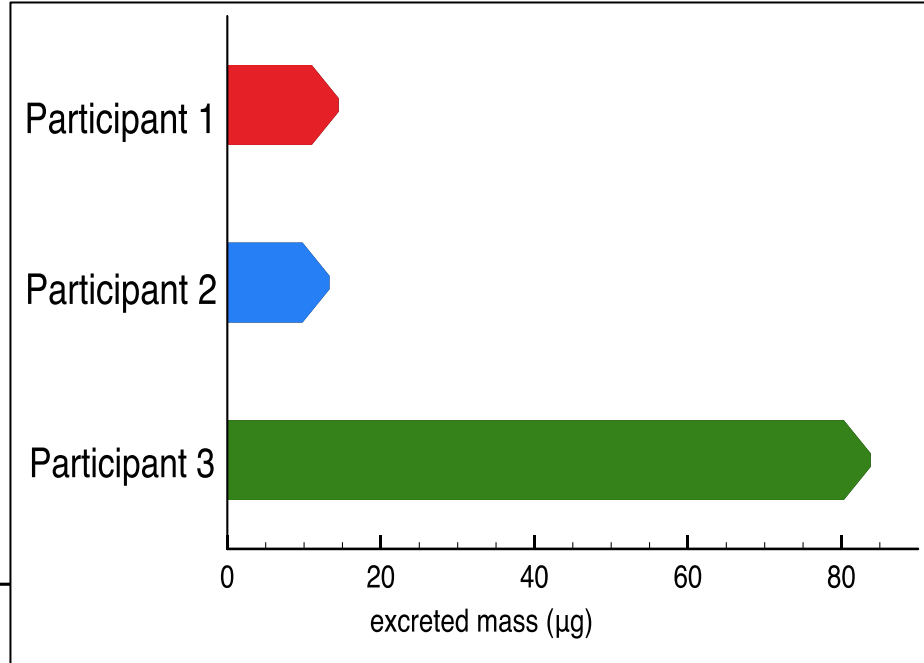
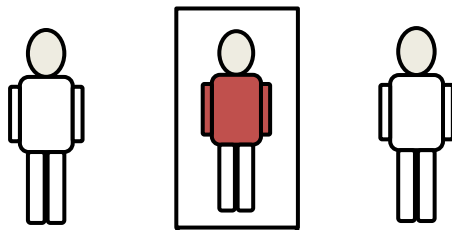
- Person 1
- Person 2
- Person 3



## Udskilleleshastigheden i urin – sum af BP-1 og BP-3



# Samlet udskillelse



## Estimering af den samlede daglige eksponering - sum BP-3 + BP-1

|                |             | Daglig eksponering<br>ng/kg/dag |                      |
|----------------|-------------|---------------------------------|----------------------|
| <b>USA</b>     | Kvinder     | 532                             | Calafat et al. 2008  |
|                | Mænd        | 245                             |                      |
| <b>Kina</b>    |             | 33                              | Gao et al. 2015      |
| <b>Belgien</b> | kun BP-3    | 22                              | Dewalque et al. 2014 |
| <b>Danmark</b> | Sommer børn | 212                             | Krause et al 2017    |
|                | Vinter børn | 56                              |                      |

Anslået optagelse fra tøj i dette studie: **9 - 35 ng/kg/dag**

Modellering baseret på:

Weschler og Nazaroff 2012 (permeabilitetsmetode)

Morrison et al. 2016 (optagelse fra tøj)

Wan et al. 2015 (luft koncentration i amerikanske bygninger)

## Konklusion

- BP-3 kan optages gennem huden fra eksponeret tøj, måles i blodet, metaboliseres og udskilles i urin som hhv. BP-3 og BP-1
- En deltager absorberede ~ 8 gange mere end andre deltagere  
→ Forskelle i hudpermeabilitet?
- Dermal optagelse fra luft og tøj bidrager sandsynligvis til den samlede BP-3 eksponering.

## Dermal Uptake of Benzophenone-3 from Clothing

Glenn C. Morrison,<sup>\*,†,Ⓞ</sup> Gabriel Bekö,<sup>‡</sup> Charles J. Weschler,<sup>‡,§</sup> Tobias Schripp,<sup>||,⊥</sup> Tunga Salthammer,<sup>||</sup> Jonathan Hill,<sup>†</sup> Anna-Maria Andersson,<sup>#,∇</sup> Jørn Toftum,<sup>‡</sup> Geo Clausen,<sup>‡</sup> and Hanne Frederiksen<sup>#,∇</sup>

<sup>†</sup>Civil, Architectural and Environmental Engineering, Missouri University of Science and Technology, Rolla, Missouri 65409, United States

<sup>‡</sup>International Centre for Indoor Environment and Energy, Department of Civil Engineering, Technical University of Denmark, Lyngby, 2800 Denmark

<sup>§</sup>Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, New Jersey 08901, United States

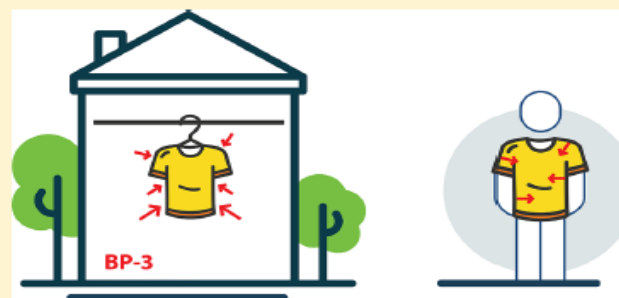
<sup>||</sup>Department of Material Analysis and Indoor Chemistry, Fraunhofer WKI, Braunschweig 38108, Germany

<sup>⊥</sup>Institute of Combustion Technology, German Aerospace Center, Stuttgart, 70569, Germany

<sup>#</sup>Department of Growth and Reproduction and <sup>∇</sup>International Center for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Rigshospitalet, University of Copenhagen, Copenhagen 2100, Denmark

### Supporting Information

**ABSTRACT:** Benzophenone-3 (also known as BP-3 or oxybenzone) is added to sunscreens, plastics, and some coatings to filter UV radiation. The suspected endocrine disruptor BP-3 has been detected in the air and settled dust of homes and is expected to redistribute from its original sources to other indoor compartments, including clothing. Given its physical and chemical properties, we hypothesized that dermal uptake from clothing could contribute to the body burden of this compound. First, cotton shirts were exposed to air at an elevated concentration of BP-3 for 32 days; the final air concentration was  $4.4 \mu\text{g}/\text{m}^3$ . Next, three participants wore the exposed shirts for 3 h. After 3 h of exposure, participants wore their usual clothing during the collection of urine samples for the next 48 h. Urine was analyzed for BP-3, a metabolite (BP-1), and six other UV filters. The rate of urinary excretion of the sum of BP-1 and BP-3 increased for all participants during and following the 3 h of exposure. The summed mass of BP-1 and BP-3 excreted during the first 24 h attributable to wearing exposed t-shirts were 12, 9.9, and  $82 \mu\text{g}$  for participants 1, 2, and 3, respectively. Analysis of these results, coupled with predictions of steady-state models, suggest that dermal uptake of BP-3 from clothing could meaningfully contribute to overall body burden.



## Mange tak til

- Stine E. Andersen, *Afdeling for Vækst og Reproduktion, Rigshospitalet*
- Anna-Maria Andersson, *Afdeling for Vækst og Reproduktion, Rigshospitalet*
- Glenn Morrison, Environmental Science and Engineering, University of North Carolina
- Charles Weschler, Environmental and Occupational Health Sciences Institute, Rutgers University, Piscataway, NJ
- Gabriel Bekö, Department of Civil Engineering, International Centre for Indoor Environment and Energy, Technical University of Denmark,

Tak for økonomisk støtte fra:

- Otto Mønsted Guest Professorship of the Technical University of Denmark
- International Center for Research and Research Training in Endocrine Disruption of Male Reproduction and Child Health (EDMaRC), Rigshospitalet,
- the National Science Foundation under grant no. 1336807.



Tak for anden økonomisk støtte til:

- Velux Fondene
- Lundbeck Fonden
- Augustinus Fonden
- Svend Andersens Fond

?

?

?

# Niveauerne af UV-filtre hos gravide

**Hanne Frederiksen**

**Afdeling for Vækst og Reproduktion, Rigshospitalet**

**Center for Hormonforstyrrende Stoffer, Informationsdag 31. Oktober 2017**

## UV-filtres hormonforstyrrende egenskaber

- Nogle UV-filtre har vist østrogene, anti-androgene og anti-thyroide egenskaber og påvirker i dyreforsøg udvikling af pubertet, skjoldbruskkirtel og reproduktive funktioner (Foster et al. 1983, Schlumpf et al. 2008, Krause et al. 2012, Kim og Choi 2014, Watanabe et al. 2015).



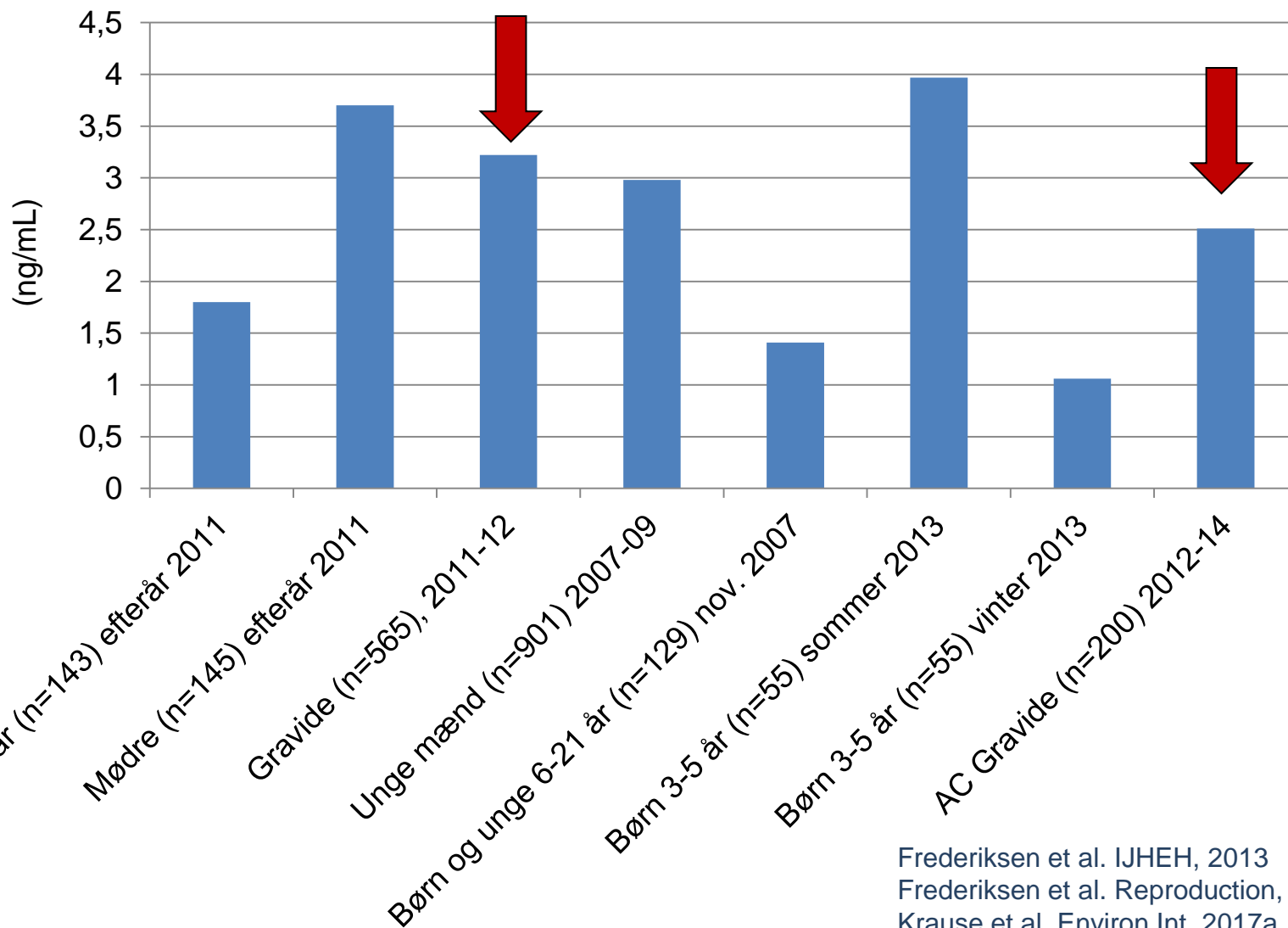
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Præ- og perinatal eksponering af rotter viser anti-androgene effekter → nedsat antal spermatozytter hos afkom (Nakamura et al. 2015).

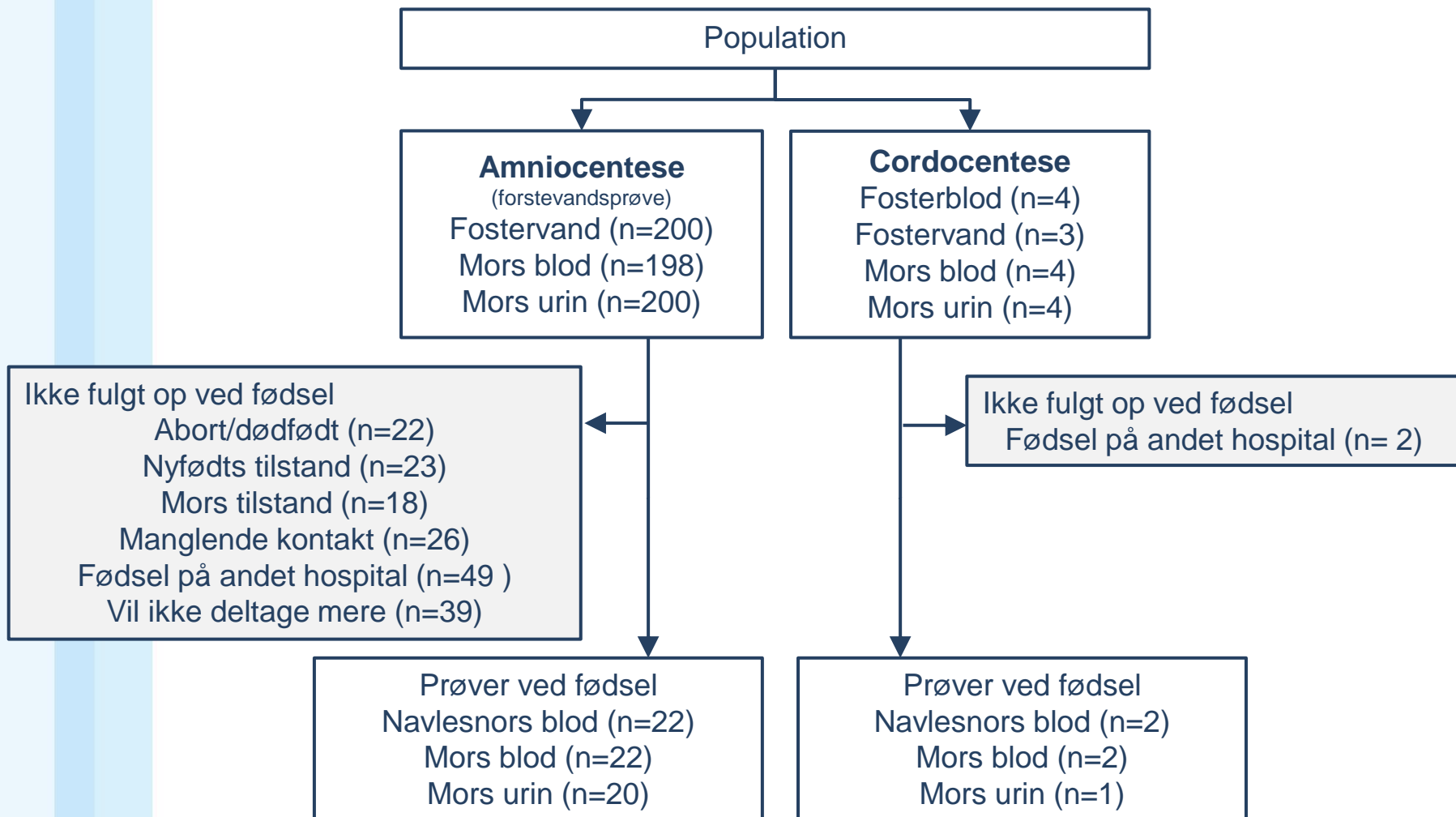
- In vitro-studier har vist, at nogle UV-filtre (bl.a. BP-3, 4-MBP, 4-MBC, 3-BC) kan aktivere den sædspecifikke CatSper-kanal (kationkanal i sædceller) og derved "snyde" sædcellerne til for tidlig at igangsætte den hyper-mobilitet, som er nødvendig for at befrugte ægget (Rehfeld et al. 2016, Schiffer et al. 2014)

## BP-3 målt i danskeres urin



# Eksponeres et foster for sin mors UV-filtre?

# Studie design



## Gravide i amniocentese projekt (n=200)

|                                  | Group 1<br>n=51 (26%) | Group 2<br>n=78 (39%) | Group 3<br>n=71 (35%) | In total<br>n=200 (100%) | p-value |
|----------------------------------|-----------------------|-----------------------|-----------------------|--------------------------|---------|
| <b>Age (n)</b>                   | 51                    | 78                    | 69                    | 198                      |         |
| median (min-max)                 | 37 (27-44)            | 34 (21-42)            | 33 (21-44)            | 35 (21-44)               | 0.000   |
| <b>Education (n)</b>             | 51                    | 78                    | 69                    | 198                      |         |
| high                             | 37 (72)               | 50 (64)               | 50 (72)               | 137 (69)                 |         |
| middel                           | 9 (18)                | 16 (21)               | 8 (12)                | 33 (17)                  | 0.526   |
| low                              | 5 (10)                | 12 (15)               | 11 (16)               | 28 (14)                  |         |
| <b>Body mass index (BMI) (n)</b> | 47                    | 77                    | 70                    | 194                      |         |
| BMI: ≤ 20: underweight           | 7 (15)                | 22 (28)               | 10 (14)               | 39 (20)                  |         |
| BMI: >20-25: normal              | 33 (70)               | 30 (39)               | 42 (61)               | 105 (54)                 | 0.006   |
| BMI > 25: overweight             | 7 (15)                | 26 (33)               | 17 (25)               | 50 (26)                  |         |
| <b>Conception (n)</b>            | 50                    | 75                    | 69                    | 194                      |         |
| Natural conception               | 46 (92)               | 65 (87)               | 63 (91)               | 169 (85)                 | 0.542   |
| Fertility treatment              | 4 (8)                 | 10 (13)               | 6 (9)                 | 20 (10)                  |         |
| <b>Sunscren use (n)</b>          | 49                    | 72                    | 66                    | 187                      |         |
| Used over 2 days ago             | 42 (86)               | 51 (71)               | 60 (91)               | 153 (82)                 |         |
| Used during last 2 days          | 1 (2)                 | 2 (3)                 | 1 (1.5)               | 4 (2)                    | 0.054   |
| Used during last day             | 2 (4)                 | 10 (14)               | 1 (1.5)               | 13 (7)                   |         |
| Used during last 2 hours*        | 4 (8)                 | 9 (13)                | 4 (6)                 | 17 (9)                   |         |

\* Including personal care products other than sunscreens known to contain UV filters.

Group 1: amniocentesis performed due to maternal request only as both ultrasound scan and karyotype of fetus was normal

Group 2: amniocentesis performed due to calculated increased risk of having an abnormal fetus, but ultrasound scan was without any malformations and karyotype results turn out to be normal.

Group 3: amniocentesis performed due to malformations on ultrasound scan and or fetuses with abnormal karyotype.

# UV-filtre i fostervand, urin og serum ved Amniocentese

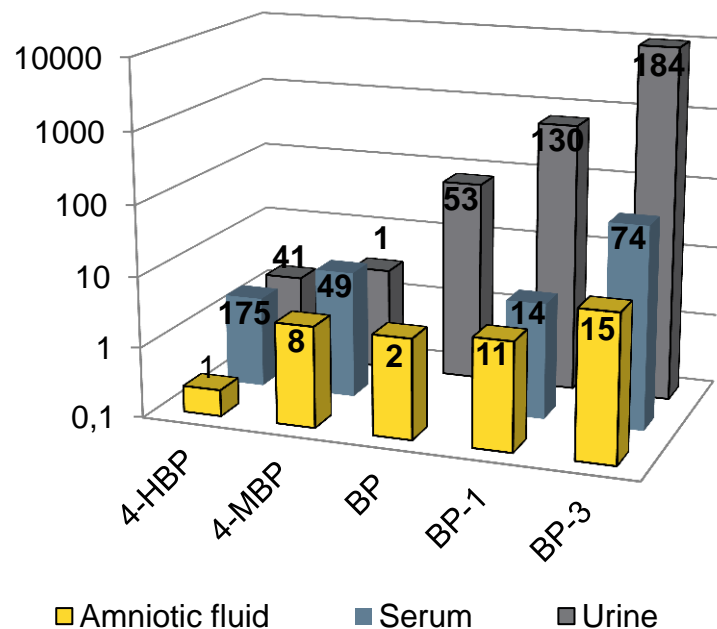
**Koncentration (ng/ml) i maternal serum (n=198), urin (n=200) og fostervand (n=200) indsamlet ved amniocentese, graviditetsuge 12-36**

|            | Benzophe none | LOD*  | n >LOD (%) | Min. | Percentile |      |      | Max.  |      |      |
|------------|---------------|-------|------------|------|------------|------|------|-------|------|------|
|            |               |       |            |      | 50         | 75   | 90   |       |      |      |
| Serum      | BP-1          | 0.13  | 14 (7)     |      |            |      | <LOD | 4.37  |      |      |
|            | BP-2          | 0.08  | 0          |      |            |      |      | <LOD  |      |      |
|            | BP-3          | 0.12  | 74 (37)    |      | <LOD       | 0.39 | 0.79 | 71.8  |      |      |
|            | BP-7          | 0.24  | 3 (2)      |      |            |      |      | <LOD  | 0.68 |      |
|            | 4-HBP         | 0.18  | 175 ( 88)  | <LOD | 0.63       | 0.92 | 1.22 | 1.96  |      |      |
|            | 4-MBP         | 0.27  | 49 (25)    |      |            | <LOD | 0.65 | 6.37  |      |      |
| Urin       | BP            | 2.35  | 53 (27)    |      |            |      | <LOD | 5.98  | 74.5 |      |
|            | BP-1          | 0.25  | 130 (65)   | <LOD | 0.46       | 2.44 | 16.1 | 665   |      |      |
|            | BP-2          | 0.41  | 3(2)       |      |            |      |      | <LOD  | 2.94 |      |
|            | BP-3          | 0.28  | 184 (92)   | <LOD | 2.59       | 10.4 | 96.2 | 10034 |      |      |
|            | BP-7          | 0.44  | 0          |      |            |      |      |       | <LOD |      |
|            | 4-HBP         | 0.23  | 41 (21)    |      |            | <LOD | 0.35 | 1.67  |      |      |
| 4-MBP      | 0.45          | 1 (1) |            |      |            |      |      | <LOD  | 2.94 |      |
| Fostervand | BP            | 2.35  | 2 (1)      |      |            |      |      | <LOD  | 2.6  |      |
|            | BP-1          | 0.25  | 11 (6)     |      |            |      |      | <LOD  | 3.38 |      |
|            | BP-2          | 0.41  | 0          |      |            |      |      |       | <LOD |      |
|            | BP-3          | 0.28  | 15 (8)     |      |            |      |      |       | <LOD | 11.6 |
|            | BP-7          | 0.44  | 0          |      |            |      |      |       | <LOD |      |
|            | 4-HBP         | 0.23  | 1 (1)      |      |            |      |      |       | <LOD | 0.24 |
| 4-MBP      | 0.45          | 8 (4) |            |      |            |      |      | <LOD  | 2.7  |      |

\* LOD: detektionsgrænse

BP: benzophenone (na i serum);  
 BP-1: benzophenone-1  
 BP-2: benzophenone-2  
 BP-3: benzophenone-3  
 BP-7: 5 chloro-2-hydroxybenzophenone  
 4-HBP: 4-hydroxy-benzophenone  
 4-MBP: 4-methyl-benzophenone

Max koncentrationer ved amniocentese



# UV-filtre i urin, serum og navlesnorsblod ved fødsel

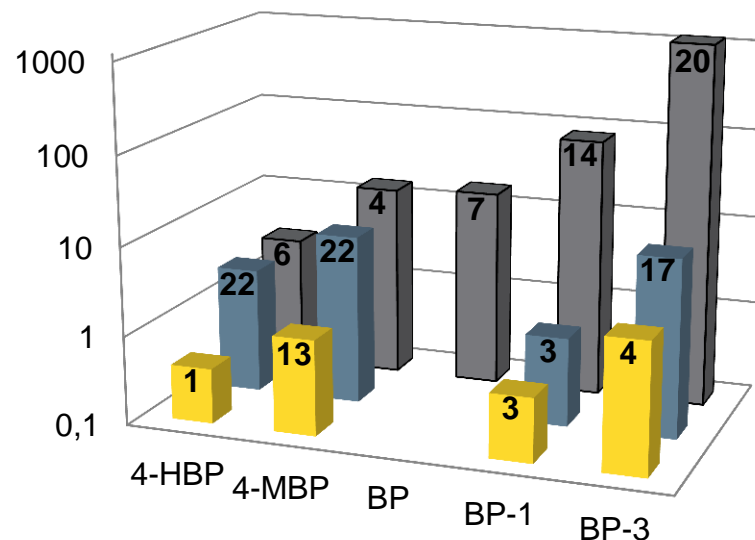
Koncentration (ng/ml) i maternal serum (n=22), urin (n=20) og navlesnorsblod (n=22) indsamlet ved fødslen fra 23 kvinder

|            | Benzophe none | LOD* | n >LOD (%) | Min. | Percentile |      |      | Max. |
|------------|---------------|------|------------|------|------------|------|------|------|
|            |               |      |            |      | 50         | 75   | 90   |      |
| Serum      | BP-1          | 0.13 | 3 (14)     |      | <LOD       | 0.33 | 0.99 |      |
|            | BP-2          | 0.08 | 0          |      |            |      | <LOD |      |
|            | BP-3          | 0.12 | 17 (77)    | <LOD | 0.27       | 0.64 | 1.96 | 10.1 |
|            | BP-7          | 0.24 | 1 (5)      |      |            |      | <LOD | 0.28 |
|            | 4-HBP         | 0.18 | 22 (100)   | 0.77 | 1.57       | 1.96 | 2.34 | 2.55 |
|            | 4-MBP         | 0.27 | 22 (100)   | 0.3  | 0.92       | 1.35 | 1.77 | 8.01 |
| Urin       | BP            | 2.35 | 7 (35)     | <LOD | 1.66       | 3.17 | 7.43 | 16.5 |
|            | BP-1          | 0.25 | 14 (70)    | <LOD | 1.04       | 5.3  | 21.8 | 81.4 |
|            | BP-2          | 0.41 | 0          |      |            |      |      | <LOD |
|            | BP-3          | 0.28 | 20 (100)   | 0.42 | 6.89       | 38.9 | 329  | 1162 |
|            | BP-7          | 0.44 | 0          |      |            |      |      | <LOD |
|            | 4-HBP         | 0.23 | 6 (30)     | <LOD | 0.44       | 1.21 | 2.84 |      |
| Fostervand | 4-MBP         | 0.45 | 4 (20)     |      | <LOD       | 1.57 | 14.6 |      |
|            | BP            | 2.35 | 3 (14)     |      | <LOD       | 0.29 | 0.53 |      |
|            | BP-1          | 0.25 | 0          |      |            |      |      | <LOD |
|            | BP-2          | 0.41 | 4 (18)     |      | <LOD       | 0.85 | 2.93 |      |
|            | BP-3          | 0.28 | 0          |      |            |      |      | <LOD |
|            | BP-7          | 0.44 | 1 (5)      |      |            |      | <LOD | 0.43 |
|            | 4-HBP         | 0.23 | 13 (59)    | <LOD | 0.35       | 0.43 | 0.9  | 1.2  |
|            | 4-MBP         | 0.45 | 3 (14)     |      | <LOD       | 0.33 | 0.99 |      |

\* LOD: detektions grænse

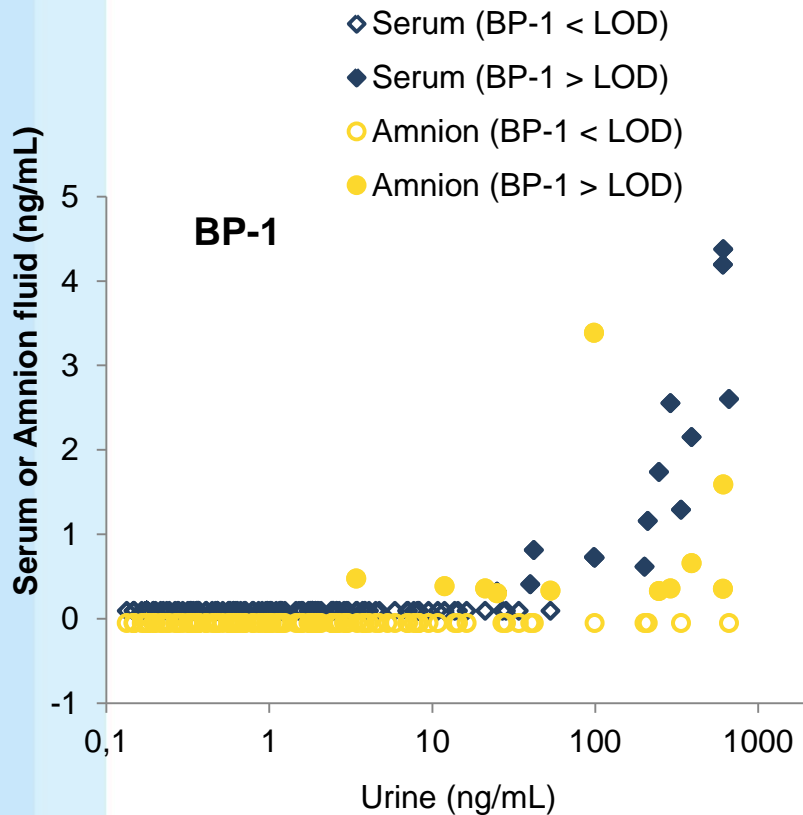
BP: benzophenone (na i serum);  
 BP-1: benzophenone-1  
 BP-2: benzophenone-2  
 BP-3: benzophenone-3  
 BP-7: 5 chloro-2-hydroxybenzophenone  
 4-HBP: 4-hydroxy-benzophenone  
 4-MBP: 4-methyl-benzophenone

Max koncentrationer ved fødsel

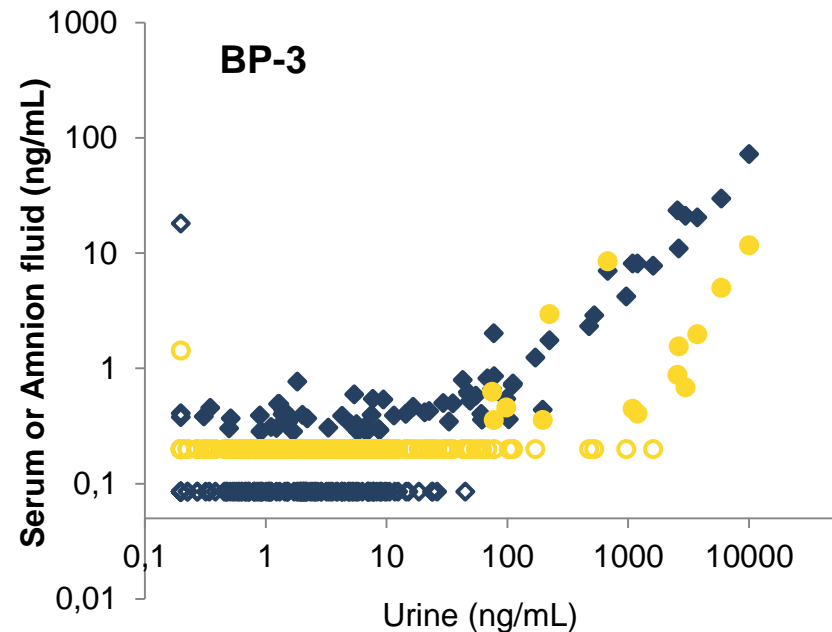


■ Cord blood ■ Serum delivery ■ Urine delivery

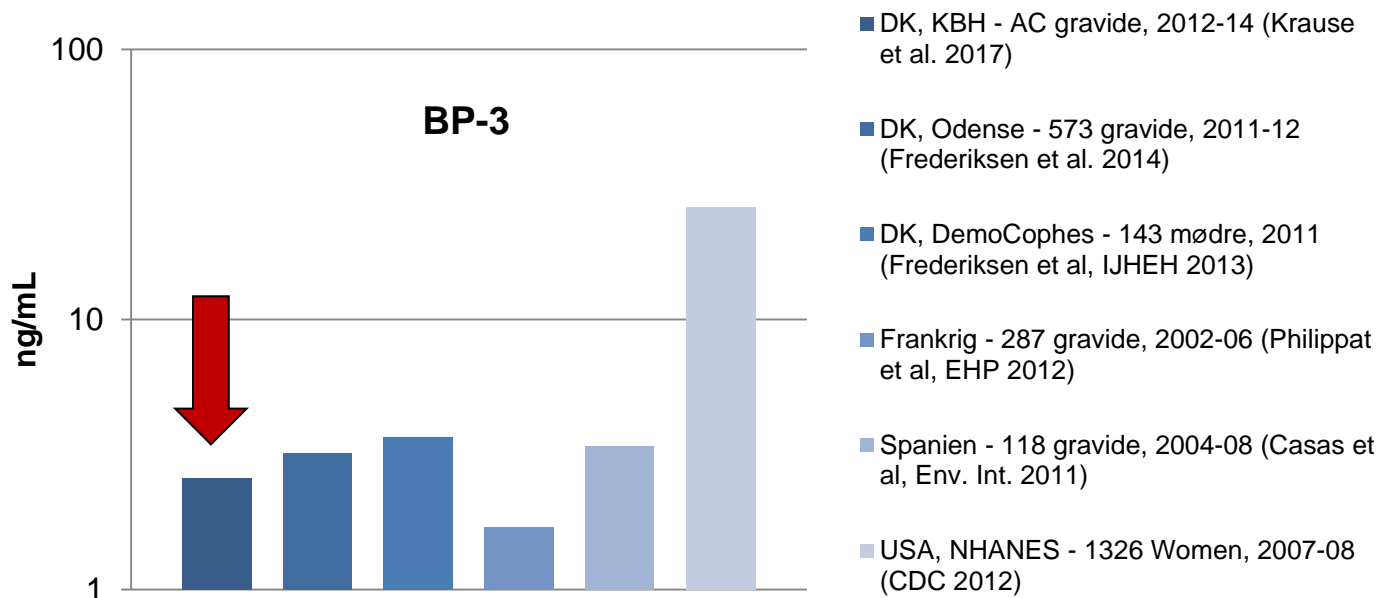
# Korrelation mellem UV-filter konc. i parrede maternale og føtale prøver ved amniocentese



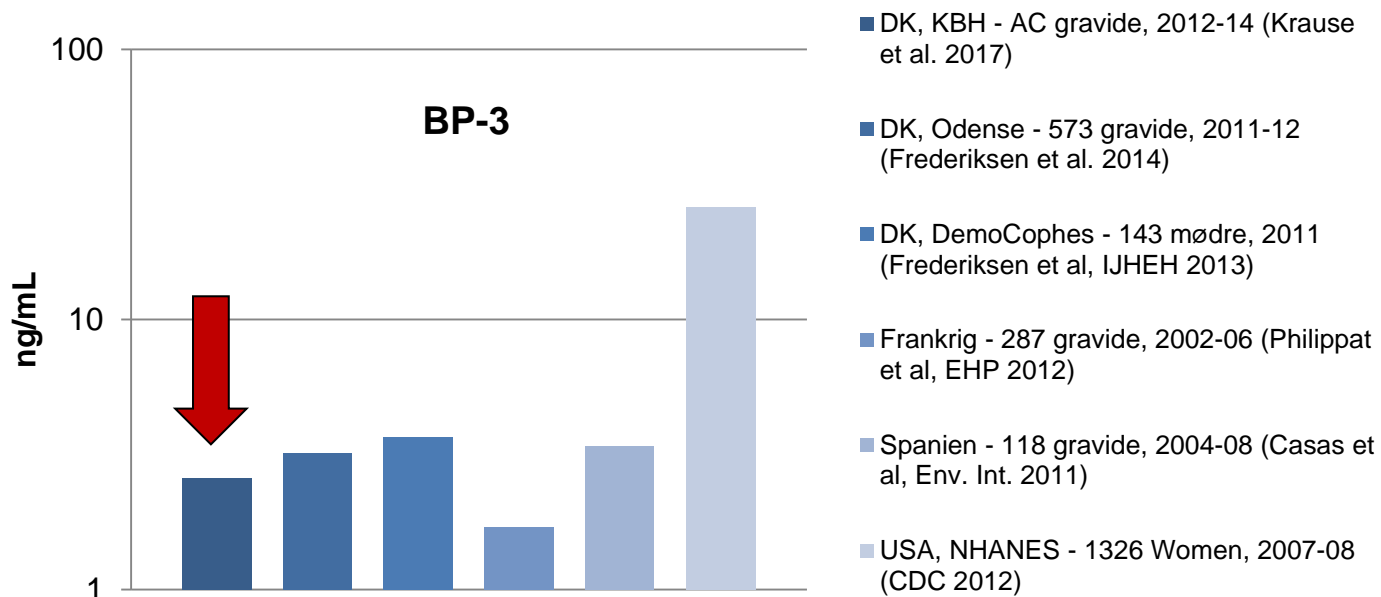
|                                 | Antal parrede prøver | Spearman coefficient | p- value |
|---------------------------------|----------------------|----------------------|----------|
| <b>Urin vs. serum</b>           |                      |                      |          |
| BP-1                            | 14                   | 0.921                | 0.000**  |
| BP-3                            | 71                   | 0.774                | 0.000**  |
| 4-HBP                           | 27                   | -0.029               | 0.887    |
| <b>Urin vs. fostervand</b>      |                      |                      |          |
| BP-1                            | 11                   | 0.127                | 0.709    |
| BP-3                            | 14                   | 0.604                | 0.022*   |
| <b>Serum vs. fostervand</b>     |                      |                      |          |
| BP-1                            | 7                    | 0.321                | 0.482    |
| BP-3                            | 15                   | 0.571                | 0.026*   |
| <b>Serum vs. navlesnorsblod</b> |                      |                      |          |
| 4-MBP                           | 13                   | -0.137               | 0.655    |



## Kvinder i Europa og USA



# Kvinder i Europa og USA



Vægt : 60 kg  
 Urin: 2 L/dag  
 Urin udskillelses faktor ?  
 x sikkerhedsfaktor 100

|                                      | BP-1 | BP-3  |
|--------------------------------------|------|-------|
| <b>200 gravide kvinder</b>           |      |       |
| Middel (median) eksponering (ug/L)   | 0.46 | 2.59  |
| Højest eksponerede gravide (ug/L)    | 665  | 10034 |
| Estimeret dagligt indtag (mg/kg/dag) | 0.02 | 0.33  |
| DI * SF (mg/kg/dag)                  | 2.22 | 33.45 |
| <b>NOALS* i rotte studier</b>        |      |       |
| Tox (mg/kg/dag)                      | 236  | 200   |
| Reprotox (mg/kg/dag)                 | 100  | 700   |

\*no observed adverse effect levels

## Konklusion

- BP-1, BP-3, 4-MBP og 4-HBP blev målt i fostervand ved amniocentese og navlesnorsblod ved fødsel
- BP-1, BP-3 og 4-MBP blev målt i føtalblod ved cordocentese
- BP-1 og BP-3 koncentrationen i føtal- og navlesnorsblod var ca. 10 gange lavere end i maternal serum og 1000 gange lavere end i maternal urin.
- BP-1 og BP-3 kunne kun måles i den føtale cirkulationen når moderen var udsat for en høj eksponering, hvilket indikerer en vis beskyttelse af fostret.
- 4-MBP passerer tilsyneladende lettere end andre UV-filtre til føtal- og navlesnorsblod (ratio 1: 3 mellem navlesnorsblod og maternal serumniveau)
- Niveauet af BP-3 i fostervand og maternal urin korrelerede og den gravide kvindes eksponering for BP-3 kan således være en gyldig proxy for fostrets eksponering.

## ARTICLE IN PRESS

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## Presence of benzophenones commonly used as UV filters and absorbers in paired maternal and fetal samples

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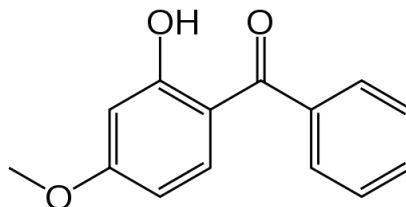
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<sup>d</sup> Fetal Medicine Unit, Department of Obstetrics and Gynecology, Copenhagen University Hospital Hvidovre, Denmark

<sup>e</sup> Department of Plastic Surgery, Breast Surgery and Burns Treatment, Rigshospitalet, University of Copenhagen, Denmark

## Perspektiver: Hvad betyder den føtale UV-filter eksponering for den senere udvikling?



## Mange tak til

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# CEHOS



Endocrine Disruption of  
Male Reproduction and Child Health



- Velux Fondene
- Lundbeck Fonden
- Augustinus Fonden
- Svend Andersens Fond