CeHoS-EDMaRC projekt

”Undersøgelse af ændringer over tid i graden og mønstret af eksponering for phthalater, bisphenoler og andre phenoler”

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Timetrend studiet

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Timetrend studiet

Formål

- at undersøge befolkningens eksponeringsmønster for de velkendte, og nu regulerede, phthalater og bispehnol A (BPA), samt for nye substitutter for disse stoffer
- at belyse om regulering og gradvis udfasning af visse phthalater og BPA har medført en ændring i eksponeringsmønstret, som samlet giver en nedsat eksponering for phthalater og bisphenoler

Studie design

- 300 unge danske mænd fra den generelle befolkning
- Urinprøver indsamlet i 2009, 2013 og 2017
- Kemisk analyse af 32 kemikalier, som er eller mistænkes for at være hormonforstyrrende

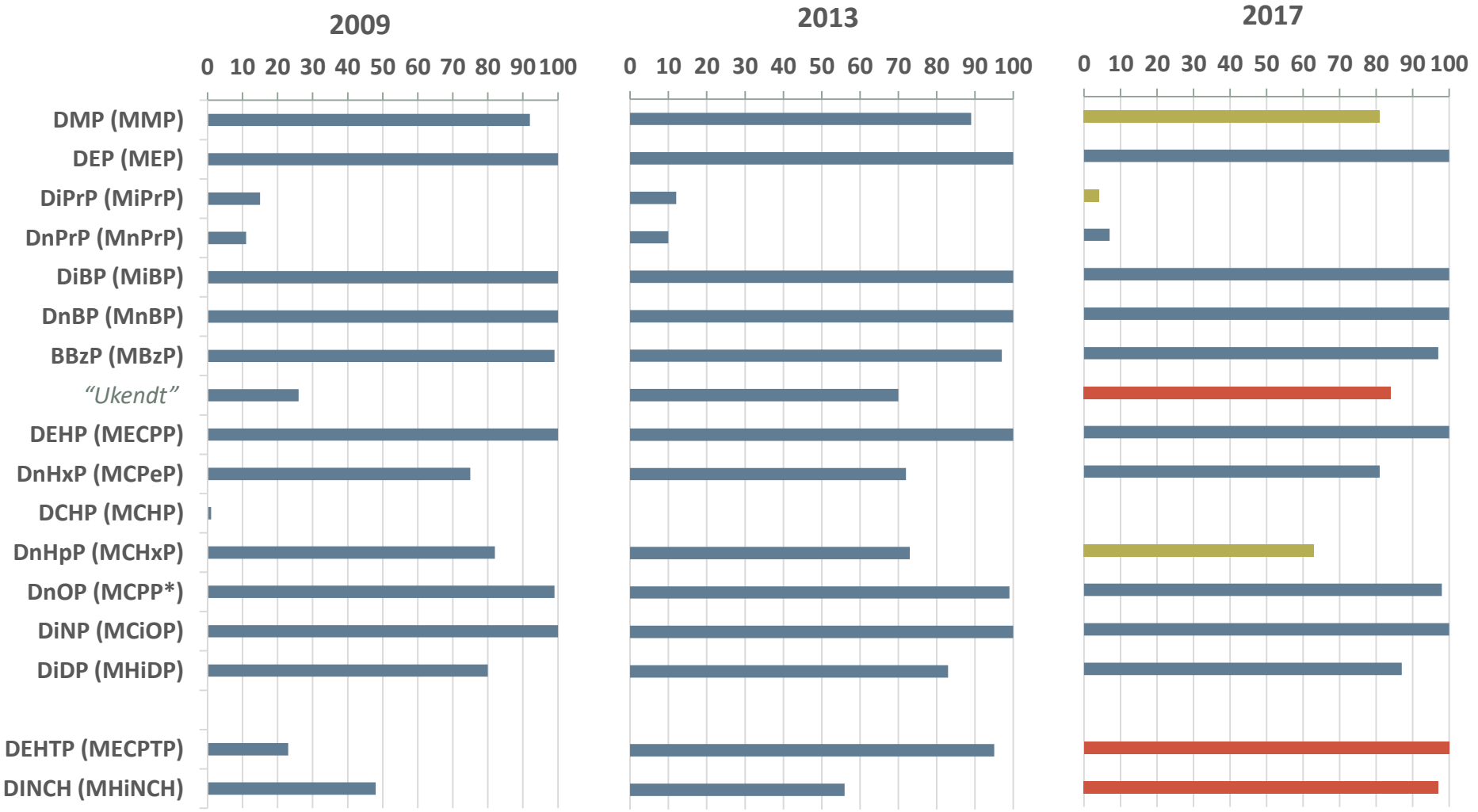
Phthalater er plastblødgørrende stoffer i industrielle produkter

Phthalate diesters and phthalate substitutes and their metabolites				
	Phthalate diester		Human urine metabolite	Abbreviation
Phthalates				
	Di-methyl phthalate	DMP	Mono-methyl phthalate	MMP
	Di-ethyl phthalate	DEP	Mono-ethyl phthalate	MEP
	Di-iso-propyl phthalate	DiPrP	Mono-iso-propyl phthalate	MiPrP
	Di-n-propyl phthalate	DPrP	Mono-propyl phthalate	MPrP
	Di-iso-butyl phthalate	DiBP	Mono-iso-butyl phthalate	MiBP
	Di-n-butyl phthalate	DnBP	Mono-n-butyl phthalate	MnBP
			Mono-(3-hydroxybutyl) phthalate	MHBP
	Butylbenzyl phthalate	BBzP	Mono-benzyl phthalate	MBzP
	Di-n-pentyl phthalate	DnPeP	Mono-n-pentyl phthalate	MnPeP
			Mono-(4-hydroxypentyl) phthalate	MHPeP
	Di-(2-ethyl-hexyl) phthalate	DEHP	Mono-(2-ethyl-hexyl) phthalate	MEHP
			Mono-(2-ethyl-5-hydroxyhexyl) phthalate	MEHHP
			Mono-(2-ethyl-5-oxohexyl) phthalate	MEOHP
			Mono-(2-ethyl-5-carboxypentyl) phthalate	MECPP
			Mono-(2-carboxymethylhexyl) phthalate	MCMHP
	Di-n-hexyl phthalate	DnHxP	Mono-n-hexyl phthalate	MHxP
			Mono-(5-hydroxyhexyl) phthalate	MHHxP
			Mono-(5-carboxypentyl) phthalate	MCPeP
	Di-cyclohexyl phthalate	DCHP	Mono-cyclohexyl phthalate	MCHP
	Di-n-heptyl phthalate	DnHpP	Mono-n-heptyl phthalate	MHpP
			Mono-(6-hydroxyheptyl) phthalate	MHHpP
			Mono-(6-carboxyhexyl) phthalate	MCHxP
	Di-octyl phthalate	DnOP	Mono-n-octyl phthalate	MnOP
			Mono-3-carboxypropyl phthalate	MCPP*
	Di-iso-nonyl phthalate	DiNP	Mono-iso-nonyl phthalate	MiNP
			Mono-hydroxy-iso-nonyl phthalate	MHiNP
			Mono-oxo-iso-nonyl phthalate	MOiNP
			Mono-carboxy-iso-octyl phthalate	MCiOP
	Di-iso-decylphthalate	DiDP	Mono-iso-decyl phthalate	MiDP
			Mono-(9-hydroxydecyl) phthalate	MHiDP
			Mono-(9-oxodecyl) phthalate	MOiDP
			Mono-(9-carboxynonyl) phthalate	MCiNP
Phthalate substitutes				
	Di-2-ethylhexyl terephthalate	DEHTP	Mono-(2-ethyl-5-hydroxy-hexyl) terephthalate	MEHHTP
			Mono-(2-ethyl-5-oxo-hexyl) terephthalate	MEOHTP
			Mono-(2-ethyl-5-caboxyl-pentyl) terephthalate	MECPTP
			Mono-(2-caboxyl-methyl-hexyl) terephthalate	MCMHTP
	Di-iso-nonyl-cyclohexane-1,2-dicarboxylate	DINCH	Cyclohexane-1,2-dicarboxylate-mono-(hydroxyl-iso-nonyl) ester	MHiNCH
			Cyclohexane-1,2-dicarboxylate-mono-(carboxy-iso-octyl) ester	MCiOCH

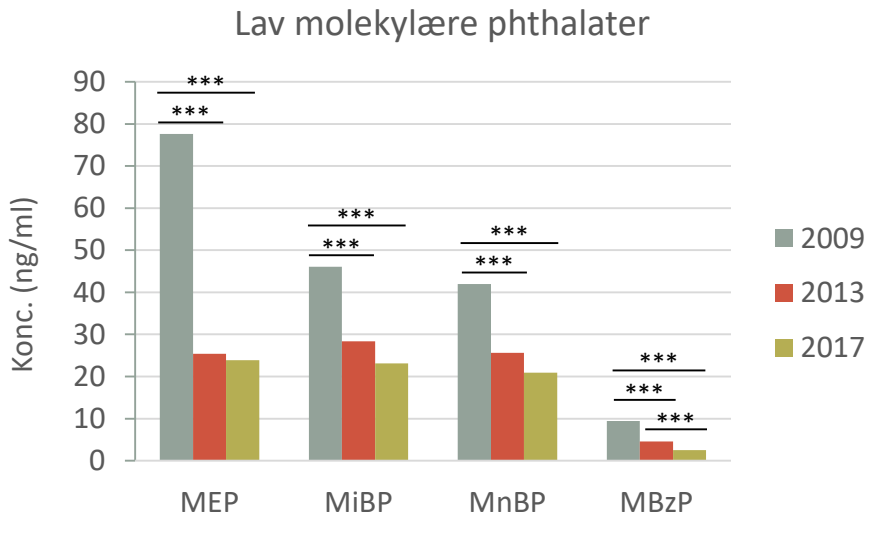
* MCPP is the major metabolite of DnOP but are not specific for DnOP

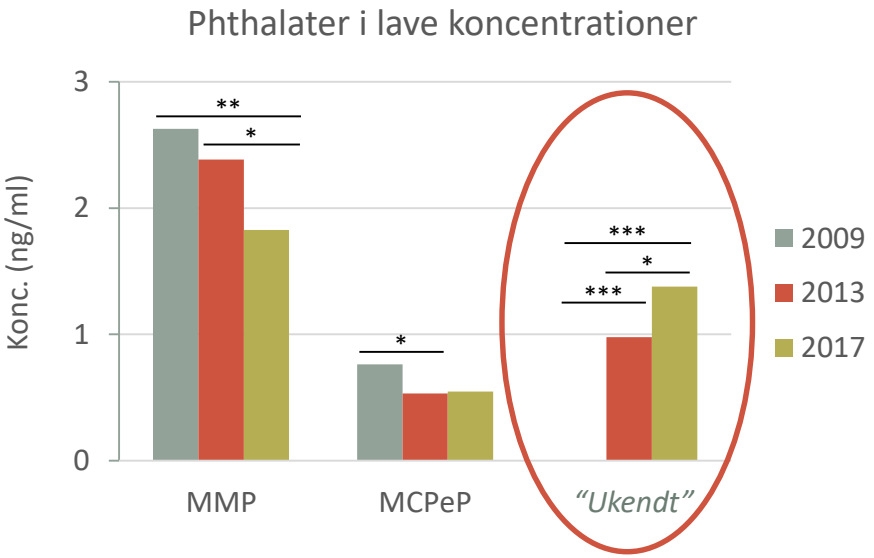
32 metabolitter fra 15 phthalater
og
6 metabolitter fra 2 phthalat substitutter
(DINCH og DEHTP)

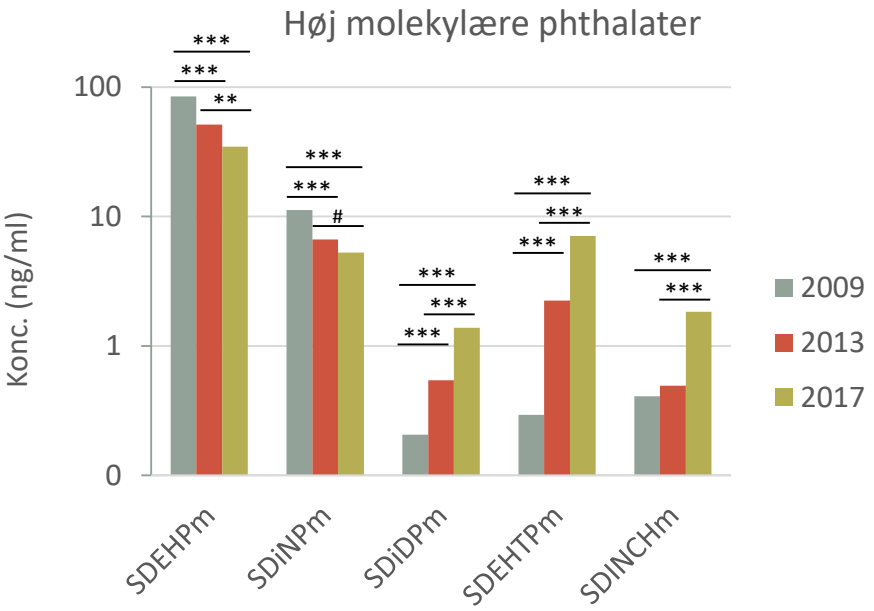
Antal mænd eksponeret for phthalater

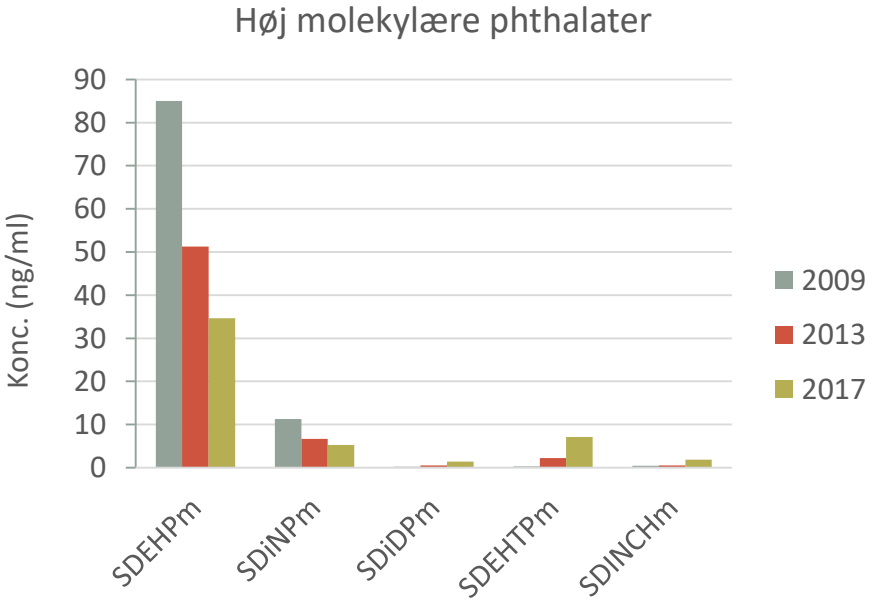


Phthalater og substitutter målt i urin

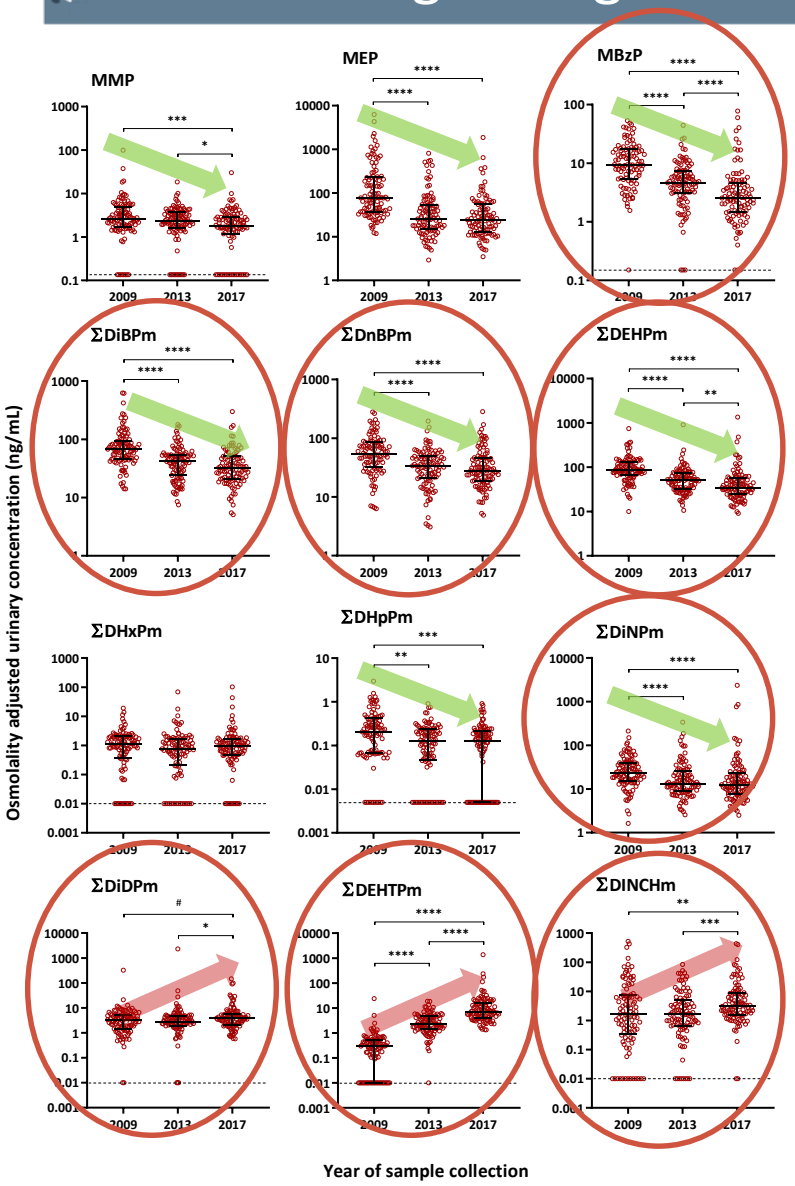








Regulering af hormonforstyrrende phthalater



Frederiksen et al, 2019, in press

De fire phthlater, DiBP, DnBP, BBzP og DEHP:

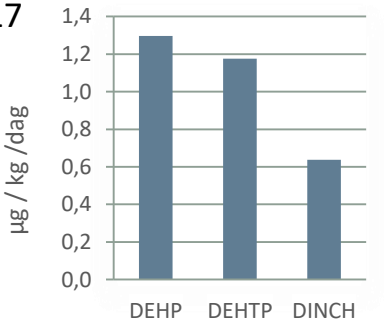
- gradvist begrænset og udfaset fra mange forbrugerprodukter, bl.a. legetøj, børneartikler og fødevarekontakt materialer
- July 2020, vil **de fire** i EU kun være tilladt i koncentrationer lig med eller under 0,1 vægtprocent hver for sig eller i en hvilken som helst kombination i plastikmaterialer til almindelige forbrugere og i indendørsmiljøer

Andre

- **DINP, DIDP og DNOP** er registreret under REACH* pga. mistanke om tilsvarende hormonforstyrrende egenskaber
- **DnPeP** er registreret under REACH på kandidatlisten som et SVHC** kemikalie, hvor der er grund til meget stor bekymring

Phthalat substitutter, **DEHTP og DINCH**

- Vurderes ikke til at have samme hormonforstyrrende egenskaber som f.x. DEHP
- Kemisk struktur og metaboliseringsmønster analogt til DEHP
- Estimeret daglig eksponering i 2017



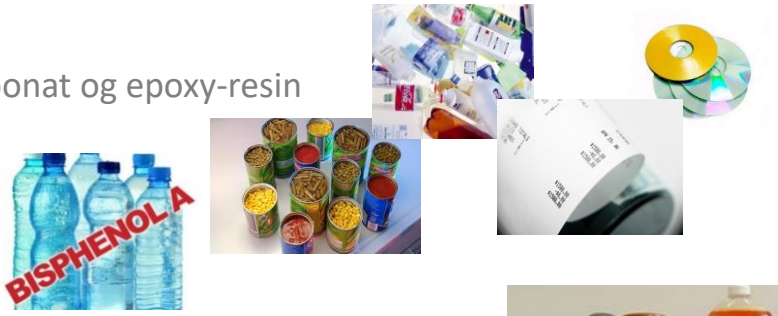
*REACH (Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals),
**SVHC substance (Substance of very high concern)

7 Bisphenoler og 6 andre phenoler

Bisphenoler		
	Bisphenol A (2,2-Bis(4-hydroxyphenyl)propane)	BPA
	Bisphenol S (4,4´-Sulfonyldiphenol)	BPS
	Bisphenol F (4,4´-Methylenediphenol)	BPF
	1,1-Bis(4-hydroxyphenyl)ethane	BPE
	2,2-Bis(4-hydroxy-3-methylphenyl)propane	BPC
	2,2-Bis(4-hydroxy-3-isopropylphenyl)propane	BPG
	1,1-Bis(4-hydroxyphenyl)-1,1diphenylmethane	BPBP

Andre phenoler		
	Triclosan	TCS
	Triclocarban	TCC
	Benzophenone-3	BP-3
	2,4-Dichlorophenol	2,4-DCP
	2,5-Dichlorophenol	2,5-DCP
	2,4,5-Trichlorophenol	2,4,5-TCP
	2-Phenylphenol	2-PP
	4-Phenylphenol	4-PP

Polykarbonat og epoxy-resin



Anti-mikrobielle konserveringsmidler

UV-filter

Pesticider og intermediater i organisk syntese

Fungicider

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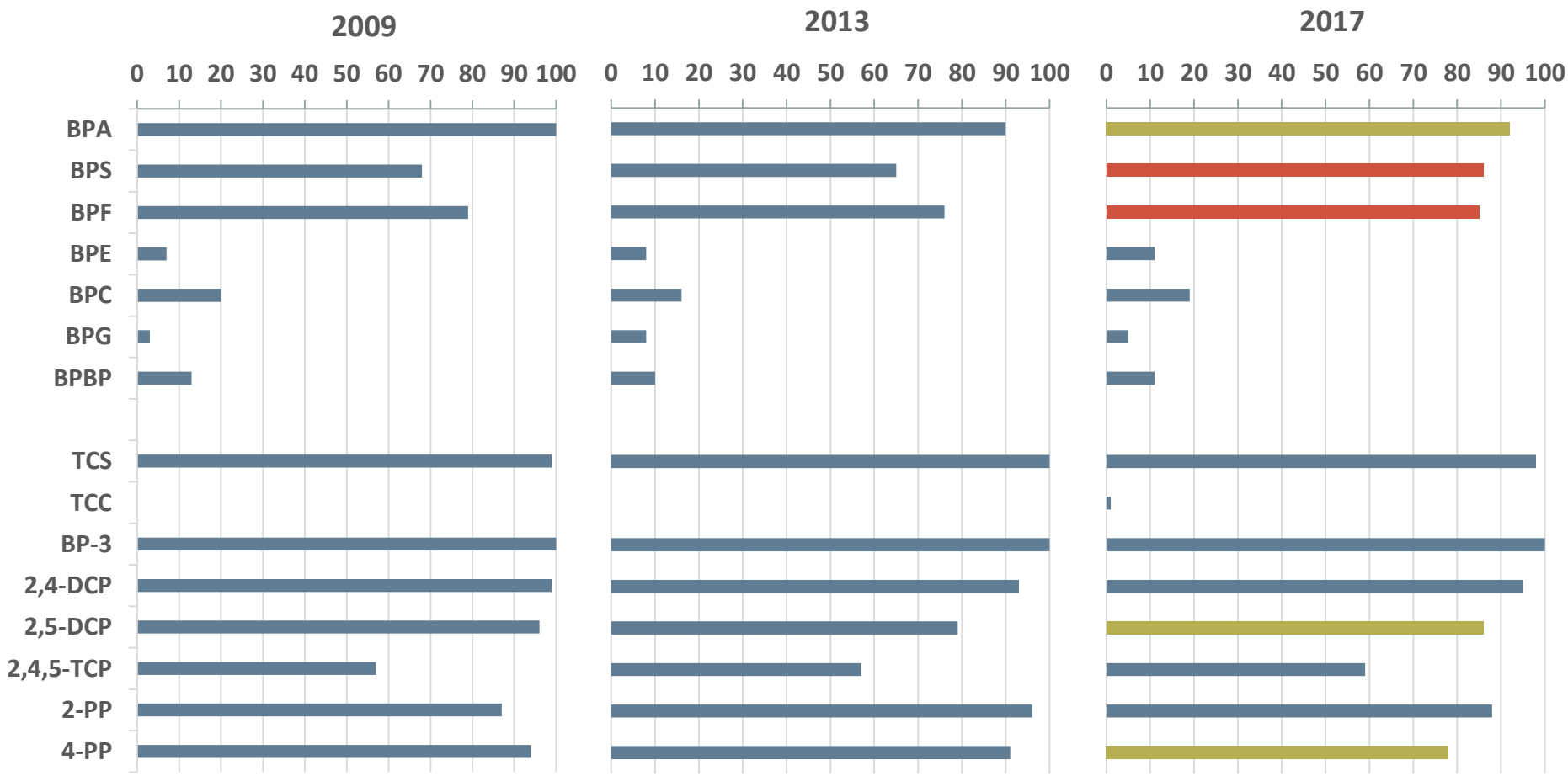
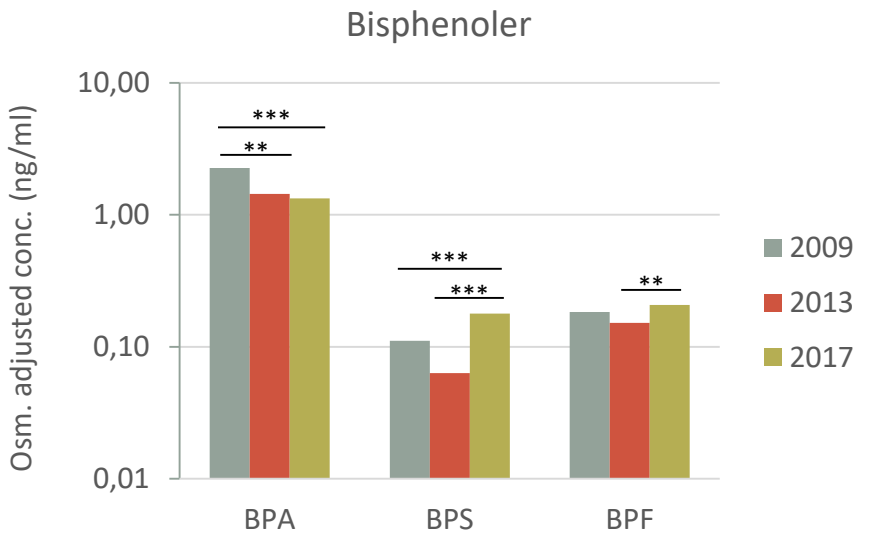
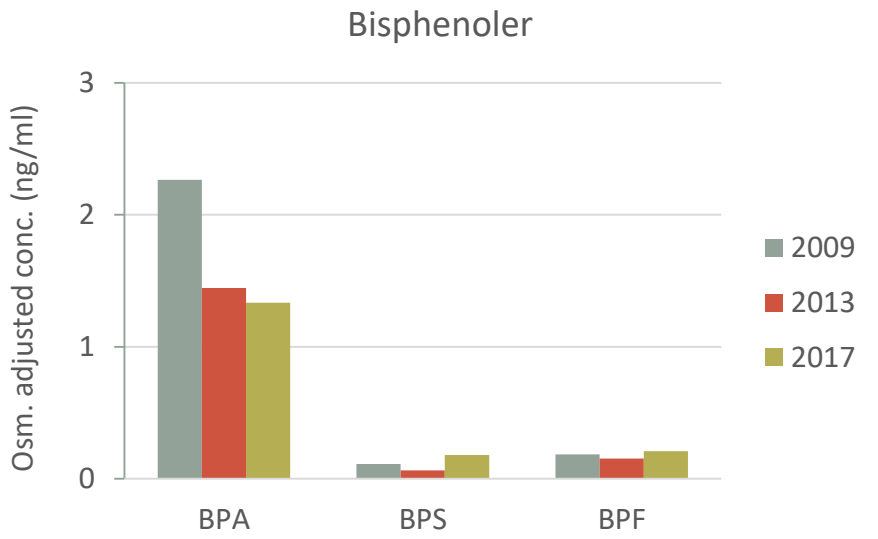
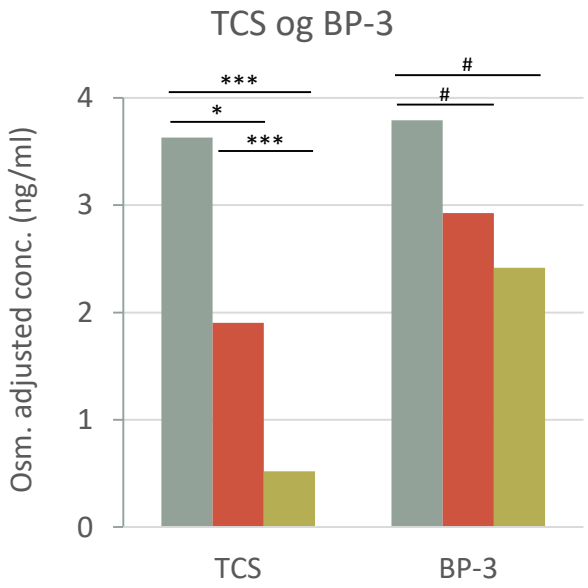
Antal mænd eksponeret for bisphenoler og andre phenoler

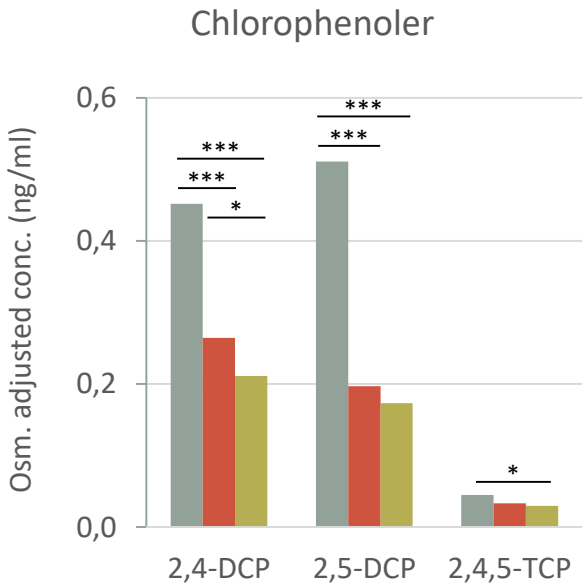


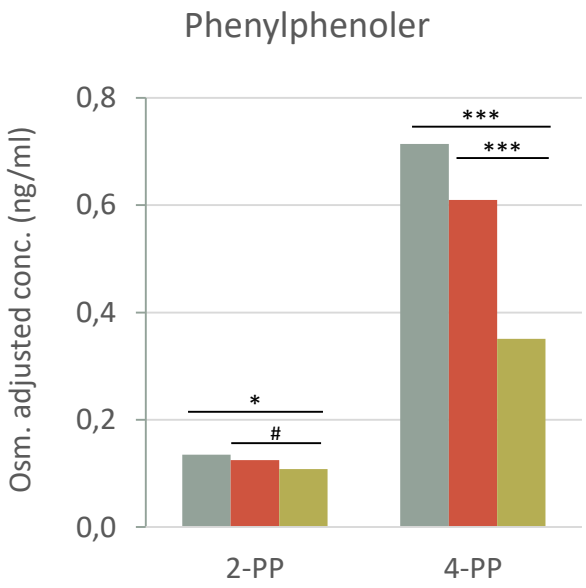
Bisphenoler og andre phenoler målt i urin



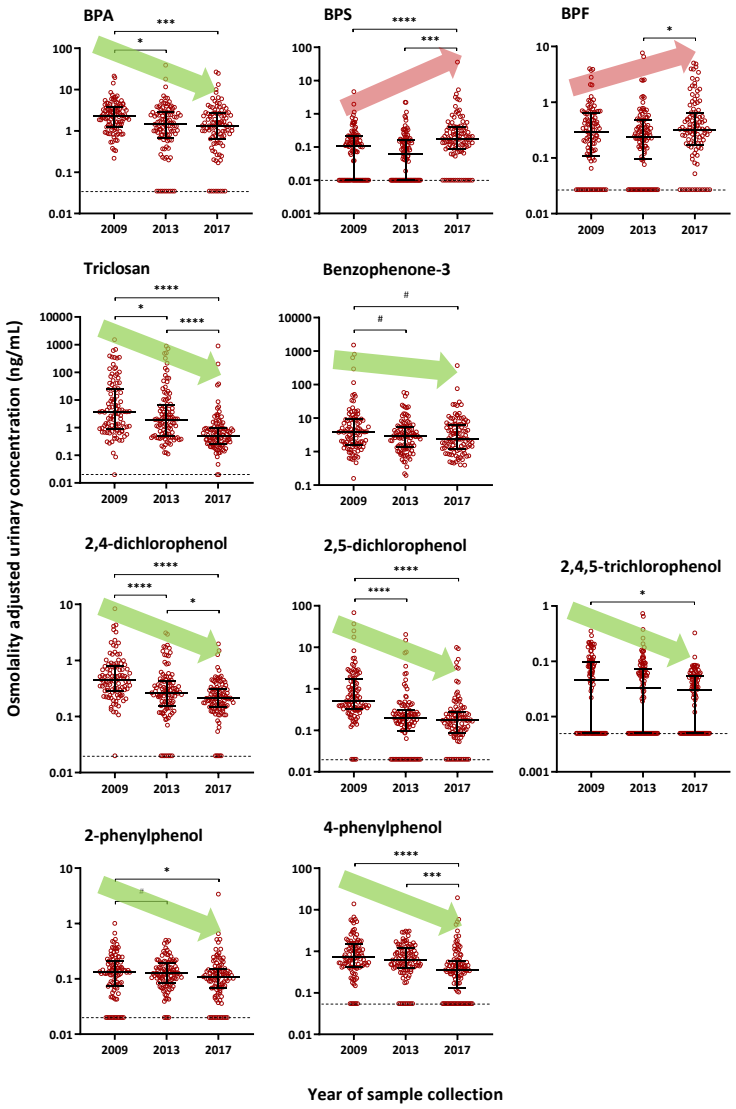








Regulering af phenoler



BPA

- **BPA** gradvist begrænset og udfaset fra mange forbrugerprodukter, bl.a. babyartikler
- Fra juli 2020, vil **BPA** i EU kun være tilladt i koncentrationer lig med eller under 0,1 vægtprocent i forbrugerprodukter og i indendørsmiljøer
- BPS og BPF koncentrationen stiger ?

Chloro- and phenylphenolerne

- bl.a. pesticider og fungicider i konventionelt landbrug
- I Danmark er produktionen af økologisk frugt og grønt fordoblet fra 2015-2017*
- I Danmark er importen af økologiske vare mere end fordoblet fra 2012-2017*

TCS

- I Danmark har **TCS** i mange år kun været tilladt i få personlige plejemidler bl.a. tandpasta og deodorenter og kun i koncentrationer ≤ 0.3%.
- Siden 2015 har **TCS** også være forbudt i mange desinfektionsmidler for at undgå bioakkumulering i vandmiljøet

BP-3

- Iflg. EU lov har **BP-3** indtil september 2017 været tilladt som UV filter i koncentrationer ≤ 10% i alle kosmetikprodukter
- Fra september 2017 blev **BP-3** begrænset til ≤ 6% i solcremer og maks. 0.5% i alle andre kosmetikprodukter
- **BP-3** bruges stadig som UV absorber i mange andre forbrugerprodukter

Frederiksen et al, 2019, in press

*Danmarks Statistic 2019

Timetrend studiet - konklusion

- 32 kemikalier blev analyseret
- 26 kemikalier blev målt i > 60% af mændene i 2017
- 15 kemikalier faldt signifikant fra 2009 til 2017
- 5 kemikalier steg signifikant fra 2009 til 2017
- Positiv ændring i eksponeringsmønstret for langt de fleste målte phthlater og BPA i takt med regulering og udfasning
- Den samlede eksponering for både phthalater og bisphenoler er på trods af substitution nedbragt
- Positiv faldende eksponering for en række andre phenoler, som TCS og nogle pesticider og fungicider
- Mange tusind andre kemikalier

Timetrend studiet

International Journal of Hygiene and Environmental Health xxx (xxxx) xxx-xxx

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: http://ees.elsevier.com

Changes in urinary excretion of phthalates, phthalate substitutes, bisphenols and other polychlorinated and phenolic substances in young Danish men; 2009–2017

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ARTICLE INFO

Keywords
endocrine disruptor
human biomonitoring
phthalate
DINCH
di-2-ethylhexyl terephthalate (DEHTP)
phenol

ABSTRACT

During the past two decades human exposure to bisphenol A (BPA) and phthalates such as di-iso-butyl phthalate (DiBP), di-n-butyl phthalate (DnBP), butylbenzyl phthalate (BBzP) and di-(2-ethyl-hexyl) phthalate (DEHP) has received substantial interest due to widespread population exposures and potential endocrine disrupting effects. Therefore, these chemicals have gradually been restricted and phased out through legislation. However, humans are still exposed to a wide range of other less studied phthalates, phthalate substitutes and BPA analogues as well as other polychlorinated and phenolic substances. In this study, we investigated human exposure to these chemicals over the past decade. Three hundred urine samples collected in 2009, 2013 and 2017 (100 samples each year) from young Danish men of the general population, participating in a large on-going cross-sectional

Tak for økonomisk støtte til:

EDMaRC
Endocrine Disruption of Male Reproduction and Child Health

CEHOS

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