Problématique des phtalates et assimilés
Où en sommes-nous ?

Point de vue du clinicien

Laurent STORME
Pédiatre Néonatologiste

CHU & Université de Lille

LILLE

EURO-PHARMAT
N'A PAS PERDU LE NORD !

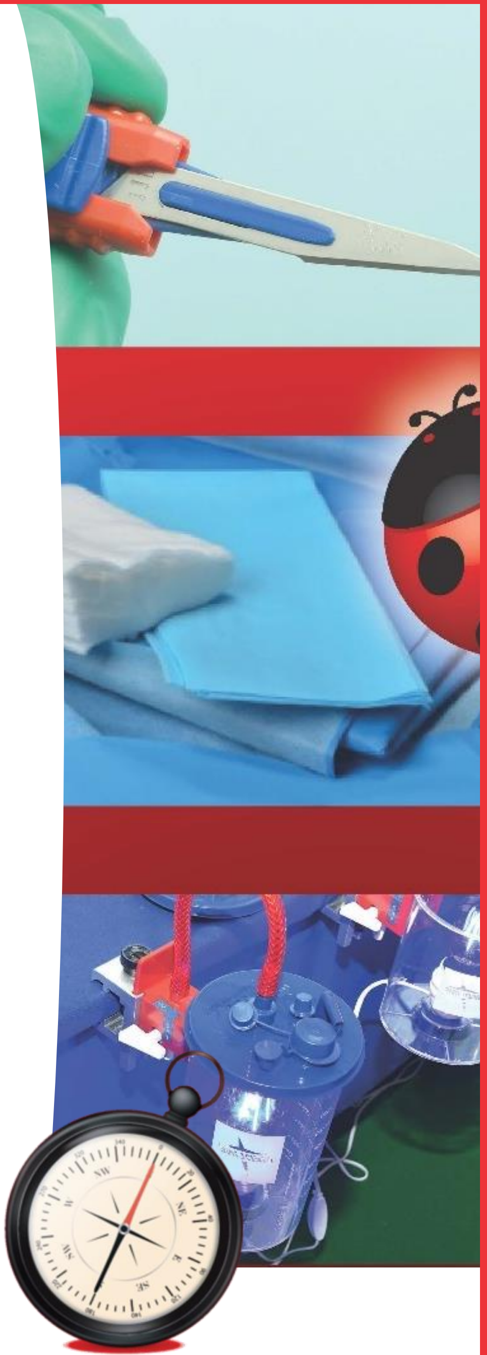
DÉBARQUEMENT SUR LILLE
LES 15, 16 ET 17 OCTOBRE 2024

POUR VIVRE ENSEMBLE

LES 34ES JOURNÉES NATIONALES SUR LES DISPOSITIFS MÉDICAUX STÉRILES

À LILLE GRAND PALAIS
1 BD DES CITÉS UNIES

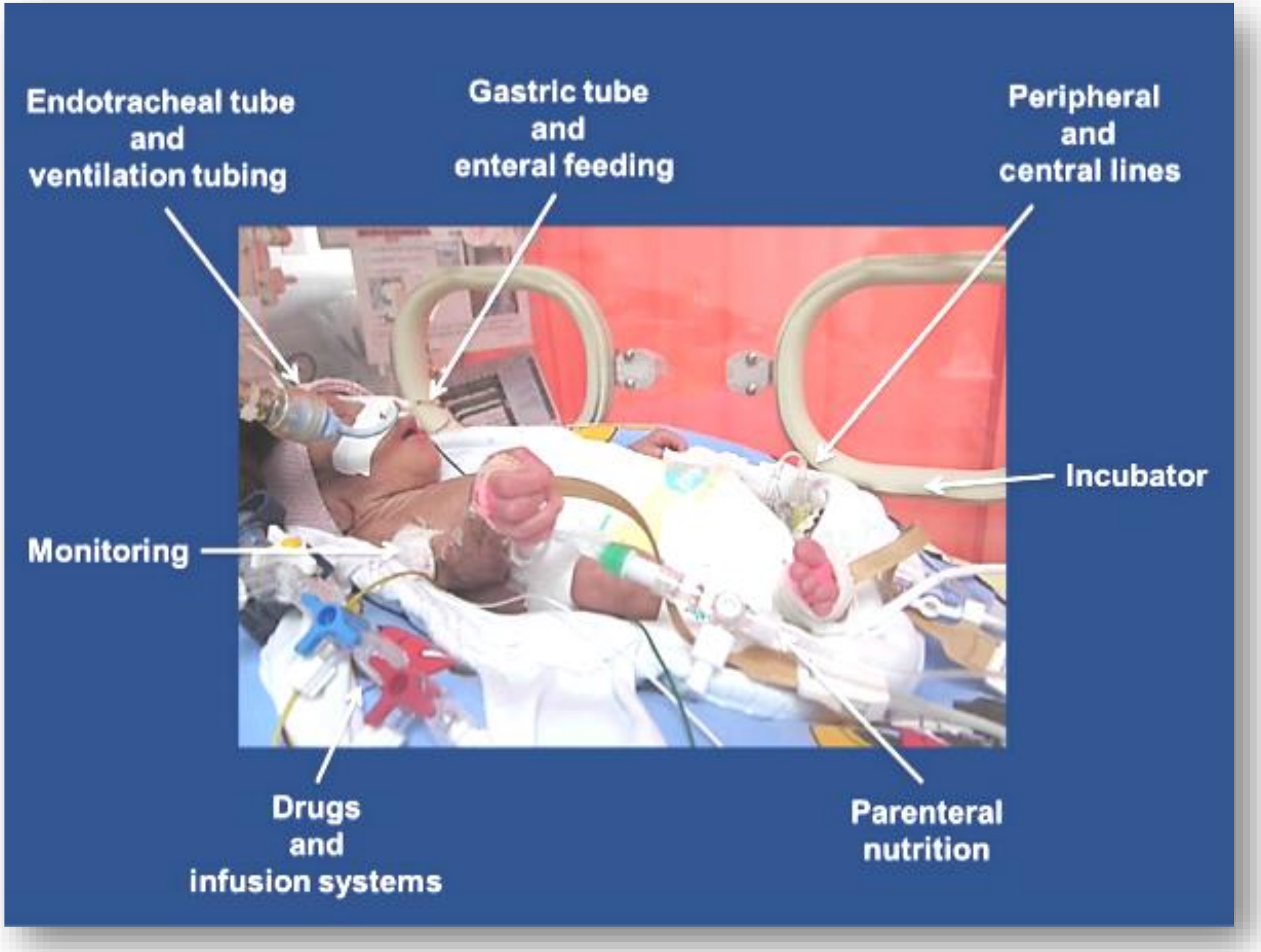
www.euro-pharmat.com
Hôtel Dieu - 2, rue Viguerie - TSA 80035 - 31059 TOULOUSE CEDEX 9 // Tél. : 05 61 77 83 70



Déclaration liens d'intérêts

- Aucun

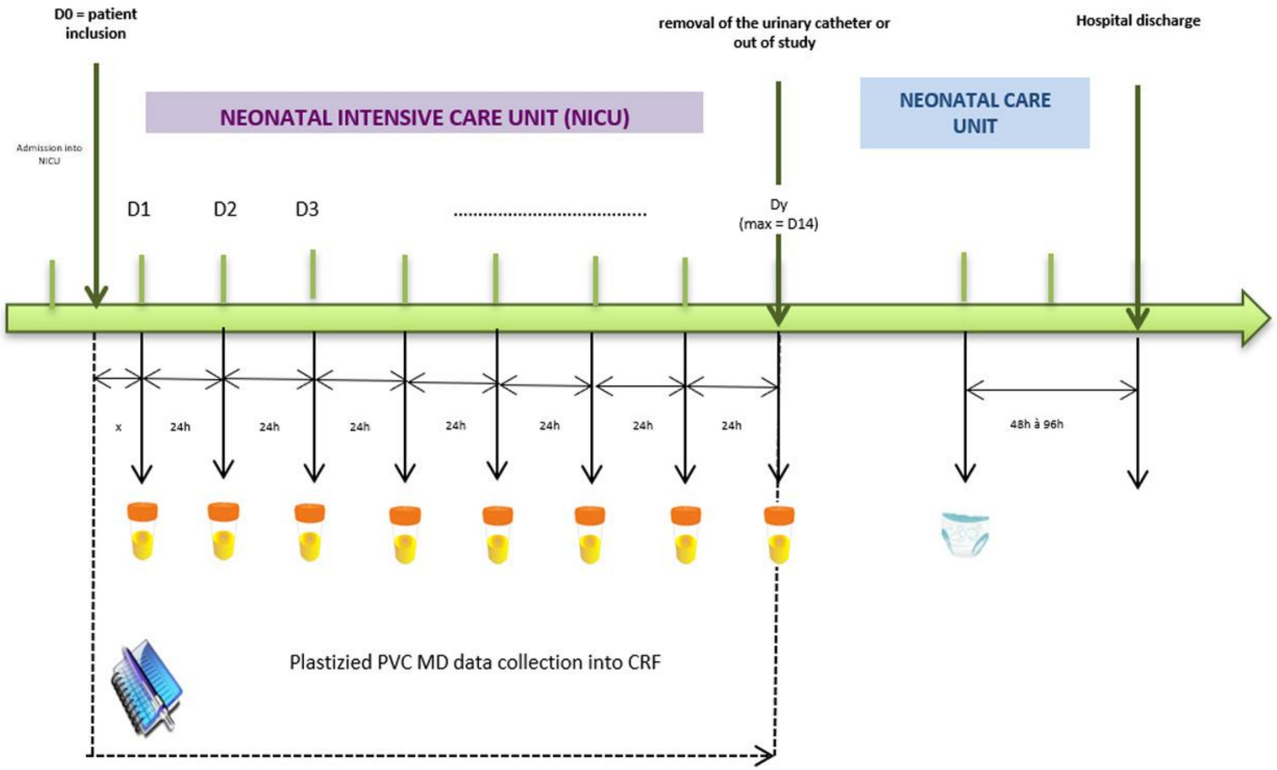
Plastifiants (Phthalates)

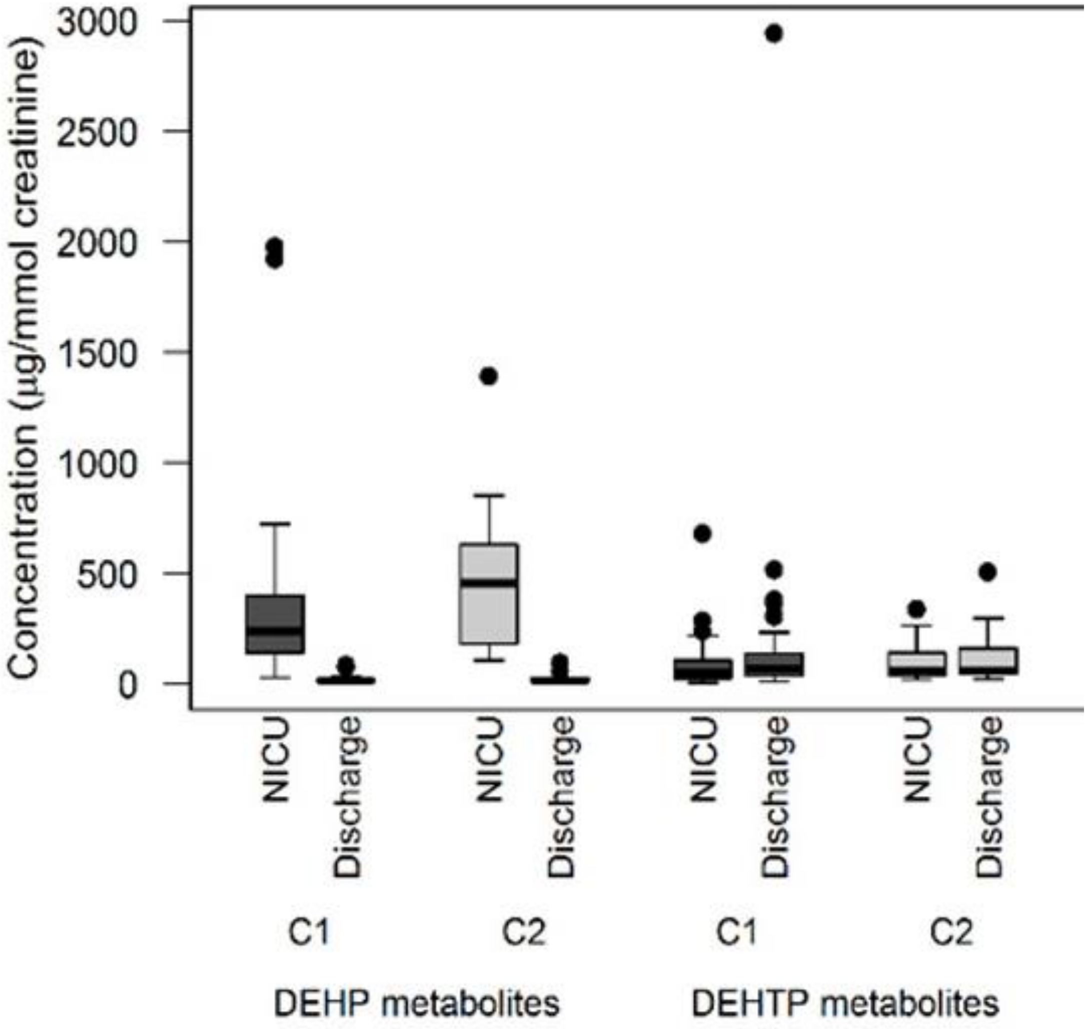

Endotracheal tube and ventilation tubing
Gastric tube and enteral feeding
Peripheral and central lines
Incubator
Monitoring
Drugs and infusion systems
Parenteral nutrition

ARMED

Financé par l'ANSM

Fischer CJ, J Paediatr Child Health. 2013
L Bernard, Sci Total Environ. 2023

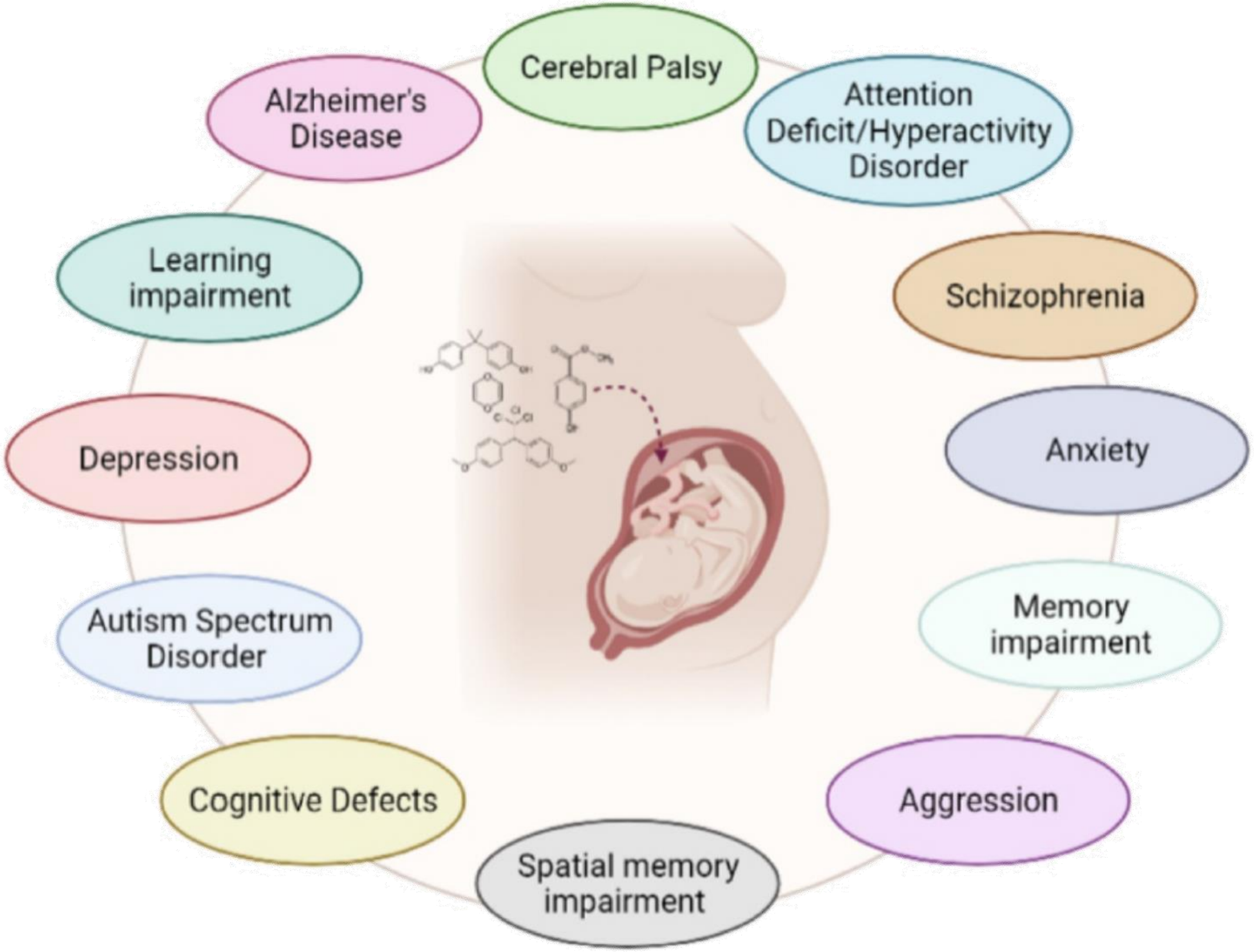

D0 = patient inclusion
removal of the urinary catheter or out of study
Hospital discharge
NEONATAL INTENSIVE CARE UNIT (NICU)
NEONATAL CARE UNIT
Admission into NICU
D1
D2
D3
……………………………
Dy (max = D14)
x
24h
24h
24h
24h
24h
24h
24h
48h à 96h
Plastizied PVC MD data collection into CRF



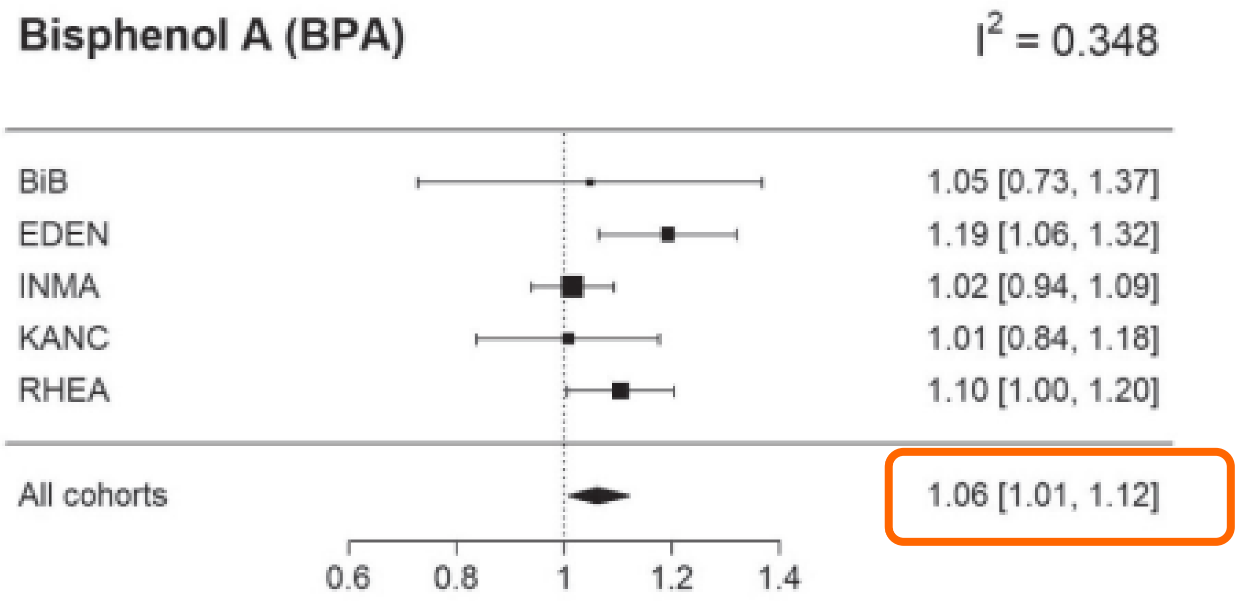
L Bernard, Sci Total Environ. 2023

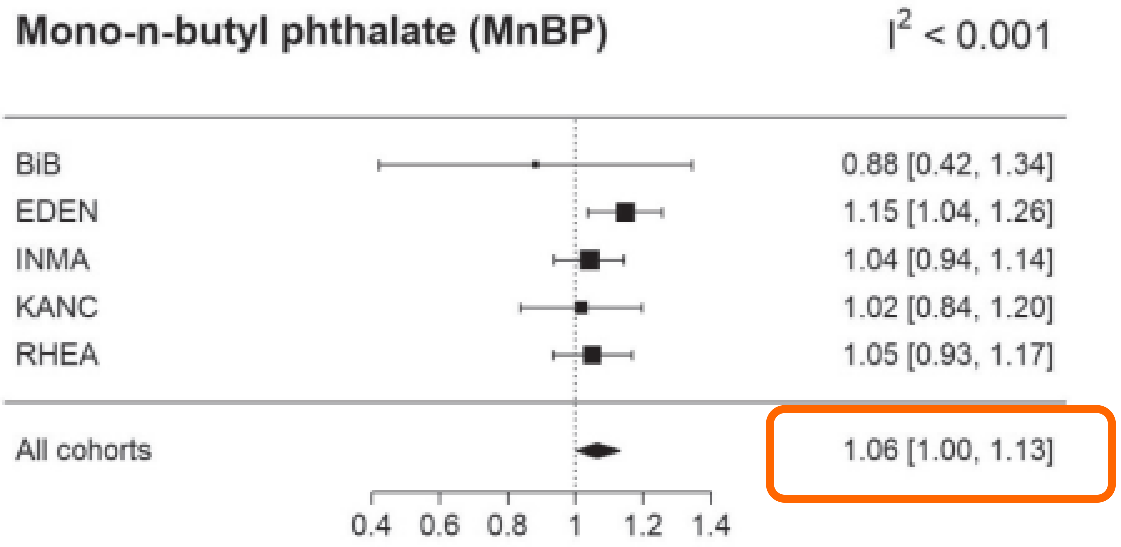
Quelles conséquences pour les patients ?

- Effets neuro-développementaux
  - Déficit de l’attention
  - Altération cognitive
- Effets perturbateurs endocriniens
  - Effet sur le système hormonal
  - Impact sur la fertilité
- Effets sur le métabolisme
  - Augmentation du risque d’obésité
  - Augmentation de la résistance à l’insuline
- Risques cancérigènes


Cerebral Palsy
Alzheimer's Disease
Attention Deficit/Hyperactivity Disorder
Learning impairment
Schizophrenia
Depression
Anxiety
Autism Spectrum Disorder
Memory impairment
Cognitive Defects
Aggression
Spatial memory impairment

Rivollier F, Int J Environ Res Public Health 2019
Raja, Environ Res 2022

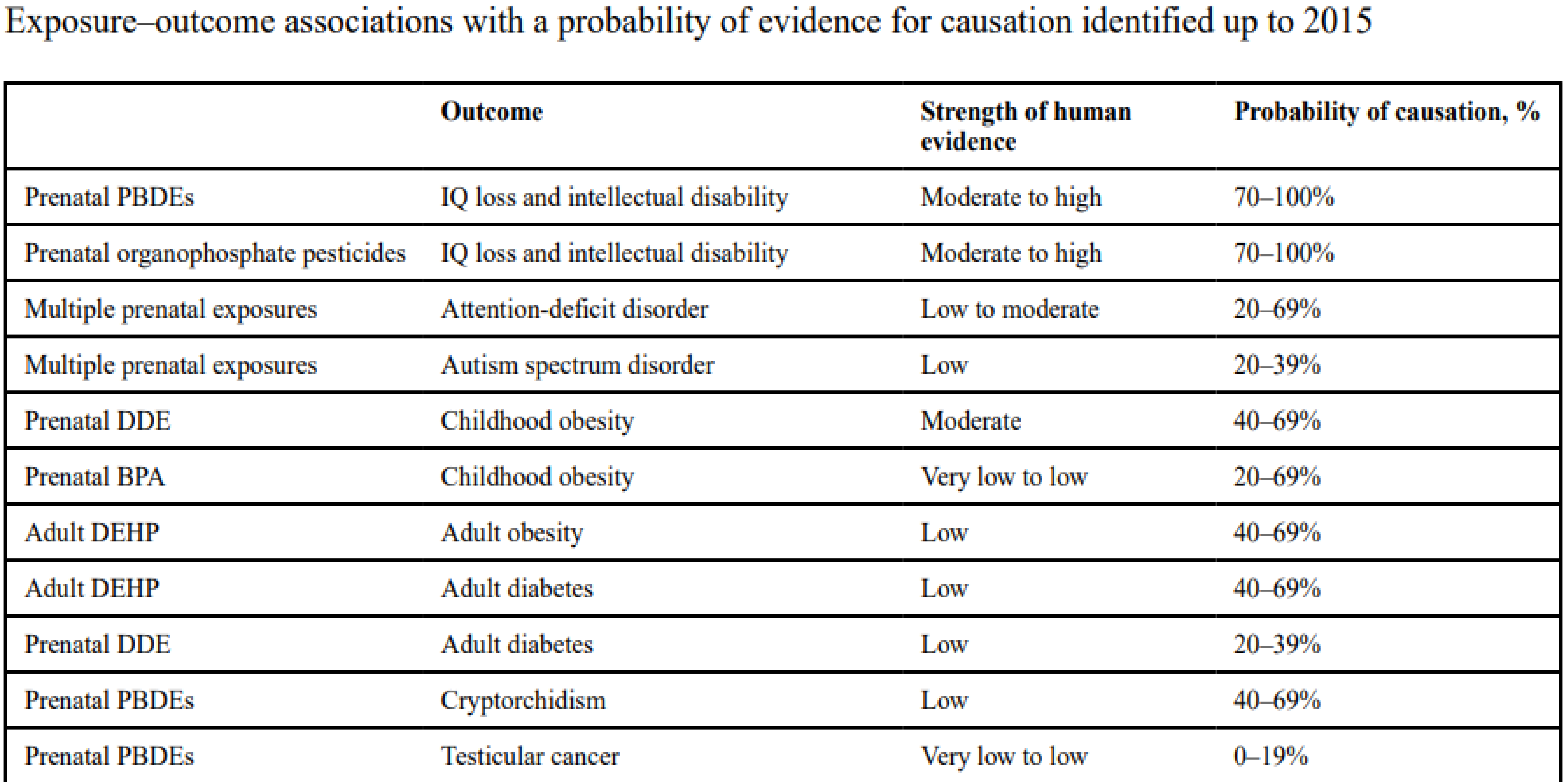




- *4 cohortes européennes dont EDEN*
- *N=708 mères enfants*
- *SDQ test*

Jedynak, Science of the Total Environment 2021

Association entre expositions précoces and devenir

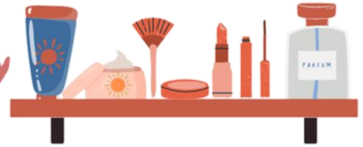


Exposure–outcome associations with a probability of evidence for causation identified up to 2015

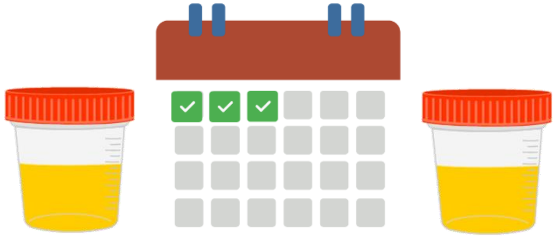
	Outcome	**Strength of human evidence**	**Probability of causation, %**
Prenatal PBDEs	IQ loss and intellectual disability	Moderate to high	70–100%
Prenatal organophosphate pesticides	IQ loss and intellectual disability	Moderate to high	70–100%
Multiple prenatal exposures	Attention-deficit disorder	Low to moderate	20–69%
Multiple prenatal exposures	Autism spectrum disorder	Low	20–39%
Prenatal DDE	Childhood obesity	Moderate	40–69%
Prenatal BPA	Childhood obesity	Very low to low	20–69%
Adult DEHP	Adult obesity	Low	40–69%
Adult DEHP	Adult diabetes	Low	40–69%
Prenatal DDE	Adult diabetes	Low	20–39%
Prenatal PBDEs	Cryptorchidism	Low	40–69%
Prenatal PBDEs	Testicular cancer	Very low to low	0–19%

Kahn LG, Lancet Diabetes Endoc 2020

Efficacité des interventions ?



100 jeunes filles
Utilisation régulière
de crème solaire, crème de jour, maquillage et parfum.



Cosmétiques sans parabène, triclosan, BP-3 ni phtalates

Etude avant-après, N=100

RÉSULTATS

Phtalates : c° ↘ 27% MEP (MnBP et MiBP : ≠ non significative)

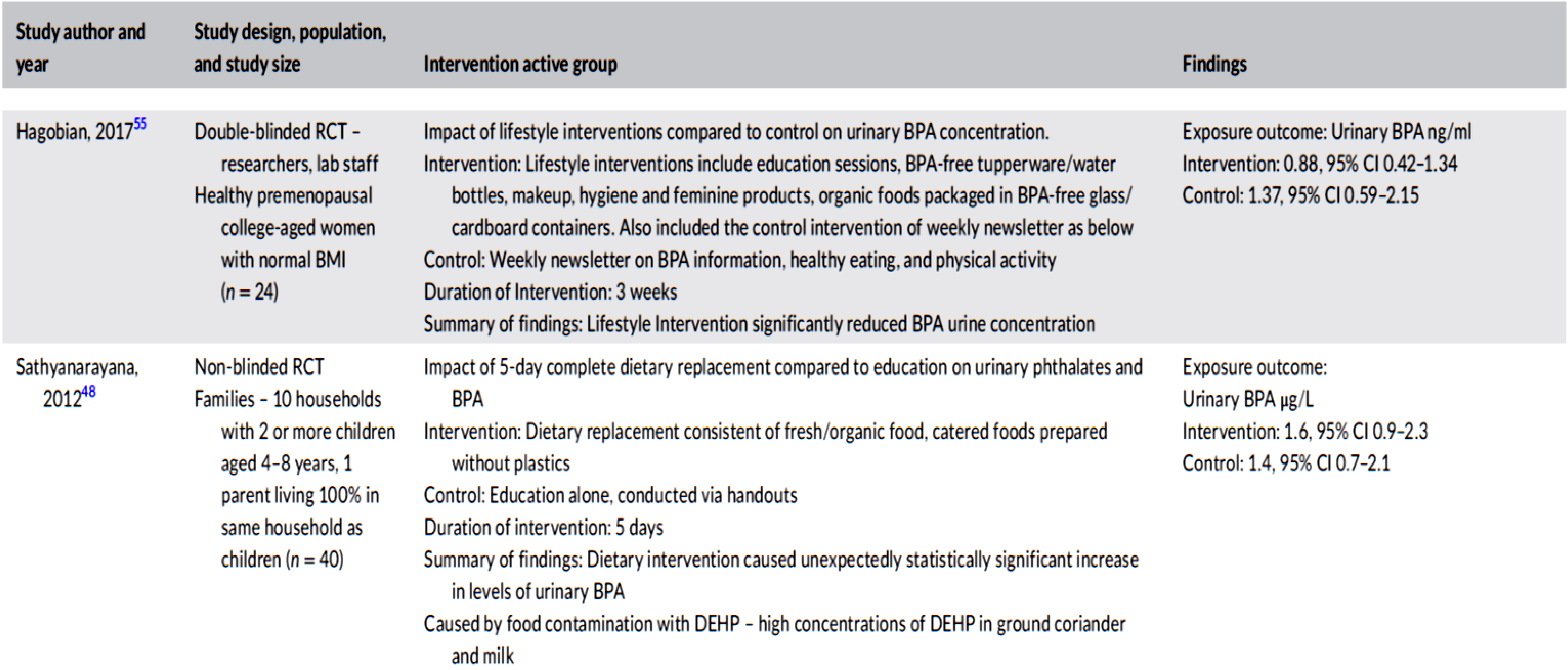
Parabènes : **c° ↘ 44%** Méthyl et **↘ 45%** Propyl. ↗ c° Ethyl et butyl (mais restent basses)

Triclosan : c° ↘ 36%

Benzophénone-3 : c°↘ 36 % (↘ 52% chez les utilisatrices de crème solaire).

Etude HERMOSA - Harley et al, Environmental Health Perspectives (2016)

Métaanalyses des études interventionnelles visant à réduire l'exposition aux perturbateurs endocriniens



Study author and year	Study design, population, and study size	Intervention active group	Findings
Hagobian, 2017[55]	Double-blinded RCT - researchers, lab staff Healthy premenopausal college-aged women with normal BMI (*n* = 24)	Impact of lifestyle interventions compared to control on urinary BPA concentration. Intervention: Lifestyle interventions include education sessions, BPA-free tupperware/water bottles, makeup, hygiene and feminine products, organic foods packaged in BPA-free glass/cardboard containers. Also included the control intervention of weekly newsletter as below Control: Weekly newsletter on BPA information, healthy eating, and physical activity Duration of Intervention: 3 weeks Summary of findings: Lifestyle Intervention significantly reduced BPA urine concentration	Exposure outcome: Urinary BPA ng/ml Intervention: 0.88, 95% CI 0.42–1.34 Control: 1.37, 95% CI 0.59–2.15
Sathyanarayana, 2012[48]	Non-blinded RCT Families - 10 households with 2 or more children aged 4–8 years, 1 parent living 100% in same household as children (*n* = 40)	Impact of 5-day complete dietary replacement compared to education on urinary phthalates and BPA Intervention: Dietary replacement consistent of fresh/organic food, catered foods prepared without plastics Control: Education alone, conducted via handouts Duration of intervention: 5 days Summary of findings: Dietary intervention caused unexpectedly statistically significant increase in levels of urinary BPA Caused by food contamination with DEHP – high concentrations of DEHP in ground coriander and milk	Exposure outcome: Urinary BPA µg/L Intervention: 1.6, 95% CI 0.9–2.3 Control: 1.4, 95% CI 0.7–2.1

N = 14 études

G Corbet, Int J Gynecol Obstet 2022

Etude PREVED – Concentration de perturbateurs endocriniens dans le lait

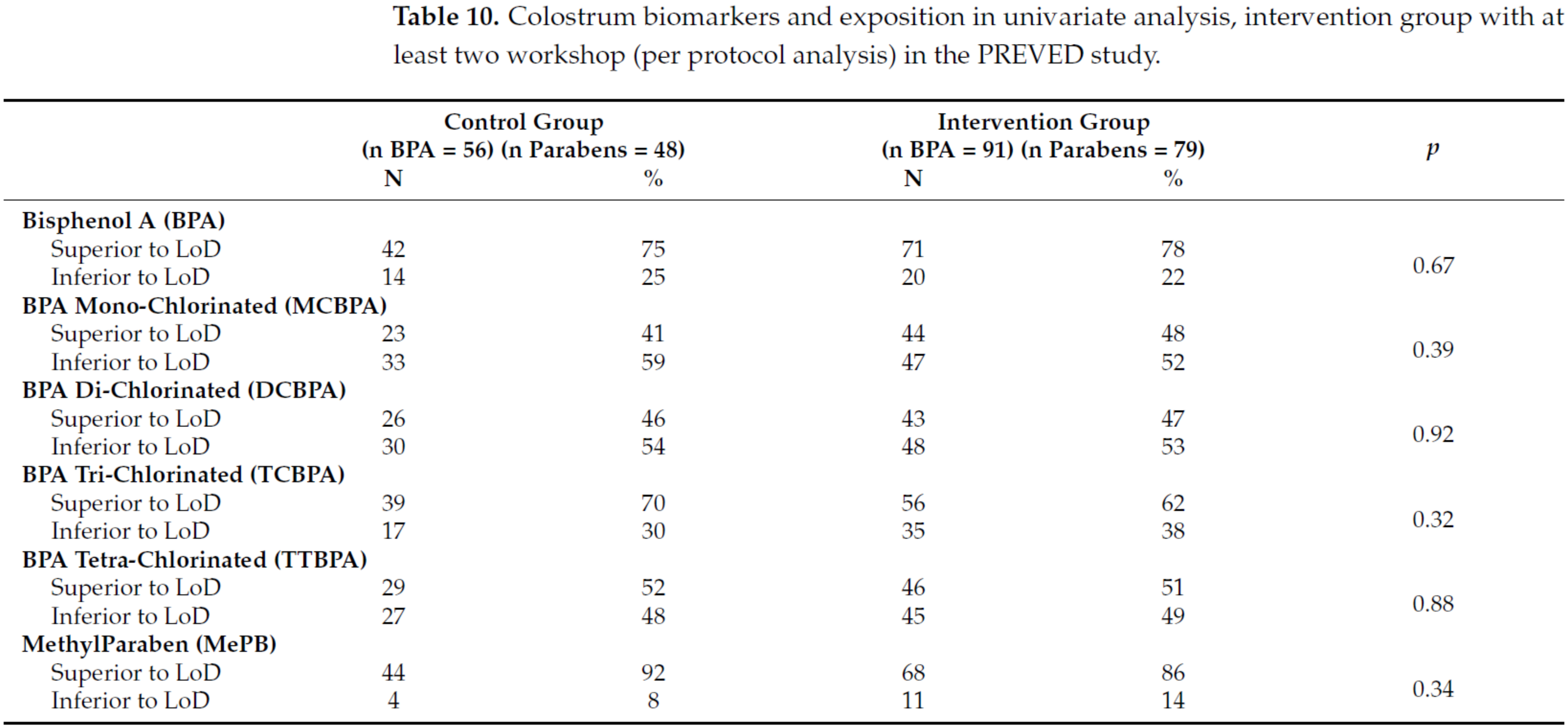


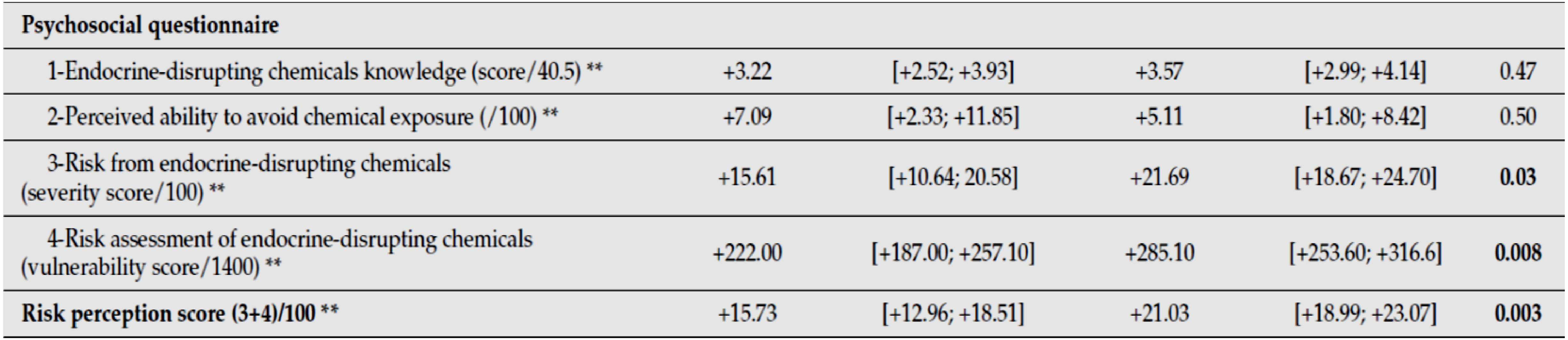
Table 10. Colostrum biomarkers and exposition in univariate analysis, intervention group with at least two workshop (per protocol analysis) in the PREVED study.

	Control Group (n BPA = 56) (n Parabens = 48)		Intervention Group (n BPA = 91) (n Parabens = 79)		*p*
	N	**%**	**N**	**%**	
Bisphenol A (BPA)					
Superior to LoD	42	75	71	78	0.67
Inferior to LoD	14	25	20	22	
BPA Mono-Chlorinated (MCBPA)					
Superior to LoD	23	41	44	48	0.39
Inferior to LoD	33	59	47	52	
BPA Di-Chlorinated (DCBPA)					
Superior to LoD	26	46	43	47	0.92
Inferior to LoD	30	54	48	53	
BPA Tri-Chlorinated (TCBPA)					
Superior to LoD	39	70	56	62	0.32
Inferior to LoD	17	30	35	38	
BPA Tetra-Chlorinated (TTBPA)					
Superior to LoD	29	52	46	51	0.88
Inferior to LoD	27	48	45	49	
MethylParaben (MePB)					
Superior to LoD	44	92	68	86	0.34
Inferior to LoD	4	8	11	14	

N=268 pregnant women

Houazzani, Int J Environ Res Public Health 2022

Etude PREVED – Questionnaires psychologiques



Psychosocial questionnaire					
1-Endocrine-disrupting chemicals knowledge (score/40.5) **	+3.22	[+2.52; +3.93]	+3.57	[+2.99; +4.14]	0.47
2-Perceived ability to avoid chemical exposure (/100) **	+7.09	[+2.33; +11.85]	+5.11	[+1.80; +8.42]	0.50
3-Risk from endocrine-disrupting chemicals (severity score/100) **	+15.61	[+10.64; 20.58]	+21.69	[+18.67; +24.70]	**0.03**
4-Risk assessment of endocrine-disrupting chemicals (vulnerability score/1400) **	+222.00	[+187.00; +257.10]	+285.10	[+253.60; +316.6]	**0.008**
Risk perception score (3+4)/100 **	+15.73	[+12.96; +18.51]	+21.03	[+18.99; +23.07]	**0.003**

Houazzani, Int J Environ Res Public Health 2022

Stress périnatal « toxique » (chronique, prolongé, répété)

Est associé à un risque accru de:

- **Pathologies neurodéveloppementales:**
  - Déficit d'attention / hyperactivité
  - Retard des apprentissages
  - Troubles du spectre autistique;
- **Maladies non communicables:**
  - Allergie
  - Diabète/obésité
  - Maladies cardio-vasculaires
  - Trouble du comportement: agressivité, contrôle émotionnel, impulsivité;
  - Dépression / Anxiété;

Babenko, Neurosci Biobehabior Rev 2015
Boyce, Pediatrics 2021

DOHaD : « Origine Développementale de la Santé »

Facteurs environnementaux

Fenêtre de vulnérabilité

Santé de l'enfant et de l'adulte

- Pratiques éducatives, Interactions parents-enfant, Langage
- Stress « toxique »
- Addictions
- Activité Physique
- Alimentation
- Expositions aux Toxiques

Les premiers 1 000 jours

Capital Santé & Compétences psycho-sociales:

- Cognitives
- Sociales
- Emotionnelles

Maladies non communicables:

- Troubles du neuro-développement
- Maladies allergiques / inflammatoires
- Maladies cardiovasculaires
- Maladies métaboliques: obésité, diabète

Impact de l’environnement précoce sur la santé psychique future

Métaanalyse	**Odds Ration (IC 95%)**
Toxiques de l’environnement	Estimation entre 1 et 2 (à confirmer)
Sédentarité	1.4 (1.03-1.52)
Obésité	1.4 (1.13-1.71)
Diabète	1.52 (1.23-1.89)
Tabagisme	2.82 (2.38-3.34)
Stress toxique	3.70 (2.62-5.22)
Dépression	4.4 (3.54-5.46)
Addiction	5.62 (4.46-7.07)
Violences intra-familiales	8.10 (5.87-11.18)

Hughes, Lancet Public Health 2017