LTAP

Development and application of non-invasive biomarkers to detect early effects of pollutants on the respiratory tract and other target organs

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Objectives

Biomarkers of early effects correspond to biological changes that are predictive of health impairment or potential impairment. They must be sensitive, specific, robust and measurable in a minimally invasive way. We are currently using such biomarkers to evaluate the health risks of exposure to various environmental or lifestyle stressors including cadmium, tobacco or wood smoke, fine particles and chlorination products.

Recent observations

Our recent observations support the hypothesis that early age exposure to some airborne stressors, especially chlorine-based oxidants, can cause persistent airways epithelium defects (A) promoting the development of allergic sensitization and later the clinical manifestations of atopy (B). Observations among adults and adolescents also suggest that some lifestyle changes (C, D) can be detrimental to the testicular function. The study of urinary cadmium levels in different age groups of the general population in Belgium (E) has revealed the existence of physiological associations (F), which call into question the long-held view that urinary Cd is a reliable indicator of the cumulative exposure to low-level environmental Cd.

A

Persistent defects of airways epithelium in adolescents with the highest attendance at chlorinated pools during childhood (top quintile). A, girls; B, boys. (Bernard *et al.*, to be published)
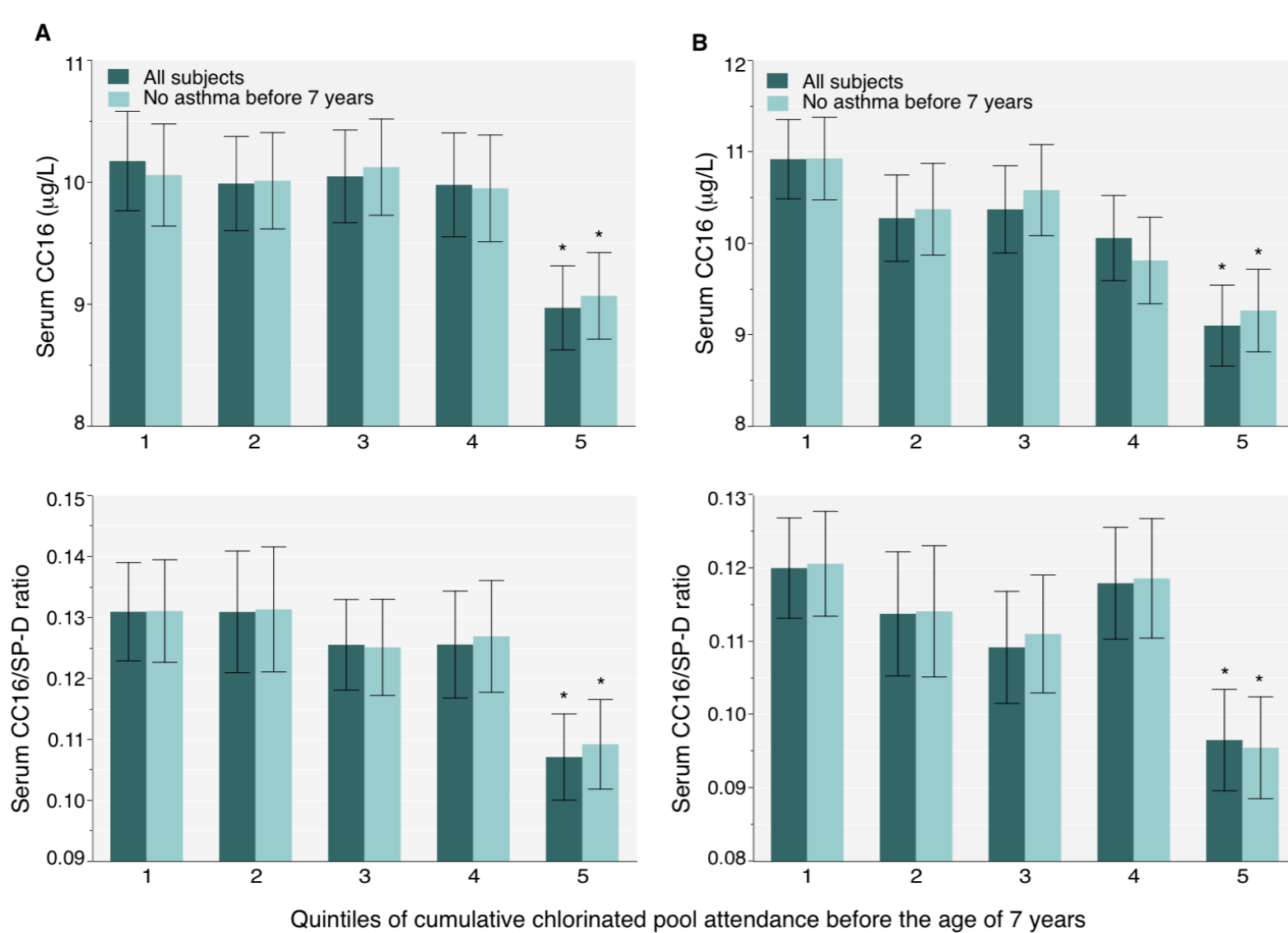
B

Sequential development of respiratory and allergic diseases in children according to age and cumulative attendance at chlorinated pools (Bernard *et al.*, Am J Resp Crit Care Med, 2011, 2013)
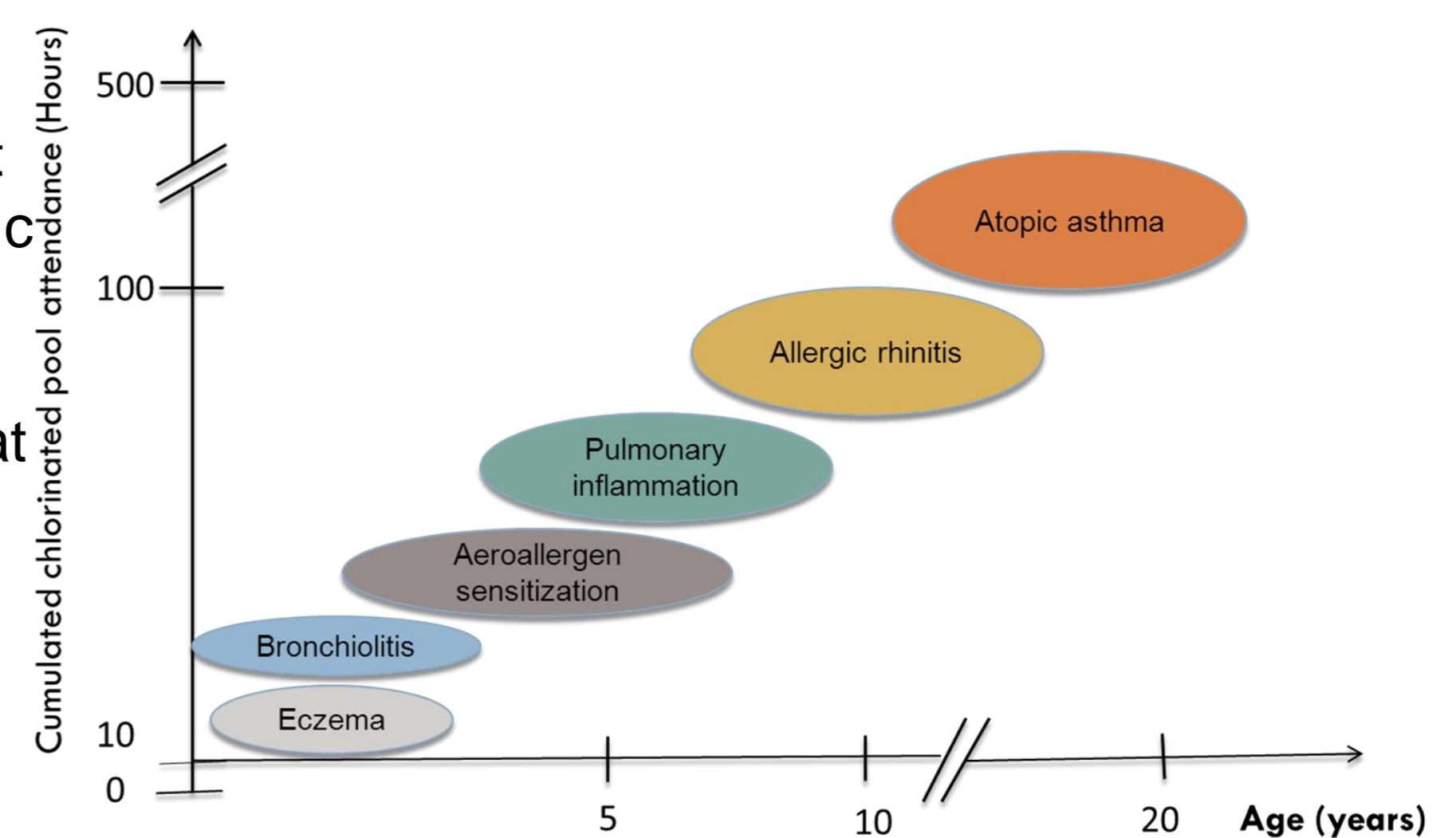
C

Decrease of inhibin B (OBI and DSL assays) and total testosterone in the serum of adolescents according to their attendance of indoor chlorinated pools before 7 years (A), 10 years (B) or over lifetime (C)(Nickmilder and Bernard, Int J Androl, 2011)
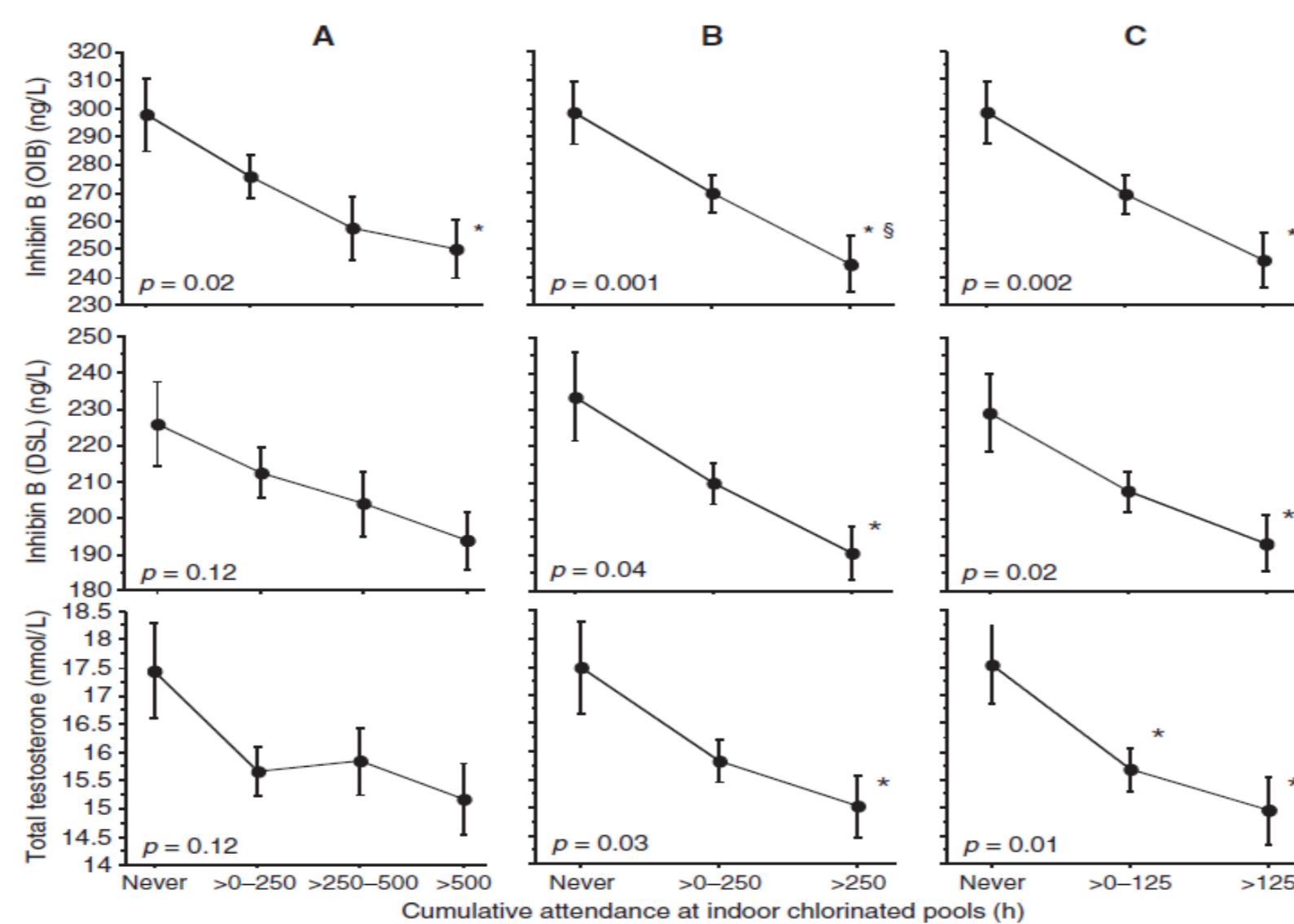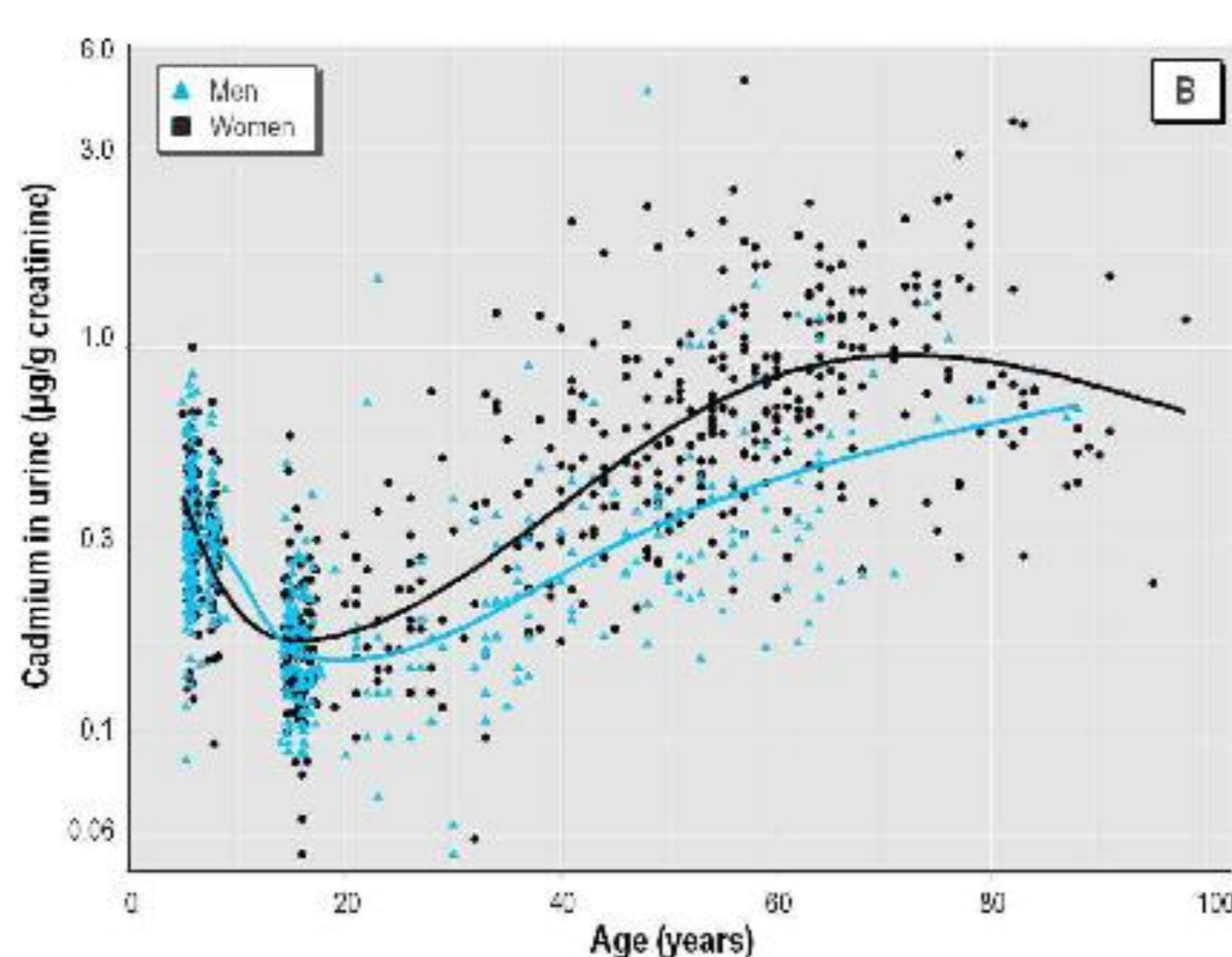
D

Increase of serum inhibin B (OBI and DSL assays) in adolescents according to the duration of breastfeeding (Bernard and Nickmilder, JAMA Pediatrics, 2013)
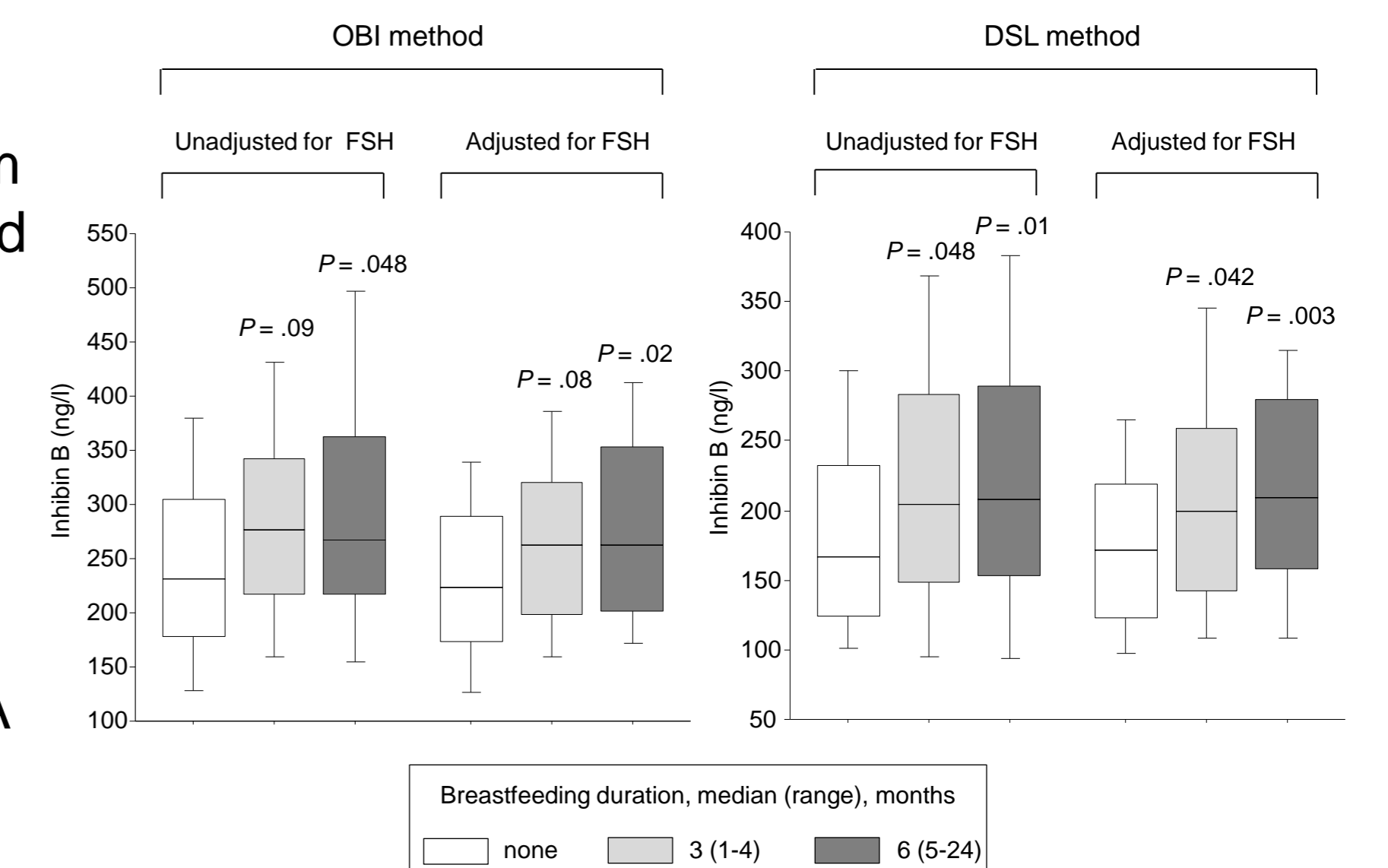
E

Variations of urinary Cd over lifetime in men and women. This nonmonotonic relationship challenges the curvilinear model recently adopted by EFSA (Chaumont *et al.*, EHP, 2013)

F

Associations between urinary Cd and retinol-binding protein in different age groups of the general population in Belgium. All these associations are most likely physiological, reflecting the co-excretion of Cd and proteins in urine. (Chaumont *et al.*, EHP, 2013)

Table 4. Multiple regression analysis of the determinants of U-RBP in the general population, stratified by age groups and adult smoking status.

Participants	n	U-RBP (μg/g creatinine) Independent variable	Coefficient (95% CI)	p-Value	r^2	U-RBP (μg/L) Independent variable	Coefficient (95% CI)	p-Value	r^2
Children	296	U-Cd	0.217 (0.057, 0.376)	0.007	0.177	U-Cd	0.198 (0.025, 0.375)	0.026	0.300
		Age	−0.100 (−0.127, −0.073)	< 0.001		U-Creat	0.756 (0.561, 0.944)	< 0.001	
						Age	−0.098 (−0.126, −0.069)	< 0.001	
Adolescents	200	U-Cd	0.313 (0.096, 0.529)	0.005	0.093	U-Cd	0.363 (0.139, 0.587)	0.002	0.409
		BMI	−1.07 (−1.66, −0.48)	< 0.001		BMI	−1.07 (−1.65, −0.477)	< 0.001	
						U-Creat	0.808 (0.549, 1.07)	< 0.001	
Adults (19–70 years)									
All	744	U-Cd	0.125 (0.073, 0.177)	< 0.001	0.049	U-Cd	0.116 (0.060, 0.173)	< 0.001	0.391
		BMI	−0.546 (−0.786, −0.305)	< 0.001		BMI	−0.545 (−0.785, −0.304)	< 0.001	
						U-Creat	0.846 (0.761, 0.932)	< 0.001	
Never-smokers	284	U-Cd	0.111 (0.029, 0.193)	0.008	0.034	U-Cd	0.103 (0.007, 0.200)	0.035	0.389
		BMI	−0.577 (−0.982, −0.173)	0.005		BMI	−0.580 (−0.986, −0.174)	0.005	
						U-Creat	0.872 (0.733, 1.01)	< 0.001	
Ever-smokers	460	U-Cd	0.138 (0.068, 0.211)	< 0.001	0.052	U-Cd	0.127 (0.052, 0.203)	0.001	0.381
		BMI	−0.515 (−0.978, −0.181)	< 0.001		BMI	−0.504 (−0.809, −0.198)		
						U-Creat	0.822 (0.709, 0.935)		
Adults (> 70 years)									
All	98	U-Cd	0.013 (−0.391, 0.188)	0.49	0.005	U-Cd	−0.077 (−0.382, 0.227)	0.6	0.197
						U-Creat	1.21 (0.720, 1.69)	< 0.001	
Never-smokers	62	U-Cd	−0.076 (−0.406, 0.255)	0.65	0.003	U-Cd	−0.053 (−0.392, 0.286)	0.8	0.259
						U-Creat	1.22 (0.673, 1.76)	< 0.001	
Ever-smokers	36	U-Cd	−0.128 (−0.699, 0.443)	0.65	0.006	U-Cd	−0.114 (−0.731, 0.503)	0.7	0.092
						U-Creat	1.19 (0.156, 2.21)	0.025	

CI, confidence interval.

Data from adults are those of the Cadmibel study (Buchet et al., 1990 Lancet). Other data are from studies carried out between 2013 and 2010 in the French speaking part of Belgium