Supplemental Material

Urinary Biomarkers for Phthalates Associated with Asthma in Norwegian Children

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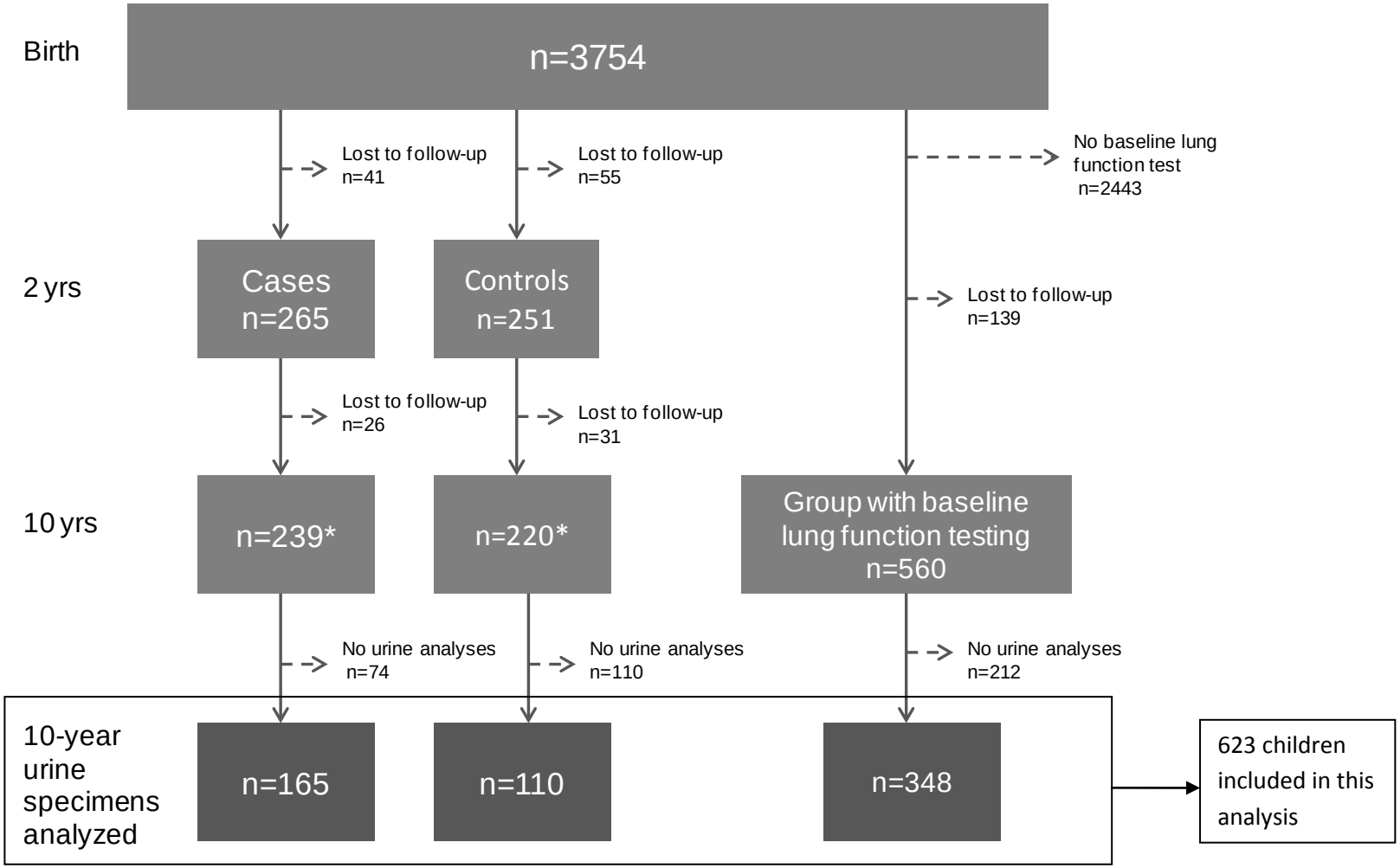

*Among the children followed up at age 10, 63 of the cases and 73 of the controls had had lung function tests at birth

Figure S1: Flow-chart of the 623 children within the Environment and Childhood Asthma study with urine analyzed for phthalate metabolites

Table S1: Comparisons of characteristics between 623 children included in the present study and the 396 *non-included* children from the 10-year follow-up. Percent of characteristics within each group, except for age (in years) reported by median (min-max)

Characteristics	**% of n=623**	**% of n=396**	**p-value**
SUBJECTS			
Age [yrs, median (min-max)]	10.7 (8.8-12.5)	10.8 (9.0-12.5)	0.001
Boys	53	56	0.4
[a]BMI ≥ 85th percentile	16	18	0.3
Firstborn	49	56	0.02
Skin prick test (SPT) positive	26	34	0.02
sIgE > 0.35 kU/L	33	39	0.04
Either SPT positive or sIgE > 0.35 kU/L	35	43	0.02
Current rhinitis	26	28	0.06
Current asthma	21	7	<0.001
Current eczema	23	18	0.05
PARENTS			
Parental asthma *or* rhinoconjuctivitis at child's birth	36	37	0.8
Maternal education, years			
≤ 12	47	53	0.1
13-16	31	27	
≥ 17	22	20	
Annual household income (in 1000 NOK[b])			
<350	13	20	0.2
> 350 - 560	28	24	
> 560 - 750	30	26	
> 750	30	30	

[a]age- and gender adjusted BMI; [b]NOK=Norwegian krone

Table S2: Demography at birth of 623 children with urine analysed for phthalate metabolites at age 10 compared to the remainder of the birth cohort (n=3131). Reported as percent of characteristics within each group

Characteristics	**% of included n=623**	**% of non-included n=3131**	**p-value**
Gender (boys)	53	52	0.5
Parental asthma[a]	14	12	0.1
Parental rhinoconjunctivitis[a]	31	27	0.08
Parental atopic eczema[a]	30	28	0.5
Maternal smoking in pregnancy			
No	75	76	
Occasionally	10	9	
Daily	15	15	0.9
Firstborn	49	56	<0.001
Pets at birth	23	23	0.9
Annual household income (in 1000 NOK[b])			
≤299	24	31	
300 -499	60	49	
≥ 500	16	20	<0.001
Maternal education			
≤ 12 years	47	47	
13-16	31	30	
≥ 17 years	22	24	0.5
Parents living together	95	94	0.3

[a]Parental allergic diseases are reported as the presence of disease in mother, father or both;
[b]NOK=Norwegian krone

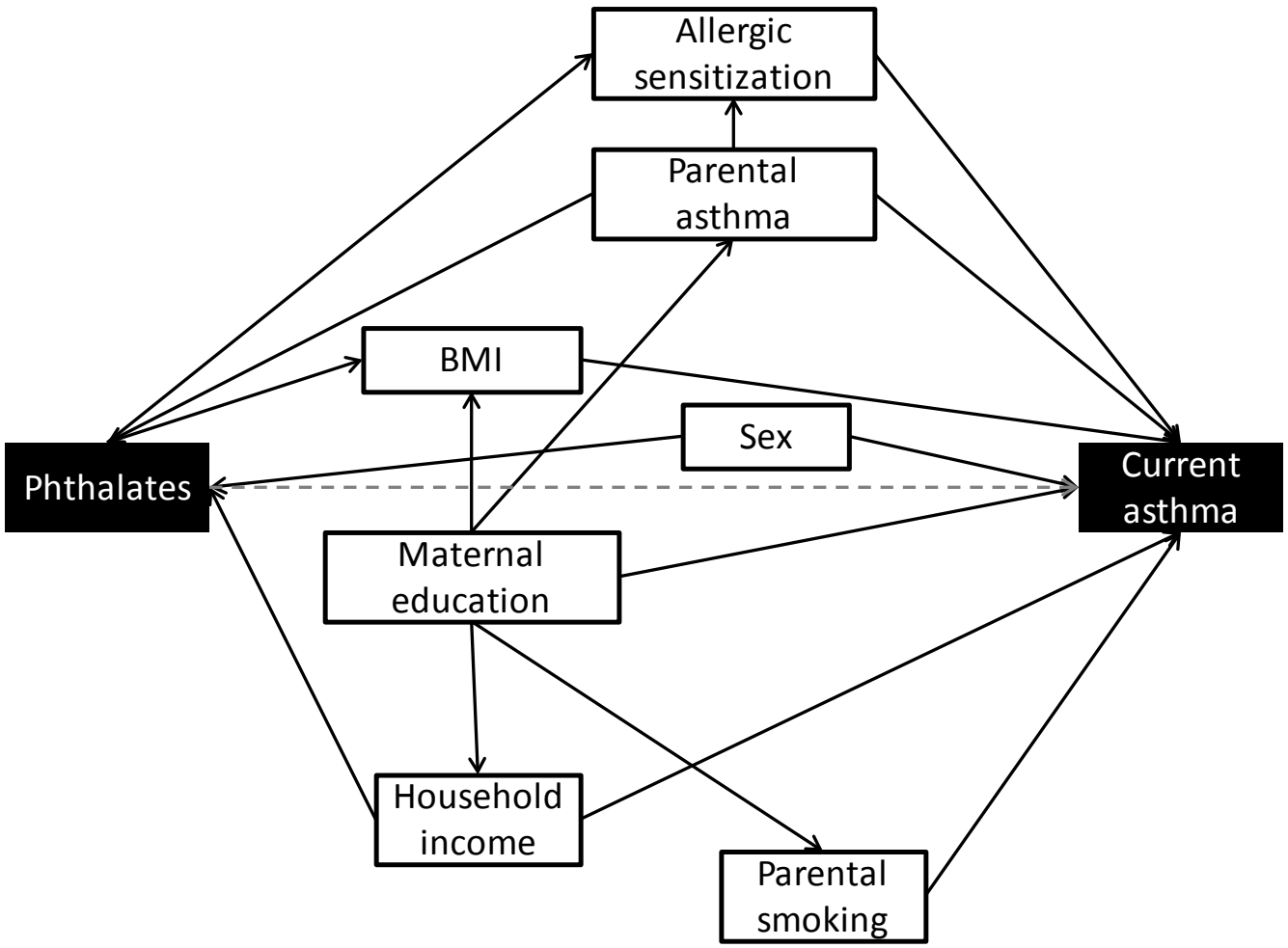

Figure S2: Directed acyclic graph (DAG) for evaluation of covariate selection in the analyses of phthalates and current asthma. The minimial adjustment set for estimating the total effect of phthalates on asthma was according to the dagitty (http://www.dagitty. net/dags/html): sex, household income, and parental asthma

Table S3: Spearman rank correlation coefficient, r_s, for correlation between the individual phthalate metabolites

	MnBP	**MiBP**	**MBzP**	**MCPP**	**MEHP**	**MEOHP**	**MEHHP**	**MECPP**	**MCOP**	**MCNP**
MEP	0.45	0.35	0.39	0.31	0.19	0.34	0.32	0.33	0.27	0.23
MnBP		0.64	0.55	0.52	0.34	0.51	0.48	0.48	0.36	0.32
MiBP			0.50	0.44	0.26	0.55	0.51	0.50	0.39	0.33
MBzP				0.47	0.30	0.48	0.46	0.47	0.41	0.38
MCPP					0.29	0.61	0.61	0.58	0.59	0.54
MEHP						0.62	0.62	0.58	0.27	0.25
MEOHP							0.98	0.94	0.51	0.44
MEHHP								0.93	0.50	0.43
MECPP									0.52	0.47
MCOP										0.75

Table S4: Geometric mean (GM) and 95% confidence interval (CI) for specific gravity adjusted urinary concentrations of individual phthalate metabolites (µg/L) and phthalate sums (µmol/L) for girls and boys (p-value for one-way ANOVA)

Phthalate	Girls GM (95% CI)	Boys GM (95% CI)	p
Individual phthalate metabolites (parent phthalate)			
MEP (DEP)	77 (69, 85)	55 (50, 60)	<0.001
MnBP (DnBP)	161 (150, 172)	135 (127, 144)	<0.001
MiBP (DiBP)	61 (56, 66)	54 (50, 59)	0.07
MBzP (BBzP)	34 (31, 37)	31 (29, 34)	0.3
MCPP (DnOP)	8.4 (7.7, 7.5)	8.1 (7.5, 8.7)	0.5
MEHP (DEHP)	8.0 (7.3, 8.7)	8.4 (7.7, 9.1)	0.4
MEOHP (DEHP)	52 (49, 56)	53 (49, 57)	0.9
MEHHP (DEHP)	83 (77, 89)	84 (78, 90)	0.8
MECPP (DEHP)	109 (101, 118)	105 (97, 113)	0.4
MCOP (DINP)	6.9 (6.4, 7.6)	6.1 (5.6, 6.6)	0.03
MCNP (DIDP)	2.5 (2.3, 2.7)	2.2 (2.0, 2.4)	0.09
Phthalate sums			
∑Low-MWP [a]	1.6 (1.5, 1.7)	1.3 (1.2, 1.4)	<0.001
∑High-MWP [b]	1.1 (1.1, 1.2)	1.1 (1.0, 1.2)	0.5
∑DEHP [c]	0.9 (0.8, 0.9)	0.9 (0.8, 0.9)	0.9

The MEP and MBzP concentrations have been multiplied by 0.66 and 0.72, respectively, to correct for the inadequate purity of the analytic standards used (Calafat, personal communication, 2012).
[a]∑Low-MWP: MEP, MnBP, and MiBP. [b]∑High-MWP: MBzP, MCNP, MCOP, MCPP, MEHP, MECPP, MEHHP, and MEOHP. [c]∑DEHP : MEHP, MECPP, MEHHP, and MEOHP.

Table S5: Adjusted odds ratio for current asthma (n=52) in children *without* allergic sensitization (n=392) and for current asthma (n=70) in children *with* allergic sensitization (n=210) per $\log_{10}$ IQR unit increase in urinary concentration of phthalate metabolites. Adjusted for urine specific gravity, parental asthma and household income

	Allergically sensitized	
Phthalate metabolites	**No (n=392) aOR (95% CI)**	**Yes (n=210) aOR (95% CI)**
MEP	1.1 (0.75, 1.5)	1.0 (0.69, 1.5)
MnBP	0.98 (0.64, 1.5)	0.76 (0.50, 1.2)
MiBP	1.2 (0.77, 1.7)	1.3 (0.86, 1.84)
MBzP	1.2 (0.83, 1.8)	1.1 (0.73, 1.8)
MCPP	1.4 (0.87, 2.2)	0.99 (0.67, 1.5)
MCOP	1.4 (0.95, 2.1)	1.4 (0.87, 2.1)
MCNP	1.6 (1.1, 2.2)	1.1 (0.77, 1.5)
Metabolite sums		
ΣLow-MWP[a]	1.1 (.075, 1.6)	1.0 (0.68, 1.5)
ΣHigh-MWP[b]	1.2 (0.79, 1.8)	1.1 (0.67, 1.6)
ΣDEHP[c]	1.2 (0.77, 1.7)	0.99 (0.64, 1.5)

[a]∑Low-MWP: MEP, MnBP, and MiBP. [b]∑High-MWP: MBzP, MCNP, MCOP, MCPP, MEHP, MECPP, MEHHP, and MEOHP. [c]∑DEHP : MEHP, MECPP, MEHHP, and MEOHP.

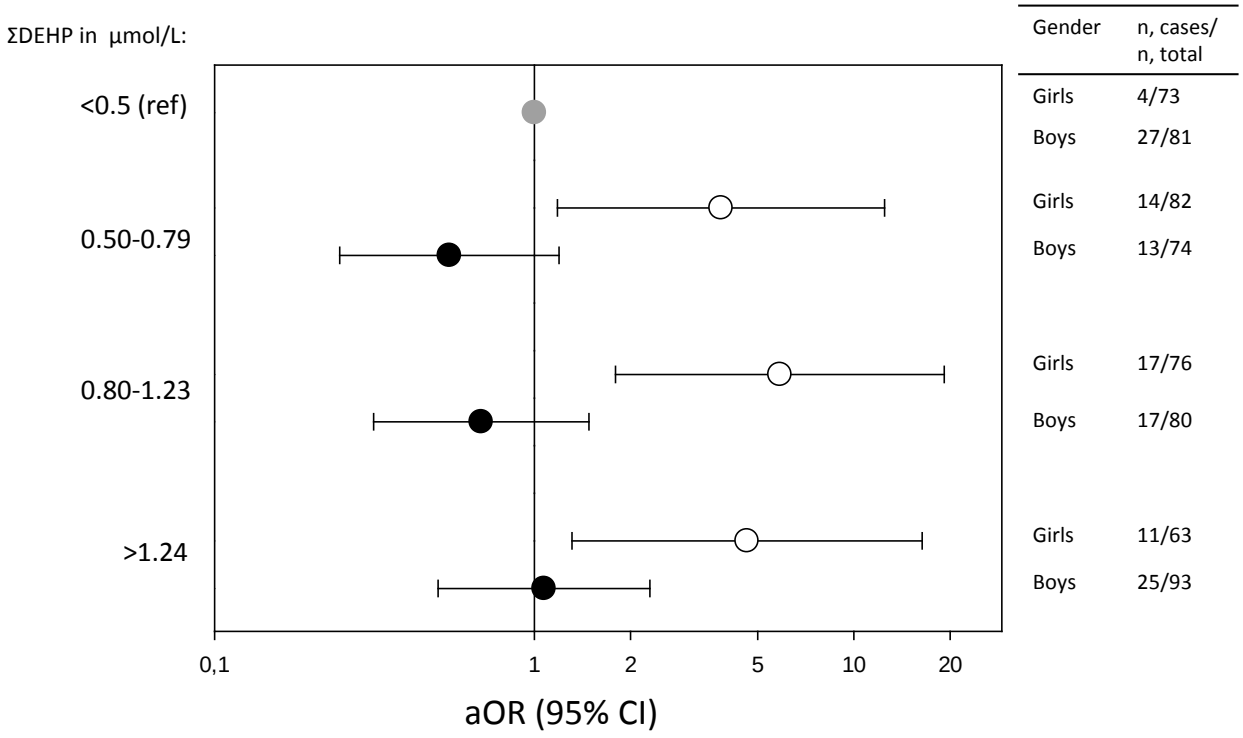

Figure S3: Adjusted oddsratio for current asthma for girls (white dots) and boys (black dots) by quartiles of ∑DEHP concentration (in µmol/L) adjusted for urine specific gravity, parental asthma, and household