

Supporting information

Phthalate metabolites in urine of Chinese children and their association with asthma and allergic symptoms

Yuxuan Zhao ¹, Yuexia Sun ^{1,*}, Changqi Zhu ¹, Ying Zhang ², Jing Hou ¹, Qinghao Zhang ¹ and Yeganeh Ataei ¹

¹ Tianjin Key Laboratory of Indoor Air Environmental Quality Control, School of Environmental Science and Engineering, Tianjin University, Tianjin 300350, China

² School of Environmental Science and Engineering, Tianjin University, Tianjin 300350, China

* Correspondence: yuexiasun@tju.edu.cn

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Table S1 Mass-charge ratio and retention time of phthalate metabolites

	Mass-charge ratio	Retention time (min)	Internal standard compounds	Mass - charge ratio	Retention time (min)
MEP	193/77	4.23	¹³ C ₄ -MEP	197/124	4.23
MiBP	221/77	5.75	¹³ C ₄ -MnBP	225/79	5.85
MnBP	221/71	5.85	¹³ C ₄ -MnBP	225/79	5.85
MBzP	255/77	6.24			
MEHP	277/134	8.09			
MECPP	307/113	5.68	¹³ C ₄ -MECPP	311/159	5.68
MEHHP	293/121	5.76			
MEOHP	297/77	5.97			

Table S2 Mean and median concentrations (µg/L) of phthalate metabolites in different seasons

		MEP	MiBP	MnBP	MEHP	MECPP	MEHHP	MEOHP
Spring	Mean	61.38	24.88	23.02	7.16	44.73	11.12	8.67
	Median	13.93	31.16	17.99	7.48	54.47	13.87	8.44
Summer	Mean	52.29	31.66	41.56	8.22	33.24	14.16	9.80
	Median	45.32	32.53	36.85	8.06	33.86	16.66	12.33
Autumn	Mean	24.91	25.43	23.08	5.96	40.96	11.41	7.35
	Median	14.32	31.12	20.27	5.53	50.66	11.79	6.35
Winter	Mean	32.01	29.26	31.87	8.58	33.95	16.17	10.11
	Median	18.90	31.86	31.43	8.05	34.42	17.24	12.30
	P ^a	0.01	0.03	0.01	0.00	0.04	0.01	0.02

^a Kruskal-Wallis test.

Table S3 Crude odds ratios (95% Confidence Intervals) of phthalate metabolites ^a with children's asthma and allergy in logistic regression models

	MEP	MiBP	MnBP	MEHP	MECPP	MEHHP	MEOHP
Wheeze ever	1.11 (0.95-1.31)	1.06 (0.83-1.35)	1.49 (0.91-2.44)	1.06 (0.70-1.59)	0.99 (0.56-1.74)	1.16 (0.73-1.84)	1.38 (0.82-2.34)
Wheeze current	1.15 (0.97-1.36)	1.25 (0.92-1.70)	1.52 (0.81-2.83)	1.19 (0.69-2.04)	0.53 (0.24-1.17)	1.31 (0.73-2.36)	1.85 (0.90-3.78)
Current dry cough	1.00 (0.85-1.19)	1.04 (0.81-1.34)	0.95 (0.56-1.62)	0.93 (0.61-1.43)	1.10 (0.62-1.96)	1.27 (0.79-2.02)	1.19 (0.70-2.02)
Diagnosed asthma	0.93 (0.68-1.26)	1.25 (0.95-1.63)	1.98 (1.16-3.38)	1.35 (0.86-2.12)	0.92 (0.49-1.73)	2.04 (1.19-3.48)	2.16 (1.16-4.02)
Rhinitis ever	1.04 (0.89-1.22)	0.93 (0.76-1.15)	1.01 (0.66-1.55)	1.00 (0.71-1.41)	0.87 (0.54-1.38)	0.83 (0.56-1.22)	1.03 (0.67-1.58)
Rhinitis current	0.92 (0.77-1.10)	0.95 (0.78-1.17)	0.96 (0.63-1.46)	1.07 (0.77-1.50)	1.06 (0.67-1.68)	0.73 (0.49-1.08)	0.82 (0.54-1.25)
Diagnosed rhinitis	0.80 (0.54-1.19)	1.12 (0.88-1.43)	1.21 (0.74-1.96)	1.09 (0.73-1.62)	1.01 (0.59-1.75)	1.19 (0.76-1.86)	1.04 (0.63-1.71)
Eczema ever	0.84 (0.65-1.07)	0.88 (0.71-1.08)	0.82 (0.54-1.25)	0.85 (0.60-1.19)	1.39 (0.87-2.22)	0.75 (0.50-1.10)	0.77 (0.50-1.18)
Eczema current	0.88 (0.66-1.18)	0.89 (0.71-1.13)	0.96 (0.60-1.54)	0.83 (0.56-1.21)	1.26 (0.75-2.10)	0.69 (0.44-1.09)	0.65 (0.40-1.05)
Diagnosed eczema	0.88 (0.72-1.09)	1.03 (0.84-1.26)	0.99 (0.65-1.51)	0.99 (0.71-1.38)	1.04 (0.66-1.64)	0.90 (0.61-1.31)	0.85 (0.55-1.29)

^a Concentrations of phthalate metabolites were coded as continues variables with an interquartile increase step. *p*-value less than 0.05 are indicated in bold for significance

Table S4 Stratification analysis on associations of phthalates metabolites with children's asthma and allergy in winter-spring and summer-autumn seasons

		MEP	MiBP	MnBP	MEHP	MECPP	MEHHP	MEOHP
Wheeze ever	Winter-spring	1.21 (0.93-1.57)	1.01 (0.84-1.21)	1.25 (0.59-2.62)	1.10 (0.53-2.29)	1.18 (0.50-2.79)	1.13 (0.74-1.71)	1.65 (0.81-3.33)
	Summer-autumn	0.97 (0.54-1.75)	0.89 (0.52-1.55)	1.52 (0.66-3.45)	1.05 (0.48-2.31)	0.88 (0.35-2.24)	0.77 (0.27-2.21)	0.89 (0.30-2.65)
Wheeze current	Winter-spring	1.26 (0.91-1.74)	1.07 (0.86-1.35)	1.94 (0.74-5.03)	1.24 (0.48-3.16)	0.58 (0.18-1.88)	1.14 (0.69-1.88)	2.67 (0.97-7.37)
	Summer-autumn	0.53 (0.13-2.21)	1.28 (0.63-2.57)	1.13 (0.34-3.78)	1.83 (0.59-5.70)	0.53 (0.13-2.11)	0.98 (0.24-3.97)	0.89 (0.20-4.04)
Current dry cough	Winter-spring	0.95 (0.73-1.22)	1.03 (0.86-1.24)	1.24 (0.56-2.74)	1.10 (0.53-2.26)	0.88 (0.36-2.17)	1.35 (0.85-2.12)	1.52 (0.74-3.14)
	Summer-autumn	1.50 (0.87-2.59)	1.15 (0.67-1.97)	1.12 (0.44-2.82)	0.59 (0.23-1.51)	0.92 (0.33-2.61)	0.93 (0.29-3.01)	0.65 (0.18-2.39)
Diagnosed asthma	Winter-spring	0.84 (0.45-1.55)	1.22 (0.95-1.57)	2.06 (0.89-4.78)	1.22 (0.54-2.75)	1.29 (0.49-3.41)	1.73 (0.97-3.11)	2.18 (0.95-4.96)
	Summer-autumn	1.50 (0.85-2.65)	0.81 (0.41-1.59)	1.95 (0.79-4.85)	2.08 (0.76-5.66)	0.48 (0.13-1.77)	1.59 (0.46-5.49)	1.79 (0.48-6.68)
Rhinitis ever	Winter-spring	1.07 (0.88-1.29)	0.89 (0.75-1.06)	0.90 (0.47-1.74)	0.75 (0.40-1.42)	1.08 (0.50-2.34)	0.76 (0.52-1.13)	0.98 (0.54-1.76)
	Summer-autumn	1.16 (0.79-1.71)	1.10 (0.76-1.61)	1.27 (0.65-2.47)	1.09 (0.58-2.06)	0.61 (0.29-1.29)	0.81 (0.36-1.83)	0.95 (0.41-2.21)
Rhinitis current	Winter-spring	0.88 (0.65-1.19)	0.91 (0.78-1.07)	0.86 (0.46-1.62)	0.86 (0.47-1.59)	1.36 (0.65-2.84)	0.66 (0.43-1.00)	0.69 (0.39-1.22)
	Summer-autumn	1.15 (0.79-1.70)	1.06 (0.73-1.55)	1.10 (0.57-2.13)	1.22 (0.65-2.30)	0.79 (0.38-1.61)	0.74 (0.33-1.65)	0.78 (0.34-1.80)
Diagnosed rhinitis	Winter-spring	0.55 (0.24-1.28)	1.06 (0.88-1.28)	1.28 (0.59-2.78)	0.91 (0.42-1.96)	1.30 (0.55-3.04)	1.02 (0.67-1.55)	0.78 (0.40-1.51)
	Summer-autumn	1.11 (0.60-2.04)	0.91 (0.50-1.65)	1.12 (0.45-2.77)	1.36 (0.58-3.21)	0.70 (0.24-2.01)	1.27 (0.43-3.80)	1.25 (0.39-3.99)
Eczema ever	Winter-spring	0.87 (0.65-1.16)	1.07 (0.91-1.26)	1.27 (0.68-2.37)	0.96 (0.53-1.75)	0.81 (0.39-1.66)	1.04 (0.72-1.50)	0.95 (0.55-1.64)
	Summer-autumn	0.83 (0.56-1.23)	0.61 (0.37-1.00)	0.49 (0.23-1.04)	0.77 (0.41-1.47)	2.25 (0.97-5.24)	0.52 (0.23-1.22)	0.61 (0.26-1.45)
Eczema current	Winter-spring	0.90 (0.63-1.27)	0.90 (0.75-1.08)	0.97 (0.48-1.97)	0.79 (0.40-1.55)	0.83 (0.38-1.85)	0.76 (0.49-1.18)	0.72 (0.39-1.32)
	Summer-autumn	0.92 (0.57-1.49)	0.96 (0.60-1.53)	0.89 (0.40-1.97)	0.67 (0.32-1.40)	2.49 (1.04-5.98)	0.68 (0.27-1.72)	0.42 (0.15-1.19)
Diagnosed eczema	Winter-spring	0.91 (0.72-1.14)	1.01 (0.86-1.18)	1.23 (0.66-2.30)	1.00 (0.55-1.81)	0.98 (0.48-2.00)	1.03 (0.71-1.48)	0.93 (0.54-1.60)
	Summer-autumn	0.97 (0.66-1.43)	1.15 (0.79-1.67)	0.79 (0.41-1.53)	1.24 (0.67-2.30)	0.89 (0.44-1.78)	0.72 (0.33-1.60)	0.77 (0.34-1.75)

Odds ratios were adjusted for age, gender, allergic history, home dampness and environmental tobacco smoke exposure. Concentrations of phthalate metabolites were coded as continuous variables with an interquartile increase step. *p*-value less than 0.05 are indicated in bold for significance

Table S5 Median concentrations ($\mu\text{g/L}$) of phthalate metabolites in children's urine in different studies

References	Country	Sampling time	Sample size	MEP	MiBP	MnBP	MBzP	MEHP	MECPP	MEHHP	MEOHP
(Lewis, 2013)	Mexico	2010	53 (boys)	62.7	11	91.2	5.6	7.5	71.8	45.4	20.9
			55 (girls)	78.4	12.7	98	5	6.4	69.8	42.5	18.7
(Koch, 2011)	Germany	2007	111	/	42.8	36.8	7.2	4.7	28.4	17.4	15.1
(Fromme, 2013)	Germany	2011-2012	663	14.5	44.7	32.4	11.6	/	/	16.5	17.9
(Bertelsen, 2013)	Norway	2001-2004	623	56.7	49.2	138	29.3	7.8	98.2	76.6	49.7
(Boas, 2010)	Denmark	2006-2007	503 (boys)	21	130		17	4.5	30	37	19
			342 (girls)	21	121		12	3.6	27	31	16
(Langer, 2014)	Denmark	2008-2009	441	16.6	72.2	80.1	13	4.7	34.5	33.2	17.6
(Liao, 2018)	China	2013-2014	434	10.1	46.2	58.1	0.2	4.5	39	24.7	14.5
			39								
(Gong, 2015)	China	2013-2014	(summer)	23.8	78.2	224	/	6.5	68.4	25.2	21.6
			39 (winter)	15.3	54.1	120	/	9.3	70.9	47.9	28.2
(Wang, 2013)	China	2012	259	15.9	37.4	47.2	0.05	21.1	29.8	15.7	22.9
This study	China	2013-2016	243	18.4	31.6	26.2	0.09	7.5	46.1	16.7	9.6

References

- Boas, M., Frederiksen, H., Feldt-Rasmussen, U., Skakkebaek, N.E., Hegedus, L., Hilsted, L., Juul, A., Main, K.M., 2010. Childhood exposure to phthalates: Associations with thyroid function, insulin-like growth factor i, and growth. *Environmental Health Perspectives*. 10, 1458-64.
- Fromme, H., Lahrz, T., Kraft, M., Fembacher, L., Dietrich, S., Sievering, S., Burghardt, R., Schuster, R., Bolte, G., Volkel, W., 2013. Phthalates in German daycare centers: Occurrence in air and dust and the excretion of their metabolites by children (lupe 3). *Environment International*. 64-72.
- Gong, M., Weschler, C.J., Liu, L., Shen, H., Huang, L., Sundell, J., Zhang, Y., 2015. Phthalate metabolites in urine samples from beijing children and correlations with phthalate levels in their handwipes. *Indoor Air*. 6, 572-81.
- Koch, H.M., Wittassek, M., Bruning, T., Angerer, J., Heudorf, U., 2011. Exposure to phthalates in 5-6 years old primary school starters in Germany-a human biomonitoring study and a cumulative risk assessment. *International Journal of Hygiene and Environmental Health*. 3, 188-95.
- Langer, S., Beko, G., Weschler, C.J., Brive, L.M., Toftum, J., Callesen, M., Clausen, G., 2014. Phthalate metabolites in urine samples from Danish children and correlations with phthalates in dust samples from their homes and daycare centers. *International Journal of Hygiene and Environmental Health*. 1, 78-87.
- Lewis, R.C., Meeker, J.D., Peterson, K.E., Lee, J.M., Pace, G.G., Cantoral, A., Tellez-Rojo, M.M., 2013. Predictors of urinary bisphenol a and phthalate metabolite concentrations in Mexican children. *Chemosphere*. 10, 2390-8.
- Liao, C.X., Liu, W., Zhang, J.L., Shi, W.M., Wang, X.Y., Cai, J., Zou, Z.J., Lu, R.C., Sun, C.J., Wang, H., Huang, C., Zhao, Z.H., 2018. Associations of urinary phthalate metabolites with residential characteristics, lifestyles, and dietary habits among young children in Shanghai, China. *Science of the Total Environment*. 1288-97.

Wang, H.X., Zhou, Y., Tang, C.X., He, Y.H., Wu, J.G., Chen, Y., Jiang, Q.W., 2013. Urinary phthalate metabolites are associated with body mass index and waist circumference in Chinese school children. *Plos One*. 2.