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Supplemental Material

Urinary Phthalate Metabolites and Slow Walking Speed in the Korean Elderly Environmental Panel II Study

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Table S1. Timeline of KEEP II data collection

	Exam I (Oct 2012- Feb 2013)	Exam II (Jan 2014- Apr 2014)	Exam III (Nov 2014- Apr 2015)
Questionnaires	x	x	x
Demographic factors	x	x	x
Socioeconomic status	x	x	x
Smoking status	x	x	x
Physical activity	x	x	x
Medical history	x	x	x
Physical examination	x	x	x
Walking speed	x	x	x
Depression	x	x	x
Anthropometric measures	x	x	x
Metabolite Measures	x	x	x
Urinary MEHHP ^a	x	x	x
Urinary MEOHP ^a	x	x	x
Urinary MnBP ^a	x	x	x
Urinary MEcPP ^b		x	
Urinary MBzP ^b		x	

^a Three metabolites were measured up to 3 times and the data from the first visit for each subject were used in the cross-sectional analysis.

^b Two metabolites had one measurement. Only cross-sectional analysis was possible.

Table S2. Distribution of urinary phthalate concentrations ($\mu\text{g/L}$) at enrollment and follow-up in KEEP II study participants^a

	N	<i>n</i> < LOD (%)	GM	\pm SD	Min	25th	50th	75th	Max
MEHHP ($\mu\text{g/L}$)									
Enrollment	1190	0 (0.0)	21.25	\pm 2.42	0.66	12.32	21.29	37.80	864.76
Follow-up 1	740	0 (0.0)	17.94	\pm 2.19	1.73	10.72	18.23	30.47	165.48
Follow-up 2	288	0 (0.0)	15.99	\pm 2.27	2.18	9.09	16.00	26.71	175.54
MEOHP ($\mu\text{g/L}$)									
Enrollment	1190	0 (0.0)	15.44	\pm 2.45	0.28	9.09	15.69	27.16	540.72
Follow-up 1	740	0 (0.0)	12.38	\pm 2.39	0.38	7.10	12.99	22.34	123.36
Follow-up 2	288	0 (0.0)	11.51	\pm 2.23	1.42	6.47	11.76	19.27	118.84
MnBP ($\mu\text{g/L}$)									
Enrollment	1190	0 (0.0)	28.50	\pm 2.15	1.33	17.32	29.06	45.79	1014.61
Follow-up 1	740	0 (0.0)	28.43	\pm 2.21	1.18	17.35	29.35	48.04	627.76
Follow-up 2	288	0 (0.0)	38.15	\pm 2.16	3.66	23.08	39.48	60.28	1446.83
MEcPP ($\mu\text{g/L}$) ^b									
Exam II (A1+B)	731	0 (0.0)	25.00	\pm 2.15	1.25	14.76	25.68	41.82	768.67
MBzP ($\mu\text{g/L}$) ^b									
Exam II (A1+B)	731	64 (8.76)	2.19	\pm 4.43	0.10	0.97	2.46	6.18	122.16

Abbreviations: GM, geometric mean; LOD, limit of detection; SD, standard deviation; MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate

^a All participants: Enrollment A+B+C in Figure 1.

^b MEcPP and MBzP had one measurement ($n = 731$) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S3. Distribution of creatinine-corrected urinary phthalate concentrations ($\mu\text{g/g cre}$) at enrollment and follow-up in KEEP II study participants^a

	N	GM	$\pm\text{SD}$	Min	25th	50th	75th	Max
MEHHP ($\mu\text{g/g cre}$)								
Enrollment	1190	26.35	± 2.08	1.07	16.78	25.93	41.74	774.97
Follow-up 1	740	21.96	± 2.09	2.28	14.31	20.89	34.05	415.01
Follow-up 2	288	20.25	± 1.91	4.33	12.73	19.60	29.10	159.26
MEOHP ($\mu\text{g/g cre}$)								
Enrollment	1190	19.00	± 2.12	0.53	12.01	18.66	30.98	582.16
Follow-up 1	740	14.86	± 2.09	0.98	9.68	14.91	24.40	415.92
Follow-up 2	288	14.58	± 1.93	2.88	9.12	14.30	21.73	118.93
MnBP ($\mu\text{g/g cre}$)								
Enrollment	1190	35.33	± 1.81	4.60	24.63	33.97	49.07	1039.10
Follow-up 1	740	34.78	± 1.84	3.75	23.87	34.46	48.48	600.78
Follow-up 2	288	48.33	± 1.78	10.05	33.07	47.47	65.65	865.74
MEcPP ($\mu\text{g/g cre}$) ^b								
Exam II (A1+B)	731	27.69	± 1.82	3.89	18.67	27.29	41.48	645.94
MBzP ($\mu\text{g/g cre}$) ^b								
Exam II (A1+B)	731	2.42	± 3.62	0.04	1.14	2.76	5.61	66.47

Abbreviations: GM, geometric mean; SD, standard deviation; MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate

^a All participants: Enrollment A+B+C in Figure 1.

^b MEcPP and MBzP had one measurement ($n = 731$) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S4. Geometric means (95% CIs) of urinary phthalate metabolite concentrations according to participant characteristics at enrollment in the KEEP II study (numeric values of Figure 2)

	N (%)	MEHHP (µg/L)	<i>P</i> -value ^a	MEOHP (µg/L)	<i>P</i> -value	MnBP(µg/L)	<i>P</i> -value
Total	1190 (100)	21.3 (20.2, 22.4)		15.4 (14.7, 16.2)		28.5 (27.3, 29.8)	
Age							
60-69 years	261 (21.9)	19.6 (17.6, 21.9)	(Ref)	13.9 (12.4, 15.5)	(Ref)	28.2 (25.7, 30.9)	(Ref)
70-79 years	692 (58.2)	20.9 (19.6, 22.3)	0.590	15.3 (14.3, 16.4)	0.272	28.4 (26.8, 30.1)	0.986
≥80 years	237 (19.9)	24.3 (21.7, 27.2)	0.021	17.8 (15.9, 19.9)	0.006	29.1 (26.4, 32.0)	0.895
Sex							
Male	365 (30.7)	22.7 (20.7, 24.9)	(Ref)	16.4 (14.9, 17.9)	(Ref)	30.2 (27.9, 32.6)	(Ref)
Female	825 (69.3)	20.6 (19.4, 21.9)	0.084	15.0 (14.2, 16.0)	0.135	27.8 (26.4, 29.3)	0.086
Region							
Urban	548 (46.1)	16.2 (15.1, 17.4)	(Ref)	12.3 (11.4, 13.2)	(Ref)	30.1 (28.2, 32.1)	(Ref)
Rural	642 (54.0)	26.7 (25.0, 28.6)	<0.001	18.8 (17.5, 20.1)	<0.001	27.2 (25.6, 28.8)	0.020
Education							
≤Elementary school	797 (67.0)	22.0 (20.7, 23.4)	(Ref)	15.9 (14.9, 16.9)	(Ref)	27.5 (26.1, 29.0)	(Ref)
Middle and high school	310 (26.1)	20.6 (18.7, 22.8)	0.505	15.0 (13.6, 16.6)	0.647	30.1 (27.6, 32.7)	0.200
>High school	83 (7.0)	16.7 (13.8, 20.3)	0.019	13.1 (10.8, 15.9)	0.150	32.4 (27.5, 38.2)	0.153
Smoking status							
No	975 (81.9)	21.0 (19.8, 22.2)	(Ref)	15.3 (14.4, 16.2)	(Ref)	28.0 (26.7, 29.4)	(Ref)
Yes	215 (18.1)	22.5 (20.0, 25.4)	0.282	16.2 (14.4, 18.3)	0.365	30.9 (27.9, 34.2)	0.092
Physical activity (METs-hours/week)							
<7.5	988 (83.0)	21.8 (20.6, 23.0)	(Ref)	15.7 (14.9, 16.6)	(Ref)	28.0 (26.7, 29.4)	(Ref)
≥7.5	202 (17.0)	18.8 (16.6, 21.2)	0.028	14.1 (12.4, 15.9)	0.096	31.0 (27.9, 34.4)	0.076
Osteoarticular disease							
No	758 (63.7)	21.9 (20.6, 23.3)	(Ref)	16.1 (15.1, 17.2)	(Ref)	29.3 (27.7, 30.9)	(Ref)
Yes	432 (36.3)	20.2 (18.5, 21.9)	0.118	14.3 (13.2, 15.6)	0.030	27.2 (25.3, 29.2)	0.101
Cardiovascular disease							
No	1053 (88.5)	21.1 (20.0, 22.3)	(Ref)	15.3 (14.5, 16.1)	(Ref)	28.2 (26.9, 29.5)	(Ref)
Yes	137 (11.5)	22.2 (19.1, 25.7)	0.547	16.6 (14.3, 19.3)	0.305	31.1 (27.4, 35.4)	0.154
Chronic respiratory disease							
No	1146 (96.3)	21.1 (20.0, 22.2)	(Ref)	15.3 (14.6, 16.2)	(Ref)	28.5 (27.3, 29.8)	(Ref)
Yes	44 (3.7)	24.7 (19.0, 32.1)	0.254	18.1 (13.9, 23.6)	0.232	27.6 (22.0, 34.6)	0.782
Cancer							
No	1117 (93.9)	21.2 (20.1, 22.4)	(Ref)	15.5 (14.7, 16.3)	(Ref)	28.4 (27.2, 29.7)	(Ref)
Yes	73 (6.1)	21.7 (17.7, 26.6)	0.822	15.3 (12.4, 18.7)	0.903	29.4 (24.7, 35.1)	0.715
Diabetes							
No	944 (79.3)	20.5 (19.4, 21.7)	(Ref)	14.9 (14.1, 15.8)	(Ref)	28.2 (26.9, 29.7)	(Ref)
Yes	246 (20.7)	24.5 (21.9, 27.3)	0.005	17.6 (15.8, 19.7)	0.009	29.5 (26.8, 32.5)	0.426
Hypertension							
No	533 (44.8)	20.4 (18.9, 22.0)	(Ref)	14.8 (13.7, 16.0)	(Ref)	28.1 (26.4, 30.0)	(Ref)
Yes	657 (55.2)	22.0 (20.6, 23.5)	0.137	16.0 (14.9, 17.1)	0.157	28.8 (27.2, 30.5)	0.599

Table S4. Continued (numeric values of Figure 2).

	MEcPP ^b (μg/L)	<i>P</i> -value	MBzP ^b (μg/L)	<i>P</i> -value
Total	25.0 (23.6, 26.4)		2.19 (1.96, 2.44)	
Age				
60-69 years	21.2 (18.6, 24.1)	(Ref)	1.90 (1.47, 2.45)	(Ref)
70-79 years	24.9 (23.2, 26.7)	0.083	2.17 (1.89, 2.49)	0.641
≥80 years	29.3 (26.0, 33.2)	0.001	2.55 (2.01, 3.24)	0.225
Sex				
Male	25.8 (23.1, 28.8)	(Ref)	2.45 (1.98, 3.02)	(Ref)
Female	24.7 (23.2, 26.4)	0.505	2.10 (1.85, 2.38)	0.224
Region				
Urban	24.3 (22.5, 26.2)	(Ref)	1.95 (1.68, 2.25)	(Ref)
Rural	25.9 (23.8, 28.1)	0.274	2.51 (2.14, 2.94)	0.021
Education				
≤Elementary school	25.1 (23.4, 26.9)	(Ref)	2.17 (1.90, 2.47)	(Ref)
Middle and high school	24.7 (22.1, 27.6)	0.970	2.20 (1.77, 2.72)	0.994
>High school	25.2 (20.5, 31.0)	0.999	2.35 (1.58, 3.50)	0.926
Smoking status				
No	25.1 (23.7, 26.7)	(Ref)	2.11 (1.88, 2.38)	(Ref)
Yes	24.2 (21.0, 27.9)	0.633	2.64 (2.00, 3.48)	0.150
Physical activity (METs-hours/week)				
<7.5	21.6 (20.4, 22.9)	(Ref)	2.29 (2.04, 2.57)	(Ref)
≥7.5	18.7 (16.5, 21.3)	0.025	1.70 (1.29, 2.24)	0.051
Osteoarticular disease				
No	25.8 (23.9, 27.8)	(Ref)	2.39 (2.06, 2.76)	(Ref)
Yes	24.1 (22.1, 26.1)	0.216	1.97 (1.68, 2.31)	0.082
Cardiovascular disease				
No	24.9 (23.4, 26.4)	(Ref)	2.19 (1.95, 2.46)	(Ref)
Yes	25.8 (22.3, 29.9)	0.631	2.18 (1.65, 2.90)	0.990
Chronic respiratory disease				
No	24.9 (23.5, 26.3)	(Ref)	2.19 (1.96, 2.44)	(Ref)
Yes	28.8 (21.5, 38.7)	0.335	2.26 (1.27, 4.01)	0.911
Cancer				
No	25.0 (23.6, 26.4)	(Ref)	2.16 (1.93, 2.41)	(Ref)
Yes	25.6 (20.4, 32.2)	0.827	2.75 (1.77, 4.28)	0.291
Diabetes				
No	24.9 (23.4, 26.5)	(Ref)	2.18 (1.93, 2.46)	(Ref)
Yes	25.4 (22.5, 28.6)	0.774	2.22 (1.77, 2.80)	0.873
Hypertension				
No	24.2 (22.2, 26.3)	(Ref)	2.10 (1.78, 2.49)	(Ref)
Yes	25.6 (23.8, 27.5)	0.314	2.25 (1.95, 2.59)	0.556

Abbreviations: SD, standard deviation; MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate

^a T-test for binomial groups and the Tukey's post-hoc test for categorical groups.

^b MEcPP and MBzP had one measurement (n = 731) at Exam II (Follow-up A1 and Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S5. Spearman's correlation coefficients between enrollment and follow-up visits for each phthalate metabolite in KEEP II study participants

	Baseline	Follow-up 1	Follow-up 2
MEHHP (µg/L)			
Enrollment	1		
Follow-up 1	0.357 (<i>p</i> <0.001)	1	
Follow-up 2	0.413 (<i>p</i> <0.001)	0.396 (<i>p</i> <0.001)	1
MEOHP (µg/L)			
Enrollment	1		
Follow-up 1	0.379 (<i>p</i> <0.001)	1	
Follow-up 2	0.463 (<i>p</i> <0.001)	0.431 (<i>p</i> <0.001)	1
MnBP (µg/L)			
Enrollment	1		
Follow-up 1	0.317 (<i>p</i> <0.001)	1	
Follow-up 2	0.296 (<i>p</i> <0.001)	0.326 (<i>p</i> <0.001)	1

Abbreviations: MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate

Note that MEcPP and MBzP had one measurement at Exam II (Follow-up A1 and enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S6. Odds ratios (95% CI) for slowness (< 1.0 m/s) according to urinary phthalate metabolite concentrations (non-adjusted and covariate-adjusted) from cross-sectional analysis at enrollment (n = 1,190 ^a) and longitudinal analysis (n = 2,218 ^b)

Phthalate metabolites	Cross-sectional analysis at enrollment		Longitudinal analysis	
	Non-adjusted for creatinine	Cre-adjusted ^c	Non-adjusted for creatinine	Cre-adjusted ^c
MEHHP (µg/L)				
Per doubling	1.15 (1.02, 1.30)	1.14 (0.99, 1.32)	1.18 (1.08, 1.29)	1.16 (1.04, 1.30)
Quartile 1 (0.66-12.27)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Quartile 2 (12.32-21.28)	1.70 (1.13, 2.55)	1.67 (1.10, 2.53)	1.44 (1.10, 1.88)	1.40 (1.06, 1.85)
Quartile 3 (21.31-37.67)	1.28 (0.85, 1.92)	1.24 (0.81, 1.90)	1.12 (0.84, 1.49)	1.07 (0.78, 1.45)
Quartile 4 (37.80-349.45)	1.58 (1.03, 2.44)	1.49 (0.89, 2.48)	1.82 (1.32, 2.51)	1.68 (1.15, 2.46)
<i>P</i> for trend	0.092	0.245	0.004	0.056
MEOHP (µg/L)				
Per doubling	1.11 (0.98, 1.25)	1.09 (0.95, 1.25)	1.12 (1.03, 1.22)	1.08 (0.97, 1.20)
Quartile 1 (0.28-9.09)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Quartile 2 (9.13-15.69)	1.38 (0.92, 2.08)	1.33 (0.87, 2.01)	1.14 (0.87, 1.51)	1.10 (0.82, 1.46)
Quartile 3 (15.70-27.16)	1.19 (0.79, 1.79)	1.11 (0.72, 1.71)	1.00 (0.75, 1.33)	0.93 (0.69, 1.27)
Quartile 4 (27.17-330.10)	1.25 (0.82, 1.91)	1.10 (0.67, 1.80)	1.62 (1.18, 2.23)	1.45 (1.00, 2.09)
<i>P</i> for trend	0.391	0.832	0.020	0.204
MEcPP^d (µg/L)				
Per doubling	1.16 (0.94, 1.42)	1.14 (0.88, 1.48)	n.a.	n.a.
Quartile 1 (1.25-14.74)	1 (reference)	1 (reference)		
Quartile 2 (14.76-25.54)	1.14 (0.62, 2.08)	1.14 (0.61, 2.15)		
Quartile 3 (25.68-41.80)	0.87 (0.47, 1.59)	0.87 (0.45, 1.68)		
Quartile 4 (41.82-232.78)	2.02 (1.00, 4.08)	2.06 (0.90, 4.75)		
<i>P</i> for trend	0.141	0.250		
MnBP (µg/L)				
Per doubling	1.17 (0.97, 1.28)	1.09 (0.91, 1.30)	0.99 (0.90, 1.09)	0.88 (0.77, 0.99)
Quartile 1 (1.33-17.24)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Quartile 2 (17.32-29.05)	1.68 (1.09, 2.58)	1.63 (1.05, 2.53)	1.21 (0.89, 1.65)	1.10 (0.81, 1.51)
Quartile 3 (29.07-45.68)	1.15 (0.77, 1.74)	1.09 (0.70, 1.71)	1.12 (0.84, 1.51)	0.93 (0.68, 1.28)
Quartile 4 (45.79-676.45)	1.53 (1.00, 2.34)	1.40 (0.83, 2.35)	1.01 (0.76, 1.35)	0.74 (0.51, 1.06)
<i>P</i> for trend	0.185	0.484	0.858	0.063
MBzP^d (µg/L)				
Per doubling	1.12 (1.01, 1.25)	1.13 (1.00, 1.27)	n.a.	n.a.
Quartile 1 (0.10-0.97)	1 (reference)	1 (reference)		
Quartile 2 (0.97-2.43)	1.12 (0.62, 2.03)	1.10 (0.60, 2.03)		
Quartile 3 (2.46-6.13)	1.49 (0.79, 2.81)	1.46 (0.75, 2.84)		
Quartile 4 (6.18-83.62)	1.64 (0.85, 3.16)	1.59 (0.77, 3.29)		
<i>P</i> for trend	0.092	0.154		

Abbreviations: CI, confidence interval; Cre, creatinine; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate; m/s, meter/second

Note: Logistic regression models were used for cross-sectional analysis and generalized estimating equation models were used for longitudinal analysis

All models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

^a All participants: Enrollment A+B+C in Figure 1

^b All observations: Enrollment A+B+C and Follow-up A1+A2+B1 in Figure 1.

^c Further adjusted for urinary creatinine concentration as a covariate.

^d MEcPP and MBzP had one measurement (n = 731) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S7. Change (95% CI) in walking speed (m/s) according to urinary phthalate metabolite concentrations (non-adjusted and covariate-adjusted) from cross-sectional analysis at enrollment (n = 1,190 ^a) and longitudinal analysis (n = 2,218 ^b)

Phthalate metabolites	Cross-sectional analysis at enrollment		Longitudinal analysis	
	Non-adjusted for creatinine	Cre-adjusted ^c	Non-adjusted for creatinine	Cre-adjusted ^c
MEHHP (µg/L)				
Per doubling	-0.01 (-0.02, 0.00)	-0.01 (-0.02, 0.00)	-0.01 (-0.02, -0.01)	-0.01 (-0.02, -0.00)
Quartile 1 (0.66-12.27)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Quartile 2 (12.32-21.28)	-0.03 (-0.07, -0.00)	-0.04 (-0.07, -0.00)	-0.03 (-0.06, -0.01)	-0.03 (-0.06, -0.01)
Quartile 3 (21.31-37.67)	-0.03 (-0.06, 0.01)	-0.03 (-0.07, 0.00)	-0.02 (-0.05, 0.00)	-0.02 (-0.05, 0.01)
Quartile 4 (37.80-349.45)	-0.04 (-0.07, -0.00)	-0.05 (-0.09, -0.01)	-0.05 (-0.08, -0.02)	-0.05 (-0.08, -0.02)
<i>P</i> for trend	0.076	0.043	0.001	0.008
MEOHP (µg/L)				
Per doubling	0.00 (-0.01, 0.01)	0.00 (-0.02, 0.01)	-0.01 (-0.01, 0.00)	0.00 (-0.01, 0.01)
Quartile 1 (0.28-9.09)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Quartile 2 (9.13-15.69)	-0.02 (-0.05, 0.02)	-0.02 (-0.05, 0.02)	-0.01 (-0.04, 0.01)	-0.01 (-0.04, 0.01)
Quartile 3 (15.70-27.16)	-0.01 (-0.05, 0.02)	-0.01 (-0.05, 0.02)	-0.01 (-0.03, 0.02)	0.00 (-0.03, 0.02)
Quartile 4 (27.17-330.10)	-0.01 (-0.05, 0.02)	-0.02 (-0.06, 0.02)	-0.03 (-0.06, -0.01)	-0.03 (-0.06, 0.00)
<i>P</i> for trend	0.559	0.540	0.027	0.161
MEcPP^d (µg/L)				
Per doubling	-0.01 (-0.02, 0.00)	-0.01 (-0.03, 0.00)	n.a.	n.a.
Quartile 1 (1.25-14.74)	0 (reference)	0 (reference)		
Quartile 2 (14.76-25.54)	-0.03 (-0.07, 0.01)	-0.04 (-0.08, 0.01)		
Quartile 3 (25.68-41.80)	-0.02 (-0.06, 0.02)	-0.03 (-0.07, 0.01)		
Quartile 4 (41.82-232.78)	-0.02 (-0.06, 0.02)	-0.04 (-0.08, 0.01)		
<i>P</i> for trend	0.353	0.217		
MnBP (µg/L)				
Per doubling	0.00 (-0.01, 0.01)	0.00 (-0.02, 0.01)	0.01 (0.00, 0.02)	0.03 (0.02, 0.04)
Quartile 1 (1.33-17.24)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
Quartile 2 (17.32-29.05)	-0.04 (-0.07, -0.01)	-0.04 (-0.08, -0.01)	0.00 (-0.02, 0.03)	0.01 (-0.01, 0.04)
Quartile 3 (29.07-45.68)	-0.01 (-0.04, 0.03)	-0.01 (-0.04, 0.03)	0.01 (-0.02, 0.03)	0.03 (0.00, 0.06)
Quartile 4 (45.79-676.45)	-0.02 (-0.05, 0.01)	-0.02 (-0.06, 0.02)	0.03 (0.00, 0.05)	0.07 (0.04, 0.09)
<i>P</i> for trend	0.623	0.608	0.018	<.001
MBzP^d (µg/L)				
Per doubling	-0.01 (-0.01, 0.00)	-0.01 (-0.02, 0.00)	n.a.	n.a.
Quartile 1 (0.10-0.97)	0 (reference)	0 (reference)		
Quartile 2 (0.97-2.43)	0.01 (-0.03, 0.05)	0.01 (-0.04, 0.05)		
Quartile 3 (2.46-6.13)	-0.01 (-0.05, 0.03)	-0.01 (-0.06, 0.03)		
Quartile 4 (6.18-83.62)	-0.02 (-0.06, 0.02)	-0.03 (-0.07, 0.02)		
<i>P</i> for trend	0.289	0.183		

Abbreviations: CI, confidence interval; Cre, creatinine; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate; m/s, meter/second

Note: Linear regression models were used for cross-sectional analysis and linear mixed-effects models were used for longitudinal analysis.

All models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

^a All participants: Enrollment A+B+C in Figure 1

^b All observations: Enrollment A+B+C and Follow-up A1+A2+B1 in Figure 1.

^c Further adjusted for urine creatinine concentration as covariate.

^d MEcPP and MBzP had one measurement (n = 731) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available..

Table S8. Odds ratios (95% CI) for slowness (< 0.8 m/s) according to urinary phthalate metabolite concentrations ($\mu\text{g/g cre}$) from cross-sectional analysis at enrollment ($n = 1,190^a$) and longitudinal analysis ($n = 2,218^b$)

Phthalate metabolites	Cross-sectional analysis at enrollment		Longitudinal analysis	
	No. with slowness / no. of participants	OR (95% CI)	No. with slowness / no. of observations	OR (95% CI)
MEHHP ($\mu\text{g/g cre}$)				
Per doubling		1.08 (0.94, 1.24)		1.07 (0.97, 1.19)
Quartile 1 (1.07-16.75)	105/299	1 (reference)	241/660	1 (reference)
Quartile 2 (16.78-25.89)	149/297	1.08 (0.74, 1.58)	270/580	0.95 (0.75, 1.20)
Quartile 3 (25.98-41.58)	151/297	1.08 (0.74, 1.58)	283/530	1.19 (0.93, 1.54)
Quartile 4 (41.74-306.32)	185/296	1.29 (0.86, 1.92)	271/446	1.15 (0.87, 1.53)
<i>P</i> for trend		0.246		0.138
MEOHP ($\mu\text{g/g cre}$)				
Per doubling		1.02 (0.89, 1.16)		0.96 (0.87, 1.06)
Quartile 1 (0.53-11.98)	121/298	1 (reference)	266/680	1 (reference)
Quartile 2 (12.01-18.66)	140/298	0.82 (0.56, 1.20)	261/573	0.85 (0.66, 1.09)
Quartile 3 (18.67-30.96)	147/297	0.76 (0.52, 1.11)	270/519	0.91 (0.70, 1.19)
Quartile 4 (30.98-263.23)	182/296	1.05 (0.71, 1.56)	268/444	1.06 (0.80, 1.41)
<i>P</i> for trend		0.914		0.703
MEcPP ^c ($\mu\text{g/g cre}$)				
Per doubling		1.08 (0.88, 1.31)	n.a.	n.a.
Quartile 1 (3.89-18.65)	95/182	1 (reference)		
Quartile 2 (18.67-27.29)	117/183	1.50 (0.95, 2.38)		
Quartile 3 (27.29-41.43)	118/183	1.32 (0.84, 2.09)		
Quartile 4 (41.48-216.94)	118/182	1.17 (0.74, 1.87)		
<i>P</i> for trend		0.602		
MnBP ($\mu\text{g/g cre}$)				
Per doubling		0.96 (0.82, 1.12)		0.82 (0.73, 0.92)
Quartile 1 (4.60-24.63)	158/298	1 (reference)	270/521	1 (reference)
Quartile 2 (24.65-33.97)	139/297	0.83 (0.57, 1.20)	254/517	0.81 (0.62, 1.06)
Quartile 3 (33.98-49.07)	148/298	0.93 (0.64, 1.36)	261/565	0.68 (0.51, 0.89)
Quartile 4 (49.15-764.57)	145/296	0.79 (0.54, 1.16)	280/614	0.58 (0.44, 0.76)
<i>P</i> for trend		0.349		<.001
MBzP ^c ($\mu\text{g/g cre}$)				
Per doubling		1.22 (1.07, 1.39)	n.a.	n.a.
Quartile 1 (0.04-1.13)	90/182	1 (reference)		
Quartile 2 (1.14-2.76)	122/183	1.80 (1.13, 2.87)		
Quartile 3 (2.76-5.53)	110/183	1.34 (0.85, 2.12)		
Quartile 4 (5.61-66.47)	126/182	1.96 (1.22, 3.13)		
<i>P</i> for trend		0.022		

Abbreviations: CI, confidence interval; Cre, creatinine; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate; m/s, meter/second

Note: Logistic regression models were used for cross-sectional analysis and generalized estimating equation models were used for longitudinal analysis.

All models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

^a All participants: Enrollment A+B+C in Figure 1

^b All observations: Enrollment A+B+C and Follow-up A1+A2+B1 in Figure 1.

^c MEcPP and MBzP had one measurement ($n = 731$) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S9. Odds ratios (95% CI) for sex-and height-adjusted slowness^a by urinary phthalate metabolite concentrations ($\mu\text{g/g cre}$) from cross-sectional analysis at enrollment ($n = 1190$ ^b) and longitudinal analysis ($n = 2218$ ^c)

Phthalate metabolites	Cross-sectional analysis at enrollment		Longitudinal analysis	
	No. with slowness / no. of participants	OR (95% CI)	No. with slowness / no. of observations	OR (95% CI)
MEHHP ($\mu\text{g/g cre}$)				
Per doubling		1.00 (0.85, 1.18)		1.12 (0.99, 1.27)
Quartile 1 (1.07-16.75)	36/299	1 (reference)	84/660	1 (reference)
Quartile 2 (16.78-25.89)	61/297	1.02 (0.62, 1.68)	107/580	1.01 (0.73, 1.39)
Quartile 3 (25.98-41.58)	64/297	1.14 (0.69, 1.86)	116/530	1.21 (0.86, 1.70)
Quartile 4 (41.74-306.32)	74/296	1.05 (0.64, 1.73)	117/446	1.28 (0.90, 1.93)
<i>P</i> for trend		0.776		0.100
MEOHP ($\mu\text{g/g cre}$)				
Per doubling		0.93 (0.79, 1.09)		1.05 (0.94, 1.17)
Quartile 1 (0.53-11.98)	45/298	1 (reference)	96/680	1 (reference)
Quartile 2 (12.01-18.66)	59/298	0.83 (0.52, 1.34)	99/573	0.84 (0.62, 1.16)
Quartile 3 (18.67-30.96)	63/297	0.83 (0.52, 1.32)	120/519	1.08 (0.78, 1.50)
Quartile 4 (30.98-263.23)	68/296	0.78 (0.49, 1.27)	109/444	1.08 (0.76, 1.54)
<i>P</i> for trend		0.369		0.392
MEcPP^d ($\mu\text{g/g cre}$)				
Per doubling		1.21 (0.97, 1.51)	n.a.	n.a.
Quartile 1 (3.89-18.65)	30/182	1 (reference)		
Quartile 2 (18.67-27.29)	44/183	1.46 (0.84, 2.54)		
Quartile 3 (27.29-41.43)	49/183	1.65 (0.96, 2.84)		
Quartile 4 (41.48-216.94)	50/182	1.48 (0.86, 2.56)		
<i>P</i> for trend		0.163		
MnBP ($\mu\text{g/g cre}$)				
Per doubling		1.04 (0.88, 1.24)		0.94 (0.82, 1.08)
Quartile 1 (4.60-24.63)	66/298	1 (reference)	109/521	1 (reference)
Quartile 2 (24.65-33.97)	56/297	0.93 (0.60, 1.44)	101/517	0.87 (0.64, 1.19)
Quartile 3 (33.98-49.07)	49/298	0.90 (0.58, 1.40)	101/565	0.85 (0.62, 1.16)
Quartile 4 (49.15-764.57)	50/296	0.94 (0.61, 1.46)	113/614	0.79 (0.57, 1.11)
<i>P</i> for trend		0.764		0.183
MBzP^d ($\mu\text{g/g cre}$)				
Per doubling		1.07 (0.97, 1.18)	n.a.	n.a.
Quartile 1 (0.04-1.13)	35/182	1 (reference)		
Quartile 2 (1.14-2.76)	52/183	1.61 (0.95, 2.73)		
Quartile 3 (2.76-5.53)	37/183	1.01 (0.58, 1.74)		
Quartile 4 (5.61-66.47)	48/182	1.36 (0.80, 2.31)		
<i>P</i> for trend		0.642		

Abbreviations: CI, confidence interval; Cre, creatinine; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate

Note: Logistic regression models were used for cross-sectional analysis and generalized estimating equation models were used for longitudinal analysis.

All models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

^a Slowest 20% of the population, by sex and standing height (cut-point: median).

^b All participants: Enrollment A+B+C in Figure 1

^c All observations: Enrollment A+B+C and Follow-up A1+A2+B1 in Figure 1.

^d MEcPP and MBzP had one measurement ($n = 731$) at Exam II (Follow-up A1+Enrollment B). Only cross-sectional analysis was possible. Thus, repeated measurements of MEcPP and MBzP were not available.

Table S10. Odds ratios (95% CI) for slowness (< 1.0 meter/second) by urinary phthalate concentrations ($\mu\text{g/g cre}$) from longitudinal analysis after further adjustments for socioeconomic status^a (n = 1,721) and depression^b (n 2,215)

Phthalate metabolites	Adjusted for SES		Adjusted for depression	
	No. with slowness / no. of observations	OR (95% CI)	No. with slowness / no. of observations	OR (95% CI)
MEHHP ($\mu\text{g/g cre}$)				
Per doubling		1.11 (0.99, 1.27)		1.16 (1.03, 1.30)
Quartile 1 (1.07-16.75)	303/496	1 (reference)	421/660	1 (reference)
Quartile 2 (16.78-25.89)	318/438	1.11 (0.82, 1.51)	427/580	1.07 (0.83, 1.40)
Quartile 3 (25.98-41.58)	313/408	1.23 (0.89, 1.70)	403/529	1.18 (0.88, 1.56)
Quartile 4 (41.74-306.32)	311/379	1.37 (0.95, 1.98)	376/446	1.50 (1.07, 2.10)
<i>P</i> for trend		0.076		0.025
MEOHP ($\mu\text{g/g cre}$)				
Per doubling		1.05 (0.92, 1.19)		1.06 (0.95, 1.19)
Quartile 1 (0.53-11.98)	316/509	1 (reference)	442/679	1 (reference)
Quartile 2 (12.01-18.66)	320/436	1.19 (0.88, 1.62)	423/573	1.05 (0.80, 1.37)
Quartile 3 (18.67-30.96)	305/409	1.01 (0.73, 1.41)	387/519	0.93 (0.69, 1.25)
Quartile 4 (30.98-263.23)	304/367	1.54 (1.06, 2.24)	375/444	1.56 (1.11, 2.18)
<i>P</i> for trend		0.083		0.075
MnBP ($\mu\text{g/g cre}$)				
Per doubling		0.84 (0.74, 0.97)		0.85 (0.75, 0.97)
Quartile 1 (4.60-24.63)	316/408	1 (reference)	401/521	1 (reference)
Quartile 2 (24.65-33.97)	281/383	0.70 (0.48, 1.00)	380/517	0.74 (0.54, 1.01)
Quartile 3 (33.98-49.07)	295/430	0.64 (0.45, 0.90)	403/565	0.70 (0.51, 0.94)
Quartile 4 (49.15-764.57)	354/501	0.59 (0.42, 0.83)	444/613	0.65 (0.48, 0.89)
<i>P</i> for trend		0.003		0.009

Abbreviations: CI, confidence interval; Cre, creatinine; SES, socioeconomic status; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; m/s, meter/second

Note: Generalized estimating equation models were used for longitudinal analysis.

All models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

^a Further adjusted for socioeconomic status including household income and living arrangement.

^b Further adjusted for self-reported depression symptoms (SGDS-K score) as a covariate.

Table S11. Odds ratios (95% CI) for slowness (< 1.0 meter/second) according to urinary phthalate concentrations ($\mu\text{g/g cre}$) in men and women, from longitudinal analysis ($n = 2,218$)

Phthalate metabolites	No. with slowness / no. of observations	OR (95% CI)		<i>p</i> for interaction	
		Men	No. with slowness / no. of observations		Women
MEHHP					
Per doubling		1.25 (1.04, 1.52)		1.10 (0.96, 1.26)	0.424
Quartile 1 (1.07-16.75)	99/159	1 (reference)	314/471	1 (reference)	
Quartile 2 (16.78-25.89)	125/166	1.60 (0.93, 2.74)	306/405	1.30 (0.94, 1.81)	
Quartile 3 (25.98-41.58)	107/158	1.04 (0.60, 1.79)	290/388	1.04 (0.71, 1.52)	
Quartile 4 (41.74-306.32)	122/150	2.14 (1.14, 4.00)	265/319	1.40 (0.87, 2.25)	
<i>P</i> for trend		0.098		0.366	
MEOHP					
Per doubling		1.22 (0.99, 1.49)		1.01 (0.89, 1.15)	0.110
Quartile 1 (0.53-11.98)	108/170	1 (reference)	332/483	1 (reference)	
Quartile 2 (12.01-18.66)	115/159	1.39 (0.80, 2.43)	294/395	0.95 (0.68, 1.34)	
Quartile 3 (18.67-30.96)	119/166	1.22 (0.72, 2.06)	276/372	0.77 (0.52, 1.14)	
Quartile 4 (30.98-263.23)	111/138	2.09 (1.12, 3.93)	273/333	1.16 (0.74, 1.84)	
<i>P</i> for trend		0.056		0.986	
MnBP					
Per doubling		1.12 (0.87, 1.44)		0.79 (0.68, 0.91)	0.018
Quartile 1 (4.60-24.63)	81/124	1 (reference)	308/399	1 (reference)	
Quartile 2 (24.65-33.97)	124/163	1.92 (1.08, 3.42)	282/373	0.90 (0.61, 1.32)	
Quartile 3 (33.98-49.07)	117/163	1.68 (0.89, 3.16)	278/375	0.71 (0.49, 1.04)	
Quartile 4 (49.15-764.57)	132/184	1.55 (0.80, 3.00)	306/435	0.51 (0.33, 0.80)	
<i>P</i> for trend		0.365		0.002	

Abbreviations: CI, confidence interval; Cre, creatinine; MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; m/s, meter/second

Note: Generalized estimating equation models were used for longitudinal analysis.

Models were adjusted for age, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

Table S12. Overall effects of phthalate metabolite mixtures on changes in walking speed (m/s, meters/second) estimated by Bayesian kernel machine regression (numeric values of Figure 3).

Quantile	Changes in walking speed (m/s)	
0.05	0.064	(0.013, 0.115)
0.10	0.048	(0.015, 0.081)
0.15	0.038	(0.014, 0.061)
0.20	0.030	(0.012, 0.049)
0.25	0.024	(0.010, 0.039)
0.30	0.018	(0.007, 0.028)
0.35	0.013	(0.005, 0.020)
0.40	0.008	(0.004, 0.013)
0.45	0.005	(0.002, 0.008)
0.50	0.000	(0.000, 0.000)
0.55	-0.003	(-0.005, -0.001)
0.60	-0.008	(-0.012, -0.003)
0.65	-0.011	(-0.019, -0.004)
0.70	-0.015	(-0.025, -0.005)
0.75	-0.021	(-0.035, -0.006)
0.80	-0.026	(-0.045, -0.007)
0.85	-0.030	(-0.054, -0.006)
0.90	-0.037	(-0.068, -0.005)
0.95	-0.047	(-0.093, -0.001)

Analysis was conducted with data at one-time point (Exam II) when all five metabolites were measured (n = 731). The model was adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension. Changes in walking speed (m/s) were estimated when all log-transformed phthalates were at the respective percentiles compared to median values. Variation is presented using 95% credible intervals.

Table S13. Posterior inclusion probabilities for individual phthalate metabolites using Bayesian kernel machine regression analysis

Phthalate metabolites	Non-hierarchical Model		Hierarchical Model		
	PIP	Group	Group PIP	Conditional PIP	
MEHHP	0.33	1	0.51	0.72	
MEOHP	0.05	1	0.51	0.08	
MEcPP	0.11	1	0.51	0.20	
MnBP	0.03	2	0.04	1.00	
MBzP	0.12	3	0.16	1.00	

Abbreviations: MEHHP, mono (2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, mono (2-ethyl-5-oxohexyl) phthalate; MnBP, mono-n-butyl phthalate; MEcPP, mono-(2-ethyl-5-carboxypentyl) phthalate; MBzP, mono-benzyl phthalate; posterior inclusion probability, PIP

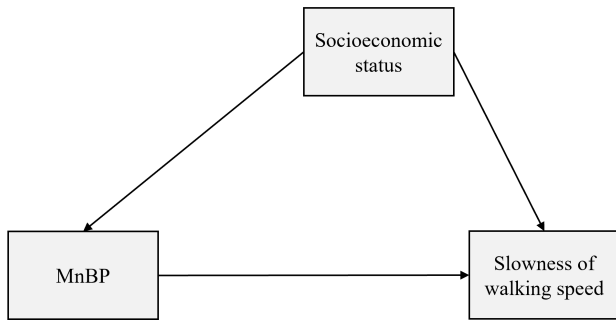
Note: Analysis was conducted with data at one-time point (Exam II), when all five metabolites were measured (n=731). Models were adjusted for age, sex, region, education level, smoking status, weight, height, physical activity, osteoarticular disease, cardiovascular disease, chronic respiratory diseases, cancer, diabetes, and hypertension.

Table S14. Spearman's coefficients between MnBP and household income at enrollment in the KEEP II study.

	MnBP ($\mu\text{g/L}$)	
	Spearman's coefficients	<i>p</i> -value
Household income		
All participants (n=854)	0.03174	0.1879
Men (n=292)	-0.04403	0.3045
Women (n=562)	0.05615	0.0541

^a Analysis was conducted with available data at enrollment, which was used in the cross-sectional analysis in Tables 3 and 4.

A) Men



B) Women

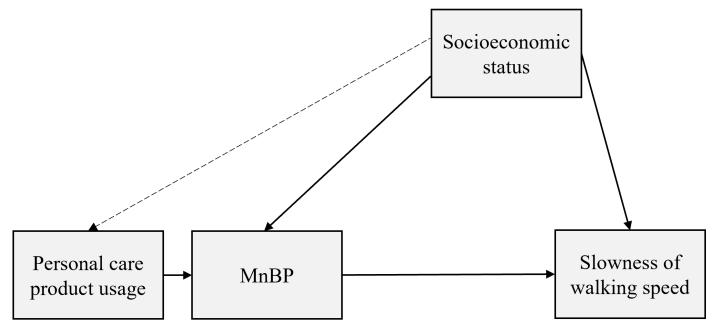


Figure S1. Directed acyclic graph (DAG) for representing the potential confounding effect of socioeconomic status (SES) on associations between MnBP and slowness of walking speed in men (A) and women (B). The potential causal relationships (either protective or adverse) between one variable on another were represented as arrows.