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Supplemental Material

Urinary Phthalate Metabolite Concentrations and Breast Cancer Incidence and Survival following Breast Cancer: The Long Island Breast Cancer Study Project

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Table S1. Distribution of urinary phthalate metabolite concentrations ($\mu\text{g/L}$) among the LIBCSP women (n=1,542) and non-Hispanic adult NHANES women.

Analyte	LIBCSP					NHANES 1999-2000 ^a		
	LOD	n	n (%) <LOD	P50 ^b	P95 ^b	n	P50 ^b	P95 ^b
MEP	0.6	1,542	0 (0.0)	108	1570	360	94.7	1173
MBP	0.4	1,542	9 (0.6)	23.4	132	364	20.6	146
MiBP	0.2	1,542	155 (10.1)	2.10	12.6	–	–	–
MCPP	0.2	1,542	2 (0.1)	3.80	19.2	–	–	–
MBzP	0.3	1,542	2 (0.1)	9.21	60.9	364	8.71	52.7
MCOP	0.2	752	0 (0.0)	4.50	36.5	–	–	–
MCNP	0.2	752	3 (0.4)	2.60	18.4	–	–	–
MEHP	0.5	1,542	342 (22.2)	2.60	24.7	364	2.30	20.8
MEOHP	0.2	1,542	6 (0.4)	12.3	94.4	–	–	–
MEHHP	0.2	1,542	0 (0.0)	20.7	155	–	–	–
MECPP	0.2	1,542	0 (0.0)	27.7	207	–	–	–

Long Island Breast Cancer Study Project (LIBCSP) women without breast cancer were age-matched to women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyoctyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate; P, percentile.

^aNHANES 1999-2000 participants restricted to non-Hispanic adult (≥ 18 years old) women with urinary phthalate metabolite measurements from: CDC (Centers for Disease Control and Prevention). 2001. NHANES 1999-2000 Laboratory Data. Available:

<https://www.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Laboratory&CycleBeginYear=1999>.

^bValues below the limit of detection (LOD) were imputed as $\text{LOD}/\sqrt{2}$.

Table S2. Distribution of creatinine-corrected urinary phthalate metabolite concentrations ($\mu\text{g/g}$ creatinine) among the LIBCSP women, by breast cancer status (n=1,308).

Analyte	Women with Breast Cancer (n=710)			Women without Breast Cancer (n=598)						
	n	P50	P95	n	P50	P95	P20 ^a	P40 ^a	P60 ^a	P80 ^a
MEP	710	138	2008	598	158	2049	60.7	118	207	492
MBP	710	33.9	128	598	34.1	141	19.3	29.1	43.6	67.9
MiBP	710	2.78	12.9	598	2.97	11.8	1.44	2.43	3.79	6.16
M CPP	710	5.13	16.2	598	5.32	19.0	3.28	4.53	6.45	9.28
MBzP	710	12.4	66.6	598	13.5	54.1	7.03	11.0	16.5	25.7
MCOP	320	5.57	47.4	205	6.07	54.9	3.42	5.03	7.54	13.6
MCNP	320	3.50	16.8	205	3.17	27.3	1.99	2.64	3.92	7.72
MEHP	710	3.72	23.6	598	4.11	27.0	1.81	3.13	4.96	9.86
MEOHP	710	16.8	86.6	598	16.8	106	9.17	14.5	20.0	34.0
MEHHP	710	28.2	158	598	28.4	170	14.9	23.8	34.2	59.4
MECPP	710	37.7	196	598	38.6	199	22.5	34.0	45.9	78.4

Long Island Breast Cancer Study Project (LIBCSP) women without breast cancer were age-matched to women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; M CPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyoctyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate; P, percentile.

^aPercentile cutpoints used for categorization of phthalate metabolite concentrations into quintiles.

Table S3. Pearson correlation coefficients between urinary phthalate metabolite concentrations ($\mu\text{g/g}$ creatinine) with each other and with continuous breast cancer covariates among LIBCSP women without breast cancer ($n=598$).

Analyte	MEP	MBP	MiBP	MCPP	MBzP	MCOP	MCNP	MEHP	MEOHP	MEHHP	MECPP
MEP	1										
MBP	0.03	1									
MiBP	-0.04	0.30*	1								
MCPP	0.00	0.31*	0.12*	1							
MBzP	0.01	0.20*	0.11*	0.11*	1						
MCOP	-0.03	0.04	-0.02	0.22*	0.02	1					
MCNP	-0.03	0.40*	0.04	0.58*	-0.01	0.10	1				
MEHP	0.02	0.05	0.06	0.29*	0.07	0.07	0.08	1			
MEOHP	0.00	0.07	0.06	0.27*	0.09*	0.06	0.05	0.86*	1		
MEHHP	0.00	0.06	0.06	0.28*	0.09*	0.06	0.06	0.90*	0.99*	1	
MECPP	0.00	0.06	0.04	0.22*	0.11*	0.08	0.08	0.65*	0.88*	0.85*	1
Covariate	MEP	MBP	MiBP	MCPP	MBzP	MCOP	MCNP	MEHP	MEOHP	MEHHP	MECPP
Age at reference	-0.01	0.02	0.05	0.06	-0.01	-0.04	0.03	0.00	0.00	0.00	0.04
Age at menarche	0.01	-0.01	-0.04	-0.10*	0.06	-0.02	-0.08	-0.02	-0.01	-0.01	0.02
Oral contraceptive use (mos.)	-0.04	-0.03	-0.02	-0.03	-0.05	-0.06	-0.04	-0.01	-0.01	-0.02	-0.03
Parity	-0.01	-0.04	0.01	-0.05	0.05	-0.05	0.04	-0.06	-0.03	-0.04	0.01
Age at first birth	-0.05	0.00	-0.06	-0.03	-0.02	-0.01	0.04	0.04	0.04	0.04	0.08
Lactation (mos.)	0.00	0.01	0.07	0.01	0.07	-0.03	0.02	-0.01	0.00	-0.01	-0.01
BMI at reference (kg/m²)	0.01	-0.03	0.05	0.01	0.04	0.01	-0.02	0.02	0.09*	0.07	0.10*
BMI at age 20 (kg/m²)	0.03	0.01	0.01	-0.00	0.04	-0.04	-0.04	0.03	0.07	0.06	0.09*

Long Island Breast Cancer Study Project (LIBCSP) women without breast cancer were age-matched to women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyethyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate.

* $P < .05$

Table S4. Chi-squared test statistics between quintiles of creatinine-corrected urinary phthalate metabolite concentrations ($\mu\text{g/g}$ creatinine) and categorical breast cancer covariates among LIBCSP women without breast cancer (n=598).

Covariates	MEP	MBP	MiBP	MCPP	MBzP	MCOP	MCNP	MEHP	MEOHP	MEHHP	MECPP
Age at reference	0.25	0.01	0.05	8.62*	1.88	2.78	2.78	6.33*	0.29	0.58	2.10
Income	0.00	1.03	4.16*	0.34	0.38	0.04	1.92	6.45*	0.41	0.31	0.62
Education	2.24	1.64	9.25*	0.11	0.12	0.08	1.13	1.37	0.02	0.07	0.06
Menopausal status	0.40	0.02	0.05	10.62*	2.20	3.44	7.05*	2.57	3.11	3.18	4.53*
Hormone replacement therapy use	4.39*	0.21	0.52	0.35	0.62	1.14	0.10	0.02	0.15	0.73	0.21
Age at menarche	0.09	1.55	3.80	1.85	0.71	2.20	0.98	0.07	0.37	0.48	0.19
Oral contraceptive use	0.03	0.34	0.05	2.44	0.00	0.48	0.16	0.16	0.27	0.00	0.66
Parity/lactation history	0.78	0.03	1.43	1.04	3.30	1.08	0.79	2.69	0.00	0.28	0.07
Age at first birth	1.07	0.79	0.65	0.11	1.22	0.01	0.06	0.03	2.45	1.34	1.21
Family history of breast cancer	0.09	2.43	0.00	0.99	0.09	0.53	0.23	0.55	0.40	0.40	0.99
BMI at reference	2.47	0.24	3.64	1.93	1.55	1.25	0.63	2.46	8.66*	7.18*	10.98*
BMI at age 20	1.31	0.04	0.00	0.08	2.62	0.16	0.05	0.03	0.55	1.04	0.68
Alcohol intake	0.29	2.07	0.00	0.03	1.59	0.38	0.01	0.01	0.00	0.00	0.61

Long Island Breast Cancer Study Project (LIBCSP) women without breast cancer were age-matched to women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyethyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate.

*p<.05

Table S5. Age-adjusted means (standard errors)^a of log-transformed creatinine-corrected urinary phthalate metabolite concentrations ($\mu\text{g/g}$ creatinine) by receipt of chemotherapy treatment prior to urinary sample collection among women diagnosed with breast cancer (n=693).

Analyte	Receipt of chemotherapy treatment ^b		<i>P</i>
	Yes (n=145)	No (n=548)	
	Ln- $\mu\text{g/g}$ creatinine (SE)	Ln- $\mu\text{g/g}$ creatinine (SE)	
MEP	4.87 (0.11)	5.13 (0.06)	0.05
MBP	3.52 (0.07)	3.54 (0.04)	0.80
MiBP	0.97 (0.09)	0.99 (0.04)	0.89
MCPP	1.67 (0.06)	1.66 (0.03)	0.93
MBzP	2.66 (0.08)	2.50 (0.04)	0.08
MCOP	1.89 (0.13)	1.92 (0.07)	0.84
MCNP	1.44 (0.11)	1.33 (0.06)	0.34
MEHP	1.47 (0.09)	1.33 (0.05)	0.14
MEOHP	2.99 (0.08)	2.85 (0.04)	0.10
MEHHP	3.55 (0.08)	3.37 (0.04)	0.04
MECPP	3.77 (0.07)	3.69 (0.04)	0.33

Long Island Breast Cancer Study Project (LIBCSP) women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyoctyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate.

^aAdjusted means, standard errors, and p-values are derived from generalized linear models regressing each of the ln-transformed creatinine-corrected phthalate metabolites on age and chemotherapy treatment prior to urinary sample collection.

^b17 breast cancer cases were missing chemotherapy status prior to urine sample collection.

Table S6. Age-adjusted means (standard errors)^a of log-transformed creatinine-corrected urinary phthalate metabolite concentrations (µg/g creatinine) by disease and treatment characteristics among women diagnosed with breast cancer (n=710).

Covariates	MEP	MBP	MiBP	MCPP	MBzP	MCOP	MCNP	MEHP	MEOHP	MEHHP	MECPP
Stage											
<i>In situ</i>	5.22 (0.13)	3.58 (0.08)	1.00 (0.10)	1.65 (0.07)	2.46 (0.09)	1.57 (0.17)	1.26 (0.15)	1.15 (0.10)	2.67 (0.09)	3.19 (0.09)	3.52 (0.08)
Invasive	5.05 (0.06)	3.52 (0.03)	0.98 (0.04)	1.67 (0.03)	2.54 (0.04)	1.94 (0.06)	1.35 (0.05)	1.40 (0.04)	2.91 (0.04)	3.44 (0.04)	3.74 (0.03)
<i>P</i>	0.24	0.52	0.81	0.87	0.42	0.04	0.58	0.02	0.01	0.01	0.01
Nodal involvement											
No	5.12 (0.14)	3.51 (0.09)	0.97 (0.11)	1.66 (0.08)	2.45 (0.10)	1.65 (0.20)	1.42 (0.15)	1.23 (0.11)	2.74 (0.10)	3.27 (0.10)	3.60 (0.09)
Yes	4.96 (0.07)	3.58 (0.05)	1.01 (0.06)	1.69 (0.04)	2.56 (0.05)	1.95 (0.09)	1.34 (0.07)	1.42 (0.06)	2.90 (0.05)	3.43 (0.05)	3.72 (0.05)
<i>P</i>	0.30	0.53	0.74	0.75	0.32	0.17	0.63	0.14	0.16	0.16	0.27
Tumor size											
≤2cm	5.02 (0.08)	3.63 (0.05)	1.06 (0.06)	1.73 (0.04)	2.58 (0.05)	2.08 (0.10)	1.41 (0.08)	1.48 (0.06)	2.92 (0.05)	3.48 (0.06)	3.76 (0.05)
>2cm	4.86 (0.13)	3.48 (0.08)	0.92 (0.10)	1.60 (0.07)	2.53 (0.09)	1.57 (0.15)	1.15 (0.12)	1.29 (0.11)	2.89 (0.09)	3.39 (0.09)	3.71 (0.09)
<i>P</i>	0.29	0.14	0.22	0.14	0.64	0.01	0.06	0.12	0.71	0.43	0.64
ER status											
ER–	5.07 (0.13)	3.52 (0.08)	0.85 (0.10)	1.75 (0.07)	2.53 (0.08)	1.84 (0.13)	1.40 (0.11)	1.37 (0.10)	2.93 (0.08)	3.48 (0.09)	3.75 (0.08)
ER+	5.04 (0.07)	3.54 (0.04)	1.02 (0.05)	1.64 (0.04)	2.56 (0.05)	1.91 (0.08)	1.27 (0.06)	1.39 (0.06)	2.90 (0.05)	3.43 (0.05)	3.70 (0.04)
<i>P</i>	0.83	0.84	0.13	0.14	0.81	0.64	0.30	0.90	0.80	0.62	0.62
Radiation therapy											
No	5.05 (0.10)	3.49 (0.06)	0.98 (0.07)	1.63 (0.05)	2.50 (0.07)	1.79 (0.11)	1.29 (0.09)	1.33 (0.08)	2.85 (0.07)	3.35 (0.07)	3.69 (0.06)
Yes	5.08 (0.08)	3.61 (0.05)	1.00 (0.06)	1.70 (0.04)	2.61 (0.05)	2.06 (0.09)	1.43 (0.07)	1.46 (0.06)	2.90 (0.05)	3.44 (0.05)	3.73 (0.05)
<i>P</i>	0.78	0.11	0.78	0.21	0.20	0.07	0.24	0.17	0.59	0.31	.63
Chemotherapy											
No	5.13 (0.08)	3.53 (0.05)	0.95 (0.06)	1.66 (0.04)	2.44 (0.06)	2.03 (0.10)	1.44 (0.08)	1.34 (0.06)	2.78 (0.05)	3.31 (0.06)	3.64 (0.05)
Yes	4.97 (0.10)	3.62 (0.06)	1.06 (0.07)	1.67 (0.05)	2.76 (0.07)	1.85 (0.11)	1.29 (0.09)	1.49 (0.08)	3.01 (0.07)	3.54 (0.07)	3.80 (0.06)
<i>P</i>	0.24	0.29	0.23	0.86	<.001	0.25	0.22	0.14	0.01	0.01	0.06
Hormone therapy											
No	5.16 (0.10)	3.56 (0.06)	1.00 (0.08)	1.72 (0.05)	2.56 (0.07)	1.92 (0.12)	1.40 (0.10)	1.34 (0.08)	2.86 (0.07)	3.39 (0.07)	3.69 (0.71)
Yes	5.04 (0.08)	3.56 (0.05)	0.99 (0.06)	1.65 (0.04)	2.57 (0.05)	1.98 (0.09)	1.35 (0.07)	1.45 (0.06)	2.89 (0.74)	3.41 (0.05)	3.72 (0.05)
<i>P</i>	0.35	0.99	0.93	0.26	0.94	0.66	0.66	0.29	0.74	0.80	0.71

Long Island Breast Cancer Study Project (LIBCSP) women diagnosed with breast cancer between August 1, 1996 and July 31, 1997.

Abbreviations: MEP, monoethyl phthalate; MBP, mono-n-butyl phthalate; MiBP, mono-isobutyl phthalate; MCPP, mono(3-carboxypropyl) phthalate; MBzP, monobenzyl phthalate; MCOP, monocarboxyoctyl phthalate; MCNP, monocarboxy-isononyl phthalate; MEHP, mono(2-ethylhexyl) phthalate; MEOHP, mono(2-ethyl-5-oxohexyl) phthalate; MEHHP, mono(2-ethyl-5-hydroxyhexyl) phthalate; MECPP, mono(2-ethyl-5-carboxypentyl) phthalate.

^aAdjusted means, standard errors, and p-values are derived from generalized linear models regressing each of the ln-transformed creatinine-corrected phthalate metabolites on age and the covariate.