Supplemental Table 1

Geometric means and 10th-90th percentile concentrations of urinary phenols, µg/g-creatinine, BCERP 2004-2011.

	N	Geometric mean	10th Pctl	90th Pctl
Benzophenone-3	1169	37	3	802
Enterolactone	1147	452	92	1,797
Bisphenol A	1169	2.7	1	8
Paraben Sum	1079	103	16	829
2,5-Dichlorophenol	1169	17	2	224
Triclosan	1157	18	3	174
Daidzein	1147	126	19	1,226
Genistein	1147	58	9	602

There were 1170 observations with at least one biomarker and creatinine. One girl was missing from the phenols (n=1169) but had phytoestrogens (enterolactone, daidzein, genistein; n=1147). In the earlier report (Wolff *et al.*, 2010), we had phenol biomarkers on 1151 girls; 22 additional laboratory values were added after that report for the phenol panel of benzophenone-3, bisphenol A, 2,5-dichlorophenol, and 10 for triclosan. Three are excluded because of two missing creatinine and one withdrawal from the study. Paraben sum is the molar sum of methyl-, ethyl-, and propyl-parabens, expressed as propylparaben (molecular weight 180.2). There were fewer paraben values as this biomarker was reported after the first round of analyses.

Suppl Table 2

Diagnostic mediation analysis exploring the relationship among age at breast stage 2, phenol (ln-ug/L) and BMI% controlling for child race, caregiver education and ln-urinary creatinine.

Urinary phenol:	Causal Mediation Analysis					Causal Mediation Analysis where B2 Age < 120 mo				
benzophenone-3	N	Estimate	Lower 95%	Upper 95%	p value	N	Estimate	Lower 95%	Upper 95%	p value
Total Effect	1141	1.01	0.51	1.48	<.01	821	0.45	0.10	0.77	0.01
Direct Effect		1.04	0.57	1.47	<.01		0.46	0.15	0.78	0.01
Indirect effect		-0.03	-0.19	0.13	0.72		0.00	-0.10	0.10	0.99
enterolactone		Estimate	Lower 95%	Upper 95%	p value		Estimate	Lower 95%	Upper 95%	p value
Total Effect	1119	0.74	-0.10	1.61	0.1	803	0.61	0.14	1.11	0.01
Direct Effect		0.15	-0.74	1.03	0.7		0.39	-0.06	0.88	0.09
Indirect effect		0.59	0.34	0.87	<.01		0.22	0.07	0.38	<.01
2,5-Dichlorophenol		Estimate	Lower 95%	Upper 95%	p value		Estimate	Lower 95%	Upper 95%	p value
Total Effect	1141	-1.05	-1.70	-0.42	<.01	821	-0.59	-1.03	-0.20	<.01
Direct Effect		-0.94	-1.53	-0.33	<.01		-0.50	-0.92	-0.14	<.01
Indirect effect		-0.11	-0.28	0.05	0.21		-0.09	-0.19	0.01	0.09
triclosan		Estimate	Lower 95%	Upper 95%	p value		Estimate	Lower 95%	Upper 95%	p value
Total Effect	1129	-0.81	-1.51	-0.09	0.02	813	-0.37	-0.82	0.04	0.08
Direct Effect		-0.88	-1.54	-0.21	0.01		-0.44	-0.88	-0.04	0.03
Indirect effect		0.07	-0.13	0.28	0.49		0.06	-0.05	0.19	0.28

Enterolactone is the only phenol that exhibits a BMI-mediating (indirect) effect, i.e. enterolactone → BMI →B2-age. Among girls at all ages, the direct effect of enterolactone on B2 (i.e., controlled for BMI%) is smaller than the indirect effect of enterolactone, i.e., supporting a pathway of enterolactone → BMI →B2-age. In contrast, among girls younger than 120 months, the direct effect of enterolactone on B2 was larger than the indirect effect. These estimates suggest that BMI% is a less important factor in the enterolactone models among younger (<120 months) compared with older girls. However, the indirect effect is significant in both age groups.

This analysis provided estimates (but risks) for the average causal mediation effect (indirect effect), average direct effect and total effect of exposure biomarker associations with age-at-B2 while controlling for race/ethnicity, education and creatinine. Estimates have no risk importance, but rather show the relative contribution of exposure and BMI% to associations that are quantified using Hazards models in Table 2 of the paper. The Total Effect can be described as the Total exposure association with age-at-B2 incorporating all pathways including BMI%. The Direct Effect excludes the contribution of BMI% to the Total. The Indirect effect is approximately the difference between the other two and is that portion of the exposure effect on B2 that operates through BMI, i.e. exposure→BMI%→B2.

Estimates were created using the R package Mediation created by Tingley (Tingley et al., 2013). The package estimates the indirect, direct and total effect using algorithms developed by Imai et al., 2010. This method requires a parametric modeling approach, and therefore we specified the Weibull distribution which in our data produced nearly identical HRs compared to the Cox Model for exposures and covariates. The estimates in this table were produced by the nonparametric bootstrap confidence intervals with the percentile method procedure. N's are those for adjusted models in Table 2, representing girls with information on urinary phenols, creatinine, caregiver education, race/ethnicity, BMI.