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Dietary sources of cumulative phthalates exposure among the U.S. general population in NHANES 2005–2014

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Abstract

Background—Anti-androgenic phthalates are reproductive toxicants that may have additive effects on male development. Diet is the primary exposure source for most phthalates, which contaminate the food supply through food contact materials and industrialized production.

Objective—To compare dietary sources of cumulative phthalates exposure between "food at home" (e.g. food consumed from a grocery store) and "food away from home" (e.g. food consumed from fast food/restaurants and cafeterias) in the U.S. general population.

Methods—We estimated cumulative phthalates exposure by calculating daily intake from metabolite concentrations in urinary spot samples for 10,253 participants (6 years old) using National Health and Nutrition Examination Survey (NHANES, 2005–2014) data. We constructed a biologically relevant metric of phthalates daily intake (Σandrogen-disruptor, μg/kg/day) by converting phthalates into anti-androgen equivalent terms prior to their summation. Particular foods and the percent of total energy intake (TEI) consumed from multiple dining out sources were ascertained from 24-hour recall surveys. Associations with Σandrogen-disruptor levels were estimated for children, adolescents, and adults using multivariable linear regression.

Results—We observed a consistent positive association between dining out and Σandrogen-disruptor levels across the study population (*p*-trend < 0.0001). Among adolescents, high

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Conflicts of interest
None

consumers of foods outside the home had 55% (95% CI: 35%, 78%) higher Σandrogen-disruptor levels compared to those who only consumed food at home. The contribution of specific dining out sources to Σandrogen-disruptor levels varied by age group. For example, cafeteria food was associated with 15% (95% CI: 4.0%, 28%) and 64% (95% CI: 40%, 92%) higher Σandrogen-disruptor levels in children and adults, respectively. Particular foods, especially sandwiches (i.e. cheeseburgers), were associated with increased Σandrogen-disruptor levels only if they were purchased away from home ($p < 0.01$).

Conclusion—Dining out may be an important source of biologically relevant cumulative phthalates exposure among the U.S. population. Future studies should evaluate modifiable production practices that remove phthalates from the food supply in addition to the efficacy of interventions that promote eating fresh foods prepared at home.

Keywords

chemical mixtures; endocrine disruption; fast food; cumulative assessment; food contact materials; consumer product chemicals

1. Introduction

Endocrine disrupting chemicals (EDCs) are associated with hormone-mediated health outcomes, such as reproductive issues, metabolic disease, and neurodevelopmental problems.[1,2] In the United States alone, researchers recently estimated the disease cost of EDCs at $340 billion, for which phthalates were the second-leading driver.[3] Anti-androgenic phthalates may have additive adverse effects on fetal sex differentiation that are associated with testosterone inhibition during critical stages of pregnancy (i.e. reproductive organ development).[4] Cumulative phthalate assessments are therefore more biologically relevant for human reproductive health than chemical-by-chemical approaches.[5,6] Although pregnancy is one critical stage of toxicity, phthalates may also contribute to health impacts across the life course, including reduced semen quality, obesity, diabetes, and cancer.[7–10] Low testosterone may influence adverse adult metabolic outcomes, suggesting a possible mode of action for androgen-disrupting phthalates along this disease pathway.[11] Thus, efforts to identify opportunities for phthalates exposure reduction may have significant implications for preventing metabolic and other hormone-mediated illnesses and decreasing the economic burden of EDCs.

Phthalates have many uses in commerce, including food contact materials (e.g. plastic and recycled cardboard food packaging), personal care products, medical tubing, and/or any material containing polyvinyl chloride (PVC).[12–14] Consequently, human exposure is ubiquitous, with multiple phthalates simultaneously detected in the vast majority of the U.S. population.[12,15] Diet is the dominant exposure pathway for most anti-androgenic phthalates, especially for high molecular weight compounds such as di(2-ethylhexyl) phthalate (DEHP) and di-isononyl phthalate (DiNP).[16–19] These phthalates are predominantly found in fatty foods such as meat and dairy,[14,20] although they have also been linked to grains and spices, [18,21] and likely enter the food supply through packaging, processing, and handling.[22–27] Thus, it is plausible that a significant source of phthalates exposure may come from foods prepared outside the home which undergo substantial industrialized production practices,

such as in the fast food and restaurant industries, school cafeterias, street food vendors, and sports and entertainment facilities.

Consumption of food prepared away from home, rather than food purchased in a store and prepared at home, has grown steadily over the last few decades in the United States. Between 1970 and 2014, household food expenditures devoted to dining out increased from 25.9% to 43. 7%, respectively, and over half of total U.S. food dollars are currently spent on foods purchased outside the home.[28,29] Like adults, children 2-17 years old are dining out more, with 35% of their total calories sourced from food prepared away from home in 2003–6 compared to 20% in 1977–8.[30] Among children, younger kids are more likely to eat meals offered by their school cafeterias, while adolescents are more likely to eat from competing vendors, such as fast food chains.[30] Although research has primarily focused on nutrition and diet quality with regard to dining out,[29–32] chemical exposures introduced through increased food packaging, handling, and processing are also important public health considerations.

Several studies have investigated the connection between food prepared outside the home and phthalate exposures. Zota et al. (2016) recently reported a consistent, positive association between fast food consumption and measured urinary metabolites of DEHP and DiNP in the U.S. general population,[33] and fast food intake has been associated with urinary DiNP and butyl benzyl phthalate (BBzP) metabolites in a cohort of young children.[34] In several smaller studies outside the United States, phthalates have been detected in takeout/delivery food containers as well as pre-cooked and immediately packaged cafeteria-style meals.[23,27,35,36] However, a broader analysis across age groups in the U.S. population which evaluates multiple sources of food prepared away from and at home is warranted to assess the extent to which these and other dietary intake sources are associated with biologically relevant phthalate exposures.

Accordingly, this study compares cumulative phthalates exposure between consumers of "food away from home" (such as fast food and food from full-service restaurants and/or cafeterias) with consumers of "food at home" (such as food purchased from a grocery store) among children, adolescents, and adults in the United States.

2. Materials and Methods

2.1 Study population

The U.S. Centers for Disease Control and Prevention (CDC) administers the National Health and Nutrition Examination Survey (NHANES) as a nationally representative interview and physical examination of the civilian, non-institutionalized general population. We combined five cycles of laboratory, questionnaire, and dietary NHANES data between 2005 and 2014 for this study (http://www.cdc.gov/nchs/nhanes.htm). Our original study population included all participants   6 years old for which phthalate data, urinary creatinine measurements, kilocalorie and dietary intake source information were available (N = 12,134). Participants with missing information on household income and educational attainment (n = 920) were excluded from the study population because we wanted to evaluate these demographic characteristics in relation to phthalates exposure. We also excluded participants who did not

self-identify as Hispanic, Mexican American, non-Hispanic white, or non-Hispanic black (*n* = 961) due to racial/ethnic ambiguity of other or multi-racial classifications. The final sample size included 10,253 study participants.

2.2 Cumulative phthalates exposure assessment

The NHANES survey provides phthalate metabolite measurements for one-third of study participants in each survey cycle. Spot urine samples are collected as part of the medical examination and analyzed at the CDC in Atlanta, GA., with analytical methods detailed elsewhere.[37,38] In summary, phthalate metabolites are quantified using high performance liquid chromatography coupled with tandem mass spectrometry. Laboratory files for 2005-12 survey cycles were downloaded from the NHANES website in March 2015 and included impurity corrections for certain previously used analytical standards.[39] NHANES 2013-14 data were downloaded in January 2017. The maximum limit of detection (LOD_{max}) was used to standardize variable detection limits across survey cycles and concentrations below LOD_{max} were substituted with LOD_{max} divided by 2 (Supplementary Table S1).[12] We used data for nine urinary metabolites to estimate exposure for six parent phthalates: di-*n*-butyl phthalate (DnBP), di-isobutyl phthalate (DiBP), BBzP, DEHP, DiNP, and diethyl phthalate (DEP). Because DiNP's primary metabolite, mono-isononyl phthalate (MiNP), was below the detection limit for most NHANES samples, the secondary metabolite, mono(carboxy-isooctyl) phthalate (MCOP), was the only metabolite used to assess DiNP exposure.

We constructed a biologically relevant metric of cumulative phthalates exposure by summing phthalates based on their relative anti-androgenic potencies, according to our previously published method.[40] In summary, phthalates were converted into anti-androgen equivalent terms by applying unitless relative potency factors (RPF) to daily intake estimates of individual parent compounds prior to their summation. A potency-weighted sum of estimated daily intake (Σandrogen-disruptor, μg/kg/day) for di-*n*-butyl phthalate (DnBP), di-isobutyl phthalate (DiBP), BBzP, DEHP, DiNP, and diethyl phthalate (DEP) was then calculated as follows (where *i* = individual phthalate): *Σandrogen-disruptor (μg/kg/day) = Σ(Daily Intake$_i$ × RPF$_i$) =* (DnBP × 1.0) + (DiBP × 0.24) + (BBzP × 0.26) + (DEHP × 0.61) + (DiNP × 0.26) + (DEP × 0.024) (**Eq. 1**).[40] RPFs were constructed previously by scaling each phthalate to a reference anti-androgen (DnBP).[40] The RPF calculation involved comparing benchmark doses (BMDs) associated with fetal testosterone inhibition that were published in a 2008 National Academy of Sciences (NAS) report (although DiNP's RPF relied on more recent toxicology data and DEP was assumed to be less potent by one order of magnitude).[5,40] While the NAS BMDs were based on a singular endpoint, their underlying dose response data have since been shown to predict phthalate mixture effects on a broader range of postnatal male endpoints,[4,6,41] suggesting these RPFs may be appropriate for other androgen-mediated outcomes. However, their applicability to neurodevelopment and metabolic disease have yet to be determined.

We back-calculated oral daily intake of parent phthalates in μg/kg/day using biomarkers (metabolites) in urine because our potency comparisons were based on atomic mass doses of parent phthalate compounds administered to rats. Consistent with prior studies and

biomonitoring guidance from the NAS, we used the following pharmacokinetic equation to estimate daily intake, or "exposure dose", from urinary metabolite concentrations: *Daily Intake$_i$ = [(ME$_i$ × CE)/(F$_{UE,i}$ × 1000)] × [(MW$_p$)/(MW$_m$)]; i = individual phthalate* (**Eq. 2**). [42–44] The equation converts creatinine-adjusted urinary metabolite concentrations (ME) (μg/g) into molar equivalents from which molar daily intakes are estimated first by multiplying with body weight-adjusted creatinine excretion rate (CE) (mg/kg/day) and subsequently dividing by the metabolite's molecular weight (MW$_m$) (g/mol). The fractional molar ratio of excreted metabolite to ingested parent phthalate (F_{UE}), determined in human kinetic and metabolism studies by measuring urinary metabolite concentrations in relation to known intake of labeled parent compound over a 24-hour period,[16,45,46] is then used to calculate molar daily intake of the parent phthalate. The parent phthalate's molecular weight (MW$_p$) (g/mol) facilitates final conversion to μg/kg/day, units that are comparable to toxicology doses and human population reference values. Phthalate-specific RPF, BMD, F_{UE}, and MW values are listed in Supplementary Table S1.

Urinary creatinine is often used as a surrogate for urine dilution, although its use is controversial because creatinine excretion rates vary across racial/ethnic groups, sex, age, and body mass index (BMI).[47] We used average creatinine excretion rates of 23 mg/kg/day and 18 mg/kg/day for men and women, respectively. For boys and girls < 20 years old, we calculated average creatinine excretion rates of 21 mg/kg/day and 19 mg/kg/day, respectively, from the literature.[48,49] Alternatively, urine flow rate can be used as a more direct volume-based measure of urine dilution if the data are available, although urine flow rate has also been shown to vary across demographic groups.[50] To use the volume-based approach, one would simply replace *(ME$_i$ × CE)* with *(UME$_i$ × UE)* in the numerator of the daily intake equation, where UME is the unadjusted measured urinary metabolite concentration (ug/L) and UE is the daily urine flow rate normalized by body weight (mL/kg/day). Sample calculations for both approaches are provided in supplementary materials of our original method publication.[40]

2.3 Dietary intake exposure assessment

As part of NHANES, the CDC also collects 24-hour dietary recall data from study participants that includes extensive information about what foods were eaten, time of eating occasion, and food source (where obtained or purchased).[51] Energy and nutrient intake are later quantified for each food recorded during participant surveys,[51–53] and cup-equivalent data are also made available by the U.S. Department of Agriculture (USDA).[54] We used dietary data from the day prior to urine sample collection because phthalates have short metabolic half-lives (12-24 hours), and it is reasonable to assume that urinary metabolite concentrations measured within ~ 24 hours of parent compound exposure would appropriately reflect dietary intake the previous day.[46,55] Participants 12 years and older completed the survey independently unless they chose otherwise, while proxy-assisted interviews were automatically provided for children 6-11 years old.

Based on the methods in Zota et al. (2016), we calculated total energy intake (TEI) in kilocalories (kcals) the prior day for each participant by summing NHANES-provided kcals for all foods recorded during each participant's dietary interview.[33] We determined total fat

in grams by summing NHANES-provided grams of fat for all recorded food items, since dining out is positively associated with total caloric and fat intake among the U.S. general population,[30,31] and high-fat foods have been linked to phthalates exposure.[14,20] Total fat in kcals was calculated using nine fat grams per calorie as the conversion factor, and the percent of TEI from fat was then determined by dividing fat kcals by TEI.[56,57] Calculating "nutrient density" (i.e. % kcals from fat) is an energy adjustment method commonly used by nutritional epidemiologists to reduce the influence of exposure misclassification from dietary recall surveys and isolate diet composition from body size, metabolism, and physical activity.[56,58,59]

We categorized all foods reported by each participant as either food away from home (prepared at a restaurant, cafeteria, etc.) or food at home (purchased or obtained at a grocery store and potentially prepared at home), ascertained from the NHANES survey question regarding where the food item (or the majority of its ingredients) was obtained or purchased. Seventeen mutually exclusive responses were provided by NHANES. We defined food away from home as follows: 1) Fast food, defined by NHANES as food purchased/obtained from restaurants without table service, pizza restaurants regardless of waiter/waitress service, and all carryout and delivery food; 2) Full-service restaurants, or restaurants with table service, including bars, taverns, and lounges; 3) Cafeterias, including K-12 school cafeterias and other types; and 4) All other marginal away-from-home sources that each contributed < 2% to TEI (and together contributed < 5% to TEI), which included child/family care centers, soup kitchen/shelter/food pantry, Meals on Wheels, community food programs, vending machines, sport/recreation/entertainment facilities, street vendor/vending trucks, residential dining facilities, and fundraiser sales. We defined food at home as items purchased at a store, anything home grown or caught, and "from someone else/gift", which the USDA has characterized as dinner cooked by a friend.[30] We summed the total NHANES-provided kcals consumed for each participant from sources of either food away from home or food at home. The contribution of each source to total dietary intake, or the "energy density" of food away from home and food at home were determined by dividing total kcals (and total fat kcals) from each source by TEI.

2.4 Statistical analysis

All statistical analyses were performed in SAS version 9.4 (SAS Institute Inc., Cary, NC) with new sample weights calculated according to analytical guidelines for combining multiple cycles of data.[37] We used survey-weighted SAS procedures (i.e. PROC SURVEYMEANS, PROC SURVEYFREQ, and PROC SURVEYREG) to adjust models for population weights as well as the stratified multi-stage sample design. Statistical significance was defined at $p < 0.05$ for two-sided tests. Degrees of freedom for variance estimation were determined by subtracting the number of strata by the number of unique clusters. Phthalate exposure estimates were log-transformed prior to statistical testing to normalize their skewed distributions.

We used linear regression to examine cumulative phthalates daily intake (Σandrogen-disruptor), our primary outcome of interest, across the following study population characteristics: Age (children 6-11, adolescents 12-19, adults 20-59, and older adults 60

years old); sex (male or female); race/ethnicity [non-Hispanic white, non-Hispanic black, or Hispanic]; body mass index (BMI) [underweight (< 18.5 kg/m^2), normal weight (18.5–25 kg/m^2), overweight (25–30 kg/m^2), or obese (30 kg/m^2)]; poverty-to-income ratio, or PIR [ratio of household income to poverty threshold adjusted to family size and inflation: < 1 (beneath poverty threshold), 1–2.99, or 3]; educational attainment (less than high school, high school graduate, or any post high school education) in adults only; NHANES survey cycle (2005–6, 2007–8, 2009–10, 2011–12, or 2013–14); time of sampling session (morning, afternoon, or evening); and dietary intake of food prepared away from home [any (participants who reported dining out the prior day) or none (participants who reported consuming only food at home the prior day)]. Univariate statistics for Σandrogen-disruptor levels were calculated from these models. We also added NHANES survey cycle and a statistical interaction term to the dining out model to observe whether the association with Σandrogen-disruptor levels varied over time.

We then compared dietary intake of food away from home (our primary exposure of interest) across several population characteristics. Specifically, we used the Rao Scott chi-square test of independence, first across age (children, adolescents, adults, and older adults), then by sex, and finally, across NHANES survey cycle. The remainder of statistical analyses focus on age-specific subgroups, since differences in Σandrogen-disruptor levels and dietary behavior across age were more pronounced than between men and women or across time.

For our primary multivariable analysis, we followed the approach of Zota et al. (2016)[33] and modeled dining out as both the dietary intake of food away from home (% TEI), or the percent of TEI consumed outside the home, and away from home-derived fat intake (% TEI), or the percent of TEI consumed as fat kcals from dining out sources. Because many participants did not consume any calories outside the home (resulting in highly left-truncated distributions for these variables), we categorized these dietary intake source variables into three groups: none (participants who consumed 100% of their calories, or fat calories, from food at home the prior day), low (participants who consumed < weighted median of those who had some dietary intake of food away from home > 0), and high (participants who consumed the weighted median of those who had a dietary intake of food away from home > 0). Covariates included all population characteristics evaluated in unadjusted regression analyses (with age modeled continuously) except for BMI, which could potentially be on the causal pathway between our exposure and outcome of interest. We did not adjust for creatinine as an independent covariate since it was included in the calculation of phthalates daily intake (**Eq. 2**).

We additionally assessed the influence of total dietary intake on phthalates exposure by replacing the away-from-home dietary intake variables in our main analysis with TEI and total fat intake (% TEI), which were each categorized into low, middle, and high tertiles from age-specific weighted distributions. These "baseline" dietary intake variables were not added as independent covariates in core regression models because our primary dietary exposures of interest were normalized by TEI, which reduces bias from dietary recall surveys.[56,58,59]

Third, we constructed separate multivariable models for specific sources of food away from home, including fast food, full-service restaurants, and cafeterias (for children, adolescents, and adults). Specific away-from-home food sources were modeled as categorical independent variables because the high proportion of away-from-home "non-consumers" results in truncated distributions that pose statistical challenges in survey-weighted data analysis. Instead, we compared each "consumer" group to the same referent population in separate models to reduce the impact of potential confounding and correlation among dietary variables. Specifically, we compared consumers of "any" fast food (followed by any restaurant food and any cafeteria food) to a standard "none" referent category consisting of participants who did not consume any food away from home the prior day (e.g. all of their calories came from foods purchased at a store), with 31% of children and 43% of adolescents and adults meeting this criteria.

We also examined the influence of food type on phthalates exposure by performing multivariable regression to estimate associations between particular foods (fruits/vegetables, sandwiches, fried potatoes, and pizza, each modeled separately as binary or categorical independent variables) and Σandrogen-disruptor levels. First, we summed USDA-converted cup-equivalents for fruit (including 100% fruit juice) and vegetables (including legumes but excluding fried potatoes) from each participant's 24-hour food record.[54] We grouped participants into yes/no categories based on whether or not their daily dietary recommendations were met for either fruit or vegetable intake.[60] Next we constructed a common referent group restricted to non-consumers of sandwiches, fried potatoes, and pizza, and we compared consumers of each food to the common referent group in separate at-home and away-from home models (since a small number of participants consumed foods from both sources). For example, away-from-home sandwich consumers (who may have also consumed at-home sandwiches but not fried potatoes or pizza) were compared to participants who did not eat any sandwiches, fried potatoes, or pizza (whether purchased at or away from home) the prior day. We selected energy-dense foods as potential sources of phthalates exposure regardless of source, restricting to sandwiches containing animal protein (meat/poultry/fish, dairy, and/or egg). Similar to Sebastian et al. (2015),[66] we counted sandwiches recorded as single items (e.g. one food record described as "cheeseburger") and those recorded as combinations of individual ingredients (e.g. multiple food records for cheese, beef patty, bun, and tomato consumed in the same meal). We added total fat and energy intake to these models to evaluate them as potential confounders or mediators.

From log-level regression models, the percent difference in cumulative phthalates exposure 95% confidence interval (95% CI) were estimated as $(e^{(\beta)} - 1) * 100$ and $(e^{(\beta \pm \text{critical value} \times \text{SE})} - 1) * 100$, respectively, where β is the beta coefficient and SE is the standard error. We tested for linear trends in our association of interest by modeling categorical dietary intake variables as ordinal terms in multivariable models. Finally, adjusted associations with dining out were evaluated for each phthalate separately. We also calculated the percent geometric mean (GM) contribution to Σandrogen-disruptor from individual phthalate daily intake estimates (µg/kg/day).

2.5 Sensitivity analysis

We performed a sensitivity analysis to evaluate alternate approaches to urine dilution correction and daily intake estimation, since these factors may introduce uncertainty and variability into regression models.[47,50,62] We specifically assessed whether alternate measures of urine dilution (i.e. urine flow rate rather than creatinine) and/or the application of potency-weights directly to metabolites impacted our results. Adjusted associations were compared between Σandrogen-disruptor (μg/kg/day) and four other potency-weighted cumulative metrics (with more details provided in the method publication)[40]: 1) Phthalate daily intake metric calculated with individual urine flow rate rather than average creatinine excretion rate (Σurine-flow, μg/kg/day); 2) Metabolite-based analyte excretion rate (mass/time) calculated using urine flow rate (Σexrate-rpf, μg/day); 3) Metabolite concentration-based metric without urine dilution correction (Σmetab-rpf, μg/L); and 4) Metabolite concentration-based metric correcting for creatinine as an independent variable in regression models (Σmetab-rpf + creat, μg/L).[40] We also re-calculated these cumulative metrics using molar mass to compare adjusted associations with atomic mass-based metrics. These models were restricted to 2009-14 data because NHANES did not report urine flow rate data prior to 2009. We selected the largest age-specific subgroup evaluated in core regression models for this analysis (adults 20-59 years old, $N = 2695$).

In additional sensitivity analyses, we performed multivariable regression to evaluate the continuous association between total energy intake (TEI) and cumulative phthalates exposure, stratified between consumers of food away from home and non-consumers (participants who consumed all of their calories from food at home). Finally, we added BMI to core multivariable regression models to evaluate its potential influence on the association between dietary intake of food away from home (% TEI) and cumulative phthalates daily intake (Σandrogen-disruptor).

3. Results

The majority of study participants were adults with at least some post-high school education, non-Hispanic white, above normal weight, and in the middle income category (Table 1). More participants reported dining out than eating only at home the prior day (61 vs 39%). Unadjusted cumulative phthalates daily intake (Σandrogen-disruptor) was 35% (95% CI: 29%, 41%) higher among consumers of food away from home compared to those who ate only at home ($p < 0.0001$). Higher Σandrogen-disruptor levels were observed in earlier NHANES cycles, with a 50% total decrease in exposure between 2005 and 2014 ($p < 0.0001$). Cumulative phthalates were also elevated in males; Hispanic and white compared to black participants; underweight compared to normal weight participants; those in the highest (3) compared the middle (1 – 3) PIR; adults with the least (< high school) compared to the most (> high school) education; and in evening rather than morning sample collection times. Unadjusted Σandrogen-disruptor levels were fairly similar for adolescents, adults, and older adults (GM range: 3.9 to 4.3 μg/kg/day), while the GM for children (GM = 6.6 μg/kg/day; 95% CI: 6.2, 6.9) was 50–70% higher ($p < 0.0001$) (Table 1 and Figure 1).

Dietary consumption patterns varied significantly by age and sex ($p < 0.0001$), with 52% of older adults (compared to ~ 30-35% of younger participants) eating only food at home the

prior day (Table 2). A higher percentage of children ate cafeteria food compared to adolescents, but a higher proportion of adolescents than children consumed calories from fast food and full-service restaurants. Among all age groups, adults (20-39 years) obtained the highest percentage of their total calories from fast food and full-service restaurants. Men were more likely to consume food outside the home than women, but the differences were less pronounced than those observed across age (Table 2). Dining out differences remained fairly consistent over time, ranging from 58% in 2009–10 to just under 65% in other years (data not shown). Differences in Σandrogen-disruptor levels between consumers of food away from home ranged from 29% (95% CI: 16%, 44%) in 2005–6 to 44% (95% CI: 32%, 58%) in 2011–12; however, we did not observe evidence of effect modification by survey cycle year ($p_{interaction} = 0.48$) for the association between eating out and Σandrogen-disruptor levels.

In our main analysis, we found a positive association between dining out and cumulative phthalates daily intake (Σandrogen-disruptor), with evidence of a linear trend across exposure categories, among all age-specific subgroups (p for trend < 0.0001) (Figure 2 and Table 3). While associations were significant in all age groups, the magnitude of association was largest for adolescents, with high consumers of food away from home having 55% (95% CI: 35%, 78%) higher Σandrogen-disruptor levels than adolescents who ate only food at home the prior day. The weakest associations were observed among children, with high consumers of food away from home having 30% (95% CI: 16%, 45%) higher Σandrogen-disruptor levels than children who consumed all their calories from food at home. Similar positive associations were observed across age-specific subgroups between food away from home-derived fat intake and Σandrogen-disruptor levels, including evidence of a linear trend between exposure categories (p for trend < 0.0001). The measures of total dietary intake, TEI and total fat intake (% TEI), were positively associated with Σandrogen-disruptor levels among adults, with 14% (95% CI: 6.6%, 22%) higher levels in high compared to low fat consumers (p for trend = 0.0002) and 9.5% (95% CI: 1.0%, 19%) increased Σandrogen-disruptor levels in high relative to low TEI consumers (p for trend = 0.03); however, these baseline associations were substantially smaller than those observed for dining out (Table 3).

Each specific source of food away from home was significantly associated with cumulative phthalates daily intake (Σandrogen-disruptor) across our study population (Table 4). However, contributions from specific dining out sources to Σandrogen-disruptor levels varied by age group. For example, when compared to a common referent group (restricted to children who consumed only food at home the prior day), children who ate cafeteria food had 15% (95% CI: 4.0%, 28%) higher Σandrogen-disruptor levels while children who ate restaurant food had 46% (95% CI: 22%, 73%) higher levels. We observed stronger associations between cafeteria food intake and Σandrogen-disruptor levels among adolescents and adults (compared to their respective referent groups), with adult cafeteria consumers having 64% (95% CI: 40%, 92%) higher Σandrogen-disruptor levels in comparison to adult non-consumers. (Table 4).

Across age-specific subgroups, consuming sandwiches, fried potatoes, and pizza at home was not associated with cumulative phthalates daily intake (Σandrogen-disruptor), with the exception of fried potatoes, which were associated with reduced Σandrogen-disruptor levels

among adolescents only (Table 5). On the other hand, consuming sandwiches outside the home was consistently associated with increased Σandrogen-disruptor levels across the study population. For example, away-from-home sandwich consumption was associated with > 30% higher Σandrogen-disruptor levels in all age groups ($p < 0.005$). Results were less consistent for other foods purchased away from home, although pizza and fried potatoes were positively associated with Σandrogen-disruptor levels in children and adults, respectively ($p < 0.01$). Meeting daily guidelines for fruit or vegetable intake was associated with reduced Σandrogen-disruptor levels in adolescents ($p = 0.03$), but the difference was no longer significant when models adjusted for TEI, indicating that total caloric intake may attenuate the association between fruit or vegetable intake and phthalates exposure (Supplementary Table S2).

When evaluated separately, daily intake of DEHP and DiNP were both positively associated with dining and we observed a linear trend between exposure categories ($p < 0.0001$), with high consumers of food away from home having 74% increased DiNP exposure compared to participants who consumed all of their calories from food at home, such as food purchased from the grocery store (Table 6). These high molecular weight phthalates were the top contributors to Σandrogen-disruptor (45% and 30%, respectively), while DnBP ranked third (16%). However, DnBP was negatively associated with dining out ($p = 0.056$), and all other phthalates were not individually associated with dietary intake of food away from home. Thus, dining out associations were largely driven by DEHP and DiNP (Table 6).

Consumption of food away from home was positively associated with cumulative phthalates exposure across all supplementary metrics that evaluated alternate approaches to urine dilution correction and daily intake estimation (Supplementary Table S3). However, the magnitude of associations varied across models. Adjusted associations for daily intake metrics, including the main outcome variable (Σandrogen-disruptor) and the metric that uses urine flow rate rather than creatinine to estimate phthalate daily intakes (Σurine-flow), were more similar to each other and larger than those observed for metabolite-based metrics. Of the three metabolite-based metrics, the metric that applied RPF weights directly to non-creatinine-corrected urinary metabolite concentrations (Σmetab-rpf) generally produced the strongest associations, followed by the metric combining RPF-weighted metabolite excretion rates (Σexrate-rpf). The metric that applied RPF weights directly to urinary metabolite concentrations and adjusted for creatinine as an independent covariate in the multivariable model (Σmetab-rpf + creat) generally produced the weakest associations. Associations were slightly attenuated when RPFs were applied directly to molar mass-based metrics (i.e. molar urinary concentrations, molar excretion rates, and molar intake rates) (Supplementary Table S3).

Results from the sensitivity analysis evaluating the continuous association between TEI and cumulative phthalates daily intake (Σandrogen-disruptor), stratified by consumption of food at home and food away from home, were reasonably consistent with our main analysis among children, adolescents, and adults 20-59 years old (Supplementary Table S4). Results were less consistent for older adults. Among older adults, an increase of 100 kcals was associated with 1.6% (95% CI: −2.6%, −0.58%) lower Σandrogen-disruptor levels among

consumers ($p = 0.002$) and 0.83% (95% CI: 0.13%, 1.5%) higher Σandrogen-disruptor levels among non-consumers ($p = 0.02$) (Supplementary Table S4).

Finally, including BMI in core regression models did not substantially influence associations between dietary intake of food away from home and Σandrogen-disruptor levels (data not shown).

4. Discussion

In this cross-sectional study of NHANES participants sampled between 2005 and 2014, dining out was positively associated with potency-adjusted exposure to multiple phthalates across age groups in the U.S. general population. Among adolescents, consuming food away from home the prior day was associated with as much as 55% higher cumulative phthalates exposure compared to eating food at home only (such as food purchased from the grocery store).

To our knowledge this is the first study to compare biologically relevant cumulative phthalates exposure between individuals eating foods from multiple sources away from home to those eating predominantly store-bought foods. While prior work has shown that phthalate exposures are associated with fast food intake among the U.S. general population, [33] this study demonstrates that other sources of food away from home, such as full-service restaurants and cafeterias, are also important sources of phthalates exposure. It also shows, for the first time, that the contribution of specific food sources varies by age group. For example, cafeteria food intake was associated with a smaller percent difference in phthalates exposure among children than teenagers and adults, even though the proportion of children who consumed cafeteria food was seven times higher than adults and double that of adolescents. This suggests that food choices in the cafeteria setting may vary with age. Indeed, adolescents have greater autonomy than younger children in their cafeteria food choices, and high-school meals are generally richer in fat and lower in nutritional quality than those prepared for younger kids. [30]

Children in our study had substantially higher cumulative phthalates exposure than other age groups (70% higher than older adults), despite the fact that adolescents and adults consumed more overall calories from restaurants and/or fast food establishments the prior day. This finding is consistent with previous research on phthalates in children, which has suggested that several age-dependent biological and behavioral differences may explain the disparity. [63,64] For example, children consume a higher proportion of food to body size, and phthalate metabolism varies with age. [63–65] Also, younger kids may ingest more phthalates from consumer and personal care products that settle in house dust by playing on the floor and engaging in hand-to-mouth activity. [66–68] Children also eat more snack foods than older groups [69] and may be consuming additional phthalates from processed or packaged foods eaten at home. For example, a recent analysis by the Coalition for Safer Food Processing and Packaging detected higher phthalate levels in processed macaroni and cheese powder than in other U.S. cheese products. [70]

Older adults consumed fewer calories than younger groups in this study (with the highest TEI reported at ~ 6300 kcals compared to > 9000 kcals in adolescents and younger adults), yet unlike other groups their TEI was negatively associated with phthalates exposure among dining out consumers in the stratified sensitivity analysis. Possible reasons for this result could be that differential food preferences and/or use of meal services influence the types of food consumed by older adults (e.g. ordering a salad instead of a sandwich at a restaurant, eating nutrition-oriented meals provided by Meals on Wheels, etc.),[71,72] and older adults who dine out appear to consume more calories overall compared to those who do not dine out (~130 more kcals on average in this study). Eating more calories away from home would reduce the estimate of association among dining out consumers if TEI is negatively associated with phthalates, as we observed in our main analysis. Moreover, a linear model with TEI and phthalates exposure may not be appropriate for this age group; we did not find a linear trend across TEI groups in our main analysis (with TEI modeled categorically), and we observed minimal linearity when we modeled TEI continuously in the sensitivity analysis. Finally, adults are more likely to use medications or require outpatient services and hospitalizations as they age,[73] which may be important non-dietary sources of phthalate exposures that we were unable to account for in this study.[74,75] Future investigation of phthalate exposures among older adults should assess the role of unique dietary patterns in conjunction with non-dietary exposure sources in this subgroup.

Interestingly, we found that particular foods, especially sandwiches (i.e. cheeseburgers), were associated with increased cumulative phthalates exposure only if consumed from fast food/restaurant, cafeteria, or other dining out establishments. While previous studies have identified important at-home sources of dietary phthalates exposure, including store-bought meats, dairy products, olive oil, cooking spices, and bread,[21,25,76–78] our findings suggest that consuming foods from the grocery store may reduce exposures relative to dining out. However, few studies have evaluated phthalates in restaurant and cafeteria food. Research on pre-cooked and immediately packaged school and hospital meals in Europe and Japan[23,26,79] may be relevant for U.S. schools, which are increasingly outsourcing their food preparations off-site.[80,81] The influence of cooking methods (i.e. phthalate levels after boiling compared to frying foods)[82] may also be pertinent for restaurants or cafeterias that cook foods on-site. However, many data gaps regarding specific contamination pathways in U.S. food industries have yet to be addressed.

Food contamination sources are difficult to distinguish between industries because phthalates may enter the food supply from many different food contact materials both upstream (e.g. processing equipment such as conveyer belts and industrial tubing) and downstream (e.g. food preparation products such as plastic wrap and food handling gloves). [14,22,26,83] Focusing on key differences between industries may help guide research directions going forward. For example, compared to large-scale supermarkets, which may have company-owned processing plants and distribution centers, restaurants and cafeterias typically rely on local distributors that potentially receive products from a variety of sources. [81] Less in-house control may be one factor that contributes to increased phthalates contamination along dining out supply channels, though more research is required to make this determination. High fat meals and large portion sizes typically offered by the U.S. food

service industry may further compound dietary exposures along this pathway,[29,30] which should also be evaluated in future work.

Despite our findings, highly processed store-bought foods may also contribute to phthalates exposure. For example, higher phthalate levels in frozen compared to home-made French fries were recently attributed to increased transport activity and contact with factory equipment.[82] Prepared foods are also rising in popularity among U.S. supermarkets,[81,84,85] and NHANES recently acknowledged that foods purchased from the store are now considered a suboptimal proxy for home preparation due to the proliferation of prepared or ready-to-eat foods among U.S. grocery stores (https://wwwn.cdc.gov/nchs/nhanes/2011-2012/DR1IFF_G.htm). However, we evaluated NHANES survey data from earlier years in which store-bought foods were classified as "prepared away from home" rather than "away from home" and did not observe changes in the association between dining out and cumulative phthalates exposure across time. Moreover, our findings suggest there may be true differences in phthalate exposures between food purchased away from home and food purchased from the store (regardless of where prepared). Future efforts to characterize food production practices that increase dietary phthalates exposure should target prepared, processed, and/or packaged foods across multiple food industries, with particular emphasis placed on fast food/restaurants and cafeterias.

Together, DEHP and DiNP comprised 75% of our cumulative phthalates exposure metric. Although DEHP contributed more to the metric than DiNP (45% compared to 30%, respectively), DiNP was more strongly associated with dining out (74% compared to 30%, respectively). This is consistent with previous research suggesting that fast food consumption may be a unique source of DiNP exposure.[34] Although fewer studies have assessed DiNP sources, especially in the United States, evidence suggests that DiNP is replacing DEHP in the global plasticizers market and in food contact materials specifically.[18,33,86] Additionally, U.S. biomonitoring trends have reported DiNP increases (coupled with steady DEHP declines) in recent years.[12,40] In this study, we observed decreased cumulative phthalates exposure over time, likely due to DiNP's lower relative potency (though it is a recognized anti-androgen of concern),[16,86] while the association between dining out and cumulative phthalates exposure remained relatively constant. Thus, if dining out trends remain constant or increase over time, food service products may continue to be important sources of anti-androgenic exposure going forward. Moreover, while DnBP, DiBP, BBzP, and DEP were not individually associated with dining out in our study, diet is suspected to be the dominant exposure pathway for most phthalates.[16,19] Thus, future studies should assess food contamination pathways more broadly for all phthalates, with a focus on emerging anti-androgens such as DiNP. Forthcoming work should also examine sources of phthalates in combination, which may inform strategies to reduce biologically relevant cumulative exposures.[5,6]

Although our cumulative metric is biologically meaningful, several limitations should be addressed in future research. First, the method assumes that relative potencies are accurately predicted from toxicology studies and are appropriate for multiple endpoints. While fetal testosterone inhibition predicts additive effects on other male developmental endpoints in laboratory studies, reproductive organ malformations,[4,6] more work is needed to examine

the method's applicability to other hormone-mediated outcomes. For example, phthalates may influence risk of obesity and diabetes by disrupting androgen (or even thyroid hormone) activity in adult men and women,[87–89] and their affinity for binding the peroxisome proliferator-activated receptor (PPAR-γ) has gained more recent attention, particularly since PPAR-γ effects may contribute to fetal programming of metabolic disease.[90–93] However, current data gaps preclude our ability to compare anti-androgenic and PPAR-γ potencies, since metabolic toxicology studies vary in terms of whether experiments were performed with phthalate metabolites or parent compounds, mouse or human cells, and so forth.[94–98] Mixture studies on PPAR-γ could resolve these issues and inform whether the metric is appropriate for metabolic disease. Relative potency data for phthalates and thyroid function during pregnancy may also help discern the method's applicability to neurological outcomes in children, since thyroid hormones are critical for fetal brain development.[99] Moreover, while our results were robust across alternate cumulative exposure metrics, future efforts to identify optimal approaches for urine dilution correction and daily intake estimation that reduce potential bias in regression models[47,50,62] would provide useful guidance for exposure scientists, risk assessors, and epidemiologists who seek to evaluate phthalate exposures in combination.

Other study limitations include the cross-sectional design of NHANES, which makes causality difficult to determine and can lead to misclassification of phthalate exposures (i.e. through use of spot samples that may not capture within-person variation over time).[100,101] However, we assessed dietary intake specifically for the day prior to urine sample collection, providing temporal support for a causal association between dining out and phthalates exposure. The NHANES sampling strategy also minimizes the effect of this misclassification at the population-level by collecting urine from study participants at varying points throughout the day (morning, afternoon, and evening). The 24-hour dietary recall survey is also prone to misclassification from inaccurate self-reporting of foods and/or portion sizes,[56,59,102] but this form of bias would likely under-estimate associations in this study. For example, the weaker associations we observed in children might be partially attributable to proxy-assisted interviews in which kids with high phthalates intake may not be honest about what foods they consumed away from home when interviewed in front of their parents. Converting self-reported foods into kcals may introduce additional uncertainty due to assumptions about accurate recording and interpretation of the amount, size, and mass-to-energy conversion of reported foods.[102] While our nutrient density approach to energy adjustment (converting to kcals and dividing by TEI) has been shown to reduce this bias,[56–59] a longitudinal dietary intervention or elimination study may be more appropriate for future identification of dietary sources. Finally, although we examined foods that are likely to contain phthalates regardless of their source (i.e. sandwiches containing meat and cheese), our results may be influenced by residual confounding, since meal type is often correlated with source. For example, ~60% of cheeseburgers and 50% of poultry sandwiches consumed by the U.S. population are from fast food restaurants whereas ~75% of cold cut sandwiches are from the store.[103] Future research should assess whether different sandwich types, which may be more or less likely to be prepared away from rather than at home (with store-bought ingredients), may confound associations between dining out and cumulative phthalates exposure.

Despite these limitations, our study provides important information about dietary sources of cumulative phthalates exposure across age groups in the U.S. general population. We found that relative to food consumed from a grocery store (and potentially prepared at home), food consumed from full-service restaurants, fast food establishments, and cafeterias (prepared away from home) was associated with increased potency-adjusted exposure to multiple anti-androgenic phthalates. Efforts should be made to identify modifiable production practices that mitigate food product contamination and ultimately remove phthalates from the food supply. The effectiveness of eating and preparing food more frequently at home as a way to reduce biologically relevant phthalate exposures should also be examined in future studies, with continued emphasis placed on less processed and packaged store-bought foods.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

1. Dining out (restaurants and cafeterias) may increase cumulative phthalates exposure

2. Sandwiches purchased away from home are associated with higher phthalate levels

3. Two thirds of the U.S. population eat at least some food outside the home daily

4. In general, children have higher phthalate levels than adolescents or adults
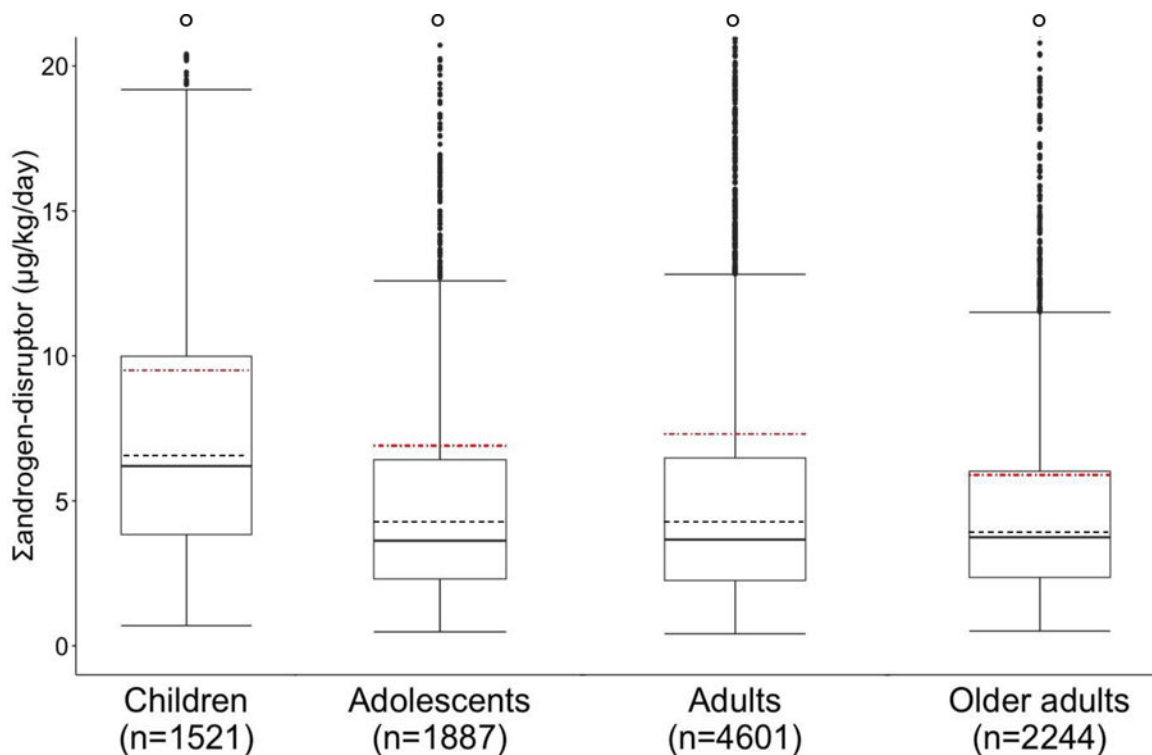
Figure 1.

Univariate distribution of cumulative phthalates daily intake (Σandrogen-disruptor, *μg/kg/ day*) among age-specific subgroups in NHANES 2005-14 (*N* = 10,253). Boxes represent interquartile range (IQR: 25th to 75th percentiles). Dark lines represent medians. Dashed lines represent geometric means. Red dot-dashed lines represent arithmetic means. Whiskers extend to min and max (Max = Most extreme values within 1.5 • IQR of the median). Outliers were defined as values below the min or max and are represented by dark points, and hollow points denote outliers off the y-axis scale. A total of 127 (8.3%), 205 (11%), 469 (10%), and 200 (8.9%) outliers were observed among children, adolescents, adults, and older adults, respectively. *P* < 0.0001 from statistical test of difference between age-specific subgroups.
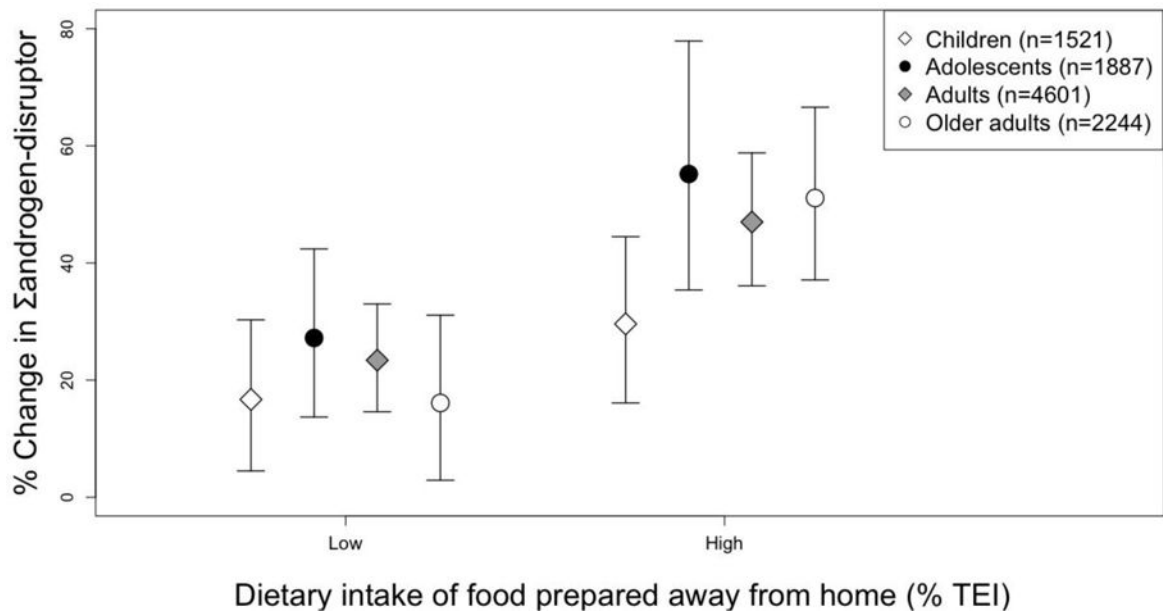
Figure 2.
Adjusted percent difference and 95% CI of cumulative phthalates daily intake (Σandrogen-disruptor, *μg/kg/day*) among age-specific subgroups in NHANES 2005-14 (*N* = 10,253). Covariates: Sex, age, race/ethnicity, poverty-to-income (PIR), education (adults only), NHANES survey cycle, and time of sampling session. *P* for trend was < 0.0001 for all age subgroups. Low and high intake divided at weighted median of participants who consumed any food away from home the prior day. Referent groups include participants who did not consume any food away from home the prior day (i.e. 100% of their calories came from food at home, such as from a grocery store). TEI = Total energy intake (kcals).

Table 1

Unadjusted association between cumulative phthalates daily intake (Σandrogen-disruptor) and study population characteristics[a] in NHANES 2005–14 ($N = 10,253$)

Population Characteristics	Σandrogen-disruptor (μg/kg/day)		
	n (%)	Percent diff (95% CI)	GM (95% CI)
Age (years)			
60	2244 (22)	Referent	3.9 (3.7, 4.2)
20-59	4601 (45)	9.2 (2.4, 17)[*]	4.3 (4.1, 4.5)
12-19	1887 (18)	9.2 (1.3, 18)[*]	4.3 (4.0, 4.6)
6-11	1521 (15)	70 (56, 81)[*]	6.6 (6.2, 6.9)
Sex			
Male	5089 (50)	Referent	4.5 (4.3, 4.6)
Female	5164 (50)	−4.4 (−8.2, −0.4)[*]	4.3 (4.1, 4.5)
Race/ethnicity			
Black	2633 (26)	Referent	3.9 (3.7, 4.1)
White	4592 (45)	15 (7.1, 26)[*]	4.4 (4.2, 4.8)
Mexican American/Hispanic	3028 (30)	16 (7.1, 26)[*]	4.5 (4.2, 4.8)
Body mass index (BMI)[b]			
Normal (18.5-25 kg/m^2)	3211 (32)	Referent	4.3 (4.1, 4.5)
Underweight (< 18.5 kg/m^2)	1230 (12)	39 (29, 49)[*]	6.0 (5.6, 6.3)
Overweight (25-30 kg/m^2)	2751 (27)	−0.8 (−6.2, 4.8)	4.3 (4.0, 4.5)
Obese (30 kg/m^2)	2985 (29)	−2.6 (−8.1, 3.2)	4.3 (4.1, 4.5)
Poverty:income ratio (PIR)			
3 (Highest income)	3389 (33)	Referent	4.5 (4.3, 4.8)
1-3 (Moderate income)	4260 (42)	−7.4 (−13, −1.8)[*]	4.2 (4.0, 4.4)
< Poverty line	2604 (25)	−5.2 (−12, 1.8)	4.3 (4.1, 4.5)
Education[c]			
> High School	3420 (50)	Referent	4.3 (4.1, 4.5)
= High School	1652 (24)	−4.0 (−10, 2.3)	4.1 (3.9, 4.4)
< High School	1773 (26)	−9.3 (−15, −2.8)[*]	3.9 (3.7, 4.1)
Survey cycle			
2013-14	1873 (18)	Referent	3.5 (3.3, 3.7)
2011-12	1735 (17)	16 (3.4, 30)[*]	4.1 (3.7, 4.5)
2009-10	2241 (22)	21 (10, 33)[*]	4.3 (4.0, 4.6)
2007-8	2193 (21)	39 (25, 55)[*]	4.9 (4.5, 5.3)
2005-6	2211 (22)	49 (34, 66)[*]	5.2 (4.8, 5.7)
Sampling session			
Morning	4833 (47)	Referent	4.2 (4.0, 4.4)
Afternoon	3629 (35)	−2.0 (−7.0, 3.2)	4.1 (4.0, 4.4)

Population Characteristics	Σ*androgen-disruptor (μg/kg/day)*		
	n (%)	Percent diff (95% CI)	GM (95% CI)
Evening	1791 (18)	22 (15, 30) [*]	5.2 (4.9, 5.4)
Self-reported dietary intake of food away from home (prior day)			
None	4024 (39)	Referent	3.6 (3.5, 3.8)
Any	6229 (61)	35 (29, 41) [*]	4.9 (4.7, 5.1)

GM = Geometric mean.

[a] From linear regression models where null hypothesis assumes no difference from referent category.

[b] Sample size restricted to 10,177 due to missing BMI data.

[c] Educational attainment restricted to adults only ($N = 6845$).

[*] $p < 0.05$

Table 2

Survey-weighted percent of participants who reported consumption of food away from home the prior day across age and by sex among the U.S. general population[a] in NHANES 2005–14 (N = 10,253)

Dietary Intake[b] *Food away from home*	Age (years)					Sex (Adults ≥ 20 years)		
	6-11 n=1521	12-19 n = 1887	20-59 n = 4601	60 n = 2244		Men n = 3337	Women n = 3508	
	% (SE)	% (SE)	% (SE)	% (SE)	*p*-value	% (SE)	% (SE)	*p*-value
NONE Away *Only food at home*	31 (1.7)	34 (1.3)	35 (1.2)	52 (1.5)	<0.0001	35 (1.1)	43 (1.0)	<0.0001
TOTAL Away *Any food away from home*	69 (1.7)	67 (1.3)	65 (0.9)	48 (1.5)	<0.0001	65 (1.1)	57 (1.0)	<0.0001
Fast food *Any*	36 (1.7)	42 (1.2)	39 (0.9)	21 (1.5)	<0.0001	38 (1.1)	33 (0.8)	<0.0001
Full-service restaurant *Any*	14 (1.2)	18 (1.5)	28 (0.8)	22 (1.1)	<0.0001	27 (0.9)	22 (0.8)	<0.0001
Cafeteria *Any*	28 (1.8)	16 (1.1)	4.0 (0.6)	3.0 (0.5)	<0.0001	8.0 (0.5)	7.0 (0.5)	0.420
Other (marginal) *Any*	17 (1.2)	12 (1.0)	17 (0.8)	12 (1.0)	<0.0001	17 (0.7)	13 (0.7)	<0.0001

[a] Percentages are weighted due to the NHANES multi-level sampling strategy. Differences evaluated using Rao Scott chi-square test for independence, where null hypothesis equates to no significant difference between age subgroups or between men and women.

[b] NONE Away indicates participants who did not consume any food away from home the prior day (i.e. 100% of their calories came from food at home, such as food purchased from the grocery store). TOTAL Away includes all participants who consumed any food away from home (including food consumed from full-service/fast food restaurants, cafeterias, and/or "other" marginal sources that together contributed less than 5% to total energy intake, or TEI).

Table 3

Adjusted association between cumulative phthalates daily intake (Σandrogen-disruptor, *μg/kg/day*) and dietary intake (total and from food away from home)[a] in NHANES 2005–14 (*N* = 10,253)

Dietary Intake	Children 6-11 yrs (n = 1521)		Adolescents 12-19 yrs (n = 1887)		Adults 20-59 yrs (n = 4601)		Older Adults 60yrs (n = 2244)	
	n	Percent difference (95% CI)	n	Percent difference (95% CI)	n	Percent difference (95% CI)	n	Percent difference (95% CI)
Away from home (% TEI)[b]								
None	471	Referent	630	Referent	1714	Referent	1209	Referent
Low	504	17 (4.5, 30)*	650	27 (14, 42)*	1462	23 (15, 33)*	526	16 (2.9, 31)*
High	546	30 (16, 45)*	607	55 (35, 78)*	1425	47 (36, 59)*	509	51 (37, 67)*
p for trend		<0.0001		<0.0001		<0.0001		<0.0001
Away from home fat (% TEI)[b]								
None	477	Referent	638	Referent	1756	Referent	1221	Referent
Low	506	18 (4.9, 32)*	647	27 (14, 42)*	1438	23 (14, 32)*	525	18 (5.1, 31)*
High	538	28 (14, 44)*	602	54 (34, 78)*	1407	46 (34, 58)*	498	51 (36, 68)*
p for trend		<0.0001		<0.0001		<0.0001		<0.0001
Total fat (% TEI)[c]								
Low	497	Referent	634	Referent	1634	Referent	795	Referent
Mid	498	-0.16 (-11, 12)	603	3.6 (-8.1, 17)	1465	3.1 (-4.0, 11)	759	-9.3 (-18, 0.8)
High	526	0.93 (-9.0, 12)	650	9.8 (-2.9, 24)	1502	14 (6.6, 22)*	690	10 (-1.4, 23)
p for trend		0.86		0.13		0.0002		0.09
Total energy intake (TEI) (kcals)[c]								
Low	528	Referent	626	Referent	1570	Referent	848	Referent
Mid	494	4.5 (-6.7, 17)	615	-7.5 (-17.0, 3.0)	1526	1.9 (-5.8, 10)	672	-8.1 (-18, 2.3)
High	499	2.6 (-8.2, 15)	646	12 (-4.6, 30)	1505	9.5 (1.0, 19)*	724	-1.1 (-13, 12)
p for trend		0.64		0.18		0.03		0.90

[a] Covariates: Sex, age, race/ethnicity, poverty-to-income ratio (PIR), education (adults only), NHANES survey cycle, and time of sampling session.

[b] Referent groups include participants who did not consume any food away from home the prior day (i.e. 100% of their calories came from food at home). Low/High divided at weighted median of dining out consumers (% TEI), which was 40, 49, 44, and 38, respectively, for children, adolescents, adults, and older adults (range 0–100%). Weighted median (range) for away from home-derived fat intake (% TEI): 14 (0–42), 18 (0–62), 17 (0–56), and 15 (0–62) for children, adolescents, adults, and older adults, respectively.

[c] Low/Mid/High calculated from weighted distributions of age-specific subgroups. Tertile divisions (range) for children, adolescents, adults, and older adults, respectively: 30, 36 (3.8–62), 30, 37 (1.8–69), 30, 37 (1.5–75), and 31, 38 (4.1–65) for total fat intake (% TEI); 1613, 2112 (171–6992), 1650, 2379 (193–9363), 1746, 2570 (89–13,133), and 1496, 2004 (188–6305) for TEI (kcals).

*
$p<0.05$

Table 4

Adjusted association between cumulative phthalates daily intake (Σandrogen-disruptor, *μg/kg/day*) and dietary intake from specific sources of food away from home[a] in NHANES 2005–14 (*N* = 10,253)

Dietary Intake (% TEI)	Children 6–11 yrs (n = 1521)		Adolescents 12–19 yrs (n = 1887)		Adults ≥20 yrs (n = 6845)	
	n	Percent diff (95% CI)	*n*	Percent diff (95% CI)	*n*	Percent diff (95% CI)
Fast food restaurant						
None[b]	471	Referent	630	Referent	2923	Referent
Any	545	29 (16, 43)*	798	47 (32, 64)*	2313	39 (31, 48)*
Full-service restaurant						
None[b]	471	Referent	630	Referent	2923	Referent
Any	165	46 (22, 73)*	251	52 (24, 86)*	1503	41 (31, 51)*
Cafeteria						
None[b]	471	Referent	630	Referent	2923	Referent
Any	488	15 (4.0, 28)*	381	45 (24, 68)*	223	64 (40, 92)*

[a] Covariates: Sex, age, race/ethnicity, poverty-to-income ratio (PIR), education (adults only), NHANES survey cycle, and time of sampling session.

[b] Common referent groups include participants who did not consume any calories from food away from home the prior day (i.e. 100% of their calories came from food at home, such food purchased from a grocery store).

*
p<0.05

Table 5

Adjusted association between cumulative phthalates daily intake (Σandrogen-disruptor, $\mu g/kg/day$) and dietary intake of particular foods at home and away from home[a] in NHANES 2005–14 (N = 10,253)

Dietary Intake	Children 6-11 yrs (N = 1521)		Adolescents 12-19 yrs (N = 1887)		Adults ≥20 yrs (N = 6845)	
	n	Percent difference (95% CI)	n	Percent difference (95% CI)	n	Percent difference (95% CI)
Fruit/veggie guideline[b]						
Yes	498	Referent	415	Referent	1890	Referent
No	751	3.0 (−8.0, 15)	1158	−13 (−23, −1.9)*	3668	4.1 (−1.7, 10)
Sandwich[c]						
None	474	Referent	619	Referent	3043	Referent
At home	253	7.4 (−4.0, 20)	323	−5.0 (−19, 11)	1485	1.8 (−4.9, 9.0)
None	474	Referent	619	Referent	3043	Referent
Away from home	145	35 (10, 64)*	218	37 (12, 68)*	729	31 (17, 47)*
Fried potatoes[c]						
None	474	Referent	619	Referent	3043	Referent
At home	35	11 (−12, 39)	39	−21 (−37, −0.3)*	154	−0.8 (−22, 25)
None	474	Referent	619	Referent	3043	Referent
Away from home	61	8.2 (−18, 42)	68	7.6 (−23, 51)	192	26 (6.9, 49)*
Pizza[c]						
None	474	Referent	619	Referent	3043	Referent
At home	50	6.3 (−17, 37)	54	−2.0 (−19, 19)	131	12 (−6.1, 34)
None	474	Referent	619	Referent	3043	Referent
Away from home	177	22 (5.2, 40)*	167	3.2 (−14, 24)	247	9.1 (−5.3, 26)

[a]Covariates: Sex, age, race/ethnicity, poverty-to-income ratio (PIR), education (adults only), NHANES survey cycle, and time of sampling session.

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[b]Fruit/veggies were evaluated separately from other foods. Referent group includes participants who met either their daily fruit or vegetable guideline (in cup-equivalents, or c-eq); "No" group includes participants who did not meet either requirement.[65] Sample sizes restricted by data availability.

[c]Six models were performed for each age-specific subgroup to separately compare *At home* and *Away from home* consumers to a common referent group of non-consumers of any of these foods. For example, consumers of sandwiches away-from-home were compared to participants who did not eat any at-home or away-from-home sandwiches, fried potatoes, or pizza the prior day. The *At home* and *Away from home* categories included a small number of overlapping participants who consumed particular foods from both sources the prior day (e.g. $n = 58$, 7, and 9 children consumed at-home and away-from-home sandwiches, fried potatoes, and pizza, respectively).

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$p < 0.05$

Table 6

Individual phthalate contributions to cumulative daily intake (Σandrogen-disruptor, $\mu g/kg/day$) and their adjusted associations with dietary intake of food away from home[a] in NHANES 2005–14 (N = 10,253)

Dietary Intake[b] (% TEI)	n	DEHP	DiNP	DnBP	DEP	BBzP	DiBP
None (0)	4024	Referent	Referent	Referent	Referent	Referent	Referent
Low (0.04 – 43.3)	3178	15 (9.1, 21)*	37 (27, 47)*	−1.3 (−5.9, 3.5)	−2.4 (−10, 6.1)	−2.3 (−8.3, 4.1)	−0.8 (−5.4, 3.9)
High (43.4 – 100)	3051	31 (22, 40)*	74 (60, 901)*	−5.8 (−11, 0.1)	−6.9 (−14, 1.0)	−3.0 (−8.7, 3.0)	−2.7 (−7.8, 2.8)
p for trend		<0.0001	<0.0001	0.056	0.088	0.314	0.333
Contribution (%)		*45*	*30*	*16*	*4*	*2*	*2*

[a] Covariates: Sex, age, race/ethnicity, poverty-to-income ratio (PIR), education (adults only), NHANES survey cycle, and time of sampling session.

[b] Low and high dietary intake divided at the weighted median of participants who consumed food away from home the prior day. None includes participants who did not consume any food away from home (i.e. 100% of their calories were consumed from food at home, such as food purchased from the grocery store.

*
p<0.05