2016

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Bisphenol-A and Sleep Adequacy among Adults in the National Health and Nutrition Examinations Surveys

Hind A. Beydoun, PhD, MPH; May A. Beydoun, PhD, MPH; Hueiwang Anna Jeng, ScD; Alan B. Zonderman, PhD; Shaker M. Eid, MD, MBA

Study Objectives: To evaluate bisphenol-A (BPA) level and its relationship to sleep adequacy in a nationally representative sample of U.S. adults.

Methods: A population-based cross-sectional study was conducted using 2005-2010 National Health and Nutrition Examination Survey whereby data were collected using in-person interviews, physical examination and laboratory testing. BPA level was measured in urine samples and analyzed as loge-transformed variable and in quartiles (< 0.9 ng/mL; 0.9 to < 1.9 ng/mL; 1.9 to < 3.7 ng/mL; ≥ 3.7 ng/mL). Sleep adequacy was operationalized with three questions: "How much sleep do you usually get at night on weekdays or workdays?", "Have you ever told a doctor or other health professional that you have trouble sleeping?" and "Have you ever been told by a doctor or other health professional that you have a sleep disorder?" Sleep duration was further categorized as (< 6 h, ≥ 6 h); (< 7 h, 7–8 h, > 8 h); (< 5 h, 5–6 h, 7–8 h, ≥ 9 h). Linear, binary, and ordinal logistic regression models were constructed.

Results: Loge-transformed BPA level was inversely related to sleep duration defined, in hours, as a continuous variable, a dichotomous variable (≥ 6, < 6), or an ordinal variable (≥ 9, 7–8, 5–6, < 5), after adjustment for confounders. Help-seeking behavior for sleep problems and diagnosis with sleep disorders were not significantly associated with loge-transformed BPA level in fully adjusted models.

Conclusions: Loge-transformed BPA level may be associated with fewer hours of sleep among U.S. adults, with implications for prevention. Further research involving diverse populations are needed to confirm these study findings.

Keywords: bisphenol-A, endocrine disruptor, sleep duration, sleep disorder, survey

Introduction

Growing evidence has implicated sleep as a key player in the regulation of appetite, metabolic and immune functions. In recent studies, suboptimal sleep duration has been linked to serious health problems, including obesity, insulin resistance, type 2 diabetes, hypertension, metabolic syndrome, cardiovascular disease, and cancer. Sleep disorders, described as difficulty initiating or maintaining sleep or non-restorative sleep, are highly prevalent and often under-diagnosed in the U.S. In particular, 10% to 15% of U.S. adults are affected by insomnia. Also, 3% to 7% of men and 2% to 5% of women have diagnoses of obstructive sleep apnea (OSA), whereas 82% of men and 93% of women with moderate to severe OSA may be undiagnosed. Identification of modifiable risk/protective factors for inadequate sleep is a prerequisite for the design, implementation, and evaluation of preventive strategies aimed at reducing its health impact. Whereas dietary habits and sedentary lifestyle have recently been correlated with sleep, little research has been done on endocrine disruptors. Bisphenol-A (BPA) is a carbon-based synthetic compound used in the manufacturing of polycarbonate plastics, epoxy resins, and food and beverage containers. It is a ubiquitous endocrine disruptor with estrogenic activity and is known to exert a wide variety of metabolic effects leading to reproductive and thyroid hormone dysregulation, weight gain, glucose intolerance, insulin resistance, type 2 diabetes, metabolic syndrome, cardiovascular disease, and fatty liver disease. Recent literature reviews have pointed out the heterogeneity of epidemiologic evidence linking BPA exposure to various health outcomes, rendering the magnitude of the association difficult to estimate via meta-analyses. BPA may impact suboptimal sleep and sleep disorders indirectly via its potential role in cardiometabolic risk factors and health problems. A direct impact of BPA on the muscle function in the upper airway leading to OSA has also been suggested based on analogous findings from biomedical research. Although the link between BPA and sleep appears to be biologically plausible, to date, only one study has correlated sleep issues with high levels of BPA.

The aim of this cross-sectional study is to evaluate level of BPA and its relationship to sleep adequacy (sleep duration, help-seeking behavior for sleep problems, and diagnosis with sleep disorders) in a nationally representative sample of U.S. adults, by performing secondary analyses using 2005-2010 National Health and Nutrition Examination Surveys (NHANES) data. We hypothesize that BPA level is inversely related to sleep duration and has a negative impact on sleep problems and disorders.

Methods

The NHANES is a program of studies conducted by the National Center for Health Statistics, a division of the Centers for Disease Control and Prevention (CDC), to assess the health and nutritional status of U.S. children and adults and to determine the prevalence of major diseases and their risk factors. The NHANES uses stratified multistage cluster sampling with...
oversampling of African Americans, Asians, Hispanics and adults 60 years and older.74 Demographic, socioeconomic, and nutritional data were collected through in-person interviews, physical examinations and laboratory tests.74,75

**Study Participants**

Since 1999, NHANES has become a continuous surveillance system. We selected 31,034 NHANES participants from three consecutive waves, namely, 2005–2006 (n = 10,348), 2007–2008 (n = 10,149), and 2009–2010 (n = 10,537). We excluded pregnant women (n = 507), individuals younger than 20 years (n = 13,902), and those with missing data on BPA (n = 23,133) and/or sleep-related questions (n = 11,467). The final sample consisted of adult non-pregnant 2005–2010 NHANES participants who were 20 years or older, and had no missing data on key variables of interest (n = 5,034).

**Variable Definitions**

**Bisphenol-A Level**

Spot urine samples were obtained from a one-third random subset of NHANES participants. Total urinary BPA, both conjugated and free, was analyzed by online solid-phase extraction coupled to high performance liquid chromatography (HPLC)-isotope dilution tandem mass spectrometry by the Division of Environmental Health Laboratory Sciences at the National Center for Environmental Health, CDC.68 The details of quality assurance and quality control procedures, including coefficients of variation (CV of 8.1% to 18.6% for the low BPA quality control pools and 5.7% to 12.1% for the high BPA quality control pools) and lower limits of detection (LLOD/√2 or 0.28 ng/mL), were described elsewhere.68 After careful examination of its distributional properties, we analyzed BPA level as a log-transformed continuous variable and in quartiles (<0.9 ng/mL; 0.9 to <1.9 ng/mL; 1.9 to <3.7 ng/mL; 3.7+ ng/mL). We used quartiles instead of tertiles or quintiles to maximize our ability to detect a relative risk of ~1.3, assuming that the proportion having the outcome is 0.1 with α = 0.05 and β = 0.2.

**Sleep Adequacy**

Three questions related to sleep adequacy were available in all 3 waves (2005–2006, 2007–2008, and 2009–2010) of NHANES data as follows: “How much sleep do you usually get at night on weekdays or workdays?” (Q1: Sleep duration), “Have you ever told a doctor or other health professionals that you have trouble sleeping?” (Q2: Help-seeking behavior for sleep problems) and “Have you ever been told by a doctor or other health professional that you have a sleep disorder?” (Q3: Diagnosis with sleep disorders). Responses to Q1 were measured on a continuous scale as number of hours, and responses to Q2 and Q3 were dichotomous “yes” or “no”.76 Q1 was also analyzed as a categorical variable using 3 distinct definitions based on recent studies of NHANES data, namely: definition 1 (“short sleep (yes): <6 h”, “short sleep (no): ≥6 h”); definition 2 (“short sleep: <7 h,” “normal sleep: 7–8 h,” “long sleep: >8 h”); and definition 3 (“very short sleep: <5 h,” “short sleep: 5–6 h,” “normal sleep: 7–8 h,” “long sleep: ≥9 h”).77

**Covariates**

Selected demographic, socioeconomic, lifestyle, and health characteristics were considered as a priori confounders for the hypothesized relationships between BPA level and sleep adequacy, based on the literature.42,43,45,74–83 These include sex (male, female), age (<30, 30–39, 40–49, 50–59, 60+ years), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other), education (less than high school, high school, more than high school), marital status (married/cohabiting, not married), poverty income ratio (continuous; <100%, 100% to <200%, ≥200%), smoking status (Current smoker, Ex-smoker, Never smoker), alcohol consumption (≥12 glasses in the past 12 months) (yes/no), body mass index (BMI) (<25, 25 to <30, 30+ kg/m²), waist circumference (High: ≥102 cm (40 in) in men or ≥88 cm (35 in) in women vs. Low: <102 cm (40 in) in men or <88 cm (35 in) in women), self-rated health (excellent/very good/good, fair/poor), depressive symptoms based on the 9-item Patient Health Questionnaire (PHQ) total score (High ≥10, Low: <10), and adjusted creatinine level which was calculated based on equations described by Silver and coworkers.68 Of note, the normal creatinine levels are estimated to be 0.6 to 1.2 mg/dL in adult males and 0.5 to 1.1 mg/dL in adult females.

**Statistical Analysis**

Statistical analyses were performed using STATA version 12 (STATA Corporation, College Station, TX). Whereas frequencies and percentages were computed for categorical variables, means and standard errors of the mean (SEM) were computed for continuous variables. Unadjusted (Model I), age- and sex-adjusted (Model II) as well as fully adjusted (Model III) models were constructed for BPA as a predictor of sleep adequacy, using ‘svy:reg’ for continuous outcomes, ‘svy:logit’ for binary outcomes and ‘svy:ologit’ for ordinal outcomes. Measures of association were presented as beta coefficients with their 95% confidence intervals (CI) for linear regression models and odds ratios (OR) with their 95% CI for logistic regression models. Sampling weights were used to produce correct population estimates accounting for differential probabilities of selection and adjusting for non-response, non-response, and oversampling of subpopulations. Two-sided statistical tests were performed at an α level of 0.05.

**RESULTS**

Between 2005 and 2010, 5,034 participants met inclusion criteria in this study; 2,564 were men and 2,470 were women. Table 1 details the demographic, socioeconomic, lifestyle, and health characteristics of the study participants by sex. Overall, the mean (±SEM) for age, BMI, waist circumference, depressive symptoms, and adjusted creatinine level were 47.0 ± 0.35 years, 28.7 ± 0.1 kg/m², 97.9 ± 0.4 cm, 2.8 ± 0.08, and 909614.2 ± 13896.9 mg/dL, respectively. Furthermore, 24% were ≥60 years, 70% were non-Hispanic White, 57% had more than high school education, 58% were married, 63% had poverty income ratio >2, 53% never smoked, and 76% drank alcohol in the past 12 months. Also, 35% had BMI ≥30 kg/m², 52% had a high waist circumference, 84% had excellent, very good, or good self-rated health, and 6% had high
Table 1—Demographic, socioeconomic, lifestyle and health characteristics of study sample by sex: National Health and Nutrition Examination Surveys 2005–2010 (n = 5,034).

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 5,034)</th>
<th>Males (n = 2,564)</th>
<th>Females (n = 2,470)</th>
<th>P value</th>
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<td><strong>Age (years)</strong></td>
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<td>20.7</td>
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<td>Never smoker</td>
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<td><strong>Alcohol (past 12 months)</strong></td>
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<td>Yes</td>
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<td>85.6</td>
<td>66.5</td>
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<td>No</td>
<td>23.9</td>
<td>14.4</td>
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<td>28.8 ± 0.2</td>
<td>28.5 ± 0.2</td>
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<td>&lt; 25</td>
<td>32.0</td>
<td>26.6</td>
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<tr>
<td>25–30</td>
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<td>38.4</td>
<td>27.8</td>
<td></td>
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<tr>
<td>≥ 30</td>
<td>34.9</td>
<td>34.9</td>
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<tr>
<td><strong>Waist circumference (cm)</strong></td>
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<td></td>
<td>&lt; 0.0001</td>
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<tr>
<td>Mean ± SEM</td>
<td>97.9 ± 0.4</td>
<td>101.4 ± 0.5</td>
<td>94.7 ± 0.4</td>
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<td>Categorical</td>
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<td>&lt; 0.0001</td>
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<tr>
<td>High</td>
<td>51.8</td>
<td>43.3</td>
<td>60.0</td>
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<tr>
<td>Low</td>
<td>48.2</td>
<td>56.7</td>
<td>39.9</td>
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<td><strong>Self-rated health</strong></td>
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<tr>
<td>Excellent/Very good/Good</td>
<td>83.5</td>
<td>83.8</td>
<td>83.1</td>
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<tr>
<td>Fair/Poor</td>
<td>16.5</td>
<td>16.2</td>
<td>16.9</td>
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<td><strong>Depressive symptoms</strong></td>
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<td>&lt; 0.0001</td>
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<tr>
<td>Mean ± SEM</td>
<td>2.8 ± 0.08</td>
<td>2.3 ± 0.08</td>
<td>3.2 ± 0.1</td>
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<tr>
<td>Categorical</td>
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<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>High (≥ 10)</td>
<td>5.9</td>
<td>4.4</td>
<td>7.3</td>
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<tr>
<td>Low (&lt; 10)</td>
<td>94.1</td>
<td>95.6</td>
<td>92.7</td>
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<tr>
<td><strong>Creatinine (mg/dL) – adjusted</strong></td>
<td></td>
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<td></td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Mean ± SEM</td>
<td>909614.2 ± 13896.9</td>
<td>1092170 ± 18177.8</td>
<td>731908.2 ± 18516.82</td>
<td></td>
</tr>
</tbody>
</table>

*“High” refers to waist circumference > 102 cm in males and > 88 cm in females.*
depressive symptoms. All these characteristics differed significantly by sex, with the exception of race, education, and self-rated health.

BPA levels and sleep adequacy of the study participants by sex are presented in Table 2. Overall, the mean (± SEM) for BPA level and duration of sleep were 4.2 ± 0.4 ng/mL and 6.9 ± 0.03 h, respectively. Furthermore, 87% reported sleeping ≥ 6 h, 55% 7 to 8 h, and 7% ≥ 9 h. Moreover, 24% reported ever telling a doctor that they had trouble sleeping, and only 8% were ever diagnosed with a sleep disorder. All these characteristics were significantly different among men and women, with the exception of the binary definition (< 6 h vs. ≥ 6 h) of sleep duration.

Table 3 presents urinary BPA level as a predictor of sleep duration defined as a continuous or categorical variable in unadjusted (Model I), sex- and age-adjusted (Model II), and fully adjusted (Model III) models. As expected, an inverse relationship was observed between sleep duration, defined as a continuous variable, and log-transformed BPA level in all three models (Model I: −0.06 [−0.09, −0.02]; Model II: −0.06 [−0.09, −0.02]; Model III: −0.05 [−0.09, −0.002]). Taking the lowest quartile as a referent group, the upper quartile of BPA was inversely related to sleep duration, defined as a continuous variable, in the unadjusted (β = −0.2, 95% CI: −0.3, −0.03) as well as sex- and age-adjusted model (β = −0.2, 95% CI: −0.3, −0.03), but not the fully adjusted model (β = −0.12, 95% CI: −0.3, 0.02). The categorical definitions 1 (short sleep (yes): < 6 h, short sleep (no): ≥ 6 h) and 3 (very short sleep: < 5 h, short sleep: 5–6 h, normal sleep: 7–8 h, long sleep: ≥ 9 h) for sleep duration were inversely and significantly related to log-transformed BPA level in unadjusted, sex- and age-adjusted and fully adjusted models. By contrast, the categorical definition 2 (short sleep: < 7 h, normal sleep: 7–8 h, long sleep: > 8 h) for sleep duration was inversely and significantly related to log-transformed BPA level only in the unadjusted and sex- and age-adjusted models. When defined as quartiles, BPA level was inversely and significantly related to categorical definition 1 of sleep duration in the unadjusted model as well as categorical definitions 2 and 3 of sleep duration in the unadjusted and sex- and age-adjusted models.

Table 4 presents urinary BPA level as a predictor of self-reported sleep problems in unadjusted, sex- and age-adjusted and fully adjusted models. Clearly, only unadjusted models yielded significant and positive relationships between having told a doctor that he/she had trouble sleeping and urinary BPA level defined either as a continuous variable (OR = 1.08, 95% CI: 1.01, 1.16) or in quartiles (Q4 vs. Q1: OR = 1.24, 95% CI: 1.01, 1.52). By contrast, no significant relationship was observed between urinary BPA level and ever being told by a doctor that he/she had a sleeping disorder in the 3 models.
DISCUSSION

In this cross-sectional study, we investigated whether BPA was associated with sleep adequacy in a nationally representative sample of U.S. adults in whom self-reported sleep duration, help-seeking behavior for sleep problems, and diagnosis with sleep disorders were considered as the main outcomes of interest. Consistent with our hypotheses, the results indicated that loge-transformed BPA level was inversely related to sleep duration defined, in hours as a continuous variable, a dichotomous variable (≥ 6 vs. < 6) or an ordinal variable (≥ 9, 7–8, 5–6, < 5), after adjustment for confounders. By contrast, help-seeking behavior for sleep problems and diagnosis with sleep disorders were not significantly associated with loge-transformed BPA level in the fully adjusted models. Also, when BPA level was defined in quartiles, its relationship with sleep adequacy did not reach statistical significance after controlling for demographic, lifestyle, and health characteristics of the study sample. The latter finding suggests a complex nonlinear relationship between BPA and indicators of sleep adequacy.

Emerging evidence suggests that BPA, atrazine, dichlorodiphenyltrichloroethane, diethylstilbestrol, dioxin, phthalates, polychlorinated biphenyls, organotins, and other endocrine disruptors may have negative health effects.84–91 Endocrine disruptors are lipophilic substances that usually act as transcription factors for nuclear hormone receptor superfamily and can either mimic or block the action of endogenous sex hormones, resulting in irreversible alterations or reversible alterations in patterns of gene expression.84,86–91 Sex steroids (androgens and estrogens) play an important role in establishing and maintaining adipose tissue84,85 and in conjunction with growth hormones can mobilize lipids and have anti-adipogenic effects; their effects are counteracted by insulin and cortisol that have

| Table 3—Urinary bisphenol level as a predictor of sleep duration defined as a continuous or categorical variable. |
|---|---|---|
| **Sleep duration (hours) – Continuous** | **Model I: Unadjusted** | **Model II: Age-and-Sex Adjusted** | **Model III: Fully Adjusted** |
| Urinary bisphenol level (ng/mL) – Continuous | β (95% CI) | β (95% CI) | β (95% CI) |
| < 0.9 | Ref. | Ref. | Ref. |
| 0.9–1.9 | −0.05 (−0.18, 0.08) | −0.05 (−0.18, 0.09) | −0.08 (−0.2, 0.06) |
| 1.9–3.7 | −0.1 (−0.3, −0.01) | −0.1 (−0.2, 0.008) | −0.09 (−0.2, 0.04) |
| ≥ 3.7 | −0.2 (−0.3, −0.03) | −0.2 (−0.3, −0.03) | −0.12 (−0.3, 0.02) |
| **Hours of sleep – Categorical 1** | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Urinary bisphenol level (ng/mL) – Continuous | 0.87 (0.79, 0.94) | 0.87 (0.79, 0.95) | 0.88 (0.79, 0.98) |
| < 0.9 | Ref. | Ref. | Ref. |
| 0.9–1.9 | 1.03 (0.78, 1.36) | 1.04 (0.79, 1.38) | 0.94 (0.70, 1.26) |
| 1.9–3.7 | 0.77 (0.57, 1.04) | 0.79 (0.58, 1.08) | 0.79 (0.57, 1.11) |
| ≥ 3.7 | 0.73 (0.53, 0.99) | 0.73 (0.52, 1.02) | 0.76 (0.52, 1.11) |

**Model I: Unadjusted**

| Sleep duration (hours) – Categorical 2 | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| Urinary bisphenol level (ng/mL) – Continuous | 0.93 (0.88, 0.98) | 0.93 (0.88, 0.98) | 0.97 (0.91, 1.03) |
| < 0.9 | Ref. | Ref. | Ref. |
| 0.9–1.9 | 0.88 (0.69, 1.12) | 0.88 (0.69, 1.12) | 0.85 (0.65, 1.12) |
| 1.9–3.7 | 0.91 (0.73, 1.13) | 0.91 (0.73, 1.14) | 0.99 (0.75, 1.32) |
| ≥ 3.7 | 0.77 (0.63, 0.93) | 0.77 (0.63, 0.93) | 0.86 (0.68, 1.08) |

**Sleep duration (h) – Categorical 3**

| Urinary bisphenol level (ng/mL) – Continuous | OR (95% CI) | OR (95% CI) | OR (95% CI) |
|< 0.9 | Ref. | Ref. | Ref. |
| 0.9–1.9 | 0.98 (0.57, 1.69) | 0.94 (0.55, 1.62) | 0.92 (0.49, 1.75) |
| 1.9–3.7 | 0.71 (0.42, 1.19) | 0.65 (0.38, 1.13) | 0.69 (0.39, 1.22) |
| ≥ 3.7 | 0.62 (0.39, 0.99) | 0.56 (0.34, 0.93) | 0.63 (0.35, 1.12) |

*Adjusted for sex (male, female), age (< 30, 30–39, 40–49, 50–59, ≥ 60 years), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other), education (less than high school, high school, more than high school), marital status (married/cohabiting, not married), poverty income ratio (continuous; < 100%, 100%–200%, ≥ 200%), smoking status (current smoker, ex-smoker, never smoker), alcohol consumption (at least 12 glasses in the past 12 months) (yes, no), body mass index (BMI) (< 25, 25–30, ≥ 30 kg/m^2), waist circumference (High: ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women vs. Low: < 102 cm (40 in) in men or < 88 cm (35 in) in women), self-rated health (excellent/very good/good, fair/poor), depressive symptoms based on the 9-item Patient Health Questionnaire (PHQ) total score (high: ≥ 10, low: < 10) and adjusted creatinine level.
which can potentially mediate suboptimal sleep. 58,59,64,66,69

with the current evidence that BPA is a chemical substance
for the manufacturing of flame retardants, dental sealants and
factors and conditions. 69,92,93,107–109


However, our results also suggest that BPA level may be nega-
tively associated with sleep duration, independently of BMI
or waist circumference, both of which are indices of obesity-
related disturbances. Therefore, it is also plausible that BPA
may have an adverse impact on muscular function in the upper
airway, causing sleep disorders such as OSA, as suggested by
biomedical researchers.41 In-depth analyses are needed to eval-
uate the mediating role of obesity-related cardiometabolic risk
factors and conditions, including components of the metabolic
syndrome, in the observed relationship between BPA and sleep
duration. While the proposed biological mechanisms are plau-
sible, reverse causality cannot be ruled out as a potential expla-
nation for the observed associations. In fact, it is also plausible
that individuals who experience shorter sleep are more likely
to experience environmental BPA exposure which, in turn, as-
sumes a state of wakefulness.

To our knowledge, this is the first study examining whether
BPA may be causally or non-causally linked to adequacy of
sleep in a nationally representative sample of U.S. adults. Pre-
vious studies have used NHANES data to examine correlates
of sleep, including race/ethnicity,43 socioeconomic status,83
eating behaviors,80 nutritional biomarkers,77,79 alcohol use,74
obesity,76 pre-diabetes,78 diabetes,76 hypertension,82 homocys-
teine,45 inflammatory biomarkers,43,81 cardiovascular disease,42
anxiety,77 and functional health.43 In a recent study, Erden and
colleagues41 evaluated the associations among OSA, BPA, vi-
tamin D, and parathyroid hormone levels using a sample of
128 subjects who had undergone polysomnography and were
classified as control (n = 43), moderate OSA (n = 23), or se-
vere OSA (n = 62).41 Consistent with our findings, their results
indicated that while vitamin D level was lower in both OSA
groups and PTH was higher in OSA groups than in the control
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subjects, and BPA levels were higher in severe OSA than mod-
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Nevertheless, our findings should be interpreted with cau-
tion and in light of several limitations. First, the study design is
cross-sectional, which precludes establishing cause-and-effect
relationships among variables under study. Second, analyses
were based on previously collected data reducing flexibility in
the definition of outcome, exposure, and covariate variables.
Third, BPA metabolites were assessed by a single assay in

Table 4—Urinary bisphenol level as a predictor of self-reported sleep problems.

<table>
<thead>
<tr>
<th>Ever told by doctor had sleeping disorder</th>
<th>Model I: Unadjusted</th>
<th>Model II: Age-and-Sex Adjusted</th>
<th>Model III: Fully Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary bisphenol level (ng/mL) – Continuous</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>&lt; 0.9</td>
<td>1.08 (1.01, 1.16)</td>
<td>1.03 (0.96, 1.11)</td>
<td>1.08 (0.99, 1.19)</td>
</tr>
<tr>
<td>0.9–1.9</td>
<td>1.19 (0.94, 1.52)</td>
<td>1.08 (0.85, 1.39)</td>
<td>1.13 (0.86, 1.49)</td>
</tr>
<tr>
<td>1.9–3.7</td>
<td>1.11 (0.88, 1.39)</td>
<td>0.96 (0.75, 1.22)</td>
<td>1.03 (0.77, 1.39)</td>
</tr>
<tr>
<td>≥ 3.7</td>
<td>1.24 (1.01, 1.52)</td>
<td>1.06 (0.85, 1.34)</td>
<td>1.19 (0.89, 1.59)</td>
</tr>
<tr>
<td>Urinary bisphenol level (ng/mL) – Quartiles</td>
<td>P = 0.1</td>
<td>P = 0.9</td>
<td>P = 0.4</td>
</tr>
<tr>
<td>&lt; 0.9</td>
<td>Ref.</td>
<td>Ref.</td>
<td>Ref.</td>
</tr>
<tr>
<td>0.9–1.9</td>
<td>1.01 (0.66, 1.54)</td>
<td>0.98 (0.63, 1.52)</td>
<td>1.18 (0.74, 1.88)</td>
</tr>
<tr>
<td>1.9–3.7</td>
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<td>0.79 (0.51, 1.22)</td>
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<td>≥ 3.7</td>
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*Adjusted for sex (male, female), age (< 30, 30–39, 40–49, 50–59, ≥ 60 years), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other), education (less than high school, high school, more than high school), marital status (married/cohabiting, not married), poverty income ratio (continuous; < 100%, 100%–200%, ≥ 200%), smoking status (current smoker, ex-smoker, never smoker), alcohol consumption (at least 12 glasses in the past 12 months) (yes, no), body mass index (BMI) (< 25, 25–30, ≥ 30 kg/m²), waist circumference (high: ≥ 102 cm (40 in) in men or ≥ 88 cm (35 in) in women vs. low: < 102 cm (40 in) in men or < 88 cm (35 in) in women), self-rated health (excellent/very good/good, fair/poor), depressive symptoms based on the 9-item Patient Health Questionnaire (PHQ) total score (high: ≥ 10, low: < 10) and adjusted creatinine level.

adipogenic effects.84 Exposure to endocrine disruptors such as
BPA is thought to promote adiposity typical of Cushing
syndrome, polycystic ovary syndrome, growth hormone defi-
ciency, menopause, aging, alcoholism, and depression.84,88

Since the 1960s, BPA has been produced in large quantities
for the manufacturing of flame retardants, dental sealants and
fillings, adhesives, protective coatings, infant feeding bottles,
food and mineral water storage containers, and food and bev-
verage can linings.84,92–98 Although studies have suggested that
low-dose BPA exposure may be associated with increased
reproductive and cancer risks,99–103 regulatory bodies in the
U.S., Canada, and Europe have distinct views on whether BPA
should be considered a hazardous substance.106

So far, a limited number of studies have used a nationally
representative sample to investigate health effects of BPA, and
several of these studies, most of which used NHANES data,
have linked high BPA to obesity-related cardiometabolic risk
factors and conditions.69,92,93,107–109 The finding of an inverse
relationship between sleep duration and BPA level is consistent
with the current evidence that BPA is a chemical substance
that has the capacity to bind nuclear and membrane surface
estrogen receptors, resulting in obesity-related disturbances
which can potentially mediate suboptimal sleep.58,59,64,66,68

However, our results also suggest that BPA level may be nega-
tively associated with sleep duration, independently of BMI
or waist circumference, both of which are indices of obesity-
related disturbances. Therefore, it is also plausible that BPA
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airway, causing sleep disorders such as OSA, as suggested by
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Third, BPA metabolites were assessed by a single assay in


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NHANES, which may not represent diurnal changes in BPA levels. Fourth, the study sample was selected on the basis of availability of exposure and outcome data, which may have resulted in selection bias. In particular, the inclusion and exclusion criteria that define the selected subset of NHANES 2005–2010 subjects may have influenced the effectiveness of weighting variables. Further analyses suggested that the selected and non-selected adult subjects differed significantly on sex, age, race/ethnicity, and education. Fifth, NHANES assessed adequacy of sleep using self-report rather than polysomnography or medical records data, which may have led to non-differential misclassification of the outcome variables of interest, potentially biasing measures of association towards the null value. Moreover, the question pertaining to sleep duration was limited in scope as it only considered week or workdays. Considering the existence of sleep compensation (short sleep during week or workdays and longer sleep on weekends or free days), the general sleep time is underestimated. Also, at least one of the sleep-related outcomes is a rare event with a prevalence of less than 10%, reducing our ability to detect an association with BPA exposure.

Sixth, although numerous covariates were included in the multivariable models, we cannot rule out residual confounding as an explanation for the observed associations due to uncontrolled factors such as area of residence and diet quality. Seventh, although sex differences were observed, we could not conduct stratified analyses according to sex as a result of sample size limitations. Finally, our findings can only be generalized to adult men and women, and further research is needed to evaluate these relationships in adolescents and children.

In conclusion, secondary analyses of 2005–2010 NHANES data involving U.S. adults suggests that sleep duration, but not help-seeking behaviors related to poor sleep, may be inversely related to BPA level, with implications for primary and secondary prevention. Regulation of environmental BPA level could potentially reduce the risk of adverse health outcomes, including poor sleep. Also, monitoring of BPA level by healthcare professionals could help identify patients at high risk for poor sleep and aid in the management of patients experiencing poor sleep. Our results support the idea that excessively high levels of BPA may, directly or indirectly, be linked to poor sleep. Further research is needed to better understand what specific environmental exposures may have led to excessive levels of BPA and consequently adverse outcomes such as inadequate sleep.

ABBREVIATIONS

BMI, body mass index
BPA, Bisphenol-A
CDC, Centers for Disease Control and Prevention
CI, confidence interval
CV, coefficient of variation
HPLC, high performance liquid chromatography
LLOD, lower limit of detection
NHANES, National Health and Nutrition Examination Surveys
OR, odds ratio
OSA, obstructive sleep apnea

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SUBMISSION & CORRESPONDENCE INFORMATION
Submitted for publication March, 2015
Submitted in final revised form August, 2015
Accepted for publication August, 2015
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DISCLOSURE STATEMENT
This was not an industry supported study. This work was supported in part by the Intramural Research Program of the National Institutes of Health, National Institute on Aging (NIA/NIH/IRP). The authors have indicated no financial conflicts of interest. The work was performed at the Eastern Virginia Medical School, Norfolk, VA.