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Original quantitative research

Tobacco smoke exposure and sleep: estimating the association of urinary cotinine with sleep quality

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Abstract

Introduction: A majority of studies on tobacco smoke exposure and sleep quality have relied on self-reported smoking, resulting in potential exposure misclassification and biases related to self-report. The objective of this study was to investigate associations between urinary cotinine, a biological marker of tobacco smoke exposure, and sleep quality measures, including sleep duration, sleep continuity or efficiency, sleep satisfaction and alertness during normal waking hours.

Methods: Using data on a national sample of 10 806 adults (aged 18–79 years) from the Canadian Health Measures Survey (2007–2013), we performed binary logistic regression analyses to estimate associations between urinary cotinine concentrations and sleep quality measures, while controlling for potential confounders. Additionally, we performed ordinal logistic regression to assess the association between urinary cotinine concentrations and increased number of sleep problems.

Results: Overall, 28.7% of adult Canadian survey respondents had urinary cotinine concentrations above the limit of detection (LOD), and the prevalence of each sleep problem ranged from 5.5% to 35.6%. Elevated urinary cotinine concentrations (quartile 4 vs. < LOD) were associated with significantly higher odds of short or long sleep duration (OR = 1.41; 95% CI: 1.02–1.95; *p*-trend = .021), trouble falling or staying asleep (OR = 1.71; 95% CI: 1.28–2.27; *p*-trend = .003), sleep dissatisfaction (OR = 1.87; 95% CI: 1.21–2.89; *p*-trend = .011), and increased number of sleep problems (OR = 1.64; 95% CI: 1.19–2.26; *p*-trend = .001). Stronger associations were observed among females compared to males.

Conclusion: Using a biological marker of tobacco smoke exposure, our study contributes to the body of literature of toxic environmental exposures on sleep quality by supporting an association between tobacco smoke exposure and poorer sleep quality. To address the limitations of a cross-sectional study design and to better assess the temporality of tobacco smoke exposure and sleep quality, longitudinal studies are recommended.

Keywords: *tobacco smoke exposure, urinary cotinine, sleep quality*

Highlights

- Over a quarter of study participants had detectable urinary cotinine levels, indicating that a large proportion of Canadian adults are likely exposed to tobacco smoke actively or passively.
- Poor sleep quality is a commonly reported problem, with approximately a third of adult survey respondents not meeting the recommended sleep duration guidelines.
- Elevated levels of urinary cotinine are associated with higher odds of short or long sleep duration, trouble falling or staying asleep, sleep dissatisfaction and overall increased sleep problems.
- The associations between increased urinary cotinine levels and poor sleep quality were stronger in females compared to males.

Introduction

Although the adverse health effects of tobacco smoke exposure, including cancer and cardiovascular and respiratory disease, have been well established,[1] there is a lack of comprehensive, population-based research on tobacco smoke exposure in relation to sleep quality using a biological marker of exposure. Tobacco smoke exposure includes first-hand smoke exposure in smokers, as well as second-hand smoke (SHS) exposure in both non-smokers and smokers. Recent estimates indicate that approximately 5.0 million (16.2%) Canadians aged 12 years or older reported being current smokers (daily or occasionally).[2] Among non-smokers, approximately 27% of Canadians aged 18 to 24 years have reported being exposed to SHS in a private vehicle or public place.[3] In 2012–2013, 11% of non-smoking Canadians with no reported SHS exposure and 34% of non-smoking Canadians with recent SHS exposure had detectable levels of cotinine (a biological marker of tobacco smoke exposure) in their urine.[4] Concurrently, 40% of Canadian adults reported symptoms of diminished sleep quality.[5] Sleep health has been defined as a multifaceted sleep-wakefulness cycle, reflective of an individual's physical and mental well-being.[6] As such, good sleep quality is

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framed under five dimensions: adequate sleep duration; sustained daytime alertness; sleep continuity or efficiency, which entails the ease and latency of falling asleep or returning to sleep; appropriate timing of sleep; and subjective satisfaction with sleep quality.[6]

Smoking has been shown to increase the risk of poor sleep quality.[7] Consequently, sleep disturbances have been observed among nicotine-dependent individuals.[8-10] Short sleep duration has been linked with an increased risk of morbidity and mortality.[8,11-14] Based on self-reported smoking, current smokers have been found to have higher odds of short sleep duration and poor sleep quality compared to never-smokers.[15] Compared to never-smokers, current smokers have also been found to have significantly higher odds of self-reported sleep deficiency or discontinuity and daytime sleepiness.[15-18] In addition, studies have demonstrated a dose-response relationship between quantities of cigarettes smoked and poor sleep quality.[17] In a longitudinal study, self-reported smoking was found to be significantly associated with increased difficulty of initiating sleep and waking up.[19] At the same time, light smoking has also been reportedly associated with reduced sleep duration.[20] Furthermore, non-smokers without SHS exposure have been reported to have lower odds of a sleep disorder compared to smokers with detectable cotinine concentrations.[21]

Nicotine, a stimulant, has been linked with reduced sleep quality. Compared to non-smokers, smokers have been shown to have reduced availability of dopamine transporters in the striatal region of the brain.[22] This phenomenon has been found to be associated with lower sleep quality among healthy adults.[23] Smokers have also been reported to experience nocturnal cravings and nicotine withdrawals, possibly because serum nicotine levels decline during sleep.[24] Consequently, sleep quality is potentially diminished due to a biological dependence on nicotine. In fact, the reported prevalence of nocturnal smoking among heavy smokers is roughly 41%.[25] By promoting the release of neurotransmitters, nicotine yields a sense of arousal and wakefulness.[26] As such, an association between nicotine and poor sleep quality has been previously demonstrated.

Using self-report of smoking is a noninvasive method of measuring tobacco smoke exposure, yet this method of surveillance is prone to underreporting. This is due to the socially undesirable nature of smoking, especially under the current public scrutiny of active and passive tobacco smoke exposure. Although the assessment of tobacco smoke exposure through the collection of biological samples is limited by associated costs, biological measurements of exposure, including urinary cotinine, have demonstrated a higher degree of accuracy than self-reports of smoking.[27]

Most published research has been limited to self-reported active smoking and SHS exposure as a measure of tobacco smoke exposure. Furthermore, most population-based studies have independently assessed only one dimension of sleep as an overall measure of sleep quality. A review of the literature has demonstrated a trend of underestimation in the prevalence of tobacco smoke exposure in studies relying on self-report, compared to studies utilizing biological markers of exposure.[27] Accordingly, this study aimed to address these research gaps by using urinary cotinine as a measure of tobacco smoke exposure, minimizing potential biases due to nonrandom and random misclassification of tobacco smoke exposure. In addition, this study encompassed four dimensions of sleep quality, including sleep duration, sleep continuity, sleep satisfaction and daytime alertness, thus providing a comprehensive understanding of the link between tobacco smoke exposure and sleep health. We sought to evaluate the association between urinary cotinine levels and sleep quality measures among Canadian adults, overall and by sex.

Methods

Data source and study population

This study used data from the Canadian Health Measures Survey (CHMS), cycles 1 (2007–2009), 2 (2010–2011) and 3 (2012–2013). The CHMS is an ongoing cross-sectional health survey that collects data from Canadians aged 6 to 79 years (cycle 1) or 3 to 79 years (cycles 2 and 3). Persons living on reserves or other Aboriginal settlements, full-time members of the Canadian Forces, residents of the three territories and those residing in certain remote regions or institutions were excluded from the survey. The CHMS was designed to cover approximately 96.0% of the Canadian population in the target age range.[28] The overall response rate for the pooled cycles is 52.9%. Details on the CHMS survey design and sampling framework are available elsewhere.[28] The survey consists of a household interview designed to collect sociodemographic and health- and lifestyle-related characteristics, followed by direct physical measurements and collection of biological samples at a mobile examination centre (MEC).[29] The complex multistage randomized sampling design and sample survey weights allow researchers to make inferences about the Canadian population, assess the quality of data, evaluate sampling errors and adjust for response rates in analyses. Our analysis included adults aged 18 years and older. To enhance statistical power and sample size, data from cycle 1 (n = 3726), cycle 2 (n = 3873), and cycle 3 (n = 3397) were pooled together. Due to their accelerated metabolism of nicotine, pregnant females (n = 93) were excluded from the analysis. Respondents with missing data on urinary cotinine or creatinine (n = 97) were also excluded. The final sample size was 10 806.

Ethics and consent

Participation in the CHMS is voluntary; respondents could opt out of any part of the survey at any point during data collection. Written informed consent was obtained from all participating respondents. All processes related to the CHMS were approved by Health Canada and the Public Health Agency of Canada (PHAC) Research Ethics Board.

Exposure: free urinary cotinine

Single spot urine samples were collected from participants upon arrival to the MEC. Respondents were asked to refrain from smoking or consuming other tobacco- and nicotine-containing products for a period of 2 hours prior to their visit. Before shipment to laboratories for testing, urine samples were refrigerated and stored at the appropriate temperature.[30] Cotinine was recovered by solid-phase extraction in a 96-well plate format on an automated PerkinElmer JANUS robotic workstation (C-550).[31] The limit of detection (LOD) for urinary cotinine was 1.1 µg/L.[32]

For the purpose of this analysis, urinary cotinine concentrations were divided into < LOD (reference category) and the remainder categorized into four quartiles, based

on the distribution in the overall population with detectable cotinine levels. Urinary cotinine levels were therefore classified into the following five categories: < LOD (< 1.1 µg/L); quartile 1 (≥ 1.1–60 µg/L); quartile 2 (61–734 µg/L); quartile 3 (735–< 1408 µg/L); and quartile 4 (≥ 1408 µg/L). We did not calculate geometric mean of urinary cotinine concentrations, since 40% of the sample had urinary cotinine concentrations below LOD.[31] We corrected for urinary creatinine concentrations in the analysis by including it as a covariate in multivariable regression models. This inclusion adjusts for potential biases due to individual differences in creatinine concentrations across population demographics and health characteristics.[33]

Outcomes: sleep quality

Information on the four dimensions of sleep was collected during the household interview. Sleep duration was assessed by asking respondents "How many hours do you usually spend sleeping in a 24-hour period, excluding time spent resting?" and was reported to the nearest half hour. Responses were dichotomized into "not meeting sleep duration guidelines," i.e. short or long sleep duration (ages 18–64 years: < 7 or > 9 hours; ages 65 years and over: < 7 or > 8 hours) than recommended in the U.S. National Sleep Foundation's age-specific recommendations[34] (ages 18–64 years: 7–9 hours; ages 65 years and over: 7–8 hours), and "recommended duration" (i.e. meeting sleep duration guidelines). Sleep continuity or efficiency was assessed by asking respondents "How often do you have trouble going to sleep or staying asleep?" Responses were dichotomized into "most of the time or all the time" versus "never, rarely, or sometimes." Sleep satisfaction was assessed by asking respondents "How often do you find your sleep refreshing?" Responses were dichotomized into "never or rarely" versus "sometimes, most of the time, or all the time." Finally, alertness was assessed by asking respondents "How often do you find it difficult to stay awake during your normal waking hours when you want to?" Responses were dichotomized into "most of the time or all the time" versus "never, rarely, or sometimes." Survey questions about the sleep dimensions asked about sleep characteristics during periods ranging from two weeks to two years prior to the survey date. Each of the four dimensions of sleep was independently analyzed in relation to urinary cotinine. Additionally, for our secondary analyses, we derived a composite measure of sleep quality by summing up the number of sleep problems based on the four binary variables described above. Participants were categorized as having 0, 1 or ≥ 2 sleep problems.

Covariates

We identified potential confounders from existing studies on the association between tobacco smoke exposure and sleep quality. Sociodemographic covariates included age; sex; race/ethnicity; marital status; education level; employment status; and household income adequacy. Household income adequacy was categorized based on total annual household earnings and total number of people living in a household.[31] Due to the high percentage of missing data (approximately 20%), household income was imputed by Statistics Canada using the nearest neighbour imputation method.[35] Health status covariates included body mass index (BMI); self-perceived mental health status; and presence (yes/no) of one of the following chronic conditions: asthma, diabetes, chronic obstructive pulmonary disease, hypertension, heart disease, stroke or cancer. Covariates related to health behaviour included self-reported physical activity, based on daily energy expenditures during leisure-time activities; and frequency of alcohol consumption.

Statistical analysis

We performed descriptive analyses to assess the distribution of covariates overall and by urinary cotinine category. We also determined the prevalence of each sleep quality measure across urinary cotinine categories. We used the Rao-Scott modified chi-square test to assess significance across categories of responses. Statistical significance was assessed at $p < .05$ (two-sided tests). To account for the complex sampling design of the CHMS, we integrated survey weights into all of our descriptive and logistic regression analyses. Bootstrap methods were used to calculate sample variances.[28]

We used univariate binary logistic regression to assess unadjusted associations between urinary cotinine and each of the four sleep dimensions of interest. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. We then applied a model building procedure, recommended by Hosmer and colleagues,[36] when selecting the final multivariable model for each sleep quality measure. The following covariates were included in all models regardless of statistical significance: age, sex and urinary creatinine concentrations. Other potential confounders identified from the literature (listed in the "Covariates" section, earlier) were included in the final multivariable model if they were significantly associated with the outcome (sleep quality measure) at $p < .05$, or if their inclusion resulted in a > 10% change in the beta coefficient of the main exposure (urinary cotinine). Furthermore, to assess whether there was a linear trend in the associations across increasing categories (< LOD and quartiles) of urinary cotinine, we calculated *p*-trend by modelling the median value within each cotinine quartile as a continuous variable.

Due to known sex differences in the metabolic processes of nicotine to cotinine,[37-39] we also performed separate analyses for males and females to explore potential effect modification of the association between cotinine and each sleep dimension by sex. A multiplicative interaction term between cotinine and sex was also tested in the models.

In our secondary analysis, using the same modelling approach described above, we performed ordinal logistic regression to assess the association between urinary cotinine concentrations and increased number of sleep problems (as defined in the "Outcomes: sleep quality" section, earlier). The increased sleep problems outcome was classified into three categories: zero sleep problems; 1 sleep problem; and ≥ 2 sleep problems. We assessed the validity of the proportional odds assumption. All analyses were performed using SAS EG version 5.1 (SAS Institute Inc., Cary, NC, USA).

Results

Sample characteristics across categories of urinary cotinine concentrations are presented in Table 1. Urinary cotinine was divided into five categories: < LOD; quartile 1; quartile 2; quartile 3; quartile 4. Accordingly, 28.7% of study participants had urinary cotinine concentrations above the LOD. Prevalence of the four sleep dimensions across levels of urinary cotinine concentrations is presented in Table 2. Among study participants, 35.6% had short

TABLE 1
Distribution of urinary cotinine concentrations (µg/L) across population characteristics, CHMS, Canada, 2007–2013

Characteristics	Cotinine levels (µg/L)						*p*-value[c]
	Total N (%)[a,b]	< LOD (< 1.1 µg/L) N = 7879 (71.3%)	Quartile 1 (1.1–60 µg/L) N = 704 (7.2%)	Quartile 2 (61–734 µg/L) N = 763 (7.1%)	Quartile 3 (735–<1408 µg/L) N = 763 (7.2%)	Quartile 4 (≥ 1408 µg/L) N = 743 (7.2%)	
Sociodemographics							
Age (N = 10 806)							
Young adults (18–25)	1296 (14.0)	786 (63.2)	190 (13.8)	155 (12.1)	94 (6.8)[d]	71 (4.1)[d]	< .0001
Adults (26–64)	7485 (72.8)	5401 (70.9)	427 (6.2)	509 (6.5)	534 (7.7)	614 (8.6)	
Older adults (≥ 65)	2025 (13.2)	1692 (82.2)	87 (5.2)	99 (4.9)	89 (4.6)	58 (3.1)[d]	
Sex (N = 10 806)							
Male	5162 (49.7)	3558 (67.2)	387 (8.2)	391 (7.5)	374 (8.3)	452 (8.8)	< .0001
Female	5644 (50.3)	4321 (75.4)	317 (6.2)	372 (6.7)	343 (6.0)	291 (5.7)	
Education (N = 10 688)							
Less than secondary school	1548 (12.9)	922 (57.2)	133 (8.7)	134 (9.6)	172 (11.8)	187 (12.7)	
Secondary school graduation or some post-secondary	2680 (26.6)	1832 (66.9)	233 (9.6)	229 (8.0)	176 (6.8)	219 (8.8)	< .0001
Post-secondary graduation	6460 (60.5)	5065 (76.9)	323 (5.6)	390 (6.1)	355 (6.0)	327 (5.4)	
Employment status (N = 10 806)							
Not employed	2183 (15.8)	1658 (72.4)	136 (7.4)	130 (7.5)	137 (7.0)	122 (5.7)	
Part-time employment (< 30 hours/week)	4469 (43.8)	3308 (72.3)	281 (6.4)	302 (7.0)	293 (7.6)	285 (6.8)	.48
Full-time employment (≥ 30 hours/week)	4154 (40.4)	2913 (69.9)	287 (7.9)	331 (7.0)	287 (6.8)	336 (8.4)	
Household income adequacy (N = 10 806)							
Lowest	723 (5.3)	377 (53.2)	69 (8.0)[d]	80 (12.3)[d]	87 (11.3)[d]	110 (15.2)	
Lower/upper middle	5215 (45.8)	3686 (67.9)	347 (7.5)	396 (8.2)	403 (7.9)	383 (8.6)	< .0001
Highest	4868 (48.9)	3816 (76.6)	288 (6.8)	287 (5.5)	227 (6.0)	250 (5.1)	
Race/ethnicity (N = 10 597)							
Non-White	2027 (21.7)	1581 (79.1)	126 (5.9)	142 (7.3)[d]	93 (4.2)	85 (3.5)[d]	< .0001
White	8773 (78.3)	6294 (69.2)	578 (7.5)	620 (7.1)	624 (8.0)	657 (8.3)	
Marital status (N = 10 800)							
Married or common-law	6607 (64.2)	5180 (75.8)	335 (5.8)	369 (5.7)	352 (6.2)	371 (6.5)	
Widowed, separated or divorced	1777 (11.3)	1229 (65.0)	96 (5.3)[d]	133 (8.0)	159 (9.9)	160 (11.7)	< .0001
Single or never married	2416 (24.4)	1465 (62.5)	272 (11.6)	261 (10.4)	206 (8.4)	212 (7.2)	
Health status							
BMI (N = 10 782)							
Underweight/normal	4041 (39.0)	2864 (69.9)	234 (6.8)	308 (7.1)	305 (8.2)	330 (8.0)	
Overweight	3895 (35.5)	2927 (72.7)	239 (6.6)	260 (7.4)	218 (6.0)	251 (7.2)	.30
Obese	3846 (25.5)	2074 (71.8)	230 (8.6)	194 (6.6)	189 (6.9)	159 (6.1)	

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TABLE 1 (continued)
Distribution of urinary cotinine concentrations (µg/L) across population characteristics, CHMS, Canada, 2007–2013

Characteristics	Cotinine levels (µg/L)						*p*-value[c]
	Total N (%)[a,b]	< LOD (< 1.1 µg/L) N = 7879 (71.3%)	Quartile 1 (1.1–60 µg/L) N = 704 (7.2%)	Quartile 2 (61–734 µg/L) N = 763 (7.1%)	Quartile 3 (735–<1408 µg/L) N = 763 (7.2%)	Quartile 4 (≥ 1408 µg/L) N = 743 (7.2%)	
Self-perceived mental health status (N = 10 772)							
Fair or poor	622 (6.0)	369 (56.3)	44 (7.8)	61 (8.0)	70 (15.1)	78 (12.8)	.0003
Good or very good	6561 (60.1)	4772 (71.7)	424 (7.4)	493 (7.5)	428 (6.7)	444 (6.6)	
Excellent	3589 (33.9)	2712 (73.3)	231 (6.6)	208 (6.3)	217 (6.3)	221 (7.5)	
Chronic comorbidities (N = 10 353)							
No	7333 (69.8)	5325 (72.0)	482 (7.0)	542 (7.4)	470 (6.5)	514 (7.0)	.23
Yes	3419 (30.2)	2523 (70.2)	221 (7.5)	215 (6.2)	236 (8.4)	224 (7.7)	
Health behaviours							
Alcohol consumption (N = 10 806)							
≤ once a month	4349 (39.6)	3271 (73.8)	242 (5.6)	242 (5.5)	282 (6.6)	312 (8.5)	< .0001
2–4 times a month	2652 (24.4)	1905 (71.5)	202 (9.0)	225 (7.8)	167 (6.1)	153 (5.5)	
2–6 times a week	2864 (26.9)	2060 (71.0)	200 (8.0)	226 (7.7)	184 (7.5)	194 (5.8)	
Everyday	941 (9.04)	643 (61.2)	60 (6.8)[d]	70 (10.2)[d]	84 (11.3)[d]	84 (10.5)[d]	
Physical activity (N = 10 789)							
Inactive (< 1.5 kcal/kg/day)	5710 (53.7)	3938 (66.3)	370 (7.6)	456 (8.4)	475 (8.9)	471 (8.8)	< .0001
Moderately active (1.5–2.9 kcal/kg/day)	2466 (21.8)	1884 (76.6)	174 (8.0)	154 (5.2)	126 (5.4)[d]	128 (4.8)	
Active (≥ 3 kcal/kg/day)	2630 (24.6)	2057 (77.6)	160 (5.6)	153 (6.0)[d]	116 (5.0)	144 (5.9)	
Self-reported smoking (N = 10 806)							
Daily	1744 (17.8)	NR	24 (0.22)[d]	415 (4.3)	615 (6.4)	680 (6.8)	< .0001
Occasionally	423 (4.0)	94 (0.87)[d]	100 (1.1)[d]	160 (1.4)	46 (0.44)[d]	NR	
Not at all	8639 (78.2)	7775 (70.3)	580 (5.9)	188 (1.4)[d]	56 (0.34)[d]	40 (0.30)[d]	

Data source: Canadian Health Measures Survey, Cycles 1–3.

Abbreviations: BMI, body mass index (kg/m^2); CHMS, Canadian Health Measures Survey; LOD, limit of detection; NR, not reportable.

[a] N represents unweighted number of respondents; percentages were weighted using sampling weights.

[b] Numbers may not sum up to totals due to missing data; percentages may not sum up to 100% due to rounding.

[c] Significance was calculated using the Rao-Scott modified chi-square test.

[d] Estimate is associated with high sampling variability (coefficient of variation is between 16.6% and 33.3%); to be interpreted with caution. NR: not reportable; estimate is associated with a very high sampling variability (coefficient of variation > 33.3%).

or long sleep duration and did not meet recommended sleep guidelines; 21.3% stated they had trouble falling or staying asleep; 15.7% of participants reported sleep dissatisfaction; and 5.5% of the participants had difficulty staying alert during normal waking hours. The proportion of short or long sleep duration (p = .004), trouble falling or staying asleep (p = .002), and sleep dissatisfaction (p < .0001) increased across higher quartiles of urinary cotinine concentrations. These differences were not significant across the urinary cotinine concentration quartiles for trouble staying alert during normal waking hours (p = .55). With the exception of sleep duration, the prevalence of poor sleep quality was higher in females compared to males. For example, female participants reported a 3.3% and 2.6% higher prevalence of trouble falling or staying asleep and sleep dissatisfaction, respectively (data not shown). The mean urinary cotinine concentrations were significantly higher among male study participants (308.9 µg/L; 95% CI: 274.0–343.8) compared to their female counterparts (209.3 µg/L; 95% CI: 179.7–238.9) (data not shown).

Urinary cotinine and sleep quality

Table 3 presents associations of urinary cotinine concentrations with the four dimensions of sleep quality, overall and by sex. Overall, compared to those with cotinine levels lower than the LOD (< 1.1 µg/L), those in quartile 4 had 1.41 (95% CI: 1.02–1.95; p-trend = .021) times the odds of short or long sleep duration (not meeting sleep duration guidelines); 1.71 (95% CI: 1.28–2.27; p-trend = .003) times the odds of trouble falling or staying asleep; and 1.87 (95% CI: 1.21–2.89; p-trend = .011) times the odds of sleep dissatisfaction. In addition, although not statistically significant, compared to those with cotinine levels below the LOD, those in quartile 4 had 1.30 (95% CI: 0.69–2.46; p-trend = .52) times the odds of difficulty staying awake during normal waking hours.

TABLE 2
Prevalence of sleep dimensions across urinary cotinine concentrations (µg/L), CHMS, Canada, 2007–2013

Sleep	Total N (%)[a,b]	Cotinine levels (µg/L)					*p*-value[c]
		< LOD (< 1.1 µg/L) N = 7879 (71.3%)	Quartile 1 (1.1–60 µg/L) N = 704 (7.2%)	Quartile 2 (61–734 µg/L) N = 763 (7.1%)	Quartile 3 (735–<1408 µg/L) N = 763 (7.2%)	Quartile 4 (≥ 1408 µg/L) N = 743 (7.2%)	
Sleep duration (N = 10 806)							
Short or long sleep duration (not meeting recommended sleep guidelines)	3 644 (35.6)	2 503 (33.6)	254 (38.6)	271 (35.9)	291 (41.9)	325 (45.0)	.004*
Recommended duration (meeting recommended sleep guidelines)	7 162 (64.4)	5 376 (66.4)	450 (61.4)	492 (64.1)	426 (58.1)	418 (55.0)	
Trouble falling or staying asleep (N = 10 796)							
Most of the time or all of the time	2 241 (21.3)	1 513 (19.9)	150 (20.6)	170 (19.5)	189 (26.7)	219 (32.5)	.002*
Never, rarely or sometimes	8 555 (78.7)	6 358 (80.1)	554 (79.4)	592 (80.5)	528 (74.3)	523 (67.5)	
Sleep satisfaction (N = 10 798)							
Never, rarely (sleep dissatisfaction)	1 651 (15.7)	1 057 (14.3)	114 (14.7)	138 (16.7)	156 (18.5)	186 (26.8)	< .0001*
Sometimes, most of the time or all of the time	9 147 (84.3)	6 816 (85.7)	590 (85.3)	624 (83.3)	561 (81.5)	556 (73.2)	
Difficulty staying alert during normal waking hours (N = 10 798)							
Most of the time or all of the time	529 (5.5)	350 (5.2)[d]	35 (5.4)[d]	34 (4.9)[d]	58 (6.8)[d]	52 (7.5)[d]	.55
Never, rarely or sometimes	10 269 (94.5)	7 523 (94.8)	669 (94.6)	728 (95.1)	659 (93.2)	690 (92.5)	

Abbreviations: CHMS, Canadian Health Measures Survey; LOD, limit of detection.

Note: Recommended sleep guidelines are from the U.S. National Sleep Foundation.[34]

[a] N represents unweighted number of respondents; percentages were weighted using sampling weights.

[b] Numbers may not sum up to totals due to missing data; percentages may not sum up to 100% due to rounding.

[c] Significance was calculated using the Rao-Scott modified chi-square test.

[d] Estimate is associated with high sampling variability (coefficient of variation is between 16.6 and 33.3%); to be interpreted with caution.

* Significant at $\alpha = .05$.

We examined the association between urinary cotinine levels and short sleep (< 7 hours) duration and long sleep (> 9 hours) duration (Table 3) and found that, compared to participants with cotinine levels below the LOD, those in quartile 4 had 1.41 (95% CI: 1.02–1.95; *p*-trend = .019) times the odds of short sleep duration. Furthermore, compared to participants with cotinine levels below the LOD, those in quartile 1 had 1.91 (95% CI: 1.22–3.01; *p*-trend = .73) times the odds of long sleep duration.

In sex-stratified analyses, we found stronger associations between increased urinary cotinine levels and poor sleep quality in females compared to males, although interaction terms were not statistically significant ($p > .05$). Specifically, elevated urinary cotinine levels were associated with significantly greater odds of short or long sleep duration, trouble falling or staying asleep and sleep dissatisfaction among females, with ORs (quartile 4 vs. < LOD) of 2.13 (95% CI: 1.29–3.51), 2.35 (95% CI: 1.43–3.84), and 2.72 (95% CI: 1.35–5.46) (all *p*-trend < .05), respectively (Table 3). The associations were weaker and not statistically significant among males.

Secondary analysis: urinary cotinine and increased number of sleep problems

Table 4 presents associations of urinary cotinine concentrations with increased number of sleep problems, overall and by sex. Compared to cotinine levels < LOD, the odds of having an increased number of sleep problems were significantly higher among those in the highest quartile of urinary cotinine (OR = 1.64; 95% CI: 1.19–2.26; *p*-trend = .001) Similar to analyses of individual sleep problems, the association between increased urinary cotinine levels and increased number of sleep problems was stronger among females (OR = 2.37; 95% CI: 1.80–2.94; *p*-trend = .007) compared to males (OR = 1.20; 95% CI: 0.86–1.54; *p*-trend = .28).

Discussion

Among study participants, 28.7% were found to have tobacco smoke exposure,

TABLE 3
Binary logistic regression analyses for the associations between urinary cotinine concentrations and sleep quality measures, overall and stratified by sex, CHMS, Canada, 2007–2013

Urinary cotinine concentrations	Overall		Males	Females
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Short/long sleep duration (not meeting vs. meeting recommended guidelines)				
	(N = 10 806)	**(N = 10 572)[a]**	**(N = 5047)[a]**	**(N = 5525)[a]**
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.24 (0.96–1.60)	1.25 (0.97–1.61)	1.00 (0.63–1.58)	1.75 (1.18–2.60)*
Quartile 2 (61–734 µg/L)	1.11 (0.84–1.46)	1.06 (0.80–1.40)	1.17 (0.75–1.82)	0.91 (0.66–1.26)
Quartile 3 (735–<1408 µg/L)	1.43 (1.04–1.95)*	1.23 (0.89–1.70)	1.15 (0.67–1.97)	1.64 (0.94–1.91)
Quartile 4 (≥ 1408 µg/L)	1.62 (1.20–2.18)*	1.41 (1.02–1.95)*	1.04 (0.70–1.56)	2.13 (1.29–3.51)*
p-trend[b]	.0001	.021	.66	.004
Short sleep duration (< 7 hours vs. 7–9 hours)				
	(N = 9975)	**(N = 9975)[a]**	**(N = 4795)[a]**	**(N = 5180)[a]**
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.13 (0.87–1.48)	1.19 (0.91–1.55)	0.95 (0.56–1.60)	1.64 (1.05–2.57)
Quartile 2 (61–734 µg/L)	1.01 (0.76–1.34)	1.04 (0.78–1.38)	1.15 (0.75–1.78)	0.87 (0.60–1.24)
Quartile 3 (735–<1408 µg/L)	1.34 (0.96–1.86)	1.24 (0.88–1.77)	1.15 (0.66–2.01)	1.40 (0.92–2.13)
Quartile 4 (≥ 1408 µg/L)	1.55 (1.16–2.08)*	1.41 (1.02–1.95)*	1.08 (0.71–1.67)	2.06 (1.27–3.33)*
p-trend[b]	.001	.019	.53	.004
Long sleep duration (> 9 hours vs. 7–9 hours)				
	(N = 7418)	**(N = 7418)[a]**	**(N = 3466)[a]**	**(N = 3952)[a]**
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.91 (1.28–2.87)*	1.91 (1.22–3.01)*	1.17 (0.61–2.26)	2.71 (1.42–5.12)*
Quartile 2 (61–734 µg/L)	1.20 (0.68–2.14)	1.16 (0.66–2.03)	1.07 (0.45–2.58)	1.16 (0.57–2.37)
Quartile 3 (735–<1408 µg/L)	1.30 (0.86–1.95)	1.17 (0.67–2.04)	0.79 (0.27–2.29)	1.63 (0.80–3.31)
Quartile 4 (≥ 1408 µg/L)	1.16 (0.63–2.16)	1.20 (0.61–2.35)	0.49 (0.19–1.29)	2.41 (0.84–6.92)
p-trend[b]	.55	.73	.093	.13
Trouble falling or staying asleep (most of the time/all of the time vs. never/rarely/sometimes)				
	(N = 10 796)	**(N = 10 563)[c]**	**(N = 5041)[c]**	**(N = 5522)[c]**
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.04 (0.69–1.58)	1.00 (0.63–1.60)	0.92 (0.46–1.85)	1.08 (0.69–1.70)
Quartile 2 (61–734 µg/L)	0.98 (0.72–1.32)	0.90 (0.64–1.28)	0.76 (0.43–1.36)	1.03 (0.62–1.70)
Quartile 3 (735–<1408 µg/L)	1.39 (0.88–2.18)	1.01 (0.62–1.64)	1.18 (0.62–2.25)	0.77 (0.45–1.33)
Quartile 4 (≥ 1408 µg/L)	1.93 (1.54–2.43)*	1.71 (1.28–2.27)*	1.26 (0.84–1.90)	2.35 (1.43–3.84)*
p-trend[b]	< .0001	.003	.24	.006
Sleep satisfaction (never/rarely vs. sometimes/most of the time/all of the time)				
	(N = 10 806)	**(N = 10 566)[d]**	**(N = 5042)[d]**	**(N = 5524)[d]**
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.03 (0.71–1.49)	0.92 (0.62–1.38)	0.82 (0.49–1.35)	0.99 (0.58–1.70)
Quartile 2 (61–734 µg/L)	1.20 (0.87–1.65)	1.11 (0.77–1.61)	1.14 (0.66–1.95)	1.04 (0.62–1.76)
Quartile 3 (735–<1408 µg/L)	1.35 (0.94–1.94)	0.85 (0.55–1.32)	0.61 (0.30–1.20)	1.24 (0.71–2.19)
Quartile 4 (≥ 1408 µg/L)	2.19 (1.52–3.16)*	1.87 (1.21–2.89)*	1.32 (0.70–2.26)	2.72 (1.35–5.46)*
p-trend[b]	< .0001	.011	.55	.004

Continued on the following page

TABLE 3 (continued)
Binary logistic regression analyses for the associations between urinary cotinine concentrations and sleep quality measures, overall and stratified by sex, CHMS, Canada, 2007–2013

Urinary cotinine concentrations	Overall		Males	Females
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)
Difficulty staying alert during normal waking hours (most of the time/all of the time vs. never/rarely/sometimes)				
	(N = 10 798)	(N = 10 565)[e]	(N = 5043)[e]	(N = 5522)[e]
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.03 (0.58–1.83)	0.78 (0.38–1.58)	0.65 (0.21–2.00)	0.92 (0.38–2.24)
Quartile 2 (61–734 µg/L)	0.94 (0.39–2.23)	0.77 (0.32–1.84)	0.73 (0.22–2.41)	0.86 (0.31–2.42)
Quartile 3 (735–<1408 µg/L)	1.32 (0.80–2.17)	0.91 (0.48–1.72)	0.75 (0.31–1.82)	1.32 (0.55–3.19)
Quartile 4 (≥ 1408 µg/L)	1.48 (0.86–2.52)	1.30 (0.69–2.46)	1.06 (0.40–2.80)	1.80 (0.79–4.11)
p-trend[b]	.13	.52	.99	.17

Abbreviations: CHMS, Canadian Health Measures Survey; CI, confidence interval; LOD, limit of detection; OR, odds ratio.

Notes: All multivariable models adjusted for age, sex (overall models only), education, alcohol consumption, perceived mental health status, physical activity and urinary creatinine concentrations. Recommended sleep guidelines are from the U.S. National Sleep Foundation.[34]

[a] Additionally adjusted for marital status, race/ethnicity and household income adequacy.

[b] *p*-value for test of increasing trend was calculated by modelling the median of each cotinine quartile as a continuous variable.

[c] Additionally adjusted for marital status, employment status, race/ethnicity, chronic comorbidities and body mass index.

[d] Additionally adjusted for employment status, household income adequacy, race/ethnicity, body mass index and chronic comorbidities.

[e] Additionally adjusted for employment status, race/ethnicity and chronic comorbidities.

* Statistically significant at $p < .05$.

with urinary cotinine concentrations above the LOD. This estimate is a larger proportion than the 16.1% of self-reported Canadians identifying as current smokers.[2] Consistent with other studies, our analyses confirm that a large number of Canadians are exposed to SHS.[3,4] Concurrently, the prevalence of sleep problems ranged from 5.5% to 35.6%. We found a positive association between increased levels of urinary cotinine concentrations and short or long sleep duration, trouble falling or staying asleep and sleep dissatisfaction. Elevated urinary cotinine concentrations were not found to be significantly associated with difficulty staying alert during normal waking hours. This finding is consistent with the previously described dose-dependent relationship between quantities of cigarettes smoked and diminished sleep quality.[17]

In our analyses, although the increasing trend between urinary cotinine levels and diminished sleep quality was evident, the association was only significant for the highest level of urinary cotinine (quartile 4 vs. < LOD) and not significant for lower levels (quartiles 1–3 vs. < LOD). Furthermore, elevated levels of urinary cotinine (quartile 4 vs. < LOD) were found to be significantly associated with higher odds of having an increased number of sleep problems. These findings indicate that active heavy smoking or excessive SHS exposure, with urinary cotinine concentrations of 1408 µg/L or higher, is strongly associated with increased odds of poor sleep quality. Accordingly, future public health campaigns targeting sleep problems should address active heavy smokers and those exposed to excessive amounts of SHS. It is

TABLE 4
Ordinal logistic regression analyses for the associations between urinary cotinine concentrations and increasing number of sleep problems, overall and stratified by sex, CHMS, Canada, 2007–2013

Urinary cotinine concentrations	Overall		Males	Females
	Unadjusted OR (95% CI)	Adjusted OR[a] (95% CI)	Adjusted OR[a] (95% CI)	Adjusted OR[a] (95% CI)
	(N = 10 794)	(N = 10 562)	(N = 5040)	(N = 5522)
< LOD (< 1.1 µg/L)	Reference	Reference	Reference	Reference
Quartile 1 (≥ 1.1–60 µg/L)	1.15 (0.87–1.54)	1.10 (0.82–1.48)	0.98 (0.55–1.42)	1.33 (0.98–1.68)
Quartile 2 (61–734 µg/L)	1.06 (0.83–1.37)	1.00 (0.76–1.32)	1.09 (0.67–1.50)	0.88 (0.50–1.26)
Quartile 3 (735–<1408 µg/L)	1.43 (1.01–2.04)*	1.14 (0.80–1.61)	1.12 (0.54–1.70)	1.15 (0.74–1.57)
Quartile 4 (≥ 1408 µg/L)	1.86 (1.41–2.45)*	1.64 (1.19–2.26)*	1.20 (0.86–1.54)	2.37 (1.80–2.94)*
p-trend[b]	< .0001	.001	.28	.007

Abbreviations: CHMS, Canadian Health Measures Survey; CI, confidence interval; LOD, limit of detection; OR, odds ratio.

[a] Additionally adjusted for age, sex (overall model only), household income adequacy, employment status, education, marital status, race, perceived mental health status, physical activity, chronic comorbidities, body mass index, alcohol consumption and urinary creatinine concentrations.

[b] *p*-value for test of increasing trend was calculated by modelling the median of each cotinine quartile as a continuous variable.

* Statistically significant at $p < .05$.

possible that some of the participants with urinary cotinine concentrations of 1408 µg/L or higher might not have followed survey instructions to refrain from smoking for 2 hours prior to the interview. The lack of association between urinary cotinine and difficulty staying alert during normal waking hours could be explained by the low prevalence of participants with this sleep problem, and potential residual confounding, as we were not able to control for factors such as caffeine intake and drug use.

Although the sex and urinary cotinine interaction terms in our models were not statistically significant, we found that the associations between urinary cotinine and measures of poor sleep quality were consistently stronger in females compared to males. This difference may be due to the fact that females tend to be more sensitive to the effects of nicotine.[40] Studies have demonstrated sex-based differences in the metabolization of cotinine; females have been found to have higher urinary cotinine levels, indicating faster cotinine metabolization rates.[41,42] Therefore, cotinine half-life among females is shorter compared to males. These sex differences in sensitivity and metabolization rate of nicotine can explain the stronger association between tobacco smoke exposure and poorer sleep quality among females compared to males. There are inconsistencies in the literature regarding sex differences in smoking or cotinine concentrations and sleep quality.[15,43] Such inconsistencies in study findings are potentially due to differences in population demographics and characteristics. Furthermore, discrepancies in definitions of the different sleep dimensions and tobacco smoke exposure assessment methods (self-reported vs. biological marker) could possibly yield inconsistent study conclusions. It has been reported that, compared with estimates based on urinary cotinine concentrations, smoking prevalence based on self-report was only 0.3% lower.[44]

Cotinine testing is widely accepted and used, despite costing more than other biomarkers or self-reported smoking or SHS. With the exception of nicotine replacement therapy use, cotinine is recognized as the most appropriate indicator of tobacco smoke exposure.[27] However, cotinine is a relevant indicator of short-term tobacco smoke exposure, and not of lifetime smoking habits. Cotinine could be measured in multiple mediums, including blood, saliva, urine and hair samples. A systematic review comparing cotinine estimates ascertained from multiple biological sources concluded that sensitivity values are consistently higher when cotinine is measured in saliva instead of blood or urine.[27]

Strengths and limitations

Our analyses were strengthened by the use of a national dataset with a large sample size, which allowed us to generate estimates with higher statistical precision and increase the generalizability of results. To our knowledge, this is the first Canadian study to examine the association between a biological marker of tobacco smoke exposure and sleep quality. The large sample size has increased the statistical power of our analyses. Furthermore, the use of urinary cotinine as a biomarker of tobacco smoke exposure, as an alternative to self-reported smoking status, reduced the chance of misclassification of exposure and biases such as the social desirability bias. Finally, our analyses provided a comprehensive understanding of the association between increased levels of urinary cotinine and sleep quality by simultaneously examining four dimensions of sleep quality.

This study has some limitations. First, sleep quality was self-reported in the CHMS. The use of a validated measure of sleep quality such as the Pittsburgh Sleep Quality Index (PSQI) could potentially fortify the results from our analyses. A validated measure such as the PSQI could also address an additional dimension of sleep quality—the timing of sleep. Second, we could not address the timing of smoking (e.g. before sleep) in our analyses, which could be a confounder. Third, detection of urinary cotinine concentrations is limited by its half-life of an average of 16 to 19 hours.[30] Furthermore, considerable individual variability exists in the rate and pattern of nicotine metabolism.[28] This could possibly affect the assessment of urinary cotinine concentrations resulting from tobacco smoke exposure. We have addressed this variability by controlling for numerous potential confounders in our analyses, including age, sex and pregnancy. Due to the relative consistency of tobacco exposure patterns over time, measurement of urinary cotinine at one time point is representative of an average daily exposure.[32] Participants of the CHMS only report on general patterns. As such, our analyses are limited by the lack of time correspondence for the measurement of urinary cotinine and sleep quality. Finally, due to the cross-sectional nature of CHMS data, temporality between elevated level of urinary cotinine and sleep quality could not be established. However, the stimulating effects of nicotine and subsequent diminishment of sleep quality can be effectively captured cross-sectionally, considering the relatively rapid effects of nicotine on the human brain.[45] Therefore, capturing the association between tobacco smoke exposure and sleep quality at one point provides a sufficient understanding of the association between exposure and outcome of interest.

Conclusion

Using national survey data on Canadian adults and urinary cotinine as a biological marker of tobacco smoke exposure, our study provides support for a positive association between tobacco smoke exposure and diminished sleep quality. Considering the high prevalence of sleep problems, our study adds to the body of literature substantiating public health efforts to reduce the prevalence of smoking and exposure to SHS. To directly infer causality, future studies should investigate the association between urinary cotinine levels and sleep quality prospectively using a validated measure of sleep quality such as the PSQI or an objective method of measuring of sleep quality, such as actigraphy.

Conflicts of interest

The authors declare there are no conflicts of interest.

Authors' contributions and statement

MZ, VC, DPR and MTD were all involved in the conceptualization of the work, study design, and the analysis and interpretation of the data. MZ led the process of drafting and revising the final manuscript for submission. MZ reviewed the titles and abstracts of articles identified in the systematic search. MZ, the primary author, contributed to the design and conceptualization of the work, data analysis, interpretation of the data, and drafting and revising of the paper. VC and MTD also contributed to the acquisition of the data, design and conceptualization of the work, data analysis, interpretation and revising of the paper.

The content and views expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

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