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Evaluation of a 24-Hour Caffeine Intake Assessment Compared with Urinary Biomarkers of Caffeine Intake among Young Adults in Canada

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Abstract

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AUTHOR CONTRIBUTIONS

L. Vanderlee and D. Hammond designed the research; L. Vanderlee, J. L. Reid, C. M. White, and R. B. Acton conducted the research; S. I. Kirkpatrick, M. E. Rybak, and C.-I. Pao provided essential materials and analyzed the data; L. Vanderlee, S. I. Kirkpatrick, and D. Hammond conducted statistics analysis; L. Vanderlee, R. B. Acton, J. L. Reid, and C. M. White wrote the paper; L. Vanderlee and D. Hammond had primary responsibility for final content. All authors read and approved the final manuscript.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, the Department of Health and Human Services, or the United States Government.

Supplementary materials:

The Figure is available at www.jandonline.org

STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

Background—Caffeine is a widely consumed stimulant, and caffeine-containing products are increasingly available on the market. Few tools are available to capture caffeine intake, particularly among young adults. To estimate caffeine consumption in the previous 24 hours, the 24-Hour Caffeine Intake Recall (CIR-24) was modeled after the Automated Self-Administered 24-Hour Dietary Assessment Tool, using a brand-specific database of caffeine-containing foods, beverages, and supplements.

Objective—To evaluate the accuracy of the CIR-24 compared with caffeine concentration biomarkers in urine and a caffeinated beverage intake frequency screener (CBQ) designed to assess usual intake among a young adult population in Canada.

Design/participants—In all, 79 young adults, aged 18 to 29 years, provided 24-hour urine samples and completed the CIR-24 and CBQ.

Main outcome measures—Excretion for caffeine and eight caffeine metabolites were quantified from urine samples using high-performance liquid chromatography-polarity switching electrospray ionization-tandem quadrupole mass spectrometry with stable isotope-labeled internal standards.

Statistical analyses performed—Pearson correlations and weighted κ coefficients were calculated for the self-report tools and caffeine biomarkers.

Results—The CIR-24 was significantly positively associated with all caffeine biomarkers (r_p=0.28 to 0.52, κ=0.39 to 0.59), and the CBQ was significantly positively associated with all but one biomarker (r_p=0.21 to 0.40, κ=0.32 to 0.45). The CIR-24 yielded a higher mean intake of caffeine than the CBQ. There was strong linear correlation between the CIR-24 and CBQ (r_p=0.60, P<0.001), but poor agreement in absolute caffeine consumed (t=2.83, P=0.006); quartile ranking concordance was 0.44 (P<0.001). The CIR-24 performed better than the CBQ across all biomarkers in both linear correlation and quartile ranking.

Conclusions—Although both the CIR-24 and CBQ performed reasonably well in capturing caffeine intake compared with urinary biomarkers of caffeine consumption, the CIR-24 had stronger agreement than the CBQ. The results suggest that the CIR-24 is a promising tool for evaluating caffeine intake among this population.

Keywords

Caffeine intake; Validation study; Biomarkers; Food frequency questionnaire; Dietary recall

CAFFEINE IS A WIDELY CONSUMED STIMULANT. Caffeine consumption among younger age groups has emerged as a public health concern with the emergence of new categories of caffeinated products, many of which are marketed directly toward young adults.[1,2] The growing popularity of caffeinated beverages and food products has raised concerns about the potential health effects of caffeine consumption among children and adolescents. Childhood and adolescence are critical periods for growth and brain development, making youth particularly vulnerable to the effects of caffeine.[3] Caffeine consumption in children and adolescents has been associated with sleep disturbances, anxiety, elevated blood pressure, impaired mineral absorption and bone health, and alcohol dependence.[3–8] In adults, regular caffeine consumption (up to 400 mg/day) has similarly

been associated with poor sleep quality and anxiety, and excess caffeine consumption (over 400 mg/day) has been linked to low bone mineral density and high blood pressure.[9] There is particular concern regarding caffeine consumption among sensitive populations, such as those with preexisting conditions or those carrying specific genotypes putting them at risk for adverse reactions to caffeine.[9]

Research examining caffeine consumption in Canada is limited. In 1992, Chou reported daily caffeine intake to be about 2.4 mg/kg body weight among Canadian adults and 1.1 mg/kg among Canadian children aged 5 to 18 years.[10] In 2001, Brown and colleagues found average caffeine intakes ranging from 288 to 426 mg/day among adults in southern Ontario.[11] Analyses of food and beverage intake data derived from the 2004 Canadian Community Health Survey indicate that 24% of men and 17% of women aged 31 to 50 consumed more than Health Canada's recommended daily limit of 400 mg of caffeine for adults.[12] Overall, coffee accounted for the majority (81%) of Canadian adults' caffeine consumption, followed by tea (12%) and soft drinks (6%).[12] More recent data from the United States suggest that 71% of children consumed caffeine on any given day in 2009–2010, and 10% of 12- to 19-year-olds exceeded the maximum daily caffeine intake of 2.5 mg/kg suggested by Health Canada for this age group.[13] The median daily caffeine intake among Americans aged 12 to 19 years was 14 mg per day overall, and as high as 41 mg per day among those of the same age who reported consuming caffeine regularly.[13] There is a need for updated accurate caffeine consumption data in Canada, and a concomitant need for low-burden tools to enable ongoing monitoring of consumption.

An emerging technique for estimating caffeine consumption is through the direct analysis of caffeine and its metabolites in serum or urine, which have been shown to be closely associated with caffeine intake in a dose-dependent manner.[14,15] Previous work has found that measurement of caffeine and its metabolites in urine can provide adequate sensitivity to detect caffeine intake as low as 0 to 8 mg per day[15] and that the majority of the metabolites are excreted within 24 hours, suggesting that 24-hour urine collections can provide realistic estimations of caffeine intake.[16] However, the implementation of biomarkers in large-scale research is rarely feasible. Population-based studies thus typically rely on more feasible and less invasive methods, such as self-reported consumption of sources of caffeine; self-report tools may range from brief questionnaires to in-depth dietary recalls or records. Compared with brief frequency-type tools, the more comprehensive data captured by recalls and records have been shown to provide more accurate estimates of overall dietary intake and are the source of most existing estimates of caffeine intake.[17] However, completion of a full dietary recall to capture the total diet can be time-consuming and is not feasible in all circumstances. Thus, a small number of brief caffeine-specific intake tools have been developed to support a variety of research areas.[18–21] Such tools tend to adopt a frequency approach that requires respondents to average intake over time (ie, intake of caffeine-containing products over the previous month); this averaging can be cognitively challenging, introducing bias. These tools are typically limited to beverages and do not capture the full spectrum of caffeine-containing products, and they also lack brand-specific information, limiting our understanding of intake of beverage subcategories that are particularly high in caffeine.

To advance the measurement of caffeine intake for studies in which a comprehensive measure of the total diet may not be viable, an in-depth targeted online 24-hour dietary recall questionnaire, the Caffeine Intake Recall (CIR-24), was developed focusing specifically on food and beverage products that are sources of caffeine to capture single-day intakes of caffeine. The objective of the analyses described in this article was to evaluate the accuracy of data on caffeine intake from the CIR-24 in comparison with caffeine biomarkers collected from urine samples, including caffeine and eight caffeine metabolites identified as concentration biomarkers.[15] The researchers hypothesized that the 24-hour caffeine recall would demonstrate validity as a measure of caffeine intake in the previous day when compared with biomarkers as an objective indicator of consumption. In addition, the study sought to contrast estimates from the 24-hour caffeine recall to those from an existing short caffeinated beverage intake frequency screener developed by the Fred Hutchison Cancer Center.[22] It was hypothesized that the 24-hour caffeine recall would more accurately capture caffeine intake in the previous day than the caffeinated beverage frequency questionnaire, because the caffeinated beverage frequency questionnaire is meant to capture usual intake rather than caffeine intake in the previous day.

METHODS

A total of 85 young adults were recruited from a university community in southwestern Ontario from June to August 2015. Young adults were identified as a target population because they have some of the highest rates of caffeine consumption, and rates of caffeine consumption are known to decrease over time.[12] Recruitment strategies included distributing flyers to students on campus and in community settings, posting flyers in public areas, and making announcements to undergraduate classes using a consecutive sampling technique. Interested participants e-mailed the research team and were contacted via telephone to assess eligibility using a brief survey. Eligible participants were between 17 and 30 years of age, could read and speak English, had not smoked a cigarette in the past month, were not pregnant or taking oral contraceptives (because the previous two factors are known to influence caffeine metabolism[23]), and reported that they consumed at least some caffeine in a typical day.

The researchers attempted to recruit an equal number of males and females, as well as students who self-reported consuming low, moderate, and high amounts of caffeinated beverages (within each sex) by self-reporting “Would you say you consume no caffeine, a little caffeine, a moderate amount, or a lot of caffeine? By moderate I mean between 1 small coffee and up to two medium coffees or up to one extra large per day; or less than two caffeinated energy drinks per day; or 3 to 4 cups of caffeinated tea or cans of soda pop per day”; and reported if they consumed no caffeine, very little caffeine, a moderate amount of caffeine, or a lot of caffeine. The caffeine consumption quotas were relaxed due to low response from high-intake consumers. Participation in the study included the collection of a 24-hour urine sample and the completion of three brief questionnaires: (1) the CIR-24; (2) a caffeinated beverage frequency questionnaire (Caffeinated Beverage Questionnaire [CBQ]); and (3) a background questionnaire. Participants were remunerated with $50 for study completion. This study was reviewed and received ethics clearance through the University of Waterloo Research Ethics Committee (ORE #20262) and all

participants provided written informed consent. The analysis of blinded specimens by the Centers for Disease Control and Prevention (CDC) laboratory was determined not to constitute engagement in human subjects research. This study was registered in the National Cancer Institute Dietary Assessment Calibration/Validation Register.

Urine Samples

Each participant attended an on-campus group session (n=22 sessions) to receive verbal and written instructions and materials for sample collection and storage. Urine samples were collected from the time participants woke the following day, for the subsequent 24-hour period. Participants were instructed to discard the first void of the 24-hour period, but to include the final void at the end of the 24-hour period (ie, the next morning). Urine was collected in 250-mL containers, which were either immediately transferred to a refrigerated 4-L container, or kept in an insulated carry bag with ice packs and added to the refrigerated 4-L container as soon as possible (within a maximum of 4 hours). Participants were instructed to refrigerate the 4-L container at all times and to return it to the laboratory in an insulated carry bag with ice packs.

When participants returned to the laboratory the day after sample collection, they completed the three brief questionnaires (the order of the CIR-24 and the CBQ alternated for each session to minimize potential order bias).

24-Hour Caffeine Intake Recall

The online, self-administered CIR-24 was developed to measure dietary intake of caffeine from food, beverages, and supplements. The tool was based on the Automated Self-Administered 24-Hour Dietary Assessment Tool (ASA24), a web-based, self-administered tool for collecting dietary recalls and records (http://epi.grants.cancer.gov/asa24/).[24,25] ASA24 uses a multiple-pass method adapted from the automated multiple-pass method used in National Health and Nutrition Examination Survey in the United States and the Canadian Community Health Survey in Canada.[25] The same general question structure was used in this custom online survey, but the items queried were limited to foods, beverages, and supplements that may contain caffeine. The tool was adapted for the Canadian context by listing Canadian products, changing container sizes to reflect the Canadian marketplace, and including a French version. The food, beverage, and supplement categories and subcategories can be found in the Figure (available at www.jandonline.org). Specific items listed were based on ASA24 and the Canadian Nutrient File,[26] with additional items identified through the US Department of Agriculture National Nutrient Databases[27] and Internet searches.

Respondents were asked about the consumption of items from each of four main categories (beverages, foods, energy products with added caffeine, and supplements) in the prior day. Based on each food or beverage reported, the participant received tailored probes to identify the specific items that may have contained caffeine (eg, if carbonated beverage consumption was reported, the participant was asked to specify the type of carbonated beverage and brand consumed).

Amounts of each item consumed were ascertained based on the particular category: food amounts were estimated by the number of items or pieces consumed, or by a volume amount (depending on the item); beverage amounts were estimated using images of container types and sizes (adapted from the ASA24) (or volume for powders, liquids, and concentrates); and supplements were estimated by unit (or volume for powders and liquids). The CIR-24 tool is available at http://davidhammond.ca/wp-content/uploads/2015/11/2014-CED-Technical-Report.pdf.

A database specifying the caffeine content of all food and beverage items in the Canadian Nutrient File listed as containing caffeine (with some additional items from the US Department of Agriculture National Nutrient Database for Standard Reference), plus energy drinks, shots, and products (sourced from the nutrition information on products purchased in previous studies, as well as Internet searches), and supplements listed as containing caffeine in Health Canada's Licensed Natural Health Products Database (http://www.hcsc.gc.ca/dhp-mps/prodnatur/applications/licen-prod/lnhpdbdpsnh-eng.php) or identified through an online pharmacy (www.well.ca) was compiled. Brand-specific values were added for popular products such as coffee, using information provided by manufacturers (eg, Starbucks, Tim Horton's, McDonald's) or websites that aggregate nutrition information (http://www.cspinet.org/new/cafchart.htm).

In this study, the CIR-24 was completed on iPads. Unlike the ASA24, the CIR-24 does not include automated coding of nutrient amounts. A trained research assistant, blinded to urine analysis results, reviewed and coded caffeine amounts in each respondent's response. Each item reported by a subject was assigned a caffeine value from the database according to the amount consumed.

Caffeinated Beverage Questionnaire

A paper version of a Supplemental Beverage Questionnaire that contained the CBQ from the Fred Hutchison Cancer Center, adapted for use in Canada (eg, milliliter measures were included in addition to fluid ounces), was also administered.[22] This measure is widely used but has not been previously evaluated for validity to the authors' knowledge. The CBQ asks, "Thinking of the last month, how often do you drink each beverage?" and includes 13 beverage categories, including caffeinated and decaffeinated coffee (brewed and instant) and tea, energy drinks and highly caffeinated soda pops, regular colas and root beer, and caffeine-free colas and root beer, that also align with caffeinated beverages in the Canadian marketplace. Nine frequency categories were included: Never or less than once per month; one to three per month; one per week; two to four per week; five to six per week; one per day; two to three per day; four to five per day; six or more per day. A reference for a medium size for each type of beverage category was provided; respondents stated whether each drink size was small, medium, or large in comparison to the reference amount.

Responses to the CBQ were used to calculate average daily caffeine consumption for each respondent to estimate usual consumption, as per instructions in the CBQ materials.[22] First, the number of annual servings consumed for each questionnaire item was calculated by multiplying the reported frequency (adjusted for annual intake, eg, one per week=52 per year) by the reported portion size, to estimate annual intake. A small size was multiplied

by a serving ratio of 0.5, and a large size was multiplied by 1.5. Next, the average annual volume of each beverage consumed was divided by 365 to estimate the daily intake of each beverage. The caffeine database that accompanies the tool was used to calculate the amount of caffeine consumed in milligrams. In cases in which frequency data for items were missing, it was assumed that none was consumed, and when a frequency was entered but no portion size was indicated, the medium size was assumed. Comparing the CBQ to the CIR-24 and urinary biomarkers allowed us to examine whether there were differences in intake between the previous day and usual intake, and also to examine whether or not usual intake accurately predicted intake for the previous day.

Background Questionnaire

The background questionnaire collected sociodemographic information, including ethnicity, formal education completed, and height and weight (used to calculate body mass index). Participants were also asked if they had smoked in the past week, or if they had used oral contraceptives, to verify data collected during screening. In addition, they were asked if there had been any issues with urine collection or storage that may have affected the urine sample.

Urine Sampling and Analysis

For each participant, all urine samples were combined, and the total volume of the entire 24-hour sample was recorded. A sample from each participant was aliquoted into a 2-mL cryovial, and immediately frozen at −80°C. Samples were moved for 8 days to a −20°C freezer due to logistical issues and were later returned to −80°C. At the end of the study period, all samples were transported in insulated containers with dry ice to the CDC Nutritional Biomarkers Branch in Atlanta, GA, for analysis.

Urine concentrations for caffeine (1,3,7-trimethylxanthine) and eight caffeine metabolites (1,7-dimethylxanthine [paraxanthine]; 1,3-dimethylxanthine [theophylline]; 1,3,7-trimethyluric acid; 1,3-dimethyluric acid; 1,7-dimethyluric acid; 1-methyluric acid; 1-methylxanthine; and 5-acetylamino-6-amino-3-methyluracil) were quantified by use of a high-performance liquid chromatography-polarity switching electrospray ionization-tandem quadrupole mass spectrometry with stable isotope-labeled internal standards based on a method reported previously.[28] Existing studies indicate that these metabolites have moderate correlation with caffeine intake.[15] The limits of detection were 0.05 μmol/L for 1-methyluric acid; 0.01 μmol/L for theophylline; 0.02 μmol/L for 1,3-dimethyluric acid and 1,7-dimethyluric acid; 0.005 μmol/L for 1,3,7-trimethyluric acid; 0.03 μmol/L for 1-methylxanthine; 0.003 mmol/L for caffeine; 0.006 μmol/L for paraxanthine; and 0.1 μmol/L for 5-acetylamino-6-amino-3-methyluracil. Samples that had amounts below the limits of detection were included in the sample at the median point between 0 and the limits of detection to reduce bias. This was required for two samples for 1,3-dimethyluric acid, one sample for theophylline, and one sample for 1,3,7-trimethyluric acid.

Statistical Analysis

Pearson correlations were estimated to examine linear associations between absolute values of self-reported caffeine intake from the self-report tools (CIR-24 and CBQ) and the

caffeine biomarkers. Weighted κ coefficients were calculated between quartile ranking of the self-report tools and the caffeine biomarkers. Both types of analyses were conducted to examine both linear correlation, as well as the ability of the tools to rank caffeine consumption according to quartiles. Pearson correlations and κ coefficients were also used to examine associations between estimates from the two self-reported tools, and one-sample *t* tests were used to examine differences between the two tools. All statistical analyses were conducted using SPSS v.24 (IBM Corp). A sample size calculation was conducted using the mean caffeine intake from a population-based study to ensure sufficient power to detect a "moderate" correlation of 0.2 or greater. Significance was considered at a level of $P<0.05$.

RESULTS

Of the 85 participants, three were excluded from the analysis because the quality of their urine samples was compromised during the urine collection process (as reported by participants or research assistants handling urine for reasons including significant spillage, improper storage, or transportation techniques that resulted in prolonged periods with no refrigeration; creatinine was not used to assess 24-hour urinary completeness). An additional three participants who reported that they had smoked tobacco in the previous week were also excluded, resulting in a final sample size of 79. As described in Table 1, the sample had large representation of nonwhite subjects (56%), was predominantly normal weight (body mass index 18.5 to 25.0), and had a range of education levels, with 18% having completed high school or less.

Caffeine Intake and Sources of Caffeine

Table 2 shows descriptive characteristics of caffeine intake according to the CIR-24 and the CBQ. Overall, the CIR-24 yielded a higher mean intake of caffeine than the CBQ (150.5 mg vs 112.6 mg). Overall, two females (5%) and three males (8%) had an intake of greater than the maximum amount to consume per day according to Health Canada (400 mg). According to the CIR-24, beverages were the primary source of caffeine. Across the entire sample (n=79), mean reported caffeine from beverages was 140.9 mg (SD=147.8), compared with 5.0 mg from food (SD=13.7), 3.7 mg from supplements (SD=19.3), and 0.9 mg from other products (SD=5.6).

From the CIR-24, among those who reported consuming any source of caffeine (n=75), beverages were the only reported source of caffeine for 41%, whereas 13% of those who consumed caffeine did not report any caffeine-containing beverages. Of those who consumed caffeine, 53% reported consumption of caffeine from food sources: for 11%, foods were the sole source of caffeine, whereas for 35%, food sources represented less than 10% of caffeine intake. Very few participants who consumed caffeine reported intake of caffeine-containing supplements (5%) or caffeine products (3%).

Comparisons between the CIR-24 and CBQ

There was strong linear correlation between the CIR-24 and CBQ (r_p=0.60, $P<0.001$), and quartile ranking concordance was 0.44 ($P<0.001$). The mean difference between total caffeine consumed according to the CIR-24 and estimated average daily intake in the CBQ

was 37.91 mg (one-sample *t* test value=2.83, *P*=0.006), indicating poor agreement in the absolute amount of caffeine consumed over the 24-hour period estimated by the CIR-24 in the previous day and usual 24-hour intake of caffeine using the CBQ. Bland-Altman plots were not constructed due to poor overall agreement.

Comparison between Self-Reported Measures and Urinary Caffeine Metabolites

Table 3 outlines the biomarker excretion levels for this study population, and Table 4 describes the Pearson correlations and κ coefficients between the CIR-24 and CBQ and caffeine biomarkers. Estimates from both the CIR-24 and the CBQ were significantly positively correlated with all metabolites, with the exception of 1,3,7-trimethyluric acid, which was not significantly associated with absolute values from the CBQ (r_p=0.21, *P*=0.06). Pearson correlation values for the CIR-24 ranged from r_p=0.28 for 1,3,7-trimethyluric acid to r_p=0.52 for caffeine. The CIR-24 performed better than the CBQ across all metabolites. The weighted κ coefficient for agreement when participants were ranked by quartiles was considered moderate to good for the CIR-24 (ranging from 0.39 for 1,3-dimethyluric acid to 0.59 for caffeine) and moderate for the CBQ (from 0.32 for 1-methyluric acid to 0.45 for caffeine).

DISCUSSION

Overall, the CIR-24 performed well in capturing caffeine intake compared with urinary caffeine metabolites from the previous day. The CIR-24 had stronger correlations and agreement with biomarkers than the CBQ, likely a result of the time frame of the recall being specific to the previous day and matching the time period of the urine collection, compared with the CBQ, which averages consumption of sources of caffeine intake over the previous 30 days, and also a result of the tool only estimating caffeine intake from beverages and not assessing intake from foods and other products containing caffeine.[22] This suggests that although tools that assess usual intake have some association with intake in the previous day, tools that examine intake in the previous day are more likely to accurately assess actual intake.

The CIR-24 indicated higher levels of caffeine than the usual intake frequency questionnaire, which is contrary to previous research comparing multiple day 24-hour dietary recalls and frequency questionnaires for caffeinated beverages only.[29] The higher caffeine intake identified by the CIR-24 in this study is not surprising, given that the recall assessed additional sources of caffeine intake, including food, supplements, and other products that contain caffeine, rather than beverages only. The ability to examine caffeine intake from nonbeverage sources is unique to the CIR-24 and an issue that has been identified in the literature as critical to estimating overall caffeine intake and understanding how less traditional caffeine sources are contributing to caffeine intake.[30] Caffeine products or highly caffeinated foods, such as caffeinated chewing gum or chocolate bars, caffeine powders and caffeine pills, are increasingly being marketed to consumers. In Canada, foods and beverages high in caffeine, such as energy drinks, have recently been regulated as food products instead of natural health products and have been identified as an area of interest to Health Canada.[31] This study found that a small but not insignificant proportion of

participants consumed caffeine from foods and energy products; therefore, it is increasingly important for tools to account for these sources.

The proportion of participants that consumed more than the recommended amount of caffeine per day (400 mg) was similar to population-level national estimates in Canada captured using 24-hour dietary recalls among those 19 to 30.[12] The results for caffeine consumption according to self-report using the CIR-24 and biomarkers of caffeine intake yielded by this study are similar to a prior study that compared data from a full 24-hour dietary recall with biomarkers obtained from spot urine samples for this age group (20 to 39 years).[15] Full 24-hour dietary recalls can be time-consuming to complete, and they place a greater burden on participants compared with brief tools. A challenge in examining caffeine intake using recall data is the lack of caffeine information and brand-specific values for some or all products within nutrient databases, such as the Canadian Nutrient File, that are associated with tools such as ASA24 and its Canadian adaptation, ASA24-Canada (asa24.ca). The CIR-24 used brand-specific values for popular products to obtain more precise estimates of caffeine intake, likely increasing the accuracy of the tool in comparison with other tools (including the CBQ), which rely on generic caffeine values. A customized database such as this has been identified as important for understanding caffeine intake globally.[30] Although CIR-24 has low respondent burden, it should be noted that the data require manual coding, a function that could be automated in future iterations to increase usability.

Study Strengths and Limitations

To the authors' knowledge, this is the first targeted tool developed for the assessment of caffeine intake. This study used biomarkers to evaluate the self-report data captured by the CIR-24, avoiding challenges, such as autocorrelation, inherent in comparing data from one self-report tool to that from another (a common approach in the evaluation of dietary measures due to the lack of markers of true intake). Although caffeine metabolites in urine represent concentration as opposed to recovery biomarkers and therefore are not markers of true intake, prior research has shown moderate correlations with consumption.[32] Until a recovery biomarker is identified for caffeine, alternative approaches to assess the validity of self-report estimates relative to unbiased estimates are unavailable, with the exception of observation, which does not capture intake among free-living subjects.

The sample was recruited both on a university campus and in the community, and almost one-fifth of the sample had completed at most high school, which increases the generalizability of the results to other young adult populations. The study excluded subjects who reported lifestyle factors known to influence caffeine pharmacokinetics, including smoking, pregnancy, and use of oral contraceptives among females; however, it is likely that individual-level factors known to influence caffeine metabolism that were not controlled for in the study, such as genetic factors, are responsible for some of the variation in the association between caffeine biomarkers and self-reported caffeine intake.

The study has several limitations. A mechanical issue with the freezer storing the urine samples resulted in the samples being temporarily transferred to freezers maintained at −20°C instead of −80°C; however, this lower temperature storage is consistent with other

studies examining urinary caffeine metabolites that typically store samples at −20°C and is not expected to have affected the metabolite concentrations in the samples.[16] Also, targeting the CIR-24 to only caffeine-containing foods and beverages may increase the likelihood of misreporting for products that are often consumed in combination (such as soda and snacks) and does not allow for the analysis of intake of caffeine-containing products in comparison with other aspects of diet. Additional research would be helpful to examine the sensitivity of the tool to changes in caffeine consumption over a longer period of time.

CONCLUSION

The CIR-24 tool performed relatively well in assessing caffeine intake among young Canadian adults ages 18 to 30 in relation to caffeine metabolites in urine. Comparability of values from the tool was greater than for an existing tool, potentially due to the focus on comprehensively capturing intake for a short period of time as well as the use of brand-specific caffeine values. The CIR-24 may serve as new easy-to-use tool to estimate caffeine intake in population-based studies with a particular focus on caffeine consumption and could also be used as a supplement to a 24-hour recall when investigating outcomes for which energy or other nutrients are potential confounders, or when interest is in examining caffeine intake in relation to overall dietary patterns or other components of concern, such as added sugars.

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RESEARCH SNAPSHOT

Research Question:

How accurate are estimates of caffeine consumption from an online 24-hour caffeine intake assessment among young adults?

Key Findings:

In a validation study that included 79 young adults, estimates of caffeine consumption based on a 24-Hour Caffeine Intake Recall (CIR-24) tool were found to be positively associated with all urinary biomarkers of caffeine concentration.

Main category	Subcategories
Beverages	Coffee or espresso beverages (eg, latte, *Frappuccino*[a]) Tea beverages (eg, hot or iced, chai) Chocolate or coffee-flavored beverages (eg, chocolate milk, hot chocolate, chocolate-flavored supplement or protein beverages, coffee liqueur) Soft drinks (eg, soda pop, *Slurpee*[b], *Starbucks Refreshers*[a]) Energy drinks (eg, *Red Bull*[c], *Monster*[d], *Rockstar*[e], *NOS*[d], *Amp*[f], and *Full Throttle*[d], but there are others; include energy "shots" and energy drinks mixed with alcohol, but *do not* include sports drinks, such as *Gatorade*[f] or *Powerade*[g]) Energy water (eg, *VitaminWater Energy*[g], *SoBe Lifewater B-Energy*[f], *RockStar Energy Water*[e], *MiO Energy*[h])
Foods	Chocolate bars, candy, and sweets Granola or protein or nutrition bars with chocolate, energy bars Baked goods with chocolate or coffee (eg, cookies, cakes) Chocolate or coffee ice cream, frozen desserts, yogurt, pudding, other desserts Chocolate syrups, dips, or spreads (including *Nutella*[i])
Energy products with added caffeine	Energy gum Energy mints Energy strips or sheets Energy candy or chews Caffeinated foods (eg, caffeinated marshmallows, jerky, waffles, ice cream, cereal, chips, *Sumseeds*[j]) Caffeine powders or absorbable caffeine (sprays, patches, or powders) Other caffeinated product
Supplements	Vitamin or mineral supplements (eg, multivitamin, vitamin C, calcium) Herbal, botanical, or dietary supplements (eg, ginseng, Echinacea, probiotics) Green tea extract or green coffee bean extract Energy or alertness supplements, pills, or medications (eg, caffeine capsules or pills, *Wake-Ups*[k], *Total Energy*[l], guarana capsules) Diet or weight-loss supplements or pills (eg, *Hydroxycut*[m], *Xenadrine*[n], *Lean+*[o]) Workout supplements (eg, *BPI Sports 1.M.R.*[p], *Cellucor C4 Extreme*[q], *Dymatize Xpand 2x*[r], *SuperPump Max*[s]) Other supplements

[a]Starbucks Corporation.
[b]7-Eleven stores.
[c]Red Bull GmbH.
[d]Monster Beverage Corporation.
[e]Rockstar, Inc.
[f]PepsiCo.
[g]The Coca-Cola Company.
[h]Kraft Foods.
[i]Ferrero.
[j]Dakota Valley Products Inc.
[k]Adrem Brands Inc.
[l]Jamieson Laboratories Ltd.
[m]Iovate Health Sciences Inc.
[n]Cytogenix Sciences.
[o]Genuine Health.
[p]BPI Sports.
[q]Cellucor.
[r]Dymatize Nutrition.
[s]Gaspari Nutrition.

Figure.

Sublists of main Caffeine Intake Recall (CIR-24) categories. Superscript letters indicate manufacturer names for products and were not shown to participants as part of the CIR-24.

Table 1.

Sample characteristics of young Canadian adults participating in a study evaluating the accuracy of a 24-Hour Caffeine Intake Recall and Caffeinated Beverage Frequency Questionnaire (n=79)

Characteristic	Total	Men	Women	χ^2 P value
		% (*n*)		
Sex				
Female	51 (40)			
Male	49 (39)			
Age, y				0.38
18–21	57 (45)	56 (22)	58 (23)	
22–25	25 (20)	31 (12)	20 (8)	
26–29	18 (14)	13 (5)	22 (9)	
Education				0.79
High school or less	18 (14)	18 (7)	19 (7)	
Some university, no degree	46 (36)	46 (18)	45 (18)	
Completed university degree	19 (15)	23 (9)	15 (6)	
Postgraduate degree	18 (14)	13 (5)	23 (9)	
Ethnicity				0.68
White	44 (35)	49 (19)	40 (16)	
Other	55 (43)	49 (19)	60 (24)	
Prefer not to say	1 (1)	2 (1)	0 (0)	
BMI [a] [b]				0.63
Underweight	1 (1)	3 (1)	0 (0)	
Normal weight	75 (59)	67 (26)	83 (33)	
Overweight	19 (15)	26 (10)	12 (5)	
Obese	1 (1)	3 (1)	0 (0)	
Missing data	4 (3)	3 (1)	5 (2)	

[a] BMI=body mass index.

[b] For χ^2 analysis, BMI was grouped to represent underweight or normal weight and overweight or obese.

Table 2.

Self-reported caffeine consumption among a sample of Canadian adults according to the CIR-24[a] and the CBQ[b] (n=79)

Parameter	CIR-24	CBQ
	mean±SD[c]	
Mean, mg	150.51±148.4	112.61±103.7
Median, mg	124.9	94.1
Range, mg	0.0–780.0	2.2–524.7
Quartiles	*range, mg*	
25th	0.0–27.3	2.2–36.4
50th	27.4–124.8	36.5–94.0
75th	124.9–197.8	94.1–147.0
100th	197.9–780.0	147.1–524.7

[a]CIR-24=24-Hour Caffeine Intake Recall.

[b]CBQ=Caffeinated Beverage Frequency Questionnaire.

[c]SD=standard deviation.

Table 3.

Metabolite excretion for the caffeine and the eight metabolites most closely associated with caffeine intake among a sample of Canadian adults (mean excretion and by intake quartile according to the CIR-24[a])

Analyte	Mean	Caffeine Intake (CIR-24)			
		Q1[b]	Q2[c]	Q3[d]	Q4[e]
		μmol/L			
Caffeine (1,3,7-trimethylxanthine)	7.42 (5.67–9.17)	0.96 (0.14–1.78)	4.24 (2.67–5.81)	10.45 (6.81–14.08)	13.55 (9.58–17.51)
Paraxanthine (1,7-dimethylxanthine)	26.55 (20.61–32.49)	4.70 (2.21–7.20)	18.84 (11.77–25.90)	35.14 (22.36–47.91)	45.90 (32.28–59.53)
Theophylline (1,3-dimethylxanthine)	2.35 (1.80–2.91)	0.55 (0.23–0.88)	1.58 (0.99–2.16)	3.38 (1.92–4.84)	3.78 (3.59–4.97)
1,3,7-Trimethyluric acid	2.29 (1.60–2.98)	0.37 (0.15–0.60)	1.47 (0.90–2.03)	3.62 (1.36–5.89)	3.59 (2.31–4.88)
1,3-Dimethyluric acid	7.87 (6.12–9.61)	2.44 (0.64–4.24)	5.24 (3.39–7.10)	11.59 (7.02–16.16)	11.91 (8.27–15.55)
1,7-Dimethyluric acid	31.84 (23.32–40.36)	7.44 (1.98–12.90)	19.36 (12.59–26.13)	48.11 (23.12–73.10)	51.09 (33.19–69.00)
1-Methyluric acid	68.55 (53.13–83.98)	20.34 (9.72–30.97)	46.40 (32.26–60.54)	99.77 (65.86–131.68)	105.92 (65.30–146.44)
1-Methylxanthine	46.54 (35.52–57.56)	10.59 (4.58–16.59)	31.50 (21.02–41.97)	71.33 (46.23–96.43)	70.97 (43.21–98.73)
5-Acetylamino-6-amino-3-methyluracil	75.84 (59.31–92.37)	27.91 (7.54–48.26)	54.92 (32.61–77.23)	88.07 (58.78–117.36)	128.07 (86.03–170.11)

[a]CIR-24=24-Hour Caffeine Intake Recall.

[b]Q1=quartile 1.

[c]Q2=quartile 2.

[d]Q3=quartile 3.

[e]Q4=quartile 4.

Table 4.

Pearson correlations and weighted κ coefficients[a] between CIR-24[b], CBQ[c], and caffeine metabolites among Canadian adults

	CIR-24				CBQ			
Analyte	r_p	***P* value**	κ	***P* value**	r_p	***P* value**	κ	***P* value**
Caffeine (1,3,7-trimethylxanthine)	0.52	<0.001	0.59	<0.001	0.40	<0.001	0.45	<0.001
Paraxanthine (1,7-dimethylxanthine)	0.41	<0.001	0.47	<0.001	0.34	0.002	0.42	<0.001
Theophylline (1,3-dimethylxanthine)	0.34	0.002	0.49	<0.001	0.33	0.003	0.40	<0.001
1,3,7-Trimethyluric acid	0.28	0.013	0.49	<0.001	0.21	0.06	0.42	<0.001
1,3-Dimethyluric acid	0.32	0.005	0.39	<0.001	0.31	0.005	0.34	<0.001
1,7-Dimethyluric acid	0.30	0.008	0.49	<0.001	0.28	0.013	0.40	<0.001
1-Methyluric acid	0.35	0.002	0.41	<0.001	0.26	0.02	0.32	<0.001
1-Methylxanthine	0.33	0.003	0.45	<0.001	0.26	0.02	0.40	<0.001
5-Acetylamino-6-amino-3-methyluracil	0.36	0.001	0.41	<0.001	0.36	0.001	0.38	<0.001

[a] Weighted κ based on quartile ranking by self-reported measures and biomarker quartiles.

[b] CIR-24=24-Hour Caffeine Intake Recall.

[c] CBQ=Caffeinated Beverage Frequency Questionnaire.