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## Factors associated with the blood and urinary selenium concentrations in the Canadian population: Results of the Canadian Health Measures Survey (2007–2011)



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## ABSTRACT

**Objective:** The objective of the present work is to assess the factors associated with whole blood and urinary selenium (Se) concentrations in Canadians aged 6–79 years old, and to interpret the data in the context of exposure guidance values.

**Methods:** Whole blood Se concentrations data collected from 10740 participants as part of the Canadian Health Measures Survey (CHMS) Cycle 1 (2007–09) and Cycle 2 (2010–11) were analyzed for associations with the demographic and dietary characteristics of the Canadian population; whereas the urinary Se concentrations were only assessed for their association with the demographic variables. Whole blood and urinary Se concentrations were compared to biomonitoring equivalents established for exposure guidance values.

**Results:** The geometric means of whole blood Se concentrations ( $\mu\text{g/L}$ ) were 197.42 (95% CI: 194.79, 200.08) and 192.35 (95% CI: 189.68, 195.06) for males and females, respectively. The corresponding urinary Se concentrations ( $\mu\text{g/L}$ ) were 56.91 (95% CI: 54.81, 59.10) and 44.10 (95% CI: 41.89, 46.43) respectively. Males, participants born in Asia, older individuals, and participants who frequently consumed nuts and vegetables had higher whole blood Se, whereas current smokers, residents of Quebec and Ontario, participants who frequently consumed meat, fruits or dairy products were associated with lower whole blood Se. Sociodemographic factors were also significantly associated with urinary Se although the direction of association sometimes differed from those observed with blood Se. More than 99.9% of the Canadian population covered by the survey had whole blood Se concentrations within the range from the lower (100  $\mu\text{g/L}$ ) and higher (400  $\mu\text{g/L}$ ) biomonitoring equivalents set for the protection from deficiency and selenosis, respectively.

**Conclusions:** The CHMS data provide a baseline for Se exposure among Canadians and indicated that the population is generally not at risk of deficiency or toxicity.

### 1. Introduction

Selenium (Se) is a naturally occurring, essential trace element present in the environment both in organic and inorganic forms. Median dietary intakes vary widely in Canadians, ranging 83–151  $\mu\text{g/day}$  for adults (Environment and Climate Change Canada and Health Canada, 2017). Exposure to drinking water, air, soil, use of consumer products, and diet are the major sources of Se for Canadians (CCME, 2009). The bio-availability of selenium is influenced by the speciation and the presence of other ions and nutritional factor (Rayman, 2012). Baked goods, cereals, and grains are the most important dietary Se sources for Canadians, and meats, fish and seafood, grains, nuts, and cereals have

the highest Se concentrations. However, Se concentrations in specific items within a single food group or within a single food item can be highly variable (Rayman, 2008). Soil Se is fundamental to Se in the food systems (Combs, 2001). The geographic variation (e.g. North America vs. Europe) in human Se biomarkers is generally in accordance with soil Se concentrations (Combs, 2001; Johnson et al., 2010; Oldfield, 2002; Rayman, 2008).

Guidance values have been developed to prevent selenium deficiency and toxicity. Although Se deficiency is not expected in individuals having a balanced diet, extremely low levels of intake have been linked to Keshan disease, a form of cardiomyopathy (Chen, 2012), male infertility (Moslemi and Tavanbakhsh, 2011) and osteoarthritis

**Abbreviations:** ATSDR, Agency for Toxic Substances and Disease Registry; BE, biomonitoring equivalent; CHMS, Canadian Health Measures Survey; EAR, estimated average requirement; GM, geometric mean; IOM, Institute of Medicine; RfD, reference dose; MEC, mobile examination center; MRL, minimal risk level; NHANES, National Health and Nutrition Examination Survey; Se, selenium; UL, tolerable upper intake level; US EPA, United States Environmental Protection Agency

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(Jirong et al., 2012). The essential roles of Se involve selenoproteins (e.g. glutathione peroxidases, iodothyronine deiodinases, and selenoprotein P) conducting redox reactions, thyroid hormone metabolism, and immune functions. To meet these requirements, the Institute of Medicine (IOM) established an Estimated Average Requirement (EAR; the nutritional requirement of half of the healthy individuals in an age and sex group) of 17–35 µg/day for children aged 1–13 years and 45 µg/day of selenium for adolescents and adults.

Excess levels of Se intake can lead to selenosis, characterized by hair and nail loss and brittleness, tooth decay, skin anomalies, garlic breath odor, and nervous system disturbances in more severe cases (intakes > 1270 µg/day) (Yang et al., 1989; Yang and Zhou, 1994). To prevent these, the IOM set the Tolerable Upper Intake Level (UL; the maximum total daily intakes likely to pose no risk of adverse effects) to 45–60 µg/day for infants up to 12 months, 90–280 µg/day for 1–13 years old, and 400 µg/day for adolescents and adults (Health Canada, 2000; Institute of Medicine, 2000). The U.S. EPA and the ATSDR have both set their selenium toxicity guidance values (reference dose (RfD) and Minimal Risk Level (MRL), respectively) at 5 µg/kg/day (ATSDR, 2003; US EPA, 1991). All these agencies have derived their toxicity guidance values based on clinical selenosis observed in a cohort of Chinese individuals exposed to very high levels in the diet (Yang et al., 1989; Yang and Zhou, 1994).

Since Se is an integral component of the cellular antioxidant system, it is commonly consumed as a dietary supplement. However, the health benefits of Se remain controversial. For example, a large U.S. study based on the NHANES data, reported a nonlinear association between serum Se concentrations and all-cause and cancer mortality, i.e. while increasing serum Se concentrations up to 130 µg/L were associated with decreased mortality, higher serum Se concentrations, in fact, increased mortality (Bleys et al., 2008; Rayman et al., 2018). Moreover, Se intake was reported to associate with a lower risk of certain type of cancer (Vinceti et al., 2014) but recent randomized trials have found associations between high levels of intake and prostate cancer and other health outcomes, such as cardiovascular diseases, type II diabetes, amyotrophic lateral sclerosis, and glaucoma (Faghihi et al., 2014; Kenfield et al., 2015; Lippman et al., 2009; Stranges et al., 2007). The difference in study design, including the difference in forms of Se used and/or the dose range of Se being exposed to, impede drawing definitive conclusions from these studies.

The Se status of the Canadian population, particularly information on how demographics and other factors are associated with exposure, is not known. Biomonitoring studies provide useful information to answer these questions by reflecting the exposure of populations across all sources and routes. These studies represent an important means to monitor trends over time, changes in the usage of chemical substances, establish research priorities, and the impact of pollution control measures (Aylward et al., 2013). As such, the Canadian Health Measures Survey (CHMS) is a nationally representative, cross-sectional survey with direct health measurements aimed at assessing the health conditions and chemical exposures of the Canadian population (Health Canada, 2013, 2010). The concentrations of chemicals measured in the blood or urine samples collected from the population can then be interpreted in a risk assessment context by relating these to guidance values using biomonitoring equivalents (BEs) (Hays et al., 2014). The BE concept is a screening tool that refers to the concentration of a substance in a biological matrix (e.g. hair, blood, etc.) corresponding to a non-cancer or cancer endpoint oral intake value established based on human or animal data, such as the Tolerable Daily Intake (TDI). Therefore, BE can be used as reference concentrations for risk assessment purposes.

By using the whole blood and urinary Se concentrations reported from the CHMS cycle 1 (2007–09) and cycle 2 (2010–11), the present work assesses the differences in exposure in Canadians, the relationships between dietary factors, social economics status, and Se status, and how the population Se status compared with BE.

## 2. Materials and methods

### 2.1. The Canadian Health Measures Survey

The CHMS is an ongoing biennial survey developed to assess the health status and environmental exposures of the Canadian population aged 3–79 years (6–79 years in cycle 1) (Health Canada, 2010). People living on reserves or in other Aboriginal settlements in the provinces or in certain remote areas institutions, and Canadian Forces were excluded (representing less than 4% of the population). Household interviews were used to collect demographic and socioeconomic data and information about lifestyle, medical history, current health status, the environment, and housing conditions as part of the CHMS. Participants who completed the household interview were invited to the mobile examination center (MEC) to conduct physical measurements and collect biological specimens to assess clinical parameters and exposure to environmental chemicals. The survey weights and bootstrap sample weights were used to account for the unequal selection probabilities and to produce nationally representative estimates and confidence intervals. Survey participants provided informed consent for the collection of data and biological specimens, and for their storage and analyses (Statistics Canada, 2010). A detailed description of the CHMS including the multistage sampling procedure for the selection of survey participants and data and biological specimens collected as part of the survey has been provided elsewhere (Tremblay et al., 2007). Data used in this study are from cycle 1 (2007–2009) and cycle 2 (2009–2011) of the CHMS. The CHMS cycle 1 included approximately 5600 respondents from 15 collection sites, and cycle 2 sampled approximately 6400 respondents from 18 collection sites. Data from respondents in Cycle 1 and Cycle 2 were combined to produce more precise estimates following standard protocols (Statistics Canada, 2015).

### 2.2. Blood and urinary Se measurement

Whole blood specimen was collected by venipuncture in K2-EDTA vacutainers and collection volumes varied according to the age group. Whole blood samples were diluted in a basic solution containing octylphenol ethoxylate and ammonia. Approximately 60 ml of urine sample (mid-stream urine in cycle 1, and first-catch urine in cycle 2) were collected in a 120 ml container. Urine creatinine concentration was measured using the colorimetric end-point Jaffe method (Barr et al., 2005). Whole blood and urinary Se were measured by inductively coupled plasma-mass spectrometry (ICP-MS) (Perkin Elmer Sciex, Elan DRC II). Laboratory analyses were performed at the Centre de Toxicologie du Québec of l'Institut national de santé publique du Québec (INSPQ), Québec, which is accredited under ISO 17025. Field blanks were performed at all 33 collection sites to ensure that samples were not being contaminated by the MEC environment and process and no significant levels of contamination were found in these blank samples. The limits of detection (LOD) for whole blood Se were 8 µg/L and 20 µg/L in the CHMS cycle 1 and cycle 2, respectively; the LODs for urinary Se were 6 µg/L in the CHMS cycle 1 and 4 µg/L in cycle 2. We assigned a value of 3 µg/L (half of higher LOD) when urinary Se concentrations were below the LOD for participants in both cycles. Full details of the collection protocol and laboratory analyses including QA/QC protocols are described elsewhere (Health Canada, 2010). Whole blood Se reflects long-term exposure and urinary Se reflects transient exposure (Alaejos and Romero, 1993; Hays et al., 2014).

### 2.3. Demographic, socioeconomic status, and health behaviors

Age, sex, education, household income, racial/cultural background, place of birth, region of residence, smoking status, and alcohol consumption of participants were included as potential covariates. Age categories (in years) were: 6–11, 12–19, 20–39, 40–59 and 60–79. Children aged 3–5 years in cycle 2 were excluded from the combined

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