Screening of population level biomonitoring data from the Canadian Health Measures Survey in a risk-based context

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HIGHLIGHTS

• The Canadian Health Measures Survey (CHMS) has been collecting biomonitoring data from the general Canadian population since 2007 and has provided, to date, nationally representative baseline concentrations for hundreds of environmental biomarkers in blood and/or urine.
• A number of screening values have been developed as tools to interpret biomonitoring data in a human health risk assessment context. These values include Biomonitoring Equivalents (BEs) derived from existing exposure guidance values.
• BEs have been derived for a number of biomarkers of exposure measured in the CHMS and were compared to biomonitoring data from the CHMS to calculate hazard quotient (HQ).
• Results suggest most chemical exposures in Canadians seem below current exposure guidance values. However, inorganic arsenic and cadmium exposure may be exceeding risk assessment-based exposure guidance values, in portions of the Canadian population at least intermittently.
• This type of analysis may contribute to screening and prioritization efforts.

ABSTRACT

Since 2007, the Canadian Health Measures Survey (CHMS) has been collecting biomonitoring data from the general Canadian population and has provided, to date, nationally representative concentrations for hundreds of environmental biomarkers in blood or urine. Biomonitoring Equivalents (BEs) have been developed as tools to help interpret biomonitoring data in a health risk context at a population level. In this paper, BEs are used to relate biomonitoring data from the CHMS (2007–2011) to existing exposure guidance values developed by Health Canada and other government agencies. Chemical-specific hazard quotients (HQs) and/or cancer risk estimates are calculated using existing BEs corresponding to environmental chemicals analyzed in the CHMS.

For the majority of environmental chemicals, calculated HQ values are less than 1 indicating exposure is below published exposure guidance values. Individual biomonitoring data for two biomarkers of metal exposure (inorganic arsenic and cadmium) resulted in HQ values exceeding 1 suggesting that exposure may be above existing guidance values for a portion of the population, at least intermittently. This type of analysis may be used by researchers, risk assessors, and risk managers in prioritization efforts.

1. Introduction

The Canadian Health Measures Survey (CHMS) is the most comprehensive and nationally representative survey that provides information on the general health and lifestyles of Canadians including weight, height, physical fitness, and chronic and infectious disease, and on the concentrations of environmental chemicals and/or their metabolites in blood and urine as biomarkers of exposure (Health Canada, 2010c, 2013b). Biomarkers

Abbreviation: CHMS, Canadian Health Measure Survey; BE, Biomonitoring Equivalent; CSF, Cancer Slope Factor; HQ, hazard quotient; POD, point of departure; RID, Reference Dose; TCS, triclosan; TDI, Tolerable Daily Intake.

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of exposure are defined as a chemical, its metabolite, or the product of an interaction between a chemical and some target molecule or cell that is measured in the human body (NRC, 2006). The latest biomonitoring report released by Health Canada provides population-level data for 91 biomarkers of exposure in Canadians aged 3–79 years collected from 2009 to 2011 (Health Canada, 2013b). Previously, from 2007 and 2009 the CHMS reported on 81 biomarkers of exposure in Canadians aged 6–79 years (Health Canada, 2010c). Additionally, pooled serum samples from CHMS (2007–2009) analyzed for additional persistent organic pollutants (POPs) include data on exposure to polychlorinated biphenyls (PCBs), dioxins, and furans (Rawn et al., 2012, 2013). The pooled study provides national estimates for POPs concentrations in the human serum of Canadians by pooling the small volumes of left over serum samples from CHMS cycle 1 collection (2007–2009).

Although, our ability to measure increasing number of chemicals at lower detection levels has improved, our interpretation of associated risks to human health is still limited (Haines et al., 2011). Health-based tissue guidelines or intervention levels are derived on the basis of toxicological and epidemiological studies and can be used to compare with biomarker concentrations to determine if levels are associated with potentially increased health risk. In Canada, and elsewhere only a few substances, including lead and mercury, have intervention levels based upon direct, quantitative relationships between biomarker measurements and health effects (CEOH, 1994; Legrand et al., 2010). Such risk assessment values come from time- and resource-intensive epidemiological studies. Data from the CHMS show that the majority of Canadians have, lead, and mercury levels below their respective provisional Canadian blood guidance values (Health Canada, 2013a; Lye et al., 2013). For other biomarkers measured in the CHMS, Biomonitoring Equivalents (BEs) can be used as tools to help interpret biomonitoring data in a health risk context at a population level. A BE is defined as an estimated concentration of an environmental chemical in humans consistent with an existing non-cancer health-based exposure guidance value, such as a tolerable daily intake (TDI) or with an exposure guidance value based on cancer endpoints, such as a risk-specific dose (RSD) (Hayes et al., 2008a). In this paper, existing BEs are used to screen biomonitoring data from the CHMS (2007–2011) and provide an assessment of which biomarkers are present at concentrations below, near, or above existing exposure guidance values. This evaluation may help to set priorities for future research, monitoring, and surveillance activities and for potential risk assessment or risk management follow-up efforts.

2. Methods

2.1. Canadian Health Measure Survey biomonitoring data

The CHMS is representative of the general Canadian population aged 6–79 years and 3–79 years for the data collected in 2007–2009 and 2009–2011, respectively (Tremblay et al., 2007; Giroux et al., 2013). For biomarkers analyzed in 2007–2009, including DDT, HCB, PBDE, and PCBs, the sample population comprised approximately 1666 individuals between the ages of 20 and 79 years. The pooled biomarkers from 2007–2009 (i.e., dioxins and HBCD) were analyzed in a total sample population comprising 5059 individuals between the ages of 6 and 79 years divided over 59 composite pools. The remaining biomarkers were analyzed in 2009–2011 in a sub-sample population of approximately 2000 individuals except for cadmium which was measured in the full sample population of 5059 individuals aged 6–79 years. In order to be representative of the Canadian population, the analyses were weighted using the CHMS survey weights (Statistics Canada, 2011, 2013). The data were analyzed with SAS 9.2 (SAS Institute Inc., U.S.) and SUDDAN 10.0.1 software (RTI International, U.S.). This analysis is provided for a subset of the CHMS environmental chemicals for which BEs were available (Table 1).

For each biomarker or sum of biomarkers, descriptive statistics (geometric means and selected percentiles with their associated 95% confidence intervals) were calculated on the volumetric (units of micrograms per liter urine or whole blood) or lipid-adjusted (units of nanogram per gram plasma lipids) concentrations. For arsenic, dichlorodiphenyldichloroethane (DDT), di-2 (ethylhexyl) phthalate (DEHP), hexabromocyclododecane (HBCD), and polychlorinated biphenyls (PCBs), descriptive statistics were calculated based upon the sum of the appropriate biomarkers according to the requirements of the screening values (ANSES, 2010; Aylward and Hayes, 2011; Aylward et al., 2009b; Hayes et al., 2010). Biomarker concentrations below the limit of detection (LOD) were assigned a value of LOD/2, except for concentrations of DDT biomarkers below the LOD which were assigned a value of zero to avoid overestimation as DDT was detected in only a small portion of the population (Statistics Canada, 2011, 2013). Pooled biomonitoring data for HBCD, polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like PCBs (DL-PCBs) were obtained from Rawn et al. (2012, 2013).

Sub-population analyses by age, sex, or smoking status were only conducted where relevance was suggested by existing information. In the case of cadmium, smoking has been identified as a major source of exposure (Environment Canada, 1994; Health Canada, 1994a; IARC, 2012) and therefore, descriptive statistics for cadmium in sub-populations of smokers and non-smokers were calculated. Smoking status was defined in terms of urinary cotinine concentrations, with smokers defined as those with concentrations exceeding 50 ng/ml, as recommended by the Society for Research on Nicotine and Tobacco (SRNT Subcommittee on Biochemical Verification 2002). No attempt was made to comprehensively assess trends with smoking, sex, or age across all chemicals in the analyses.

2.2. Biomonitoring Equivalents

BEs are based on exposure guidance values established by government agencies, such as Health Canada, the United States Environmental Protection Agency (U.S. EPA), or the World Health Organization (WHO) (Hayes et al., 2007, 2008a). Biomarkers selected for this analysis are presented in Table 1. BE values based upon risk specific doses from cancer risk assessments (i.e., $BE_{\text{RSD}}$) were available for three biomarkers: arsenic, DDT, and hexachlorobenzene (HCB) and are presented in Table 5 (Aylward et al., 2010; Hayes et al., 2010; Kirman et al., 2011).

The methods for deriving BEs are reviewed in Angerer et al. (2011). For interpreting CHMS biomarkers, BE values based on Health Canada exposure guidance values were favored. When these values were not available, BEs based on risk assessment values from U.S. EPA or other international health organizations were selected. A provisional BE value was identified for HBCD (Aylward and Hayes, 2011). Provisional values are derived based on the point of departure from Health Canada screening and risk assessments in the absence of established exposure guidance values. A concentration of concern was identified for PCBs (ANSES, 2010).

2.3. Risk-based approach: screening with Biomonitoring Equivalents

For non-cancer endpoints, hazard quotients (HQ) were calculated as the ratio of the biomarker concentration to the chemical-specific BE value:
Table 1 Environmental chemicals and their respective biomarkers from the Canadian Health Measures Survey for which existing Biomonitoring Equivalents were identified.

<table>
<thead>
<tr>
<th>Concentration of concern</th>
<th>Biomarkers (if different)</th>
<th>Relevance of biomarker*</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCBs</td>
<td>PCB 138, PCB 153, PCB 180</td>
<td>–</td>
<td>ANSES, 2010</td>
</tr>
</tbody>
</table>

Biomonitoring Equivalents

2,4-D Arsenic, inorganic

Bisphenol A

Cadmium

Cyfluthrin

Deltamethrin

DEP

Dioxins

Hexachlorobenzene

PBDE 99

Triclosan

Provisional Biomonitoring Equivalent

HBCD

HQC = \frac{[\text{Biomarker}]}{[\text{BE}]}

HQs were calculated for biomarker concentration at the population geometric mean (GM) and upper bound (95th percentile or maximum value), as appropriate for each environmental chemical. Since BEs are based on RfD or TDI values, HQs near or exceeding a value of 1 provide an indication that exposure levels are near or exceeding the existing exposure guidance values.

For carcinogens such as inorganic arsenic, DDT and HCB, risk-specific doses (RSD) have been calculated for a range of risk levels of interest from 1 in 10,000 \( (1 \times 10^{-4}) \) to 1 in 1,000,000 \( (1 \times 10^{-6}) \). BE_{RSD} provide an estimate of the steady-state concentrations that would result from chronic exposure, over a lifetime, at the RSDs (Aylward et al., 2013). In this evaluation, cancer risks corresponding to 5th, 25th, 75th, and 95th percentile were estimated with information provided in chemical specific BE derivation, and assuming linear extrapolation (Aylward et al., 2010; Hays et al., 2010; Kirman et al., 2011).

3. Results

Descriptive statistics for individual and summed biomarkers of exposure for environmental chemicals included in the CHMS are summarized alongside their respective BE values in Tables 2–4. Environmental chemicals were divided into two groups based upon estimated half-lives. Table 2 contains chemicals with short estimated half-lives of elimination (< 1 day) including inorganic arsenic, phthalates, environmental phenols and pesticides. Concentrations of persistent environmental chemicals including cadmium, DDT, HCB, PCBs, polybrominated diphenyl ether (PBDE), HBCD and PCDD/F + DL-PBCs are presented in Tables 3 and 4.

The HQ values for the population geometric means and 95th percentile for biomarkers of inorganic arsenic, phthalates, pesticides, and environmental phenols are presented in Fig. 1. These chemicals have short estimated half-lives of elimination relative to expected exposure frequencies; for example, biomarkers of inorganic arsenic have estimated half-lives of 4–28 h (Hays et al., 2010). When the biomarker’s half-life in urine is short, large variations may be expected in urine concentrations from an individual over the course of a single day (Aylward et al., 2012). For these short-lived chemicals, biomarker concentrations at the tails of the distributions (e.g., 95th percentile) may not be very indicative of long-term exposure levels. If the BE is based on an exposure guidance value derived for chronic exposures, then interpretation of the tails of the distributions should be interpreted with caution.

The calculated HQ values for persistent environmental chemicals are presented as a function of age in Fig. 2. The biomonitoring levels measured for these chemicals are expected to be stable, with little intra-individual variability. Since available data from pools do not provide information on the distribution of concentrations expected in a given age or gender group (i.e., 95th percentile), maximum values are provided as a means of screening the data at the upper range.

Cancer risk levels corresponding to population percentiles are presented in Fig. 3 for biomarkers of inorganic arsenic, DDT, and HCB. The frequency of detections for these biomarkers was all above 60% in the CHMS.

4. Discussion

4.1. Cross-chemical evaluation

This evaluation across a range of selected biomarkers provides a novel interpretation of the CHMS (2007–2011) biomonitoring data in a risk-based context. The general pattern of these results presented here is consistent with a similar evaluation previously
conducted on U.S. biomonitoring data from the National Health and Nutrition Examination Survey (NHANES; 2001–2010) (Aylward et al., 2013). For non-cancer effects, HQ values for the CHMS data exceeded 1 at the 95th percentile for only two (inorganic arsenic and cadmium) biomarkers of environmental chemicals or groups of chemicals selected for this evaluation, suggesting most chemical exposures in Canadians are below current exposure guidance values. Similarly, for the NHANES data, of the substances common to both analyses, HQ values at the 95th percentile exceeded 1 for inorganic arsenic, dioxins/furans/DL-PCBs, cadmium (in smokers) and DEHP (Aylward et al., 2013). As with the CHMS analysis, all environmental chemicals included in NHANES had HQ values below 1 at the geometric mean. These results suggest both populations are likely exposed below the exposure guidance value at the time of sampling. For DEHP, the differences in HQ values between the CHMS analysis and that of the NHANES data may be due to the use of a different BE value; the CHMS analysis was based upon a Health Canada derived TDI and considered only three metabolites while the NHANES analysis was based upon an U.S. EPA derived RfD and considered four metabolites (Aylward et al., 2009b, 2012). For dioxins/furans/DL-PCBs, the CHMS analysis was based upon the maximum concentrations from pooled samples which are not comparable to the upper bound 95th percentile of the distribution in the general population used in the NHANES analysis.

For the majority of short-lived chemicals, the results of this evaluation suggest that, in general, exposures to short-lived compounds do not exceed current exposure guidance values. However, HQ values approached 1 at the geometric mean of the sum of inorganic arsenic-derived urinary biomarkers, monomethylarsinic acid (MMA) and dimethylarsinic acid (DMA), suggesting that exposures may be near the existing Health Canada exposure guidance value on non-cancer endpoints (Health Canada, 2008a). The estimated cancer risks were also calculated for the sum of MMA and DMA, based on Health Canada cancer slope factor (Health Canada, 2006). Cancer risk level for the geometric mean of these biomarkers exceeded 1 × 10⁻⁴, which is slightly above the range defined as essentially negligible (e.g.: 1 × 10⁻⁵–1 × 10⁻⁶) (Health Canada, 2010b). However, caution is required when interpreting data for biomarkers of inorganic arsenic, as the predominant metabolite, DMA, has shown associations with organic arsenic species exposure. Aylward et al. (2014) showed a strong correlation between DMA and organic arsenic species in NHANES data, suggesting co-exposure or even metabolism of the organic species to DMA. Hence, it seems DMA when used as a biomarker of inorganic arsenic exposure may overestimate the actual exposure. Thus, a more focused chemical-specific analysis for inorganic arsenic including a detailed examination of exposure data may be required to determine whether current exposures are of concern.

The HQ values did not exceed 1 at the geometric mean for any of the persistent chemicals. However, calculated HQ values for cadmium exceed 1 at the 95th percentile of the smoking and non-smoking population aged 40–59 and 60–79 years. In the case of cadmium with a long biological half-life of 6–38 years in the kidney, concentrations at the 95th percentile are considered

Table 2

<table>
<thead>
<tr>
<th>Chemical group, CHMS cycle</th>
<th>Environmental chemical (biomarker, if different)</th>
<th>Exposure guidance values (type, reference)</th>
<th>BE and matrix</th>
<th>Age group</th>
<th>n</th>
<th>CHMS data (µg/L urine)</th>
<th>GM (95% CI)</th>
<th>95th percentile (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metals, 2009–2011</td>
<td>Arsenic, inorganic (sum of DMA, MMA)</td>
<td>3E-04 mg/kg-d-TDI; Health Canada, 2008a</td>
<td>5.8 µg/L urine</td>
<td>6–79</td>
<td>2022</td>
<td>4.2 (3.6, 4.8)</td>
<td>20 (11, 28)</td>
<td></td>
</tr>
<tr>
<td>Phthalates, 2009–2011</td>
<td>Benzylobutyl phthalate (MBzP)</td>
<td>1.3 mg/kg-d-TDI; Health Canada, 2000</td>
<td>31.000 µg/L urine</td>
<td>6–79</td>
<td>2037</td>
<td>2.7 (2.6, 6.6)</td>
<td>75 (48, 65)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diethyl phthalate(MEP)</td>
<td>8E-01 mg/kg-d-RfD; U.S. EPA, 1993</td>
<td>18,000 µg/L urine</td>
<td>6–79</td>
<td>2038</td>
<td>44 (36, 54)</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Di-n-butyl phthalate (MBP)</td>
<td>6.3E-02 mg/kg-d-TDI; Health Canada, 1994</td>
<td>1400 µg/L urine</td>
<td>6–79</td>
<td>2033</td>
<td>20 (18, 22)</td>
<td>87 (74, 100)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Di-2(ethylhexyl) phthalate (sum of MEHP, MEHHP)</td>
<td>4.4E-02 mg/kg-d-TDI; Health Canada, 1994</td>
<td>610 µg/L urine</td>
<td>6–79</td>
<td>2038</td>
<td>22 (20, 24)</td>
<td>100 (78, 120)</td>
<td></td>
</tr>
<tr>
<td>Environmental Phenois, 2009–2011</td>
<td>Bisphenol A</td>
<td>2.5E-02 mg/kg-d-pTDI; Health Canada, 2008b</td>
<td>1000 µg/L urine</td>
<td>6–79</td>
<td>2036</td>
<td>1.2 (1.1, 1.3)</td>
<td>6.7 (4.8, 8.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Triclosan</td>
<td>0.3 mg/kg-d-RfD; U.S. EPA, 2008</td>
<td>6400 µg/L urine</td>
<td>6–79</td>
<td>2027</td>
<td>15 (12, 19)</td>
<td>710 (540, 880)</td>
<td></td>
</tr>
<tr>
<td>Pesticides, 2009–2011</td>
<td>2,4-D</td>
<td>1E-03 mg/kg-d-RfD; U.S. EPA, 2004</td>
<td>200 µg/L urine</td>
<td>6–79</td>
<td>2028</td>
<td>–</td>
<td>1.0 (0.86, 1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deltamethrin (cis-DRCA)</td>
<td>1E-03 mg/kg-d-RfD; U.S. EPA, 2010</td>
<td>7 µg/L urine</td>
<td>6–19</td>
<td>1016</td>
<td>0.01 (0.01, 0.02)</td>
<td>0.20 (0.13, 0.27)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cyfluthrin (4-F-3-PBA)</td>
<td>1E-02 mg/kg-d-RfD; U.S. EPA, 2010</td>
<td>50 µg/L urine</td>
<td>20–79</td>
<td>993</td>
<td>0.01 (0.009, 0.06)</td>
<td>0.14 (0.050, 0.24)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2E-02 mg/kg-d-RfD; U.S. EPA, 2002</td>
<td>200 µg/L urine</td>
<td>6–79</td>
<td>2022</td>
<td>–</td>
<td>0.11 (0.035, 0.38)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BE, Biomonitoring Equivalent; CHMS, Canadian Health Measures Survey; CI, confidence interval; 24-D; 2,4-dichlorophenoxyacetic acid; cis-DRCA, cis-3-(2,2-dichromomvinyl)-2,2-dimethylcyclopropane-1-carboxylic acid; DMA, dimethylarsinic acid; 4-F-3-PBA, fluoro-3-phenoxobenzoic acid; GM, geometric mean; HQ, Health Canada; MnBP, mono-n-butyl phthalate; MBzP, mono-benzyl phthalate; MEHHP, mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEHP, mono-2-ethylhexyl phthalate; MEOHP, mono-(2-ethyl-5-oxohexyl) phthalate; MEP, mono-ethyl phthalate; MMA, monomethylarsenic acid; pTDI, provisional tolerable daily intake; RfD, reference dose; TDITolerable daily intake.

* If >40% of samples were below the limit of detection, the GM was not calculated.**DMA + MMA only due to low detection rates for other inorganic arsenic species (arsenite and arsinite).

Data are used with caution as coefficient of variation is between 16.6% and 33.3%.

Data are considered too unreliable to be published as coefficient of variation is greater than 33.3%.
representative of relatively long-term exposures at elevated levels (Hays et al., 2008b). Based on previous studies, urinary cadmium levels were anticipated to be higher in smokers than non-smokers (NTP, 2011; Riederer et al., 2012). However, cadmium HQ values approached 1 at the 95th percentile even in non-smokers of older age groups. Urinary cadmium levels are considered to be a highly relevant biomarker for the critical dose metric of renal cortex cadmium concentrations (Hays et al., 2008; Järup et al., 1998; Järup et al., 1998). For these reasons, HQ values approaching or exceeding 1 for cadmium provide an indication that exposure levels may be exceeding exposure guidance values, at least for a portion of the population. Thus, a more focused chemical-specific analysis for cadmium including a detailed examination of exposure data may be required to determine whether current exposures are of concern.

4.2. Limitations of screening with Biomonitoring Equivalents

Calculated HQ values using BEs do not represent medical diagnostic criteria and cannot be used to evaluate the likelihood of an adverse health effect in an individual or among a population. HQ values above 1 indicate exposures at or above the current exposure guidance values which may lessen the safety margin, but do not necessarily result in any significant adverse health effects. Therefore, similar to when other exposure guidance values are exceeded; chemical-specific HQ values above 1 should result in further investigation and can be used to determine priorities for further efforts when multiple contaminants are evaluated.

For a single substance, there may exist multiple BE values each derived based upon exposure guidance values from different environmental chemicals.
traditional values existing approach assessment does practise human consideration in.

Table 4
Exposure guidance values, corresponding Biomonitoring Equivalents and pooled biomonitoring data from the Canadian Health Measures Survey for biomarkers of persistent environmental chemicals, hexabromocyclododecane and dioxins.

<table>
<thead>
<tr>
<th>Environmental chemical, CHMS cycle (biomarkers)</th>
<th>Exposure guidance values (type, reference)</th>
<th>BE</th>
<th>Units and matrix</th>
<th>CHMS data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dioxin TEQ, 2007–2009(PCDD/F + DL-PCB)</td>
<td>0.7 pg/kg-d (RID; U.S. EPA, 2012a,b)</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7 pg/kg-d (RID; U.S. EPA, 2012a,b)</td>
<td>15</td>
<td>pg/g serum lipid</td>
<td>6–11</td>
</tr>
<tr>
<td></td>
<td>21 pg/g serum lipid</td>
<td>20</td>
<td>pg/g serum lipid</td>
<td>10: 880</td>
</tr>
<tr>
<td></td>
<td>60–79</td>
<td>40</td>
<td>ng/g serum lipid</td>
<td>0.51</td>
</tr>
<tr>
<td>HBCD, 2007–2009(γ of α-, β, γ and HBCD)</td>
<td>10 mg/kg-d (NOAEL, Point of departure; Health Canada, 2010a)</td>
<td>10000</td>
<td>ng/g serum lipid</td>
<td>6–11</td>
</tr>
</tbody>
</table>

Abbreviations: BE, Biomonitoring Equivalent; CHMS, Canadian Health Measures Survey; DL-PCB, dioxin-like polychlorinated biphenyls; GM, geometric mean; HBCD, hexabromocyclododecane; HC, Health Canada; NOAEL, no observed adverse effect level; PCDD, polychlorinated dibenzo-p-dioxins; PCDF, polychlorinated dibenzofurans; RID, reference dose; TEQ, toxic equivalent.

a Appropriate BE values for children under the age of 12 have not yet been identified (Aylward et al., 2012).
b Data are used with caution as coefficient of variation is between 16.6% and 33.3%.

In general, the urinary VE values were derived using assumptions regarding urinary flow and excretion fraction for people ages 6 and above (Hays et al., 2010). Therefore in this evaluation, urinary data for children under six were excluded due to the uncertainties in extrapolation of the BE values for application to younger children. As for plasma there are no existing data for children since the survey population in the CHMS was limited to 20–79 years.

4.3 CHMS data gaps and limitations

Relevance of the various biomarkers to the critical effect varies for the different chemicals considered here and this is reflected in the measures of relevance in Table 1. In fact, some biomarkers are highly relevant while other are only moderately relevant for the critical dose metric (Hays et al., 2008a). Most biomarkers analysed in this manuscript were considered to have medium to high relevance. Biomarkers for inorganic arsenic however were considered to be of low relevance to the critical dose metric (Hays et al., 2010).

Table 5
Cancer reference values, risk levels and corresponding Biomonitoring Equivalents identified for biomarkers of environmental chemicals measured in the Canadian Health Measures Survey.

<table>
<thead>
<tr>
<th>Environmental chemical (biomarker, if different)</th>
<th>Cancer reference value</th>
<th>Risk level</th>
<th>BE&lt;sub&gt;EQ&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic (sum of MMA, DMA)</td>
<td>Oral CSF (Health Canada, 2006): 1.8 (mg/kg-d)&lt;sup&gt;−1&lt;/sup&gt;</td>
<td>10&lt;sup&gt;−4&lt;/sup&gt;</td>
<td>1.1 μg/L urine</td>
</tr>
<tr>
<td>DDT (sum of DDT, DDE)</td>
<td>Oral CSF (U.S. EPA, 1991): 0.34 (mg/kg-d)&lt;sup&gt;−1&lt;/sup&gt;</td>
<td>10&lt;sup&gt;−4&lt;/sup&gt;</td>
<td>4000 ng/g plasma lipid</td>
</tr>
<tr>
<td>Hexachlorobenzene</td>
<td>TC&lt;sub&gt;90&lt;/sub&gt; (Health Canada, 1996): 0.06 mg/kg-d</td>
<td>10&lt;sup&gt;−5&lt;/sup&gt;</td>
<td>1500 ng/g plasma lipid</td>
</tr>
</tbody>
</table>

Abbreviations: BE, Biomonitoring Equivalent; CSF, cancer slope factor; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; DMA, dimethylarsinic acid; HC, Health Canada; MMA, monomethylarsonic acid; RSD, risk specific dose; TD, tumorigenic dose.
Fig. 1. Hazard quotients (HQ) for environmental chemicals with short elimination half-lives based upon biomonitoring data from the Canadian Health Measures Survey (CHMS) and existing Biomonitoring Equivalents for the relevant biomarkers of exposure. Biomonitoring Equivalents and CHMS data are reported in Table 2. Squares (■) represent HQ values at the geometric mean of the CHMS population data and diamonds (●) represent HQ values at the 95th percentile. The absence of a marker indicates that the geometric mean was not calculated as >40% of samples were below the limit of detection.

Abbreviations: BBP, benzyl butyl phthalate; BPA, bisphenol A; 2,4-D, 2,4-dichlorophenoxyacetic acid; DnBP, di-n-butyl phthalate; DEHP, di-2(ethylhexyl)phthalate; DEP, diethyl phthalate.

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Fig. 2. Hazard quotients (HQ) for persistent environmental chemicals based upon biomonitoring data from the Canadian Health Measures Survey (CHMS), as a function of age group, and existing Biomonitoring Equivalents for the relevant biomarkers of exposure. Biomonitoring Equivalents and CHMS data are reported in Table 3 and 4. Squares (■) represent HQ values at the geometric mean and diamonds (●) represent HQ values at the 95th percentile. For the pooled CHMS population data, HQ values at the geometric mean are represented by small squares (■) with error bars presenting the HQ values at the maximum and minimum data points. The absence of markers indicates that the either the estimate was too unreliable to be reported or that the geometric mean was not calculated as >40% of samples were below the limit of detection.

Abbreviations: DDT, dichlorodiphenyltrichloroethane; HBCD, hexabromocyclododecane; HCB, hexachlorobenzene; PBDE, polybrominated diphenyl ether; PCBs, polychlorinated biphenyls; TEQ, toxic equivalent.
The sampled medium may have been chosen on the basis of ease of collection rather than ease of interpretation in the toxic responses. For example, total BPA (free plus conjugated) is measured in urine, although free BPA in blood would be a more relevant biomarker for the target organ (Krishnan et al., 2010). The more distant the sampled medium and measured biomarker is from the target organ, the more uncertainty may exist in the interpretation of the data in a risk-based context. Other times, the target organ or system is unknown, because the mode of action is not fully understood, as in the case of biomarkers of inorganic arsenic.

5. Conclusions

The biomonitoring component of the CHMS provides a snapshot of population exposure integrated from all sources and when coupled with BE values, it offers a unique opportunity to screen population and prioritize environmental chemicals based on exposure. The results have the potential to be used by researchers, risk assessors, and risk managers.

The CHMS biomonitoring program includes future cycles in which additional analytes will be added or rotated in. Future work in the interpretation of biomonitoring data may include evaluation of combined chemical exposures with anticipated common toxicity endpoints or mode of action (Aylward et al., 2013; Meek et al., 2011). Derivation of additional BEs would increase the usability of this approach.

Conflict of interest

The authors declare that there are no conflicts of interest.

Transparency document

The Transparency document associated with this article can be found in the online version.

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