Note to reader

This draft version of Chapter 8 in the Technical Background Report to the Global Mercury Assessment 2018 is made available for review by national representatives and experts. The draft version contains material that will be further refined and elaborated after the review process. Specific items where the content of this draft chapter will be further improved and modified are:

1. Quality of all graphics (Figures, Tables) will be improved prior to publication.
2. Content of all graphics (Figures, Tables) will be double-checked, updated, and refined prior to publication.
3. The report's section on "Vulnerable Populations" is in preliminary draft form. It has not been reviewed yet by all authors. It will be updated after reviews have been received.
4. The report "Summary Section" is in preliminary draft form. It has not been reviewed yet by all authors. It will be updated after reviews have been received.
5. Table in Appendix #3 (Birth Cohort studies) will be further updated and cleaned-up.
6. Linkages will be made to the "Biotic Indicators" chapter once we have co-reviewed the two pieces.
7. We welcome comments and suggestions!!!

GMA Draft for review. Chapter 8 Mercury levels and trends in human populations worldwide. Nil Basu, Joanna Tempowski, David Evers, Milena Horvat, Pál Weihe, Irina Zastenskaya, Carla Achcar (WHO coordinated working group)

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Chapter 8 Mercury levels and trends in human populations worldwide

8.1 Background

8.1.1 Health effects of mercury

Mercury (Hg) is a pollutant of global concern principally due to its adverse effects towards human health. Mercury is also found in a number of items of great public health benefit such as seafood, dental amalgams, and vaccines. The current state of knowledge concerning Hg's human health impacts has been reviewed by Ha et al. (2017) and Karagas et al. (2012), and extends upon solid background papers by WHO/UNEP/IOMC (2008), Mergler et al. (2007), Clarkson and Magos (2006), the U.S. CDC's ATSDR (1999), and the U.S. EPA (1997). In brief, all individuals worldwide are exposed to some amount of Hg, and the possibility of exposure-related adverse health effects is dependent upon a range of factors (e.g., chemical form, concentration, duration, life stage). It is widely agreed that developing organs are the most sensitive to the toxic effects of Hg. Mercury has been documented to impair a range of physiological systems with the nervous, renal, and cardiovascular systems being most susceptible. Exposures to elemental Hg (Hg^0) may affect the nervous system with key symptoms including tremors, emotional lability, neuromuscular changes, and polyneuropathies. Exposures to inorganic Hg compounds may affect the kidneys. Exposures to methylmercury (MeHg) have received the most attention largely due to notorious poisoning events in Japan and Iraq which showed exposures to relatively high levels to be associated with adverse neurodevelopmental outcomes. This work has expanded over recent decades, and there is a growing body of evidence to illustrate that chronic exposures to relatively low-level MeHg exposures can be associated with a range of adverse health outcomes.

8.1.2 Mercury exposure assessment

Detailed reviews concerning the conduct and approaches of Hg exposure assessment have been reviewed by WHO/UNEP/IOMC (2008) and the U.S. EPA (1997). Mercury is a naturally occurring element that can enter the ecosystem via natural or anthropogenic-mediated process. Three major chemical forms of Hg relevant to human exposures are found in the environment: elemental Hg (Hg^0), inorganic Hg compounds (Hg^{2+}), and organic methylmercury (MeHg). The source, environmental fate, exposure, and toxicity of these different Hg forms vary.

Mercury has unique physical and chemical properties that have rendered it attractive for use in a range of industrial and medical applications. Major sources of elemental and inorganic Hg exposure to humans include occupational use (e.g. in artisanal and small-scale gold mining (ASGM) and dentistry), the use of products containing Hg (e.g. dental amalgams, skin-lightening creams, traditional medicines, thermometers, compact fluorescence lamps), and as a result of environmental pollution (e.g., fish and rice from contaminated ecosystems). Some notable examples are highlighted (Figure 1).

Mercury released into the environment may be converted to organic MeHg, which bioaccumulates and biomagnifies through the food chain, particularly in aquatic systems. For many communities worldwide, consumption of fish, shellfish and marine mammals that are contaminated with MeHg is arguably the most important source of exposure with key examples highlighted in Figure 1.

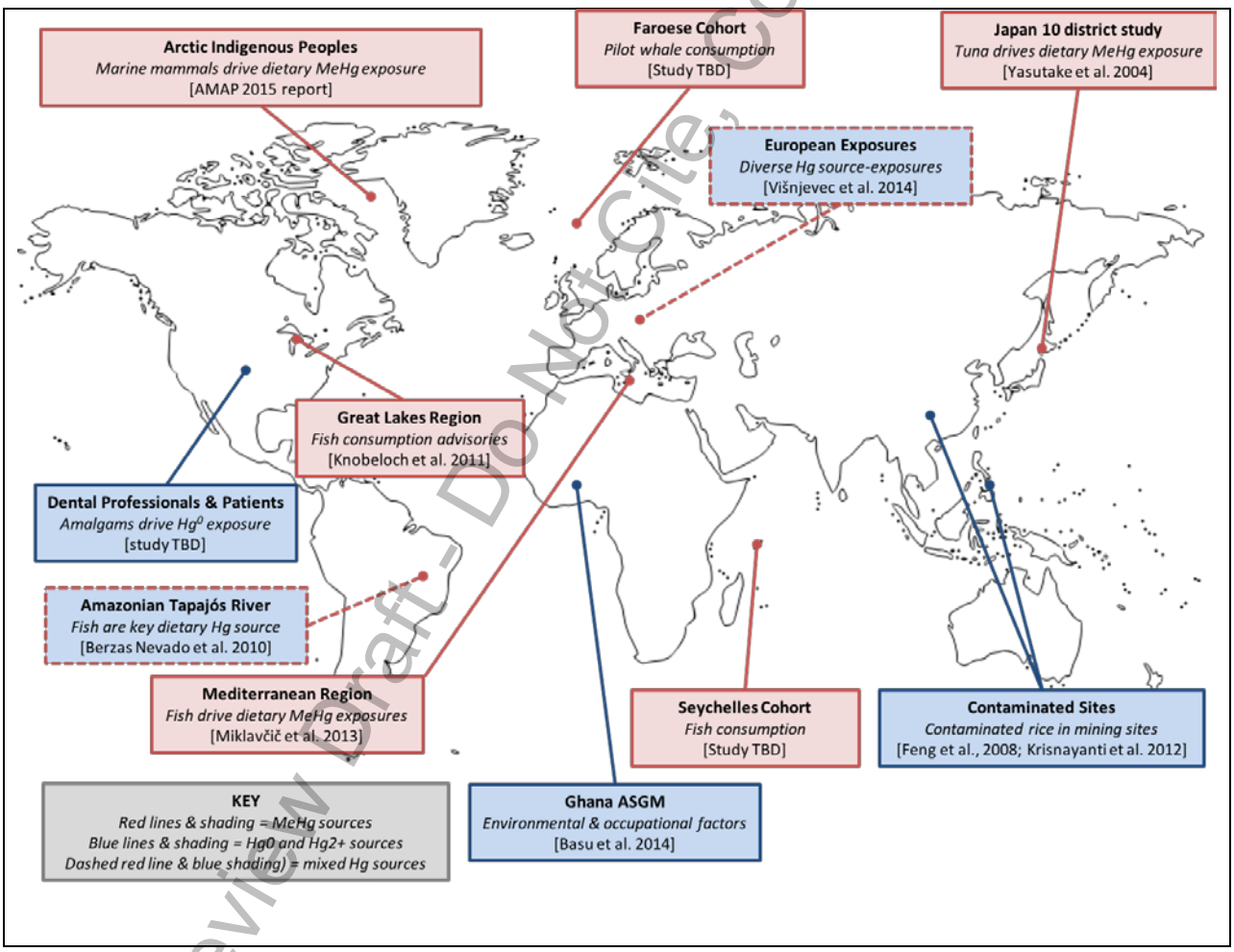

Figure 1. Selected studies across the world depicting strong and representative evidence of mercury source-exposure relationships.

8.1.3 Biomarkers of mercury exposure

Human exposure to Hg is estimated by the use of human tissues that serve as biomarkers (WHO/UNEP/IOMC, 2008). This report focuses on biomarkers of Hg exposure for which there are well-validated methods of measurement and interpretation and for which there is a reasonably large body of knowledge. Within the scientific community there are four established biomarkers of Hg exposure - hair (for MeHg), urine (for inorganic Hg), whole blood (mostly MeHg but can contain inorganic Hg), and cord blood (to gauge developmental exposures). Blood measurements indicate recent exposures (~1-2 months) and speciation measures can deepen understanding of potential sources, though blood collection, storage, and transport poses certain logistical and financial barriers. Hair and urine samples are particularly suitable as they provide information on the two main forms of Hg, and their collection is relatively non-invasive, requires no specialized training, and is cost-effective (e.g., sampling and analyses can likely be achieved for <$50 USD/measure). Further, hair grows at approximately 1 cm per month and thus Hg measurements can be tracked over time. Each biomarker can provide pertinent exposure information on the type of Hg (organic vs. inorganic) and timeline of exposure (acute or chronic). When multiple biomarker measures are taken from a given individual, and also combined with surveys, a deeper exposure assessment may be performed.

To maximize the use of Hg biomarker data, it is sometimes necessary to convert across biomarker types and there are two conventions to be noted. First, the Joint Food and Agriculture Organization (FAO) and World Health Organization (WHO) Expert Committee on Food Additives (JECFA 2004) established a MeHg hair-to-blood ratio of 250 that is now commonly used by the research community. Second, cord blood levels are on average 70% higher than maternal blood as discussed by Stern and Smith (2003). While we use these two biomarker ratios in the current report, we acknowledge on-going debate in the literature concerning the validity of these approaches particularly in consideration of heterogeneity across individuals with respect to influential factors such as sex, age, and ethnicity (Stern and Smith, 2003; Bartell et al., 2000). Nonetheless, biomarker conversions facilitate comparability across studies, and have been effective at helping derive large, regional biomonitoring assessments and maps (e.g., Europe, Miklavcic et al., 2014; Arctic, AMAP 2015) that are effective communication tools. In addition, to make judgements from biomarker measures it is necessary to have reference guidelines and as such we briefly summarise key propositions by stakeholder organizations (Appendix 1 and 2). For the purposes of this report we have adapted the colour scale used by Miklavcic et al. (2014) in their European assessment of Hg exposure (Appendix 3).

8.2 Objective

The overall goal of this chapter is to provide an overview about worldwide human exposures to Hg as reflected by concentrations in biomarker samples. The specific objectives of this study are to outline:

- whether exposures have changed over time in specific populations;
- geographical variations in exposure;
- exposures in vulnerable groups because of high exposures and susceptibility to toxic effects;
- exposure biomarker data with respect to guideline values;
- links between Hg sources and biomarker levels; and
- key knowledge gaps.

8.3 Method

8.3.1 Identification of studies

An international advisory group of scientific experts (i.e., report authors) on Hg exposure was convened to guide the work. The group decided to focus this initial global assessment on three study population types:

A-National human biomonitoring programs. These programs are usually sponsored and/or run by official government agencies and provide high quality data. A list of such programs was compiled by UN Environment (UNEP 2016), and augmented by report authors.

B-Longitudinal birth cohort studies. These studies are usually well designed and most pertinent for establishing exposure-outcome relationships. They tend to provide high quality exposure data for vulnerable groups (pregnant women, newborns, and children), and these data can be used to explore geographic differences, temporal trends, and characterize Hg source-exposure-biomarker relationships.

C-Cross-sectional studies on vulnerable populations. While many vulnerable populations exist, here we focused on two broad groups: a) populations exposed to inorganic Hg from point sources (i.e., artisanal and small-scale gold miners (ASGM) and community members; people living and working in former Hg contaminated sites); and populations exposed to organic Hg from dietary sources (i.e., Indigenous Peoples; recreational or subsistence fishers; pregnant women and foetuses).

8.3.2 Search strategy

A systematic search of the peer-reviewed scientific literature was performed in three databases (PubMed, SCOPUS, Web of Science). The search strategy included the following two Boolean search phrases: #1 – "mercury OR methylmercury OR (methyl AND mercury) OR MeHg"; and #2 - "blood OR hair OR urine". In addition to the systematic search, we considered grey literature and polled key scholars identified by report authors. There were no language restrictions as the committee was willing to devote resources to having pertinent foreign language papers properly translated. When a study was reported upon in multiple articles, we chose the article with the most complete dataset to serve as a representative piece.

Scientific papers were reviewed through a two-stage process: First, the title and abstract fields were searched to ascertain relevancy; and second, the full text was reviewed on papers that were deemed relevant. In brief, national biomonitoring studies (Study Type A) were identified through the 2016 UN Environment survey, authors' knowledge, and an electronic search. All national biomonitoring programs that measured Hg in hair, blood, urine, or cord blood were included (i.e., no exclusion criteria were applied). Longitudinal birth cohort studies (Study Type B) were identified through the 2016 UN Environment survey, authors' knowledge, and an electronic search. Similar to national biomonitoring studies, we did not apply any exclusion criteria except that these studies needed to: A) include at least two discrete sampling periods, one of which needed to be a biomarker measured during pregnancy or birth; and B) measure a health outcome in the newborn during some later lifestage. Vulnerable population group studies (Study Type C) were selectively identified (i.e., most illustrative works) through bibliographic searches.

8.3.3 Data analyses

For all studies, we extracted data on population characteristics (age, lifestage, sex, city/country/region location), Hg exposure measurements (sample size, Hg biomarker and speciation information, quality control measures), and measures of central tendencies (geometric mean, median) and high-end (90th or 95th percentile or maximum) biomarkers. To compare across the biomarker types, we normalized datasets to blood THg equivalents using the conventions mentioned earlier. To further interpret the results, we compared the values against the aforementioned reference guidelines (Appendix 1) and used a colour scale to visually represent the findings (Appendix 3).

8.4 Results

8.4.1 National Biomonitoring Studies

We obtained national data from seven countries (Belgium, Canada, Czech Republic, Germany, Republic of Korea, Sweden, USA), of which three surveys were designed to be nationally representative (Canada, Republic of Korea, USA). The other surveys were included here as they were either legally mandated or government-run to yield actionable information. The total sample population of these surveys was 97,696 people from which 150,929 biomarker measurements of Hg exposure were extracted. The survey data were compared with a particular focus on the following factors: country, lifestage, sex, sampling year(s), and biomarker type.

Table 1. Summary of National Biomonitoring programs that measure mercury

Country	Survey	Lead Organization	Year Started	# Cycles; Frequency	Size /Cycle	Age; Sex	Biomarkers
Canada	CHMS	Statistics Canada	2007	4; every 2 yrs	~5,000	3-79; both	Blood, urine
Germany	GerES	Umwelt Bundesamt	1985	5; variable	~5,000	3-69; both	Blood, urine
Sweden	Riksmaten	Swedish National Food Agency	1990	2; variable	~300	18-80; both	Blood
Korea	KoNEHS	Korean Ministry of Environment	2005	3; every 2 yrs	~5,000	3-19+; both	Blood, urine
USA	NHANES	Centers for Disease Control and Prevention	1960	6; every 2 yrs	~8,000	1-70+; both	Blood, urine
Czech Republic	CZ-HBM	National Institute of Public Health	1994	16; ~every yr	~400	8-64; both	Blood, urine, hair
Belgium	FLEHS	Vlaanderen Departement Omgeving	2002	2; every 2 yrs	~5,000	1-65; both	Hair

Table 2. Count of individuals and mercury biomarker measures from the National Biomonitoring programs.

	Demographics					Mercury Measures				
Country	**Total Sample Size**	**Children**	**Adults**	**Males**	**Females**	**Total # Measures**	**Blood (THg)**	**Blood (MeHg)**	**Urine**	**Hair**
Canada	**17,210**	6,983[1]	10,227[2]	8,418	8,792	**29,099**	16,927	1,032	11,140	
Germany	**10,520**	2,466	8,054			**16,757**	6,237		10,520	
Sweden	**297**			128	145	**297**	297			
Korea	**14,688**	2,346	12,342			**14,688**	14,688			
USA	**46,974**	19,086[3]	27,888[4]	23,292	23,682	**75,778**	46,974	13,016	15,788	
Czech Republic	**7,542**	3,623	3,919			**13,845**	4,700		6,459	2,686
Belgium	**465**	210	255		255	**465**				465
Totals	**97,696**					**150,929**				

Across the national biomonitoring programs the majority of participants had blood Hg levels that fell below 5 ug/L. Blood Hg levels were consistently highest in Korea versus the other countries. Blood Hg levels in adults were approximately 2.1-fold higher than in children, and this varied across lifestage. For example, median blood Hg levels in Canadians from the CHMS increased with age as follows: 0.24 μg/L for 6-11 yr olds, 0.28 μg/L for 12-19 yr olds, 0.76 μg/L for 20-39 yr olds, 1.1 μg/L for 40-59 yr olds, and 0.96 μg/L for 60-79 yr olds. Similar trends were observed in the U.S. and Korean datasets.

Urine Hg levels were consistent across the countries from which data were obtained, with a majority of the values falling under 3 μg/L. Like blood, urine Hg levels were higher in adults than in children.

[1] includes study participants ages 3-19
[2] includes study participants ages 20-79
[3] includes study participants ages 1-19
[4] includes study participants ages 20+

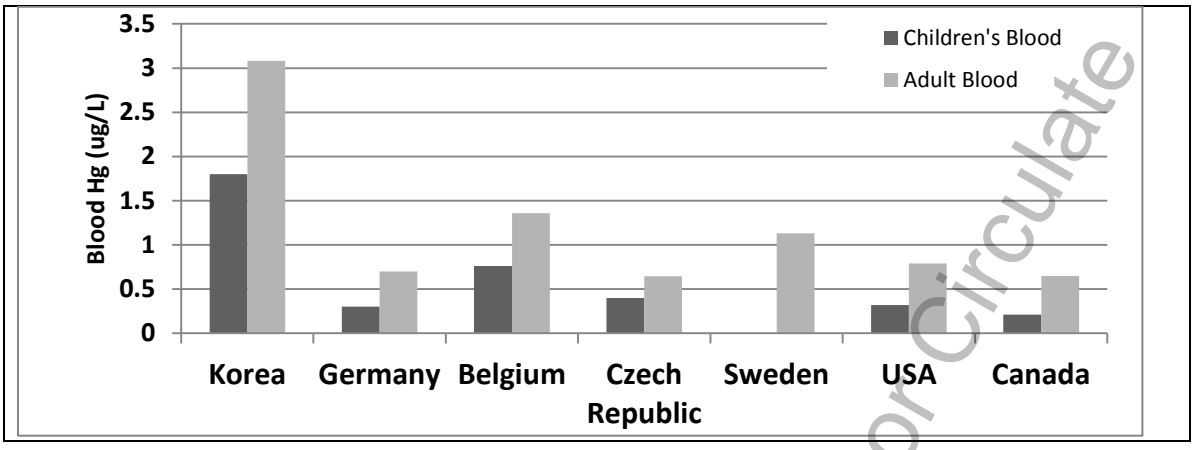

Figure 2. Comparison of median whole blood total Hg (μg/L) measurements across children (<19 years) and adults from national biomonitoring datasets between the years 2003-2014.

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TABLE 3. Cross-sectional comparison of whole blood total mercury measurement (μg/L) in adults and children via national biomonitoring data. Males and females are grouped together.

		Korea	Germany	USA	Canada	Belgium	Czech Republic	Sweden
	Survey Name	KHANES (Adults), KorEHS-C (Children)	GerES-3 (Adults), GerES-2 (Children)	NHANES	CHMS Cycle 2	FLEHS2	CZ-HBM	Riksmaten
Adults	Year	2011	1998	2011-2012	2009-2011	2007-2011	2015	2010-2011
	Age	19+	18-69	20+	20-39	18-42	18-64	18-80
	Sample Size	2014	3973	5030	1313	255	302	297
	Whole Blood Hg (50%)	3.08 (GM)	0.70	0.79	0.65	1.36	0.65	1.13
	Whole Blood Hg (95%)	??	2.40	5.02	5.20	3.44	2.50	3.45
Children	Year	2012-2014	2003-2006	2011-2012	2009-2011	2007-2011	2008	
	Age	3-18	3-14	6-11	6-11	14-16	8-10	
	Sample Size	2346	1240	1048	961	210	198	
	Whole Blood Hg (50%)	1.80	0.30	0.32	0.21	0.76	0.40	
	Whole Blood Hg (95%)	3.68	1.00	1.40	2.00	1.88	1.40	

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TABLE 4. Cross-sectional comparison of urinary total mercury measurement (μg/L) in adults and children via national biomonitoring data. Males and females are grouped together.

		Germany	USA	Canada	Czech Republic
Adults	Year	1998	2011-2012	2012-2013	2009
	Age	18-69	20+	20-39	18-64
	Sample Size	4052	1716	1048	373
	Urine Hg (50%)	0.40	0.34	0.20	0.80
	Urine Hg (95%)	3.00	1.93	1.10	5.30
Children	Year	2003-2006	2011-2012	2012-2013	2008
	Age	3-14	6-11	6-11	8-10
	Sample Size	1734	401	1010	318
	Urine Hg (50%)	<0.1 [LOD is 0.1]	.22	<LOD	0.2[5]
	Urine Hg (95%)	0.5	1.37	.93	1.1

14198

14199 Temporal changes in Hg exposure were evaluated by reviewing national datasets in which there were 2
14200 or more comparable sampling periods. For blood Hg, datasets from four countries were reviewed and in
14201 general they showed declining exposures. For example, combining the work from USA, Canada, and the
14202 Czech Republic into a linear regression model showed annual decreases in blood Hg of approximately
14203 0.026 μg/L or 2.25% (i.e., over 10 years this would be a decrease of 0.26 μg/L or ~22.5%) with median
14204 blood Hg levels levelling around 0.75 μg/L (Figure 3A). For urinary Hg, similar over-time decreases can
14205 be observed particularly when examining the US NHANES dataset as the Hg levels in the latest dataset is
14206 approximately 50% lower than it was 10 years earlier (Figure 3B). The urinary Hg values now in the US
14207 are similar to Canada and hover around 0.2 μg/L.

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[5] creatinine corrected

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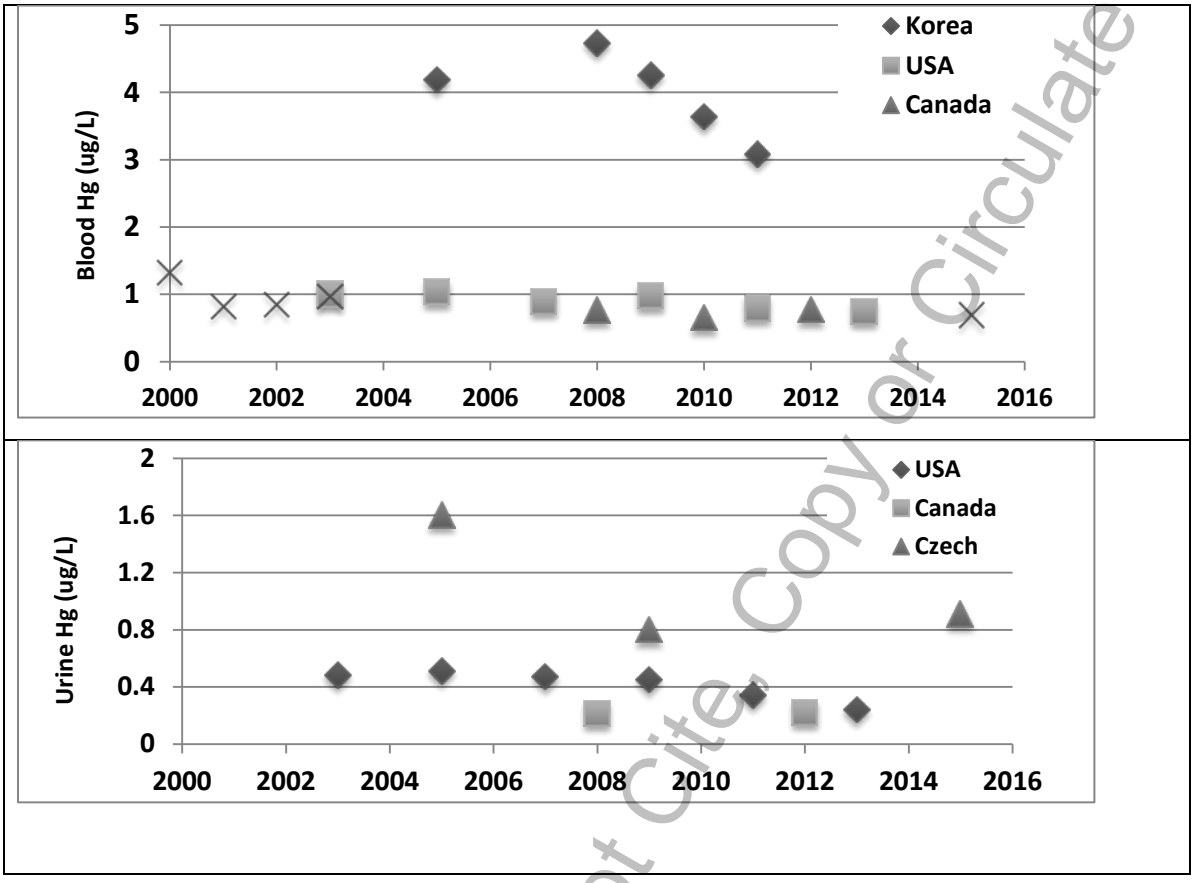

Figure 3. Temporal trends of adult A) whole blood and B) urinary total Hg (μg/L; median values) measurements across the national biomonitoring studies in which data was available from 2+ comparable sampling periods.

14210 **8.4.2 Longitudinal birth cohorts**

14211 We found 26 birth cohort studies in which at least there was one Hg exposure measurement during
14212 pregnancy or birth, as well as a follow-up time period in which an outcome measurement was taken
14213 (Appendix 4). The total sample population of these birth cohort studies was 19,940 mother-child pairs
14214 from which 42,750 biomarker measurements were taken. Of these birth cohort studies, 16 (62%)
14215 measured Hg in cord blood, 9 (35%) measured Hg in maternal blood during pregnancy, and 14 (54%)
14216 measured Hg in maternal hair, and these are summarized in Figures 4 and 5.

14217 From this dataset, there are some noteworthy observations: A) groups consuming large amounts of
14218 seafood (Seychelles, Spanish) and/or marine mammals (e.g., Faroe Islands, Inuit) have the highest Hg
14219 cord blood values, which often exceed 10 μg/L; B) cord blood Hg levels range between 5 and 10 μg/L
14220 across several Mediterranean populations, are approximately 5 μg/L in Asia, and generally less than 5

14221 μg/L across communities in North America and Europe (excluding Indigenous Peoples and
14222 Mediterranean); and C) exposures in the Faroe Islands have dropped nearly five-fold from ~1987 to
14223 ~2008 (whole blood Hg from 22.3 to 4.6 μg/L), and in the Seychelles approximately two-fold from ~1989
14224 to ~2008 (hair Hg from 5.9 to 2.9 μg/g);

Figure 4. **Cord blood mercury measurements (μg/L) across the birth cohort studies.**

[aside, graphics quality and content will be improved]

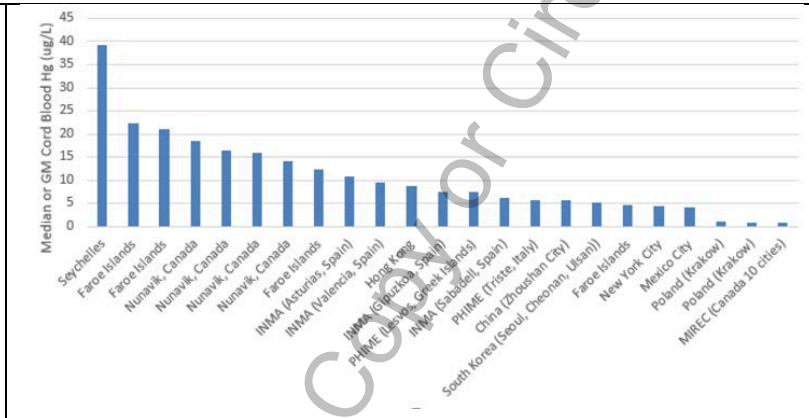

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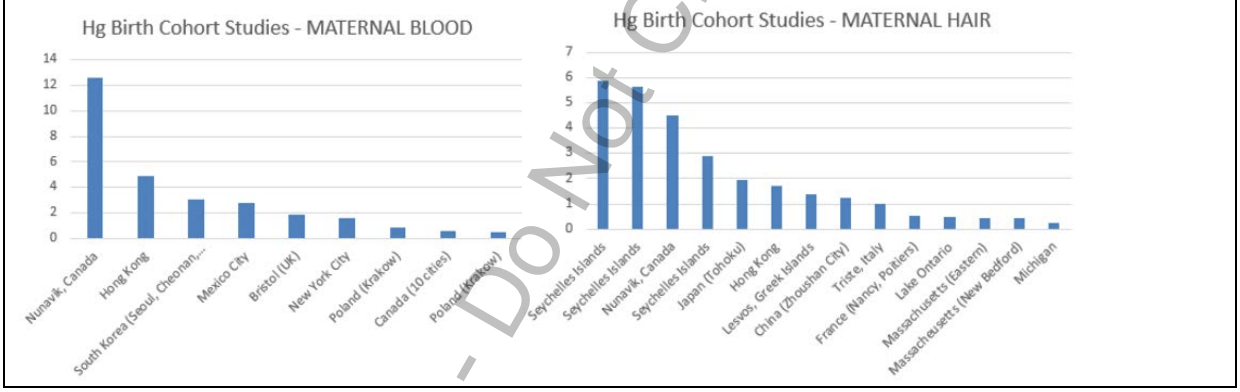
Figure 5. **Maternal A) blood (ug/L) and B) hair (μg/g) mercury values across the birth cohort studies. [aside, graphics quality and content will be improved]**



14226

14227 In these birth cohort studies a range of health outcomes were measured in the newborn, infant, toddler,
14228 or child, including for example, birth weight, motor function, and intelligence (see reviews by Ha et al.
14229 2017, Karagas et al. 2012). Here, we flag the cohorts in which a Hg-associated adverse health outcome
14230 was observed, and in doing so we see that these span a range of exposures and are not restricted to
14231 highly exposed groups or particular regions (Figure 6).

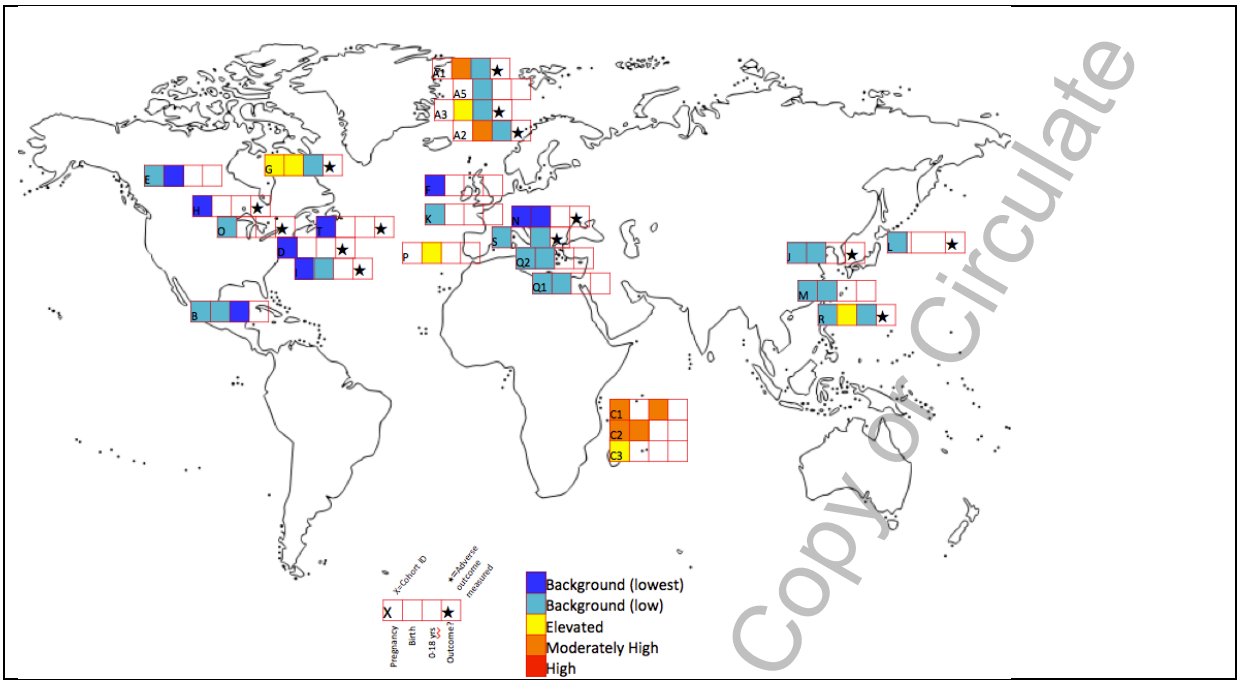


Figure 6. Map outlining the locations of the selected mercury birth cohort studies. Data represents 26 cohort studies and 42,750 Hg biomarker measures. The first three boxes refer to mercury measures taken during pregnancy, at birth, and up until age 18 according to the colour scale (see Appendix 3; cohort ID is indicated in the first box via a letter). If the final box has a star, then a Hg-associated adverse outcome was reported in that cohort.

8.4.3 Vulnerable populations

*** this Section is in EARLY DRAFT phase. It has not been reviewed by all team members. It will be updated following the review ***

From the bibliometric search and group discussions, a selection of exemplary and representative papers was identified and discussed here to showcase the current state of knowledge mercury exposure in notable vulnerable groups. In general we prioritized conclusions from high-quality review papers. Some of these examples were captured in Figure 1.

Pregnant women and foetuses. MeHg-contaminated seafood poses particular risk-benefit dilemmas (Mahaffey et al. 2011). Sheehan et al. (2014) conducted a systematic review of Hg exposure biomarkers in these populations worldwide (164 studies from 43 countries) and drew some meaningful conclusions: 1) exposures are highest amongst riverine gold mining communities (median hair Hg 5.4 µg/g; n=10,152 participants) and Arctic Indigenous Peoples (median hair Hg 2.1 µg/g; n=5,935 participants); 2) coastal Pacific regions of Asia have higher median hair Hg levels (1.3 µg/g; n=14,704 participants) than

Mediterranean (0.7 μg/g; n=6,536), Atlantic (0.4 μg/g; n=9,675), as well as inland populations (0.4 μg/g; n=10,745)

Indigenous Peoples. Groups in the Arctic are exposed to some of the highest MeHg levels globally largely due to their reliance on marine mammals and seafood as culturally important food staples. The 2015 AMAP Human Health Report reviewed several human biomonitoring programs across the circumpolar region. As an example, in Canada as part of the International Polar Year study the geometric mean of whole blood Hg across 4 study regions ranged from 2.8 to 12 μg/L, with individual values ranging from 0.1 to 240 μg/L. Beyond the Arctic region, there are studies from several other communities documenting elevated exposures in Indigenous Populations (e.g., selected examples to be listed here) especially since fish are a vital component of the culture of these communities. For example, Cisneros-Montemayor et al. (2016) compiled data from over 1,900 coastal Indigenous groups (27 million people from 87 countries) to show that per capita seafood consumption in these communities is 15-times higher than in non-Indigenous groups.

Artisanal and small-scale gold mining (ASGM). ASGM is rapidly growing worldwide with upwards of 15 million miners estimated to be directly involved in the sector and potentially 100 million people living in ASGM communities (World Health Organization, 2016; United Nations, 2012). There are a number of public health concerns in ASGM communities (Basu et al., 2015; World Health Organization, 2016) as well as a growing number of human biomonitoring studies (reviewed by Gibb and O'Leary, 2014). A noteworthy meta-analysis of 1,245 miners from across Indonesia, Philippines, Tanzania, Zimbabwe, and Mongolia reporting median urine Hg values of 3.6 μg/L (95th percentile 119 μg/L) with upward values in excess of 1,000 μg/L, and median blood Hg levels in 1,121 miners being 5.1 μg/L (95th percentile 38.2 μg/L) (Baeuml et al., 2011).

8.5 Summary of findings

*** this Summary is in EARLY DRAFT phase. It has not been reviewed by all team members. It will be updated following the review ***

The current assessment documents great variability in Hg exposures worldwide. All people are exposed to some amount of Hg. Individuals in select background populations worldwide have blood Hg levels that generally fall under 5 μg/L and urine Hg levels that fall under 3 μg/L, and corresponding levels in

hair and cord blood may be determined using the ratios outlined in Appendix 1. There are a number of notable groups with relatively high Hg exposures. Elevated exposures to Hg in key populations of concern for which there exist a relatively robust dataset include Arctic Indigenous Peoples who consume fish and marine mammals, coastal and/or small-island communities who are avid seafood consumers, and individuals who either work or reside amongst ASGM sites.

Despite a relatively large dataset to work from (e.g., here we had 150,929 and 42,750 biomarker measurements from national biomonitoring programs and birth cohort studies, respectively) there remain outstanding questions. Foremost is that there exist a number of countries and geographic regions for which data is completely lacking. There are several other groups of potential concern (e.g., individuals living in Hg contaminated sites; consumers of rice from contaminated sites; users of skin-lightening creams) but relatively little data to draw firm conclusions. In addition to focusing on vulnerable groups due to elevated exposures to Hg, there remain concerns about Hg susceptibility during certain lifestages (e.g., pregnancy and infancy), the range of physiological systems targeted (Karagas et al., 2012), the complex interactions between Hg and other chemical and non-chemical stressors particularly in the context of global change drivers (Eagles-Smith et al., 2017), and the increasing acceptance that genetic differences in sub-populations can influence exposure biomarkers and exposure-outcome relationships (Basu et al., 2014).

There are also success stories to be noted. Through our review identified studies that showed that steps to reduce Hg exposure may be effective. First, the approximately two-fold reduction in urinary Hg levels measured over the past decade across the U.S. has been linked with the phase-down on the use of dental amalgam (Figure 3B). Similar trends have been observed elsewhere, such as in German children (Link et al., 2007) and dental professionals (Goodrich et al., 2016). Second, across Arctic circumpolar regions Hg exposures are elevated though over the past two decades these have dropped likely as a result of local dietary advisories and changing consumption patterns. According to AMAP (2015) these decreases may be a sign that risk management efforts are having a beneficial effect, but that there remain concerns about changing consumption patterns and how this may affect culture and spirituality, recreational opportunities, and human nutrition. In other jurisdictions, there have been cases of decreased Hg exposures as a result of dietary consumption advisories (e.g., Kirk et al., 2017; Knobeloch et al., 2011), and we also note that decreases have also been observed in both the Faroe Islands and the Seychelles (Figure 6). Third, within the ASGM sector there is increasing interest in assessing the efficacy

of interventions in terms of reducing exposures. Calys-Tagoe et al. (2017) found that urinary Hg levels are significantly lower in workers from licensed ASGM sites versus unlicensed ones in Ghana.

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APPENDIX 1. Reference Values for Mercury Biomarkers. Italicized values are estimated based on biomarker conversions indicated in the text.				
	Whole Blood	**Hair**	**Cord Blood**	**Urine**
NAS/NRC BMDL (concerning women of child-bearing age)	*3.5 ug/L*	1 ug/g	5.8 ug/L	
Qualitative conclusions by expert panel (Karagas) on "High" Levels	>12 ug/L	>4 ug/g	>20 ug/L	
Health Canada (Legrand Paper)	8 ug/L (pregnant women); 100ug/L for "general" men/women	*2 ug/g* *25 ug/g*	*13.6 ug/L* *and* *170 ug/L*	
German HBM-1[6] [no risk, background]	5	*1.25 ug/g*	*8.5 ug/L*	7
German HBM-2 [increased risk for adverse outcome]	15	*3.75 ug/g*	*25.5ug/L*	25
World Health Organization (WHO). Recommended Health-Based Limits in Occupational Exposure to Heavy Metals; WHO: Geneva, Switzerland, 1980.		<0.5 ug/g (non fish consumers); 1-2 ug/g (low and moderate fish consumers); >10 ug/g (frequent consumers)		50 ug/l
The ACGIH (2007) https://www.osha.gov/dts/osta/otm/otm_ii/pdfs/otmii_chpt2_appb.pdf				35 µg/g of creatinine.
Florida Health Department[7]	<10 ug/L (background); 50 and above (clinical effects)	*<2.5 (background); 12.5 and above (clinical effects)*		<40ug/L (no clinical effects); 40-60 (medium); 60+ (high)

[6] https://www.umweltbundesamt.de/sites/default/files/medien/355/bilder/dateien/hbm-werte_engl_stand_2017_02_06.pdf

[7] http://www.floridahealth.gov/environmental-health/mercury-spills/mercury-poisoning/_documents/guidelines-for-mercury.pdf [document HG05-2009]

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APPENDIX 2. Reference Values for Mercury Intake.				
		Inorganic Hg	**MeHg**	**REF**
European Food Safety Authority[8] (CONTAM panel), 2012	Tolerable Weekly Intake;	4 ug/kg bw for Inorganic Hg	1.3 ug/kg/bw for MeHg	
Joint FAO/WHO Expert Committee on Food Additives (JECFA), 2010	Tolerable Weekly Intake;	Similar to EFSA Above	1.6 ug/kg bw for MeHg	
U.S. EPA Reference Dose	Daily Intake	0.3 ug/kg/d mercuric chloride	0.1 ug/kg/d for MeHg	
U.S. EPA Reference Dose	Weekly Intake	0.3 ug/kg/d mercuric chloride	0.7 ug/kg/d for MeHg	
Canada (adopted 1997)	Weekly Intake		1.4 ug/kg wk for MeHg	WHO Doc Ref 6,7
Japan (adopted 2005)	Weekly Intake		2 ug/kg wk for MeHg	WHO Doc Ref 8
Netherlands	Weekly Intake		0.7 ug/kg/d for MeHg	WHO Doc ref 9

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[8] http://www.efsa.europa.eu/en/press/news/121220

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Appendix 3. Colour scale related to mercury biomarker values. Adapted from Mikalavcic et al. with minor modifications.				
	Hair (ug/g)	**Whole Blood (ug/L)**	**Cord Blood (ug/L)**	**Urine (ug/L)**
Background-non seafood consumers [BLUE]	<0.5	<2	<3.4	<1
Background-seafood consumers [Turquoise]	0.5-2	2-8	3.4-13.6	1-3
Elevated [yellow]	2-5	8-20	13.6-34	3-10
Moderately High [orange]	5-10	20-40	34-68	10-50
High [red]	>10	>40	>68	>50

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Appendix 4. Summary of birth cohort studies that were included in the current report. [NOTE this will be updated with new studies and cleaned accordingly prior to publication]

				LIFESTAGE EXPOSURES							
Cohort-ID	Cohort-Name	n	Yr	Pregnancy	Birth	Infant (0-1	Toddler (1	Child (3-11	Adolescen	Adult (18+	Outcome?
H	POUCH (Michigan)	1024	1998	0.92							★
N	Poland	313	2002	0.83	1.09						★
E	MIREC	1673	2008	2.24	0.802						
D	VIVA	135	2002	1.8							★
T	Massacheusetts	421	1993	1.8							★
F	ALSPAC	4131	1991	1.86							
O	Oswego	212		2							★
K	EDEN	665	2003	2.08							
I	World Trade Center	280	2001	1.6	4.44						★
S	Italy	128	2001	3.2				2.16			★
B	ELEMENT	348	1994	2.8	4.1			1.37			
J	MOCEH (Korea)	797	2006	3.1	5.2						★
A5	Faroe Islands	500	2008		4.6						
Q1	PHIME-Italy	573		4	5.6						
M	Zhoushan	406	2004	4.98	5.58						
Q2	PHIME-Greece	281		5.6	7.5						
R	Hong Kong	1057	2000	4.92	8.8			2.62			★
L	Tohoku	498	2001	7.8							★
P	INMA	1883	2004		8.2						
C3	Seychelles		2008	11.68							
A3	Faroe Islands	475	1999		12.4			2.6			★
G	Nunavik Child Development	130	1994	12.6	15.9			5.9			★
A2	Faroe Islands	182	1995		21			3.2			★
A1	Faroe Islands	1022	1987		22.3			8.4	4.1		★
C1	Seychelles	779	1989	23.6		26.4	19.2	25.2	32.4	27.3	
C2	Seychelles		2001	22.5	39.3						