

Global methylmercury exposure from seafood consumption and risk of developmental neurotoxicity: a systematic review

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Objective To examine biomarkers of methylmercury (MeHg) intake in women and infants from seafood-consuming populations globally and characterize the comparative risk of fetal developmental neurotoxicity.

Methods A search was conducted of the published literature reporting total mercury (Hg) in hair and blood in women and infants. These biomarkers are validated proxy measures of MeHg, a neurotoxin found primarily in seafood. Average and high-end biomarkers were extracted, stratified by seafood consumption context, and pooled by category. Medians for average and high-end pooled distributions were compared with the reference level established by a joint expert committee of the Food and Agriculture Organization (FAO) and the World Health Organization (WHO).

Findings Selection criteria were met by 164 studies of women and infants from 43 countries. Pooled average biomarkers suggest an intake of MeHg several times over the FAO/WHO reference in fish-consuming riparians living near small-scale gold mining and well over the reference in consumers of marine mammals in Arctic regions. In coastal regions of south-eastern Asia, the western Pacific and the Mediterranean, average biomarkers approach the reference. Although the two former groups have a higher risk of neurotoxicity than the latter, coastal regions are home to the largest number at risk. High-end biomarkers across all categories indicate MeHg intake is in excess of the reference value.

Conclusion There is a need for policies to reduce Hg exposure among women and infants and for surveillance in high-risk populations, the majority of which live in low- and middle-income countries.

Abstracts in **عربي**, **中文**, **Français**, **Русский** and **Español** at the end of each article.

Introduction

The World Health Organization (WHO) considers mercury (Hg) among the top 10 chemicals of “major public health concern”.¹ Evidence of ubiquitous Hg contamination globally led to the recent Minamata Mercury Convention, a binding international treaty to control anthropogenic Hg emissions.² A principal form of Hg to which general populations are exposed is methylmercury (MeHg). Transformation of Hg emissions to organic MeHg takes place in the aquatic environment, where MeHg bioaccumulates in food webs. In human beings MeHg exposure occurs predominantly through the consumption of seafood (including freshwater and marine varieties, shellfish and marine mammals).^{3–6} MeHg is a neurotoxin particularly harmful to the developing fetal brain.^{3–6} A large body of research has demonstrated an association of exposure *in utero* with developmental neurotoxicity (e.g. deficits in fine motor skills, language and memory) among populations that consume seafood regularly.^{3,7–9} Such studies have been used to develop health-based reference doses below which no appreciable risk of harm is thought to occur, including the provisional tolerable weekly intake (PTWI), established by the Joint Expert Committee on Food Additives (JECFA) of the Food and Agriculture Organization (FAO) and WHO.^{6,10} Recent research suggests harm at doses associated with relatively infrequent seafood consumption.¹¹

Seafood species vary in MeHg content depending on contamination source, trophic level and other factors.^{12–14} Seafood, on the other hand, is an important source of nutrients, including neuroprotective omega-3 polyunsaturated

fatty acids.¹⁵ Research on the benefits and harms of seafood highlights the importance of choosing species low in MeHg and high in these polyunsaturated fatty acids and of ensuring that consumers have sufficient information to make such choices.^{15,16} Well-designed seafood advisories can be helpful to this end,^{17,18} but they exist in a small number of countries, most of which are high-income.¹⁹ An estimated 400 million women of reproductive age in the world rely on seafood for at least 20% of their intake of animal protein; a large share of them live in low- and middle-income countries where access to information on MeHg content in seafood is not widely available.^{20–22} Although the research conducted in the last two decades has highlighted the risk in subsistence fishing communities that practise artisanal and small-scale gold mining²³ and among Arctic peoples whose diet consists of apex marine predators such as the pilot whale,²⁴ few researchers have compared MeHg exposures globally in women who consume seafood.

Human exposure to chemical contaminants can be characterized by examining biomarkers.²⁵ Total Hg in hair (THHg) and total Hg in blood (TBHg) are both validated biomarkers of MeHg intake correlated with seafood consumption in general human populations.^{4,26} Our goal was to review and synthesize the evidence from published studies reporting THHg and TBHg biomarkers to systematically compare global MeHg exposure among women and their infants from seafood-consuming populations. By identifying populations at higher risk, we aim to provide policymakers with scientific evidence for the prioritization of risk reduction messages and targeted population surveillance.

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Methods

Based on a pre-defined study protocol,²⁷ we performed a systematic electronic search of the peer-reviewed scientific literature (Box 1). Studies were selected in two stages: title and abstract screening, followed by full text review after application of exclusion criteria. We excluded studies not involving women or infants from general populations and not reporting a central THHg or TBHg biomarker estimate. When multiple articles reported on a single sample, we chose the most recent one with complete data. To ensure robust summary statistics, we excluded studies with less than 40 participants.

We extracted data on study design, population characteristics, measures of average (geometric mean or median) and high-end (90th or 95th percentile or maximum) biomarkers, exposure conditions and main covariates examined. Extracted biomarkers were organized into three subpopulation groups: non-pregnant women; pregnant women and mothers who had recently given birth; and infants (up to 12 months of age). Because biomarkers for more than one subpopulation with different levels of exposure were often reported in the same study, the subpopulation was our main level of analysis.

We stratified subpopulations into six mutually exclusive categories based on predictors of the body burden of MeHg. The most important of these predictors are seafood consumption frequency and seafood MeHg content. In most seafood species MeHg represents the largest fraction of total Hg (inorganic Hg representing a much smaller share). Thus, seafood MeHg concentration is commonly measured as total Hg in tissue.^{3,4} Seafood consumption estimates were reported in some studies; data on total Hg concentrations were rarely provided. Research suggests the following general hierarchy: marine mammals, other apex marine predators and some industrially-contaminated fish [containing several parts per million (ppm)]; large marine fish [containing up to 1 or more ppm]; most commercially purchased marine and freshwater fish [often containing less than 0.5 ppm] and most shellfish [often containing less than 0.2 ppm].^{23,24,28–31} Seafood intake is generally higher in coastal regions than inland^{30,32} and seafood from globalized commercial sources predominates in

Box 1. Literature search strategy for global systematic review of methylmercury exposure from seafood in women and infants

1. "fetus" OR "infant" OR "newborn" OR "maternal" OR "mother" OR "pregnant" OR "women"
 2. "fish" OR "marine" OR "shellfish" OR "seafood"
 3. "mercury" OR "methylmercury" OR "methyl AND mercury" OR "biomonitoring"
- Combined terms: 1 AND 2 AND 3.

Note: The following databases were searched for studies published from January 1991 to September 2013: PubMed, Embase, SCOPUS, Web of Science, TOXNET and LILACS. References were hand-checked and there were no restrictions on language or study design.

many urban areas.¹⁴ We therefore generated six categories based on the following proxy predictors, reported in most studies: seafood source; seafood type; likely Hg contamination pathway; and residential context. Four categories included populations consuming seafood that was mainly self-caught and two included populations consuming seafood that was commercially purchased primarily (Table 1).

As recommended in guidelines for the systematic review of observational studies,²⁷ we evaluated study quality by examining the risk of bias in three areas: selection of participants (selection methods and reporting of exposure characteristics); exposure measurement (laboratory methods and quality control); and statistical methods and covariate analysis (evaluation of distribution shape, reporting of seafood intake and exposure to non-seafood sources of Hg).

We derived two summary distributions – central and upper bound – for each exposure category by pooling average and high-end biomarkers. For comparability, all TBHg biomarkers were converted to THHg-equivalent at a hair-to-blood ratio of 250:1.^{3,5} We summarized resulting statistical distributions using medians and percentiles. To interpret results, we compared distribution medians with the THHg-equivalent value of the PTWI dose (approximately 2.2 µg/g) established by the JECFA.¹⁰ We also determined the share of subpopulations with average and high-end biomarkers over this reference. In sensitivity analysis we evaluated the impact on pooled biomarkers taking into account differences in participant selection, exposure measurement and statistical methods identified in the quality review. Given substantial heterogeneity in population exposure conditions, study designs and reporting, we did not undertake a meta-analysis. All data analysis was performed in Stata10 (StataCorp, College Station, United States of America).

Results

Selected studies

Of 3042 articles identified in the published literature, we screened 1402 non-duplicates (1379 were identified by electronic search and 23 by hand search); we excluded 1120 and we reviewed the full texts of the remaining 282, from which we excluded 118 (Fig. 1). The remaining 164 articles, which reported total Hg biomarkers for 239 distinct subpopulations, were included in this review. Selected articles report biomarker concentrations for 63 943 women and infants from 43 countries (Table 2). Most (73%) studies were cross-sectional and over half (56%) reported THHg measures; the majority (79%) were published after 2001. Studies published in 1991–2001 were conducted primarily in populations consuming self-caught seafood; since 2001, the number of studies in consumers of seafood that is predominantly commercially purchased has increased notably in both absolute and relative terms (Fig. 2). The characteristics of the selected studies are provided in Table 3 and Table 4 (both available at: <http://www.who.int/bulletin/volumes/92/04/13-116152>).

Pooled biomarker concentrations

For 43 subpopulations of women and infants living near small-scale gold mining sites in Bolivia (Plurinational State of),^{33,34} Brazil,^{35–53,59,60} Colombia,⁵⁴ French Guiana,^{55–57} Indonesia⁵⁸ and Surinam⁶¹ the pooled central distribution median THHg biomarker concentration was 5.4 µg/g (upper bound median: 23.1) (Table 5). Values were higher (8.2 µg/g; upper bound: 27.5) in the subgroup of rural riverine dwellers reliant on local freshwater fish and lower (1.4 µg/g; upper bound: 11.8) among urban dwellers consuming less fish. For 21 subpopulations from Arctic regions, including in Canada,^{62–66} Denmark (Greenland and the Faroe Islands),^{67–69}

Table 1. Methylmercury exposure categories^a for women and infants from seafood-consuming populations

Category/subcategory	Predominant Hg pathway to seafood	Predominant seafood type	Seafood intake range (kg per month) ^b	Residential context
Locally self-caught seafood is important share of diet				
Arctic – Traditional diet – Mixed diet	Unique polar meteorology and Hg deposition/mobilization, Arctic food-chain (marine mammals as apex predators)	Traditional: marine fish and marine mammals Mixed: marine fish and non-seafood protein sources, few if any marine mammals	0.6–7.1	Far northern Arctic, where people rely on apex Hg-contaminated marine mammals and fish
Gold mining – Rural riverine – Urban	Artisanal and small-scale gold mining, soil lixiviation, forest fires releasing Hg emissions	Rural: high share of locally-caught freshwater fish Urban: mixed diet including non-seafood protein, low share of locally-caught freshwater fish	0.6–14.9	Rural and urban tropical areas near artisanal and small-scale gold mining, where the diet includes fish from rivers contaminated by gold mining activity
Fishing	Local and general global transport of Hg emissions	Marine and freshwater fish and shellfish	0.1–3.8	Recreational or subsistence fishing areas near rivers, reservoirs or lakes without a particular Hg contamination source
Industry	Local Hg-emitting industry (chloralkali, power generation, mining other than gold mining)	Marine and freshwater fish and shellfish	0.2–5.8	Recreational or subsistence fishing areas near water bodies with active or disused industrial facilities
Seafood consumed is mostly from commercial sources (i.e. non-self-caught)^c				
Coastal – Atlantic – Mediterranean ^d – Pacific	Local and general global transport of Hg emissions in all three regions; natural Hg emission sources in the Mediterranean	Marine and freshwater fish and shellfish	0.3–5.6	Atlantic, Mediterranean or Pacific coastal areas where seafood intake is frequent
Inland	Local and general global transport of Hg emissions	Marine and freshwater fish and shellfish	Very little–2.0	Inland areas where seafood intake is low

Hg, mercury.

^a Exposure categories based on proxy predictors reported in selected studies.

^b Estimated per capita seafood intake ranges were derived from data reported in selected studies. They were converted to kg per month for comparability.

^c Several subpopulations consume an important share of self-caught marine seafood in addition to commercially-purchased varieties.

^d Because Indian Ocean and Persian Gulf subpopulations were not numerous and reported seafood intake and total Hg biomarkers similar to those of the more numerous Mediterranean subpopulations, the former were included with the latter.

Norway,^{70,71} the Russian Federation⁷² and the United States (state of Alaska),⁷³ the pooled central distribution median result was 2.1 µg/g (upper bound: 9.8); values were higher (3.6 µg/g; upper bound: 24.3) for marine mammal and other self-caught seafood consumers and lower (0.4 µg/g; upper bound: 1.4) among those with a diet including less seafood and less reliant on these traditional foods.

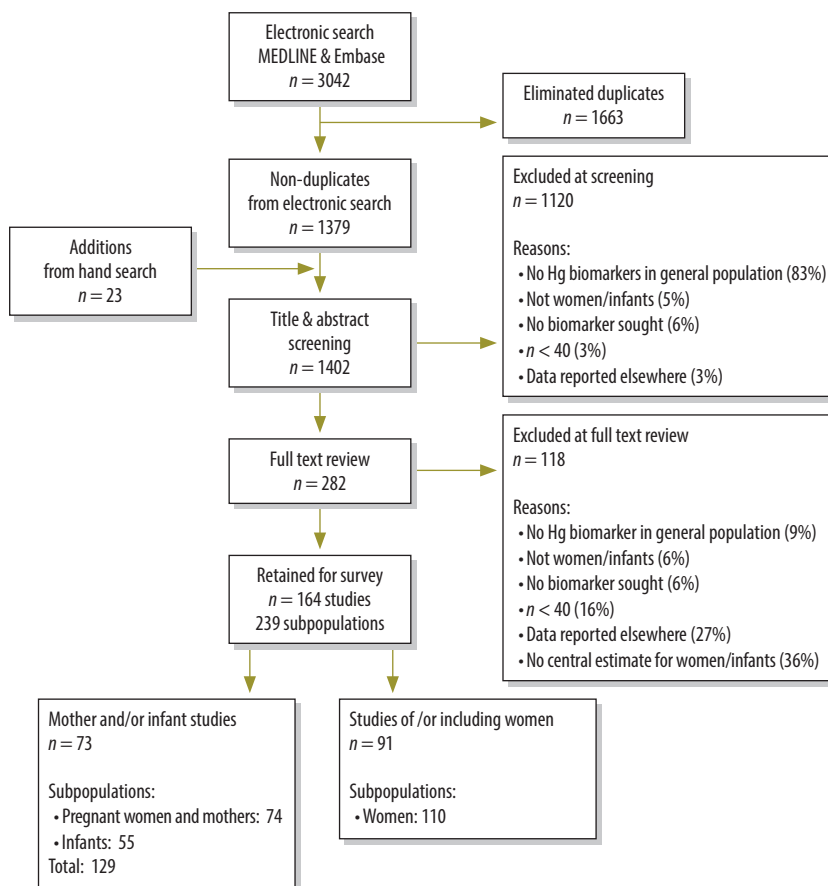
For 25 subpopulations whose self-caught fish from local waterways is affected by Hg-emitting industries in Brazil,^{74,75} Chile,⁷⁶ China,^{77–81} Colombia,⁸² Italy,^{83,84} Kazakhstan,⁸⁵ Mexico,⁸⁷ Morocco,⁸⁸ Nicaragua,⁸⁹ Norway,¹¹⁵ the

Republic of Korea,⁸⁶ Romania,⁹⁰ Slovakia,^{81,91} Sweden,⁹² Taiwan, China,⁹³ the United States⁹⁴ and Venezuela (Bolivarian Republic of),⁹⁵ the pooled central THHg median biomarker was 0.8 µg/g (upper bound: 4.6). In 14 subpopulations consuming fish periodically from non-industry-contaminated waters in Botswana,⁹⁶ Canada,^{97–102} Norway,¹⁰³ Sweden¹⁰⁴ and the United States,^{105–107} the value was 0.4 µg/g (upper bound: 2.8).

For 102 coastal or island-dwelling subpopulations consuming seafood that is predominantly commercially purchased, the combined central median THHg concentration was 0.8 µg/g (upper bound: 6.8). On the Atlantic coast,

the pooled result for 35 subpopulations in Brazil,¹⁰⁸ Canada,^{99,109} France,^{110,111} Norway,¹¹⁵ Portugal,¹¹⁷ Spain,¹¹⁸ Sweden,^{81,92,112–114,119} the United Kingdom of Great Britain and Northern Ireland^{120,121} and the United States^{122–131} was 0.4 µg/g (upper bound: 2.9). For 27 subpopulations from the Mediterranean, Persian Gulf and Indian Ocean (combined because of similar THHg ranges and referred to as “Mediterranean”) in Albania,¹³² Croatia,¹³³ Greece,^{133,135} the Islamic Republic of Iran,^{136–139} Italy,^{83,133,140} Kuwait,¹⁴¹ Morocco,¹⁴² Seychelles,¹⁴³ South Africa,^{144,145} Spain¹⁴⁶ and Turkey,¹⁴⁷ the pooled central THHg concentration was 0.7 µg/g (upper bound: 8.5). For 40 Pa-

Fig. 1. Selection of articles for the review of studies on methylmercury exposure in women and infants from seafood-consuming populations



cific coast subpopulations in China,^{148–151} Japan,^{153–160} Peru,¹⁷² the Republic of Korea,^{161–171} Taiwan, China¹⁷⁴ and the United States,^{175,176} the pooled result was 1.3 µg/g (upper bound: 6.0).

For 34 subpopulations living in inland regions of Austria,¹⁷⁷ Brazil,¹⁷⁸ Canada,¹⁷⁹ Croatia,⁸¹ the Czech Republic,^{81,180,181} France,^{142,182} Italy,⁸⁴ Morocco,⁸¹ Pakistan,¹⁸³ Poland,¹⁸⁴ the Republic of Korea,¹⁶⁹ Saudi Arabia,^{186–188} Slovenia,^{81,189} Spain,^{190,191} Sweden¹⁹² and the United States,^{193–196} the pooled central TTHg median was 0.4 µg/g (upper bound: 2.9).

Comparison with provisional tolerable weekly intake

The median of the pooled central TTHg biomarker distribution for women and infants in rural riverine communities near tropical gold mining sites reached nearly four times the FAO/WHO PTWI reference level of 2.2 µg/g (Fig. 3), while the upper-bound median reached more than 10 times this reference. Some individual high-end biomarkers exceeded

50 µg/g, the lower end of the range found in the neurological syndrome known as Minamata disease,⁴ associated with accidental industrial Hg poisoning in Japan in the 1950s and 1960s (Fig. 4). The median of the central TTHg biomarker distribution in Arctic traditional food consumers exceeded the reference by 63%, while the upper bound median was over 10 times the value. For women and infants in the industry and fishing categories, central estimate medians were below the international reference, although the industry central median was twice that of the fishing category; most high-end biomarkers were above it. For those in the Pacific coastal subcategory, the 75th percentile approached the reference value; the upper bound median was nearly three times this value and nearly all high-end biomarkers exceeded it. Central biomarkers were below the PTWI in the Atlantic. However in many subpopulations in the Mediterranean they exceeded this reference, while the upper bound median was nearly four times the reference and most

high-end biomarkers exceeded it. For the inland category, the central estimate median was well below the reference, but nearly 80% of the high-end biomarkers exceeded it.

Study quality

A majority (78%) of selected studies were based on convenience samples taken from seafood-consuming populations. Some details of the seafood context were provided in most (71%) studies, but in the others this information was sparse. Laboratory protocols for TTHg and TBHg detection were nearly universally reported (91%). Most (82%) protocols were based on cold vapour atomic absorption spectrometry (CV-AAS) or inductively-coupled plasma mass spectrometry (ICP-MS) and a majority (74%) reported laboratory quality control procedures. In 86% of studies, distributions were transformed to lognormal scale and summarized using geometric means or medians. More than half (55%) of the studies reported maximums as high-end estimates, while the remainder reported 90th or 95th percentiles. Only 51% of studies reported some seafood intake data and 25% evaluated non-seafood sources of Hg.

Discussion

We found that biomarkers of MeHg intake were of greatest health concern among three categories of seafood-consuming women and their infants: (i) rural riverside dwellers living near tropical small-scale gold mining with diets dependent on locally-caught freshwater fish; (ii) those in Arctic regions for whom apex food-chain marine mammals are a dietary staple; and (iii) coastal inhabitants, particularly in the Pacific and Mediterranean, who probably consume seafood that is primarily commercially sourced. In the first group, average Hg biomarkers suggest MeHg intake exceeds by several fold the level considered by WHO and FAO to pose no substantial risk of developmental neurotoxicity. In the second group, average biomarkers suggest MeHg intake well over the reference value. In the third group, biomarkers suggest an important share of the population approach or exceed the reference level. High-end biomarkers in all three groups indicate body burdens of MeHg in the range associated in epidemiological studies with observable neurological damage. While

Table 2. Summary of studies assessing total mercury in hair (THHg) or total mercury in blood (TBHg) among women and infants from seafood-consuming populations, by exposure category

Study characteristics	No. of studies	Exposure categories					
		Self-caught seafood				Commercially-purchased seafood	
		Arctic	Gold mining	Fishing	Industry ^a	Coastal	Inland
Population studied							
Mothers and/or infants ^b	73	9	10	3	5	37	9
Women in general	91	3	19	9	15	32	13
All	164	12	29	12	20	69	22
Study design							
Cross-sectional	119	10	28	9	13	44	15
Other	45	2	1	3	7	25	7
Biomarker reported							
Reporting THHg biomarkers ^c	92	1	27	5	16	37	6
Reporting TBHg biomarkers ^b	72	11	2	7	4	32	16
Reporting of seafood data							
Some	84	6	14	10	11	37	6
None	80	6	15	2	9	32	16
Publication date							
Published in 1991–2001	34	6	10	3	4	9	2
Published in 2002–2013	130	6	19	9	16	60	20
Subpopulation studied^d							
Infants	55	7	9	3	3	27	6
Pregnant women or mothers	74	10	13	2	4	35	10
Non-pregnant women	110	4	21	9	18	40	18
All	239	21	43	14	25	102	34
Study participants							
Average participants per study	390	495	350	263	152	448	48
Average participants per subpopulation	268	283	236	236	121	303	316
Total no. of participants	63 943	5935	10 152	3161	3035	30 915	10 745
Countries represented	43	5	6	5	17	23	16

^a Other than gold mining.

^b Mother and infant studies include pregnant women, mothers who have recently given birth and infants (i.e. children up to 12 months of age).

^c Some studies reported both TBHg and THHg biomarkers. When both were reported, THHg biomarkers were extracted.

^d Of these studies, 48 reported on two or more distinctly-defined exposed subpopulations of more than 40 non-pregnant women, pregnant women, women who had recently given birth, or infants (i.e. children up to 12 months of age).

average biomarkers in other groups suggest that MeHg intake is below the recommended level, most upper bound biomarkers in these categories exceed the reference, which shows that even in groups with lower average exposure certain populations are at risk.

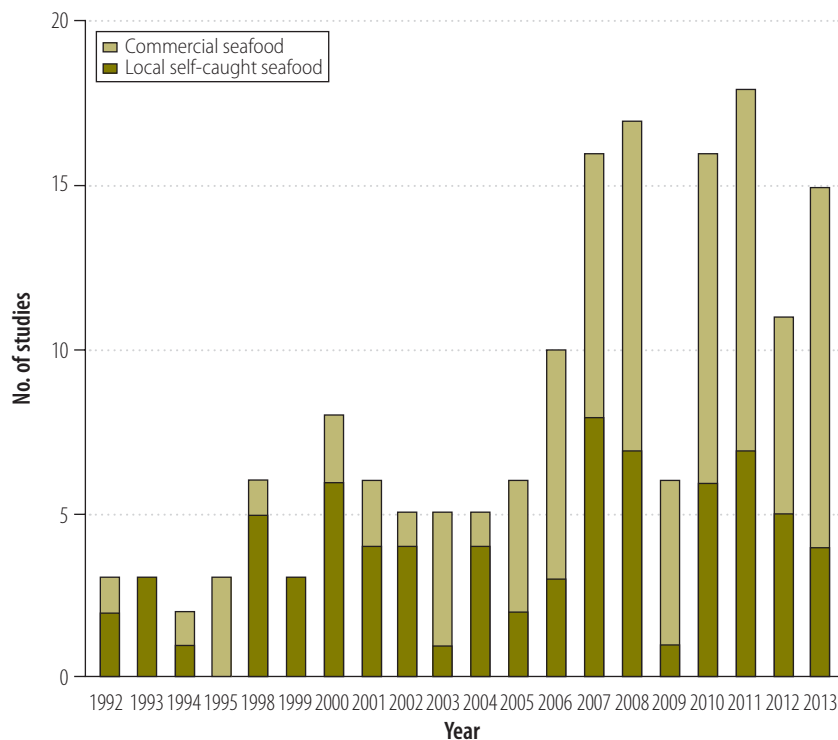
Before this study, few researchers had systematically compared the global exposures and risks linked to MeHg intake from seafood. Brune et al. reviewed Hg biomarker studies – published from 1976 to 1990 – of general populations exposed through various sources and found the highest values among seafood consumers in Greenland and Japan.¹⁹⁷ Sioen et al. estimated contaminant and nutrient intake in general populations based on global seafood availability data and found the estimated MeHg intake to

be highest in Japan and the Pacific islands, followed by the Nordic and Mediterranean regions.¹⁹⁸ A recent European regional study examining biomarkers showed the highest MeHg exposure to be in Mediterranean countries.¹⁹⁹ Our findings are broadly consistent with these studies and with the literature describing MeHg exposure and risk in specific subsistence fishing communities. This review adds to the evidence by synthesizing the findings from the two most recent decades of published international Hg biomarker data specifically for women and infants and by examining, in a single study, MeHg exposure in populations consuming self-caught and commercially purchased seafood.

Several limitations affect the interpretation of our results. Our goal was to

compare MeHg exposure across various international groups of women and infants from seafood-consuming populations. However, incomplete reporting prevented us from evaluating the share of non-consumers of seafood in each study. Furthermore, most studies used convenience samples that may not have been representative of the populations from which they were taken. In sensitivity analysis we pooled biomarkers excluding the several large representative population surveys (which have a higher share of non-consumers of seafood than other studies). However, this did not alter our findings. Physiological differences in MeHg metabolism and elimination by life stage are well known²⁰⁰ and the FAO/WHO reference dose was established based on maternal

Fig. 2. **Number of selected studies reporting total mercury in hair (THHg) or total mercury in blood (TBHg) in women and infants from seafood-consuming populations, by predominant seafood type (local self-caught or commercially purchased) and year of publication**



biomarkers. Thus, in sensitivity analysis we also combined biomarkers excluding infants. This resulted in slightly lower medians for the Arctic and gold mining categories and higher ones for the coastal and inland categories.

TBHg is a better indicator of recent MeHg exposure than THHg, which is a better measure of longer-term MeHg exposure.^{3,4,6} Although this difference may be important among sporadic seafood consumers, the majority of our subpopulations were regular seafood consumers. Conversion of TBHg biomarkers to THHg equivalents is likely to have resulted in some measurement error. However, the range of hair-to-blood ratios reported in our studies was similar to the range on which the standard conversion ratio is based, which minimizes this bias.⁵ When we pooled only THHg biomarkers, medians were slightly higher across most categories (although some categories had few observations). Despite the use of laboratory methods that relied on commonly employed protocols, detection techniques are subject to variation^{3,11} and quality control practices were not uniformly reported. Sensitivity analysis examining only stud-

Table 5. **Pooled total THHg biomarker distributions in women and infants from seafood-consuming populations, by exposure category and subcategory**

Category and subcategory	No. of sub populations	No. of participants	Central distribution ^a			Upper bound distribution ^a		
			THHg (µg/g) ^b 75th, 95th percentile	25th, 50th	Percentage > PTWI ^c	THHg (µg/g) ^b 75th, 95th percentile	25th, 50th	Percentage > PTWI ^c
Gold mining	43	10 152	1.80, 5.36, 10.00, 14.70		77	11.94, 23.07, 39.40, 125.00		98
Rural	34	8 283	2.50, 8.24, 11.20, 14.70		85	18.53, 27.45, 53.80, 130.70		97
Urban	9	1 869	0.19, 1.41, 1.80, 5.36		44	6.09, 11.80, 19.60, 24.14		100
Arctic	21	5 935	0.47, 2.09, 4.18, 6.33		52	2.30, 9.76, 26.13, 45.25		81
Traditional	12	4 958	2.34, 3.61, 4.56, 6.33		75	18.90, 24.25, 41.08, 45.25		100
Mixed diet	9	977	0.31, 0.40, 0.55, 0.64		11	0.93, 1.38, 6.35, 7.82		56
Industry	25	3 035	0.25, 0.75, 1.27, 3.54		32	3.04, 4.62, 9.93, 35.00		89
Fishing	14	3 161	0.13, 0.38, 0.70, 2.50		6	0.70, 2.75, 4.00, 5.38		71
Coastal	102	30 915	0.36, 0.82, 1.51, 3.70		23	2.83, 6.76, 10.65, 26.46		86
Atlantic	35	9 675	0.27, 0.35, 0.69, 2.70		16	1.16, 2.93, 9.75, 22.14		76
Mediterranean	27	6 536	0.29, 0.65, 1.45, 5.90		32	4.18, 8.53, 16.50, 26.46		96
Pacific	40	14 704	0.85, 1.34, 1.94, 4.66		23	2.83, 6.03, 10.65, 28.50		98
Inland	34	10 745	0.31, 0.38, 0.77, 1.47		18	1.93, 2.90, 7.59, 13.00		79
Total	239	63 943	–		34	–		86

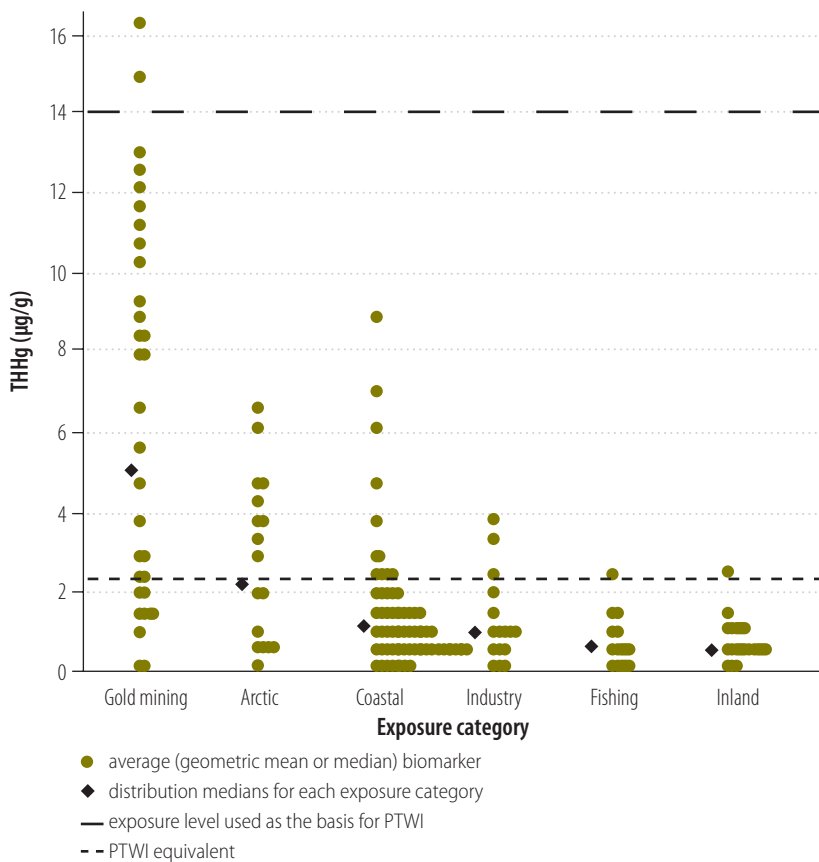
PTWI, provisional tolerable weekly intake; THHg, total mercury in hair.

^a Central distribution reflects pooling of geometric mean and median biomarkers from reported studies; upper bound distribution reflects pooling of 90th, 95th percentiles and maximums from reported studies.

^b Biomarkers measuring total mercury in blood converted to THHg equivalent at a hair-to-blood ratio of 250:1.

^c Share of total subpopulations with a reported average or high-end biomarker greater than the PTWI equivalent of 2.2 µg/g of THHg.

Fig. 3. Distributions of central estimate for total mercury in hair (THHg) reported in selected studies of women and infants from seafood-consuming populations, by exposure category



PTWI, provisional tolerable weekly intake.

ies using CV-AAS or similar procedures resulted in slightly higher biomarkers for the Arctic category.

Population Hg biomarker distributions are often skewed to the right, so that central tendency is best captured by geometric means or medians.³ Thus, in reporting our main results we chose to exclude the small number of studies reporting only arithmetic means. Including arithmetic means yielded higher results for the inland category. To give greater weight to estimates from larger samples, we pooled biomarkers using sample-size weighting. Doing so yielded higher summary biomarkers in the Arctic and coastal categories. Variations in the share of MeHg in total Hg have been reported, both among frequent and infrequent seafood consumers,^{23,201} depending in part on exposure to Hg sources other than seafood (such as elemental Hg in dental amalgams or inorganic Hg compounds in skin-lightening creams).^{3,29} Most of the one quarter of selected studies examining

non-seafood sources of Hg assessed the presence of dental amalgams, mainly in infrequent consumers of seafood; while this inorganic Hg source is best measured with urinary biomarkers, in cases where this exposure is important TBHg biomarkers may overestimate MeHg.²⁶ We eliminated high outlier biomarkers due to suspected non-seafood sources wherever these were noted by authors (most were in subpopulations where skin-lightening creams were used). Nevertheless, other sources of Hg exposure influencing high-end measures cannot be excluded. These limitations in the underlying data suggest that our findings should be interpreted cautiously. However, most sensitivity analyses resulted in higher biomarker summary statistics than the main findings we report; we chose conservative assumptions for our main results.

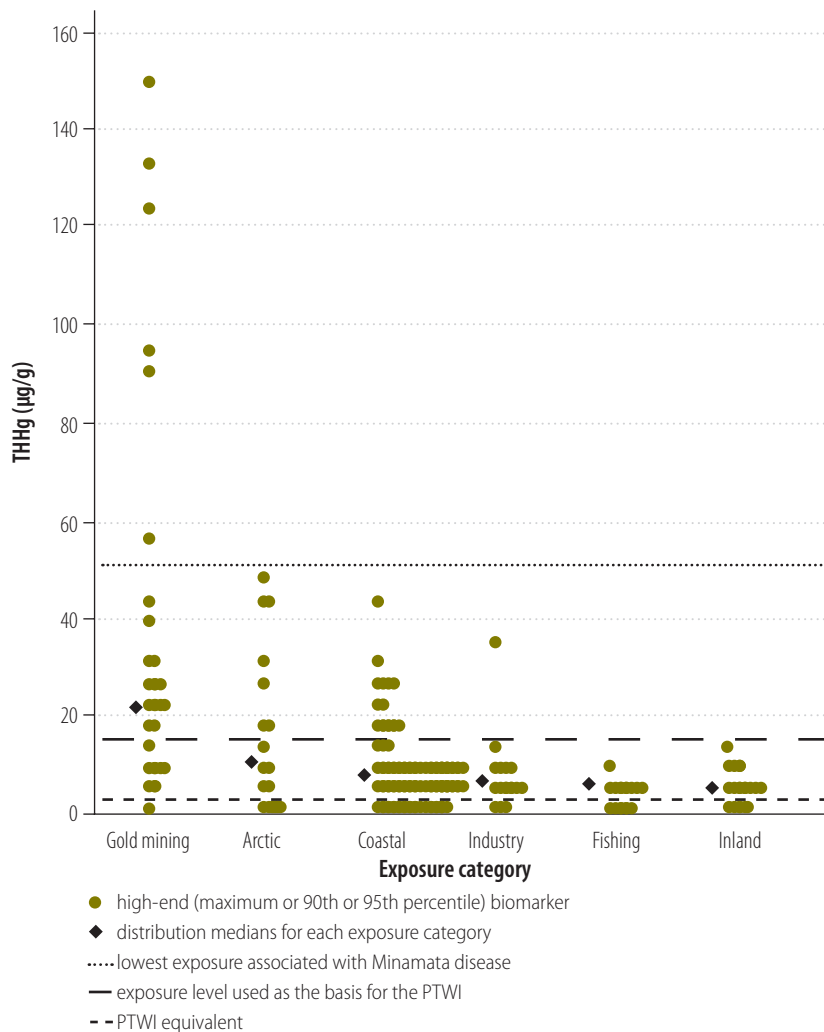
Estimated IQ losses in infants born to seafood consuming mothers serve as an alternative means of characterizing the public health impact of MeHg ex-

posure. As an illustration, we applied a dose–response relationship (0.18 infant IQ point lost for every ppm increase in maternal THHg)²⁰² that has been used to estimate the economic costs associated with Hg contamination^{203,204} to our pooled upper bound biomarkers. The resulting interquartile range of estimated IQ loss spanned from 1 to 13 points for the gold mining, Arctic and coastal subpopulation categories. IQ losses at the higher end of this range may be sufficient to contribute to mild mental retardation, defined as an IQ between 50 and 69 points. Among subsistence fishing populations in the Amazon, an assessment of global burden of disease showed an incidence of mild mental retardation of up to 17.4 cases per 1000 infants²⁰⁵ and separate research identified MeHg-associated deficits in memory and learning in adults.²⁰⁶ IQ losses in the lower end of the range may contribute to borderline intellectual functioning, characterized by memory and executive function deficits.²⁰⁷ Although such minor losses in IQ may go unnoticed in an individual, they can cause an important shift in intellectual capacity at the population level, as documented in the case of lead.²⁰⁸ IQ loss represents only one facet of the neurological harm resulting from MeHg; our analysis did not include recent research suggesting neurological effects at lower dose¹¹ or other documented effects, such as adverse cardiovascular outcomes.²⁰⁹

Systematic reviews provide an opportunity to identify gaps in a body of research. Small-scale gold mining is practiced in 70 countries,²¹⁰ but we found Hg biomarker studies meeting our criteria in only six. We identified studies in 23 coastal countries, although per capita seafood consumption data suggest that many other such countries warrant study.²⁰ Although reviews of subsistence fishing populations in the Amazon and Arctic are available, few have been conducted for coast-dwelling frequent seafood consumers (e.g. in south-eastern Asia or the Mediterranean) or for fishing populations near abandoned chloralkali plants and other aquatic sources of Hg contamination. We found population-based Hg biomonitoring surveys in only a handful of countries; most are high-income and have relatively low per capita seafood consumption.

It was beyond the scope of this review to assess time trends in Hg

Fig. 4. Distributions of upper-bound total mercury in hair (THHg) reported in selected studies of women and infants from seafood-consuming populations, by exposure category



PTWI, provisional tolerable weekly intake.

Note: High-end biomarkers in the gold mining, Arctic and coastal categories reach into the range associated with observable neurological damage.

biomarkers. Without major policy changes, projections indicate that global anthropogenic Hg emissions are likely to increase.²¹¹ Moreover, modelling suggests that any reduction in Hg emissions is likely to take time to translate into reduced MeHg in seafood.²¹² Declines in Hg biomarkers in humans have been observed in association with changes in seafood consumption habits in various populations. This finding reinforces the importance of carefully designed public health messages intended to reduce MeHg exposure.^{199,212} In subsistence fish-

ing populations, the cultural importance of seafood harvesting and the scarcity of alternative animal protein sources suggest the existence of complex tradeoffs in guiding seafood consumption and the need for well-targeted messages. In predominantly urban seafood-consuming coastal populations, commercial seafood advisories may be an appropriate choice for reaching at-risk populations.¹⁹ Because of seafood's important nutritional benefits, all such messages should aim to encourage a shift away from large apex predator species and towards those

with lower MeHg and higher polyunsaturated fatty acid content, rather than to reduce seafood intake.

Conclusion

In this review of biomarkers of MeHg intake in women and infants from 164 studies across 43 countries, we found a very high risk in tropical riverine populations near gold mining sites and in traditional Arctic populations. In both groups, biomarkers suggest average MeHg intake exceeds the FAO/WHO recommendation, although their share of the global total of seafood-consuming women and infants is likely to be fairly small. We also found an elevated risk among seafood consumers in the coastal regions of south-eastern Asia, the western Pacific and the Mediterranean; a large share of the world's seafood-consuming women and their infants is likely to be found in this group because of its large population. In other populations for whom data were available, average indicators of risk were lower and generally within international intake recommendations. However, women and infants with high exposure to MeHg were evident across all exposure categories. Although sources of bias were present, these results should help to set broad priorities for preventive policy and research.

The findings of this review underscore the importance of WHO's call for enhanced population monitoring and risk communication to women of reproductive age regarding healthful seafood choices.¹ One of the provisions of the Minamata Convention aims to protect vulnerable populations from Hg exposure through public education and other measures.²¹³ The Convention is a potentially important strategic tool to reach the populations at highest risk through development of seafood advisory risk messages for commercial seafood consumers, targeted community-based interventions for subsistence fishing groups and regular population surveillance. ■

Competing interests: None declared.

ملخص

التعرض العام لميثيل الزئبق من تناول المأكولات البحرية ومخاطر السمية العصبية التنموية: مراجعة منهجية
 الغرض فحص الواصلات البيولوجية لمدخول ميثيل الزئبق (MeHg) لدى المرأة والطفل من السكان الذين يتناولون المأكولات البحرية على مستوى العالمي، وتمييز المخاطر المقارنة للسمية العصبية التنموية للجنين.
 الطريقة يشير بحث تم إجراؤه في المؤلفات المنشورة إلى إجمالي الزئبق (Hg) في شعر ودم النساء والرضع. ويتم التحقق من هذه الواصلات البيولوجية من خلال التداير غير المباشرة لميثيل الزئبق، وتوجد السمية العصبية بشكل أساسي في المأكولات البحرية. وتم استخلاص الواصلات البيولوجية المتوسطة والعليا، وتم تقسيمها إلى طبقات حسب سياق استهلاك المأكولات البحرية، وتم تجميعها حسب الفئات. وتم مقارنة متوسطات التوزيعات المتوسطة والعليا التي تم تجميعها مع المستوى المرجعي المحدد من قبل لجنة خبراء مشتركة تابعة لمنظمة الأغذية والزراعة ومنظمة الصحة العالمية.
 النتائج استوفت 164 دراسة للنساء والرضع من 43 دولة معايير الاختبار. وتشير الواصلات البيولوجية التي تم تجميعها إلى مدخول

ميثيل زئبق يتجاوز مرات عديدة مرجع منظمتي الأغذية والزراعة والصحة العالمية لدى سكان الشواطئ الذين يتناولون الأسماك ويعيشون بالقرب من مناجم الذهب صغيرة الحجم، وبشكل زائد عن المرجع الخاص بمستهلكي الثدييات البحرية في مناطق القطب الشمالي. وفي المناطق الساحلية لجنوب شرق آسيا، وغرب المحيط الهادي والبحر المتوسط، يقترب متوسط الواصلات البيولوجية من المرجع. ورغم أن المجموعتين السابقتين معرضتان لمخاطر أعلى للإصابة بالسمية العصبية عن المجموعة الأخيرة، إلا أن المناطق الساحلية تعد موطناً لأكثر عدد معرض للخطر. وتشير الواصلات البيولوجية العليا عبر جميع الفئات إلى أن مدخول ميثيل الزئبق (MeHg) يتجاوز القيمة المرجعية.
 الاستنتاج هناك حاجة لسياسات تحد من التعرض للزئبق بين النساء والرضع، والترصد بالنسبة للسكان المعرضين لمخاطر عالية، والذين يعيش أكثرهم في البلدان المنخفضة الدخل والمتوسطة الدخل.

摘要

全球海产品消费甲基汞暴露和发育性神经中毒的风险：系统回顾

目的 调查在全球范围内妇女和婴儿从海产品消费中摄入的甲基汞 (MeHg) 的生物标志物，表征胎儿发育性神经中毒的相对风险。
方法 对报告妇女和婴儿毛发和血管中的总汞 (Hg) 含量的已发表文献进行检索。这些生物标志物是对 MeHg 经过验证的间接量度，MeHg 是一种主要在水产品中发现的神经毒素。提取平均和高端生物标志物，并按海鲜消费环境进行分层，按类别汇集。将平均和高端汇集分布的中位值与联合国粮农组织 (FAO) 和世卫组织 (WHO) 联合专家委员会制定的参考水平进行比较。
结果 来自 43 个国家的 164 个有关妇女和婴儿的研究

符合入选标准。汇集的平均生物标志物显示，居住在靠近小型金矿河边的鱼类消费人群中摄入 MeHg 超过 FAO/WHO 参考值数倍，在北极圈地区海洋哺乳动物的消费人群摄入量也大大超过参考水平。在东南亚、西太平洋和地中海沿海地区，平均生物标志物接近参考水平。尽管前两组的神经中毒风险比后者更高，沿海地区却是风险数量最多的地方。各个类别中，高端生物标记物表明 MeHg 摄入量超过了参考值。
结论 需要通过政策来减少妇女和婴儿的汞接触，同时对高风险人群进行监测，这些人群绝大多数在中低收入国家。

Résumé

Exposition globale au méthylmercure par la consommation de poisson et fruits de mer et risque de neurotoxicité sur le développement: un examen systématique

Objectif Examiner les biomarqueurs de l'ingestion de méthylmercure (MeHg) chez les femmes et les enfants des populations consommant des poisson et fruits de mer au niveau mondial et caractériser le risque comparatif de la neurotoxicité sur le développement du fœtus.

Méthodes Une recherche a été effectuée dans la documentation publiée rapportant les quantités totales de mercure (Hg) dans les cheveux et le sang des femmes et des enfants. Ces biomarqueurs ont été validés comme étant des mesures indirectes du MeHg, une neurotoxine que l'on trouve principalement dans les poissons et fruits de mer. Les biomarqueurs moyens et terminaux ont été extraits, stratifiés par contexte de consommation de poissons et fruits de mer et groupés par catégorie. Les médianes pour les distributions groupées des biomarqueurs moyens et terminaux ont été comparées avec le niveau de référence établi par un comité mixte d'experts de l'Organisation des Nations Unies pour l'alimentation et l'agriculture (FAO) et l'Organisation mondiale de la Santé (OMS).

Résultats Les critères de sélection ont été satisfaits par 164 études

concernant des femmes et des enfants dans 43 pays. Les biomarqueurs moyens groupés suggèrent une ingestion de MeHg plusieurs fois supérieure à la référence FAO/OMS chez les riverains consommateurs de poissons et vivant à proximité d'une zone d'orpaillage à petite échelle et bien au-delà de la référence chez les consommateurs de mammifères marins dans les régions arctiques. Dans les régions côtières de l'Asie du Sud-Est, du Pacifique occidental et de la Méditerranée, les biomarqueurs moyens se rapprochent de la référence. Bien que les deux premiers groupes aient un risque de neurotoxicité plus important que les derniers groupes, les régions côtières abritent le plus grand nombre de personnes à risque. Les biomarqueurs terminaux dans toutes les catégories indiquent que l'ingestion de MeHg est supérieure à la valeur de référence.

Conclusion Il y a un besoin de politiques pour réduire l'exposition au Hg chez les femmes et les enfants, ainsi que pour surveiller les populations à haut risque, dont la majorité vit dans les pays à revenu faible et intermédiaire.

Резюме

Риск отдаленной нейротоксичности и подверженность воздействию метилртути в глобальном масштабе вследствие потребления морепродуктов: систематический обзор

Цель Изучить биомаркеры поступления метилртути (MeHg) у женщин и детей из группы населения, потребляющего морепродукты, в мировом масштабе и охарактеризовать сравнительный риск отдаленного нейротоксического действия на плод.

Методы Был проведен поиск опубликованной литературы, в которой сообщалось об общем содержании ртути (Hg) в волосах и крови женщин и детей. Эти биомаркеры являются подтвержденными репрезентативными индикаторами содержания MeHg – нейротоксина, обнаруживаемого главным образом в морепродуктах. После отбора биомаркеры среднего и высокого уровней были разделены по контексту потребления морепродуктов и сгруппированы по категориям. Медианные значения распределений биомаркеров для среднего и высокого уровней сравнивались с контрольным уровнем, установленным объединенным экспертным комитетом Продовольственной и сельскохозяйственной организации ООН (ФАО) и Всемирной организацией здравоохранения (ВОЗ).

Результаты Критериям выбора соответствовали 164 исследования женщин и детей из 43 стран. Сгруппированные биомаркеры

среднего уровня позволяют заключить, что поступление MeHg в несколько раз превышает контрольный уровень ФАО/ВОЗ у представителей населения прибрежных районов, потребляющих морепродукты и проживающих вблизи небольших месторождений золота, и значительно выше контрольного уровня – у потребителей морских млекопитающих в Арктике. В прибрежных районах Юго-Восточной Азии, Западной части Тихого океана и Средиземноморье биомаркеры среднего уровня близки к контрольному уровню. Несмотря на то, что две первые группы подвержены более высокому риску нейротоксичности, чем вторая, в указанных прибрежных районах проживает наибольшее число подверженных риску. Биомаркеры высокого уровня во всех категориях указывают на то, что поступление MeHg превышает контрольный уровень.

Вывод Необходима разработка стратегий уменьшения воздействия Hg на женщин и детей и эпидемиологического надзора над населением, составляющим группу повышенного риска, большая часть которого проживает в странах с низким и средним уровнями доходов.

Resumen

La exposición global al metilmercurio a partir del consumo de pescado y marisco y el riesgo de neurotoxicidad del desarrollo: una revisión sistemática

Objetivo Examinar los biomarcadores de la ingesta de metilmercurio (MeHg) en mujeres y niños procedentes de poblaciones que consumen pescados y mariscos a nivel global y describir el riesgo comparativo de neurotoxicidad del desarrollo fetal.

Métodos Se realizó una búsqueda de la literatura publicada que informa sobre el mercurio total (Hg) en el cabello y la sangre de mujeres y niños. Estos biomarcadores son medidas indirectas validadas de MeHg, una neurotoxina que se encuentra sobre todo en el pescado y marisco. Se extrajeron biomarcadores de gama media y alta, los cuales se estratificaron por contexto de consumo de pescado y marisco y se agruparon por categorías. Se compararon las medianas de las distribuciones por grupos de gama media y alta con el nivel de referencia establecido por un comité mixto de expertos de la Organización para la Agricultura y la Alimentación (FAO) y la Organización Mundial de la Salud (OMS).

Resultados 164 estudios de mujeres y niños de 43 países cumplieron los criterios de selección. El grupo de biomarcadores de gama media indica una ingesta de MeHg varias veces superior a la referencia de la FAO/OMS en los ribereños que consumen pescado que viven cerca de una pequeña mina de oro, y muy superior a la referencia en los consumidores de mamíferos marinos en las regiones árticas. En las regiones costeras del sudeste de Asia, el Pacífico occidental y el Mediterráneo, los biomarcadores de gama media se acercan a la referencia. Aunque el riesgo de neurotoxicidad es mayor en los dos grupos anteriores que en el último, las regiones costeras albergan el mayor número de personas en riesgo. En todas las categorías, los biomarcadores de alta gama indican que la ingesta de MeHg es superior al valor de referencia.

Conclusión Se necesitan políticas que reduzcan la exposición al Hg entre mujeres y niños, así como una vigilancia en las poblaciones de alto riesgo, la mayoría de las cuales viven en países de bajos y medianos ingresos.

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Table 3. Characteristics of studies assessing total mercury in hair (THHg) or total mercury in blood (TBHg) in women and infants consuming self-caught seafood, by exposure category and subcategory

Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg per month)	Sub population	n	THHg, average ^b (µg/g)	THHg, High-end ^b (µg/g)
Gold mining^c							
Gold mining: rural riverine							
Monrroy et al. 2008 ³³	Cross-sectional	Bolivia (Plurinational State of), Beni valley	2.2	W	163	3.9	20.0
Barbieri et al. 2009 ³⁴	Cross-sectional	Bolivia (Plurinational State of), Beni valley	5.1	W	77	2.5	–
Boischio et al. 1993 ³⁵	Cross-sectional	Brazil, upper Madeira (river)	–	W	70	10.0	125.0
Barbosa et al. 1998 ³⁶	Cross-sectional	Brazil, upper Madeira (river)	–	MO	98	12.8	94.7
Lebel et al. 1998 ³⁷	Cross-sectional	Brazil, Tapajos	6.9	W	46	11.2	26.6
Grandjean et al. 1999 ³⁸	Cross-sectional	Brazil, Tapajos	10.2	W	114	11.6	–
Amorim et al. 2000 ³⁹	Cross-sectional	Brazil, Tapajos	–	W	46	10.8	–
Boischio et al. 2000 ⁴⁰	Cross-sectional	Brazil, Madeira	–	MO	90	12.6 ^d	28.3
Dolbec et al. 2000 ⁴¹	Cross-sectional	Brazil, Tapajos	9.0	W	40	8.7	–
Harada et al. 2001 ⁴²	Cross-sectional	Brazil, Barreiras	–	W	44	16.4 ^d	53.8
Crompton et al. 2002 ⁴³	Cross-sectional	Brazil, Jacareacanga	–	W	113	6.7 ^d	–
Santos et al. 2002 ⁴⁴	Cross-sectional	Brazil, Sai Cinza	5.1	W	192	14.7	90.4
Santos et al. 2003 ⁴⁵	Cross-sectional	Brazil, Pakaanova	–	W	549	8.55	39.4
Santos et al. 2007 ⁴⁶	Cross-sectional	Brazil, Itaituba	–	IN	1510	4.2 ^d	–
				MO	1510	2.9 ^d	–
Passos et al. 2008 ⁴⁷	Cross-sectional	Brazil, Tapajos	–	W	121	16.3 ^d	150.0
Grotto et al. 2010 ⁴⁸	Cross-sectional	Brazil, Tapajos	–	W	54	8.8	–
Fillion et al. 2011 ⁴⁹	Cross-sectional	Brazil, Tapajos	–	W	126	9.4	–
Dórea et al. 2012 ⁵⁰	Cross-sectional	Brazil, Bom Futuro	1.6	IN	166	1.6	–
Barcelos et al. 2013 ⁵¹	Cross-sectional	Brazil, Tapajos	14.9	W	193	16.3	–
Marques et al. 2013 ⁵²	Cross-sectional	Brazil, Madeira (river)	–	IN	396	3.0	18.5
		Brazil, Madeira (river)	4.3	MO	396	12.1	130.7
		Brazil, Madeira (tin region)	–	IN	294	0.8	2.0
		Brazil, Madeira (tin region)	0.9	MO	294	4.5	11.9
		Brazil, Madeira (rural)	–	IN	67	2.0	8.8
		Brazil, Madeira (rural)	2.6	MO	67	7.8	41.1
Vieira et al. 2013 ⁵³	Cross-sectional	Brazil, Porto Velho (river)	4.4	MO	75	8.2	20.1
Olivero-Verbel et al. 2011 ⁵⁴	Cross-sectional	Colombia, Antioquia	–	W	757	1.4	10.0
Cordier et al. 1998 ⁵⁵	Cross-sectional	French Guiana	–	PW	109	1.6	22.0
Cordier et al. 2002 ⁵⁶	Cross-sectional	French Guiana, upper Maroni	10.2	W	90	12.7	–
		French Guiana, Camopi	–	W	63	6.7	–
		French Guiana, Awala	–	W	55	2.8	–
Fujimura et al. 2012 ⁵⁷	Cross-sectional	French Guiana, upper Maroni	8.63	W	234	9.9 ^d	26.6
Bose-O'Reilly et al. 2010 ⁵⁸	Ecological	Indonesia, Kalimantan	–	W	64	2.5	29.6
Gold mining: urban							
Hacon et al. 2000 ⁵⁹	Cross-sectional	Brazil, Alta Floresta	0.6	MO	75	1.1 ^d	8.2
Marques et al. 2007 ⁶⁰	Cross-sectional	Brazil, Porto Velho	0.7	IN	100	0.2	–
			0.7	MO	100	0.1	–
Dorea et al. 2012 ⁵⁰	Cross-sectional	Brazil, Porto Velho	1.4	IN	82	1.8	–
Marques et al. 2013 ⁵²	Cross-sectional	Brazil, Madeira (urban)	–	IN	676	1.5	4.8
			1.7	MO	676	5.4	24.1
Vieira et al. 2013 ⁵³	Cross-sectional	Brazil, Porto Velho (urban)	0.7	MO	82	1.3	6.1
Mohan et al. 2005 ⁶¹	Cross-sectional	Surinam, Paramaribo	–	IN	39	1.6 ^d	19.6
			–	MO	39	0.8 ^d	15.4

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Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg per month)	Sub population	n	THHg, average ^b (µg/g)	THHg, High-end ^b (µg/g)
Arctic^e							
Arctic: Traditional diet							
Dewailly et al. 2001 ⁶²	Cross-sectional	Canada, Nunavik	–	W	284	4.2	28.0
Muckle et al. 2001 ⁶³	Cohort	Canada, Nunavik	–	IN	95	4.6	24.3
			–	MO	130	2.6	11.1
Lucas et al. 2004 ⁶⁴	Cross-sectional	Canada, Nunavik	4.9	IN	439	3.5	–
Butler-Walker et al. 2006 ⁶⁵	Cross-sectional	Canada, Northwest Territories (Inuit)	–	IN	132	1.7	19.0
			3.5	MO	132	0.9	8.5
Fontaine et al. 2008 ⁶⁶	Cross-sectional	Canada, Nunavik	1.5	W	308	2.1	41.1
Grandjean et al. 1992 ⁶⁷	Cohort	Denmark, Faroe Islands	–	IN	1020	6.1	–
			2.2	MO	1020	4.5	–
Bjerregaard et al. 2000 ⁶⁸	Cross-sectional	Denmark, Greenland (Disko Bay)	–	IN	178	6.3	45.3
			7.1	MO	180	3.2	18.9
Nielsen et al. 2012 ⁶⁹	Cross-sectional	Denmark, Greenland	–	W	1040	3.7	42.5
Arctic: Mixed diet							
Butler-Walker et al. 2006 ⁶⁵	Cross-sectional	Canada, Northwest Territories (Caucasian)	–	IN	124	0.3	3.2
			0.6	MO	124	0.2	1.1
Odland et al. 1999 ⁷⁰	Cross-sectional	Norway, northern (Norwegian)	–	MO	81	0.6	0.6
		Norway, northern (Russian)	–	MO	151	0.4	1.4
Hansen et al. 2011 ⁷¹	Cross-sectional	Norway, northern	–	MO	211	0.3	0.9
Klopov et al. 1998 ⁷²	Cross-sectional	Russian Federation, Norilsk-Sakelhard	–	IN	42	3.1 ^d	–
			1.5	MO	42	3.9 ^d	–
Arnold et al. 2005 ⁷³	Cross-sectional	United States, Alaska	–	MO	150	0.5	6.4
			–	W	52	0.6	7.8
Industry^f							
Nilson et al. 2001 ⁷⁴	Cross-sectional	Brazil, Itapessuma	–	W	84	1.9 ^d	12.5
Kuno et al. 2010 ⁷⁵	Cross-sectional	Brazil, São Paulo state	0.2	W	265	0.3	1.1
Bruhn et al. 1994 ⁷⁶	Cross-sectional	Chile, 8th district	–	PW	59	1.7	7.1
Li et al. 2006 ⁷⁷	Ecological	China, Chanchung	0.6	W	69	0.5 ^d	10.5
Zhang et al. 2006 ⁷⁸	Cross-sectional	China, Wujiazhan	–	W	40	0.6	–
Tang et al. 2008 ⁷⁹	Cohort	China, Tongliang	–	IN	110	1.8 ^d	9.9
Fang et al. 2012 ⁸⁰	Cross-sectional	China, Zhejiang	1.9	W	50	0.8 ^d	3.0
Pawlas et al. 2013 ⁸¹	Cross-sectional	China, Guiyang	–	W	49	2.2	35.0
Olivero-Verbel et al. 2008 ⁸²	Cross-sectional	Colombia, Cartagena (bay)	4.3	W	258	1.0	–
Madeddu et al. 2008 ⁸³	Case control	Italy, Sicily Augusta	–	W	100	1.2	5.0
Deroma et al. 2013 ⁸⁴	Cohort	Italy, Venice (region)	–	IN	70	0.7	–
			–	MO	79	1.2	–
Hsiao et al. 2011 ⁸⁵	Cross-sectional	Kazakhstan, Temirtau	1.1	W	174	0.4	4.6
Lim et al. 2010 ⁸⁶	Cohort	Republic of Korea, Sinha-Banud	0.4	W	852	0.7	–
Trasande et al. 2010 ⁸⁷	Cross-sectional	Mexico, Lake Chapala	–	W	91	0.5	–
Elhamri et al. 2007 ⁸⁸	Cross-sectional	Morocco, Martil	1.2	W	40	1.4	7.9
Lacayo et al. 1991 ⁸⁹	Cross-sectional	Nicaragua, Lake Xolotlan	–	W	40	3.4	–
Bravo et al. 2010 ⁹⁰	Cross-sectional	Romania, Babeni	1.5	W	38	1.0	–
Palkovicova et al. 2008 ⁹¹	Cohort	Slovakia, eastern	–	IN	99	0.2	0.64
			–	MO	99	0.2	0.73
Pawlas et al. 2013 ⁸¹	Cross-sectional	Slovakia, Baska Bystrica	–	W	52	0.6	3.3
Oskarsson et al. 1994 ⁹²	Cross-sectional	Sweden, Boliden	–	MO	124	0.3 ^d	–
Chang et al. 2008 ⁹³	Cross-sectional	China, Taiwan, Tainan	5.8	W	99	3.7	–
Lincoln et al. 2011 ⁹⁴	Cross-sectional	United States, Louisiana (gulf)	1.5	W	44	0.7	3.6
Rojas et al. 2007 ⁹⁵	Case control	Venezuela (Bolivarian Republic of), Valencia	–	W	50	0.9 ^d	4.31

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Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg per month)	Sub population	<i>n</i>	THHg, average ^b (µg/g)	THHg, High-end ^b (µg/g)
Fishing^g							
Black et al. 2011 ⁹⁶	Cross-sectional	Botswana, Okavango delta	2.6	W	60	0.1	0.9
Girard et al. 1995 ⁹⁷	Cross-sectional	Canada, St James	–	MO	991	2.5	–
Mahaffey et al. 1998 ⁹⁸	Cross-sectional	Canada, St Lawrence	0.6	W	99	0.04	–
Belles-Isles et al. 2002 ⁹⁹	Cohort	Canada, St Lawrence	3.8	IN	40	0.5	2.8
Cole et al. 2004 ¹⁰⁰	Cross-sectional	Canada, Ontario	2.2	W	38	1.5	5.4
Morrisette et al. 2004 ¹⁰¹	Cohort	Canada, St Lawrence (river)	0.6	IN	101	0.1	0.4
			0.6	MO	101	0.1	0.3
Abdelouahab et al. 2008 ¹⁰²	Cross-sectional	Canada, St Lawrence (river)	1.2	W	87	0.4	3.9
Jenssen et al. 2012 ¹⁰³	Cross-sectional	Norway	2.2	W	100	0.9	4.0
Johnsson et al. 2004 ¹⁰⁴	Cross-sectional	Sweden, Hagfors	–	W	51	0.7	–
Stewart et al. 2000 ¹⁰⁵	Cohort	United States, New York (state)	–	W	296	0.5	0.7
Knobeloch et al. 2007 ¹⁰⁶	Cross-sectional	United States, Wisconsin	1.3	W	1050	0.4	5.3
Schantz et al. 2010 ¹⁰⁷	Cross-sectional	United States, Wisconsin	0.1	W	79	0.4	3.3

IN, infants; MO, mothers; PW, pregnant women; W, women.

^a Seafood intake as reported in studies, converted to kg per month (assuming average meal size of 170 g if not stated) and shown for mothers if reported for both mothers and infants; not all studies reported seafood intake.^b Biomarker concentrations shown as THHg, either as reported or as converted from TBHg using the hair-to-blood ratio of 250:1. All THHg concentrations are rounded to one decimal place. Average THHg is the geometric mean or median (unless noted with ⁴⁹); high-end THHg is the maximum or the 95th or 90th percentile.^c Women and infants near tropical small-scale gold mining sites who consume freshwater fish from Hg-contaminated rivers.^d The average is the arithmetic mean and was not included in main pooling results.^e Women and infants living in the Arctic or far-Northern regions consuming apex marine foods, including marine mammals.^f Women and infants periodically consuming marine and freshwater fish caught locally from water bodies contaminated by mercury-emitting industry.^g Women and infants periodically consuming marine and freshwater fish caught locally from water bodies not affected by industrial emissions.

Table 4. Characteristics of studies assessing total mercury in hair (THHg) or total mercury in blood (TBHg) in women and infants consuming seafood that is predominantly commercially purchased, by exposure category and subcategory

Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg/mo)	Subpopulation	n	THHg, average ^b (µg/g)	THHg, high-end ^b (µg/g)
Coastal^c							
Coastal: Atlantic							
Carneiro et al. 2011 ¹⁰⁸	Cross-sectional	Brazil, Porto Alegre	0.5	W	107	0.1 ^d	–
Legrand et al. 2005 ¹⁰⁹	Cross-sectional	Canada, Bay of Fundy	1.5	W	77	0.5 ^d	0.7
Albert et al. 2010 ¹¹⁰	Risk assessment	France, north-western	–	PW	125	0.7	2.8
Drouillet-Pinard et al. 2010 ¹¹¹	Cohort	France, Poitiers	–	IN	645	0.4	–
	Cohort		1.4	MO	645	0.5	–
Vahter et al. 2000 ¹¹²	Cohort	Sweden, Solna	–	IN	148	0.4	1.2
	Cohort		–	MO	148	0.2	0.7
Björnberg et al. 2003 ¹¹³	Cross-sectional	Sweden, Uppsala	–	IN	123	0.3	1.4
	Cross-sectional		0.8	MO	123	0.4	1.5
Rosborg et al. 2003 ¹¹⁴	Cross-sectional	Sweden (acid region)	–	W	47	0.4	3.5
	Cross-sectional	Sweden (alkaline region)	–	W	43	0.3	1.0
Brantsaeter et al. 2010 ¹¹⁵	Cohort	Norway, Baerum	1.2	MO	119	0.4	1.1
Gerhardsson et al. 2010 ¹¹⁶	Cross-sectional	Norway, Simrishamn	0.7	PW	50	0.2	–
Renzoni et al. 1998 ¹¹⁷	Cross-sectional	Portugal, Maderia	–	W	181	8.6	42.6
Ramon et al. 2011 ¹¹⁸	Cohort	Spain, Asturias	2.7	IN	340	2.7	17.3
	Cohort	Spain, Gipuzkoa	2.4	IN	529	1.9	12.5
Oskarsson et al. 1994 ⁹²	Cross-sectional	Sweden, Homsund	–	MO	79	0.3 ^d	–
Björnberg et al. 2005 ¹¹⁹	Cross-sectional	Sweden	2.1	W	127	0.7	6.6
Pawlas et al. 2013 ⁸¹	Cross-sectional	Sweden, southern	–	W	54	1.4	9.8
Bates et al. 2007 ¹²⁰	Cross-sectional	United Kingdom	0.7	W	44	0.2	–
Dewailly et al. 2012 ¹²¹	Cross-sectional	United Kingdom (Bermuda)	–	MO	49	1.1	5.0
Stern et al. 2001 ¹²²	Cross-sectional	United States, New Jersey	1.2	MO	143	0.3 ^d	8.0
Ortiz-Roque et al. 2004 ¹²³	Cross-sectional	United States, Puerto Rico	2.0	W	45	0.4	–
	Cross-sectional	United States, Vieques	3.6	W	41	0.3	–
Oken et al. 2005 ¹²⁴	Cohort	United States, eastern Massachusetts	0.9	MO	135	0.1	0.6
McKelvey et al. 2007 ¹²⁵	Cross-sectional	United States, New York City	1.5	W	1049	0.7	2.8
Karouna-Renier et al. 2008 ¹²⁶	Cross-sectional	United States, Florida panhandle	–	PW	83	0.2	10.7
			–	W	515	0.3	22.1
Lederman et al. 2008 ¹²⁷	Cross-sectional	United States, New York City (non-Asian)	–	IN	178	0.7	–
		United States, New York City (Chinese)	–	MO	83	1.1	–
		United States, New York City (non-Asian)	–	MO	176	0.4	–
Caldwell et al. 2009 ¹²⁸	Cross-sectional	United States (national)	–	W	1888	0.2	1.1
Wells et al. 2011 ¹²⁹	Cross-sectional	United States, Maryland	–	IN	300	0.3	–
King et al. 2013 ¹³⁰	Cross-sectional	United States, Pawtucket	–	IN	538	0.1	9.8
Traynor et al. 2013 ¹³¹	Cross-sectional	United States, Duval County, Florida	2.1	W	698	0.3	3.0
Coastal: Mediterranean, Indian Ocean, Persian Gulf							
Babi et al. 2000 ¹³²	Cross-sectional	Albania, Tirana	0.3	W	47	0.6	2.0
Miklavčič et al. 2013 ¹³³	Cohort	Croatia, Rijeka	0.8	IN	210	0.7	8.0
			0.8	MO	255	0.5	5.3
Gibičar et al. 2006 ¹³⁴	Cohort	Greece, islands	1.5	PW	246	1.4	17.5
Vardavas et al. 2011 ¹³⁵	Cohort	Greece, Heraklion Crete	–	PW	47	0.4	1.7
Miklavčič et al. 2013 ¹³³	Cohort	Greece, Lesvos and Chios	1.0	MO	391	1.5	8.3
Fakour et al. 2010 ¹³⁶	Cohort	Islamic Republic of Iran, Mahshahr	1.3	W	195	3.0 ^d	26.5

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Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg/mo)	Subpopulation	n	THHg, average ^b (µg/g)	THHg, high-end ^b (µg/g)
Salehi et al. 2010 ¹³⁷	Cross-sectional	Islamic Republic of Iran, Mahshahr	2.9	PW	149	2.0	10.0
Barghi et al. 2012 ¹³⁸	Cross-sectional	Islamic Republic of Iran, Noushahr	3.9	PW	59	0.3	0.6
Okati et al. 2012 ¹³⁹	Cross-sectional	Islamic Republic of Iran, Mazandaran	–	IN	93	1.9 ^d	6.9
			1.1	MO	93	3.6 ^d	9.0
Díez et al. 2008 ¹⁴⁰	Cross-sectional	Italy, Naples	–	W	114	0.5	1.5
Maddedu et al. 2008 ⁸³	Case control	Italy, Sicily, Catalina	–	W	100	0.9	4.2
Miklavčić et al. 2013 ¹³³	Cohort	Italy, Trieste	1.2	IN	614	1.0	8.3
			1.2	MO	871	0.6	10.0
Bou-Olayan et al. 1994 ¹⁴¹	Cross-sectional	Kuwait	2.2	W	68	4.1 ^d	25.0
Khassouani et al. 2001 ¹⁴²	Cross-sectional	Morocco, Rabat	–	W	70	1.6 ^d	–
Myers et al. 1995 ¹⁴³	Cohort	Seychelles, Mahe	–	PW	740	5.9	26.7
Channa et al. 2013 ¹⁴⁴	Cross-sectional	South Africa, KwaZulu-Natal	–	IN	350	0.2	4.6
			–	MO	350	0.2	3.1
Rudge et al. 2009 ¹⁴⁵	Cross-sectional	South Africa	–	IN	62	1.2	9.7
			–	MO	62	0.7	8.8
			–	W	50	2.9 ^d	20.0
Ramon et al. 2011 ¹¹⁸	Cohort	Spain, Valencia	2.1	IN	554	2.4	16.5
Spain, Sabadell		2.3	IN	460	1.6	15.0	
Unuvar et al. 2007 ¹⁴⁷	Cohort	Turkey, Istanbul	1.1	IN	143	0.1	–
			1.1	MO	143	0.1	–
Coastal: Pacific coast							
Choy et al. 2002 ¹⁴⁸	Case control	China, Hong Kong Special Administrative Region	–	W	155	1.7	–
Fok et al. 2007 ¹⁴⁹	Cohort	China, Hong Kong Special Administrative Region	1.3	IN	1057	2.2	–
			1.3	MO	1057	1.2	–
Gao et al. 2007 ¹⁵⁰	Cohort	China	2.9	IN	408	1.4	–
			2.9	MO	408	1.3	–
Liu et al. 2008 ¹⁵¹	Cross-sectional	China, 5 cities	2.1	W	321	0.7	8.5
Dewailly et al. 2008 ¹⁵²	Cross-sectional	French Polynesia, Tahiti	5.6	IN	234	2.6	12.1
Nakagawa et al. 1995 ¹⁵³	Cross-sectional	Japan, Tokyo	–	W	177	1.9	–
Iwasaki et al. 2003 ¹⁵⁴	Cross-sectional	Japan, Akita	–	W	154	1.7	5.8
Yasutake et al. 2003 ¹⁵⁵	Cross-sectional	Japan	–	W	1666	1.4	25.8
Arakawa et al. 2006 ¹⁵⁶	Cohort	Japan, Sendai	2.6	MO	180	2.0	9.4
Ohno et al. 2007 ¹⁵⁷	Cohort	Japan, Akita	–	W	59	1.5	3.6
Sakamoto et al. 2007 ¹⁵⁸	Cross-sectional	Japan, 3 cities	–	IN	115	2.5	–
			–	MO	115	1.3	–
Sakamoto et al. 2008 ¹⁵⁹	Biomarker valid	Japan, Fukuoka	–	IN	40	0.4	–
			–	MO	40	0.4	–
Miyake et al. 2011 ¹⁶⁰	Cohort	Japan, Osaka	–	W	582	1.5	3.2
Kim et al. 2006 ¹⁶¹	Case control	Republic of Korea, Seoul	–	IN	63	1.0	5.0
			–	MO	63	0.6	7.4
Kim et al. 2008 ¹⁶²	Cross-sectional	Republic of Korea (coastal)	4.4	W	111	0.8	–
Jo et al. 2010 ¹⁶³	Cross-sectional	Republic of Korea, Busan	4.4	W	146	1.9	11.4
Kim et al. 2010 ¹⁶⁴	Cross-sectional	Republic of Korea, 3 cities	4.4	IN	312	3.7	–
Lee et al. 2010 ¹⁶⁵	Cohort	Republic of Korea, 3 cities	4.4	IN	417	1.4	6.0
			4.4	PW	417	0.8	4.6
Kim et al. 2011 ¹⁶⁶	Cohort	Republic of Korea, 3 cities	–	IN	797	1.3	2.3
			–	MO	797	0.8	1.4
Kim et al. 2012 ¹⁶⁷	Cross-sectional	Republic of Korea	–	W	2964	1.0	–
You et al. 2012 ¹⁶⁸	Cross-sectional	Republic of Korea, Busan and Ulsan	–	W	200	4.7	–
Eom et al. 2013 ¹⁶⁹	Cross-sectional	Republic of Korea (coastal)	–	W	308	1.1	–
Hong et al. 2013 ¹⁷⁰	Cross-sectional	Republic of Korea, Seoul	–	W	79	1.4 ^d	–

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Studies, by category and subcategory	Study design	Location	Seafood intake ^a (kg/mo)	Subpopulation	n	THHg, average ^b (µg/g)	THHg, high-end ^b (µg/g)
Kim et al. 2013 ¹⁷¹	Cross-sectional	Republic of Korea (urban)	1.5	W	117	0.9	–
		Republic of Korea (coastal)	1.5	W	114	0.9	–
		Republic of Korea (rural)	1.5	W	105	0.7	–
Marsh et al. 1995 ¹⁷²	Cohort	Peru, Mancora	–	MO	131	7.1	28.5
Hsu et al. 2007 ¹⁷³	Cross-sectional	China, Taiwan, Taipei	–	IN	65	2.3	7.0
			1.9	MO	65	2.2	5.3
Chien et al. 2010 ¹⁷⁴	Risk assessment	China, Taiwan (northern)	1.5	W	263	1.7	16.3
Sato et al. 2006 ¹⁷⁵	Cross-sectional	United States, Honolulu, Hawaii	0.6	IN	188	0.7 ^d	5.0
Tsuchiya et al. 2009 ¹⁷⁶	Cohort	United States, Washington state (Koreans)	1.8	W	108	0.6	–
		United States, Washington state (Japanese)	1.8	W	106	1.2	–
Inland^e							
Gundacker et al. 2006 ¹⁷⁷	Cross-sectional	Austria, Vienna	–	W	78	0.6 ^d	–
Rudge et al. 2011 ¹⁷⁸	Cross-sectional	Brazil, São Paulo state	–	MO	155	0.2	1.1
Rhainds et al. 1999 ¹⁷⁹	Cross-sectional	Canada, southern Quebec	–	IN	109	0.2	3.4
Pawlas et al. 2013 ⁸¹	Cross-sectional	Croatia, Koprivnica	–	W	60	0.4	7.6
Puklová et al. 2010 ¹⁸⁰	Cross-sectional	Czech Republic	0.5	W	163	0.2	2.3
Cerna et al. 2012 ¹⁸¹	Cross-sectional	Czech Republic	–	W	494	0.2	0.7
Pawlas et al. 2013 ⁸¹	Cross-sectional	Czech Republic	–	W	51	0.9	8.0
Khassouani et al. 2001 ¹⁴²	Cross-sectional	France, Angers	–	W	62	0.9	–
Huel et al. 2008 ¹⁸²	Cohort	France, Paris	–	MO	81	1.2	2.9
Deroma et al. 2013 ⁸⁴	Cohort	Italy, northern	–	IN	58	0.9	–
			–	MO	72	0.9	–
Eom et al. 2013 ¹⁶⁹	Cross-sectional	Republic of Korea (inland)	–	W	886	0.8	–
Pawlas et al. 2013 ⁸¹	Cross-sectional	Morocco, Fez	–	W	50	1.0	9.1
Anwar et al. 2007 ¹⁸³	Cross-sectional	Pakistan, Lahore	0.7	W	75	0.2	2.5
Jędrychowski et al. 2007 ¹⁸⁴	Cross-sectional	Poland, Krakov	–	IN	313	0.1	–
		Poland	0.7	MO	313	0.2	–
Pawlas et al. 2013 ⁸¹	Cross-sectional	Poland, Wroclaw	–	W	51	0.7	2.9
Al-Saleh et al. 2006 ¹⁸⁵	Case control	Saudi Arabia	–	W	185	0.9 ^d	5.4
Al-Saleh et al. 2008 ¹⁸⁶	Case control	Saudi Arabia, Riyadh	–	W	434	0.9 ^d	7.6
Al-Saleh et al. 2011 ¹⁸⁷	Cross-sectional	Saudi Arabia, Riyadh	–	IN	1561	0.6	1.9
		Saudi Arabia, Riyadh	–	MO	1574	0.5	2.2
Al-Saleh et al. 2013 ¹⁸⁸	Cross-sectional	Saudi Arabia	–	MO	150	0.3	–
Miklavčič et al. 2011 ¹⁸⁹	Cohort	Slovenia, Ljubljana	–	IN	446	0.4	–
		Slovenia, Ljubljana	0.8	MO	574	0.3	–
Miklavčič et al. 2013 ¹³³	Cohort	Slovenia, Ljubljana	1.3	MO	446	0.4	3.5
Pawlas et al. 2013 ⁸¹	Cross-sectional	Slovenia, Ljubljana	–	W	50	0.7	13.0
Díez et al. 2009 ¹⁹⁰	Cohort	Spain, Madrid	1.4	IN	57	1.5	5.1
Díez et al. 2011 ¹⁹¹	Case control	Spain, Toledo	2.0	W	64	2.5	–
Bjermo et al. 2013 ¹⁹²	Cross-sectional	Sweden	–	W	145	0.2	0.7
Gerhardsson et al. 2010 ¹¹⁶	Cross-sectional	Sweden, Hasselholm	0.4	PW	50	0.2	–
Knobeloch et al. 2005 ¹⁹³	Cross-sectional	United States, 12 states	0.7	W	414	0.3	1.6
Xue et al. 2007 ¹⁹⁴	Cohort	United States, Michigan	0.6	MO	1024	0.1	–
Pollack et al. 2011 ¹⁹⁵	Cross-sectional	United States, western New York state	–	W	252	0.3	–
Pollack et al. 2012 ¹⁹⁶	Cross-sectional	United States, Buffalo	–	W	248	0.4	–

IN, infants; MO, mothers; PW, pregnant women; W, women.

^a Seafood intake as reported in studies, converted to kg per month (assuming average meal size of 170 g if not stated) and shown for mothers if reported for both mothers and infants; not all studies reported seafood intake.

^b Biomarker concentrations shown as THHg, either as reported or as converted from TBHg using the hair-to-blood ratio of 250:1. All THHg concentrations are rounded to one decimal place. Average THHg is the geometric mean or median (unless noted with “^d”); high-end THHg is the maximum or the 95th or 90th percentile.

^c Women and infants living in coastal regions and consuming marine and freshwater seafood mainly purchased from local and global markets.

^d The average is the arithmetic mean and was not included in the main pooled results.

^e Women and infants living inland and consuming marine and freshwater seafood mainly purchased from local and global markets.