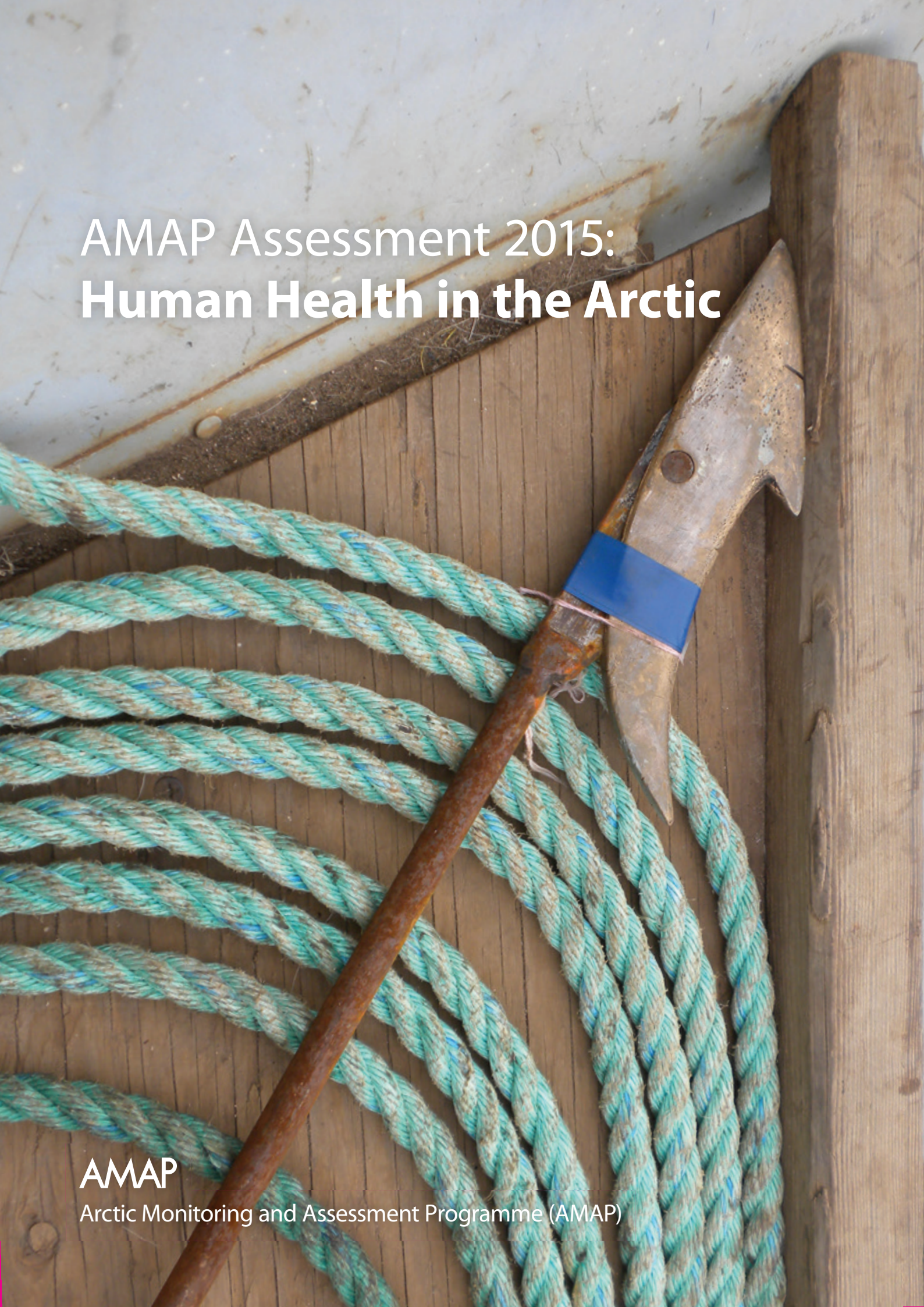

AMAP Assessment 2015:
Human Health in the Arctic

AMAP

Arctic Monitoring and Assessment Programme (AMAP)

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As ice conditions change, indigenous whalers in Alaska are using modern boats during the spring hunt in combination with traditional hunting methods. Photo: Michael Brubaker

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DEDICATION

In memory of a great scientist and friend

The AMAP Human Health Assessment Report 2015 is dedicated to our esteemed colleague, Dr. Éric Dewailly. He died in a tragic accident at La Réunion in June 2014, while on vacation together with his family.

Éric was a leading expert in the AMAP Human Health Assessment Group. He was very clear that we needed not only to monitor levels of contaminants in humans, but also to study the human health effects arising from these contaminants. His early research papers from Quebec are still outstanding and must be regarded as foundational pioneer work. The combination of public health and toxicology research was the basis for the development of a great network; in Canada, in all circumpolar countries, and, not least, across all the scientific disciplines needed for good research in environmental medicine. His laboratory in Quebec and the generous contribution from Health Canada to the first AMAP human health assessment made it possible to produce compatible and reliable data from all circumpolar countries, for the first time in history.

Éric's scientific portfolio speaks for itself. He published a few hundred papers in his decades-long career, always filled with new ideas and new questions; otitis media, cardio-vascular effects, reproductive effects, and immune effects, just to mention a few. The 2015 report contains substantial results of his excellent work. We hope that his fear of a 'boring report' has not been realized.

Just as important as his scientific life was his social contribution to a large group of colleagues with very different backgrounds and perspectives. We could have very open and interesting discussions in a friendly atmosphere, and then we could have a good (and long lasting!) dinner. To enjoy life meant that his pipe was with him, and there was no fanatical talk about risk factors. Another not well known side of Éric was his talent as a story teller. Those of us who participated in the Svalbard meeting will remember hours of funny stories from all the places in the world he visited, of course with his special French way of expressing himself.

We lost some of our future with Éric. He was a mentor and a supervisor for the most brilliant scientists of the new generation. Even so, some of us are in the same generation and we will continue the work in the spirit of how we think Éric would have continued. We are certain that he would agree with that. We will do the best we can, and hopefully he will send his strong corrections from above if we are not on the right track. Thank you for everything, Éric!

Jon Øyvind Odland and Shawn Donaldson (Co-chairs AMAP Human Health Assessment Group)

Contents

Preface

This assessment report presents the results of the 2015 AMAP Assessment of Human Health in the Arctic. This is the fourth AMAP assessment dealing with this issue in a sequence and updates the assessments delivered in 1998, 2002 and 2009.

The Arctic Monitoring and Assessment Programme (AMAP) is a group working under the Arctic Council. The Arctic Council Ministers have requested AMAP to:

- produce integrated assessment reports on the status and trends of the conditions of the Arctic ecosystems
- identify possible causes for the changing conditions
- detect emerging problems, their possible causes, and the potential risk to Arctic ecosystems including indigenous peoples and other Arctic residents
- recommend actions required to reduce risks to Arctic ecosystems.

This report provides the accessible scientific basis and validation for the statements and recommendations made in the *Summary for Policy-makers: Arctic Pollution Issues 2015* report[i] that was delivered to Arctic Council Ministers at their meeting in Iqaluit, Canada in April 2015. It is also the basis for a related AMAP State of the Arctic Environment report *Arctic Pollution Issues 2015: Overview*[ii]. It includes extensive background data and references to the scientific literature, and details the sources for graphics reproduced in the overview report. Whereas the Summary for Policy-makers report contains recommendations that focus mainly on policy-relevant actions concerned with addressing contaminant impacts on Arctic human populations, the conclusions and recommendations presented in this report also cover issues of a more scientific nature, such as proposals for filling gaps in knowledge, and recommendations relevant to future monitoring and research work.

This assessment of Arctic human health impacts of contaminants and other stressors was conducted between 2012 and 2014 by an international group of over 60 experts. AMAP Human Health assessment group members and lead authors are appointed following an open nomination process coordinated by AMAP. A similar process was used to select international experts who independently reviewed this report.

Information contained in this report is fully referenced and based first and foremost on peer-reviewed and published results of research and monitoring undertaken since 2009. It also incorporates some new (unpublished) information from monitoring and research conducted according to well-established and documented national and international standards and quality assurance/quality control protocols. Care has been taken to ensure that no critical probability statements are based on non-peer-reviewed materials.

Access to reliable and up-to-date information is essential for the development of science-based decision-making regarding ongoing changes in the Arctic and their global implications. Related assessment summary reports[i,ii] have therefore been developed specifically for policy-makers, summarizing the main findings of the assessment. The assessment lead authors have confirmed that both this report and its derivative products accurately and fully reflect their scientific assessment. All AMAP assessment reports are freely available from the AMAP Secretariat and on the AMAP website: www.amap.no, and their use for educational purposes is encouraged.

AMAP would like to express its appreciation to all experts who have contributed their time, efforts and data, in particular the lead authors who coordinated the production of this report. Thanks are also due to the reviewers who contributed to the human health assessment peer-review process and provided valuable comments that helped to ensure the quality of the report. A list of contributors is included in the acknowledgements at the start of this report and lead authors are identified at the start of each chapter. The acknowledgements list is not comprehensive. Specifically, it does not include the many national institutes, laboratories and organizations, and their staff, which have been involved in various countries in human health-related monitoring and research. Apologies, and no lesser thanks are given to any individuals unintentionally omitted from the list.

The support from the Arctic countries and non-Arctic countries implementing research and monitoring in the Arctic is vital to the success of AMAP. The AMAP work is essentially based on ongoing activities within these countries, and the countries that provide the necessary support for most of the experts involved in the preparation of the AMAP assessments. In particular, AMAP would like to acknowledge Canada and Norway for taking the lead country role in this assessment and thank Canada, Denmark, Norway, and the Nordic Council of Ministers for their financial support to the human health assessment work. The contribution of the Inuit Circumpolar Council (ICC) to the preparation of this assessment is also greatly appreciated.

The AMAP Working Group is pleased to present its assessment to the Arctic Council and the international science community.

Shawn Donaldson (Human health assessment Co-lead, Canada)

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Oslo, December 2015

[i] AMAP, 2015. Summary for Policy-makers: Arctic Pollution Issues 2015. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway. 12 pp.

[ii] AMAP, 2015. Pollution Issues 2015: Overview report. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

1. Introduction

Authors: Jon Øyvind Odland, Shawn Donaldson, Alexey Dudarev, Anders Carlsen

The 2015 Human Health Assessment Report follows three previous AMAP assessments on human health (AMAP 1998, 2003, 2009) and represents the current knowledge base after 25 years of focused study. This report includes new knowledge, updates and fills information gaps identified in past reports, and focuses attention on the most recent integrated scientific knowledge related to environmental contaminants and human health. It does not update information concerning the levels and effects of radioactivity and UV-radiation; these topics were addressed in the first comprehensive AMAP Assessment Report (AMAP 1998).

1.1 AMAP 1998 human health assessment

The Arctic Monitoring and Assessment Programme (AMAP) began in 1991. Phase 1 was designed to implement components of the Arctic Environmental Protection Strategy (AEPS) as adopted by the Ministers of the eight Arctic countries. The main task was to prepare an assessment of the state of the Arctic environment with respect to defined pollution issues. Based on this, AMAP designed and implemented a monitoring program largely based on adaptation of ongoing national and international activities and initiated new monitoring and research work only where necessary to fill out the AEPS. The first AMAP assessment, entitled *AMAP Assessment Report: Arctic Pollution Issues*, was published in 1998 (AMAP 1998).

The first AMAP assessment was not an environmental risk assessment. Rather, it was a compilation of current knowledge about the Arctic region and a statement of the prevailing conditions in the area. The assessment was prepared in a systematic and uniform manner to provide the means for intercomparisons with other regional environmental conditions, and for assessing the nature and extent of anthropogenic influences on the circumpolar region related to global environmental pollution.

The 1998 report had a broad and holistic perspective; the issues related to population health and exposure to environmental contaminants were contained in a single chapter (Hansen et al. 1998). The health chapter provided the very first quality assured comparison of persistent organic pollutants (POPs) and metals in human biological materials at the circumpolar level[1] (Odland and Nieboer 2012).

It was clearly evident from the 1998 AMAP Assessment Report that several groups of people in the Arctic were highly exposed to environmental contaminants, that others were less exposed and that exposures for Inuit people were substantially greater than for non-Arctic residents. It was also concluded that variation in human exposure depended upon a combination of factors: different environmental concentrations of contaminants across the Arctic; local physical and biological pathways which make the contaminants more or less available; and the local dietary habits of the exposed individuals. The overall report concluded that current understanding of contaminant transport processes into the Arctic, the relative importance of contaminant concentrations between compartments (air, land, water, ice, sediments, biota) and the ability to quantify them were inadequate.

The fundamental importance of good and reliable biomonitoring programs and health effects studies was a key conclusion of the health chapter (Hansen et al. 1998). Despite concern over the levels of some contaminants found in blood samples, the health chapter emphasized that breastfeeding (with its well-established benefits) and consumption of traditional (country) food items (i.e., food from wild animals and plants that are hunted, caught or collected locally in the Arctic) should continue even though there was not a full understanding of the effects of the contaminants on human health. A separate chapter of the 1998 AMAP Assessment Report described characteristics of human populations in the Arctic relevant to pollution issues. One result of this overview has been the development of a comprehensive set of circumpolar health indicators (Young and Bjerregaard 2008).

1.2 AMAP 2002 human health assessment

The 2002 human health assessment (AMAP 2003) went deeper into health effects, reporting case studies in different geographical areas. It focused upon the combined effects of 'multiple environmental stressors'. Evidence from analyses of banked blood samples from Norway (non-Arctic donors) demonstrated an exponential increase in polybrominated diphenylethers since 1977. Progress was made on studies of interactive effects of mixtures of POPs found in some traditional diets. Also, information on concentrations of contaminants found in species consumed as traditional food and in the various organs of these species improved. Subtle, dose-related neurotoxic effects of methylmercury were reported in children in some Arctic regions. These findings enhanced the basis for targeted dietary advice for specific local populations which would benefit from lowering their exposures. The success of carefully developed public health strategies was demonstrated in the Faroe Islands where interventions related to consumption of pilot whale meat resulted in an 80% reduction in mean mercury body burdens.

The 2002 assessment opened up the issue of how to conduct risk assessments when dealing with exposure to mixtures of contaminants rather than exposure to individual contaminants. New epidemiological approaches and mechanistic biomarker

[1] Health Canada provided funding for the analyses of blood samples from all eight Arctic countries in a single QA/QC assured laboratory to enable direct comparisons of data from country to country.

effects studies made it possible to examine for the first time the effects of current contaminant exposure, possible interactions, and the modifying effects of nutrients ('combined effects').

It was clear that in some areas, indigenous peoples enjoyed the same level of health as the non-indigenous populations, but in most areas of the Arctic population health for indigenous peoples was significantly poorer. Among indigenous peoples, lifestyle-related conditions such as obesity, diabetes, and circulatory diseases were shown to be more frequent than previously reported. Suicide and injuries remained significant causes of death in parts of the Arctic.

1.3 AMAP 2009 human health assessment

The 2009 assessment (AMAP 2009) presented more evidence, more data and an accelerated understanding of population health and well-being issues in the Arctic. Epidemiological study designs were improved, molecular research was in rapid development and several of the ongoing mother/child cohorts provided results of developmental effects. Risk communication and risk management were on the public health agenda. Human adaptation to climate change became part of the discussion, and several new substances emerged as contaminants of potential concern.

Extensive new data for Arctic Russia were available for the first time in the 2009 assessment report, indicating elevated levels of oxychlordane and polychlorinated biphenyls (PCBs) in indigenous coastal peoples from Chukotka (AMAP 2004). These levels have been linked to consumption of marine mammals by these coastal peoples. DDE, the major metabolite of the pesticide DDT, was reported at the highest concentrations in Arctic Russia, despite its decline in most other areas of the Arctic. These data suggested that the likely source was recent use of DDT in Russian agriculture or its use as a pesticide in northern communities, rather than long-range atmospheric transport and local accumulation in the marine mammal food chain.

Mercury levels were reported to be declining in many populations across the Arctic; however, Inuit people still had blood mercury levels three to ten times higher than populations which consumed imported store-bought foods, as determined in the 1998 and 2002 assessments. This finding of elevated blood mercury was especially prominent in Greenland and parts of Arctic Canada. The proportion of Inuit women of childbearing age who exceeded guidelines for blood mercury was seen to be decreasing. The pattern in Arctic Russia was, however, different; even in areas with relatively high levels of POPs, mercury concentrations were low. Overall, the influences of social, cultural, and economic change on diet, together with peoples' responses to risk advisories in the Arctic, were considered to be the primary reasons for these decreases in human blood mercury levels. The decreases in human blood mercury levels were in contrast to the increasing levels of mercury seen in many marine species in some parts of the Arctic.

The 2009 assessment provided public health authorities with more detailed information on contaminant health effects at the molecular and clinical level than before. The challenge for policymakers and public health authorities was the conversion of these findings into new or altered contaminant management strategies and health advisories. Risk communication must be carried out with great care and must be sensitive to cultural preferences at a community level. Within a community there may be a need for specific and targeted advice to address the potential health risks for a particular subgroup (such as women of childbearing age). The 2009 assessment report clearly stated that it could not provide specific public health advice in local and regional situations, but could evaluate the circumpolar impacts of efforts by local health authorities to develop and disseminate advice.

1.4 Challenges for the AMAP 2015 human health assessment

It is an ongoing challenge to facilitate a holistic health impact assessment of the influences of environmental pollution on the health of Arctic peoples and the associated risk factors affecting them. This requires an interdisciplinary approach. Climate adaptation has increasing importance for all aspects of human life in the Arctic. Considering the importance of general health and the influence of changing diets and contaminants on disease outcomes, more efforts were made over the five-year period leading up to the 2015 assessment to systematically collect, analyze, and report on the evolving health status of Arctic populations and especially indigenous peoples (see Fig. 1.1 for locations of systematic health studies). The present report describes activities for maintaining and expanding current human population cohorts which are now ongoing in all eight Arctic countries, as well as in human cohorts in several European and southern hemisphere countries. These long-term prospective studies will provide the information needed to track adverse health outcomes associated with contaminants and changing conditions related to climate change, socio-cultural conditions, and diet. The health-related parts of the EU-funded FP7 project ArcRisk (*Arctic Health Risks: Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling, 2009–2014*; www.arcrisk.eu), coordinated by the AMAP Secretariat, were based on a number of the ongoing cohorts in the Arctic, Europe and in the Mediterranean area. It provided a complementary approach to the assessment of hazard and risk in the Arctic situation. Uniform reporting of human levels of contaminants as well as health status indicators is planned to occur every three to five years, including trend information, broken down by age and gender, and should be provided by all circumpolar jurisdictions at appropriate regional levels.

The following chapters report a detailed assessment of changes in contaminant concentrations in Arctic populations, additional results from a number of contaminant-effects studies, a comprehensive update on best practice for risk communication, information on adaptation strategies for small Arctic communities to the environmental impacts of climate change, and recommendations for future work.

Figure 1.1 Location of recent and ongoing blood monitoring, temporal trend and human health cohort studies around the Arctic.

2. Overview of ongoing cohort and dietary studies in the Arctic

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2.1 Introduction

This chapter gives an overview of the ongoing cohort and dietary studies underlying the assessment of population health in the Arctic. The description of each study begins with a table containing key information about the study, such as year established, sample size, and average exposure levels (i.e. concentration levels) for different contaminants in different matrices. The emphasis here is on a description of the material, methods and results or preliminary results for each study. Detailed exposure information is available in Chapter 3, while Chapter 4 describes the effects associated with contaminant exposure in the Arctic.

The cohort descriptions have been arranged geographically, beginning in Norway and moving east to Finland, Sweden, Russia, and the other Arctic countries and ultimately to the Faroe Islands. No cohort studies have been reported for Alaska or Iceland; however, biomonitoring data for these areas are provided in Chapter 3.

2.2 Arctic cohort and dietary studies

2.2.1 The MISA study

The northern Norway mother-and-child contaminant cohort study – the MISA study – is a cross-sectional study with longitudinal aspects aimed at establishing a new northern Norway mother-and-child contaminant cohort study (see Table 2.1). The MISA database is considered suitable for exploring associations between contaminant exposure and diet, enhancing understanding of the interplay between physiological changes that occur in mothers and contaminant pharmacokinetics

Table 2.1 Key details of the MISA Study.

Year	Start year: 2007		
Sample size	515		
Follow-up	None		
Matrix	Blood:		
	early pregnancy n=515		
	3 days postpartum n=458		
	6 weeks postpartum n=394		
	Urine:		
	early pregnancy n=509		
	3 days postpartum n=444		
	6 weeks postpartum n=392		
	Hair: n=459		
	Cord blood: n=413		
	Meconium: n=448		
Analytes	PCB99, PCB101, PCB118, PCB138, PCB163, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187, PCB194		
	p,p'-DDE, HCB		
	trans-Nonachlor		
	cis-Nonachlor		
	As, Cd, Co, Hg, Pb, Cu, Mn, Mo, Se, Zn		
PCB exposure level, median pg/g lipid	PCB153	n=508	24.46
	p,p'-DDE	n=508	36.72
MeHg exposure level, median µg/L whole blood	Hg	n=282	1.35

(including transfer to the infant before and after birth), and conducting prospective health studies of the children.

Recruitment for the MISA Study began in May 2007 and continued for the next 25 months (until June 2009). A total of 515 eligible women were enrolled in early pregnancy, with 391 completing the study protocol that included a self-administrated food frequency questionnaire (FFQ) and donation of biological samples for contaminant analysis in the second trimester of pregnancy, just after delivery, and six weeks postpartum. Daily dietary intake was converted to energy intake, and estimates were made of macro- and micronutrients ingested. Some of the MISA findings were compared to data available in the Medical Birth Registry of Norway (MBRN). Compared to all 2004–2006 mothers in northern Norway, the MISA Study women were about two years older and smoked less. Parity, gestational age and birth weight of the newborn were comparable. The estimated average dietary intake of 8.1 MJ per day was less than that recommended by the Nordic Nutritional Recommendations (NNR), but the intake of micronutrients per MJ complied.

Although the final MISA cohort sample size was less than targeted, the generally good comparisons observed between MBRN-registered information for the study cohort and dropouts suggest that this introduced minimal bias. Agreement between the demographic and clinical characteristics of the cohort women and newborns with all births in northern Norway implied acceptable external validity. The dietary findings also aligned well with Norwegian national data and guidelines and other studies, as did the high prevalence of breastfeeding (Veyhe et al. 2012).

Meconium was analyzed to establish whether it could be used to predict fetal exposure to organochlorines (OCs) and hydroxylated polychlorinated biphenyls (PCBs). A subset of 40 meconium samples and complementary maternal serum were selected. Multivariate linear regression modelling confirmed that maternal serum was the most consistent predictor of meconium concentrations, adding gestational age and time of meconium sampling improved the models. Although more challenging to analyze, the lipid-adjusted OC concentration in meconium appears a sensitive and informative fetal exposure index when taking into account gestational age and its postpartum sampling time (Veyhe et al. 2013).

In a subset of 211 pregnant women, maternal blood concentrations of selected essential and toxic elements in the second trimester of pregnancy were compared with concentrations three days and six weeks postpartum. Ten selected elements (arsenic, As; cadmium, Cd; cobalt, Co; copper, Cu; lead, Pb; manganese, Mn; mercury, Hg; molybdenum, Mo; selenium, Se; zinc, Zn) featured three general but distinct concentration patterns across the three collection periods (see Fig. 2.1): a progressive increase, a V-shaped curve with a minimum at day three, and an inverted V-shaped curve with a maximum at day three (Hansen et al. 2011).

In a subset of 50 women, blood concentrations of common OCs in the second trimester of pregnancy were compared with concentrations three days and six weeks postpartum. Lipids and wet-weight OC levels both peaked at birth and were lowest at six weeks postpartum. However, this peak was no longer evident when the OC concentrations were lipid-adjusted. Wet-weight OC concentrations appear to be driven by the physiological lipid profiles and are interpreted to constitute biomarkers of lipidemia. This observation may have implications for the biomonitoring of individuals at risk of Type 2 diabetes. Both age and parity were strong predictors for the OCs measured, but no consistent association with body mass index (BMI) was evident. Independent of lipid-adjustment, all compounds were positively and significantly correlated with each other (within and across the three collection periods). The peak in OCs during pregnancy suggests that the period spanning the last weeks of the third trimester and the early postpartum days constitutes an optimum sampling window purely from the analytical perspective (Hansen et al. 2010).

2.2.2 The Tromsø study

Human exposure to both the legacy and newer persistent organic pollutants (POPs) has changed over past decades. Exposure routes have been largely dietary for the legacy POPs, while other routes have also been important for the newer POPs. The legacy POPs have often been observed to increase with age in cross-sectional studies and this association probably reflects birth-cohort differences in duration and intensity of exposure to these compounds. For the newer POPs, associations with age are not consistent.

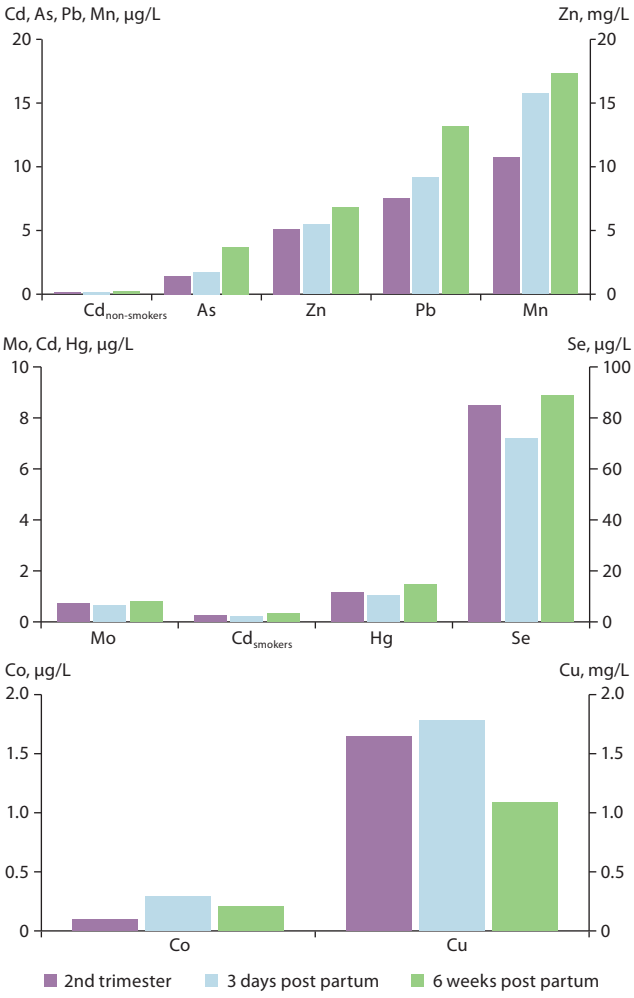

Figure 2.1 Contaminant concentrations in the MISA cohort mothers followed one of three patterns: a progressive increase (upper plot), a V-shaped curve (middle plot), and an inverted V-shaped curve (lower plot) (Hansen et al. 2011).

Table 2.2 Key details of the Tromsø Study.

Study type	Longitudinal study
Year	1979, 1986–1987, 1994, 2001–2002, 2007–2008
Sample size	53
Matrix	Serum
Analytes	POPs (PCBs, organochlorine pesticides and PFASs)
PCB exposure level, median µg/g lipid	PCB153: 0.36 (1979), 0.36 (1986–1987), 0.25 (1994), 0.24 (2001–2002), 0.17 (2007–2008)
DDE exposure level, median µg/g lipid	*p,p'*-DDE: 1.10 (1979), 0.80 (1986–1987), 0.35 (1994), 0.32 (2001–2002), 0.21 (2007–2008)

The Tromsø Study (see Table 2.2) is a population-based health survey initiated in 1974 to investigate the reasons for high mortality due to cardiovascular disease in northern Norway. Six surveys have been undertaken since 1974 and the health research topics included have increased. A total of 40,051 people have participated in at least one survey and 15,157 have participated in three or more surveys. The Tromsø Study was also used to explore changes in POP concentrations from 1979 to 2007 on an individual basis with a repeat measurement design. Serum samples were obtained from the freezer archive for 54 men who participated in all of the survey points: 1979, 1986, 1994, 2001, and 2007. The archived serum samples were analyzed for PCBs, chlorinated pesticides, and per-and polyfluoroalkyl substances (PFASs).

Median summed concentrations of PCBs and OC pesticides decreased by 22% (1979–1986), 52% (1979–1994), 54% (1979–2001), and 68% (1979–2007) (Nøst et al. 2013). Concentrations of DDT and DDE decreased from 1979, whereas most PCBs decreased from 1986. The median summed PFAS burdens increased from 1979 to 2001 and then decreased from 2001 to 2007 (Nøst et al. 2014). The results indicate that concentrations followed calendar year trends rather than 'increasing with age' *per se* and concentrations have followed birth year-dependent patterns over time. Furthermore, the composition of POPs in serum has changed over the almost 30-year period. Assessments of age, calendar year and birth cohort trends showed that calendar time was the dominant influence.

The concentrations and time trends of four PCBs were compared to predicted concentrations from a human exposure mechanistic model (Nøst et al. 2013). The predicted and measured concentrations, time trends and birth-year patterns were in good agreement and so inspire confidence in such models.

The trends observed between 1979 and 2007 probably reflect overall trends in the use and emission of the different POPs, together with compound-specific persistency, bioaccumulation potential and long-range transport. Study design and population characteristics must also be considered in monitoring studies. The Tromsø Study has increased knowledge of intra-individual variation in POP concentrations with respect to time and exposure history, which is essential for understanding past exposure and predicting future exposure. The findings have important implications for future studies of exposure and vulnerable groups (Nøst et al. 2013).

2.2.3 Northern Finland 1966 Birth Cohort

Information is available on individuals born into the Northern Finland 1966 Birth Cohort in the provinces of Oulu and Lapland since the 24th gestational week as well as on their mothers and, to a lesser extent, fathers. A total of 12,058 live-born children were born into the cohort (around 96% of all eligible) and 11,665 were alive in 1997 (Table 2.3). Data were collected by questionnaire, from hospital records and various registers and databases (social benefits, medication reimbursement, hospital discharges and

Table 2.3 Key details of the northern Finland 1966 birth cohort study.

Year	Start year: 1966		
Sample size	n=12,058		
Follow-up	At birth, age 1 and 14, 31 and 47 years (during pregnancy)		
Matrix	Blood (contaminants at age 31 and 47 years)		
	Age 31 years: n=250 samples analyzed		
Analytes	As, Cd, Co, Hg, Pb, Cu, Mn, Mo, Se, Zn		
Exposure level, median µg/L whole blood	As	n=250	0.46
	Cd	n=250	0.05
	Cu	n=250	858
	Hg	n=250	2.06
	Mn	n=250	6.40
	Pb	n=250	13.50
	Se	n=250	101
	Zn	n=250	4210

deaths, community wealth), as well as by interview and clinical examination at birth, age 1 year and 14 years, and at age 31 years when a comprehensive follow-up was conducted on each subject's well-being, social standing and health. In 1997, all members of the cohort that lived in the provinces of Oulu and Lapland (n=7191) or that had moved to the capital region (n=1272) completed a questionnaire and underwent a health examination. Those living in other parts of the country (n=2164) or abroad (n=695) were also sent the questionnaire. In total, 8676 people returned the questionnaire, making a response percentage of about 77%. About 71% attended the health examination. Selected blood samples (n=250) from the 1997 sampling were analyzed for toxic and essential elements to establish levels in persons born and living for the last five years in the eastern and western part of Lapland.

2.2.4 The Northern Sweden Health and Disease Study

The Northern Sweden Health and Disease Study (NSHDS) consists of three study cohorts in northern Sweden: the Northern Sweden MONICA study; the Västerbotten Intervention Program (VIP); and the Mammography Screening Program (MSP). See Table 2.4 for key details of the NSHDS.

The Northern Sweden MONICA Study was originally part of the multicenter WHO survey MONICA (Multinational Monitoring of Trends and Determinants in Cardiovascular Disease). In the northern Sweden MONICA Study, 2000 or 2500 randomly selected participants aged 25–75 years (25–65 years before 1994) have been invited to the health survey every fourth or fifth year since 1986. Seven surveys have been conducted to date and 11,800 individuals have participated, of whom 3500 have participated more than once. Participants undergo a medical examination focusing on risk factors for cardiovascular disease and complete an extensive questionnaire on lifestyle factors, including a food frequency questionnaire. Participants are asked to donate fasting blood samples to be stored in a biobank for future research. Urine samples were collected from a proportion of the participants in the surveys from 2009 and 2014.

The VIP began in 1985 and was designed after the MONICA Study. In addition to the health examination, questionnaires and collection of blood samples to the biobank, VIP includes an intervention in which participants are offered counseling regarding lifestyle modifications with a trained nurse. The inhabitants in the county Västerbotten are invited to the intervention the year they become 40, 50 and 60 years old (until 1994 also 30 years old). By March 2015, 98,300 individuals had participated with 36,100 having participated more than once. No urine has been sampled.

The MSP was conducted between 1995 and 2006. Women 40–70 years of age were invited to mammography screening and asked to donate blood samples to the biobank. Limited information on lifestyle factors was collected. In total, 28,800 women have participated with 14,600 having participated more than once.

The stored blood samples make prospective studies of environmental contaminants possible within the NSHDS.

Environmental contaminants have been analyzed in sub-groups of the Northern Sweden MONICA Study. Concentrations are available for Cd and Pb in blood for 1990–2014 and Hg for 1990–2009. In the latest survey from 2014 some organic pollutants were analyzed in urine (ten phthalates, Bisphenol A, Bisphenol F, hydroxypyrene, triclosan, pesticides, trichloropyridinol and 3-phenyoxybenzoic acid). Bisfenol A was also analyzed in urine in 2009.

Various case-control studies concerning health effects of environmental pollutants have been conducted within the NSHDS. For example, those on Hg in relation to myocardial infarction and stroke; Cd, Pb and Hg in relation to kidney disease; Cd in relation to fractures; Cd and Pb in relation to B-cell malignancies; and data from NSHDS are included in international collaboration on POPs and various cancers. Case-control studies concerning exposure to Cd and POPs and risk of diabetes is ongoing.

Table 2.4 Key details of the Northern Sweden Health and Disease Study.

Study type	Cohort with blood samples stored in biobank
Years of sampling	1986–ongoing
Sample size	140,000 (about 5000 with analyses on one or more environmental contaminants)
Matrix	Blood, urine
Analytes	Cd, Pb, Hg, PCBs, DDE, HCB
Medians based on analyses of samples from sub-groups	Blood Cd: men 0.14 µg/L; women 0.20 µg/L
	Blood Pb: men 16 µg/L; women 12 µg/L
	Blood Hg: men 0.91 µg/L; women 0.98 µg/L
	Plasma PCB118: men 101 pg/ml; women 115 pg/ml
	Plasma PCB138: men 536 pg/ml; women 503 pg/ml
	Plasma PCB153: men 1075 pg/ml; women 937 pg/ml
	Plasma PCB156: men 100 pg/ml; women 81 pg/ml
	Plasma PCB170: men 375 pg/ml; women 303 pg/ml
	Plasma PCB180: men 740 pg/ml; women 595 pg/ml
	Plasma DDE: men 1438 pg/ml; women 1636 pg/ml
	Plasma HCB: men 186 pg/ml; women 191 pg/ml

There are plans to create an environmental contaminant cohort within the NSHDS. This will include individuals for whom analyses of metals and POPs have been carried out.

2.2.5 Chukotka dietary and exposure study

Data were collected in 2001–2003 in Chukotka (Russia) on PCB and DDT contamination (Table 2.5) of different local foods and indoor materials. Exposure of indigenous people was evaluated by comparing pollutant levels in foods with levels in human blood in people living in coastal and inland regions (Dudarev 2012; Dudarev et al. 2012a,b). Because DDT degrades to DDE, the ratio of *p,p*'-DDE to *p,p*'-DDT is commonly used in environmental epidemiology practice as a measure of the remoteness of DDT exposure events: the higher the score, the lower the concentration of the original DDT and the longer the exposure.

The DDE:DDT ratios in Chukotka fresh local foods vary widely. High ratios were found in whale meat (up to 16), seal meat (up to 27), and bearded seal fat (up to 65), which indicates little fresh

Table 2.5 Key details of the Chukotka 2001–2003 cross-sectional study.

Study type	Cross-sectional
Years of sampling	2001–2003
Sample size	Coastal:
	Men: n=24 (average age 35; range 19–68)
	Women: n=26 (average age 38; range 21–68)
	Pregnant women: n=68 (average age 26; range 15–41)
	Inland:
	Men: n=14 (average age 32; range 19–54)
	Women: n=28 (average age 37; range 19–81)
	Pregnant women: n=58 (average age 25; range 18–40)
Follow-up	None
Matrix	Human serum and whole blood
Analytes	POPs, Hg, Pb
PCB153 exposure level, median µg/kg lipid	Coastal:
	Men: 948 (177–2645)
	Women: 344 (65.6–1406.92)
	Pregnant women: 261 (20.9–1393)
	Inland:
	Men: 139 (69.1–384)
	Women: 78.4 (15.6–415)
	Pregnant women: 36.8 (11.9–817)
Total Hg exposure level, µg/L whole blood, median	Coastal:
	Men: 10.9 (3.6–25.7)
	Women: 7.6 (2.4–22.9)
	Pregnant women: 1.3 (0.5–6.2)
	Inland:
	Men: 8.5 (0.5–15)
	Women: 6.5 (1.0–28.6)
	Pregnant women: 1.0 (0.5–7.7)
p,p'-DDE exposure levels, µg/kg plasma lipids, median	Coastal:
	Men: 694 (297–1633)
	Women: 447 (90.7–1087)
	Pregnant women: 478 (140–2148)
	Inland:
	Men: 814 (229–1628)
	Women: 387 (64.1–1264)
	Pregnant women: 334 (8.7–1642)

contamination, while low DDE:DDT ratios were observed in walrus meat (up to 1.5) and fat (up to 8.5) and bearded seal meat (up to 6.2). As well as exposure, these widely varying ratios could reflect differences in nutritional habit (bearded seals and walrus feed on benthic invertebrates, whales feed on krill, and seals feed on fish), variability in DDT metabolism (still poorly studied) and DDE/DDT accumulation/elimination processes in these large marine animals with a thick layer of subcutaneous fat. Fish (migratory and freshwater), poultry and venison are characterized by low DDE:DDT ratios (1–5) which could indicate 'fresh' exposure. Extremely low DDE:DDT ratios in washouts and scrapes from the walls inside dwellings (0.4) are conclusively linked to the use of 'fresh' DDT as a household insecticide (Dudarev et al. 2012b).

Comparison of DDE:DDT ratios in the food and blood of aboriginal Chukotka people suggests that the higher ratios in marine mammals are responsible for the higher ratios in the blood of coastal natives, and the much lower ratios in reindeer meat, poultry and fish are responsible for the lower blood ratios for inland residents.

Despite considerable variation, the indigenous coastal residents have a blood DDE:DDT ratio (18–19) that is almost double that of their inland neighbors (11–12), which indicates a substantial amount of relatively 'fresh' DDT contamination in the inland regions (10–15% vs 4–6% of 4,4DDT, respectively). This implies that marine food-chain DDT has a more 'long-standing' global origin than terrestrial food-chain DDT (Dudarev et al. 2012b).

Blood PCB congener 'composition' in indigenous coastal residents shows a low percentage of low-chlorinated and dioxin-like PCB congeners and a large share (up to 60%) of 'triad' congeners (PCB128–PCB138–PCB153). Inland residents are characterized by a much higher proportion of low-chlorinated and dioxin-like congeners and a lower share of 'triad' congeners (35–38%). The composition of PCB congeners in the blood of inland residents differs from that of inland local foodstuffs, unlike the coastal residents whose blood PCB 'formula' is very similar to that of marine mammal tissues. There was no similarity between the PCB congener structure of household indoor materials (washouts and scrapes from the walls) and the blood of natives (Dudarev et al. 2012a).

2.2.6 Follow-up Chukotka coastal mother-child study 2001–2007: exposure and infection disease study

Levels of persistent toxic substances (PTS) in blood from 17 mothers and cord blood from the corresponding 17 babies born in the Chukotka coastal area in 2001–2002 were compared with PTS levels in blood sampled from the same women and their five-year old children in 2007 (see Table 2.6) with the aim of examining the influence of breastfeeding on maternal POPs serum levels and the link between children's POPs blood levels and the frequency of infectious diseases (Dudarev et al. 2010, 2011).

Maternal blood levels of POPs decreased significantly during the five-year period (by 33–74%), blood Pb levels decreased by 21%, and blood Hg levels remained the same. The infant blood serum levels of most POPs increased considerably over this period, while blood Pb levels were unchanged and Hg levels decreased by 31%.

Results showed that, during the five-year period, maternal PCB levels became similar to those observed in cord blood in 2001, and vice versa – infant PCB levels in 2007 became similar to maternal levels in 2001. The ratio of PCB congeners in blood

Table 2.6 Key details of the follow-up Chukotka coastal mother-child 2001–2007 study.

Study type	Follow up
Years of sampling	2001–2002 and 2007
Sample size	17 pregnant women / mothers (average age at delivery 25; range 15–33);
	17 fetuses / children (newborns and 5-year olds)
Follow-up	Yes
Matrix	Human and cord blood and serum
Analytes	POPs, Hg, Pb
PCB153 exposure levels, µg/kg plasma lipids, median	Cord: 232 (33.3–1132)
	Children: 378 (15.5–1165)
	Pregnant women: 261 (40.4–1393)
	Mothers: 174 (19.3–579)
Total Hg exposure levels, µg/L whole blood, median	Cord: 1.7 (0.5–3.3)
	Children: 1.0 (1.0–2.7)
	Pregnant women: 2.0 (0.5–3.9)
	Mothers: 1.8 (1.0–4.8)
p,p'-DDE exposure levels, µg/kg plasma lipids, median	Cord: 543 (255–1882)
	Children: 462 (79.0–1094)
	Pregnant women: 537 (169–2148)
	Mothers: 198 (58.6–517)

of puerperia–mother and fetus–child in coastal Chukotka was unchanged five years after the first examination, which indicates that elimination/accumulation rates for the various congeners were effectively the same both in mothers and children. The average elimination half-life of PCB congeners PCB105–PCB187 in maternal blood was 4–6 years, and for total PCB was 5.7 years.

The maternal DDT metabolite levels fell by 70% each, while the DDE:DDT ratio stayed at about 12, which could indicate 'old' sources of exposure. The infant DDE:DDT ratio increased by 84%, from 10.6 to 19.5.

On average, the medical files showed 4.8 infectious disease occurrences per child per year (range 0.9–9.6). For each individual child, there was no significant association between the annual number of infectious diseases (2001–2007) and POPs cord blood serum concentrations (2001). An interesting observation was that two children maximally exposed (to POPs and metals) got sick less often than others (Dudarev et al. 2010, 2011).

2.2.7 Chukotka birth cohort 2001–2003: exposure and reproductive effects

In 2001–2002 in Chukotka delivery departments, 126 indigenous pregnant women (68 coastal and 58 inland) were interviewed and gave blood samples (Table 2.7). Births with adverse outcomes were observed in almost every fourth woman (23%): premature births (22 cases) partially accompanied by low birth weight (13 cases), stillbirths (3 cases), and congenital malformations (3 cases – a heart defect and two multiple defects, one stillborn).

Negative (but insignificant) associations were found between high POPs levels and premature births and low birth weight. No associations were found for metals. Average POPs blood levels among mothers with preterm births were lower than those with a normal length of gestation: PCBs by 13–16%, hexachlorocyclohexane (HCH) by 14%, oxychlordane by 43%, ΣDDT by 11%, and Mirex by 33%.

Maternal POPs blood levels were higher in cases of stillbirth: for ΣPCBs by 27%, 4,4DDE by 84%, 4,4DDT by 304%, ΣDDT by 94%, and hexachlorobenzene (HCB) by 20%, but the differences were not statistically significant.

Maternal POPs blood levels were also higher in cases of congenital malformation: for ΣPCB by 156%, DDT metabolites by 38–54%, HCB by 119%, ΣHCH by 95%, and oxychlordane by 575%. These associations were statistically significant for oxychlordane (p=0.04) and HCB (p=0.02) only.

In terms of POPs and the sex ratio of newborns (70 boys and 56 girls), women with higher exposure to PCBs and other POPs gave birth to girls more often than boys. On average, PCB blood levels among mothers of boys were 13–30% lower than for mothers of girls, and for other POPs 18–44% lower. The differences were statistically significant for ΣHCH (p=0.033) and 4,4 DDT (p=0.042). Average levels of metals in the blood of mothers having boys and mothers having girls were similar.

Higher POPs blood levels were noted among women with earlier menarche, shortened menstrual cycle and prolonged bleeding (Dudarev and Chupakhin 2014).

2.2.8 Kola Lapland 2001–2006: POPs and diabetes mellitus

In 2006, and under the framework of the International Barents Secretariat project 'Revealing the hidden diabetes mellitus in Lovozero district of Murmansk Oblast', 4359 residents of Kola Lapland in Murmansk Oblast were interviewed and had their blood glucose levels analyzed (2736 rural and 1623 urban, including Sami – 694, Komi – 910, Nenets – 80). This showed that risk of Type 2 diabetes (overweight/obesity, enhanced blood pressure, sedentary lifestyle, malnutrition, alcohol abuse) was 3- to 7-fold lower in indigenous residents than non-indigenous residents. Signs of diabetes were absent among Sami people of the remote villages. Elevated blood glucose levels were found mainly in large settlements. Indigenous residents in remote villages demonstrate minimum risk for diabetes mellitus and this may be related to their traditional diet based on local foods, a physically active lifestyle, and minimal consumption of high carbohydrate foods.

Table 2.7 Key details of the Chukotka birth cohort 2001–2003 study.

Study type	Cross-sectional
Years of sampling	2001–2003
Sample size	126
	Coastal pregnant women: n=68 (average age 26, range 15–41)
	Inland pregnant women: n=58 (average age 25, range 18–40)
Follow-up	None
Matrix	Human blood and serum
Analytes	POPs, Hg, Pb
PCB153 exposure levels, μg/kg plasma lipids, median	Coastal: 262 (20.9–1393)
	Inland: 36.8 (11.9–817)
Total Hg exposure levels, μg/L whole blood, median	Coastal: 1.3 (0.5–6.2)
	Inland: 1.0 (0.5–7.7)
p,p'-DDE exposure levels, μg/kg plasma lipids, median	Coastal: 478 (140–2148)
	Inland: 334 (8.7–1642)

Table 2.8 Key details of the Kola Lapland 2001–2006 study.

Study type	Cross-sectional
Years of sampling	2001 and 2006
Sample size	83 persons
	Lovozero
	men: n=4 (average age 55; range 45–77)
	women: n=47 (average age 44; range 18–78)
	Krasnoschelje
	men: n=15 (average age 41; range 18–57)
	women: n=17 (average age 47; range 26–76)
Follow-up	None
Matrix	Human blood
Analytes	POPs, Hg, Pb
PCB153 exposure levels, µg/kg plasma lipids, median	Lovozero
	men: 744 (501–1003)
	women: 186 (23.2–1767)
	Krasnoschelje
	men: 199 (43.9–585)
	women: 128 (32.9–338)
Total Hg exposure levels, µg/L whole blood, median	Lovozero
	men: 5.5 (3.0–11.8)
	women: 3.6 (1.0–8.2)
	Krasnoschelje
	men: 7.0 (0.5–22.1)
	women: 5.5 (1.3–29.2)
p,p'-DDE exposure levels, µg/kg plasma lipids, median	Lovozero
	men: 1701 (1579–8820)
	women: 985 (68.2–15614)
	Krasnoschelje
	men: 621 (94.2–1614)
	women: 919 (65.1–3135)

Data collected as part of the Russian Arctic PTS study (2001–2003) on blood POPs levels in indigenous residents of Kola Lapland (83 residents had blood sampled for PTS analyses) gave an opportunity to compare the results of both projects.

A comparison of diabetic status and POPs exposure showed that overweight/obesity, high blood glucose and Type 2 diabetes diagnoses were associated with higher blood levels of POPs (ΣPCB, DDTs, ΣHCH, HCB), although this was not statistically significant (Dudarev et al. 2012c). Key details of the Kola Lapland 2001–2006 study are shown in Table 2.8.

2.2.9 Nunavik Child Development Study

The Nunavik Child Development Study (NCDS), is a prospective mother-child cohort study taking place in Nunavik (Arctic Quebec), Canada (see Table 2.9). It was designed to extend previous findings on the effects of OCs, Hg and Pb on child health and development by following up a sample of mother-child dyads that were found to be prenatally and postnatally exposed to high levels of POPs and heavy metals. The primary objective of the NCDS was to document the growth, neurobehavioral and cardiac effects of pre- and postnatal exposure to OCs with endocrine-related disruptive properties, as well as to Hg and Pb. A secondary aim was to test whether nutritional variables (e.g. prenatal polyunsaturated fatty acid intake, breastfeeding, and childhood vitamin deficiency) mediate and/or mitigate the effects of environmental contaminants on health and development. The NCDS was made possible by the Nunavik Cord Blood Monitoring Program, through which exposure to environmental contaminants was determined from umbilical cord blood samples obtained from almost all Nunavik infants born between 1994 and 2001 (Dallaire et al. 2003; Muckle et al. 1998). Between November 1995 and March 2001, pregnant Inuit women from the three largest communities of the Hudson Bay coast were invited to participate in a first follow-up (Muckle et al. 2001), which allowed the testing of 190 infants at 6 and 12 months of age. Between 1999 and 2001, 110 preschool aged children that had not participated in the follow-up during infancy underwent neuromotor and neurophysiological testing

Table 2.9 Key details of the Nunavik Child Development study.

Study type	Prospective cohort study
Year	Birth years: 1994–2001
	Follow-up at 11 years old: 2005–2010
Sample size	294 11 year-old children
Follow-up	6 and 12 months, 5 and 11 years
Matrix	Cord blood/maternal blood/child blood/child hair
Analytes	POPs, Hg, Pb, Se, PUFAs
PCB exposure level, median (μg/kg lipid)	Cord blood PCB153: 93.6 μg/kg lipid
	Child blood PCB153: 45.9 μg/kg lipid
MeHg exposure level, median (μg/L)	Cord blood Hg: 16.6 μg/L
	Child blood Hg: 3.0 μg/L

(Després et al. 2005; Saint-Amour et al. 2006). Between 2005 and 2010, 294 eleven-year-old children were tested, whether or not they had been assessed during the infancy or preschool periods. The cohort is currently being followed-up at adolescence (2013–2016).

Mothers that had volunteered to provide cord blood samples at the birth of their child under the Cord Blood Monitoring Program were contacted by phone, provided with information about the study protocol, and invited to participate with their children in the NCDS. Inclusion criteria were children of 8.5–14.5 years in age, a birth weight of 2.5 kg or above, a gestation duration of 35 weeks or more and the absence of either birth defects, neurological or health problems, or pervasive developmental disorders. Over a five-year period (September 2005 to February 2010), 294 children and their mothers participated in neurocognitive assessments in the three largest villages in Nunavik. Participants residing in other communities were flown by plane to one of the three villages selected for testing. Children were assessed to establish physical growth, vision, intellectual function and cognitive development, behavioral development, and heart rate and blood pressure. A maternal interview was conducted to provide information on demographic background, lifestyle during pregnancy, and family environment. Cord blood samples collected at birth and child blood samples collected at the time of testing were analyzed for chlorinated pesticides, PCBs, Hg, Pb and total plasma lipids. Many potentially confounding variables and effect modifiers were assessed through blood biomarkers, medical files and maternal self-reporting.

2.2.10 Inuit Adult Cohorts: Canada

The Nunavik Health Survey Qanuippitaa was conducted between 30 August and 1 October 2004 on the scientific research vessel CCGS *Amundsen*. The research group visited the 14 communities of Nunavik (www.qanuippitaa.com) and recruited 917 participants. Samples were analyzed for POPs that had also been determined during the 1992 Santé Québec Health Survey. Plasma concentrations of new halogenated hydrocarbons such as PBDEs, PFOS, hydroxy-PCBs, methyl-sulfone PCBs and chlorophenols were also determined.

The Inuit Health Survey (2007–2009) was a comprehensive study that included the measurement of dietary intake of contaminants, contaminant body burden, as well as other determinants of health and their relationship with health outcomes of the participants. It was the first time that such a complete set of data had been collected from Inuit in Nunavut, the Inuvialuit Settlement Region, and Nunatsiavut. The study was the result of the integrated efforts of Inuit, Inuit Organizations, the Departments of Health of the Territorial and regional Inuit governments, and scientists from a variety of different disciplines. Of the 2595 individuals participating in the Inuit Health Survey, 2172 provided blood samples. The body burden of several metals (e.g. Cd, Pb) and POPs (e.g. PCBs, DDT, DDE, toxaphene, chlordane, PBDEs) were measured for Inuit participants (n=2172) from 36 communities in Nunavut, Nunatsiavut, and the Inuvialuit Settlement Region, in Canada (Smith et al. 2009; Chateau-Degat et al. 2010a,b,c, 2011a,b; Lucas et al. 2010a,b; Medehouenou et al. 2010; Ayotte et al. 2011; Valera et al. 2011a,b; Kellett et al. 2012; Labonte et al. 2012, 2014; Messier et al. 2012; Noel et al. 2012; Alkazemi et al. 2013; Laird et al. 2013a; Paunescu et al. 2013a; Rudkowska et al. 2013; Proust et al. 2014). The Greenland part of the circumpolar cohort is described in Sect. 2.2.16.

2.2.11 INUENDO

The INUENDO project: 'Biopersistent organochlorines in diet and human fertility. Epidemiological studies of time-to-pregnancy and semen quality in Inuit and European populations' was supported by the European Union Fifth Framework (FP5) program (Bonde et al. 2008). The cohort was established in 2002–2004 and involved about 1400 pregnant women from Greenland, Poland and Ukraine (Table 2.10 covers Greenlandic participants only), as well as studies on about 600 fertile couples from Sweden (fishermen and their wives).

The study included measurement of PCB153 and *p,p*'-DDE and bioeffect markers of serum legacy POP-induced estrogen- and androgen-receptor transactivity and epidemiological cross-sectional studies on male and female reproductive health on these individuals in relation to the measured exposures.

The associations between previous exposure to PCB153 and *p,p*'-DDE and fetal loss were studied in this cohort. The risk of ever experiencing a fetal loss increased at higher levels of PCB153 and *p,p*'-DDE exposure although the results were inconsistent between countries (Toft et al. 2010).

Table 2.10 Key details of the INUENDO study.

Study type	Cross-sectional
Year	2002–2004
Sample size	Men: n= 438 (average age 31; range 18–72)
	Pregnant women: n=572 (average age 27; range 18–42)
Matrix	POPs in µg/kg plasma lipid, metals in µg/L whole blood
Analytes	*p,p*'-DDE, PCB153, HCB, Hg, Pb, Cd, PFOS, PFOA
PCB exposure level, median (µg/kg lipid)	Men: 209 (5.1–5455)
	Women: 107 (2.6–2223)
MeHg exposure level, median (µg/L)	Men: 8.7 (0.2–386)
	Women: 4.8 (0.4–51.6)
DDE levels, median (µg/kg lipid)	Men: 523 (4.4–13197)
	Women: 280 (5.3–3122)

The association between fetal exposure to PCB153 and *p,p*'-DDE and birth weight and gestational age was also evaluated, indicating lower birth weight and shorter gestational age at higher POP exposure (Wojtyniak et al. 2010). These results were included in a large European meta-analysis of birth weight in relation to PCB and DDE exposure confirming the negative association between PCB exposure and birth weight (Govarts et al. 2012). However, it has been questioned whether the results could have been biased by maternal weight gain during pregnancy (Verner et al. 2013).

2.2.12 CLEAR

The CLEAR project: Climate Change, Environmental Contaminants and Reproductive health was supported by the EU's Seventh Framework Programme for Research (FP7) (Table 2.11). In addition to modelling the effects of climate change on long-range transport of contaminants, the project includes a series of cross-sectional studies on male and female reproductive health combined with a follow-up study on childhood growth and development at 6–9 years of age in a cohort of about 1400 mothers, fathers and offspring from Greenland, Poland and Ukraine. The original INUENDO cohort was established in 2002–2004 and the CLEAR follow-up on the children was undertaken in 2009–2012. In addition to PCB153 and *p,p*'-DDE, serum or full blood were analyzed for HCB, six PBDEs, one PBB, six phthalate metabolites, eight PFCs, bisphenol A, cotinine, Pb, Cd, and Hg (Lindh et al. 2012; Lenters et al. 2013). The contaminant distribution varied widely between countries with the highest level generally found in Greenland.

2.2.13 IVAAQ

The Greenland Child Cohort IVAAQ recruited 403 mothers and newborn children in West Greenland during 1999–2005 (Table 2.12). Several follow-up studies have since been carried out. The IVAAQ study has a strong focus on contaminant exposure but information about lifestyle factors such as diet, physical activity, smoking and alcohol are also part of the study.

2.2.14 ACCEPT

The aim and perspectives of the ongoing ACCEPT project – Adaptation to Climate Change, Environmental Pollution, and Dietary Transition – are to establish a geographical Greenlandic mother-child cohort (Table 2.13; Long et al. 2015). The overall aim was to obtain a cohort compatible with international and especially other circumpolar child cohorts. ACCEPT

Table 2.11 Key details of the CLEAR study.

Study type	Cross sectional/follow up
Year	2002–2004 baseline (INUENDO) and 2009–2012 follow up
Sample size	440 men and 575 pregnant women, 531 children at follow-up
Follow-up	6–9 year-old children
Matrix	Maternal and paternal serum and full blood; offspring buccal swabs
Analytes	PCB, DDE, PFAS, PBDEs, phthalates, bisphenol A, Hg, Pb, Cd
PCB exposure level, geometric mean (range) µg/kg lipid	Men: 209 (5.1–5455)
	Women: 107 (2.6–2223)
Hg exposure level, geometric mean (range) µg/L	Men: 8.7 (0.2–386)
	Women: 4.8 (0.4–51.6)
DDE levels, geometric mean (range) µg/kg lipid	Men: 523 (4.4–13197)
	Women: 280 (5.3–3122)

Table 2.12 Key details of the IVAAQ study.

Study type	Longitudinal study
Year	1999-2005
Sample size	403
Follow-up	6–10 years of age
Matrix	Maternal blood, cord blood, hair
Analytes	POPs, MeHg
PCB153 exposure level, median (µg/kg lipid)	100
MeHg exposure level, median (µg/L)	4.3
DDE exposure level, median (µg/kg/lipid)	237

Table 2.13 Key details of the ACCEPT project.

Study type	Longitudinal study
Year	2010–2015
Sample size	Total 587; 192 sampled 2010-2011, 395 sampled 2013-2015
Follow up	52 children at age 3-4 years followed by questionnaires to the mothers concerning skills and health
Matrix	Blood, hair, (n=586), some maternal milk
Analytes	POPs, PFAS, PBDEs, Hg, Se
PCB153 exposure level, median (µg/kg lipid)	57
Hg exposure level, median (µg/L)	4.23
DDE levels, median (µg/kg lipid)	130

will explore possible health outcomes of lifestyle and dietary changes during a period of rapid global change, particularly climate change. Being a part the FETOTOX (http://fetotox.au.dk) international network of mother-child cohort studies (Norway - the MISA study, Denmark, and Shanghai, China) carried out with similar protocols, ACCEPT will compare contaminant related health effects between populations in several countries with regard to differences in exposure patterns, genetics, and lifestyle factors.

The ACCEPT study has established a prospective mother-child cohort designed to determine exposure to environmental contaminants during pregnancy and the development of the fetus and child as well as health effects later in life in the Greenlandic population. ACCEPT is being undertaken in cooperation with the Greenlandic health care system and the Institute of Nurse and Health Sciences at the University of Greenland, Nuuk. ACCEPT represents a formal and ongoing information service on environmental health issues for local communities in Greenland (health professionals as well as the general population). The ACCEPT study protocol includes the enrollment of women in early pregnancy (before the end of gestation week 13). A questionnaire on lifestyle and food frequency is administered by midwives, and women donate biological samples for a biobank, as well as blood samples for determining contaminant levels and several effect biomarkers in the first trimester and cord blood, and some breast milk before day 6 postpartum. Data on the newborn child are obtained from a perinatal journal maintained by the visiting nurse. The children will be followed up on skills at year 3–4 by telephone interview. The ACCEPT database is considered suitable for exploring associations between POP exposure and diet, providing information on contaminant pharmacokinetics (including maternal transfer to the infant before and after birth), and for prospective child health studies. Recruitment occurred between August 2010 and August 2011 and 192 pregnant women were enrolled. Unforeseen problems prevented recruitment between summer 2011 and summer 2013. Another 395 pregnant women were enrolled during the last six months of 2013, 2014 and 2015 increasing the cohort to include 587 mother-child pairs.

In total 587 pregnant women are enrolled in the ACCEPT cohort: North (Qaanaaq, Upernavik, Uummannaq) 13; Disko Bay (Ilulissat, Aasiaat, Qeqertarsuaq, Qasigiannguit) 88; West (Sisimiut, Maniitsoq, Nuuk, Paamiut) 455; South (Qaqortoq, Nanortalik, Narsaq) 10; East (Tasiilaq, Ittoqqortoormiit) 21. The first data from the 192 pregnant women sampled in 2010–2011 on maternal serum POP levels have been published (Long et al. 2015). A trend of higher intake of marine mammals in the eastern and northern regions was reflected by a higher *n-3:n-6* fatty acid ratio. Participants in the eastern region also tended to have a higher intake of terrestrial species. A higher percentage intake of seabird species was seen for pregnant women in the western region. Compared to earlier reports, decreased levels of legacy POPs, Hg and Pb and perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) were observed, but the levels of PFAS congeners perfluorohexane sulfonate and perfluorononanoic acid remained similar to those reported previously.

A sub-study on lifestyle, reproductive factors and food intake for the same pregnant women sampled in 2010–2011 showed

a relatively higher BMI and high smoking frequency; age and regional differences were found for alcohol consumption, breastfeeding plans and food intake profile (Knudsen et al. 2015).

2.2.15 Follow-up of children from the IVAAQ and CLEAR cohorts in Greenland

In 2010, 223 children from the IVAAQ cohort (see Sect. 2.2.13) were followed up for the presence of otitis media by otoscopy, tympanometry and review of hospital records. The hypothesis of a positive association between maternal POP concentrations in pregnancy and increased prevalence of chronic otitis media in children aged 4 to 10 years was not confirmed in this study (Jensen et al. 2013). Thus, these results contrast with the results obtained for otitis media in the study by Dewailly and Dallaire.

In 2012, 311 children from the IVAAQ (n=198) and CLEAR (n=113) cohorts (Sects. 2.2.11 and 2.2.12) were followed up to assess the growth pattern and health (assessed by contact with the health care system) among children aged 6–10 years. Children aged 0–18 months had higher weight and height than the reference populations. The study concluded that growth among Greenlandic children older than 18 months corresponded with growth reference curves from Sweden but did not match those from Japan or WHO data (www.who.int/childgrowth/en). On average, the Greenlandic children had 40 contacts with the health care system during a period of 6 to 10 years. They were hospitalized more often than Danish children, but had fewer contacts with the primary sector (Sørensen 2013).

A total of 409 children now aged 7–9 years were invited to a follow-up in 2013–2014 to test the hypothesis that exposure to POPs may negatively affect the immune response to vaccines (diphtheria, tetanus).

2.2.16 The Greenland Population Health Studies

Cross-sectional countrywide studies of the adult indigenous population in Greenland have been undertaken three times since the early 1990s: 1993–1994, 1999–2001 and 2005–2010 (Table 2.14). The data were obtained by questionnaire and for most participants also by clinical examination and sampling of biological media. The main themes of the studies were general health and living conditions, mental health, substance abuse including smoking, diet, physical activity, diabetes and cardiovascular disease. All studies included dietary information and some data on contaminants (Table 2.15).

In 2014, all 6008 participants were followed up in disease registers (mortality registry, cancer registry and registry of hospital discharges) and 2102 participants was re-examined. In a subsample of these participants (n=547), blood samples were drawn and analyzed for Hg and selected POPs. The numbers in Tables 2.14 and 2.15 relate to only those participants in the previous surveys for which blood samples are available.

A food frequency questionnaire with portion sizes was used to create dietary pattern groups (Bjerregaard and Jeppesen 2010). The questionnaire was validated against blood Hg and it was shown that frequency of meals of marine mammals showed similar associations with blood Hg as did calculated intake in grams (Jeppesen et al. 2012). The dietary pattern 'Traditional food' was positively associated with Type 2 diabetes (Jeppesen et al. 2013). Results from the three population health surveys demonstrated a decreasing trend for PCBs and pesticide levels in blood (Bjerregaard et al. 2013). Neither Hg nor POPs showed any association with blood pressure in Greenlandic Inuit (Nielsen et al. 2012; Valera et al. 2013c).

Table 2.14 Key details of the Greenland Population Health studies.

Study type	Cross sectional and longitudinal studies
Year	1993–2010
Sample size	4398
Follow-up	25+
Matrix	Blood
Analytes	POPs, MeHg
PCB153 exposure level, median (μg/kg lipid)	724 (1993–1994), 770 (1999–2001), 620 (2005–2010)
MeHg exposure level, median (μg/L)	31.8 (1993–1994), 16.4 (2005–2010)
DDE levels, median (μg/kg lipid)	1633 (1993–1994), 1500 (1999–2001), 1300 (2005–2010)

Table 2.15 Three population health surveys in Greenland.

Year	n	n with blood samples	Contaminants included in survey (n)	Geographical coverage of contaminant data
1993–1994	1728	264	14 PCB congeners and 11 pesticides (225) and mercury (211)	West Greenland
1999–2001	2001	1314	14 PCB congeners and 11 pesticides (692)	West Greenland
2005–2010	2958	2820	14 PCB congeners and 11 pesticides (1725) and mercury (2814)	Nationwide

2.2.17 Birth Cohort 1 in the Faroe Islands

A cohort of 1022 singleton births was assembled in the Faroe Islands during a 21-month period in 1986 and 1987 (Grandjean et al. 1992) (Table 2.16). Frequent whale meat dinners during pregnancy, frequent consumption of fish (to a much lesser degree) and increased parity or age are associated with high Hg concentrations in cord blood and maternal hair. Mercury concentrations in cord blood correlated moderately with blood-selenium. Lead concentrations in cord blood were low (median, 82 nmol/L). Because the effects of fetal childhood exposure to MeHg are persistent, detailed examination of children with prenatal exposure to this neurotoxicant were performed at age 7 years (1993–1994). A total of 917 of the children (90.3%) completed the examinations. Past medical history, current health status and social factors were recorded on a self-administered form. The physical examination included a functional neurological examination with emphasis on motor coordination and perceptual-motor performance. The main emphasis was placed on detailed neurophysiological and neuropsychological tests that had been selected on the basis of a range of considerations (Grandjean et al. 1997, 2012d). A follow-up examination was performed using the same test methods when the cohort members were 14 and 22 years of age. Cohort 1 is currently undergoing a follow-up at the age of 27 years, with special emphasis on how glucose metabolism and immune response are associated with environmental contaminants. The neurobehavioral effects found in Cohort 1 at age 7, 14 and 22 years are described in Chapter 4.

2.2.18 Birth Cohort 2 in the Faroe Islands

The findings from Birth Cohort 1 (see Sect. 2.2.17) suggested that exposure assessment should encompass several lipophilic pollutants in addition to MeHg. As a follow-up, Cohort 2 was therefore established during a 12-month period in 1994–1995 and included 182 singleton term births from consecutive births at the National Hospital in Tórshavn, Faroe Islands (Table 2.17). Relevant obstetric data were obtained by standardized procedures and supplemented by a brief nutrition questionnaire. The geometric mean (GM) for MeHg was 20.96 μg/L in cord blood and 4.13 μg/g in maternal hair. The maximum maternal hair-Hg concentration was 16.31 μg/g. The GM for maternal serum PCB was 1126 μg/kg lipid with a maximum of 18,446 μg/kg lipid. The children were first examined by the Neurological Optimality Score (NOS) at age two weeks (adjusted for gestational age). Subsequent examinations occurred at age 18 months and then at 12-month intervals to age 66 months. At 42 months, a comprehensive medical examination with the NOS was included (Steuerwald et al. 2000). For comparison with Cohort 1, detailed neurobehavioral tests were carried out at age 7 years. A repeat examination was undertaken at age 10 years. The complete profile of neurobehavioral development has been analyzed and the study suggests that prenatal MeHg exposure may have an adverse effect on Visual Evoked Potential (VEP) findings despite the absence of clinical toxicity to the visual system. However, this association was apparent only after adjustment for *n*-3 PUFA status (Yorifuji et al. 2013). This cohort also participated in a study of serum antibody concentrations as a measure of the effects of routine childhood immunizations, showing that increased perinatal exposure to PCBs may adversely impact on immune responses to childhood

Table 2.16 Key details of Birth Cohort 1 in the Faroe Islands.

Study type	Longitudinal study
Year	1986–1987
Sample size	1022
Follow-up	7, 14, 22 and 28 years
Matrix	Cord blood and tissue, child blood, hair, semen (n=240)
Analytes	POPs, MeHg, Se, PFC
Cord blood PCB exposure level, geometric mean (μg/kg lipid)	604 (17–5606)
MeHg exposure level in cord blood, geometric mean (μg/L)	22.3 (0.9–351)
DDE level, geometric mean (μg/kg lipid)	270 (4.2–4487)

Table 2.17 Key details of Birth Cohort 2 in the Faroe Islands.

Study type	Longitudinal study
Year	1994–1995
Sample size	182
Follow-up	2 weeks, 7, 18, 30, 42, 60, 66, 90, 120 months
Matrix	Maternal blood and milk, cord blood, child blood, hair
Analytes	POPs, MeHg, Se
Maternal PCB exposure level, geometric mean (μg/kg lipid)	1126 (440–18,446)
MeHg exposure level in cord blood, geometric mean (μg/L)	21.0 (1.9–102)
Maternal DDE levels, geometric mean (μg/kg lipid)	725 (201–8038)

vaccinations (Heilmann et al. 2006). The clinical implications of insufficient antibody production emphasize the need for prevention of immunotoxicant exposures.

2.2.19 Birth Cohort 3 in the Faroe Islands

New insight into health risks caused by environmental pollutants and changing exposure patterns in the Faroes led to the formation of Cohort 3 from 656 consecutive births in Tórshavn between November 1997 and March 2000 (Table 2.18). Following dietary recommendations from the Faroese health authorities, MeHg exposure had now decreased thus allowing better characterization of possible effects of PCBs and other persistent contaminants. Additional attention was turned to the perfluorinated compounds (PFCs), as they have been documented as contaminants of marine food chains with possible toxicity to the immune system. Cohort 3 is similar to the two previously generated cohorts in that serum was collected from the mother at the last antenatal examination (34th week of pregnancy). Other samples collected from the mother-child pairs include cord blood and serum, maternal hair at parturition, and milk on days 3–5 (before mother and child were discharged) and at two weeks. Nutritional habits were recorded by questionnaire. A subgroup of cohort children was examined with regard to immunological parameters at ages 11 and 18 months. The first comprehensive medical examination was carried out just before the booster vaccination at age 5 years, with a follow-up blood sample one month after vaccination. The children were examined again at age 7 years, with a main focus on immunological parameters such as formation of antibodies and allergic response (Heilmann et al. 2010). The conclusion of this study was that developmental PCB exposure is associated with immunotoxic effects on serum concentrations of specific antibodies against diphtheria and tetanus vaccinations. The immune system development during the first years of life appears to be particularly vulnerable to this exposure. Elevated exposures to PFCs were associated with reduced humoral immune response to routine childhood immunizations in children aged 5 and 7 years. (Grandjean et al. 2012a). A follow-up study at 13 years was undertaken with 533 (86.7%) participating (255 females and 278 males). This follow-up study aimed (i) to describe the most vulnerable age to effects of immunotoxicant exposure on antibody responses to vaccines and further to detect whether these effects continue into adolescence; (ii) to investigate whether early postnatal or cumulative exposure to immunotoxicants affect the occurrence during childhood of allergic diseases and raised serum IgE concentrations; (iii) to determine whether blood lymphocyte populations and cytokine production elicited by a toxoid challenge are affected by immunotoxicant exposures; and (iv) to describe which environmental immunotoxicants are responsible for these effects, and at which exposure levels. The follow-up study also encompassed a thorough clinical examination. The main focus was on development of allergic disease, using International Study of Asthma and Allergies in Childhood (ISAAC) criteria. A questionnaire similar to previous examinations was used and included the child's current health, diet and past medical history with emphasis on infectious and allergic disease, as well as family history for asthma, chronic bronchitis, atopic dermatitis, allergic eczema and rhinitis/pollinosis. Blood samples were obtained for measurements of antibodies and exposure biomarkers. Skin prick tests were also used to detect allergic reactions.

2.2.20 Birth Cohort 5 in the Faroe Islands

The most recent of the Faroe Islands' cohort studies began during an 18-month period between October 2007 and April 2009 (Table 2.19). The total number of mother-child pairs was 501 (70% of the eligible population). Blood was taken from the cord, and blood, hair, and milk were obtained from the mother. The analytical results show Hg exposure to have declined substantially, with the GM being 4.8 μg/L cord blood and 0.71 μg/g hair. The maximum maternal hair-Hg concentration was 6.3 μg/g. Organochlorine exposure has also begun to decline. The GM for serum-PCB was 420 μg/kg lipid, with a maximum of 2965 μg/kg. In connection with the birth cohort formation, detailed data were obtained about time-to-pregnancy and obstetric parameters. In addition, 281 fathers participated in an examination of sperm quality along with a blood sample for OC analysis. Both grandmothers were invited to complete a dietary questionnaire and provide blood for OC analyses – as a possible reflection of prenatal exposure of the birth cohort parents. A total of 343 maternal and 206 paternal grandmothers participated. The children were examined at age 18 months. Follow-up includes a questionnaire at 42 months and a clinical examination at 5 years of age, with emphasis on immunological parameters.

Table 2.18 Key details of Birth Cohort 3 in the Faroe Islands.

Study type	Longitudinal study
Year	1997–2000
Sample size	656
Follow-up	1.5, 5, 7.5, 13 years
Matrix	Maternal blood and milk, cord blood, child blood, hair
Analytes	POPs, MeHg, PFC
Maternal PCB exposure level, geometric mean (μg/kg lipid)	1214 (181–15150)
MeHg exposure level in cord blood, geometric mean (μg/L)	12.4 (1.6–193)
Maternal DDE levels, geometric mean (μg/kg lipid)	538 (43.1–11,414)

Table 2.19 Key details of Birth Cohort 5 in the Faroe Islands.

Study type	Longitudinal study
Year	2007–2009
Sample size	501
Follow-up	18, 42 and 60 months
Matrix	Maternal blood and milk, cord blood and tissue, child blood, hair
Analytes	POPs, MeHg, PFC
Maternal PCB exposure level, geometric mean (µg/kg lipid)	420 (16.0–2965)
MeHg exposure level in cord blood, geometric mean (µg/L)	4.6 (0.8–44.5)
Maternal DDE levels, geometric mean (µg/kg lipid)	131 (6.0–1517)

2.2.21 The septuagenarian cohort of the Faroe Islands

To complement the birth cohort studies, studies are also being undertaken to examine the health status of elderly Faroese residents regarding their lifetime exposure to marine pollutants (Table 2.20). A cohort of 1131 Faroese residents aged 70–74 years was formed and 713 were examined (64% of the eligible population). All subjects underwent a thorough physical examination, with a focus on neurobehavioral and cardiovascular function, as well as body weight, diabetes, and general health. Birth weights were obtained from midwife charts at the Faroese National Archives. Cumulative exposure to major marine pollutants was determined from blood sample analysis. Dietary habit concerning the consumption of traditional food during childhood and adolescence, adulthood, and the most recent year was recorded (Grandjean et al. 2011). Information concerning current health and past medical history, including medication, risk factors such as smoking and alcohol use, and body weight at age 20 years was also recorded (Dalgard et al. 2011).

Serum 25-hydroxyvitamin D3 (S-25(OH)D3) was measured in 669 of the 713 subjects for whom sufficient serum was available: 19% had S-25(OH)D3 concentrations <25 nmol/L and only 10.3% had S-25(OH)D3 concentrations >80 nmol/L. In a logistic regression analysis, BMI <30 kg/m^2, blood sampling in summer season, eating pilot whale blubber more than once per month and female sex were positively associated with vitamin D levels of >80 nmol/L. The high prevalence of low vitamin D levels among the elderly Faroese population reflects the low skin synthesis during most months of the year, which is caused by the limited sun exposure and insufficient benefits from marine diet (Dalgard et al. 2010).

Septuagenarians with Type 2 diabetes or impaired fasting glycemia tended to have higher PCB concentrations and higher past intake of traditional foods, especially during childhood and adolescence. In non-diabetic subjects, the fasting insulin concentration decreased by 7% (95% CI = -12% to -2%) for each doubling of the PCB concentration after adjustment for sex and BMI at age 20. Conversely, the fasting glucose concentration increased by 6% (-1% to 13%) for each doubling in PCB. Similar associations were seen in subjects without impaired fasting glycemia, while further adjustment for current BMI and lipid metabolism parameters attenuated some of the associations. According to this study impaired insulin secretion appears to constitute an important part of the Type 2 diabetes pathogenesis associated with exposure to persistent lipophilic food contaminants (Grandjean et al. 2011).

2.2.22 Type 2 Diabetes in middle-aged Faroese residents

In total 3324 people were included in the Faroese Diabetes project (Table 2.21). The individuals were derived from three different groups: 460 subjects with diabetes or prediabetes found in a cross-sectional population-based study (MARK) conducted in 2007–2008; 577 individuals from the septuagenarians cohort (see Sect. 2.2.21) with increased or marginally elevated HbA1c or blood glucose levels; and a new group of 2187 randomly selected individuals aged between 40 and 70 years.

About 26% of the study population had some carbohydrate disturbance. The overall prevalence of T2DM in the study population was 13.1% (95% CI = 11.7–14.5%). Of these, about a quarter had unknown diabetes: 3.4% (2.7 to 4.1%). The

Table 2.20 Key details of the septuagenarian cohort of the Faroe Islands.

Study type	Cross sectional
Year	2008–2009
Sample size	713
Follow-up	2011–13 (partly)
Matrix	Blood, hair and nails
Analytes	POPs, MeHg, PFC
ΣPCB exposure level, geometric mean (µg/kg lipid)	8076 (685–70049)
Blood Hg, mean (µg/L)	4.6 (0.8–44.5)
DDE levels, geometric mean (µg/kg lipid)	2929 (7.0–47604)

Table 2.21 Key details of the Type 2 Diabetes study for middle-aged Faroese residents.

Study type	Cross sectional
Year	2011–2013
Sample size	3324
Matrix	Blood, hair
Analytes	POPs, MeHg, PFC
ΣPCB exposure level, mean (μg/kg lipid)	Not yet analyzed
Blood Hg, mean (μg/L)	Not yet analyzed
DDE levels, mean (μg/kg lipid)	Not yet analyzed

prevalence of isolated IFG, isolated IGT and combined IFG-IGT were 4.8% (3.9–5.7%), 4.5% (3.7–5.4%) and 3.5% (2.8–4.3%) respectively. The prevalence of diabetes and other disorders increased significantly with age (p <0.05) and was higher in men than in women (p <0.0001). Age and sex specific prevalence of T2DM were 2.1% (6/284), 6.0% (16/266), 8.9% (20/225) and 18.8% (60/319) for women aged 40–49, 50–59, 60–69 and 70+; and 3.8% (12/313), 9.5% (27/283), 24.2% (64/264) and 28.3% (96/339), respectively, for men (Andreassen 2014).

2.3 Conclusions and recommendations

An increasing number of exposure studies have been performed in the circumpolar Arctic over the past three decades. Exposure in this context means exposure to contaminants in the Arctic environment. The main source of contaminant exposure is the consumption of traditional foods of marine origin, such as whales, seals, polar bears and some fish species. AMAP has generated a vast amount of data on contaminant levels in human tissues, especially in hair and blood, and in some studies even human milk. Exposure levels vary in different regions of the Arctic, which can be largely explained by variation in contaminant levels in the traditional diet.

Several studies have been designed as birth cohorts, giving the opportunity for later examination of health effects associated with prenatal or early postnatal exposure. However, conducting human health effects studies in the Arctic can be a challenging for several reasons, including issues associated with logistics, the wide range of languages and cultures, and a lack of qualified staff when estimating the function of the central nervous system.

To maximize the returns from such studies requires a harmonized study design and harmonized reporting of results. This will make it possible to merge studies and perform strong meta-analysis. AMAP guidance on the design of cohort and dietary studies for assessing the effects of environmental contaminants on population health in the Arctic as well as a protocol for the full reporting of results, including statistical methodology, would be very useful. This will enhance the ability to compare and combine the outcome of such studies from different circumpolar regions and should thus result in a more statistically valid assessment of effects.

3. Levels and trends of contaminants in humans

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3.1 Introduction

This chapter reports on biomonitoring data developed in the eight Arctic countries since the previous AMAP human health assessment (AMAP 2009). The focus is on blood concentrations of several persistent organic pollutants (POPs), organochlorine pesticides (OCs) and metals, updates on concentrations of contaminants first reported in the previous assessment report, and data for some of the newest contaminants reported in the Arctic. Contaminant concentrations are also reported for other human tissues and fluids, such as hair, breast milk and urine.

Exposure to environmental contaminants through the traditional diet remains one of the risks to human health in the Arctic. Due to unique geographic and climatic characteristics, the Arctic has become a repository for contaminants transported long distances through the atmosphere and via ocean currents. Often persistent, these chemicals then bioaccumulate and biomagnify through Arctic food chains into the species that make up traditional (country) food sources for many Arctic peoples. The traditional diet of these Arctic populations tends to rely on foraged plant matter, fish, and terrestrial and marine mammals for sustenance, because store-bought foods (sometimes also termed market foods or commercial foods) are difficult to access or are not as nutrient-rich as traditional foods (Donaldson et al. 2010a). Many of the marine mammals, some of which are top predators in the Arctic marine food web, and some fish species can be highly contaminated with persistent, bioaccumulative chemicals. General trends of POPs in biota are not included in this chapter; however they have been reported on in other AMAP reports, including a recent report prepared for the Stockholm Convention's Second Global Monitoring Plan (AMAP 2014). Biomonitoring studies investigating the changing levels of contaminants in human populations are an essential part of the management of these risks, including the ability to analyze the risks and benefits for human populations that consume traditional food.

3.2 Synthesis

3.2.1 AMAP 1998

The first AMAP human health assessment (AMAP 1998) marked the first international, circumpolar report from the Arctic Monitoring and Assessment Programme (AMAP). Seven of the eight circumpolar countries (Canada, Denmark/Greenland/Faroe Islands, Iceland, Finland, Sweden, Norway, and Russia) contributed data to this report. Several polychlorinated biphenyls (PCBs), OCs, and metals were reported in different Arctic populations, both indigenous and non-indigenous populations.

The preliminary data identified in the 1998 assessment suggest that levels of POPs and methylmercury (MeHg) in breast milk and cord blood were two- to ten-fold higher than levels found south of the Arctic region. Despite worldwide risk management put in place for several POPs during the 1970s and 1980s, there seemed to be no evidence that levels in Arctic populations had decreased. Persistence, ubiquity and continued use in different parts of the globe contributed to continuous exposure levels for Arctic populations. This report presented the first amalgamation of human biomonitoring data for Arctic populations. While the 1998 assessment could not indicate temporal trends, it did provide the first Arctic-wide perspective.

Levels of hexachlorobenzene (HCB), Mirex and three chlordane metabolites were markedly higher in Greenland and eastern Canadian Inuit maternal blood samples than in corresponding samples from the other participating countries. PCBs were highest in maternal blood samples from Greenland. Organochlorines such as β-hexachlorocyclohexane (β-HCH) and *p,p'*-dichlorodiphenyltrichloroethane (*p,p'*-DDT) were found to be higher in Russian populations than in populations examined from other countries, indicating potential uses in Russia or that these pesticides were being used on the food products consumed by these Arctic populations. Levels of *p,p'*-dichlorodiphenyldichloroethylene (*p,p'*-DDE) in Greenland and Russian populations were three to five times higher than those in other Arctic countries.

Greenland and Canada emerged as hotspots for metals, particularly mercury (Hg), lead (Pb) and cadmium (Cd). This exposure to Hg and Pb was attributed to specific traditional food consumption in these two populations in comparison with the food species consumed by populations in other parts of the Arctic; and smoking behavior was linked with levels of Cd.

Exposure levels found in the Arctic in the 1998 assessment were identified as unacceptable. While temporal trends for Hg and Cd could not be determined from the data sets available, it was evident that Pb levels were decreasing in the Arctic in a similar way as levels in the south, probably in response to the risk management action taken on Pb emissions, and the partial ban on lead shot.

3.2.2 AMAP 2002

The second AMAP human health assessment (AMAP 2003) provided the first opportunity to compare contaminant levels over time, especially in the Canadian and Greenlandic data sets for the maternal blood contaminant study. Data were submitted by all eight circumpolar countries. Fewer contaminants were reported in the 2002 assessment, but core contaminants of concern were consistently tested and reported in the Arctic countries, allowing for geographical comparison.

Levels of contaminants in blood samples from the populations living in the Arctic region again showed that certain POPs and Hg were high in Arctic people that consumed certain traditional foods. Greenland Inuit mothers, in particular, were found to have levels of PCBs, HCB, total chlordanes and Hg higher than any other Arctic population. Russian non-indigenous populations had the highest levels of DDT and β-HCH; and elevated levels were also observed in Iceland and in the non-Caucasian, non-Dene/Métis, non-Inuit 'Others' group for the Canadian Arctic.

3.2.3 AMAP 2009

The third AMAP human health assessment report (AMAP 2009) contained the first comparison of all Arctic regions in Russia as a part of the overall assessment. It provided some of the first trend data for particular OCs and metals. Data from Canada, Greenland, Iceland, Sweden, Finland and Russia showed that levels of contaminants such as PCBs, oxychlordane, and Hg were decreasing in a broad range of Arctic populations. It was apparent that the consumption of marine mammals as a part of a healthy traditional diet seemed to result in elevated contaminant levels in Inuit regions of Greenland and Canada.

A new set of contaminants were measured in the Arctic for the 2009 assessment. It was possible to report the levels of brominated flame retardants (BFRs) and perfluorinated compounds (PFCs) due to advances in detection techniques and methodologies. Levels of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) were found throughout the Arctic and were elevated compared to other POPs. Polybrominated diphenyl ethers (PBDEs) were found at low levels across the Arctic, with the exception of high levels found in Alaska. Tetrabromobisphenol A (TBBPA) and hexabromocyclodecane (HBCD) had limited data but showed low blood levels. Concentrations of PFOS were significantly higher in consumers of fish and marine mammal meat in Nunavik, Canada. PBDEs were found to require more data before a source or trend could be identified. In general, more monitoring data were needed for the emerging contaminants, as some were very data-limited but anticipated to be of potential concern in the future.

3.2.4 AMAP 2015

Since the 2009 assessment, biomonitoring activities have continued in the eight Arctic countries. POPs and metals are still undergoing long-range transport to the Arctic and are bioaccumulating and bioconcentrating within the Arctic food chains relied on for a socially, economically, culturally and nutritionally beneficial traditional food supply. However, declines are beginning to be detected in certain Arctic populations, and public health interventions have been instituted based on some of the biomonitoring results presented. Different contaminants are also being detected in the Arctic, indicating that new international risk management may be necessary. The use and production of PFCs started in the 1950s, increased during the 1970s, and continues today with PFCs still in demand in industrial and consumer applications (Nøst et al. 2014). Although PFCs do not bioaccumulate in fatty tissues, they are exhibiting similar patterns of concentration in Arctic populations as for most other POPs, however the patterns for BFRs are slightly different. Further monitoring of BFRs is being pursued to identify their potential threat to Arctic populations.

3.3 Methodology for AMAP 2015

Since the first meeting of the AMAP Expert Group on Human Health in 1991, considerable efforts have been made to ensure the measurement of high quality human biomonitoring data for POPs and metals of concern to AMAP. The AMAP Human Health Assessment Group recommended in 2000 that a quality assessment (QA) program be established for POPs in human biological fluids (the AMAP Ring Test). The 2009 assessment report (AMAP 2009) described in detail the implementation and evolution of this external quality assessment scheme (EQAS), which has provided a means of comparing the quality of data produced by laboratories involved in the measurement of POPs in samples of human origin from Arctic countries (Weber 2002).

Since its inception in 2001, the scope of the AMAP Ring Test has been revised to add or remove different POPs, with a substantial revision occurring in 2007 to add more POPs and to modify the scoring system. The scheme now considers 37 analytes (11 pesticides, eight PBDEs, nine PCBs, six PFCs, total lipids, cholesterol and triglycerides). Described earlier (see AMAP 2009), several international EQAS already exist for metals in biological fluids, as well as a number of national schemes. Participation in the AMAP Ring Test by both AMAP and non-AMAP countries has fluctuated over the years – from 25 to 29 participating laboratories during the period 2002 to 2008. Currently, 32 laboratories are registered participants (Table 3.1).

It is important for AMAP to present spatial and temporal trends of exposure with confidence and to demonstrate that the trends are not influenced unduly by analytical uncertainty. The AMAP Ring Test has thus established criteria for good (within 20% of target) and acceptable (within 40% of target) EQAS performance. Although fluctuations in individual performance are expected, the proportion of laboratories showing excellent or good performance generally increased between 2001 and 2007, often with pronounced improvements for some analytes (AMAP 2009). Ongoing participation in the AMAP Ring Test (or another suitable intercomparison program) is therefore highly encouraged, as this seems to have provided impetus for participating laboratories to examine and refine analytical procedures and organizational protocols necessary for meeting performance targets. All laboratories submitting data to this assessment were active participants in a QA/QC program.

The data for POPs, OCs and PBDEs in this chapter are expressed on a lipid weight basis (μg/kg plasma lipid) because these analytes accumulate in lipids, and lipid levels in plasma increase throughout pregnancy and vary in response to meals. The data for PFCs are expressed on a wet weight basis (μg/L plasma or serum) as they do not accumulate in lipids. The data for metals are expressed on a whole blood basis (μg/L whole blood). Data are provided for mothers and children, women of childbearing age (WCBA), and women and men of all ages. The geographical areas represented in this update are found in Chap. 1 (Fig. 1.1).

Table 3.1 Overview of QA/QC participation by laboratories supplying data to the 2015 AMAP Human Health assessment.

Country	POPs		Metals	
	Laboratory	QA/QC scheme	Laboratory	QA/QC scheme
USA	CDC	AMAP	CDC	QA/QC programs from independent sources as required by CLIA
Canada	CTQ	AMAP	CTQ	QMEQAS
Greenland	CTQ University of Aarhus, Department of Bioscience, Roskilde (PFCs)	AMAP (including PFCs)	University of Aarhus, Department of Bioscience, Roskilde	None for metals in serum, but QUASIMEME for metals in the marine environment and Seronorm™ controls
Iceland	DPTUI NILU (PFCs)	AMAP	na	
Faroe Islands	University of Southern Denmark	EQUAS	University of Southern Denmark	EQUAS and QMEQAS
Norway	NILU	AMAP	Jožef Stefan Institute, Department of Environmental Sciences, Slovenia	PHIME and PHAPAS
Sweden	National Food Agency, Department of Science, Sweden	None for POPs in serum, but several for other matrices including human milk (EU-RL PT)	Occupational and Environmental Medicine, Lund University, Sweden	QMEQAS, EQUAS and NEQAS
Finland	National Institute for Health and Welfare, Finland	AMAP	Jožef Stefan Institute, Department of Environmental Sciences, Slovenia	PHIME and PHAPAS
Russia	Typhoon, NW branch, Russia	AMAP	Typhoon, NW branch, Russia	STAMI

Laboratories: CDC: Center for Disease Control, Atlanta, GA, USA; CTQ: The Centre de toxicologie du Québec, Montreal, Canada; DPTUI: Department of Pharmacology and Toxicology, University of Iceland, Reykjavik, Iceland; NILU: Norwegian Institute for Air Research, Tromsø, Norway. QA/QC scheme: AMAP: Ring test for POPs in human serum from CTQ; EQUAS: The German external quality assessment scheme for analyses in biological materials; CLIA: Clinical Laboratory Improvement Amendments; QMEQAS: Multi-element external quality scheme in human material, including serum and urine from CTQ, Canada; QUASIMEME: Quality Assurance of Information for Marine Environmental Monitoring in Europe Laboratory Performance Studies; PHIME: An EU project 2006-2011 with six intercomparison exercises on metals in blood; PHAPAS: Proficiency testing for elements in milk samples organised by FERA: Food and Environment Research Agency, UK; NEQAS: United Kingdom National External Quality Assessment Schemes for clinical chemistry; STAMI: QA/QC program offered by the National Institute of Occupational Health, Norway.

This chapter focuses on spatial or temporal trends for several POPs which are expected to be found in higher concentrations in some Arctic populations. The observation of trends is also undertaken for metals such as Hg and Pb, for which individuals have often exceeded tolerable daily intakes. Data have also been provided for new contaminants discussed in the previous assessment report (AMAP 2009).

The studies described in this chapter often provide an update for contaminants and populations examined in previous assessments. In some cases, differences that are statistically significant are identified within single studies or cohorts. However, due to the nature of human biomonitoring data and privacy concerns, the individual raw data sets were not usually available from the different studies and limited statistical analyses have thus been attempted. The data are usually presented as geometric means for populations, and the minimum and maximum concentrations in the range of values measured are often also presented. Where geometric means are not available for the data, this is clearly indicated.

With these additional data, this chapter discusses how contaminant levels are changing with time, and provides an indication of differences between populations, geographical areas, and traditional practices. In doing so, insight is obtained about how international risk management efforts, dietary shifts, and risk communication interventions from public health officers and other officials may be affecting Arctic residents' exposure. For several Arctic countries, there are now almost 20 years of biomonitoring data available to assess changes in contaminant concentrations.

3.4 National reports

3.4.1 Alaska

The Alaskan Native Maternal Organics Monitoring (AN MOM) program began in 1998. The Yukon-Kuskokwim Delta regions specifically requested to participate in this study. Data representing the continuing biomonitoring of Yup'ik mothers were generated by the AN MOM project from 1999 to 2012. Prospective repeat sampling of the same population resulted in recruitment of a cohort of 160 participants for the most recent sampling period (2009–2012), from the Yukon and Kuskokwim River Delta in southwestern Alaska.

3.4.1.1 Persistent organic pollutants

Concentrations of POPs are lower in maternal samples from the 2009–2012 sampling period than in previous periods (Table 3.2). Oxychlordane, *p,p*'-DDT, *p,p*'-DDE, Mirex and PCB138 declined steadily between 1999–2003 and 2009–2012. In fact, more than 50% of samples for *p,p*'-DDT and Mirex were below the limit of detection. The pattern for *trans*-nonachlor, HCB, β-HCH and

Table 3.2 Concentrations of POPs in Yup'ik maternal and infant blood from Alaska. Data presented as geometric means (range), calculated for the specified period of sampling, in µg/kg plasma lipid. Source: 1999–2003 data and 2004–2006 data (AMAP 2009); 2004–2006 PFCs data (Kostick and Berner pers. comm. 2013); 2009–2012 data (Berner pers. comm. 2014).

	1999–2003	2004–2006	2009–2012	2009–2012
Mean age	26	26.4	26.5	Infant
Sample size	n=106	n=206	n=156	n=77
Oxychlordane	29	12 (1.5–234)	7.3 (<LOD–72.5)	7.7 (<LOD–58.8)[a]
trans-Nonachlor	5.3	21 (1.8–310)	9.9 (<LOD–107)	8.8 (<LOD–87.4)
p,p'-DDT	6.4	3.4 (1.2–23)	2.5 (<LOD–12.6)[a]	–[b]
p,p'-DDE	135	124 (3.1–777)	82.7 (13.8–373)	80.7 (15.4–280)
HCB	14	22 (2.4–188)	15.9 (2.7–98.8)	19.6 (<LOD–105)
β-HCH	6.7	7.7 (1.1–138)	3.6 (<LOD–36.8)	–[b]
Mirex	24	3.3 (1.1–36)	2.3 (<LOD–12.7)[a]	–[b]
PCB99	na	na	3.0 (<LOD–28.6)	2.8 (<LOD–21.4)
PCB118	na	5.6 (0.4–78)	3.4 (<LOD–27.5)	3.5 (<LOD–29.3)
PCB138	35	14 (0.2–221)	9.1 (1.0–77.8)	8.3 (<LOD–56.3)
PCB153	17	24 (0.8–416)	14.8 (1.5–148)	12.5 (2.0–90.1)
PCB180	na	10 (0.4–192)	5.4 (<LOD–56.8)	4.2 (<LOD–30.1)
PBDE47	na	26 (1.2–455)	19.8 (2.4–395)	16.1 (<LOD–265)
PBDE99	na	6.3 (0.2–1359)	4.5 (<LOD–186)	2.5 (<LOD–36.3)
PBDE100	na	5.3 (0.1–87)	4.6 (0.7–60.5)	3.0 (<LOD–46.6)
PBDE153	na	8.0 (0.3–76)	9.5 (2.3–58.6)	4.3 (<LOD–23.9)
PBDE209	na	1.9 (1.2–15)	–[b]	–[b]
PBB153	na	na	0.7 (<LOD–28.1)	–[b]
PFOS	na	0.9 (0.2–27.6)[c]	2.2 (<LOD–9.0)[d]	0.5 (<LOD–2.7)[e]
PFOA	na	0.3 (0.1–3.8)[f]	1.0 (<LOD–4.3)[d]	0.6 (<LOD–2.6)[e]
PFNA	na	0.4 (0.1–5.7)[c]	0.7 (<LOD–3.4)[d]	0.2 (<LOD–1.3)[e]
PFDA	na	0.2 (0.2–2.1)[g]	0.2 (<LOD–1.1)[d]	–[b]
PFHxS	na	na	0.3 (<LOD–3.2)[d]	0.2 (<LOD–0.7)[e]

LOD: Limit of detection. For statistical purposes, values <LOD were replaced by LOD/√2; [a]over 50% of samples <LOD; [b]over 70% of samples <LOD, so data not reported; [c]n=134; [d]n=159; [e]n=78; [f]n=132; [g]n=123.

PCB153 is less clear, as concentrations in the sample population from 2004–2006 were higher than those found in 1999–2003. For *trans*-nonachlor and HCB, concentrations in 2009–2012 were lower than those of 2004–2006, but not yet as low as 1999–2003. For both β-HCH and PCB153, the current concentrations are lower than those seen in the past two sampling periods, despite the higher concentrations in 2004–2006. The concentrations of PBDE153 were higher in 2009–2012 than in 2004–2006, although the other PBDEs were lower than in 2004–2006. More than 70% of samples were below the detection limit for PBDE209. Several PFCs increased in the current sampling year compared to the previous sampling period. PFOS and PFOA increased in mothers over the time period. Perfluorononanoate (PFNA) also showed a small increase. The geometric mean concentration of perfluorodecanoate (PFDA) remained similar, although the maximum decreased. Perfluorohexane sulfonate (PFHxS) was measured for the first time.

Infants of the mothers sampled during the 2009–2012 sampling period were also sampled. Not every infant had umbilical cord blood collected, but those that did are shown compared to the maternal values. Five contaminants within the infant population had more than 70% of samples below the limit of detection, compared with one in the maternal population. Many of the PCBs and OCs measured were similar between maternal blood and infant blood. However, two contaminants were higher in infants than in mothers – oxychlordane by 5% and HCB by 19%. All PBDEs and PFCs were lower in infants than in mothers.

3.4.1.2 Metals

Comparing the recent metals analysis with data reported by AMAP (2009) shows that levels have decreased in Yup'ik mothers in Cd, Pb and Hg (Table 3.3). Although the statistical significance of these trends was not measured, there has been a steady decline in Cd concentrations across the three sampling periods, and Pb and Hg concentrations in 2009–2012 are less than half the values of 2004–2006. Selenium (Se) is also reported for the first time. Levels reported in Yup'ik mothers are similar to those found in US females (all ages), which had a geometric mean of 188 µg/L blood Se in the National Health and Nutrition Examination Survey (NHANES) (US CDC 2014a).

Table 3.3 Concentrations of metals in Yup'ik maternal blood from Alaska. Data presented as geometric means, calculated for the specified period of sampling, in µg/L whole blood. Source: 1999–2003 data and 2004–2006 data (AMAP 2009); 2009–2012 data (Berner pers. comm. 2014).

	1999–2003	2004–2006	2009–2012
Mean age	25	25	26.5
Sample size	n=43	n=75	n=160
Total Hg	1.1	5	2.2
Pb	11	18	7.4
Cd	0.6	0.4	0.2
Se	na	na	181

3.4.1.3 Conclusion

Although levels of contaminants have declined in Yup'ik mothers, it is likely that the change is not equally distributed across the population of the Yukon-Kuskokwim Delta due to environmental change, community accessibility and the possibility that there has been a gradual decrease in consumption of traditional foods in the younger population of the Yukon-Kuskokwim, as has been documented elsewhere in the Arctic. Traditional dietary choices have been influenced by the availability of commercial food and advertising is influencing dietary choices to replace the traditional diet by store-bought food, especially among the younger residents (Berner pers. comm. 2014). Of those eating traditional food, there is generally more marine mammal availability for coastal settlements. There is an unequally distributed transition along the coast to incorporate muskox, moose and caribou, where available, into the traditional diet rather than relying heavily on marine resources (Berner pers. comm. 2014). Riverine settlements depend more on freshwater fish and land mammals for traditional food, unless there is sharing occurring between the riverine and coastal villages.

Some of this adaptation is due to climate change (see Chap. 7). In Alaska, and across the Arctic, snowmobiles and outboard motors have changed hunting patterns and capabilities, increasing the ability of village hunters to deal with climate variability, particularly unpredictable ice conditions, and increasing hunting ranges, which can help to maintain the traditional diet.

3.4.2 Canada

Canadian biomonitoring studies reported by AMAP (2009) indicated decreases in contaminant concentrations over time. However, in the Inuvialuit Settlement Region and Nunavut, due to the small number of time points available more data were considered necessary before a trend could be reliably identified. New data presented in this report include additional time points for concentrations of contaminants among pregnant women in Nunavik through continued biomonitoring in the regions of Hudson Bay and the Ungava Coast, as well as blood concentrations of contaminants among children in Nunavik, collected through the Nunavik Child Development Study (NCDS). The Inuit Health Survey (2007–2008; IHS), which was not available in time for inclusion in the previous AMAP human health assessment, is presented here and provides coverage of three Inuit regions in northern Canada: the Inuvialuit Settlement Region, Nunavut, and Nunatsiavut (Chan 2012a,b,c). Nunatsiavut is not an Arctic region, because it covers the northern coast of Labrador in the province of Newfoundland and Labrador, but it is an Inuit region and so is included due to its many similarities with other Arctic Inuit regions. Previous AMAP assessment reports have not presented data from the Nunatsiavut region; biomonitoring data from the IHS presents the first comprehensive overview of human exposure to contaminants in this region.

Combined with another extensive survey, the Nunavik Health Survey (2004), these studies provide comprehensive biomonitoring datasets of contaminant levels among Inuit across the Canadian North. The similar random sample study methodology used for these surveys, as outlined in detail by Dewailly et al. (2007), Saudny et al. (2012) and Laird et al. (2013a) allows for a reliable Arctic-wide comparison of biomonitoring data to highlight geographical trends in northern Canada.

3.4.2.1 Persistent organic pollutants

Concentrations of POPs among WCBA in the Inuvialuit Settlement Region, Nunavut, Nunavik and Nunatsiavut are presented in Table 3.4. Concentrations among men and women (18+) of the general population were also collected and are presented in Table 3.5. Nunavik biomonitoring data from 2004 were presented in the previous AMAP report but are included here for comparison purposes.

Concentrations of POPs among WCBA were usually highest among Inuit from Nunavik, and generally lowest among Inuit from Nunatsiavut (Table 3.4). Concentrations in Nunavik were higher than in Nunavut by as much as two-fold for some POPs, and were between two and fifteen times higher than most contaminant concentrations in Nunatsiavut. Concentrations of POPs in Inuvialuit were generally slightly higher than in Nunatsiavut although still much lower than in Nunavut or Nunavik. PBDE concentrations appear similar across all four regions, although concentrations were lower in Nunavik. Among the PBDEs, PBDE209 is the most predominant congener.

The geographical differences observed for the POPs reflect the distinct cultures, traditional lifestyles and dietary habits of Inuit in the Canadian Arctic. In general, the higher POP concentrations observed in the eastern Arctic (Nunavut and Nunavik) are due to the higher consumption of marine mammals. Research by Curren et al. (2015) analyzed older maternal biomonitoring datasets from the Inuvik and Baffin-Nunavut regions of Canada, and also noted significant regional differences in the concentrations of several contaminants in an east-west comparative analysis. When blood contaminant levels of Inuit are compared to those from the general population of Canada (Health Canada 2010, 2013), it is evident that Inuit face elevated exposure to several POPs, as mean concentrations of contaminants such as PCB153 are generally between three- and eleven-fold higher among Inuit men and women from the four regions of northern Canada. This is also supported by other studies, such as that by Curren et al. (2014) which compared biomonitoring data for women in their first pregnancy from the Inuvik (Armstrong et al. 2007) and Baffin (Potyrala et al. 2008) regions in the mid-2000s, and from southern Canada collected as part of the Trinational Biomonitoring Study

Table 3.4 Blood concentrations of POPs in Inuit women of childbearing age across the Canadian Arctic. Data presented as geometric means (range), in lipid weight (µg/kg plasma lipid). Source: Chan (2012a,b,c); Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	Inuvialuit Settlement Region	Nunavut	Nunavik	Nunatsiavut
	2007–2008	2007–2008	2004	2007–2008
Mean age (range)	28 (18–39)	28 (18–39)	28 (18–39)	30 (20–39)
Sample size	n=74	n=485	n=283	n=61
Oxychlordane	8.5 (0.4–222)	21.6 (0.4–420)	34 (2.3–440)	2.5 (0.4–58.6)
trans-Nonachlor	17.3 (0.8–457)	33.8 (0.8–441)	62 (4.7–1000)	4.1 (0.7–84.7)
p,p'-DDT	5.0 (2.0–65.1)	6.8 (2.1–97.8)	8.5 (1.3–130)	4.5 (2.8–6.9)
p,p'-DDE	79.5 (13.4–1024)	148 (1.8–2680)	279 (27.1–3100)	55.6 (13.1–239)
HCB	15.7 (1.6–304)	32.2 (1.4–294)	37 (4.1–650)	8.7 (1.9–115)
β-HCH	3.7 (0.8–72)	5.5 (0.7–108)	4.8 (0.7–40)	1.6 (0.6–11.5)
Toxaphene Parlar 26	2.0 (0.3–95.5)	6.1 (0.3–98.1)	8.1 (0.4–200)	0.8 (0.3–14.7)
Toxaphene Parlar 50	2.9 (0.3–152)	8.4 (0.4–130)	15 (0.4–310)	0.9 (0.3–19.7)
PCB99	4.5 (1.6–65.1)	8.9 (1.7–146)	14 (1.4–140)	3.2 (1.7–17.1)
PCB118	4.6 (0.8–94.1)	7.5 (0.7–97.5)	13 (1.9–190)	2.9 (0.7–36.9)
PCB138	8.9 (0.8–180)	19.9 (0.8–387)	40 (3.7–310)	7.0 (1.0–93.3)
PCB153	17.6 (0.8–249)	46.9 (0.9–1022)	82 (5.7–550)	17.7 (2.2–304)
PCB180	7.4 (0.8–84.4)	22.4 (0.9–848)	38 (3.3–350)	11.4 (1.1–239)
PBDE47	9.9 (2.1–676)	8.8 (1.7–477)	6.6 (1.5–340)	7.0 (1.7–111)
PBDE99	3.3 (1.1–184)	2.6 (1.1–101)	–[a]	2.4 (1.1–30.4)
PBDE100	2.5 (1.1–127)	2.6 (0.9–379)	–[a]	2.2 (1.1–38.4)
PBDE153	3.4 (1.1–59.9)	3.3 (1.1–84)[b]	1.9 (1.1–60)	2.9 (1.1–36.4)
PBDE209	15.8 (4.0–189)[c]	13.8 (4.4–406)[d]	na	6.9 (3.9–54.6)

[a]Over 60% of samples below the limit of detection, so data not reported; [b]n=132 (2008 only); [c]n=71 (2008 only); [d]n=131 (2008 only).

conducted by the Commission of Environmental Cooperation during the same period (CEC 2011). Significant differences in concentration for several POPs, Hg and Pb were noted between the pregnant women from these northern and southern Canadian populations after adjusting for age. The highest age-adjusted geometric mean levels of POPs and metals were usually observed among Inuit in northern populations, with the exception of PBDE153, which was significantly higher in the southern women. Southern Canadian mothers born outside Canada also showed the highest individual concentrations of *p,p*'-DDE and β-HCH measured in the study, although northern mothers as a group showed a higher adjusted geometric mean concentration for β-HCH, and Inuit mothers from Baffin were higher for *p,p*'-DDE (Curren et al. 2014).

Concentrations of POPs among men in the Inuvialuit Settlement Region, Nunavut and Nunatsiavut regions were usually higher than in all women or WCBA, often by as much as two- or three-fold (Table 3.5). However, differences in POPs concentrations between men and all women studied in Nunavik did not show a clear trend by gender, and concentrations were often quite similar. WCBA had lower concentrations of contaminants compared to all women, which is expected for most contaminant concentrations that have previously been found to be associated with increasing age. Concentrations of contaminants such as PCBs, toxaphene, *p,p*'-DDT and *p,p*'-DDE all increased with age, except the PBDEs, which either decreased with age or were similar among age groups (Chan 2012a,b,c). Dietary information collected (24-hour recall and food frequency questionnaire) as part of the IHS (Chan 2012a,b,c) indicated that men ate larger portions of traditional foods more frequently than women, and that older adults (>40 years old) ate more traditional foods than younger adults (<40 years old). The main traditional foods consumed overall (by weight) were caribou and Arctic char, which are both relatively low in contaminants (Laird et al. 2013b). Since 2008 however, there have been dramatic declines in the availability of some traditional foods (e.g. caribou), such that the food consumption data collected in this survey may not reflect current usage. Like other Inuit regions in northern Canada, Inuit from Nunavik also consumed large amounts (by weight) of caribou meat and Arctic char (Lemire et al. 2015).

Concentrations of PBDEs appeared to be lower in men and women from Nunavik compared to the other three regions (Table 3.5). Concentrations of PBDE47, PBDE99 and PBDE100 were similar across the Inuvialuit Settlement Region, Nunavut and Nunatsiavut, although levels of PBDE209 appear to be higher in the Inuvialuit Settlement Region and Nunavut than in Nunatsiavut. No data for PBDE209 were available for Nunavik. PBDE concentrations in the Canadian Arctic appear to be lower than the general population of Canada, except for PBDE209 which was found to be higher in Inuit than the general population, as measured in pooled samples from Cycle 1 of the Canadian Health Measures Survey (CHMS; Rawn et al. 2014). This may be a result of different exposure

Table 3.5 Blood concentrations of POPs in men and women across the Canadian Arctic. Data presented as geometric means (range), in lipid weight (µg/kg plasma lipid). Source: Chan (2012a,b,c); Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	Inuvialuit Settlement Region		Nunavut		Nunavik		Nunatsiavut	
	Men	Women	Men	Women	Men	Women	Men	Women
	2007–2008	2007–2008	2007–2008	2007–2008	2004	2004	2007–2008	2007–2008
Mean age (range)	46.2 (18–81)	42.6 (18–90)	42.2 (18–89)	40.7 (18–90)	37.0 (18–74)	37.3 (18–74)	45.7 (18–89)	43.4 (20–79)
Sample size	n=92	n=187	n= 650	n=977	n=408	n=506	n=98	n=165
Oxychlordane	91 (1.1–1802)	34 (0.4–2888)	105 (0.3–3675)	56 (0.4–3872)	66 (0.9–1600)	66 (2.3–2700)	14 (0.5–209)	8.0 (0.4–226)
trans-Nonachlor	167 (1.6–3094)	63 (0.8–1181)	145 (0.8–2087)	80 (0.8–2478)	120 (1.5–3900)	120 (4.7–3700)	23 (0.7–394)	14 (0.7–339)
cis-Nonachlor	23 (0.4–364)	9.0 (0.4–223)	24 (0.3–401)	14 (0.4–435)	16 (0.2–410)	18 (0.4–590)	4.2 (0.3–98)	2.6 (0.3–72)
p,p'-DDT	16 (2.7–273)	10 (2.0–165)	12 (2.1–177)	10 (2.0–193)	10 (0.9–140)	13 (1.3–250)	4.4 (2.0–29)	4.2 (2.2–20)
p,p'-DDE	466 (9.4–8189)	238 (13–3251)	414 (1.4–4337)	282 (1.5–7727)	460 (13–7000)	470 (27–8300)	190 (18.9–2834)	150 (13.1–2789)
HCB	104 (1.6–1656)	54 (1.6–993)	97 (1.7–1147)	71 (1.4–1773)	51 (1.6–1200)	64 (4.1–1200)	26 (1.3–171)	21 (2.0–199)
β-HCH	28 (0.8–382)	13 (0.8–517)	19 (0.7–360)	12 (0.6–248)	8.1 (0.8–130)	8.1 (0.7–200)	3.9 (0.6–37)	3.5 (0.6–30)
Mirex	16 (0.8–227)	6.0 (0.6–152)	14 (0.5–720)	6.0 (0.5–734)	13 (0.5–290)	8.7 (0.6–640)	7.2 (0.6–103)	3.3 (0.6–55)
Toxaphene Parlar 26	20 (0.3–655)	8.5 (0.3–271)	20 (0.3–401)	14 (0.4–580)	11 (0.2–410)	15 (0.4–510)	2.7 (0.3–138)	1.8 (0.3–42)
Toxaphene Parlar 50	28 (0.3–855)	12 (0.3–367)	28 (0.3–433)	19 (0.4–725)	20 (0.2–720)	26 (0.4–890)	3.9 (0.3–185)	2.5 (0.3–60)
PCB99	28 (1.7–255)	14 (1.6–258)	26 (1.8–540)	18 (1.7–649)	23 (0.5–530)	26 (1.4–850)	9.2 (1.7–151)	6.5 (1.7–99)
PCB118	28 (0.8–619)	16 (0.8–240)	20 (0.7–486)	17 (0.7–631)	18 (0.5–500)	24 (1.9–710)	11 (0.7–116)	9.0 (0.7–167)
PCB138	69 (0.9–855)	30 (0.8–445)	69 (0.7–1273)	43 (0.8–1985)	77 (3.0–1400)	73 (3.7–2500)	39 (0.7–672)	24 (1.0–436)
PCB153	148 (1.9–2730)	62 (0.8–4408)	195 (0.7–5747)	106 (0.8–6181)	190 (6.3–3400)	160 (5.7–5800)	112 (1.3–1622)	61 (2.2–1291)
PCB180	70 (2.2–1346)	26 (0.8–3040)	109 (0.8–4766)	51 (0.9–4765)	110 (6.2–1900)	75 (3.3–3500)	94 (0.7–927)	44 (1.1–904)
PBDE47	6.6 (1.7–250)	8.8 (1.7–675)	7.9 (1.5–1587)	7.9 (1.4–518)	5.9 (1.6–100)	5.9 (1.3–340)	9.6 (1.2–570)	7.1 (1.6–215)
PBDE99	2.3 (1.1–75)	2.8 (1.0–184)	2.4 (0.7–312)	2.4 (0.7–137)	–[a]	–[a]	2.9 (1.1–255)	2.3 (0.9–42)
PBDE100	2.1 (1.1–48)	2.5 (1.0–127)	2.4 (0.7–227)	2.3 (0.7–379)	–[a]	–[a]	2.6 (0.8–122)	2.2 (0.9–76)
PBDE153	4.7 (1.1–82)	3.5 (1.0–225)[b]	5.7 (1.2–235)[c]	3.4 (1.1–84)[d]	4.0 (1.1–140)	2.1 (1.1–60)	6.9 (1.4–48)	3.7 (1.1–151)[e]
PBDE209	27.5 (3.9–702)[f]	19.8 (3.5–2252)[g]	27.8 (4.4–6953)[h]	18.6 (4.0–6001)[i]	na	na	8.7 (2.8–370)	6.8 (3.1–202)[j]

[a]Over 60% of samples below the limit of detection, so data not reported; [b]n=186 (2008 only); [c]n=191 (2008 only); [d]n=281 (2008 only); [e]n=166 (2008 only); [f]n=91 (2008 only); [g]n=181 (2008 only); [h]n=187 (2008 only); [i]n=277 (2008 only); [j]n=164 (2008 only).

pathways for PBDEs (e.g. indoor air and dust – Whitehead et al. 2015) compared to other POPs, which most Inuit are exposed to due to consumption of high trophic level traditional foods (e.g. marine mammals and long-lived predatory fish). Recent studies have shown that diet is a poor predictor of PBDE body burden and instead that indoor dusts were significantly correlated with exposure (Watkins et al. 2012). The congener with the highest mean concentrations was PBDE209, which is one of the few groups of PBDEs not listed under the Stockholm Convention on Persistent Organic Pollutants.

Concentrations of contaminants among children who participated in the NCDS are presented in Table 3.6. Blood samples were collected in the same children between 2000 and 2002 (average age 5 years) and between 2005 and 2007 (average age 11 years). Concentrations of POPs declined by more than 40% between the two time points; this decrease could be due to a decrease in levels in the environment but is most likely to be due to a dilution of concentrations of lipophilic POPs as the body grows with age. The decrease could also reflect changes in consumption of traditional foods between toddlers and pre-teens, however this would be contrary to the few current dietary studies that suggest traditional food intake in children may increase with age (Gagne et al. 2012). The concentrations of POPs in the younger children (at 5 years) could also be influenced by exposure from more recent breastfeeding.

The previous AMAP assessment (AMAP 2009) presented data for pregnant Inuit women in the Inuvialuit Settlement Region and Nunavut using two time points available from baseline and follow-up studies. Other than the IHS, there are no other time points available in these regions for further comparisons. Due to differences in sampling methodologies and target population, further comparisons were not done.

Using new biomonitoring data from the Nunavik monitoring program conducted in the Ungava Bay and Hudson Bay regions among pregnant women from 2011–2013, time trends of POPs in Nunavik are presented in Tables 3.7 and 3.8. Data from 2011 and 2012 are combined due to small sample size. Blood data from pregnant women are most appropriate for time trend comparisons in Nunavik, since extensive sampling occurred

Table 3.6 Concentrations of POPs in children from the Nunavik Child Development Study, Canada. POPs and OCs are in µg/kg plasma lipid. PFCs, TBBPA and PCP are in µg/L whole blood. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	2000–2002	2005–2007
Mean age (range)	5.4 (4.7–6.2)	11.3 (10.2–14.3)
Sample size	n=93	n=93
Oxychlordane	40 (2.9–620)	24 (0.5–240)
trans-Nonachlor	56 (4.1–710)	40 (1.4–350)
p,p'-DDT	7.8 (1.7–95)	4.5 (1.2–31)
p,p'-DDE	290 (38–3100)	170 (23–1800)
HCB	47 (10–280)	26 (4.2– 150)
β-HCH	6.6 (1.9–44)	3.1 (0.6–21)
Mirex	4.1 (1.1–72)	2.3 (0.6–29)
Toxaphene Parlar 26	na	3.1 (0.4–23)
Toxaphene Parlar 50	na	5.1 (0.4–35)
PCB99	19 (2.2–210)	8.8 (0.8–84)
PCB118	16 (1.8–130)	8.4 (0.8–50)
PCB138	54 (7.4–590)	23 (2.3–180)
PCB153	84 (7.5–1500)	45 (3.5–430)
PCB180	31 (2.6– 520)	18 (1.0–220)
PBDE47	na	14 (2.5–710)
PBDE99	na	4.0 (1.4–190)
PBDE100	na	3.4 (1.2–110)
PBDE153	na	6.0 (0.6–120)
PFOS	na	9.2 (1.9–32)
PFOA	na	2.5 (1.1–12)
TBBPA	na	0.01 (0.01–0.05)
PCP	na	1.4 (0.3–15)

between 1992 and 2013 with data available from 11 points during this period (Table 3.7). Decreasing concentrations of contaminants over time are observed (see Appendix Fig. A3.1 for graphical illustrations of this change). Overall, levels of POPs have declined by an average of 80% in the 20 years that biomonitoring has taken place in Nunavik. For example, maternal blood concentrations of POPs have decreased 64% for *trans*-nonachlor and 83% for PCB138.

Trends in concentration for some POPs can be extended back to 1987 (Dewailly et al. 1989) and 1989–1990 (Dewailly et al. 2000), when 24 and 109 breast milk samples were collected from Inuit women in Nunavik, respectively (Appendix Fig. A3.1). In 1989–1990, mean concentrations in breast milk samples were 962 µg/kg for *p,p*'-DDE, 107 µg/kg for HCB, and approximately 14 µg/kg for Mirex. In blood, the most recent measurements for *p,p*'-DDE, HCB and Mirex have shown a decline to 130, 20, and 3.0 µg/kg plasma lipid, respectively. Some caution should be used in interpreting blood plasma and milk concentrations together because, although concentrations between these compartments are strongly correlated for many OCs (Anda et al. 2007), the assumption that mean concentrations in blood and milk samples are equal (Aylward et al. 2003) may not be true for all POPs as noted in several recent studies (Lakind et al. 2009; Mannetje et al. 2012). There is a strong trend nonetheless that POPs in general are significantly declining over time in Nunavik, and the average annual decrease is often between 4% and 8%. It may be that successful international action has caused the levels of PCBs in the Arctic environment to decrease appreciably over the past 20 years (Muir et al. 1999; Braune et al. 2005; Gamberg et al. 2005). Although not presented here, a trend of declining POPs concentrations has also been observed in other regions of the Canadian Arctic, such as in the blood of Inuit mothers in Baffin (Nunavut) and the Inuvik Region, when comparing follow-up studies to early baseline studies conducted in the 1990s (AMAP 2009; Donaldson et al. 2010a).

Table 3.8 compares data for pregnant women from 2004, 2012 and 2013 for a select number of contaminants for which there are limited data over the past 20 years. Comparisons were made on a lipid basis (toxaphene and PBDEs), and on a wet weight basis (pentachlorophenol, PCP; PFOS and PFOA). All POPs showed distinct declines between 2004 and 2012 by roughly a factor of 2, while concentrations between 2012 and 2013 were fairly similar. The exception is PBDE153, which increased between 2004 and 2012. Note that *p*-values were based on data adjusted by age and region (Hudson Bay and Ungava Bay).

Table 3.7 Trends in POPs concentrations in pregnant Inuit women from Nunavik, Canada. Data presented as geometric means (range) in µg/kg plasma lipid. Results

	1992	1996	1997	1998	1999
Mean age (range)	24 (18–35)	24 (17–34)	25 (15–41)	25 (15–37)	26 (17–36)
Sample size	n=11	n=25	n=53	n=46	n=26
Oxychlordane	77 (32–240)	41 (6.1–180)	48 (8.6–390)	34 (7.0–340)	47 (15–140)
trans-Nonachlor	114 (49–320)	66 (15–250)	75 (14–330)	55 (17–580)	61 (21–170)
cis-Nonachlor	28 (11–84)	14 (5.8–40)	16 (3.7–61)	9.6 (<LOD–110)	13 (<LOD –31)
p,p'–DDT	26 (9.5–96)	17 (4.2–63)	18 (<LOD–86)	13 (<LOD –130)	8.6 (<LOD –46)
p,p'-DDE	640 (292–1600)	290 (71–1000)	370 (59–1400)	270 (67–2300)	290 (140–900)
HCB	95 (47–220)	41 (15–120)	51 (9.2–190)	36 (6.7–350)	37 (15–100)
β-HCH	12 (2.3–30)	4.7 (<LOD–14)	6.5 (<LOD–24)	5.3 (<LOD –31)	5.4 (<LOD –11)
Mirex	13 (5.6–29)	10 (2.3–36)	10 (<LOD–60)	6.5 (<LOD–32)	9.7 (<LOD–39)
PCB138	110 (45–220)	58 (10–210)	69 (12–310)	46 (13–390)	62 (17–220)
PCB153	170 (71–290)	110 (19–410)	130 (23–610)	83 (83–710)	120 (29–470)
PCB180	90 (34–150)	43 (7.6–190)	51 (11–220)	35 (12–280)	53 (14–380)

LOD: Limit of detection. For statistical purposes, values <LOD were replaced by LOD/2. [a]Special analysis: Pereg pers. comm. (2007) and Dewailly pers.

Table 3.8 Time series of POPs concentrations in pregnant Inuit women from Nunavik, Canada. Data presented as geometric means (range). Results presented only for contaminants with more than 60% of data detected. Concentrations of toxaphenes and PBDEs presented in µg/kg plasma lipids. Concentrations of PFOS, PFOA and PCP presented in µg/L whole blood. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	2004	2012	2013	$p<0.05$[a]
Mean age (range)	27 (18–42)	24 (18–39)	24 (18–41)	
Sample size	n=31	n=112	n=95	
Toxaphene Parlar 26	9.8 (<LOD–70)	4.5 (<LOD– 49)	5.8 (<LOD–47)	0.0252
Toxaphene Parlar 50	17 (<LOD–133)	7.1 (<LOD–65)	9.1 (<LOD–63)	0.008
PBDE47	7.7 (<LOD–33)	<LOD	na	
PBDE153	2.0 (<LOD–12)	2.9 (<LOD–15)	na	0.0399[b]
PFOS	9.8 (3.1–20)	3.9 (0.7–23)	na	<0.0001[b]
PFOA	na	0.7 (0.2–2.4)	na	
PCP	0.5 (0.2–1.5)	0.3 (<LOD–1.8)	na	<0.0001[b]

LOD: Limit of detection. For statistical purposes, values <LOD were replaced by LOD/2. [a]Special analysis: Dewailly pers. comm. (2014) based on orthogonal polynomial contrast, adjusted for age, region (Hudson and Ungava). [b]P-value based on ANOVA test, adjusted for age and region.

3.4.2.2 Metals

Concentrations of metals among WCBA are presented in Table 3.9. Concentrations of metals appear to be highest in the Nunavik region, and lowest in the Nunatsiavut region, which are similar to concentrations in the Inuvialuit Settlement Region. Mean Hg concentrations in Nunavik are four-fold higher than in the Nunatsiavut and Inuvialuit Settlement regions, while only two-fold higher than in Nunavut. Concentrations of Pb and Se are only slightly lower in the Inuvialuit Settlement Region and Nunatsiavut region compared to Nunavut and Nunavik, which are both quite similar.

While the consumption of dried caribou meat and Arctic char meat by participants from the IHS was approximately ten-fold higher than for ringed seal liver (by weight), these were not the main source of Hg intake among traditional foods reported during the IHS. Despite the small quantity of ringed seal liver consumed by Inuit in this study, it was the largest source for Hg (59%), with Arctic char meat the second highest dietary source at 8.4% (Laird et al. 2013b).

Like other Inuit regions in northern Canada, caribou meat and Arctic char were also consumed in higher quantities (by weight) than other traditional foods by Inuit from Nunavik (Lemire et al. 2015). In Nunavik, where traditional beluga hunting takes place, the main source of Hg intake is beluga *nikku* and meat, particularly for Inuit in the Hudson Strait region. Seal liver was also an important exposure source for Hg (Lemire et al. 2015).

Concentrations of Hg and Pb among men (Table 3.10) were generally higher than among all women and WCBA (Table 3.9) across the four Inuit regions of northern Canada, sometimes by as much as two-fold. However, in Nunavik, women's Hg concentrations slightly exceeded men's, although men reported consuming significantly higher amounts of traditional foods (by weight) (Lemire et al. 2015). Selenium concentrations appeared similar between men and all women in each region. WCBA had lower concentrations of metals compared to all women, who had a higher mean age.

presented only for contaminants with more than 60% of data detected. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

2000	2001	2004	2007	2012	2013	$p<0.05$[a]
26 (17–39)	27 (17–39)	27 (18–42)	24 (18–37)	24 (18–39)	24 (18–41)	
n=36	n=20	n=29	n=39	n=112	n=95	
40 (7.5–210)	36 (8.2–130)	35 (<LOD–230)	22 (<LOD–180)	20 (<LOD–120)	22 (0.9–130)	<0.0001
61 (13–300)	53 (12–200)	66 (14–410)	44 (2.5–260)	37 (<LOD–220)	42 (2.0–220)	<0.0001
14 (1.7–66)	9.6 (<LOD–35)	10 (2.3–62)	7.0 (<LOD–42)	5.3 (<LOD–41)	5.9 (<LOD–29)	<0.0001
11.3 (<LOD–68)	6.6 (<LOD–38)	9.1 (<LOD–44)	5.5 (<LOD–50)	4.4 (<LOD–33)	na	<0.0001
270 (64–1300)	230 (54–1700)	230 (55–930)	150 (30–720)	123 (11–520)	130 (22–480)	<0.0001
37 (12–110)	34 (11–140)	36 (8.9–170)	22 (5.1–83)	18 (<LOD–110)	20 (<LOD–92)	<0.0001
5.6 (<LOD–16)	na	4.4 (0.8–23)	3.8 (1.1–26)	2.4 (<LOD–16)	2.4 (LOD–19)	<0.0001
9.2 (<LOD–47)	7.3 (<LOD–30)	4.0 (<LOD–24)	2.0 (<LOD–16)	3.0 (<LOD–19)	3.0 (<LOD–24)	<0.0001
56 (7.9–300)	53 (11–170)	37 (8.6–120)	22 (3.0–91)	17 (<LOD–77)	19 (2.0–120)	<0.0001
97 (15–500)	82 (16–420)	72 (32–250)	40 (4.5–220)	39 (2.4–230)	40 (3.5–320)	<0.0001
42 (5.0–260)	44 (7.5–240)	32 (4.9–130)	16 (2.0–95)	17 (<LOD–160)	17 (1.7–200)	<0.0001

comm. (2014) using regression adjusted for age and region (Hudson or Ungava) and smoking status (smoker vs. non-smoker).

Table 3.9 Blood concentrations of metals in Inuit women of childbearing age across the Canadian Arctic. Data presented as geometric means (range), in µg/L whole blood. Source: Chan (2012a,b,c); Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	Inuvialuit Settlement Region	Nunavut	Nunavik	Nunatsiavut
	2007–2008	2007–2008	2004	2007–2008
Mean age (range)	28 (18–39)	28(18–39)	28.1 (18–39)	30 (20–39)
Sample size	n=74	n=491	n=283	n=60
Total Hg	2.1 (0.5–39)	5.0 (0.5–52)	8.4 (0.2–160)	1.7 (0.1–25)
Pb	18.2 (4.5–92)	21.9 (5.1–290)	27 (6.6–210)	15.1 (5.6–63)
Se	238 (150–550)	286 (85–2000)	280 (91–1300)	191 (140–530)

Table 3.10 Blood concentrations of metals in Inuit men and women across the Canadian Arctic. Data presented as geometric means (range), in µg/L whole blood. Source: Chan (2012a,b,c); Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	Inuvialuit Settlement Region		Nunavut		Nunavik		Nunatsiavut	
	Men	Women	Men	Women	Men	Women	Men	Women
	2007–2008	2007–2008	2007–2008	2007–2008	2004	2004	2007–2008	2007–2008
Mean age (range)	46.2 (18–81)	42.6 (18–90)	42.2 (18–89)	40.7 (18–90)	37 (18–74)	37.3 (18–74)	45.7 (18–89)	43.4 (20–79)
Sample size	n=92	n=187	n=650	n=977	n=408	n=506	n=98	n=165
Total Hg	5.6 (0.3–50)	4.1 (0.1–55)	9.4 (0.1–110)	7.9 (0.1–130)	9.2 (0.1–240)	12 (0.2–160)	4.2 (0.2–50)	2.8 (0.1–25)
Pb	44.5 (8.1–220)	27.6 (4.5–190)	46.1 (7.4–380)	32.2 (5.1–400)	46 (9.1–500)	34 (5.8–310)	40.1 (8.4–170)	22.4 (5.6–160)
Se	317 (160–1300)	293 (150–1200)	348 (130–2800)	342 (85–2500)	280 (130–3500)	300 (120–2400)	233 (150–1500)	204 (140–960)

Among NCDS children from Nunavik (Table 3.11), concentrations of metals are much lower among 11-year olds than 5-year olds. At 5 years, Hg levels were 5.9 µg/L whole blood but declined to 3.2 µg/L whole blood by 11 years. Lead also declined from 41 to 22 µg/L over that time frame. A similar decline was observed for Se, which decreased from 330 to 190 µg/L. Selenium is known to have been constant over time in the environment, so the decline in blood Se in children may be a sign of decreased ingestion of traditional food between 5 and 11 years of age, or the expected dilution due to body growth.

Temporal trends for metals are presented in Table 3.12, using new biomonitoring data from the Nunavik monitoring program conducted in the Ungava Bay and Hudson Bay regions among pregnant women from 2011–2013, combined with previous datasets collected since 1992. Since 1992, significant declines in concentrations of metals have been observed among Inuit in Nunavik. Mercury decreased by 59% with an average annual decrease of 4%. The decrease in maternal blood Pb concentrations is less consistent than for Hg, showing an irregular pattern of increases and decreases. There is, however, a strong decrease after the temporary lead shot ban in 1998.

Table 3.11 Concentrations of metals in children from the Nunavik Child Development Study, Canada. Data presented as geometric means (range), in µg/L whole blood. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	2000–2002	2005–2007
Mean age (range)	5.4 (4.7–6.2)	11.3 (10.2–14.3)
Sample size	n=93	n=93
Total Hg	5.9 (0.2–38)	3.2 (0.1–28)
Pb	41 (10–370)	22 (5.0–130)
Se	330 (160–2600)	190 (71–750)

Selenium concentrations have decreased over time but not nearly to the same degree as for Hg and Pb, although most recent Se concentrations actually appear to have risen slightly. It is interesting to note the differences in the trends for Hg and Se, as shown in Fig. 3.1. The divergence between decreasing Hg and increasing Se concentrations could indicate a transition in diet to one that includes food items containing less Hg but the same level of Se. Traditional foods represent the main source of intake of Hg, with some food items containing more Hg than others, but almost all traditional foods also provide a rich source of Se as well as several vitamins, minerals and fatty acids. Despite a significant decrease in consumption of traditional foods between 1992 and 2004 (Blanchet and Rochette 2008), concentrations of Se remain high in Nunavik. When compared to the general population of Canada, Se levels are higher among northern populations of the Canadian Arctic.

3.4.2.3 Conclusion

There appears to be a distinct pattern in the concentrations of contaminants across the Canadian Arctic, with the highest mean concentrations of most POPs and metals observed in the Inuit populations of the Nunavut and Nunavik regions – regions with high consumption of marine mammals such as beluga and ringed seal. In regions where time trend data are available, concentrations of many POPs and metals appear to be decreasing. Despite this decrease, concentrations of most POPs and metals are still appreciably higher among Inuit in northern Canada than in the general population of Canada (Health Canada 2010, 2013). PBDEs may be an exception, as adult men and women from the four Canadian Arctic regions

Table 3.12 Trends in metals concentrations in pregnant Inuit women from Nunavik, Canada. Data presented as geometric means (range), in µg/L whole blood. Results presented only for contaminants with more than 60% of data detected. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

	1992	1996	1997	1998	1999	2000	2001	2004	2007	2012	2013	$p<0.05$[a]
Mean age (range)	24 (18–35)	24 (17–34)	25 (15–41)	25 (15–37)	26 (17–36)	26 (17–39)	27 (17–39)	27 (18–42)	24 (18–37)	24 (18–39)	24 (18–41)	
Sample size	n=11	n=25	n=53	n=27	n=16	n=29	n=19	n=31	n=42	n=111	n=95	
Total Hg	12 (3.6–33)	13 (4.2–29)	11 (3.8–44)	7.2 (3.2–27)	8.5 (2.6–31)	9.0 (1.8–38)	9.9 (1.6–33)	7.6 (1.2–30)	4.0 (0.7–24)	5.0 (0.2–40)	5.2 (0.3–32)	<0.0001
Pb	41 (8.3–170)	48 (17–140)	56 (10–260)	54 (27–130)	53 (19–110)	44 (10–140)	33 (5.2–130)	19 (5.8–85)	16 (6.6–77)	13 (2.7–230)	14 (4.2–62)	<0.0001
Se	na	370 (190–620)	320 (190–980)	290 (180–470)	300 (150–580)	340 (190–1200)	260 (200–390)	270 (130–700)	230 (134–710)	320 (120–3000)	300 (130–1400)	0.0068

[a]Special analysis: Pereg pers. comm. (2007) and Dewailly pers. comm. (2014) using regression adjusted for age and region (Hudson or Ungava) and smoking status (smoker vs. non-smoker).

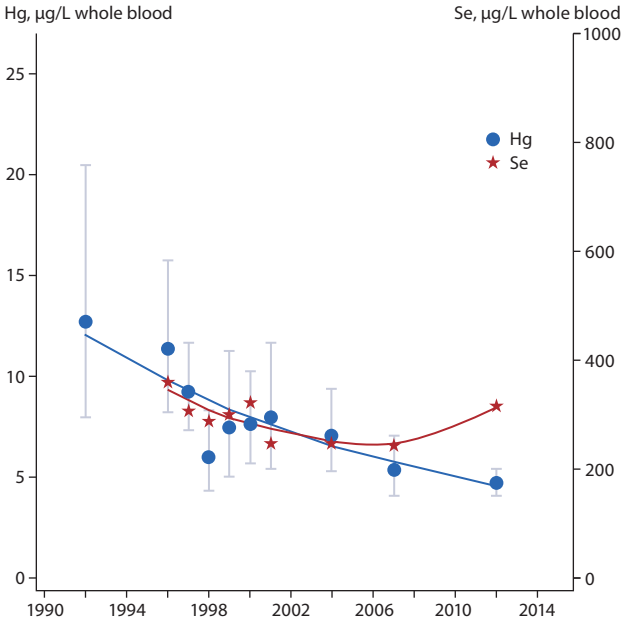

Figure 3.1 Trends in Hg and Se in maternal blood from Nunavik, Canada. Data are presented as geometric means adjusted for age and region (Hudson, Ungava) and 95% confidence intervals. Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

have lower mean concentrations of PBDE47 than the general population of Canada, and concentrations of PBDE153 were significantly higher in first-time mothers from southern Canada compared with women from Nunavut and the Northwest Territories. Moreover, mean concentrations of several PBDEs were similar across the Canadian Arctic, particularly between adult populations from the Inuvialuit Settlement Region, Nunavut and the Nunatsiavut region.

3.4.3 Greenland

Greenland is home to an extensive biomonitoring network, and several studies have been carried out with the cooperation of Greenland Inuit and other Greenlanders to monitor levels of contaminants in a population historically subject to some of the highest concentrations of POPs and metals in the Arctic.

The Inuit Health in Transition study is a general health study among adults (18+ years) in Greenland (Nielsen et al. 2012; Bjerregaard et al. 2013; Valera et al. 2013c). The study was carried out between 2005 and 2010 and included nine towns and 13 villages representing all geographical areas and community sizes (Bjerregaard 2010). For analytical purposes, the sample sites can be divided into five areas: Avanersuaq (Qaanaaq and villages 2010), North-west Greenland (Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik and villages 2006), South-west Greenland (Qaqortoq 2005–2006, Maniitsoq and villages 2006–2009, villages in Nanortalik and Narsaq districts 2007), East Greenland (Tasiilaq and villages 2008) and Nuuk (2007) (see Chap. 1, Fig. 1.1). PCBs and OCs were measured in approximately 1900 adult Inuit, and Hg and Se were measured in about 3000 adult Inuit. Data were obtained on 15 PCB congeners, 11 pesticides, Hg and Se.

A birth cohort including 598 pregnant women and 440 male spouses from Greenland was established in 2002–2004 as part of the INUENDO study (Toft et al. 2005). The study involved collection of detailed information on lifestyle factors and reproductive history. Several persistent environmental contaminants were measured in a subset of these pregnant women and male partners, including PCB153, *p,p'*-DDE, HCB, Hg, Pb, Cd, and a series of PBDEs and PFCs.

The Adaptation to Climate Change, Environmental Pollution, and Dietary Transition (ACCEPT) project is a new Greenlandic mother-child cohort study, which began in 2010–2011, restarted in 2013 and is still ongoing, recently including data for 2015. This section presents initial data from 2010–2011 and some from 2013. The aim of the ACCEPT project is to establish a geographically widespread, Greenlandic mother-child cohort study compatible with international cohorts, to detect and explore the interactions and possible health outcomes of environmental contaminants, changes to traditional lifestyle, and global climate change. It includes a follow-up on the children at age 4–5 years (see Long et al. 2015).

3.4.3.1 Persistent organic pollutants

The Inuit Health in Transition study found three PCB congeners (PCB138, PCB153, PCB180) in high concentrations in both men and women across all age groups (≥112.4 µg/kg plasma lipid in men and ≥81.2 µg/kg plasma lipid in women) and increased significantly with increasing age. PCB99, PCB118, PCB153, PCB170 and PCB187 were also present in high levels in the

highest age groups (Tables 3.13 and 3.14, see also Appendix Tables A3.1 and A3.2). This supports the well-known age-related bioaccumulation of organochlorine compounds. Among the OCs, oxychlordane, HCB, *trans*-nonachlor and *p,p*'-DDE appeared with the highest geometric mean levels in both sexes and all age groups (Bjerregaard et al. 2013; Valera et al. 2013c).

In all geographical areas, the geometric mean levels of PCBs were, in general, higher in villages than in towns (Table 3.15). Thus, in south-western Greenland the levels of PCB99, PCB105, PCB118, PCB138, PCB156, PCB170, PCB180, PCB183, and PCB187 in villages were more than twice the levels in towns, and PCB153 was more than three times higher (Table 3.15, Appendix Table A3.3). The lowest levels were observed in Nuuk. This pattern is expected mainly to result from a higher intake of a traditional diet based on marine mammals and fish in remote areas (Bjerregaard and Jeppesen 2010) and, to a lesser extent, age-related differences.

With a few exceptions, the highest levels of OCs were also observed in villages (Table 3.15, see also Appendix Tables A3.3 and A3.4). Among the pesticides with the highest concentrations (oxychlordane, HCB, *cis*-nonachlor, *trans*-nonachlor and *p,p*'-DDE) the highest geometric means were measured in Avanersuaq or in villages in East Greenland (*p,p*'-DDE). Again the lowest levels were observed in Nuuk.

In data provided through the INUENDO study, it was generally found that levels of persistent environmental contaminants in males were approximately double those in females, except for HCB which was roughly the same in both (Table 3.16 and 3.17). Age and seafood consumption were also related to OC and PFOS exposure in Greenland (Jönsson et al. 2005; Lindh et al. 2012). PBDEs were determined in serum samples from 97 men from this population. Age and seafood consumption were not significant determinants of PBDE exposure (Lenters et al. 2013), but geographical location within Greenland was

Table 3.13 Concentrations of PCBs and OCs (µg/kg plasma lipid) among Inuit men in Greenland by age group (years). Data presented as geometric means (range). Data from the Inuit Health in Transition study, 2005–2010. Source: Bjerregaard et al. (2013); Valera et al. (2013c).

Mean age (range)	24 (18–29)	41 (30–49)	61 (≥50)	*p*
Oxychlordane	69.9 (4.2–750)	204 (5.6–3500)	488 (6.4–4000)	<0.001
trans-Nonachlor	141 (7.6–820)	373 (9.8–5000)	797 (12–3500)	<0.001
cis-Nonachlor	27.7 (1.0–180)	69.7 (2.0–970)	136 (2.4–560)	<0.001
p,p'-DDT	17 (6.0–130)	26.7 (4.0–410)	39.3 (7.0–2300)	<0.001
p,p'-DDE	559 (36–3000)	1067 (97–16000)	1816 (70–10000)	<0.001
DDE:DDT	33.2 (3.6–300)	39.9 (11.6–190)	46.2 (1.7–235)	<0.001
HCB	76.5 (10–360)	174 (8.0–2300)	368 (13–1800)	<0.001
β-HCH	11.4 (2.0–110)	28.5 (2.0–530)	52.6 (2.2–440)	<0.001
Mirex	12.8 (1.0–110)	35.8 (1.0–760)	90.5 (1.0–720)	<0.001
PCB99	33.7 (4.0–230)	63.9 (5.0–1100)	110 (3.5–890)	<0.001
PCB118	27.9 (3.0–160)	68.3 (3.1–1300)	154 (5.2–660)	<0.001
PCB138	112 (6.5–480)	226 (21–3800)	400 (27–1600)	<0.001
PCB153	253 (13–1800)	545 (50–7700)	1048 (54–4600)	<0.001
PCB180	134 (5.8–1300)	332 (32–5600)	747 (60.4–300)	<0.001

Sample size for OC pesticides: n=856–859; sample size for PCBs: n=796–859.

Table 3.14 Concentrations of PCBs and OCs (µg/kg plasma lipid) among Inuit women in Greenland by age group (years). Data presented as geometric means (range). Data from the Inuit Health in Transition study, 2005–2010. Source: Bjerregaard et al. (2013); Valera et al. (2013c).

Mean age (range)	24 (18–29)	40 (30–49)	61 (≥50)	*p*
Oxychlordane	55.8 (5.6–780)	134 (2.0–2100)	436 (11–3600)	<0.001
trans-Nonachlor	108 (11–940)	239 (5.0–1500)	695 (31–4000)	<0.001
cis-Nonachlor	22 (2.3–180)	45.4 (1.0–330)	119 (5.1–650)	<0.001
p,p'-DDT	15.3 (6.0–120)	22.8 (4.1–270)	35.6 (6.0–2000)	<0.001
p,p'-DDE	444 (69–3100)	832 (10–6600)	1847 (130–27000)	<0.001
DDE:DDT	29.1 (6.9–140)	36.4 (1.2–171)	51.9 (1.8–365)	<0.001
HCB	69.5 (13–490)	145 (6.0–910)	391 (36–1700)	<0.001
β-HCH	10.2 (1.0–85)	22 (1.6–170)	52.6 (5.1–400)	<0.001
Mirex	7.7 (1.0–60)	20.4 (1.0–340)	65 (3.0–610)	<0.001
PCB99	26.6 (5.0–250)	51.6 (4.0–450)	110 (2.7–800)	<0.001
PCB118	27.8 (3.7–220)	59.2 (2.5–460)	161 (14–1400)	<0.001
PCB138	81.2 (16–500)	171 (4.1–1200)	394 (1.0–3500)	<0.001
PCB153	170 (28–1400)	382 (7.5–2600)	997 (93–6700)	<0.001
PCB180	79.2 (12–720)	204 (4.2–1800)	609 (67–4000)	<0.001

Sample size for OC pesticides: n=1051–1053; sample size for PCBs: n=995–1053.

Table 3.15 Unadjusted concentrations of PCBs and OCs (µg/kg plasma lipid) by region and residence in towns or villages, Greenland. Data presented as geometric means. Data from the Inuit Health in Transition study, 2005–2010. Source: Bjerregaard and Jeppesen (2010).

	Avanersuaq[a]		North-west[b]		South-west[c]		East[d]		Nuuk[e]
	Town	Villages	Towns	Villages	Towns	Villages	Town	Villages	Town
Sample size	n=245–246	n=30	n=265–331	n=123–187	n=325–350	n=188–251	n=171–172	n=180	n=125–154
Oxychlordane	347	498	241	450	80.3	289	186	384	59.6
trans-Nonachlor	574	692	449	480	179	513	324	567	134
cis-Nonachlor	99.3	123	74.7	78.1	36.6	98.9	61.7	110	27.3
p,p'-DDT	31.5	40.7	24.3	28.2	14.6	33.7	35.9	67.5	16.2
p,p'-DDE	1206	1519	1227	1283	599	1557	1256	2076	486
DDE:DDT	38.3	37.3	50.6	45.5	41.3	46.1	34.9	30.8	30
HCB	261	344	318	260	108	202	141	275	96.8
β-HCH	48.7	73	30.4	46.7	15.3	31.6	22.7	42.6	15.2
Mirex	40.5	62.6	28.1	46.3	17.4	46.3	35.9	67	11.9
PCB99	78.7	105	75.8	105	31.9	78.5	81.4	129	27.8
PCB118	98.3	138	105	99.6	37.4	94.7	83.5	165	33
PCB138	228	282	256	246	134	329	270	457	99.4
PCB153	591	766	603	774	290	816	603	998	213
PCB180	313	402	323	469	175	492	373	645	122

[a]Qaanaq 2010; [b]Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik 2006; [c]Nanortalik 2007, Qaqortoq 2005–2006, Narsaq 2007, Maniitsoq 2007; [d]Tasiilaq 2008; [e]Nuuk 2007.

Table 3.16 Concentrations of POPs in the blood of Inuit men (2002–2004), Greenland. Mean age 31 years (range 18–72 years). POPs in µg/kg plasma lipid. PFOS and PFOA in µg/L serum. Data presented as geometric means (range). Data from the INUENDO/Clear project. Source: Jönsson et al. (2005); Lindh et al. (2012); Lenters et al. (2013); Specht et al. (2015).

	North[a]	Disko Bay[b]	Mid-west[c]	South-west[d]	South[e]	East[f]	All
p,p'-DDE	987 (300–2625)	650 (74.4–4027)	513 (37.6–4802)	315 (4.4–2631)	616 (38.5–2684)	1228 (88.9–13197)	523 (4.4–13197)
HCB	na	76.4 (14.7–255)	52.9 (21.2–161)	45.5 (9.5–258)	48.6 (16.4–146)	94.4 (18.6–863)	58.8 (9.5–863)
PCB153	244 (32–623)	231 (15.5–1765)	197 (5.1–1299)	145 (18.4–1698)	266 (39.6–1593)	527 (101–5455)	209 (5.1–5455)
PBDE47	na	1.7 (0.05–6.6)	1.2 (0.02–4.4)	1.7 (0.1–12.5)	2.5 (0.9–8.1)	3.1 (0.8–7.7)	1.8 (0.02–12.5)
PBDE99	na	0.2 (0.01–1.4)	0.3 (0–1.7)	0.2 (0–2.0)	0.4 (0.03–2.6)	0.6 (0.4–1.5)	0.3 (0.02–2.6)
PBDE100	na	0.1 (0.001–1.3)	0.1 (0–1.2)	0.2 (0–1.8)	0.6 (0.04–2.3)	0.8 (0.4–1.6)	0.2 (0–2.3)
PBDE153	na	2.8 (0.03–8.3)	2.0 (0.03–5.5)	3.0 (1.2–22.4)	3.0 (1.5–7.6)	4.0 (2.3–8.7)	2.6 (0.03–22.4)
PFOS	na	53.2 (23.8–112)	43.1 (24.1–91.6)	41.3 (12.3–146)	46.5 (20.9–118)	61 (26.8–161)	47.4 (12.3–161)
PFOA	na	4.7 (2.2–9.8)	4.6 (2.7–6.5)	4.8 (1.5–10)	4.6 (2.8–13.7)	4.3 (2.3–6.6)	4.6 (1.5–13.7)

Sample sizes for PCB/*p,p*'-DDE: North (n=10), Disko Bay (n=134), Mid-west (n=90), South-west (n=130), South (n=45), East (n=29), All (n=438); sample sizes for HCB: Disko Bay (n=51), Mid-west (n=27), South-west (n=57), South (n=33), East (n=23), All (n=191); sample sizes for PBDEs: Disko Bay (n=24), Mid-west (n=17), South-west (n=29), South (n=19), East (n=6), All (n=95); sample sizes for PFCs: Disko Bay (n=52), Mid-west (n=27), South-west (n=59), South (n=33), East (n=23), All (n=194). Regions include the following towns and nearby settlements: [a]Qaanaaq, Uummannaq; [b]Ilulissat, Aasiaat, Qasigiannguit, Qeqertarsuaq; [c]Sisimiut, Maniitsoq; [d]Nuuk, Paamiut; [e]Qaqortoq, Nanortalik, Narsaq; [f]Tasiilaq.

Table 3.17 Concentrations of POPs in the blood of pregnant Inuit women (2002–2004), Greenland. Mean age 27 years (range 18–42 years). POPs in µg/kg plasma lipid. PFOS and PFOA in µg/L serum. Data presented as geometric means (range). Data from the INUENDO/Clear project. Source: Jönsson et al. (2005); Lindh et al. (2012); Lenters et al. (2013).

	North[a]	Disko Bay[b]	Mid-west[c]	South-west[d]	South[e]	East[f]	All
p,p'-DDE	544 (146–1661)	300 (25.7–2942)	227 (5.2–1648)	201 (5.3–3033)	397 (7.8–2661)	903 (108–3122)	280 (5.2–3122)
HCB	105 (70.1–158)	68.7 (6.0–564)	61.1 (18.3–261)	54.4 (8.4–282)	45.6 (22.2–122)	103 (14–238)	61.2 (6.0–564)
PCB153	179 (50.2–619)	106 (5.3–829)	87.3 (2.6–648)	79.9 (3.3–1306)	166 (23.1–2223)	389 (23.4–1846)	107 (2.6–2223)
PFOS	24.7 (13.5–36.3)	21.6 (8.4–72.9)	20.9 (7.8–73.8)	17.2 (4.1–87.3)	23.2 (9.0–72.4)	30.1 (8.5–86.7)	20.6 (4.1–87.3)
PFOA	1.9 (1.0–4.2)	1.8 (0.5–4.3)	1.7 (0.5–4.2)	1.9 (0.5–5.1)	1.7 (0.7–4.9)	1.6 (0.8–3.9)	1.8 (0.5–5.1)

Sample sizes for PCB, *p,p*'-DDE and PFCs: North (n=12), Disko Bay (n=178), Mid-west (n=124), South-west (n=167), South (n=58), East (n=33), All (n=572); sample sizes for HCB: North (n=2), Disko Bay (n=62), Mid-west (n=41), South-west (n=63), South (n=22), East (n=11), All (n=201). Regions include the following towns and nearby settlements: [a]Qaanaaq, Uummannaq; [b]Ilulissat, Aasiaat, Qasigiannguit, Qeqertarsuaq; [c]Sisimiut, Maniitsoq; [d]Nuuk, Paamiut; [e]Qaqortoq, Nanortalik, Narsaq; [f]Tasiilaq.

an important determinant for PFOS and PBDE exposure, with higher levels in the southern and eastern regions compared to the mid- and south-western region (Lindh et al. 2012; Lenters et al. 2013).

In the ACCEPT study, among 14 tested PCB congeners, three were in the higher concentration ranges (PCB138, PCB153, PCB180; Table 3.18). There were significant differences for PCB99, PCB118, PCB138, PCB153 and PCB180 among regions. Pregnant women living in the East (Tasiilaq, n=3) and North (n=15) had higher PCB levels than other regions. In the West and South, the level of the dioxin-like PCB118 was significantly lower than in the East and North. The OC showing the highest concentrations in the blood of pregnant women pooled from all regions of Greenland was *p,p*'-DDE with a geometric mean of 131 µg/kg plasma lipid. Similar to PCBs, higher levels of OCs such as oxychlordane, *trans*-nonachlor, HCB and β-HCH were found in pregnant Inuit women living in the East and North (Long et al. 2015). These results support a previous report of bioaccumulation of POPs in traditional Inuit food in these regions (Deutch et al. 2007a).

PBDE47 and PBDE153 were detected in up to 5% of samples while PBDE99 and PBDE100 were detected in 1% to 2% of samples (Table 3.18). No significant differences were found among the different regions of Greenland for all tested PBDEs. Among the measured PFCs, only six (PFOS, PFHxS, PFOA, PFNA, PFDA, PFUnDA) were detected in all samples and four (perfluoroheptane sulfonate, PFHpS; perfluoroheptanoate, PFHpA; perfluorododecanoate, PFDoDA; perfluorotridecanoate, PFTrDA) were detected in 1.9% to 86.8% of samples, while the remaining PFCs were below the detection limit in all samples (Table 3.18, see also Appendix Table A3.5). Although there is an age difference (ACCEPT mean age 27), these levels are lower (PFOS and PFOA, 10.5 and 1.2 µg/L, respectively) than the levels found in samples taken across the country during 1997–2006

Table 3.18 Comparison of POPs in pregnant women from different regions in Greenland for 2010–2011 and 2013. Data presented as geometric means (range). Data from the ACCEPT project. PCBs, OCs and PBDEs in µg/kg plasma lipid. PFCs in µg/L serum. Source: Long et al. (2015).

	North	Disko Bay	West	South	East	*p*	All districts[a]
Mean age (range)	28 (21–35)	27 (19–40)	27 (17–44)	28 (21–41)	33 (31–37)		27 (17–44)
No. individuals sampled	n=15	n=50	n=124	n=15	n=3		n=207
No. individuals measured	n=15	n=45	n=118	n=13	n=3		n=194
Oxychlordane	41.1 (2.0–470)	25.8 (5.9–110)	13.8 (0.2–130)	20.5 (6.5–55)	104 (61–270)	<0.0001	18.4 (0.2–470)
trans-Nonachlor	85.1 (7.6–320)	57.7 (12–220)	35.2 (4.9–400)	41.2 (15–110)	184 (130–320)	<0.0001	44.2 (4.9–400)
p,p'-DDT	7.7 (2.5–35)	4.2 (2.0–20)	3.6 (2.0–34)	3.9 (2.5–10)	23.9 (10–68)	<0.0001	4.1 (2.0–68)
p,p'-DDE	221 (18–990)	148 (35–430)	112 (16–1100)	135 (39–430)	587 (300–1300)	<0.0001	131 (16–1300)
DDE:DDT	28.9 (6.0–76.7)	35.2 (14.3–123)	30.9 (4.6–104)	34.6 (13–123)	24.6 (19.1–30)	0.56	31.8 (4.6–123)
HCB	40.1 (5.8–130)	31.9 (13–100)	21.9 (6.4–170)	24.4 (10–41)	62.8 (47–110)	<0.0001	25.6 (5.8–170)
β-HCH	6.0 (0.5–34)	4.6 (0.5–18)	3.8 (0.5–28)	3.9 (1.0–7.8)	12.5 (7.9–25)	<0.0001	3.8 (0.5–34)
Mirex	5.8 (1.0–54)	2.8 (0.5–11)	2.6 (0.4–32)	3.4 (1.0–8.6)	17.1 (9.6–40)	0.001	2.9 (0.4–54)
PCB99	16.1 (2.0–91)	9.2 (2.0–37)	6.6 (1.5–61)	8.1 (2.0–20)	45.8 (27–91)	<0.0001	8.0 (1.5–91)
PCB118	16.7 (2.4–63)	11.6 (3.5–38)	7.9 (1.5–74)	8.6 (2.8–20)	42.3 (27–100)	<0.0001	9.5 (1.5–100)
PCB138	44.5 (4.8–180)	31.1 (8.9–110)	26 (4.0–210)	31.5 (11–82)	146 (81–320)	<0.0001	29.4 (4.0–320)
PCB153	99.2 (8.9–950)	62.4 (17–210)	53.7 (11–400)	63.1 (23–180)	288 (160–680)	<0.0001	60.5 (8.9–950)
PCB180	49.4 (6.6–810)	27.2 (6.6–80)	27.7 (4.7–220)	29.2 (16–68)	132 (89–290)	0.001	29.6 (4.7–810)
ΣPCB_{14}	324 (57.1–2714)	203 (69.8–593)	184 (55.7–1129)	203 (96.6–469)	837 (507–1839)	<0.0001	203 (55.7–2714)
PBDE47	1.7 (1.5–2.5)	1.8 (1.0–12)	1.8 (1.0–13)	2.0 (1.5–4.0)	2.4 (1.5–6.0)	0.572	1.8 (1.0–13)
PBDE99	1.1 (1.0–1.5)	1.1 (0.5–3.0)	1.1 (0.5–2.5)	1.4 (1.0–4.0)	1.3 (1.0–2.0)	0.168	1.2 (0.5–4.0)
PBDE100	1.1 (1.0–1.5)	1.2 (0.5–7.6)	1.2 (0.5–2.5)	1.2 (1.0–1.5)	1.0 (1.0–1.0)	0.761	1.2 (0.5–7.6)
PBDE153	1.7 (1.5–2.5)	1.8 (1.0–10)	1.8 (1.0–5.0)	1.9 (1.5–4.0)	1.5 (1.5–1.5)	0.691	1.8 (1.0–10)
PBB153	1.7 (1.5–3.0)	1.7 (1.0–2.5)	1.7 (1.0–3.5)	1.7 (1.5–2.5)	1.5 (1.5–1.5)	0.872	1.7 (1.0–3.5)
PFCs	n=14	n=50	n=122	n=15	n=3		n=204
PFOS	15.8 (4.7–50.7)	12 (3.7–32.8)	9.8 (2.5–61.3)	7.8 (3.2–18)	15.8 (6.1–26.5)	0.001	10.5 (2.5–61.3)
PFHxS	0.9 (0.2–4.5)	0.6 (0.1–1.6)	0.7 (0.2–2.6)	0.6 (0.3–1.4)	1.2 (0.6–2.9)	0.001	0.7 (0.1–4.5)
PFOA	1.0 (0.4–1.8)	1.2 (0.5–3.1)	1.2 (0.3–6.2)	1.1 (0.4–2.4)	0.9 (0.6–1.4)	0.449	1.2 (0.3–6.2)
PFDA	1.3 (0.4–3.3)	0.9 (0.3–2.9)	0.7 (0.1–7.8)	0.6 (0.3–1.1)	1.4 (0.4–4.4)	<0.0001	0.8 (0.1–7.8)

The *p* value is the difference among five regions in Greenland (one-way ANOVA analysis); ΣPCB_{14} includes PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187. [a]Includes the 15 Greenland districts.

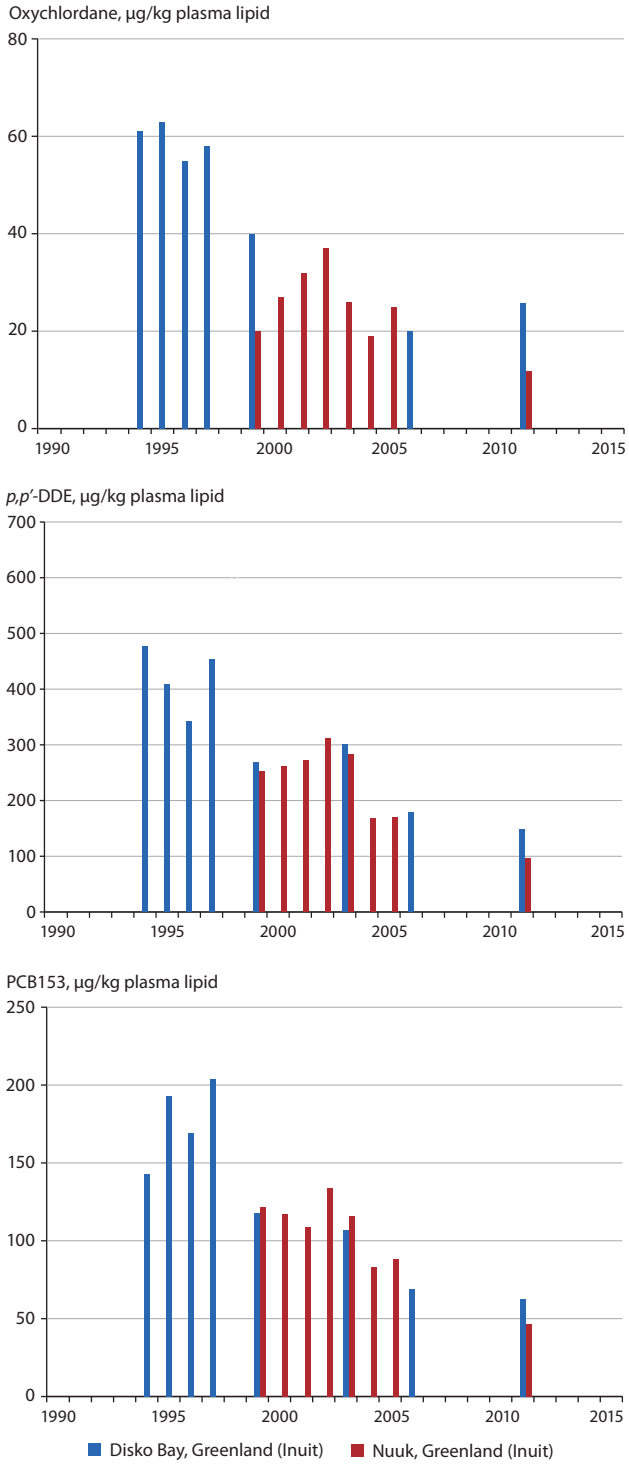

Figure 3.2 Trends in oxychlordane, *p,p'*-DDE, and PCB153 in pregnant women from Disko Bay and Nuuk, Greenland. Most recent data collected in the years 2010-2011 and 2013, presented in the 2011 bars.

(Nuuk 2000–2002) where female (mean age 49) PFOS and PFOA geometric mean levels were 21.0 and 1.5 µg/L serum, respectively (Long et al. 2012). The levels are also lower than those found in pregnant Danish women during 1996–2002 who had 35.3 and 5.6 µg/L serum, respectively (Fei et al. 2007). Serum levels of PFOS, PFHxS, PFHpS, PFNA, PFDA and PFUnDA in pregnant women from the North and East (Tasiilaq) were significantly higher than those living in the other regions. Women in the South and West had the lowest levels of PFCs (Table 3.18, Appendix Table A3.5) (Long et al. 2015).

For pregnant women in Disko Bay, plasma levels of PCB153, oxychlordane, and *p,p'*-DDE in the present study period were lower than those reported in the period 1994–2006 (AMAP 2009). Levels of oxychlordane, *p,p'*-DDE and PCB153 in Nuuk pregnant women in the ACCEPT study were 12, 96 and 47 µg/kg plasma lipid, which were lower than those found during 1995–2006 (AMAP 2009; Long et al. 2015). Added to the existing time trend data from AMAP (2009), the dataset now extends for almost 20 years, showing a general decreasing trend in concentration (Fig. 3.2).

A small subset of the Greenland population participating in the ACCEPT project had lived for longer in Denmark than in Greenland, and thus the participants were defined as Danish (n=5). Levels of lipophilic POPs such as OCs and PCBs in the Danish pregnant women were much lower than in the Greenlandic pregnant women (Table 3.19, see also Appendix Table A3.6). However, concentrations of most PBDEs and PFCs did not show much difference between the Danish and Greenlandic pregnant women. In fact, the Danish pregnant women had significantly higher levels of PBDE153.

3.4.3.2 Metals

Concentrations of metals like Pb, Hg, Cd and manganese (Mn) did not show much difference between pregnant Danish and Greenlandic women, although the blood Se levels of pregnant Greenlandic women were higher (Table 3.19). The pooled data of metals in blood sampled from the ACCEPT project population of pregnant Greenlandic women were detected in 39% (Pb), 85% (Hg), 5% (arsenic, As), and 9% (Cd) of the subjects. Pregnant women from northern Greenland had significantly higher Hg levels than women from the other regions (Table 3.20). However, no significant differences were found among regions for Pb, As and Cd. The trace elements Se and Mn were detected in 100% and 97% of subjects, respectively. No significant differences among regions were found for these two elements (Long et al. 2015).

From samples collected in the Inuit Health in Transition study across Greenland, the geometric mean of Hg ranged from 7.8 to 28.3 µg/L whole blood among men, and 8.3 to 22.1 µg/L whole blood among women (Table 3.21) (Bjerregaard et al. 2013; Valera et al. 2013c).

Mercury levels were highest in Avanersuaq, particularly in the villages. Again, levels were generally higher in villages than towns (Table 3.22, see also Appendix Table A3.7). A remarkable finding was a mean concentration of Hg five times higher in villages in the East compared with the town, Tasiilaq. Towns in the North-west had a relatively high geometric mean level of Hg compared with towns in South-west, East and Nuuk. Selenium was also highest in Avanersuaq, and almost twice as high in the villages compared to the town, Qaanaaq. Likewise, the highest Se levels were observed in the villages in the South-west and East compared with towns, whereas relatively low levels were measured in Nuuk.

The INUENDO study (Lenters et al. 2015) identified that metal levels in males were approximately double those in females, except for Cd which was similar in both (Tables 3.23 and 3.24).

For the pregnant women in Disko Bay, the Hg and Pb levels were lower in the ACCEPT study period (2010-2011 and 2013) than in the previous study period. In Nuuk pregnant women, Pb

Table 3.19 Concentrations of POPs (µg/kg plasma lipids), PFCs (µg/L serum) and metals (µg/kg whole blood) in pregnant Inuit women from Denmark and Greenland. Data presented as geometric means (range). Data from the ACCEPT project (2010–2011 and 2013). The district is given by where the Inuit lived for the longest time. Source: Long et al. (2015).

	Denmark	Greenland[a]	*p*	All[b]
Arithmetic mean age (range)	32 (29–41)	27 (17–44)		27 (17–44)
No. individuals sampled	n=5	n=207		n=212
No. individuals measured	n=5	n=194		n=199
Oxychlordane	2.0 (0.4–6.2)	18.4 (0.2–470)	<0.0001	17.4 (0.2–470)
trans-Nonachlor	3.9 (0.5–15)	44.2 (4.9–400)	<0.0001	41.6 (0.5–400)
p,p'-DDT	3.1 (2.0–5.0)	4.1 (2.0–68)	0.35	4.1 (2.0–68)
p,p'-DDE	47.1 (28–65)	131 (16–1300)	0.005	127 (16–1300)
DDE:DDT	15 (8.0–32.5)	31.8 (4.6–123)	0.004	31.2 (4.6–123)
HCB	11.5 (6.7–14)	25.6 (5.8–170)	0.006	25.1 (5.8–170)
β-HCH	2.9 (1.9–5.3)	3.8 (0.5–34)	0.45	3.8 (0.5–34)
Mirex	0.7 (0.4–1.8)	2.9 (0.4–54)	0.002	2.8 (0.4–54)
PCB99	3.0 (2.0–4.7)	8.0 (1.5–91)	0.01	7.8 (1.5–91)
PCB118	3.9 (1.6–5.3)	9.5 (1.5–100)	0.01	9.2 (1.5–100)
PCB138	13.1 (5.8–21)	29.4 (4.0–320)	0.02	28.8 (4.0–320)
PCB153	24.2 (9.6–41)	60.5 (8.9–950)	0.01	59.1 (8.9–950)
PCB180	13.4 (4.6–25)	29.6 (4.7–810)	0.03	29.0 (4.6–810)
ΣPCB_{14}	99.2 (53.6–140)	203 (55.7–2714)	0.02	199 (53.6–2714)
PBDE47	1.8 (1.0–3.0)	1.8 (1.0–13)	0.9	1.8 (1.0–13)
PBDE99	1.4 (1.0–2.0)	1.2 (0.5–4.0)	0.2	1.2 (0.5–4.0)
PBDE100	1.4 (1.0–2.0)	1.2 (0.5–7.6)	0.22	1.2 (0.5–7.6)
PBDE153	2.9 (1.0–23)	1.8 (1.0–10)	0.001	1.8 (1.0–23)
PBB153	1.8 (1.0–3.0)	1.7 (1.0–3.5)	0.74	1.7 (1.0–3.5)
PFCs	n=5	n=204		n=209
PFOS	10.8 (5.6–21.9)	10.5 (2.5–61.3)	0.28	10.5 (2.5–61.3)
PFHxS	0.6 (0.4–0.8)	0.7 (0.1–4.5)	0.33	0.7 (0.1–4.5)
PFHpS	0.2 (0.1–0.3)	0.2 (0.1–1.4)	0.39	0.2 (0.1–1.4)
PFOA	1.4 (0.8–2.3)	1.2 (0.3–6.2)	0.68	1.2 (0.3–6.2)
PFNA	1.1 (0.8–1.9)	1.3 (0.4–7.7)	0.3	1.3 (0.4–7.7)
PFHpA	0.04 (0.03–0.09)	0.03 (0.03–0.3)	0.96	0.03 (0.03–0.3)
PFDA	0.7 (0.5–1.6)	0.8 (0.1–7.8)	0.29	0.8 (0.1–7.8)
PFUnA	1.8 (0.7–6.6)	1.7 (0.2–18.2)	0.26	1.7 (0.2–18.2)
PFDoA	0.4 (0.2–0.7)	0.3 (0.2–1.8)	0.21	0.3 (0.2–1.8)
PFTrA	0.2 (0.2–0.2)	0.2 (0.2–0.9)	0.21	0.2 (0.2–0.9)
Metals	n=5	n=202		n=207
Hg	2.0 (1.0–7.0)	3.6 (0–70)	0.22	3.6 (0–70)
Pb	9.0 (5.0–20)	7.0 (10–50)	0.41	7.0 (1.0–50)
Cd	0.9 (0–1.0)	0.9 (0–10)	0.84	0.9 (0–10)
Se	80 (50–130)	120 (40–2660)	0.19	120 (40–2660)
As	0 (0)	3.0 (0–33)	0.99	3.0 (0–33)

[a]Includes the 15 Greenland districts; [b]includes the 15 Greenland regions and Denmark. ΣPCB_{14} includes PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187.

Table 3.20 Concentrations of metals (µg/kg whole blood) in pregnant Inuit women, Greenland. Data presented as geometric means (range). Data from the ACCEPT project (2010–2011 and 2013). Source: Long et al. (2015).

	North[a]	Disko Bay[b]	West[c]	South[d]	East[e]	*p*	All[f]
Mean age (range)	28 (21–35)	27 (19–40)	27 (17–44)	28 (21–41)	33 (31–37)		27 (17–44)
No. individuals sampled	n=15	n=50	n=124	n=15	n=3		n=207
No. individuals measured	n=14	n=49	n=121	n=15	n=3		n=202
Hg	8.0 (2.0–50)	4.0 (1.0–10)	3.1 (0–70)	4.0 (0.2–16)	7.0 (3.0–16)	0.02	3.6 (0–70)
Pb	7.0 (1.0–40)	7.0 (2.0–30)	7.0 (1.0–50)	7.0 (3.0–30)	6.0 (1.0–20)	0.97	7.0 (1.0–50)
Cd	0.5 (0–4.0)	1.0 (0–10)	0.9 (0–7.4)	1.1 (0–4.5)	0.7 (0–0.7)	0.36	0.9 (0–10)
Se	160 (60–1040)	110 (60–360)	120 (40–2660)	110 (70–250)	140 (90–190)	0.38	120 (40–2660)
As	3.0 (0–6.0)	3.0 (0–30)	3.0 (0–30)	3.0 (0–7.0)	3.0 (0–5.0)	0.99	3.0 (0–30)

The *p* value is the difference among five regions in Greenland (one-way ANOVA analysis). [a]Qaanaaq, Upernavik, Uummannaq; [b] Ilulisat, Qasigiannguit, Qeqertarsuaq, Aasiaat; [c] Sisimiut, Maniitoq, Nuuk, Paamiut; [d]Nanortalik, Narsaq, Qaqortoq; [e]Tasiilaq. [f]Includes the 15 Greenland districts.

Table 3.21 Concentrations of total Hg and Se (µg/L whole blood) among Inuit men and women by age group (years), Greenland. Data presented as geometric means (range). Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012).

	Men				Women			
Mean age in category (range)	24 (18–29)	41 (30–49)	61 (≥50)	*p*	24 (18–29)	40 (30–49)	61 (≥50)	*p*
Total Hg	7.8 (0.1–160)	17 (0.4–490)	28.3 (0.1–400)	<0.001	8.3 (0.1–120)	12.9 (0.1–230)	22.1 (0.1–320)	<0.001
Se	188 (70–2600)	280 (77–4800)	352 (82–5600)	<0.001	203 (84–1600)	266 (68–4800)	374 (71–4400)	<0.001

Sample size for men: Total Hg (n=1375), Se (n=1366); sample size for women: Total Hg (n=1730), Se (n=1721).

Table 3.22 Unadjusted concentrations of total Hg and Se (µg/L whole blood) by region and residence in towns or villages, Greenland. Data presented as geometric means. Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012).

	Avanersuaq[a]		North-west[b]		South-west[c]		East[d]		Nuuk[e]
	Town	Villages	Towns	Villages	Towns	Villages	Town	Villages	Town
	n=246	n=30	n=576–578	n=244	n=897–902	n=283	n=172	n=179	n=430–441
Total Hg	72.6	89.4	17.9	47.1	8.7	22.4	9.4	47.1	6.1
Se	745	1331	238	318	262	400	184	265	209

[a]Qaanaaq 2010; [b]Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik 2006; [c]Nanortalik 2007, Qaqortoq 2005–2006, Narsaq 2007, Maniitsoq 2007; [d]Tasiilaq 2008; [e]Nuuk 2007.

Table 3.23 Concentrations of metals (µg/kg whole blood) in Inuit men (2002–2004) by geographical area, Greenland. Mean age 31 years (range 18–72 years). Data presented as geometric means (range). Data from the INUENDO/Clear project. Source: Lenters et al. (2015).

	Disko Bay[a]	Mid-west[b]	South-west[c]	South[d]	East[e]	All
Sample size	n=50	n=29	n=59	n=32	n=23	n=193
Total Hg	17.6 (2.0–386)	5.4 (0.5–30.9)	3.9 (0.2–41.1)	7.8 (0.5–30.8)	28.5 (3.6–317)	8.7 (0.2–386)
Pb	29.3 (10.7–80.5)	44.4 (15.6–276)	28.7 (14–178)	24.6 (11.3–84.5)	31 (8.4–84.9)	29.9 (8.4–276)
Cd	0.8 (0.2–3.2)	1.1 (0.2–5.2)	0.6 (0.1–4.2)	0.6 (0.1–2.2)	0.9 (0.1–11.1)	0.7 (0.1–11.1)

[a]Ilulissat, Aasiaat, Qasigiannguit, Qeqertarsuaq; [b]Sisimiut, Maniitsoq; [c]Nuuk, Paamiut; [d]Qaqortoq, Nanortalik, Narsaq; [e]Tasiilaq.

Table 3.24 Concentrations of metals (µg/kg whole blood) in pregnant Inuit women (2002–2004) by geographical area, Greenland. Mean age 27 years (range 18–42 years). Data presented as geometric means (range). Data from the INUENDO/Clear project. Source: Bonefeld-Jørgensen, pers. comm. (2014).

	North[a]	Disko Bay[b]	Mid-west[c]	South-west[d]	South[e]	East[f]	All
Sample size	n=2	n=61	n=30	n=56	n=22	n=13	n=184
Total Hg	12.5	6.3 (1.4–46.5)	3.6 (0.9–14.7)	3.2 (0.4–29.2)	3.8 (0.9–13.4)	17.6 (6.3–51.6)	4.8 (0.4–51.6)
Pb	13.4	14.5 (4.9–62.8)	18.1 (5.4–141)	13.7 (5.4–61.5)	12.5 (6.0–36.1)	18.8 (9.4–50.5)	14.8 (4.9–141)
Cd	0.7	0.7 (0.2–1.8)	0.7 (0.2–3.4)	0.6 (0.2–3.5)	0.6 (0.3–2.9)	1.0 (0.2–3.0)	0.7 (0.2–3.5)

[a]Qaanaaq, Uummannaq; [a]Ilulissat, Aasiaat, Qasigiannguit, Qeqertarsuaq; [c]Sisimiut, Maniitsoq; [d]Nuuk, Paamiut; [e]Qaqortoq, Nanortalik, Narsaq; [f]Tasiilaq.

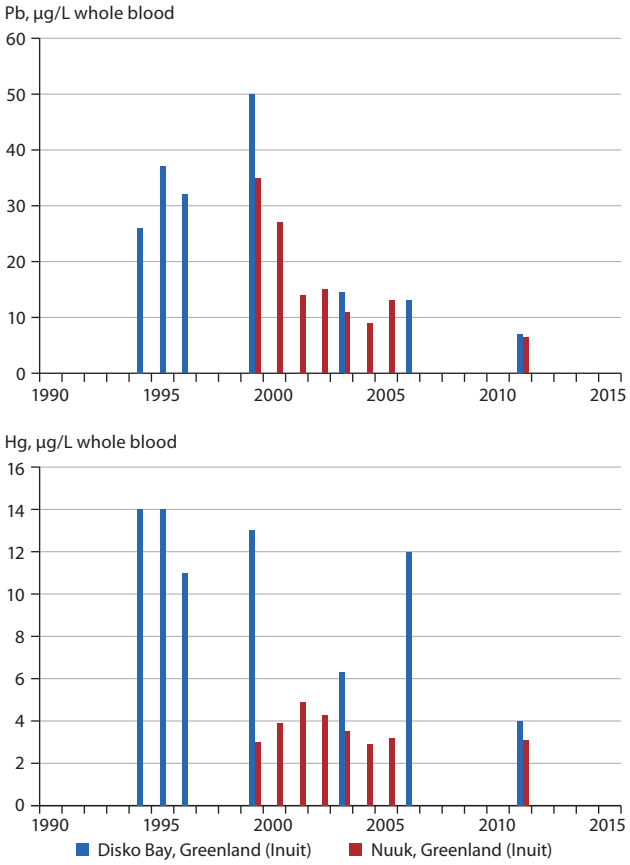

Figure 3.3 Trends in lead and mercury in pregnant women from Disko Bay and Nuuk, Greenland, since 1994. Most recent data collected in the years 2010-2011 and 2013, presented in the 2011 bars.

levels were also lower in the ACCEPT study period (2010–2011 and 2013) than in the previous study period, but the Hg levels were very similar (Long et al. 2015) (Fig. 3.3). Adding recent data to the time trend analysis undertaken by AMAP (2009) shows that Hg levels seem to have stabilized in pregnant women from Nuuk, although they continue to decline in pregnant women from Disko Bay. Lead levels continue to decline in both populations.

3.4.3.3 Conclusion

Lower levels of contaminants were observed during the most recent biomonitoring studies in Greenland compared to levels reported in the previous AMAP human health assessment (AMAP 2009). It should be noted, however, some of the Greenland data reported in the previous assessment (AMAP 2009) have since been corrected; the corrected data are shown in Appendix Tables A3.8 to A3. In general, younger women had lower OC levels than men (Jönsson et al. 2005), probably resulting from a lower intake of a traditional diet consisting of marine mammals and fish (Jeppesen 2008), the loss of contaminants through pregnancy and breastfeeding for women with children, and their younger age. This could also be a result of dietary guidance (see Chap. 6, Sect. 6.4.4) successfully reaching WCBA in Greenland. Older women and men showed smaller differences in contaminant levels, and their levels were also the highest overall during the period 2005–2010. Notably, levels of *p,p'*-DDE in Inuit women over 50 years old were four times higher than those in women of 18 to 29 years of age, while levels in Inuit men over 50 years old were three times higher than those of men of 18 to 29 years of age. This follows the expected accumulation of POPs with age and may reflect differences in POPs exposure based on birth year relative to global action to reduce the production and use of POPs (Quinn et al. 2011; Nøst et al. 2013).

The differences in POPs levels between populations that live predominantly in either towns or villages indicates a potential difference in food sources. For example, village populations may rely more on traditional food items and so experience higher contaminant exposures, while there may be greater access to store-bought food in towns. In all Greenlanders, PFOS levels were the highest of all PFCs measured. PBDE levels did not vary much between regions but some gender differences were observed. Concentrations of PBDE99 and PBDE100 tended to be lower in Inuit men than in pregnant women, while PBDE47 levels were similar, and PBDE153 concentrations tended to be higher.

Levels of metals mostly declined in pregnant Inuit women between the 2002–2004 INUENDO study and the more recent 2010–2011 and 2013 ACCEPT project. Lead has shown a considerable decrease, as has Hg in some, but not all, regions.

3.4.4 Iceland

Concentrations of POPs in maternal plasma from Reykjavik are being monitored in a new study, similar to three prior studies reported in the previous AMAP human health assessments. In these studies, when visiting a medical center, 50 pregnant women in their third trimester were invited to participate in biomonitoring sampling. This activity took place every five years in Iceland (AMAP 1998, 2003, 2009). A similar suite of contaminants were measured in this study, and all samples were collected from pregnant women during their third trimester (Olafsdottir pers. comm. 2014). The mean age of the mothers and the parity remained similar between this study and the previous ones, and sampling was conducted in Reykjavik only. Concentrations of metals in these maternal blood samples are not available. Reykjavik data are compared to data aggregated from all Iceland sampling done in previous years as it was determined that the city of the mother's residence did not appear to influence measured contaminant levels. Iceland is considered to have a socially and culturally homogenous population (AMAP 2009).

Table 3.25 (see also Appendix Table A3.13) shows the most recent concentrations measured in pregnant women from Reykjavik. The contaminants sampled in the 2009 cohort included BFRs and PFCs in addition to POPs. These data were not available in previous years. While the higher brominated congeners were detected in some participants (PBDE99, PBDE100, PBDE153), the geometric mean of the population was below the detection limit (<1.3 µg/kg plasma lipid). However, the lowest brominated congener, PBDE47, was found up to a maximum of 21 µg/kg plasma lipid, and the geometric mean was higher than the detection limit, at 1.7 µg/kg plasma lipid. These levels are still low, as the geometric means are near or below the detection limit, but these contaminants need continued monitoring to obtain additional data over time, and project how the levels might change in the future. The PFCs, PFOS and PFOA, were also analyzed for the first

Table 3.25 Trends in blood concentrations of POPs (µg/kg plasma lipid) in pregnant Icelandic women in their third trimester. Data presented as geometric means (range). Lipid normalization of data in 1999 and 2004 based on average lipid concentrations from 1995. PFOS and PFOA in µg/L plasma. Source: AMAP (2009); Olafsdottir pers. comm. (2014).

	Reykjavik	All Iceland	All Iceland	Reykjavik
	1995	1999	2004	2009
Mean age (range)	30 (18–41)	28.7 (20–42)	30.3 (20–40)	30.4 (21–43)
Sample size, mean parity	n=40; p=1.9	n=39; p=1.9	n=40; p=1.8	n=33; p=1.7
Oxychlordane	6.7 (2.6–30)	4.7 (1.3–22)	6.5 (1.3–22)	3.5 (1.3–8.9)
trans-Nonachlor	12 (3.8–50)	15 (6.4–47)	7.1 (1.3–29)	6.7 (3.6–15.5)
p,p'-DDT	na	na	na	1.4 (<1.3–5.7)
p,p'-DDE	113 (42–514)	100 (33–306)	54 (19–226)	36 (12.1–139)
DDE:DDT	na	na	na	26 (11–62)
HCB	41 (17–147)	49 (23–96)	27 (13–51)	20 (12–35)
β-HCH	32 (11–142)	24 (10–71)	9.0 (2.5–20)	7.1 (3.0–28)
Toxaphene Parlar 26	na	na	1.6 (1.3–6.4)	1.3 (<1.3–4.6)
Toxaphene Parlar 50	na	na	2.8 (1.3–10)	2.9 (<1.3–8.0)
PCB99	na	na	na	3.7 (<1.3–11)
PCB118	16 (7.7–37)	14 (3.8–38)	11 (5.1–24)	8.4 (4.7–18)
PCB138	46 (18–99)	40 (17–90)	23 (11–57)	15 (6.0–60)
PCB153	68 (26–158)	60 (24–143)	40 (19–98)	34 (18–108)
PCB180	34 (14–106)	35 (14–98)	22 (6.4–60)	16 (6.1–79)
ΣPCB_{14}	na	na	na	110 (55–370)
PBDE47	na	na	na	1.7 (<1.3–21)
PBDE99	na	na	na	<1.3 (<1.3–3.7)
PBDE100	na	na	na	<1.3 (<1.3–5.0)
PBDE153	na	na	na	<1.3 (<1.3–3.9)
PFOS	na	na	na	6.2 (4.2–13)[a]
PFOA	na	na	na	4.8 (1.4–40)[a]

ΣPCB_{14} includes PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187; [a]n=10. For statistical purposes, values <1.3 (the limit of detection, LOD) were replaced by LOD/2.

time in this population, and levels were above the detection limit, and comparable with international numbers reported by AMAP (2009).

There was an overall decrease in levels of contaminants in pregnant women from Reykjavik between the years 1995 and 2009 (Table 3.25). *p,p*'-DDE, PCBs, and β-HCH have strong decreasing trends from 1995 to 2009. There is no consistent trend for oxychlordane, although concentrations in 2009 decreased appreciably from the levels measured in 2004 and 1995, which were similar. *Trans*-nonachlor and HCB show a slight increase between 1995 and 1999 before a decrease occurs. Toxaphene Parlars 26 and 50 remained the same between the two sampling periods, which could be due to continual exposure combined with the long half-life of the contaminant and the low likelihood of measureable declines over a five-year period. Although toxaphene is banned for use in North America, it is still used in other parts of the world, so there may still be inputs into the global circulation and bioaccumulation in marine food chains. Toxaphene is known to bioaccumulate in the tissues of fish, shellfish and marine mammals and Parlar 50 is the dominant organochlorine found in cod liver in the marine environment around Iceland (Sturludottir et al. 2014).

3.4.5 Faroe Islands

Researchers in the Faroe Islands have undertaken several biomonitoring cohort studies over the past 25 years, in response to the growing awareness of environmental contaminants and their possible effects on human health. The data presented in this section represent several follow-ups of four of the cohorts – Cohorts 1, 2, 3 and 5.

Cohort 1 was established to assess the health significance of MeHg exposure during early life, and consists of 1022 singleton births assembled in the Faroe Islands during a 21-month period in 1986–1987 (Grandjean et al. 1992). It was intended to represent the entire community. These children were examined at ages 7, 14, and 22 years. Cohort 2 was established as a follow-up study during a 12-month period in 1994–1995, to respond to the findings of Cohort 1 that exposure assessment should encompass several lipophilic pollutants as well as MeHg. It included 182 singleton term births from consecutive births at the National Hospital in the capital city, Tórshavn (Steuerwald et al. 2000). Cohort 3 was formed from 656 consecutive births in Tórshavn between November 1998 and March 2000 (Heilmann et al. 2010). Cohort 5 is the most recent cohort, born during an 18-month period between October 2007 and April 2009 involving 500 mother-

Table 3.26 Time series of blood POPs concentrations from the Faroe Islands Cohort 1 (1986–1987). All participants are Faroese children born in 1986–1987. Data presented as geometric means (range). POPs in µg/kg plasma lipid. PFCs in µg/L. Source: Weihe pers. comm. (2013).

	1986–1987	1993–1994	2000–2001	2008–2009
Mean age (range)	Cord blood	6.9 (6.3–8.3)	13.8 (12.8–15.2)	22.1 (20.9–23.7)
Sample size	n=1022	n=922	n=792	n=849
Oxychlordane	na	na	15.6 (1.0–201)	na
trans-Nonachlor	na	na	40 (1.5–526)	na
p,p'-DDT	na	na	6.4 (0.9–211)	0.8 (0.1–176)
p,p'-DDE	270 (4.2–4487)	na	468 (25.4–8050)	122 (5.4–3257)
DDE:DDT	na	na	76.6 (1.2–614)	150 (0.7–7025)
HCB	45.9 (3.4–1469)	na	94.3 (22.1–858)	18.9 (3.1–164)
β-HCH	na	na	8.4 (2.8–41.5)	5.3 (0.1–232)
Mirex	na	na	6.4 (0.1–83.5)	na
PCB118	na	na	na	11.8 (0.1–282)
PCB138	83 (0.3–1068)	na	na	64.6 (0.1–790)
PCB153	130 (0.3–1127)	na	na	93 (8.2–1006)
PCB180	72 (0.3–889)	na	na	60.8 (3.4–673)
ΣPCB[a]	604 (17–5606)	1525 (210–7040)	708 (4.2–4941)	443 (36–4940)
PFOS	na	31.1 (7.2–96.9)	na	na
PFOA	na	5.4 (1.3–17.3)	na	na

[a](PCB138 + PCB153 + PCB180) × 2.

child pairs (Weihe pers. comm. 2014). Additional information, including observations of the health effects of contaminant exposure, is available for these cohorts in Chaps. 2 and 4.

3.4.5.1 Persistent organic pollutants

Each cohort underwent biomonitoring sampling at birth, and in follow-up years. Cohort 1 has the oldest time series, as biomonitoring began in 1986–1987 (Table 3.26). Changes over time can only be seen for a select group of contaminants that have undergone testing, as certain contaminants were not included in each sampling follow-up. There is an increase in levels of *p,p*'-DDE from cord blood to the sampling event at 13 years of age, and a decrease from 13 years of age to the most recent sampling event, when cohort participants were on average 22 years of age. Changes in PCB levels show a decrease from cord blood to the sampling event at 22 years of age. The sum of several PCBs was available for all sampling years, and shows a steady declining trend after an increase between birth and 7 years of age. HCB concentrations also increase between birth and 13 years of age, before concentrations decrease by age 22 years. Levels of β-HCH decrease between the final two sampling events. Mirex was only sampled during the 13-year follow up. PFCs were only sampled at the 7-year follow up, so recent changes are not known. That concentrations were measureable in 1993–1994 suggests that they may warrant follow-up sampling.

Cohort 2 has two data points available – that of the maternal blood at parturition in 1994–1995, and that of the children's blood at an average age of 7.5 years (Table 3.27). *p,p*'-DDE levels were not determined for the children. Almost all POPs levels found in the children at 7.5 years of age are lower than those for maternal blood at the time of giving birth, with the exception of PCB180, for which levels are essentially the same. PCB180, along with PCB153, are estimated to have a half-life of seven to nine years in children, as calculated using the Faroese biomonitoring data (Grandjean et al. 2008). PCB153 and PCB180 are particularly prevalent in food, which indicates that, despite the food recommendations at the time (Weihe and Joensen 2012) (see Chap. 6, Sect. 6.4.3), dietary exposure was providing enough PCB congeners to children to bring their PCB180 levels at age 7 years into line with their mother's levels at age 28 years. Using calculated partition ratios, levels of contaminants in cord blood for these children at birth are expected to have been approximately 58% of the levels found

Table 3.27 Time series of blood POPs concentrations from the Faroe Islands Cohort 2 (1994–1995). All participants were Faroese women and their children born in 1994–1995. Data presented as geometric means (range). POPs in µg/kg plasma lipid. Source: Weihe pers. comm. (2013).

	1994–1995	2001–2002
Population	Mothers	Children
Mean age (range)	28 (16–44)	7.5 (7.4–7.8)
Sample size	n=182	n=158
p,p'-DDT	9.0 (0.1–520)	na
p,p'-DDE	725 (201–8038)	na
DDE:DDT	80.1 (6.6–13040)	na
HCB	82.5 (35–663)	na
PCB118	67.2 (5.0–1410)	35.7 (3.4–202)
PCB138	185 (22–3529)	87.5 (6.3–560)
PCB153	265 (10–3933)	176 (11.6–1032)
PCB180	112 (9.0–1761)	117 (6.6–824)
ΣPCB[a]	1126 (440–18446)	765 (50–4500)

[a](PCB138 + PCB153 + PCB180) × 2.

Table 3.28 Time series of blood POPs concentrations from the Faroe Islands Cohort 3 (1998–2000). All participants were Faroese women and their children born in 1998–2000. Data presented as geometric means (range). POPs in μg/kg plasma lipid. PFCs in μg/L. Source: Heilmann et al. (2010); Tang-Péronard et al. (2014).

	1998–2000	2000–2001	2002–2005	2005–2007	2011–2012
Population	Mothers	Children	Children	Children	Children
Mean age (range)	28 (16–44)	1.5 (1.3–1.8)	5.0 (4.8–5.2)	7.5 (7.0–7.9)	13.2 (12.6–14.3)
Sample size	n=475	n=115	n=555	n=498	n=526
p,p'-DDT	0.7 (0.1–139)	na	37.6 (0.1–452)	13.2 (0.1–1216)	3.6 (0.6–101)
p,p'-DDE	538 (43.1–11414)	613 (68–10265)	476 (38.1–6631)	270 (20–4190)	92.8 (1.5–2738)
DDE:DDT	775 (24.1–40694)	na	12.6 (2.4–974)	20.5 (0.2–11595)	26 (0.1–404)
HCB	na	na	53.2 (15.7–565)	38.1 (2.1–447)	59.5 (14.4–240)
β-HCH	8.0 (0.1–100)	na	18 (0.1–84.4)	64.7 (2.1–4674)	2.0 (1.1–27.9)
PCB118	51 (0.1–788)	na	46.4 (2.8–637)	25.3 (1.0–550)	6.9 (0.9–131)
PCB138	180 (0.1–2722)	na	176 (12.2–1631)	115 (4.2–2869)	44.8 (1.5–788)
PCB153	274 (36.7–320)	na	257 (17.6–2162)	152 (6.7–3223)	86 (1.6–924)
PCB180	146 (20.8–1658)	na	127 (5.8–1421)	97.8 (0.1–2402)	38.8 (1.5–547)
ΣPCB[a]	1214 (181–15150)	1171 (166–10050)	1130 (71.4–9561)	750 (50–16990)	347 (19.5–4518)
PFOS	27.4 (9.4–68.8)[b]	na	16.7 (3.3–48.2)	15.3 (5.6–35.5)	6.6 (1.0–16.6)
PFOA	3.2 (0.8–8.4)[b]	na	4.1 (0.8–15.4)	4.5 (1.7–19.2)	2.0 (0.6–6.1)

[a](PCB138 + PCB153 + PCB180) × 2; [b]arithmetic mean age (range) = 30.2 (16.7–43.2, n=618).

in maternal serum (Needham et al. 2011), from which can be extrapolated the increase in these PCBs from birth.

Cohort 3 provides several time points of biomonitoring follow-up post parturition, following the children to the average age of 13 years in 2011–2012 (Table 3.28). The intent of Cohort 3 was to follow up on the possible effects of PCBs and other lipophilic contaminants, as dietary advice had decreased the potential for MeHg exposure (Weihe and Joensen 2012; see Chap. 6, Sect. 6.4.3). Few data were collected in the 2000–2001 follow up with children at the average age of 1.5 years, but nevertheless do provide an early measurement of *p,p'*-DDE and ΣPCB congeners (twice PCB138+PCB153+PCB180) which can measure the effects of breastfeeding in transferring lipophilic contaminants. At that time point, it can be seen that the child's levels of *p,p'*-DDE slightly exceeded the maternal blood levels taken at birth, and the ΣPCB level is only slightly lower than the maternal blood levels. The following sampling period, at 5 years of age, shows a decline in *p,p'*-DDE and ΣPCB to below the maternal blood levels. However, comparisons of other contaminant levels in the 5-year old sampling event show that levels of PCB118, PCB138, PCB153 and PCB180 are similar to those in maternal blood. Generally, each follow-up year of biomonitoring testing shows a decline in levels of contaminants in this sample population, with the exception of HCB and β-HCH (Heilmann et al. 2010; Tang-Péronard et al. 2014). HCB shows no trend, remaining essentially the same from age 5 years to 13 years. β-HCH shows an increase to the age of 7.5 years and then decreases dramatically by 13 years. Children exhibit higher levels of *p,p'*-DDT over the sampling timeframe than their 28-year old mothers did at their birth. This pattern is also consistent for β-HCH and PFOA. Levels of PFOS in 7.5-year old Cohort 3 children were dramatically lower than levels in Cohort 1 children at 7 years of age. PFOA levels were only slightly lower in Cohort 3 than Cohort 1 (Grandjean et al. 2012a).

Cohort 5 is the most recent cohort, which can show the effects of the ongoing dietary advice to the Faroese population and its effect on the transfer of lipophilic contaminants through breastfeeding (Table 3.29; see Chap. 6, Sect. 6.4.3). Mothers in Cohort 5 were born 20 years later than the mothers of Cohort 1, and so should have experienced prenatal and postnatal exposure to PCBs only after the PCB phase-outs (Quinn et al. 2011),

Table 3.29 Time series of blood POPs concentrations from the Faroe Islands Cohort 5 (2007–2009). All participants were Faroese women with their children born in 2007–2009. Data presented as geometric means (range). POPs in μg/kg plasma lipid. PFCs in μg/L. Source: Weihe pers. comm. (2013).

	2007-2009	2009-2011
Population	Mothers	Children
Mean age (range)	30.7 (17.2–49.4)	1.5 (1.4–1.7)
Sample size	n=500	n=363
p,p'-DDT	7.0 (0.1–110)	16.6 (15–194)
p,p'-DDE	131 (6.0–1517)	180 (15–4414)
DDE:DDT	19.6 (1.8–1030)	10.9 (0.7–294)
HCB	17.3 (3.0–116)	26.5 (15–144)
β-HCH	16.7 (2.0–110)	20.8 (15–296)
PCB118	14.8 (1.0–134)	29.7 (15–224)
PCB138	53.7 (3.0–383)	80.1 (15–796)
PCB153	91.2 (1.0–694)	105 (15–1214)
PCB180	60.1 (3.0–496)	61 (3.0–872)
ΣPCB[a]	420 (16–2965)	500 (70–5760)
PFOS	na	6.5 (1.4–28.3)
PFOA	na	2.9 (0.5–22.5)

[a](PCB138 + PCB153 + PCB180) × 2.

whereas mothers in Cohort 1 would have accumulated body burden during the years that PCBs were in use.

Even the ten-year difference in birth years between Cohort 3 and Cohort 5 mothers may affect the body burden accumulated. This may be indicated in the data with levels of all PCBs lower in Cohort 5 mothers than Cohort 3 mothers. Yet β-HCH levels in Cohort 5 mothers were twice those of Cohort 3 mothers. And, compared to Cohort 3, Cohort 5 maternal blood levels of *p,p'*-DDT were higher by one order of magnitude, while levels of *p,p'*-DDE were lower.

Cohort 5 children at 1.5 years of age had very similar blood concentrations to maternal blood concentrations at birth, but with higher *p,p'*-DDT and slightly higher *p,p'*-DDE. However, Cohort 5 children at 1.5 years of age had lower *p,p'*-DDE and ΣPCBs levels than 1.5 year olds in Cohort 3. This may be due to the positive effect of dietary advice in reducing exposure to PCBs and certain other lipophilic contaminants from the meat and blubber of pilot whale in particular (see Chap. 6, Sect. 6.4.3), also acknowledging that levels of POPs are generally declining in the environment and that children from Cohort 5 may thus be expected to have lower levels of POPs (Quinn et al. 2011). Cohort 5 children were also the first cohort to have PFOS and PFOA tested in blood at age 1.5 years.

3.4.5.2 Metals

Metals other than MeHg have not been a major focus of Faroese biomonitoring in recent years, and the dietary advice regarding pilot whale meat and blubber developed through the analysis of the results of the first cohorts has greatly reduced the extent of Hg exposure (see Chap. 6, Sect. 6.4.3). Table 3.30 shows the metals analyses from the four cohorts available, and Hg data are the most abundant. Comparing 7-year old children from Cohort 1 with 7.5-year olds from Cohort 3 shows the difference that approximately 20 years of dietary advice can make in addressing elevated levels of Hg, with measured levels decreasing from 8.36 to 1.99 µg/L. Even the 80% decline between the cord blood of Cohort 1 and Cohort 5 shows the great benefit recent lifestyle practices have had on levels of metals in the Faroese population. The decrease came in more recent years, probably after the 1998 recommendation to restrict pilot whale meat and blubber consumption came into effect (Weihe and Joensen 2012) (see Chap. 6, Sect. 6.4.3), because cord blood levels of Hg from Cohort 5 sampled in 2007–2009 were lower compared to those sampled in 1994–1995. Lead levels have also declined since 1986–1987, comparing the three data points available, although the most recent Pb concentration was in children 7 years of age, whereas the other two data points are from cord blood. There are not enough Se data to indicate a trend, and numbers taken from the 1986–1987 and 1994–1995 cord blood are fairly similar.

3.4.5.3 Conclusion

Overall declines in contaminant levels in the Faroese population provides insight into the impact of the recommendation in 1998 to reduce, and in 2008 to cease the use of pilot whale meat, blubber and internal organs for human consumption, and validation for the difficult public health risk management decision that was made. As indicated by Weihe and Joensen (2012), pilot whale harvesting had provided many Faroese with sustenance during times of food insecurity, but was also an important exposure source for contaminants. However, the known effects (see Chap. 4) of elevated levels of contaminants called for intervention for the health of the population. The risk communication of this public health decision is discussed in more detail in Chap. 6.

It is also possible that the concentrations of POPs which have been measured across three decades for the Faroese cohorts may be affected by the birth years of the mothers and their children relative to the implementation of global action to reduce production and use of POPs (Quinn et al. 2011), along with the timing and extent of changes to diets that included pilot whales and other traditional foods (Binnington et al. 2014).

3.4.6 Norway

The northern Norway mother-and-child contaminant cohort study (MISA study) is designed to investigate maternal concentrations of OCs and metals in the context of a northern-southern latitude perspective, to identify exposure predictors and investigate the influence of physiological changes and related pregnancy adaptations during the gestational and

Table 3.30 Time series of blood concentrations of metals from the Faroe Islands. Data presented as geometric means (range), in µg/L whole blood. Source: Heilmann et al. (2010); Weihe pers. comm. (2013); Tang-Péronard et al. (2014).

Cohort	Year	Sample size	Mean age (range)	Total Hg	Pb	Se
Cohort 1	1986–1987	1022	Cord blood	22.3 (0.9–350)	15.8 (1.0–110)	111 (69.4–217)
	1993–1994	922	7	8.4 (0.1–62.8)	na	na
	2000–2001	792	13.8 (12.8–15.1)	4.1 (0.3–39.8)	na	na
	2008–2009	849	22.1 (20.9–23.7)	2.5 (0.1–46.3)	na	na
Cohort 2	1994–1995	182	Cord blood	21 (1.9–102)	10.4 (1.2–41.4)	103 (77.1–158)
	2001–2002	158	7.5 (7.4–7.8)	3.2 (0.1–22.1)	na	na
Cohort 3	1998–2000	475	Cord blood	12.4 (1.6–193)	na	na
	2002–2005	555	5.0 (4.8–5.2)	2.6 (0.0001–36.5)	na	na
	2005–2007	498	7.5 (7.0–7.9)	2.0 (0.1–58)	6.2 (0.02–47.7)	na
Cohort 5	2007–2009	500	Cord blood	4.6 (0.8–44.5)	na	na
	2009–2011	363	1.5 (1.4–1.7)	1.4 (0.1–21.3)	na	na

postpartum periods. The work took place between 2007 and 2009, and included pregnant and delivering women from the MISA study (n=516). A suite of OCs, five toxic metals and five essential elements were analyzed (Hansen et al. 2010). More information on the MISA study is given in Chap. 2.

The Tromsø Study explored changes in POPs concentrations from 1979 to 2008 by following individuals over this period. Five surveys took place in Tromsø, northern Norway, in 1979, 1986–1987, 1994–1995, 2001 and 2007–2008. Sixty adult men were randomly selected from the total of 1438 participants, with the qualifier that they had donated blood in all five surveys. Fifty-three of the randomly selected men had sufficient remaining sample volumes in more than three sampling events. The range in birth years was 1925 to 1950, and the median ages at first and last sampling were 43 and 71, respectively (Nøst et al. 2013).

3.4.6.1 Persistent organics pollutants

Low maternal concentrations of contaminants were generally observed in the MISA study participants (Table 3.31, see also Appendix Table A3.14). Data are presented only in cases where detection frequencies were greater than or equal to 70%. Some contaminants were not reportable due to the coefficient of variation exceeding 70% and concentrations being too low, these include oxychlordane, *trans*-chlordane, *cis*-chlordane, *trans*-nonachlor, *cis*-nonachlor, heptachlor, Mirex, and PCB28, PCB52, PCB101, PCB105, PCB149, PCB156, and PCB194.

Comparing the northern Norway MISA data from 2006–2008 with data previously reported (AMAP 1998, 2003, 2009) (Table 3.32), the recent geometric mean of *p,p'*-DDE is almost half that reported in Bodø in 2004, although the range is wider. For PCB153, while the geometric mean for northern Norway participants is slightly higher than that reported for those in Bodø, with a wider range, the geometric means for participants from both Bodø and northern Norway show levels almost half those observed in 1996 in Kirkenes.

The MISA study showed links between traditional and store-bought food consumed, and measured serum concentrations of PFCs. In the MISA study women, levels of PFOS were greater than any other PFCs, followed by PFOA (Table 3.33). Berg et al. (2014) demonstrated that women consuming more marine food had significantly elevated concentrations of PFOS and other PFCs. Women who consumed a large amount of game had higher concentrations of PFHxS, PFHpS, and PFNA, while elevated concentrations of PFHpS and PFOS were detected in high consumers of white meat. There was also a relationship between the consumption of beef and salty snacks and higher PFOA concentrations. However, the strongest significant predictor of all the investigated PFCs was parity (Fig. 3.4), which resulted in lower maternal levels. Moreover, total months of breastfeeding were significantly associated with lower serum concentrations of PFHpS, PFOS and PFOA, across parity groups. While no association with age was observed for PFHxS, PFHpS, PFOS and PFOA concentrations, age was positively associated with PFNA, PFDA and PFUnDA concentrations. These observations may be explained by compound differences in half-lives, bioaccumulation potential and continued production after 2002 for PFNA, PFDA and PFUnDA (Armitage et al. 2009; Zhang et al. 2013).

Table 3.31 Concentrations of PCBs and OCs in pregnant women (early pregnancy) from northern Norway (mean parity = 0.9 (0–4)). Data presented as geometric means (range), in µg/kg plasma lipid. Average values presented for compounds with detection frequencies ≥70%. Source: Hansen et al. (2010).

	2006–2008
Mean age (range)	30.6 (18–43)
Sample size	n=515
trans-Nonachlor	2.8 (0.6–17.6)
cis-Nonachlor	0.6 (0.1–4.5)
p,p'-DDE	38.7 (10.9–351)
HCB	9.6 (3.5–53.3)
PCB99	2.2 (0.4–18.1)
PCB118	4.1 (1.0–38.3)
PCB138	14.9 (2.8–118)
PCB153	24.8 (5.3–201)
PCB180	16.5 (3.0–159)

For statistical purposes, all values below the limit of detection (LOD) were replaced by LOD/√2.

Table 3.32 Trends of OCs and PCBs in mothers from northern Norway (µg/kg plasma lipid). Data show geometric mean (range) for specified periods of sampling. Oxychlordane not available for northern Norway due to the coefficient of variation exceeding 70% and low concentrations. Source: Kirkenes (AMAP 1998), Bodø (SPFO 2005), northern Norway (Hansen et al. 2010; Odland pers. comm. 2014).

	Kirkenes	Bodø	Northern Norway
	1996	2004	2006–2008
Mean age (range)	29 (19–44)	30 (20–35)	30.6 (18–43)
Sample size	n=66	n=10	n=515
Oxychlordane	3.9 (1.6–11)	2.6 (1.0–6.1)	na
p,p'-DDE	79 (19–436)	67 (26–176)	38.7 (10.9–351)
PCB153	52 (25–130)	23 (10–50)	24.8 (5.3–201)

Table 3.33 Serum concentrations of PFCs (µg/L) in the northern Norway MISA study group (mean parity = 0.9 (0–4)). Data show arithmetic mean (range) for PFCs with detection frequencies greater than 50%. Source: Berg et al. (2014).

Mean age (range)	31 (18–43)	
Sample size	n=391	
	Median	Arithmetic mean (range)
PFHxS	0.4	0.6 (<LOD–14.8)
PFHpS	0.1	0.1 (<LOD–1.1)
ΣPFOS	8.0	8.8 (0.3–35.8)
PFOS Linear	4.7	5.1 (<LOD–19.1)
PFOS Branched	3.4	3.7 (<LOD–18.2)
% linear PFOS	59	59.1 (36–80)
PFOA	1.5	1.7 (0.3–11)
PFNA	0.6	0.7 (0.2–4.4)
PFDA	0.2	0.3 (0.05–2.3)
PFUnDA	0.3	0.3 (0.03–1.5)
PFDoDA	0.03	0.04 (<LOD–0.2)

LOD: Limit of detection; ΣPFOS = PFOS Branched + PFOS Linear; % linear PFOS = 100 × (PFOS Linear/ΣPFOS).

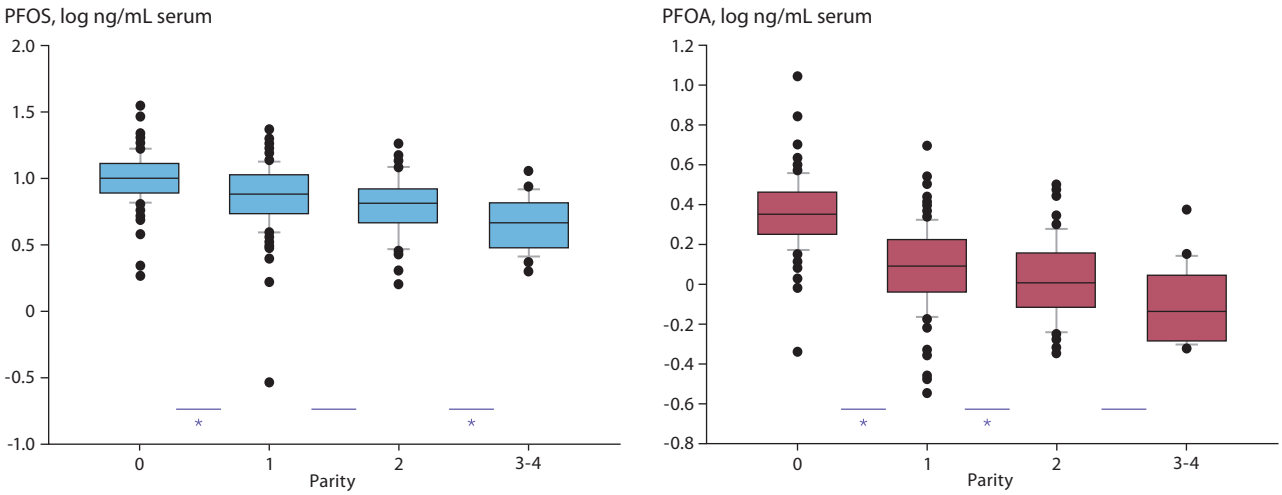

Figure 3.4 Concentrations of the two most prevalent PFCs in serum of pregnant women in the northern Norway MISA study, according to parity: 0 (n=150); 1 (n=135); 2 (n=69); 3-4 (n=24). Asterisk denotes significant differences between parity groups (p<0.05, pairwise comparisons: Bonferroni correction). Boxes represent the 25th to 75th percentiles, horizontal lines represent the median, and whiskers represent the 5th and 95th percentiles with outliers represented as data points. Source: Berg et al. (2014).

The Tromsø Study (Nøst et al. 2013) showed that levels of several POPs declined in the same Norwegian men between 1979 and 2007–2008 (identified as 2007), with significant declines observed for most POPs between pairs of five different consecutive sampling years (Fig. 3.5). *p,p'*-DDE and *p,p'*-DDT each declined at least 10-fold between 1979 and 2007. These two contaminants and HCB showed significant declines over the entire time frame. Parlar 50 (representing toxaphenes) and *trans*-nonachlor (representing the chlordanes) also showed significant differences between all consecutive sampling years. Both contaminants were

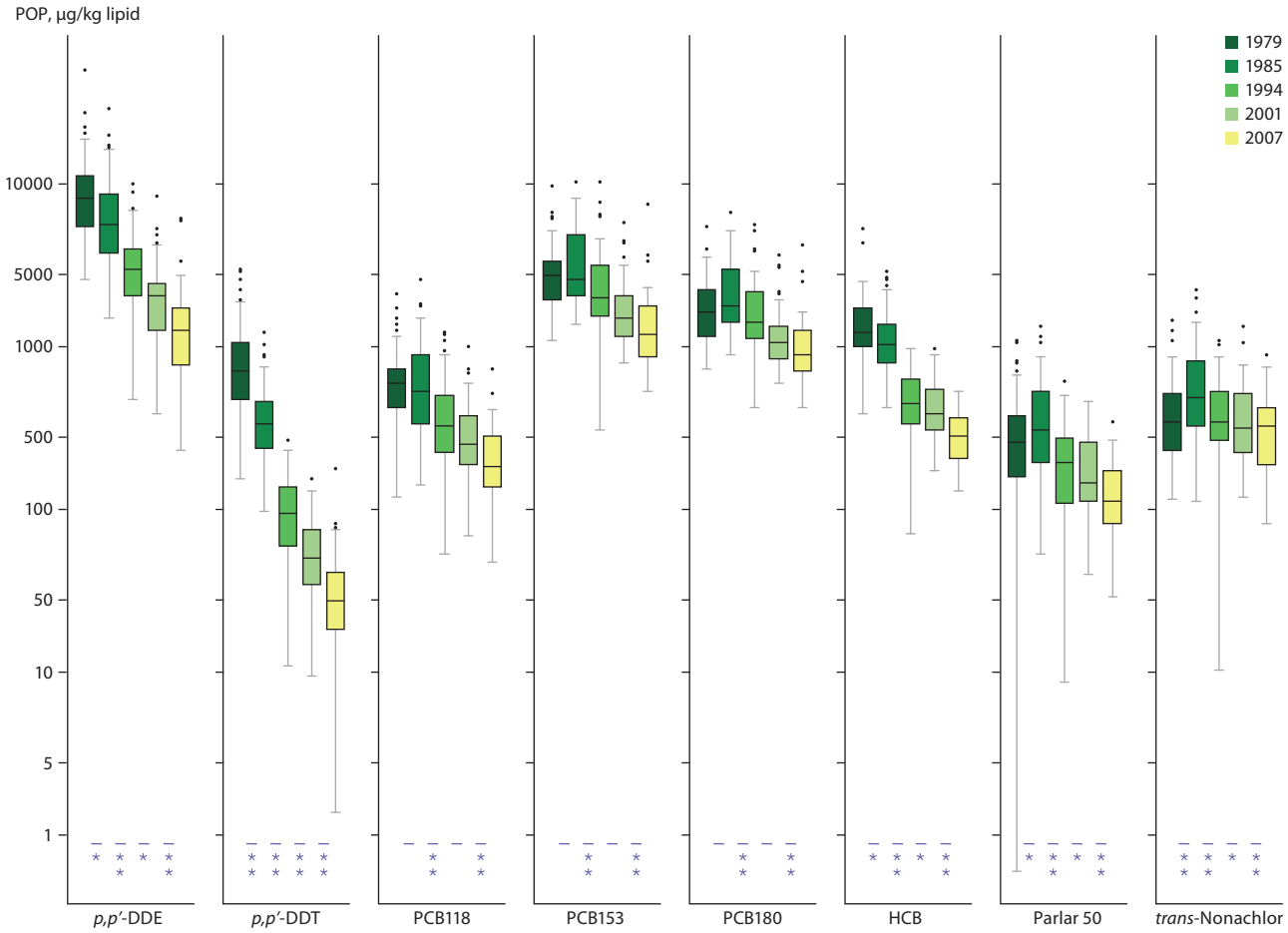

Figure 3.5 Concentrations (log$_e$ scale) of selected POPs analyzed in repeat serum samples of men (1979, n=51; 1985, n=51; 1994, n=45; 2001, n=48; 2007, n=52) from northern Norway. Parlar 50 represents toxaphenes and *trans*-nonachlor represents the chlordanes. Boxes represent the 25th to 75th percentiles, horizontal lines represent the median, whiskers indicate 1.5 times the length of the interquartile range above and below the 75th and 25th percentiles, respectively, and outliers are represented as data points. The asterisks denote significant differences (* p<0.05 and ** p<0.001) for comparisons between pairs of consecutive sampling years. Source: Nøst et al. (2013).

observed to increase between 1979 and 1986, but then declined. The smallest decline overall was for chlordanes. Each of three PCBs (PCB118, PCB153, PCB180) showed similar blood concentration patterns across 1979 and 2007, with two significant periods of decline, 1986 to 1994 and 2001 to 2007.

A similar analysis was performed by Nøst et al. (2014) for PFC concentrations in the same cohort of Norwegian men between 1979 and 2007 (Fig. 3.6). The highest measured concentrations were also for PFOS, in 2001; however, the greatest percentage change in concentration was for PFUnDA (850%) between 1979 and 1986. Three PFCs (PFDA, PFNA, PFOS) showed significant changes in concentration across all consecutive paired years; in all cases contaminant levels increased, the exception being a significant decline for PFOS in men between 2001 and 2007. PFOA and perfluorooctanesulfonamide (FOSA) also showed

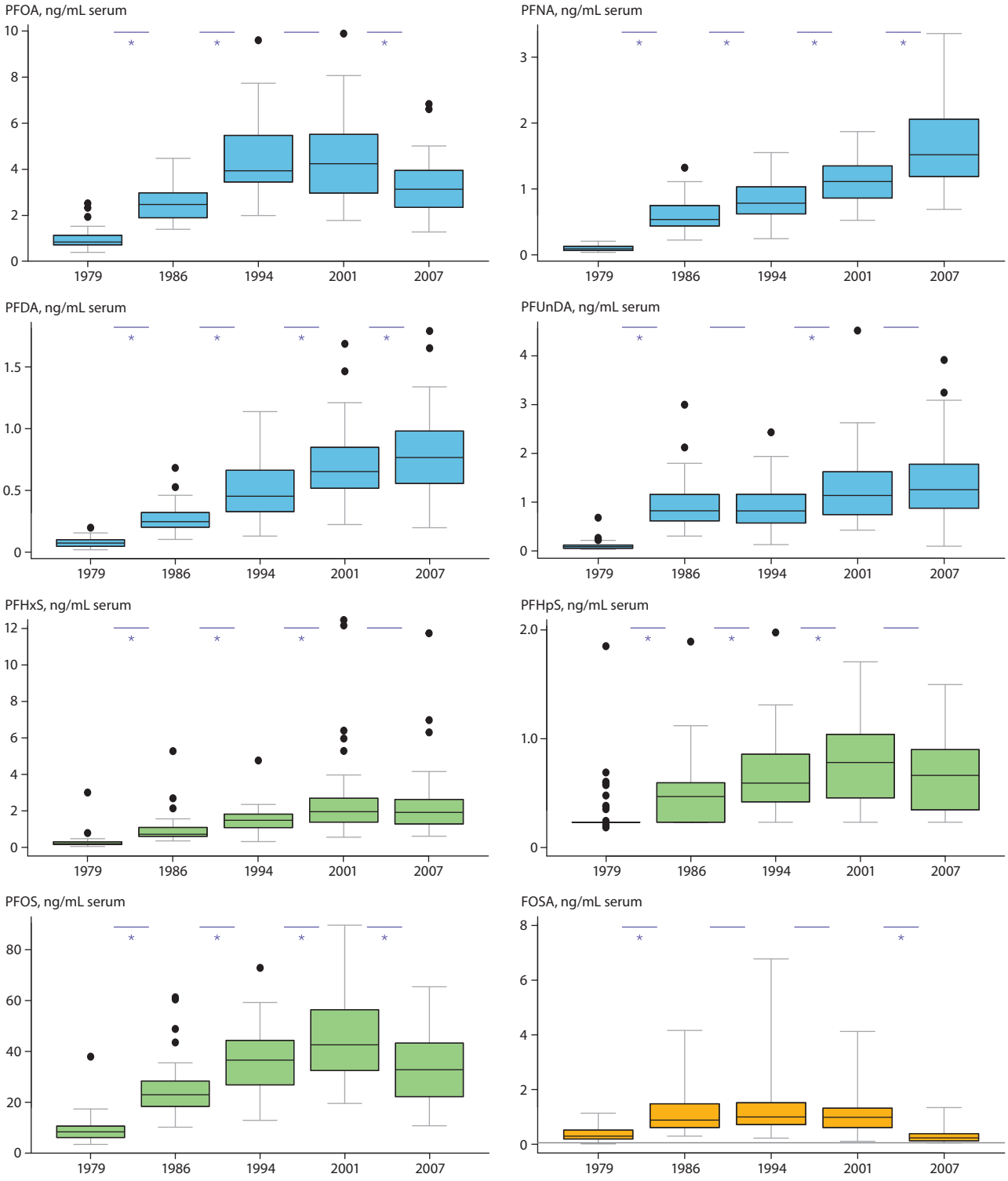

Figure 3.6 Concentrations of the most abundant PFCs analyzed in repeat serum samples of men from northern Norway (1979, n=53; 1986, n=52; 1994, n=48; 2001, n=49; 2007, n=52). The asterisks (*) denote significant differences in consecutive sampling years (p<0.001, Wilcoxon signed rank test). The boxplots for FOSA are censored box plots with the horizontal line indicating the limit of detection (LOD). One outlier for FOSA (13 µg/L) in 2001 is not shown. Source: Nøst et al. (2014).

Table 3.34 Concentrations of metals (µg/L whole blood) in pregnant women (early pregnancy) from northern Norway, in 1994–1995 and 2006–2008. Data presented as geometric mean [standard deviation] or geometric mean (range). Source: AMAP (1998), Hansen et al. (2011).

	Kirkenes	Hammerfest	Bergen	Tromsø	Northern Norway[a]
	1994	1994	1994	1995	2006–2008
Sample size	n=40	n=57	n=50	n=15	n=282
Total Hg	3.4 [±1.2]	2.5 [±0.8]	3.4 [±1.1]	na	1.2 (0.1–6.6)
Pb	12.4 [±6.2]	12.4 [±6.2]	14.5 [±6.2]	10.4 [±6.2]	7.4 (2.2–25.8)[b]
Cd	0.5 [±0.8]	0.5 [±0.6]	0.5 [±0.5]	0.4 [±0.5]	0.2 (0.04–2.7)
Se	124 [±15]	106 [±17.4]	107 [±18.2]	93.2 [±18.2]	84.7 (58.2–128)[c]

[a]Mean age (range)=30.6 (18–43), mean parity (range)=0.9 (0–4); [b]n=280; [c]n=281.

significant declines between 2001 and 2007, otherwise all other significant changes were for increasing levels of the eight most abundant PFCs in serum samples of men in this study.

3.4.6.2 Metals

Table 3.34 (see also Appendix Table A3.15) shows the most recent sampling of pregnant women in northern Norway (2006–2008) juxtaposed with metal levels in pregnant women in various regions of northern Norway in 1994–1995 (AMAP 1998). Levels are compared with specific cities in northern Norway that are geographically appropriate, as the MISA study populations lived in Nordland, Troms and Finnmark counties (Hansen et al. 2011).

Levels of Cd, Hg, and Pb have declined since 1994–1995 in pregnant women, which indicates that fetal exposure *in utero* has also declined. However, Se levels are also lower than those in 1994–1995, which could indicate a reduction in the consumption of marine mammals and fish. Fish consumption has been found to be a positive predictor for Se and Hg levels, along with multivitamin intake for Se (Hansen et al. 2011). Additionally, age reached significance only for Hg, while an inverse association was observed between parity and Hg. The observed concentrations for Pb and Cd suggest exposures from hunting traditional foods and smoking, respectively. Moreover, smoking may be increasing the body burden of Pb, reinforced by the association between Pb levels and Cd concentrations for smokers (Hansen et al. 2011).

3.4.6.3 Conclusion

Levels of most POPs have declined significantly since 1979 in a single cohort of Norwegian men. This is consistent with the expected reduction in environmental exposure following international action across several decades to reduce or eliminate production or use of POPs (Nøst et al. 2013). Several PFCs show no decline, however, while some even show increases in the same cohort of men in 2007–2008. Although trends in PFC concentrations tend to follow overall trends in production and usage, differences between individual compounds probably reflect differences in global transport mechanisms, bioaccumulation potentials and variations in consumer exposure. The influence of calendar year during sampling was evident for most POPs and PFC compounds (Nøst et al. 2013, 2014).

Berg et al. (2014) found parity to be a predictor of PFC body burden in pregnant women, and also that the relative importance of traditional and store-bought foods varied. Consumption of marine mammals and fish was associated with increased levels of PFOS, PFNA, PFDA and PFUnDA, while beef consumption was significantly associated with increased levels of PFOA. Consumption of game (e.g. reindeer, moose, grouse) was significantly associated with increased levels of PFHxS, PFHpS and PFNA. Seven of ten PFCs were measured in the majority of women (>80%) from this study during the period 2007–2009, suggesting that ongoing monitoring of these compounds is warranted to determine long-term trends in pregnant women following the decline in PFC production and use.

Three studies spanning 1996 to 2008 indicate a decreasing trend for several POPs in pregnant women, highlighted in Table 3.32 with the key contaminants oxychlordane, *p,p*'-DDE and PCB153.

Concentrations of metals declined in pregnant women in northern Norway during a similar period, but seafood consumption may have also declined, as noted through a coincident decrease in Se levels. According to Hansen

Table 3.35 Concentrations of contaminants in the general population of Sweden, (maximum). Data from the Riksmaten 2010–2011 study. Data adjusted for age, µg/L. Source: Bjermo et al. (2013a,b,c).

	Lund	Gothenburg region
Oxychlordane	2.3 (2.0–3.1)	1.8 (1.4–2.3)
trans-Nonachlor	4.7 (3.7–6.0)	3.5 (2.7–4.5)
p,p'-DDT	na	na
p,p'-DDE	98.7 (68.9–141)	68.5 (46.4–101)
HCB	14 (11.9–16.6)	10.7 (9.0–12.7)
β-HCH	5.9 (4.5–7.8)	3.1 (2.3–4.3)
PCB118	6.4 (4.7–8.4)	4.3 (3.1–5.9)
PCB138	35.9 (28.5–45.3)	23 (18–29.7)
PCB153	76.9 (62.4–94.8)	53.3 (42.5–66.9)
PCB180	48.2 (39.4–58.9)	35.7 (28.7–44.5)
PFHxS	1.7 (1.3–2.2)	1.3 (1.0–1.7)
PFOA	2.1 (1.6–2.6)	1.6 (1.3–2.1)
PFOS	8.7 (7.1–11)	7.0 (5.7–8.6)
PFDA	0.3 (0.2–0.4)	0.3 (0.3–0.4)

[a]n=267; [b]n=292.

et al. (2011), the recent metal concentrations are considered relatively low and not of clinical importance for WCBA and their children.

3.4.7 Sweden

Several biomonitoring studies have recently been undertaken in Sweden. The population-based Northern Sweden Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Study is performed approximately every five years, a part of which involves the collection of biomonitoring samples from adults living in the two northernmost counties of Sweden (Norrbotten and Västerbotten) for environmental exposure to certain contaminants (Wennberg et al. 2006). The most recent sampling of this population was carried out in 2014. The samples obtained have all been analyzed and the data are currently being analyzed (MONICA 2014).

Two biomonitoring reports were commissioned by the Swedish Environmental Protection Agency (EPA). The first was a follow-up to the health related environmental monitoring (HAMI) that began in 1994 to analyze concentrations of Hg in women from Sweden's northern, southern and western regions (Barregård 2006). Using the established HAMI methodology, samples of blood and hair were taken from early- and late-term pregnant women in these regions between 2001 and 2004. The purpose of the second study was to analyze concentrations of Pb, Hg and Cd in non-pregnant young and middle-aged women from the two northernmost counties (Norrbotten and Västerbotten) and the southernmost county (Skåne) (Wennberg et al. 2007). Samples analyzed for the second study were taken between 2004 and 2007.

In 2010–2011, a national food consumption survey was performed by the Swedish National Food Agency, the Riksmaten 2010–11 study, which included biomonitoring sampling. In total, 5000 adults (18–80 years old) from all parts of the country were asked to register their dietary habits during four days. Blood and urine samples were taken from a randomly recruited subgroup of participants (n=297). Data were adjusted for age, sex and education using a linear model, as described by Bjermo et al. (2013a,b,c).

Additional small investigations of contaminant levels in the Swedish population are also reported in this section.

3.4.7.1 Persistent organic pollutants

In the general population biomonitoring study, the Riksmaten 2010–11 study, only small regional differences in the mean levels of a few pollutants in serum were found, with the highest levels in southern (PCBs, PFOS, PFOA) or east-central Sweden (HCB, β-HCH) after statistical adjustment of the results for age, sex, education level and body mass index (Bjermo et al. 2013a) (Table 3.35, Appendix Table A3.16). Generally, the highest mean level of POPs was approximately 30% to 50% higher than the lowest across all regions (Bjermo et al. 2013a). Regional differences were observed in all PFCs, with the exception of PFNA. Median levels of PFOS and PFOA were 60% to 70% higher in Lund than in Umeå. Bjermo et al. (2013c) also examined very long-chain fatty acid levels in blood as a biomarker for fish consumption, and found that they were stronger predictors of PFOS, PFNA, PFDA and PFUnDA than the fish consumption results calculated from dietary records and questionnaires. Fish consumption was positively associated with levels of some highly chlorinated PCB congeners, *trans*-nonachlor, oxychlordane, *p,p'*-DDE, and some PFCs. There was also a positive association between serum PFOS and potato consumption, although it did not remain statistically significant after the data were adjusted for age, sex and education (Bjermo et al. 2013c). The highest median levels of PFHxS were found in Stockholm and Uppsala, and it was suggested that this may be due to drinking water contamination, potentially from fire-fighting foams. The northernmost city (Umeå in Västerbotten

by region arranged south to north. Data presented as arithmetic mean (95% confidence interval), except for the collective Sweden data which are the median sex and education. Data lipid-adjusted as by Bjermo et al. (2013b) using 0.5% as per Glynn et al. (2000). PCBs and OCs in μg/kg plasma lipid and PFCs in

Linköping	Stockholm	Örebro	Uppsala	Umeå	Sweden (maximum)
2.1 (1.7–2.9)	2.3 (1.8–2.9)	2.1 (1.7–2.7)	2.1 (1.7–2.7)	2.0 (1.5–2.5)	3.2 (26.4)[a]
3.9 (3.1–4.9)	4.5 (3.5–5.9)	3.9 (3.1–5.1)	4.1 (3.3–5.3)	3.9 (3.1–5.1)	6.9 (52.1)[a]
na	na	na	na	na	1.6 (29.7)[a]
69.9 (48.6–100)	93.7 (64.2–137)	72.8 (50–106)	87.8 (60.9–127)	70.8 (49.2–102)	84.8 (3023)[a]
12.9 (10.9–15.4)	15 (12.7–18)	11.7 (9.8–13.9)	11.9 (10–14)	12.9 (10.9–15.2)	15.4 (152)[a]
4.5 (3.3–6.0)	5.1 (3.9–6.8)	3.7 (2.9–5.1)	3.5 (2.7–4.7)	3.9 (2.9–5.3)	5.1 (71.9)[a]
5.5 (4.1–7.2)	6.6 (4.9–9.0)	5.3 (3.9–7.2)	5.3 (3.9–7.0)	6.6 (4.9–9.0)	7.3 (190)[a]
27.3 (21.7–34.7)	29.5 (23–37.7)	27.3 (21.5–34.9)	27.9 (22–35.3)	31 (24.6–39.4)	36.9 (283)[a]
61.3 (49.6–75.7)	62.2 (49.8–77.7)	58.5 (47–73)	61.7 (49.8–76.5)	62.6 (50.5–77.7)	87.7 (544)[a]
39.8 (32.4–49)	38 (30.8–47.2)	36.1 (29.1–44.5)	39.6 (32.2–48.6)	35.7 (29.1–43.9)	71.1 (307)[a]
1.5 (1.2–2.0)	2.8 (2.1–3.8)	1.5 (1.2–2.0)	2.3 (1.8–3.1)	1.3 (1.0–1.7)	2.0 (49.6)[b]
2.0 (1.6–2.6)	2.4 (1.9–3.0)	1.9 (1.5–2.4)	1.7 (1.3–2.1)	1.4 (1.1–1.7)	2.3 (9.5)[b]
7.7 (6.3–9.3)	8.8 (7.1–11)	7.6 (6.2–9.3)	7.2 (5.9–8.8)	6.3 (5.1–7.7)	11.1 (40.1)[b]
0.3 (0.3–0.4)	0.3 (0.3–0.4)	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.2 (0.2–0.3)	0.4 (2.0)[b]

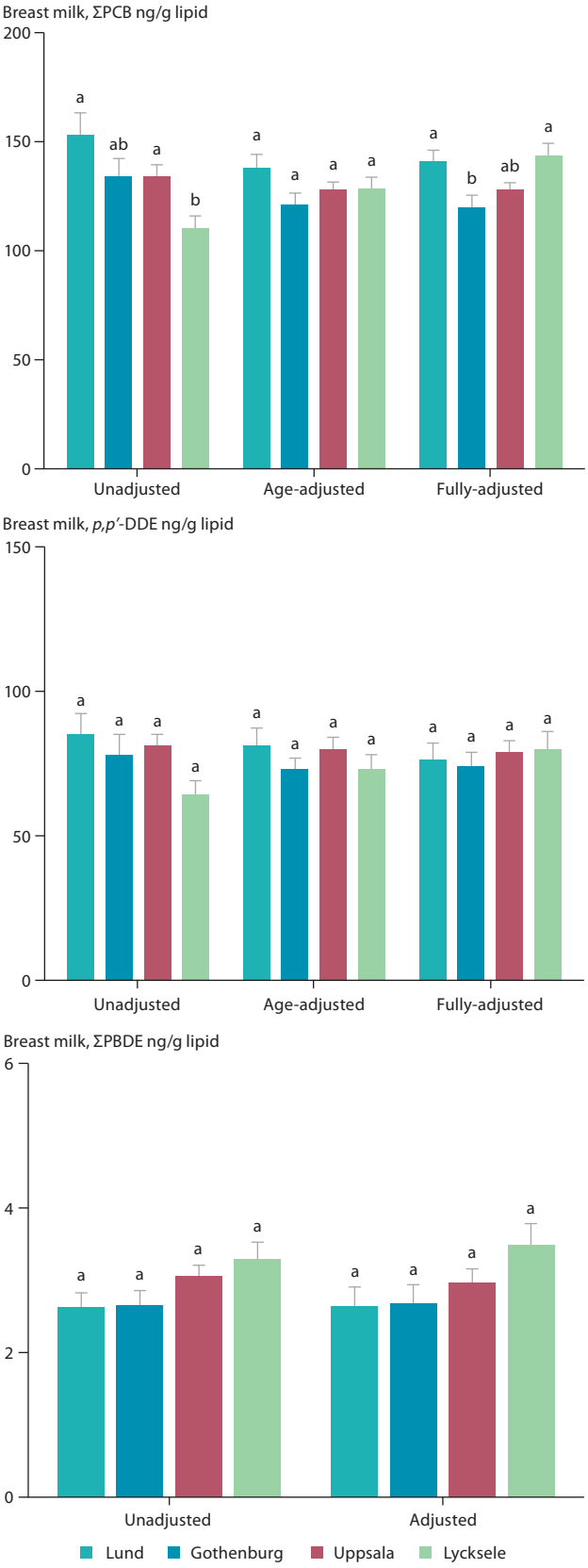

Figure 3.7 Un-adjusted, age-adjusted and fully-adjusted geometric means (standard error, SE) of ΣPCB and *p,p´*-DDE, and un-adjusted and adjusted geometric means (SE) of ΣPBDE in breast milk from first-time mothers living in different areas of Sweden in 2002–2004. Results presented by bars with at least one common letter did not differ significantly. Fully-adjusted data include the independent variables: age, weight gain during pregnancy, weight loss between delivery and milk sampling, and education level for *p,p'*-DDE; for ΣPCB, pre-pregnancy body mass index was also added to the aforementioned variables; for ΣPBDE, smoking during pregnancy was added to all of the aforementioned variables. Source: Glynn et al. (2011a).

county) mainly showed lower concentrations of contaminants but there was no consistent north-south gradient. The data were lipid-adjusted using the estimated lipid conversion factor of 0.5% used by Bjermo et al. (2013b) from Glynn et al. (2000). The wet weight values are presented in Appendix Table A3.17.

Breast milk was sampled in four different geographical locations from a total of 204 randomly recruited first-time mothers three weeks after delivery in 2000–2004. The study areas were chosen because they were both geographically and demographically well separated, in order to improve the possibility that regional differences may be detected. For compounds and compound groups that showed statistically significant temporal trends in the Uppsala group, the measured individual concentrations from all regions were back-calculated to 1 January 2000 ('un-adjusted'). As expected, mother's age was a strong determinant of mother's breast milk levels for many of the compounds, thus age-adjusted geometric means were calculated separately for ΣPCBs and *p,p'*-DDE (see Fig. 3.7). Fully adjusted geometric means were also calculated for these contaminants and ΣPBDEs after considering significant independent lifestyle and medical variables (Glynn et al. 2011a).

Mothers from the Lycksele area, who were on average 2–3 years younger than women from the other regions, tended to have lower median levels of individual PCB congeners (Glynn et al. 2011a). However, after fully-adjusting the data, Lycksele women showed the highest ΣPCB levels of all regions sampled. Fully-adjusted concentrations of ΣPCBs in the population from Lund were also significantly higher than for women from Gothenburg, however the populations in Lund and Lycksele were not significantly different from each other. No significant differences were seen in either fully adjusted or un-adjusted levels of *p,p'*-DDE between the different geographical locations. While levels of PBDEs did not show significant differences either, about 50% of the women with ΣPBDE levels exceeding 10 µg/kg lipid in this study came from the Lycksele region (Glynn et al. 2011a). The reason for this observation was not determined. Including food consumption variables did not change the observed differences.

A time series from 1996 to 2012 of POPs (Fig. 3.8) in breast milk samples from Swedish first-time mothers in Uppsala shows a steady decline in all contaminants analyzed except PBDE153 (Lignell et al. 2014). PBDE153 fluctuated only marginally over the time series, reaching its highest concentration in 2004–2006, with an unclear pattern in recent years. A similar time series for PFCs (Fig. 3.9) was analyzed in blood samples from Swedish first-time mothers, between 1996 and 2010 (Glynn et al. 2011b, 2012). PFOS and PFOA both have a general declining trend with few data points that fall outside that trend; however PFHxS and PFDA both show an increase over time (Kärrman et al. 2007; Gyllenhammar et al. 2013; Lignell et al. 2012, 2013).

3.4.7.2 Metals

In the follow-up HAMI study, a comparison was made of Hg in blood and hair from pregnant women in Sweden's north (the northern part of Västerbotten county, 2003–2004), south (Hässleholm and Simrishamn, 2002–2003) and west (Gothenburg and Lysekil, 2001) (Table 3.36) (Barregård 2006). Mercury concentrations were higher in blood and

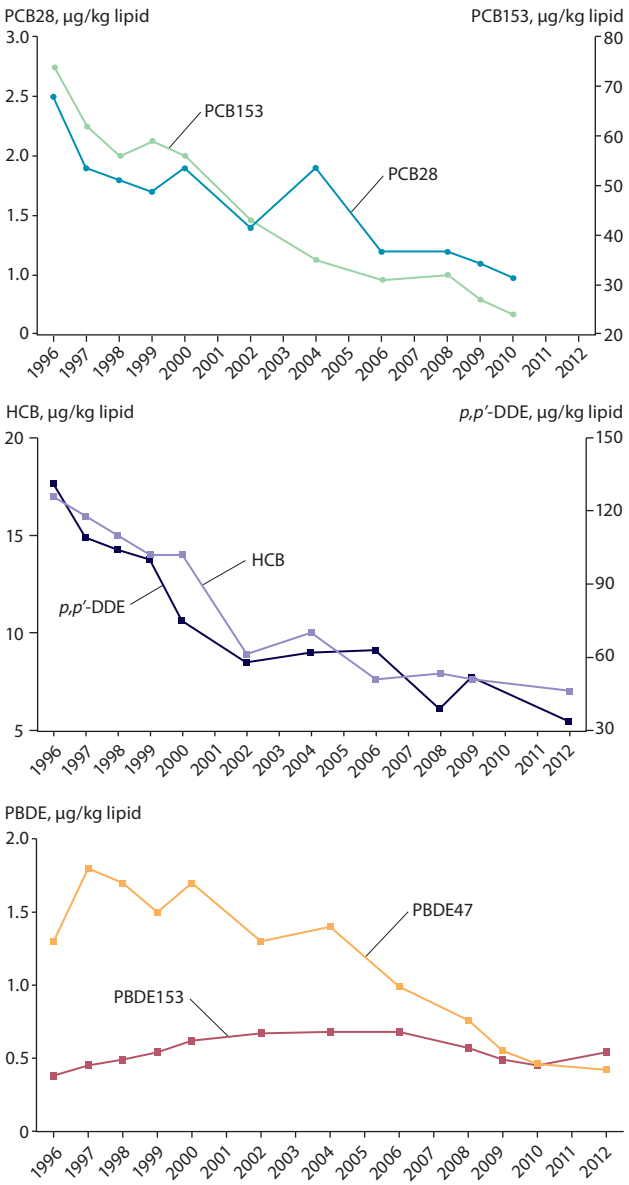

Figure 3.8 Trends in POPs concentrations in breast milk samples from Swedish first-time mothers (µg/kg lipid). Samples collected three weeks after delivery. Data are presented as median concentrations and tabulated in Appendix Table A3.18. Source: Lignell et al. (2014).

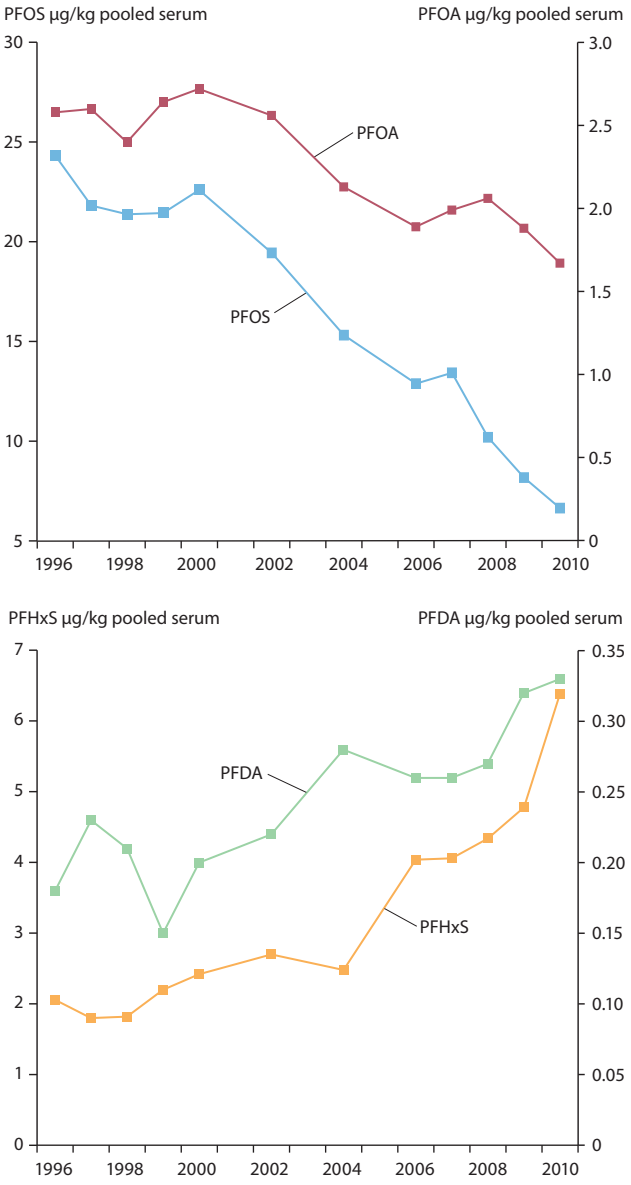

Figure 3.9 Trend in PFC concentrations (µg/kg pooled serum) in blood drawn three weeks after delivery from nursing Swedish first-time mothers. Three pools per year analyzed, with serum from 5 to 25 individuals in each pool. Data are presented as geometric means and tabulated in Appendix Table A3.19. Source: Glynn et al. (2011b, 2012).

hair in western Sweden, with a median level of 1.2 µg/L in whole blood, which is probably mainly due to the higher fish consumption in that area (Barregård 2006; Bergdahl et al. 2006). By contrast, none of the 96 women sampled in Västerbotten had hair-Hg concentrations above 1 µg/g (Naturvårdsverket 2007). Despite women from southern Sweden eating more fish per week than those in Västerbotten, Hg levels in blood and hair were comparable, and blood MeHg levels were higher in Västerbotten.

Mercury in hair from pregnant women has been determined on an annual basis in east-central Sweden, in Uppsala County, by Official Statistics of Sweden (Fig. 3.10). No strong time trend has been shown, but a slight decrease during the last 10–15 years is suggested, with medians of 0.23–0.35 µg/g in 2010–2013, compared to 0.36–0.39 µg/g in 2000 (Official Statistics of Sweden 2014). The levels in pregnant women in Uppsala are higher than levels measured in northern or southern Sweden, but lower than in western Sweden (Table 3.36).

Table 3.36 Median concentrations of Hg in blood (µg/L) and hair (µg/g) in pregnant women in northern, western, and southern Sweden. Source: Barregård (2006); Naturvårdsverket (2007).

	Year	Sample size	Age (median)	Hg in blood	MeHg in blood	Hg in hair	Fish (≥once/week)
Västerbotten (North)	2003–2004	96	28	0.6	0.5	0.19	38%
Gothenburg and Lysekil (West)	2001–2002	99	30	1.2	0.7	0.43	62%
Hässleholm and Simrishamn (South)	2002–2003	100	30	0.6	0.3	0.22	50%

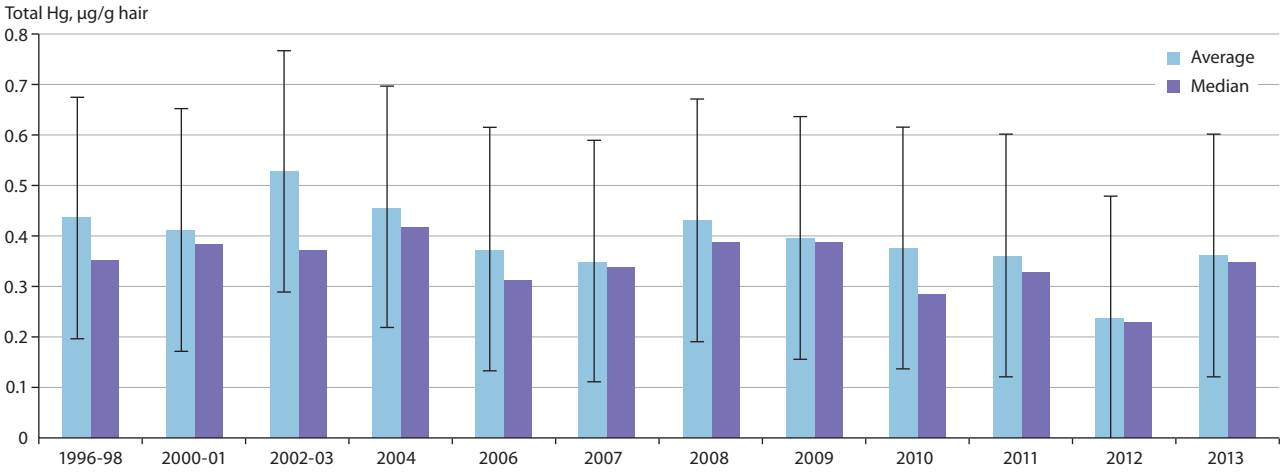

Figure 3.10 Total Hg in hair in first-time mothers, Uppsala County, 1996–2013. Source: Official Statistics of Sweden (2014).

On behalf of the Swedish EPA, Wennberg et al. (2007) measured concentrations of Cd, Hg and Pb in young (20–35 years) and middle-aged (50–60 years) women of southern (Skåne) and northern Sweden (Norrbotten and Västerbotten) (Table 3.37), and results were separated by smoking behavior. The variation in levels between smoking and non-smoking women was not large. Generally, levels of Cd and Pb were higher in the population that included smokers than in non-smokers. Mercury did not show this pattern, as non-smokers from Skåne had higher levels than the entire population. In the young women, levels between Skåne and northern Sweden for Cd and Pb were comparable, with the northern Sweden population having slightly higher levels of Hg than Skåne. In the middle-aged population, Cd and Hg patterns were similar, with slightly lower levels of Pb in the northern population. However, differences within the region between the two age groups showed that older women had higher levels of these three metals than the younger population. This is to be expected due to lifetime bioaccumulation of certain contaminants, such as Pb. Blood concentrations of other contaminants with short half-lives relative to Pb or POPs, such as MeHg, are expected to be more reflective of recent exposure. The similarity of blood Hg levels for the middle-aged women (Table 3.37) to pregnant women from western Sweden (Table 3.36), the majority of whom reported weekly consumption of fish, suggests both populations may be experiencing higher dietary exposure than other age or regional groups also reported in these studies (Table 3.36).

From the Riksmaten 2010–11 study, concentrations in the general population were comparable (Table 3.38) to those seen in Skåne and Norrbotten and Västerbotten women, and there was very little regional variation. There were no perceptible north-south trends in the regions sampled. In fact, the more northerly regions had lower levels of Hg, Pb and Cd than Stockholm. Fish consumption was positively associated with Hg level, with levels increasing with increased fish consumption. As previously noted, populations in southern and western Sweden were found to eat more fish than in Västerbotten. It has also been suggested that Skåne may receive more Cd via long-range transport (WHO 2007), and has higher levels of naturally occurring Cd in bedrock, leading to locally grown food as a potential source of Cd exposure (Wennberg et al. 2007).

Table 3.37 Concentrations of total Hg, Pb and Cd in blood (µg/L whole blood) represented as median (range) from 501 young and middle-aged women from Skåne (southern Sweden) and Norrbotten and Västerbotten (northern Sweden) with a subset of 258 young and middle-aged women who have never smoked. Source: Wennberg et al. (2007).

Age	Contaminant	Skåne, 2006–2007		Norrbotten and Västerbotten, 2004	
		All	Never smoked	All	Never smoked
20–35	Total Hg	0.5 (0–5.3)	0.6 (0–5.3)	0.8 (0.04–2.7)	0.7 (0.04–2.7)
	Pb	9.7 (3.7–120)	8.7 (3.7–120)	10 (4.9–70)	11 (4.8–70)
	Cd	0.2 (0.09–2.0)	0.2 (0.09–0.6)	0.2 (0.07–3.0)	0.1 (0.07–0.4)
50–60	Total Hg	1.4 (0.01–9.8)	1.5 (0.2–3.4)	1.5 (0.04–7.1)	1.7 (0.3–7.1)
	Pb	19 (4.5–110)	18 (7.9–110)	15 (6.0–60)	14 (6.0–45)
	Cd	0.4 (0.1–2.7)	0.3 (0.2–2.2)	0.3 (0.09–2.0)	0.2 (0.09–0.7)

Table 3.38 Concentrations of metals in the general population of Sweden, by region arranged south to north. Data presented as arithmetic mean (95% confidence interval), except for the collective Sweden data which are the median (maximum). Data from the Riksmaten 2010–2011 study. Data adjusted for age, sex and education and presented in µg/L whole blood. Source: Bjermo et al. (2013a).

	Lund	Gothenburg region	Linköping	Stockholm	Örebro	Uppsala	Umeå	Sweden (maximum)
Total Hg	0.9 (0.6–1.2)	1.1 (0.8–1.6)	0.8 (0.6–1.1)	1.0 (0.7–1.3)	0.8 (0.6–1.1)	0.7 (0.5–1.0)	0.7 (0.5–1.0)	1.1 (15.6)[a]
Pb	12 (9.6–14)	12 (9.7–15)	11 (9.5–14)	14 (11–17)	11 (9.3–14)	12 (9.7–14)	11 (9.1–13)	13.4 (102)[a]
Cd	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.3 (0.2–0.4)	0.5 (0.3–0.6)	0.3 (0.2–0.4)	0.3 (0.2 –0.4)	0.3 (0.2–0.4)	0.2 (2.9)[a]

[a]n=297.

An analysis of Hg levels in blood in men and women from Västerbotten showed that women 25–35 years of age had slightly higher levels of Hg than men of the same age (Table 3.39) (Sundkvist et al. 2011). In the 50–60 year age bracket, levels were more similar, although men who had never smoked had slightly higher levels than women in 2009. Smoking status did not have a clear association with Hg level. The change in Hg levels between 2004 and 2009 for women also showed no clear trend, as non-smoking 25–35 year olds saw an increase in blood Hg, while the entire population of 25–35 year olds and the 50–60 year old women both had a slight decrease. The 50–60 year old population for both men and women had higher Hg levels than for 25–35 year olds, as seen by Wennberg et al. (2007), suggesting a potential difference in fish or seafood consumption between age groups.

There is a trend of decreasing blood Pb concentrations in men in northern Sweden (Sundkvist at al. 2011) (Fig. 3.11; see also Appendix Table A3.20). Both the 25–35 year-old and 50–60 year-old populations show a decrease in blood Pb since 1990, although a small increase was seen in 1994 for the 50–60 year-old population. The impact of smoking status on blood Pb seems to decrease the variation of measured blood Pb concentrations, as the non-smoking populations tended to have smaller ranges than the entire population including smokers, especially in 1994 and 1999. The trends of blood Pb concentration in women over the same period also indicate a decline from 1990 to 2009 (Fig. 3.12; see also Appendix Table A3.20), although in the latter years, more extremes and outliers are seen in the overall population (Fig. 3.12a). For both populations, it is visually apparent that the

Table 3.39 Concentrations of total Hg (µg/L whole blood) in men and women grouped by age (25–35 years and 50–60 years) and smoking behavior from Västerbotten for 2004 (women only) and 2009 (women and men). Data show median (range). Source: Sundkvist et al. (2011).

	Women				Men	
	2004		2009		2009	
	Median (range)	n	Median (range)	n	Median (range)	n
25-35						
All	0.8 (0.04–2.7)	164	0.8 (0.06–4.1)	91	0.6 (0.06–3.6)	68
Never smoked	0.8 (0.04–2.7)	111	0.8 (0.06–4.1)	64	0.6 (0.06–3.6)	57
50-60						
All	1.4 (0.04–7.1)	123	1.3 (0.2–6.4)	86	1.1 (0.1–5.4)	82
Never smoked	1.6 (0.3–7.1)	54	1.2 (0.4–3.0)	35	1.6 (0.4–5.4)	32

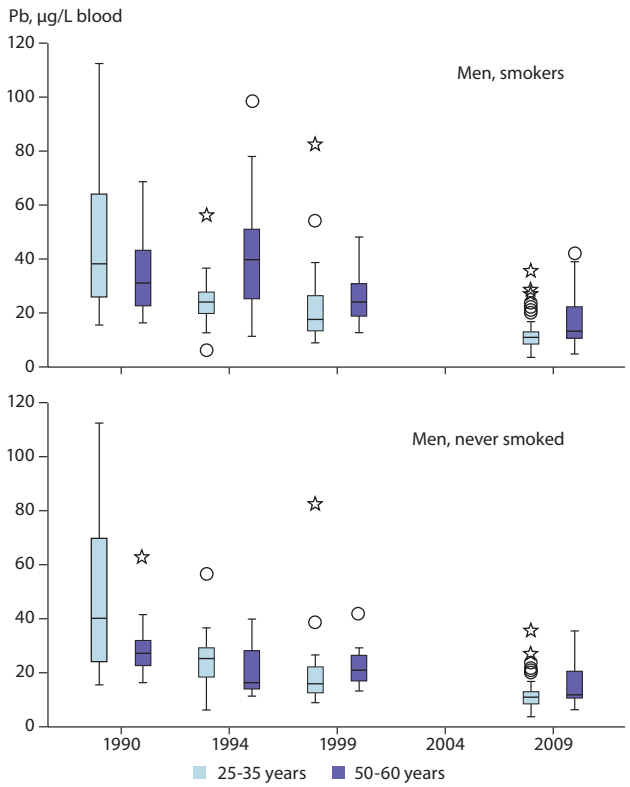

Figure 3.11 Trends in blood Pb concentration between 1990–2009 in men in northern Sweden, in the 25–35 and 50–60 year-old age groups; all men (n=291, upper) and men who have never smoked (n=165, lower). Each box shows the median and quartiles, whiskers represent minimum and maximum after removal of outliers and extremes. Outliers (○) and extremes (*) are shown. Source: data from Sundkvist et al. (2011).

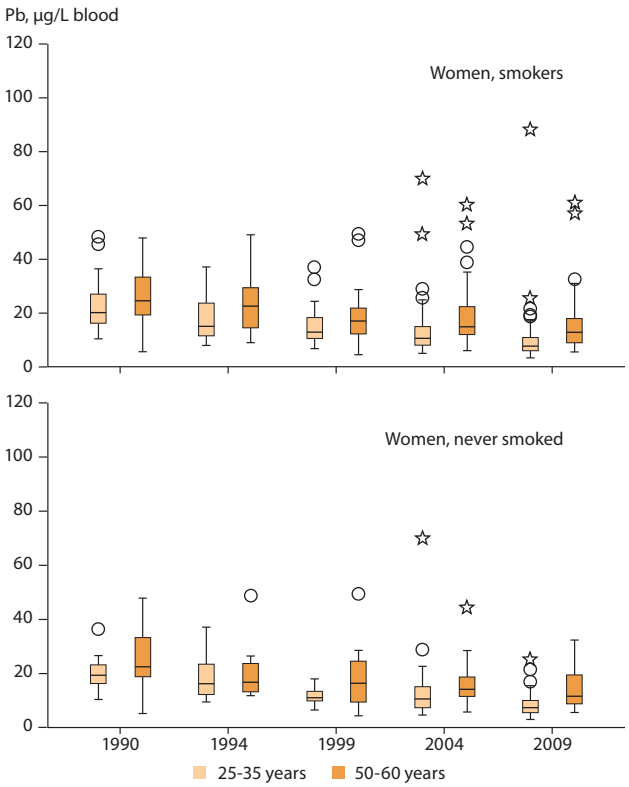

Figure 3.12 Trends in blood Pb concentration between 1990–2009 in women in northern Sweden, in the 25–35 and 50–60 year-old age groups; all women (n=615, upper) and women who have never-smoked (n=342, lower). Each box shows the median and quartiles, whiskers represent minimum and maximum after removal of outliers and extremes. Outliers (○) and extremes (*) are shown. Source: data from Sundkvist et al. (2011).

50–60 year-old population generally has higher blood Pb levels than the 25–35 year-old population, with the exception of the general population of men from 1990, where the younger age bracket median was above that of the 50–60 year-old bracket. However, these relationships may not be significant. Similarly, within the non-smoking male population, the median for the younger age bracket exceeded that of the middle-aged bracket for both 1990 and 1994.

Of regional concern is the higher consumption of game meat, such as reindeer and moose, in northern Sweden compared to many other regions of Sweden. Results from the Riksmaten 2010–11 study showed higher blood Pb levels among those consuming more game according to the food frequency questionnaire (Bjermo et al. 2013d). In this case, a possible source of Pb could be fragments of lead shot present in the game meat.

See Appendix Table A3.21 for trends in blood Cd concentration in men and women in northern Sweden between 1990–2009, grouped by age (25–35 years and 50–60 years) and smoking behavior.

3.4.7.3 Emerging contaminants

The DemoCophes Sweden study population included children aged 6–11 years of age and their mothers aged 45 years or under. The Uppsala area of central Sweden and a part of Västerbotten in northern Sweden were chosen as study areas, and the biomonitoring markers tested were expanded to include phthalates, Bisphenol A (BPA), and parabens (Democophes 2014; Democophes-Cophes 2014). Urinary concentrations of contaminants in mothers and children (Table 3.40) show different levels of excretion for certain biomarkers. Children had significantly higher levels of phthalates, with the exception of monocarboxylated mono-*iso*-nonylphthalates (cx-MiNP). Mothers had significantly higher levels of parabens compared to children, some five times higher. Children's urinary BPA levels were significantly higher than maternal urinary levels. In mothers, certain phthalate metabolites were associated with cosmetics such as fragrances, the use of sunscreen, decreased meat consumption and increased chocolate or fast food consumption. For children, certain phthalate metabolites were associated with increased ice cream consumption, rural versus urban living area, the use of eye makeup or decreased meat consumption. Both maternal and child paraben levels were associated with cosmetics and personal care product use, such as lotion, shampoo or sunscreen (Larsson et al. 2014).

Compared to the Riksmaten (2010–2011) general population study (Table 3.41), which is adjusted for age, sex and education, maternal BPA levels in Table 3.40 were lower than adjusted general population levels, whereas children's BPA levels agreed well with the median for all of Sweden at 1.6 µg/g creatinine. Adjusted general population levels of mono-ethyl phthalate (MEP) were higher in all regions than those found in mothers and children. For the less persistent phthalates, adjusted mean levels of a few metabolites in urine were slightly higher in the northern part of Sweden, but in most cases no regional differences were found. No regional differences were found in BPA levels in urine. No consistent trend is found for the measured phthalate metabolites. Only mono-*n*-butyl phthalate (MnBP) and monobenzyl phthalate (MBzP) show an increasing trend in urinary levels south to north. Levels of mono(2-ethyl-5-hydroxyhexyl) phthalate (5-OH-MEHP) are similar through most regions of Sweden, with only an increase to 27 µg/g creatinine in Umeå, whereas MEP shows a large decrease in Umeå compared to locations further south. This suggests that sources of exposure for these contaminants are generally similar throughout Sweden. Those that show more of a trend or a difference between regions may warrant further investigation.

Table 3.40 Concentrations of contaminants in urine (µg/g creatinine) from mothers and children in Sweden. Data presented as geometric mean (range). Data from the DemoCophes Sweden (2010–2012) study. Source: Larsson et al. (2014).

	Mothers			Children		
		n	Significantly higher level in mothers ($p<0.05$)		n	Significantly higher level in children ($p<0.05$)
MEHP	2.2 (<LOD–33.4)	95		3.1 (0.2–24.2)	97	✓
5-OH-MEHP	14.1 (2.4–218)	95		27.8 (6.7–237)	97	✓
5-oxo-MEHP	8.2 (0.9–99.3)	95		17.7 (4.4–87.8)	97	✓
5-cx-MEPP	10.9 (3.0–122)	95		24.3 (7.0–224)	97	✓
MBzP	12.1 (1.5–209)	95		22.5 (9.3–142)	97	✓
MnBP	59.4 (15.8–418)	95		86.8 (19.5–621)	97	✓
MEP	40.9 (5.3–464)	95		32.6 (5.1–2146)	97	
cx-MiNP	18.6 (2.8–1137)	95		24.5 (3.5–2675)	97	
OH-MiNP	7.8 (0.6–810)	95		11 (0.9–2009)	97	✓
Oxo-MiNP	4.6 (0.6–320)	95		6.4 (0.8–782)	97	✓
BPA	1.2 (0.3–7.8)	95		1.7 (0.5–35.2)	97	✓
Methyl-paraben	36 (1.5–1181)	76	✓	7.5 (<LOD–1000)	80	
Ethyl-paraben	3.0 (<LOD–659)	76	✓	0.8 (<LOD–140)	80	
Propyl-paraben	13 (<LOD–482)	76	✓	2.3 (<LOD–137)	80	

LOD: Limit of detection.

Table 3.41 Concentrations of contaminants in urine (µg/g creatinine) in the general population of Sweden, by region arranged south to north. Data presented as arithmetic mean (95% confidence interval), except for the collective Sweden data which represent the median (maximum). Data from the Riksmaten (2010–2011) study and adjusted for age, sex and education. Source: Bjermo et al. (2013a).

	Lund	Gothenburg region	Linköping	Stockholm	Örebro	Uppsala	Umeå	Sweden (maximum)[a]
BPA	2.0 (1.4–2.7)	2.1 (1.5–2.9)	2.5 (1.8–3.4)	2.2 (1.6–3.1)	1.9 (1.4–2.6)	1.8 (1.3–2.4)	2.1 (1.5–2.9)	1.6 (14.3)
MEP	86 (50–147)	70 (40–122)	76 (45–129)	71 (41–123)	76 (45–129)	81 (48–136)	57 (33–97)	51.2 (3260)
MnBP	54 (43–67)	65 (51–83)	51 (41–64)	60 (48–76)	64 (51–80)	63 (51–79)	74 (59–92)	49.2 (541)
MBzP	9.3 (6.5–13)	14 (10–21)	11 (7.6–15)	10 (6.9–15)	17 (12–24)	16 (11–23)	23 (16–33)	9.6 (118)
MEHP	3.0 (2.1–4.2)	3.6 (2.5–5.2)	3.4 (2.4–4.7)	4.2 (2.9–5.9)	3.5 (2.5–4.9)	3.1 (2.2–4.3)	4.7 (3.3–6.6)	3.0 (66.7)
5-OH-MEHP	21 (16–29)	21 (16–28)	22 (17–30)	23 (17–31)	20 (15–27)	19 (14–25)	27 (20–36)	16.6 (245)
5-oxo-MEHP	12 (9.2–17)	12 (8.9–16)	12 (8.6–15)	12 (9.2–17)	11 (8.3–15)	10 (7.8–14)	14 (11–19)	8.9 (156)
5-cx-MEPP	17 (13–22)	18 (13–25)	17 (13–23)	18 (13–24)	16 (12–21)	15 (12–20)	21 (16–28)	11.2 (206)
7-OH-MMeOP	8.2 (5.2–13)	5.0 (3.1–8.2)	10 (6.5–16)	10 (6.2–16)	7.6 (4.8–12)	8.3 (5.3–13)	7.3 (4.6–12)	6.9 (728)
7-oxo-MMeOP	3.5 (2.2–5.6)	2.0 (1.3–3.3)	3.9 (2.5–6.2)	3.9 (2.4–6.4)	3.1 (1.9–4.9)	3.4 (2.2–5.3)	2.8 (1.8–4.5)	2.6 (485)
7-cx-MMeHP	10 (6.6–16)	7.3 (4.6–12)	12 (7.7–19)	13 (8.5–21)	9.1 (5.9–14)	13 (8.4–20)	10 (6.2–15)	8.2 (324)

[a]n=293.

3.4.7.4 Conclusion

Concentrations of POPs in breast milk and serum in Sweden are decreasing, and there are no strong indications for generally higher concentrations in northern Sweden, which could be expected to have Arctic characteristics, than in other parts of Sweden. The overall conclusion of the Glynn et al. (2011a) study was that, as long as store-bought foods make up the main proportion of the diet, there are only small or no regional differences in POP exposure at a population level. This is mainly due to the highly centralized food distribution system in Sweden, covering the whole country, although the mobility of the population also reduces regional differences. Swedish adults are exposed to a mixture of PFCs, with PFOS currently dominating the mixture (Bjermo et al. 2013c). Biomarkers of fish consumption correlate well with serum levels of PFOS, PFNA, PFDA and PFUnDA, strongly suggesting that fish is an important source of exposure to certain contaminants (Wennberg et al. 2007; Bjermo et al. 2013c).

Regional differences in metal concentrations did not show an obvious trend towards accumulation in the north. In fact, many of the higher Hg levels were found in the south and west, in areas identified as consuming higher amounts of fish than populations in the north of Sweden. However, the differences between Hg levels in the north and south are not as large as the difference in fish consumption, so there still remains a need to identify sources of Hg in Västerbotten (Barregård 2006). Mercury levels decreased in women between 2004 and 2009, and a slight decreasing trend was observed in maternal hair samples from 1996 to 2012, followed by a slight increase in 2013. Lead levels are decreasing in the Swedish population, although there is concern that hunting practices remain a source of exposure for populations in the north.

Emerging contaminants measured in urine show differences between adult and child levels, as well as some small regional differences in the general population, however sources were most often associated with personal care products and store-bought food. Whether practices in Arctic populations will result in different patterns of exposure remains to be seen, but exposure to many of these contaminants may not be as a result of long-range transport.

3.4.8 Finland

Breast milk has been sampled in Finland as part of a follow-up study coordinated by the World Health Organization on levels of PCBs in human milk. The Finland component carried out a larger population-based study, which recruited consecutive women giving birth in one of the maternity clinics from each of southern, central and northern Finland, the latter being the only Arctic population (Kiviranta et al. 1999). Analyses of breast milk sampled between 1987 and 2010 from these study areas are presented in Table 3.42. New data for maternal blood concentrations of OCs and metals are not available.

3.4.8.1 Persistent organic pollutants

The observable trend in southern Finland for PCB153 levels in breast milk indicates a decline from 1987 to 2010. A decline is also seen in levels in central Finland, which also has lower levels of PCB153 than southern Finland on a year by year basis. Levels in northern Finland are only available for 2005 and 2010, however these resemble those for central Finland for the same years. No change is evident from these two time points in the north. PBDE levels also show a declining trend from 2000 to 2010 for all three regions. Levels do not vary widely between regions.

3.4.8.2 Conclusion

Twenty-three years of biomonitoring POPs in breast milk shows a decline in PCB153 and PBDEs. While the PBDE data span only a ten-year period, a declining trend is still evident. The strongest declines in PCB153 were seen early in the time series, with levels remaining relatively similar between 2005 and 2010.

Associated with the breast milk analyses, initial analyses of Finnish food sources for PCBs show that most store-bought foods have relatively low levels (Kiviranta et al. 2001), although elevated levels are present in seafood originating from the Baltic Sea. This is due to known PCB pollution in the Baltic Sea (Vartiainen et al. 1997; Kiviranta et al. 1999). Seafood from the Baltic Sea is more commonly consumed in Helsinki, and

Table 3.42 Trends of contaminants in breast milk from first-time mothers in southern Finland (non-Arctic), central Finland (non-Arctic) and northern Finland (Arctic). Data presented as geometric means (range) in µg/kg lipid. Source: 1987 data (Vartiainen et al. 1997); 1993–1994 data (Kiviranta et al. 1999); 2000, 2005 and 2010 data (Kiviranta pers. comm. 2014).

	1987	1993–1994	2000	2005	2010
Southern Finland					
Mean age (range)	26.9 (20–37)	27.9 (19–36)	29.2 (22–35)	28.7 (20–39)	31.2 (19–37)
Sample size	n=47	n=14	n=29	n=39	n=32
PCB153	113 (47.8–373)	85.2 (24.3–148)	38.7 (14.6–80.7)	24.8 (9.2–80)	22 (7.8–54.1)
PBDE[a]	na	na	2.9 (0.8–16)	2.3 (0.6–31.8)	1.3 (0.3–4.9)
Central Finland					
Mean age (range)	25.4 (19–34)	27 (18–39)	28.3 (19–36)	27.3 (19–40)	30.2 (19–36)
Sample size	n=37	n=28	n=31	n=40	n=19
PCB153	92.5 (38.9–209)	52.4 (18.2–110)	30.5 (10.5–72.7)	17.9 (4.8–65.1)	16.3 (7.2–50.3)
PBDE[a]	na	na	3.1 (0.6–13.5)	2.2 (0.5–11.3)	1.6 (0.5–6.6)
Northern Finland					
Mean age (range)				26.3 (21–41)	27.3 (20–32)
Sample size				n=11	n=20
PCB 153	na	na	na	19 (9.3–50.9)	18.7 (6.8–58.1)
PBDE[a]	na	na	na	2.5 (1.4–6.3)	1.6 (0.6–3.8)

[a]PBDE47+PBDE99+PBDE100+PBDE153+PBDE209.

potentially southern Finland, than in other regions of Finland, which could explain the differences in PCB levels seen between southern, central and northern Finland.

3.4.9 Russia

This section presents a follow-up study conducted in Russia involving the Chukotka 2001–2003 birth cohort reported by AMAP (2009) and the 2007 follow-up involving biomonitoring sampling and investigation of health effects. Individual data on contaminant levels in blood samples from 17 mothers and cord blood from their corresponding 17 babies born in the Chukotka coastal area in 2001–2002 were compared with levels in blood sampled from the same women and their five-year old children in 2007 (Dudarev et al. 2010). The possible influence of breastfeeding on maternal POPs serum levels and association of children's POPs blood levels and frequency of infectious diseases was also assessed, and are further discussed in Chap. 4.

Data reported by Rylander et al. (2011) are also presented, from recent sampling for contaminants in women and men from three north-western Russian communities in 2009 and early 2010 – Nelmin-Nos, Usinsk and Izhma. The three study sites are separated geographically and the residents are expected to have different dietary habits and living conditions. Blood samples were collected from volunteers at the same time as they took part in a general health examination. The population of Nelmin-Nos was also sampled during the 2001–2003 Persistent Toxic Substances (PTS) study, of which the Chukotka 2001–2003 birth cohort was a part.

As a part of the international KolArctic project (KO467), samples were taken in 2013 and 2014 in the Pechenga district of Murmansk Oblast in north-western Russia, near the Norwegian border. In two cities, Nickel and Zapolyarny, 400 people were interviewed and for the first time in this region, blood samples were taken to assess concentrations of contaminants. The sampled population included pregnant women, non-pregnant women and adult men (Dudarev pers. comm. 2014).

3.4.9.1 Persistent organic pollutants

Maternal blood levels of all POPs decreased, by 33–74%, during the five-year period between 2001–2003 and 2007. The child blood serum concentrations of most POPs during the same period increased, by 24–132%. Only oxychlordane and *p,p'*-DDT decreased in children from birth to 2007. After five years, maternal PCB levels are approaching those observed in cord blood in 2001–2003. Conversely, child PCB levels after five years resemble maternal PCB levels from 2001 (Table 3.43). The same PCB congeners were measured in mothers and children (Fig. 3.13).

In this 2007 follow-up study, based on measured maternal levels of PCBs, the calculated average elimination half-life of PCB congeners (PCB105–PCB187) in maternal blood was 4 to 6 years (for ΣPCB, 5.7 years) (Dudarev et al. 2010). For comparison, Ritter et al. (2011) calculated maximum intrinsic human elimination half-lives for PCBs ranging from 10 to 15 years, and Wolff et al. (2000) calculated a half-life of 11.2 years for PCBs using adult female blood levels, which are longer timeframes than experienced by the Chukotka women. A shorter calculated half-life for ΣPCBs may indicate that the women had an increased mechanism for elimination (e.g. additional pregnancies). While the duration of breastfeeding for the infants from 2001–2003 was not significantly correlated with maternal blood serum levels for POPs in 2007, it is known that almost 50% of the women in the study had at least one additional child between their pregnancy in 2001–2003 and the 2007 follow-up, with two women having two additional children in this period. The additional pregnancies may have reduced maternal PCB body burdens during gestation and subsequent breastfeeding, although additional breastfeeding duration was not tested for significance. It is known that the major source of contaminant exposure in this maternal group was via the consumption of traditional food items (Dudarev et al. 2010). While important dietary changes may have occurred during extended or cumulative hospital stays for pregnant women (Dudarev et al. 2010), it remains unclear if such short-term

Table 3.43 Maternal, cord and child blood concentrations of POPs and metals, 2001–2002 and 2007, from coastal Chukotka (Lavrentia and Lorino, Russia). Data presented as geometric means (range). POPs in µg/L plasma (wet weight) and metals in µg/L whole blood. Source: Dudarev et al. (2010).

	Maternal (n=17)			Cord (n=17)	Child (n=17)	
	2001–2002	2007	%[a]	2001–2002	2007	%[a]
Mean age (range)	24.6 (15–33)				5.5	
Oxychlordane	0.9 (0.09–3.5)	0.2 (0.02–0.8)	-73	0.4 (0.06–3.6)	0.3 (0.06–1.0)	-27
trans-Nonachlor	0.9 (0.1–2.9)	0.2 (0.05–1.0)	-72	0.3 (0.03–3.2)	0.4 (0.01–1.3)	+14
p,p'-DDT	0.2 (0.06–1.2)	0.06 (0.02–0.1)	-72	0.1 (0.02–0.4)	0.08 (0.03–0.3)	-33
p,p'-DDE	2.7 (1.0–6.6)	0.8 (0.2–2.5)	-70	1.2 (0.3–7.4)	1.5 (0.3–3.7)	+24
DDE:DDT	11.9 (5.5–76.8)	12.8 (4.0–37.3)	+8	10.6 (2.3–34.3)	19.5 (5.8–102)	+84
HCB	2.1 (0.5–6.0)	1.7 (0.4–10.7)	-19	1.3 (0.2–5.1)	2.2 (0.3–6.3)	+72
β-HCH	2.1 (0.8–7.6)	1.4 (0.3–2.9)	-33	1.2 (0.2–8.1)	2.3 (0.7–7.7)	+90
Mirex	0.1 (0.04–0.5)	0.08 (0.03–0.2)	-43	0.07 (0.01–0.5)	0.09 (0.04–0.2)	+28
ΣPCBs	3.5 (0.8–8.9)	2.0 (0.3–6.6)	-44	1.4 (0.2–10.8)	3.3 (0.3–7.6)	+132
Total Hg	1.6 (0.5–3.9)	1.6 (0.5–4.8)	+1	1.4 (0.5–3.3)	0.9 (0.5–2.7)	-31
Pb	37.5 (18.3–76.8)	29.6 (4.9–137)	-21	37.6 (14.3–78.3)	38.2 (6.9–102)	+2

[a]Geometric mean values of 2007 relative to geometric mean values of 2001–2002 (100%).

dietary transitions (Binnington et al. 2014) would significantly reduce the body burden of long-lived contaminants such as PCBs in Russian women.

Maternal *p,p'*-DDT and *p,p'*-DDE levels declined by approximately 70% and 72%, respectively in this study. *p,p'*-DDT levels decreased in children by 33% over the five-year period, potentially indicating that exposure to *p,p'*-DDT decreased during early childhood, or dilution through growth. *p,p'*-DDE levels increased by 24%, which is likely to reflect the metabolism of existing *p,p'*-DDT body burden in the children and potentially continued exposure to *p,p'*-DDE in food or from the environment. The average duration of breastfeeding of all babies in 2001–2007 was 24.4 months (range 1–72), thus ongoing exposure through breastfeeding seems likely (Dudarev et al. 2010). The DDE:DDT ratio among mothers did not change, remaining around 12, which might indicate continued historical sources of exposure, whereas in children the ratio increased substantially over this five-year time frame by 84% (from 10.6 to 19.5 µg/L plasma).

Statistical analysis of arithmetic mean concentrations of PCB, HCB, and *p,p'*-DDE in women (Table 3.44) and men (Table 3.45) from Nelmin-Nos, Izhma, and Usinsk (Rylander et al. 2011) indicates that men had significantly higher concentrations of PCB138, PCB153, and PCB180 than women during the period of 2009 and early 2010. Older people had higher concentrations of PCB153, PCB180, HCB and *p,p'*-DDE. When the blood data were adjusted for age and sex, no differences were found between the three communities for PCB138, PCB153 and PCB180, although men from Izhma had significantly higher concentrations of HCB than men from other sites. When adjusted for parity, the women of Usinsk had significantly higher levels of *p,p'*-DDE. Parity was only a significant predictor of *p,p'*-DDE (Rylander et al. 2011).

Figure 3.14 illustrates changes in mean concentrations of POPs in the Nelmin-Nos populations of men and women between the 2001–2003 sampling and the more recent sampling in 2009–2010. There is a clear decrease for both women and men

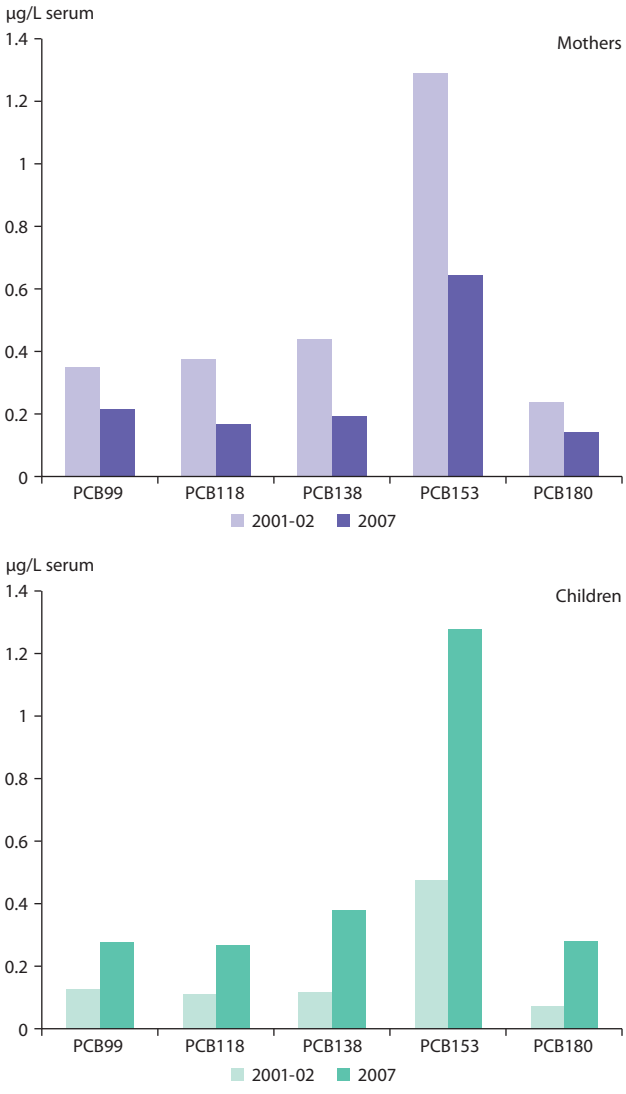

Figure 3.13 Maternal, cord and child blood concentrations of PCB congeners, sampled in 2001–2002 and 2007. Data are presented as geometric means. Source: Dudarev et al. (2010).

Table 3.44 Concentrations of POPs (µg/kg plasma lipid) in women from three regions of Russia in 2009–2010. Data presented as arithmetic means [medians] and (range). Source: Rylander et al. (2011).

Region	Nelmin-Nos	Izhma	Usinsk
Sample size	n=87	n=25	n=25
Mean parity (range)	2.8 (0–9)	2.3 (1–3)	2.1 (1–4)
trans-Nonachlor	na	na	3.6 [1.3] (<LOD–21)
p,p'-DDE	246 [163] (<LOD–1342)	127 [107] (41–517)	234 [203] (91–600)
HCB	135 [110] (<LOD–373)	122 [102] (32–297)	117 [103] (35–320)
PCB99	31 [20] (<LOD–304)	16 [9.4] (<LOD–56)	25 [25] (<LOD–35)
PCB118	48 [30] (<LOD–268)	41 [35] (<LOD–66)	44 [40] (<LOD–106)
PCB138	46 [35] (<LOD–169)	32 [31] (<LOD–61)	40 [37] (<LOD–66)
PCB153	98 [78] (<LOD–534)	65 [59] (<LOD–156)	72 [67] (<LOD–137)
PCB180	57 [47] (<LOD–286)	23 [8.5] (<LOD–108)	30 [25] (<LOD–113)

LOD: Limit of detection

Table 3.45 Concentrations of POPs (µg/kg plasma lipid) in men from three regions of Russia in 2009–2010. Data presented as arithmetic means [medians] and (range). Source: Rylander et al. (2011).

	Nelmin-Nos	Izhma	Usinsk
Sample size	n=22	n=25	n=25
trans-Nonachlor	na	na	8.9 [4.6] (3.1–26)
p,p'-DDE	245 [176] (51–732)	168 [138] (20–428)	228 [190] (53–782)
HCB	98 [86] (<LOD–203)	183 [160] (46–361)	122 [107] (53–427)
PCB99	36 [26] (<LOD–136)	29 [22] (<LOD–175)	33 [31] (<LOD–70)
PCB118	57 [26] (<LOD–532)	43 [15] (<LOD–478)	39 [28] (<LOD–106)
PCB138	58 [36] (<LOD–291)	54 [36] (<LOD–270)	53 [55] (<LOD–104)
PCB153	104 [92] (<LOD–222)	123 [106] (<LOD–297)	110 [97] (36–236)
PCB180	64 [57] (<LOD–152)	79 [73] (<LOD–170)	63 [59] (<LOD–158)

LOD: Limit of detection

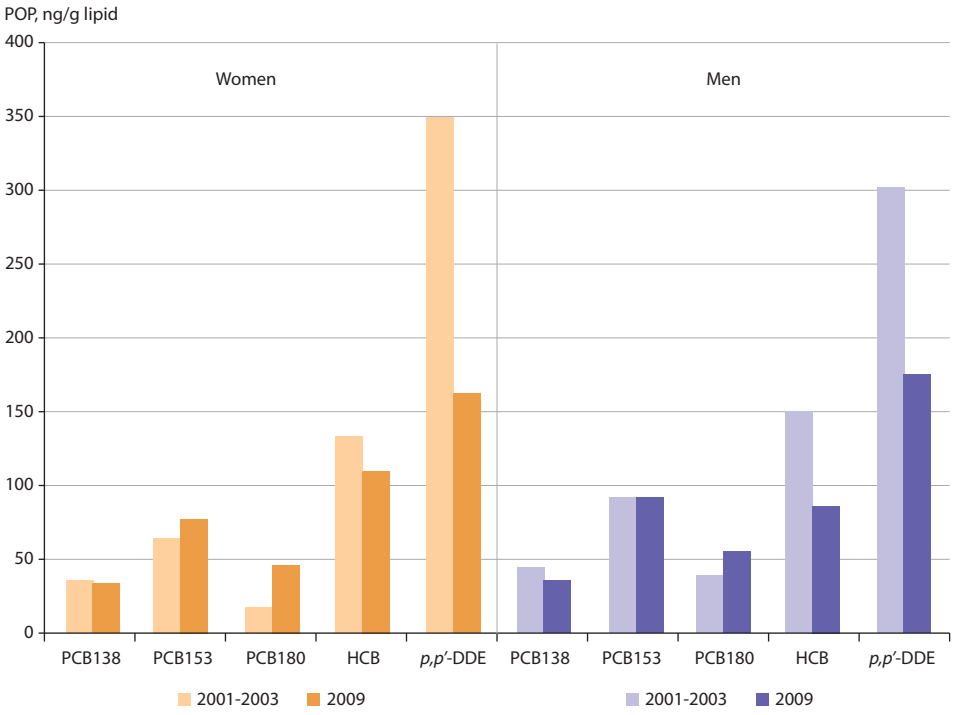

Figure 3.14 Differences in blood concentration of POPs in Nelmin-Nos from 2001–2003 to 2009. Source: Rylander et al. (2011).

Table 3.46 Concentrations of POPs in pregnant women, non-pregnant women, men and the general population (men and non-pregnant women of all ages) in the Pechenga district of Murmansk Oblast, 2013–2014. Data from the KolArctic Project (KO467). Data lipid-adjusted (µg/kg plasma lipid) and presented as geometric means (range), including age. Source: Dudarev pers. comm. (2014).

	Pregnant women	Women	Men	General population
Geometric mean age (range)	28.2 (16–41)	44.2 (26–65)	39.2 (27–54)	42.3 (26–65)
Sample size	n=50	n=17	n=33	n=50
p,p'-DDT	11.4 (1.3–376)	18.9 (6.5–124)	39.5 (11.6–132)	24.9 (6.5–132)
p,p'-DDE	102 (16–1221)	141 (39.4–538)	167 (51.6–940)	150 (39.4–940)
HCB	18.2 (5.3–252)	33.3 (12.8–85.1)	40.6 (10.9–189)	35.5 (10.9–189)
β-HCH	8.5 (0.8–146)	55.8 (17.6–157)	46 (27.8–100)	52.6 (17.6–157)
PCB118	26.1 (9.4–119)	35.6 (12.1–98.2)	46 (9.9–134)	38.6 (9.9–134)
PCB138	9.2 (1.0–48.2)	28 (6.4–74.9)	44.3 (14.8–106)	32.5 (6.4–106)
PCB153	12.2 (1.3–56.7)	27.5 (8.5–61)	47.9 (21.6–141)	32.8 (8.5–141)

in *p,p'*-DDE concentrations and, to a lesser extent, decreases for HCB. Small increases in concentration are observed for PCB153 and PCB180 across the two sampling points, however the significance of these differences has not been assessed.

Table 3.46 shows recent levels of POPs in pregnant women, and in the general population of non-pregnant women and men combined, of the Pechenga district of Murmansk Oblast for the KolArctic project (KO467) (Dudarev pers. comm. 2014). Levels of POPs in pregnant women were consistently lower than in non-pregnant women and men in the general population. Levels of POPs were consistently lower in women than men, with the exception of β-HCH, where women had higher levels, 55.8 compared to 46.0 µg/kg plasma lipid in men, and a wider range of levels than men. The maximum concentration of β-HCH in women was 157.1 compared to 100.5 µg/kg plasma lipid for men. Arithmetic means in the Pechenga district (Appendix Table A3.22) of PCB118 are comparable to those found in Nelmin-Nos, Izhma and Usinsk. PCB138 levels in those regions are slightly elevated compared to men and women in the Pechenga district, while differences in PCB153 and HCB concentrations in these regions were even greater.

3.4.9.2 Metals

Maternal blood Pb levels decreased by 21% between 2001–2003 and 2007 (Table 3.43), although the range broadened to include much lower and much higher levels in 2007. Maternal Hg levels remained essentially the same between the two sampling periods. This suggests a continuous exposure to Hg, probably through fish and seafood. Blood Pb levels in children have not changed, whereas concentrations of Hg in blood decreased by 31%. The decrease in Hg concentration in 2001–2003 cord blood compared with 2007 infant blood indicates Hg exposure during early life was less than *in utero*. There may be differences in Hg exposure between mothers and their children; however, due to the relatively short half-life of MeHg in the body (Yaginuma-Sakurai et al. 2012), it cannot be determined from these results whether the potential differences are the result of long-term behavior or if there were more recent changes in exposure prior to the 2007 sampling.

Rylander et al. (2011) also reported levels of Hg, Pb, Cd and Se in whole blood in men and women from the Komi Republic in Izhma and Usinsk (Table 3.47). Statistical analysis of these data indicated that Hg and Pb concentrations increased with increasing age, and that men had significantly higher concentrations of Pb than women. The study group from Izhma had significantly higher concentrations of Cd when controlling for age and sex, and the study group from Usinsk had higher concentrations of Se than the others. Parity did not affect metal concentration.

Table 3.47 Concentrations of metals (µg/L whole blood) in study participants from the Komi Republic, Russia in 2009–2010. Data presented as geometric means (range). Source: Rylander et al. (2011).

	Men		Women	
	Izhma	Usinsk	Izhma	Usinsk
Sample size	n=25	n=25	n=25	n=25
Total Hg	2.3 (1.0–8.1)	2.2 (1.0–10)	2.3 (1.0–10)	2.3 (1.0–6.4)
Pb	33 (14–88)	32 (11–63)	27 (11–57)	23 (11–63)
Cd	0.4 (0.1–1.4)	0.3 (0.1–1.0)	0.4 (0.1–1.5)	0.2 (0.1–1.3)
Se	88 (61–130)	99 (61–134)	87 (57–119)	100 (63–139)

3.4.9.3 Conclusion

There was a large decrease in blood concentrations of POPs for mothers from Chukotka over the period between 2001–2003 and 2007 (Dudarev et al. 2010). The major source of exposure in this study group of mothers and children is the contamination of traditional food items, including marine mammals, both from global and local sources. It was expected that the decline in POPs levels in maternal blood serum would be due in part to the displacement of contaminants during breastfeeding, but no associations were found with the duration of breastfeeding for the children born during the 2001–2003 sampling period. However, this observation does not account for additional pregnancies and breastfeeding that occurred in the interim period. The increase in POPs levels in children's blood may be explained by the transfer of contaminants from the mother through breastfeeding as well as through the consumption of local traditional food.

The study of male and female volunteers from Nelmin-Nos, Izhma, and Usinsk indicated that older people in north-western Russian communities may have significantly higher blood concentrations for many contaminants that accumulate in

people over time, and this was also the case for PCBs and Pb in men compared with women. Mercury concentrations also increased with age, suggesting that older people from these communities might be consuming greater amounts of fish and marine mammals than younger people. Although the three study sites were geographically separated and the residents were expected to have different dietary habits and living conditions, few regional differences were observed when the data were controlled for both age and sex. However, men had significantly higher concentrations of HCB in Izhma, a rural inland district of the Komi Republic mainly populated by reindeer herders, and the Izhma study group overall showed higher concentrations of Cd. The study group from Usinsk had higher concentrations of Se and *p,p'*-DDE (women only), where most people make their living as oil and gas workers.

Levels of POPs in pregnant women in the Pechenga district of Murmansk Oblast were lower than levels in the general population (combined men and non-pregnant women). Murmansk POPs levels were comparable to those for Nelmin-Nos, Izhma and Usinsk for PCB118, but PCB138, PCB153 and HCB were lower in Murmansk (Dudarev pers. comm. 2014). Comparing wet weight concentrations (Appendix Table A3.23) to the 2007 Chukotka maternal concentrations, HCB and β-HCH concentrations are lower in Pechenga non-pregnant women, whereas *p,p'*-DDT and *p,p'*-DDE are similar in each population.

3.5 International comparisons

3.5.1 Persistent organic pollutants

Greenland remains one of the Arctic areas with populations still experiencing high levels of POPs. Eastern Greenland populations were found to have the highest levels of *trans*-nonachlor, *p,p'*-DDE, PCB153, HCB, and PFOS (Fig. 3.15). Compared across the Arctic, Greenland populations had the highest measured levels for more POPs than any other Arctic country, with the exception of PBDEs. The maternal population in Alaska had the most elevated levels of PBDE47 and PBDE99, although the levels of PCB153, HCB and *trans*-nonachlor were among the lowest in the Arctic. Populations in Nunavik (Canada) had the second highest level of *p,p'*-DDE. However, Canada also has some of the lowest levels of PCB153, as shown for populations from the Inuvialuit Settlement Region and Nunatsiavut, and for PFOS and PFOA measured in populations from Nunavik. The Faroese PCB153 levels were elevated, sometimes by three- to four-fold, compared to populations in other countries, except eastern and northern Greenland. Populations sampled in Reykjavik (Iceland) had the highest PFOA levels, however they also had the lowest levels of *p,p'*-DDE and levels of PCB153, *trans*-nonachlor, PBDEs, and PFOS were also among the lowest.

Sampled Swedes and Norwegians had the next highest levels of PFOA, while levels of PFOS in Swedish populations are among the lowest in Arctic countries with data. The sampled population of Norway also had the lowest levels of *trans*-nonachlor, and some of the lowest levels of *p,p'*-DDE, PCB153 and HCB. Levels of *p,p'*-DDE and PCB153 in the pregnant women of the Pechenga District of Murmansk (Russia) are among the lowest reported here.

3.5.2 Metals

The highest levels of total Hg were observed in the blood of WCBA (including pregnant women) from Nunavik in Canada (Fig. 3.15). WCBA from northern and eastern Greenland had slightly lower levels of total Hg in blood, at 8.0 and 7.0 µg/L whole blood respectively. The lowest levels occurred in women from western Greenland, Sweden and Norway, with levels between the limit of detection and 1.2 µg/L whole blood.

Russian maternal blood from Chukotka taken in 2007 had the highest circumpolar levels of Pb at 29.6 µg/L whole blood. Women from the Nunavut, Inuvialuit Settlement Region and Nunatsiavut region in Canada all had levels ranging from 18 to 27 µg/L whole blood, which was only slightly higher than levels found in 2002–2004 in women from eastern and mid-western Greenland, although recent levels are much lower at 6.0 to 7.0 µg/L whole blood. Low levels were also found in Yup'ik mothers in Alaska (7.4 µg/L whole blood) and Norwegian women (7.44 µg/L whole blood).

A study by Fillion et al. (2014) identified a different exposure mechanism to Pb than the expected lead shot in game meat. In examining the diets of participants in the Inuit Health Survey (2007–2008) in Nunavut in particular, it was found that Pb levels in traditional food were low. However, the Pb isotope ratios found in their environments, when compared with those in the blood of IHS participants, suggested that paint and ammunition were contributing Pb to house dust, which were probably key exposure sources for high blood Pb levels in the IHS participants.

Selenium levels were not measured in pregnant women or WCBA in all circumpolar countries. The highest levels were found in women from the Canadian Arctic. Nunavut and Nunavik women had geometric means of 286 and 280 µg/L whole blood, respectively. The lowest mean blood concentrations for Se were found in women from Norway and Alaska. Cadmium levels were also not measured in all circumpolar countries, but appeared to be comparatively low, although the highest levels were again found in women from the Canadian Arctic and Greenland. The lowest levels occurred in women from Norway and Alaska.

3.6 Tissue concentrations of contaminants and guidelines: case studies

The guidance values highlighted in this chapter include the current Canadian blood intervention level for Pb of 100 µg/L whole blood (CEOH, 1994) and the recently lowered US CDC Pb blood reference value for pregnant women and children of 50 µg/L whole blood (US CDC, 2014b); Health Canada's guidance value for MeHg in blood of 20 µg/L whole blood for women aged 50 years of age or greater and men over 18 years of age (Health Canada, 1999), and the provisional blood guidance value of 8 µg MeHg/L whole blood for pregnant women, WCBA and children of both sexes (Legrand et al. 2010). The case studies also make use of the US EPA's blood MeHg level equivalent to the current US EPA reference dose, 5.8 µg/L whole blood (US EPA, 2015) which is intended for the entire population,

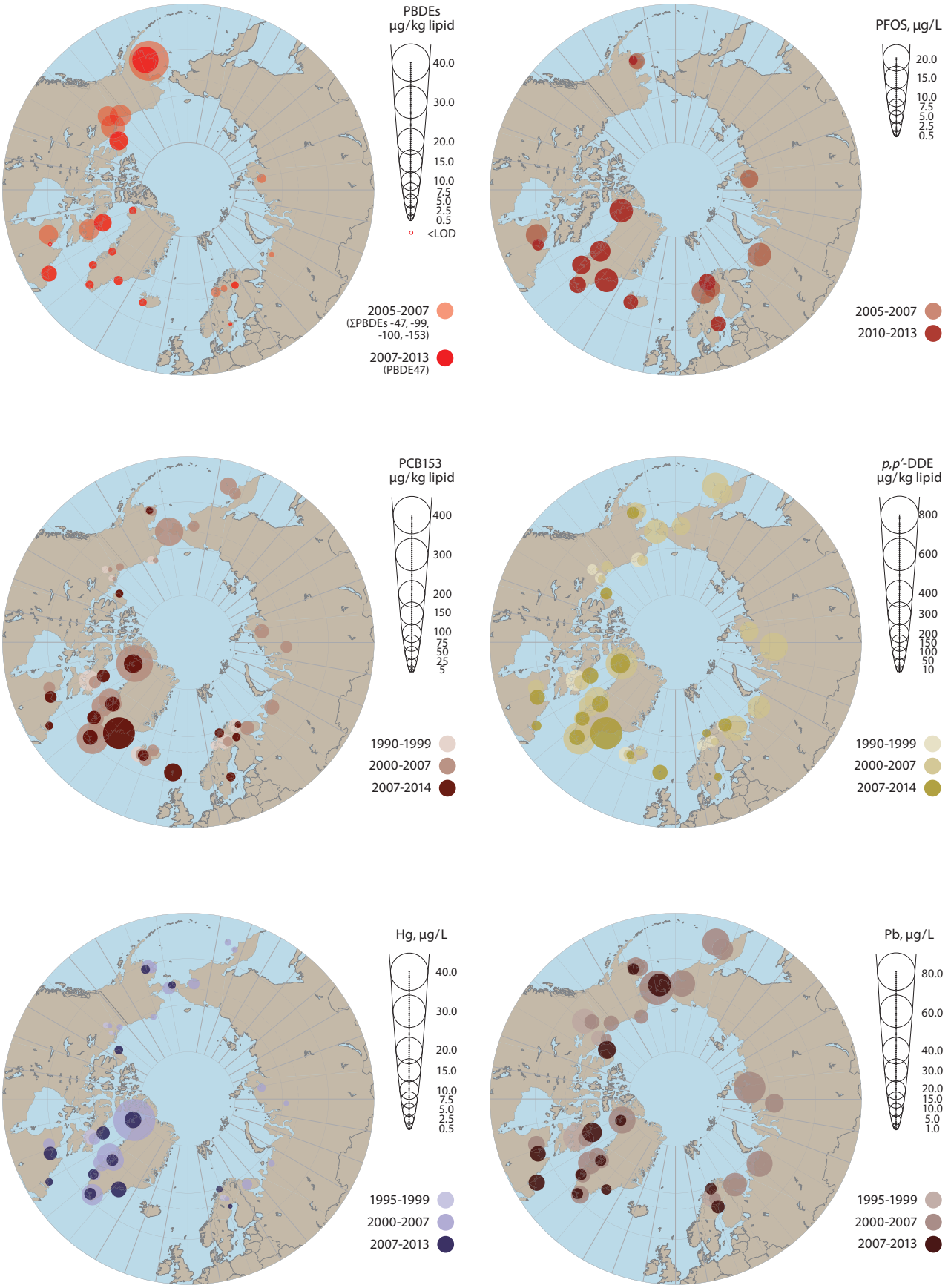

Figure 3.15 Circumpolar concentrations of PBDEs, PFOS, PCB153, *p,p'*-DDE, Hg and Pb. Unless otherwise indicated, POPs and PBDEs are presented in µg/kg plasma lipid; PFCs in µg/L; and metals in µg/L whole blood. Data for Alaska, Faroe Islands, Sweden (except metals) and coastal Chukotka (Russia) are derived from maternal blood. Data for the Inuvialuit Settlement Region (NWT, Canada), Nunavut (Canada) and Nunatsiavut (NL, Canada) are derived from the blood of women of childbearing age. Data for Nunavik (QC, Canada), Greenland, Iceland, Norway, Sweden (metals only) and the Pechenga district (Russia) are derived from the blood of pregnant women. Data for Sweden (PBDE47, PCB153, *p,p'*-DDE) and Finland are derived from breast milk.

Box 3.1 Biomonitoring equivalents and AMAP

AMAP has done extensive work on characterizing Arctic people's exposure to chemicals via biomonitoring. This wealth of data provides unique opportunities for researchers investigating exposures and potentially related health effects, while at the same time posing challenges to researchers asked to explain the meaning of the results to the participating communities.

Biomonitoring Equivalents (BEs) are estimations of the concentration of a chemical or metabolite in a biological specimen (such as blood or urine) that are consistent with a guidance value, such as a Tolerable Daily Intake. BEs can be used by researchers to place biomonitoring data in a public health risk context. Comparing biomonitoring data to these identified 'tolerable' exposure levels provides a framework to help communicate the interpretation of biomonitoring results at the population level.

Biomonitoring Equivalents have been developed for over 100 compounds (Hays et al. 2007, 2008; Kirman et al. 2011; Krishnan et al. 2011), including many persistent compounds measured in AMAP studies. Many factors need to be considered when correlating biomonitoring data with potential health effects. Potential confounders have been identified for biomarkers in urine (body mass index, age, race, time since last void, fasting time) and blood (serum lipids and proteins, etc.). Inter-individual variability can also affect measured concentrations, although this issue pertains mostly to short-lived compounds. Also, the effects of mixtures are not considered in these calculations. Additional work into the application of BEs could be a valuable additional tool for researchers and public health practitioners in interpreting Arctic biomonitoring data at the population level.

including WCBA. While guidelines are predominantly set for MeHg, total Hg blood data can be compared to MeHg guidelines as approximately 80% of total Hg in blood is expected to be MeHg (Hansen et al. 1990; Oskarsson et al. 1996, Mortensen et al. 2014). For additional guidelines available for contaminants, see Chap. 5. See also Box 3.1.

3.6.1 Exceedances in Canada

Tables 3.48 and 3.49 present Hg and Pb exceedance data for four Inuit regions of northern Canada. The relative frequency of Hg concentrations above Health Canada's guidance value of 20 μg/L whole blood was higher in Nunavut for men, all women, and WCBA, compared to other regions of northern Canada (Table 3.48). Men had higher mean concentrations of metals than women and Table 3.48 indicates that more than 27% of men in Nunavut had values exceeding 20 μg/L of total Hg in blood. When comparing concentrations to the lower provisional blood guidance value of 8 μg/L whole blood, over 36% of WBCA in Nunavut exceeded this guidance value, and 48% exceeded the US EPA blood MeHg level equivalent of 5.8 μg/L whole blood. In Nunavik, it appears that the proportion of pregnant women exceeding MeHg guidance values is decreasing (Table 3.49), however a small percentage are still above the 20 μg/L whole blood value, and 38% of pregnant women exceed the 8 μg/L whole blood value. It appears that the body burden for Hg in northern Canada is still high. Laird et al. (2013b) showed that ringed seal liver is the major source of Hg, particularly among Inuit in Nunavut. In response, the Nunavut government issued dietary advice for WCBA to lower their intake of ringed seal liver in June 2012 (see Chap. 6, Sect. 6.4.2). In Nunavik, beluga meat is the major source of Hg for Inuit (Lemire et al. 2015), which has also been the subject of recent dietary advice, issued by the Nunavik government.

Men had a higher proportion of individuals exceeding the Canadian blood Pb intervention level of 100 μg/L whole blood, than either all women or WCBA. More than 10% of men in Nunavut and the Inuvialuit Settlement Region have blood Pb concentrations above 100 μg/L whole blood. In contrast, a small percentage of Inuit WCBA from Nunavut showed blood Pb concentrations in excess of the 100 μg/L whole blood level. The percentage of all women in Nunavut above this value is higher than in either the Inuvialuit Settlement Region or Nunatsiavut. Interestingly, the percentage of men exceeding the 100 μg/L whole blood value was actually higher among those in Inuvialuit Settlement Region than in Nunavut, despite Inuit from Nunavut having slightly higher mean concentrations. In Nunavik (Table 3.49), the percentage of pregnant women exceeding the 100 μg/L whole blood level in 2011–2012 was 1.8%, although further sampling in 2013 found all pregnant women were below 100 μg/L whole blood. It is clear from Table 3.49 that the percentage of pregnant women and WCBA exceeding the 100 μg/L whole blood intervention level has decreased steadily over time in Nunavik, with exceedances approaching 0% since 2004.

Recent advances in Pb toxicology have shown that adverse health effects from Pb are possible even below 100 μg/L whole blood (e.g. Lanphear et al. 2005; Crump et al. 2013). For this reason, the US CDC recently lowered its blood Pb reference value for children to 50 μg/L whole blood. When comparing concentrations of blood Pb in pregnant women to this lower level, a small percentage of exceedances in Nunavik is seen. As mean concentrations of Pb among pregnant women are well below 50 μg/L whole blood, the exceedances observed are reflective of a small percentage of the population exposed to potentially concerning levels of Pb.

3.6.2 Exceedances in Greenland

Table 3.50 shows that two WCBA (may include pregnant women) in northern Greenland both had levels of Hg exceeding the blood Hg level equivalent to the current US EPA reference dose, 5.8 μg/L, and the Canadian provisional blood guidance value of 8 μg/L. However, neither exceeded the 20 μg/L Health Canada guidance value for MeHg or the 100 μg/L Canadian blood intervention level for Pb. All of the sample population from eastern Greenland also exceed the 5.8 μg/L MeHg value, and almost half of the sample population still exceed the 20 μg/L MeHg guidance value. With the exception of eastern Greenland, most women do not exceed the 20 μg/L MeHg guidance value. Disko Bay and south-western Greenland both show a small section of the population exceeding this level. Also, given that women in Greenland have been shown to have lower levels than men, it is likely that a higher proportion of men are exceeding the 20 μg/L guideline for adult MeHg levels (Lenters et al. 2015, Long et al. 2015).

Table 3.48 Exceedance (% calculated as greater than the guideline value) of North American blood guidelines for total Hg and Pb in participants of the Inuit Health Survey (2007-2008): women of childbearing age (18-39 years), all women (18-90 years) and men (18-89 years). Source: Chan pers. comm. (2014).

Region	n	Total Hg			Pb	
		>5.8 µg/L[a]	>8 µg/L[b]	>20 µg/L[c]	>50 µg/L[d]	>100 µg/L[e]
WCBA						
Inuvialuit Settlement Region	74	16.2	12.2	1.4	5.4	0
Nunavut	491	48.3	36	10.2	11.2	2.2
Nunatsiavut	60	9.3	9.3	1.7	5.0	0
All 3 regions	625	40.6	30.6	8.3	9.9	1.8
Women						
Inuvialuit Settlement Region	187			8.0		2.7
Nunavut	977			20.5		6.6
Nunatsiavut	165			0.6		2.4
All 3 regions	1329			16.2		5.5
Men						
Inuvialuit Settlement Region	92			12		12
Nunavut	650			27.9		10.5
Nunatsiavut	98			3.1		6.1
All 3 regions	840			23.2		10.1

[a]US EPA blood MeHg equivalent (US EPA, 2015); [b]provisional interim blood guidance value (Legrand et al. 2010); [c]Canada's guidance value for MeHg in blood of women aged 50+ years and men over 18 years of age (Health Canada, 1999); [d]US CDC Pb blood reference value for pregnant women and children (US CDC, 2014b); [e]Canada's blood intervention level (CEOH, 1994).

Table 3.49 Exceedance (% calculated as greater than or equal to the guideline value) of North American blood guidelines for total Hg and Pb in pregnant women and women of childbearing age (18–39 years) from Nunavik (1992–2013). Source: Dewailly pers. comm. (2014); Ayotte pers. comm. (2014).

		n	Mean age (range)	Total Hg			Pb	
				≥5.8 µg/L[a]	≥8 µg/L[b]	≥20 µg/L[c]	≥50 µg/L[d]	≥100 µg/L[e]
1992	WCBA	170	28 (18–39)	90.2	76.2	22.6	73.8	26.2
1996–1997	PW	78	25 (15–41)	92.3	71.8	19.2	60.3	11.5
1998–1999	PW	43	25 (15–37)	60.5	51.2	7.0	48.8	16.3
2000–2001	PW	47	26 (17–39)	74.5	61.7	21.3	38.3	8.5
2004	WCBA	283	28 (18–39)	72.7	53.2	15.5	15.8	2.9
2004[f]	PW	31	27 (18–42)	67.7	51.6	6.4	6.4	0
2007	PW	42	24 (18–37)	33.3	16.7	2.4	4.8	0
2011–2012	PW	111	24 (18–39)	49.6	36	5.4	3.6	1.8
2013	PW	95	24 (18–41)	52.6	37.9	3.2	1.0	0
p-trend[g]				<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

PW: pregnant women; WCBA: women of childbearing age. [a]US EPA blood MeHg equivalent (US EPA, 2015); [b]provisional interim blood guidance value (Legrand et al. 2010); [c]Canada's guidance value for MeHg in blood of women aged 50+ years and men over 18 years of age (Health Canada, 1999); [d]US CDC Pb blood reference value for pregnant women and children (US CDC, 2014b); [e]Canada's blood intervention level (CEOH, 1994); [f]not included in the trend test; [g]based on Cochrane-Armitage trend test.

Table 3.50 Exceedance (% calculated as greater than the guideline value) of North American blood guidelines for total Hg and Pb in pregnant women and women of childbearing age in Greenland. All data collected in 2002–2004, except for samples from the western Greenland site which were collected in 2010–2011 and 2013. Source: Bonefeld-Jørgensen and Long pers. comm. (2014).

Region	n	Total Hg			Pb	
		>5.8 µg/L[a]	>8 µg/L[b]	>20 µg/L[c]	>50 µg/L[d,e]	>100 µg/L[f]
Greenland (all)	184	43	28	7	0.5[g]	1
North	2	100	100	0	0[h]	0
Disko Bay	61	49	38	8	0[i]	0
Mid-West	30	27	17	0	na	7
West	121	na	na	na	0.8	na
South-West	56	21	13	4	na	0
South	22	36	18	0	0[j]	0
East	13	100	85	46	0[k]	0

[a]US EPA blood MeHg equivalent (US EPA, 2015); [b]provisional interim blood guidance value (Legrand et al. 2010); [c]Canada's guidance value for MeHg in blood of women aged 50+ years and men over 18 years of age (Health Canada, 1999); [d]exceedances derived from ACCEPT project, 2010–2011 and 2013; [e]US CDC Pb blood reference value for pregnant women and children (US CDC, 2014b); [f]Canada's blood intervention level (CEOH, 1994); [g]sample size: n=202; [h]sample size: n=14; [i]sample size: n=49; [j]sample size: n=15; [k]sample size: n=3.

Very few Greenlandic pregnant women and WCBA exceeded the 100 µg/L Pb blood intervention level, with mid-western Greenland having the most at 7% of 30 sampled women. Using the more recent ACCEPT sampling, very few pregnant women and WCBA exceeded the 50 µg/L Pb blood reference value for children (Long et al. 2015).

In the previous AMAP assessment (AMAP 2009), a high proportion of Greenlandic pregnant women and WCBA exceeded the Hg blood guidance value. In particular, women in Qaanaaq (North) had an exceedance of 94% for the 20 µg/L value. For all eight regions, the 5.8 µg/L blood MeHg level equivalent was exceeded by 76% of women (AMAP 2009) compared to 43% in this assessment, and the 20 µg/L value was exceeded by 35% of women (AMAP 2009) compared to the current 7%. Although blood Hg levels remain elevated, the proportion of the population exceeding guidance values is gradually being reduced.

3.7 Discussion

In Russia and the Faroe Islands, levels of contaminants in children by 5 to 7 years of age matched levels in their mother's blood at parturition. Using calculated partition ratios, levels of certain contaminants in cord blood are expected to range from approximately 29 to 74% of levels found in the mother's serum (Needham et al. 2011). As mentioned previously, it is expected that pregnancy and breastfeeding lead to a displacement of contaminants for mothers (Vartiainen et al. 1997; Kiviranta et al. 1999; Dudarev et al. 2010). However, this also translates into the possibility of ongoing exposure for children during early childhood, during critical developmental stages, which may lead to adverse effects (see Chap. 4). This is why the focus on managing contaminant exposure for WCBA and pregnant women remains important, until levels of contaminants decline in sources of exposure.

As indicated in the Canadian, Greenlandic and Russian data sets, there were many cases of lower levels of POPs and OCs in women, and WCBA, than in men. This may be an indicator of the success in reaching the target population with the risk communications messages (see Chap. 6), or indicate a dietary shift from traditional foods to store-bought foods. The lower levels in younger women could also reflect the age difference between groups, where older men or women may have higher body burdens. However, it also highlights a potential issue that men may not be receiving similar dietary advisories or appropriate information to make dietary choices for their own health. Studies are beginning to examine the potential contribution of epigenetic changes in sperm due to exposure to contamination, including contaminants of concern under the Stockholm Convention (Delbès et al. 2010; Anderson et al. 2014). These epigenetic changes could result in adverse effects in children due to damage to the sperm cells. However, even without the concern about transmissible damage to germ cells, it is known that high body burdens of these contaminants of concern can lead to health effects in all adults (see Chap. 4).

For certain countries, AMAP data now span almost 20 to 30 years, due in part to sample biobanking which allows for retrospective analysis with newer laboratory techniques of the stored samples for more recent contaminants of concern. In comparing changes in these contaminant concentrations, for example, changes in POPs concentrations in Norwegian men (Fig. 3.5), with the toxicokinetic analyses performed using these long-term biomonitoring data sets (e.g. Grandjean et al. 2008), the alignment of estimated elimination rates can be examined in the context of observed concentrations, and potential outside influences on contaminant levels, such as dietary advisories, market shifts and international risk management.

Comparing levels in this assessment with other biomonitoring activities that occur globally, it is clear that some Arctic populations are still experiencing elevated levels of exposure to certain contaminants of concern, compared to populations elsewhere (Table 3.51). For example, blood Hg concentrations are elevated in all countries where data are available, except in Sweden, where levels are comparable to those reported in the Canadian Health Measures Survey (CHMS) and the National Health and Nutrition Examination Survey (NHANES) from the USA. The CHMS is representative of the general Canadian

Table 3.51 Concentrations of selected contaminants across Arctic countries, compared with biomonitoring in non-Arctic areas. Data presented as geometric means, in blood of pregnant women or WCBA, except for DDE and PCB153 in Sweden and Finland which are levels in breast milk. POPs presented in µg/kg plasma lipid and metals in µg/L whole blood. Source: AMAP (2009), US CDC (2009, 2011a, 2014a), Health Canada (2010, 2013), Jones et al. (2010), Glynn et al. (2011b); Lignell et al. (2014); Ayotte pers. comm. (2014), Berner pers. comm. (2014), Dewailly pers. comm. (2014), Dudarev pers. comm. (2014), Weihe pers. comm. (2014), Long et al. (2015).

	Alaska[a]	Canada (Nunavik)	Greenland (East)[a]	Iceland[a]	Faroe Islands[a]	Norway[a]	Sweden	Finland	Russia	CHMS	NHANES
DDE	82.7	130[a]	587	36	131	38.7	34[b,c]	na	102[a]	102[d]	241[e]
PCB153	14.8	40[a]	288	34	91.2	24.8	24[b,c]	18.7[b]	12.2[a]	8.2[d]	19.7[e]
PBDE47	19.8	<LOD[a]	2.4	1.7	na	na	0.4[b,c]	1.6[b,f]	na	10.8[d]	19.6[e]
PBDE99	4.5	<LOD[d]	1.3	<1.3	na	na	na	1.6[b,f]	na	N/C[g]	N/C[g]
PFOS	2.2	3.9[a]	15.8	6.2	na	8.0[c]	6.7[d]	na	na	4.4[d]	7.6[e]
Total Hg	2.2	5.2[a]	7.0	na	na	1.2	0.6[a,c]	na	1.6[d]	0.7[d]	0.7[e]
Pb	7.4	14[a]	6.0	na	na	7.4	10[d,c]	na	29.6[d]	8.5[d]	8.4[e]
Se	181	300[a]	140	na	na	84.7	na	na	na	190[d]	188[e]

CHMS: Canadian Health Measures Survey; NHANES: US National Health and Nutrition Examination Survey. [a]Pregnant women; [b]data are for breast milk from first-time mothers (µg/kg lipid); [c]median value; [d]WCBA; [e]data for all females, aged 12+ years; [f]PBDE47 and PBDE99 result combined with other PBDEs; [g]geometric mean not calculated as proportion of results below limit of detection was too high to provide a valid result.

population that does not include the Canadian Arctic (Health Canada 2010, 2013). NHANES is also a nationally representative survey, representing the non-Arctic general population of the United States (US CDC 2009). Lead is also elevated in certain Arctic regions, especially in the Chukotka Peninsula of Russia, and Nunavik and Nunavut in Canada, but other Arctic countries have levels similar to those in the non-Arctic biomonitoring results. Levels of DDE in Eastern Greenland populations are higher than those found in other countries. However, levels of DDE in all females aged 12 and older from the USA are higher than pregnant women from the ACCEPT project in the rest of Greenland, and women from other Arctic countries. WCBA sampled in Nunavik (Canada) and mothers in the Faroe Islands have elevated levels compared to the CHMS. Levels of DDE in pregnant women from Russia's Murmansk region are comparable to those found in Canadian women aged 20–39 years from the CHMS.

Comparisons of PBDEs and PFOS and PFOA concentrations in blood samples obtained in Arctic countries and non-Arctic countries may point to different exposure pathways. PBDE47 levels in the maternal population in Alaska exceed those tested under the CHMS or NHANES, and they far exceed those found in other Arctic countries. PBDE99 levels in all Arctic populations exceed those found in the general population tested by the CHMS and NHANES, in that a geometric mean could not be reliably calculated for this contaminant because so few of the analyzed population in the CHMS and NHANES had levels above the limit of detection. Populations in Greenland showed very high levels of PFOS, whereas concentrations found in pregnant women in Iceland and first-time mothers in Sweden are more comparable to the concentrations found in the CHMS and NHANES. Geographical differences in concentrations of PBDEs and PFCs between Arctic populations may also be due to large-scale differences in the movements of the air masses and ocean currents carrying pollutants into the Arctic via long-range transport, or animal migration (AMAP 1998; Möller et al. 2012).

3.8 Conclusions and recommendations

3.8.1 Conclusions

Biomonitoring studies are an essential component of managing human health risks from exposure to environmental contaminants, including the ability to analyze the risks and benefits for human populations which consume traditional food. Biomonitoring activities are currently ongoing in the eight Arctic countries.

Maternal transfer of POPs and metals to infants is decreasing as maternal levels decrease (e.g. Faroe Islands), resulting in levels in newborns presently being lower than they were 20 years ago. However, data show that children are still accumulating higher levels of contaminants in their early years, with levels decreasing later in adolescence and early adulthood (e.g. Faroe Islands, Russia), potentially due to dilution through growth, changes in dietary preference and/or other factors.

Levels of most POPs have declined significantly since 1979, as seen in Norwegian men, although certain PFCs show no such decline. Changes in PBDE levels follow a different pattern to most other POPs, suggesting an alternative exposure route, such as dust from indoor furnishings (e.g. Whitehead et al. 2015). PBDEs may not accumulate in the same way as other POPs, such as PCBs in the food chain, or a combination of sources of exposure from food and consumer products or furnishings causes a different accumulation pattern. This still needs investigation.

Blood Hg concentrations are still elevated in Greenland, parts of Canada, and the Faroe Islands, although they are lower now in maternal blood than in 1986. Levels in Norway and Sweden have decreased and are now equivalent to those found in non-Arctic North America, such as for US women aged 16–49 years in 2009–2010 (0.86 μg/L) (US EPA 2013) and Canadian women aged 20–39 years from the general population in 2007–2009 (geometric weighted mean 0.70 μg/L) (Lye et al. 2013).

Blood Pb concentrations are still elevated in parts of Russia and Canada, whereas levels in other Arctic countries have declined. As suggested by Fillion et al. (2014), there may be other important sources of exposure in addition to lead shot in country food, such as paint and ammunition dust contributing to the Pb load in house dust.

Precaution, including dietary advice (see Chap. 6), is still important for WCBA and pregnant women in the Arctic. Despite elevated levels, certain high concern contaminants (e.g. *p,p'*-DDT, PCB153, HCB, Hg) in the presented Arctic populations are continuing to decrease relative to previous years. It is possible that this is evidence that international and national risk management of long-range transport contaminants may be having a positive effect, an indicator being the decline in measured body burdens after considering the population demographic and birth years for sampled populations. While local dietary advice and dietary transitions may also be resulting in decreased current exposure (see Chap. 6), for the more persistent POPs, older individuals born prior to the regulatory actions may nonetheless be expected to have a greater lifetime accumulation. Differences in levels seen between men and women may also be evidence that specific dietary recommendations for WCBA and pregnant women may be reaching their target populations, although this may depend on the length of time of dietary advisory compliance required to see changes in body burden. Moreover, a woman's reproductive behaviors, such as breastfeeding and number of children born, can have additional impacts on their chemical body burden. Although the observation that decreasing levels of contaminants in women are resulting in a decline in contaminant exposure for the fetus, there have been fewer studies across time involving men, thus it is less clear whether adult men are protected from the potential health effects of elevated body burdens of contaminants of concern.

Despite global action through the Stockholm Convention to reduce the production and use of POPs, contaminants are still being transported to and recycled within the Arctic environment (Möller et al. 2012; Garmash et al. 2013). In addition to long-range transport as a source of contaminants to the Arctic, there is evidence that global warming may affect the cycling of contaminants within the Arctic environment (Carrie et al. 2010), with the potential for release of contaminants currently held in soil, permafrost or ice,

although few changes have been seen in the Arctic food webs to date (Garmash et al. 2013) (see also Chap. 7). Nevertheless, changes in the structure and dynamics of the Arctic food webs, especially in relation to species forming part of the traditional diet, could have implications for contaminant levels in Arctic populations, with associated impacts on human health. Although time series data sets indicate a current decline in concentration for most POPs in Arctic biota, particularly PCBs and DDT, and contaminants such as PBDEs and PFOS that, prior to 2000 appeared to be increasing now appear to show either no trends or a decrease (AMAP 2014), the potential implications for human health highlight the clear need to continue biomonitoring contaminants of concern. Further biomonitoring will also aid in measuring the success of international risk management strategies for reducing risk for all Arctic and vulnerable populations.

3.8.2 Recommendations

- Analytical laboratories are highly recommended to **participate in an external QA/QC program** and are encouraged to submit compound-specific performance results.
- **Continue coordinated international biomonitoring** in order to provide a globally comparable data set, using as similar a study design as possible or a single international effort, especially for Stockholm Convention contaminants and Hg.
- Recognizing the varying requirements of ethics approval committees, **store samples for longer periods of time in biobanks** to facilitate the identification of long-term trends in new contaminants of concern.
- **Continue research concerning dietary and non-dietary sources of PBDEs and PFCs**, to complement knowledge of exposure sources of other POPs.
- **Undertake monitoring for new contaminants and elucidate sources of exposure** for Arctic populations.
- **Increase focus on the effects and levels of POPs and metals in men** in the Arctic to protect their health, and **further research effects for the fetus from health impacts for men**, such as epigenetic changes in sperm due to contaminant exposure.
- **Sustain and expand international effort on the monitoring of contaminants transported over long distances** to the Arctic, to support international conventions and risk management, and communication activities with Arctic populations.
- **Investigate the use of Se levels as a biomarker for a traditional diet**, and the potential health benefits of Se.
- **Investigate the speciation of Se in traditional Arctic diets**.
- **Increase efforts to find specific evidence of selenosis or Minamata disease in Arctic populations**.
- **Develop and apply tools for measuring changes of significance in contaminant body burdens** for Arctic nations, and **attribute identified trends to external factors** such as changes in lifestyle or dietary practices, or improvements in the Arctic environment.
- **Continue to develop innovative tools** (e.g. Biomonitoring Equivalents, comparative and accessible sampling methodologies, new or novel laboratory techniques) to help generate, analyze and interpret biomonitoring data and to support public health authorities.

Chapter 3 Appendix

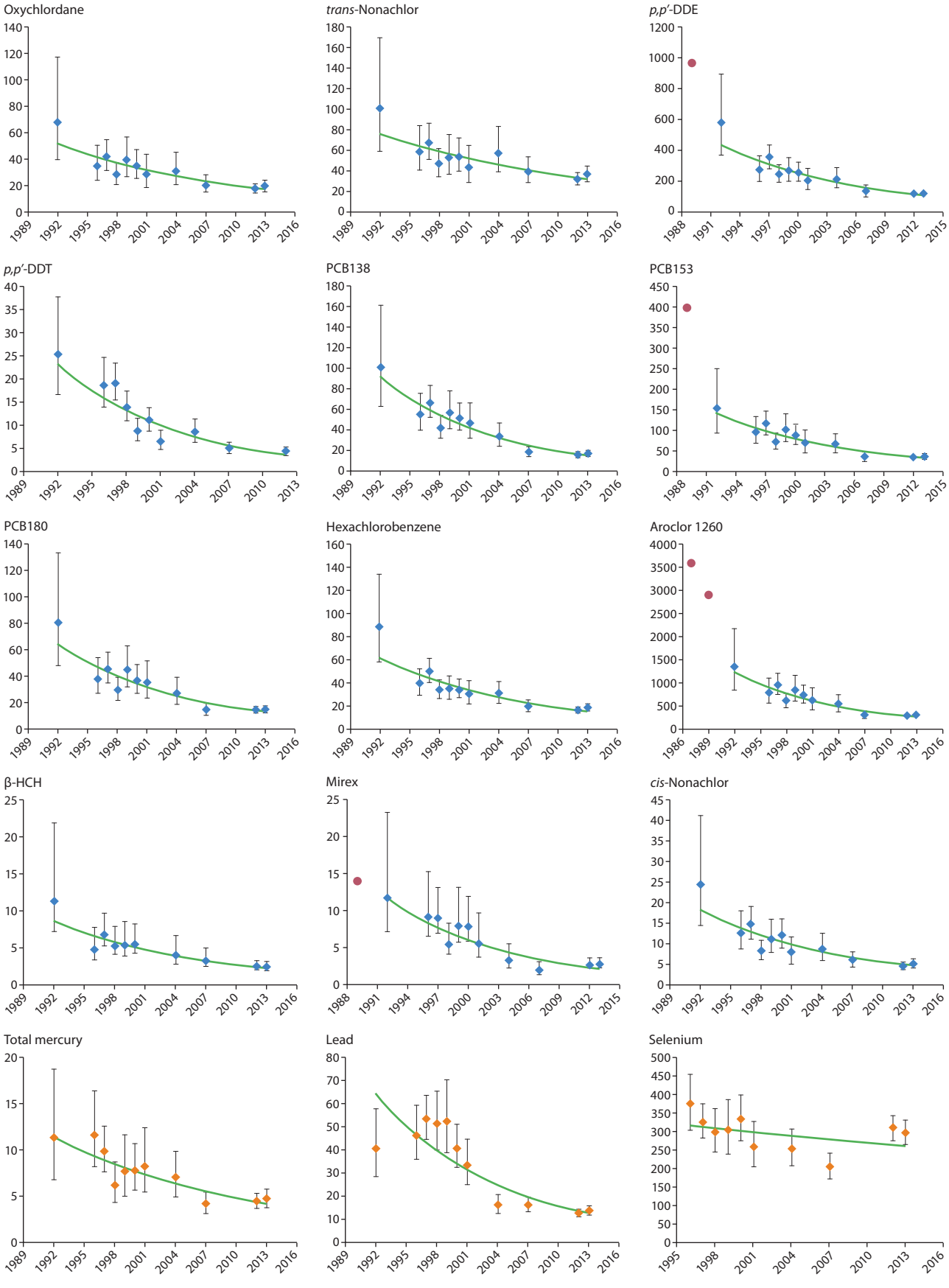

Fig. A3.1 Trends in contaminant concentrations (geometric means, 95% confidence intervals) in pregnant Inuit women from Nunavik, Canada. A special analysis (Pereg pers. comm. 2007) was performed on the data, using regression adjusted for age and region (Hudson or Ungava) and smoking status (smoker vs. non-smoker). Source: Dewailly pers. comm. (2014).

Table A3.1 Confidence intervals (95%) for data presented in Sect. 3.4.3.1 and 3.4.3.2, as well as geometric means of additional contaminants among Inuit men in Greenland by age group (years). POPs in µg/kg plasma lipid, metals in µg/L whole blood. Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012); Bjerregaard et al. (2013); Valera et al. (2013c).

Mean age (range)	24 (18–29)		41 (30–49)		61 (≥50)		*p*
	Mean (range)	95% CI	Mean (range)	95% CI	Mean (range)	95% CI	
Aldrin	1.8 (1.0–3.0)	1.7–1.9	1.5 (0.6–4.0)	1.4–1.5	1.6 (0.4–440)	1.5–1.8	<0.001
α-Chlordane	1.8 (1.0–4.4)	1.7–1.9	1.5 (0.3–4.7)	1.4–1.6	1.6 (0.2–440)	1.5–1.8	<0.001
γ-Chlordane	0.88 (0.6–1.0)	0.86–0.9	0.77 (0.3–13)	0.75–0.79	0.84 (0.1–230)	0.78–0.89	0.004
Oxychlordane		57.2–85.5		180–231		443–538	
trans-Nonachlor		119–168		335–414		735–865	
cis-Nonachlor		23.3–32.8		63–77		126–147	
p,p'-DDT		14.8–19.6		24.4–29.4		35.8–43.1	
p,p'-DDE		470–664		970–1172		1682–1962	
DDE:DDT		29.6–37.3		38–41.9		43.5–49.1	
HCB		66.6–87.8		159–190		341–398	
β-HCH		9.8–13.3		26.1–31.2		48.7–56.8	
Mirex		10.6–15.4		31.7–40.5		81.5–100	
PCB28	8.8 (6.0–20)	8.6–9.1	7.4 (0.6–27)	7.2–7.7	7.8 (1.0–1400)	7.3–8.4	0.004
PCB52	54.7 (30–80)	52.7–56.8	46.6 (7.2–170)	45.3–47.9	49.3 (2.3–14000)	45.9–53	0.006
PCB99		28.3–40		57.7–70.7		101–119	
PCB101	7.2 (3.0–40)	6.6–7.9	8.7 (1.8–120)	8.1–9.3	11.6 (1.3–440)	10.7–12.6	<0.001
PCB105	5.2 (1.0–29)	4.5–6.1	11.3 (1.0–230)	10.2–12.5	24.2 (1.0–440)	22.2–26.4	<0.001
PCB118		23.5–33.1		61.6–75.7		142–167	
PCB128	3.2 (1.0-16)	2.7–3.4	3.6 (0.7–51)	3.4–3.9	5.0 (1.0–440)	4.6–5.5	<0.001
PCB138		95.8–132		207–246		372–429	
PCB153		232–300		497–598		997–1159	
PCB156	13.6 (1.0–110)	11.8–15.9	34.4 (3.2–590)	31.6–37.5	82.3 (6.3–510)	76.6–88.4	<0.001
PCB163	42.1 (3.0-260)	35.6–49.9	102 (7.3–1600)	92.9–113	247 (9.2–1200)	227–268	<0.001
PCB170	45.9 (3.0–460)	38.4–54.9	111 (11–2000)	100–122	234 (19–1400)	217–254	<0.001
PCB180		112–160		302–366		690–809	
PCB183	13.7 (1.0–89)	11.7–16	26.5 (2.5–380)	24.3–28.9	46.9 (3.1–440)	43.6–50.6	<0.001
PCB187	53.7 (3.0–280)	45.7–63.1	123 (11–1700)	112–134	249 (15–1100)	232–267	<0.001
Hg		6.7–9.2		15.4–18.2		25.8–31	
Se		173–203		264–297		329–377	

Sample size for OC pesticides: n=856–859; sample size for PCBs: n=796–859; sample size for Hg: n=1375; sample size for Se: n=1366.

Table A3.2 Confidence intervals (95%) for data presented in Sect. 3.4.3.1 and 3.4.3.2, and geometric means of additional contaminants among Inuit women in Greenland by age group (years). POPs in µg/kg plasma lipid, metals in µg/L whole blood. Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012); Bjerregaard et al. (2013); Valera et al. (2013c).

Mean age (range)	24 (18–29)		40 (30–49)		61 (≥50)		*p*
	Mean (range)	95% CI	Mean (range)	95% CI	Mean (range)	95% CI	
Aldrin	1.7 (1.0–5.0)	1.6–1.8	1.5 (0.7–3.0)	1.5–1.6	1.4 (0.8–400)	1.3–1.5	<0.001
α-Chlordane	1.7 (0.7–3.0)	1.6–1.8	1.5 (0.2–5.7)	1.5–1.6	1.4 (0.2–400)	1.3–1.5	<0.001
γ-Chlordane	0.84 (0.2–200)	0.82–0.86	0.78 (0.2–1.4)	0.77–0.8	0.76 (0.2–200)	0.71–0.81	0.022
Oxychlordane		48.2–64.8		120–149		401–475	
trans-Nonachlor		95.6–122		218–262		649–744	
cis-Nonachlor		19.5–24.8		41.5–49.6		112–127	
p,p'-DDT		13.8–16.9		21.2–24.6		32.5–39	
p,p'-DDE		394–499		764–906		1723–1981	
DDE:DDT		26.9–31.4		34.7–38.3		48.6–55.4	
HCB		62.5–77.3		134–157		367–416	
β-HCH		9.1–11.4		20.4–23.8		49.4–56.1	
Mirex		6.8–8.8		18.6–22.5		59–71.7	
PCB28	8.4 (5.0–20)	8.2–8.6	7.3 (0.9–20)	7.1–7.5	7.0 (0.4–1200)	6.5–7.5	<0.001
PCB52	50.6 (30–100)	49.3–52	47.4 (9.7–170)	46.4–48.4	45 (4.4–12000)	41.8–48.3	0.014
PCB99		23.4–30.2		47.4–56.3		103–119	
PCB101	6.5 (4.0–32)	6.1–6.9	7.9 (2.6–77)	7.5–8.4	10.6 (1.3–400)	9.8–11.4	<0.001
PCB105	5.3 (1.0–44)	4.7–5.9	10.4 (1.0–95)	9.6–11.3	25.1 (2.0–400)	23.3–27	<0.001
PCB118		24.7–31.4		54.4–64.5		151–172	
PCB128	2.6 (1.0–16)	2.5–2.9	3.3 (0.6–35)	3.1–3.6	4.9 (0.8–400)	4.4–5.3	<0.001
PCB138		72.5–90.9		158–185		366–424	
PCB153		150–192		350–416		930–1069	
PCB156	8.2 (1.0–56)	7.3–9.1	21.6 (1.0–250)	19.9–23.5	73.4 (8.3–480)	68.2–79.1	<0.001
PCB163	27.6 (4.7–200)	24.4–31.2	67.6 (2.0–550)	61.8–74	219 (21–1600)	202–238	<0.001
PCB170	27.4 (4.1–270)	24.1–31.4	68.9 (2.0–690)	62.9–75.5	196 (23–1200)	181–212	<0.001
PCB180		69.6–90		187–223		562–659	
PCB183	9.4 (1.8–53)	8.5–10.6	20.9 (2.0–170)	19.3–22.6	46.9 (2.2–420)	43.7–50.3	<0.001
PCB187	34.5 (5.7–190)	30.8–38.7	82.1 (2.2–520)	75.7–89	230 (27–2000)	215–246	<0.001
Hg		7.3–9.5		12–14		20.3–24.1	
Se		191–217		255–279		351–397	

Sample size for OC pesticides: n=1051–1053; sample size for PCBs: n=995–1053; sample size for Hg: n=1730; sample size for Se: n=1721.

Table A3.3 Confidence intervals (95%) for data presented in Sect. 3.4.3.1, and geometric means of additional contaminants by region and residence in towns or villages, Greenland. POPs in µg/kg plasma lipid. Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012); Bjerregaard et al. (2013); Valera et al. (2013c).

	Avanersuaq[a]		North-west[b]		South-west[c]		East[d]		Nuuk[e]
	Town	Villages	Towns	Villages	Towns	Villages	Town	Villages	Town
Sample size	n=245–246	n=30	n=265–331	n=123–187	n=325–350	n=188–251	n=172	n=180	n=125–154
PCB28	7.5 (7.3–7.8)	7.7 (7.2–8.2)	5.7 (5.3–6.1)	8.5 (8.2–8.8)	7.5 (7.3–7.7)	7.8 (7.6–8.1)	7.8 (7.5–8.0)	8.1 (7.9–8.4)	10.7 (8.9–12.9)
PCB52	45.6 (44–47.2)	44 (42–48.1)	45.3 (42.9–47.8)	49.3 (47.6–51.1)	46 (44.7–47.2)	45.6 (44.5–46.7)	47.2 (45.6–48.8)	49.1 (47.4–51)	67.3 (55.2–81.9)
PCB99	(70.9–87.5)	(79.1–140)	(69.4–82.8)	(93.4–118)	(28.6–35.6)	(71–86.8)	(71.6–92.5)	(118–142)	(23.1–33.4)
PCB101	11.7 (10.8–12.8)	14.8 (11.6–18.8)	8.9 (8.4–9.6)	10.8 (9.9–11.8)	5.8 (5.5–6.0)	7.9 (7.5–8.5)	9.7 (8.8–10.7)	15.5 (13.7–16.4)	6.9 (5.9–8.2)
PCB105	17.9 (16–20.1)	26 (19.7–34.2)	15.6 (14.3–17.1)	17.6 (15.6–19.9)	5.9 (5.3–6.6)	14.3 (12.8–15.8)	15.5 (13.5–17.8)	29.6 (26.7–32.7)	6.6 (5.4–8.0)
PCB118	(87–111)	(102–187)	(95.4–115)	(87.9–113)	(33.3–42)	(85.3–105)	(72.7–95.9)	(149–184)	(27.6–39.4)
PCB128	4.0 (3.7–4.3)	5.4 (4.3–6.6)	3.3 (3.0–3.5)	4.1 (3.7–4.5)	2.5 (2.3–2.6)	4.1 (3.7–4.4)	5.9 (5.2–6.7)	8.6 (7.7–9.4)	2.9 (2.4–3.5)
PCB138	(205–254)	(208–382)	(234–278)	(220–276)	(120–149)	(297–365)	(233–313)	(415–504)	(86–115)
PCB153	(525–666)	(531–1105)	(551–660)	(681–879)	(258–326)	(730–912)	(522–697)	(897–1112)	(183–247)
PCB156	32.1 (28.1–36.7)	34.7 (22.2–54.1)	41.2 (37.4–45.4)	41.1 (35.4–47.6)	19.9 (17.6–22.5)	50 (44.4–56.4)	34.1 (29–40.2)	66.1 (57.9–75.8)	17.4 (14.5–20.8)
PCB163	110 (96.7–125)	136 (91.1–202)	110 (98.6–124)	123 (107–142)	48.1 (42.4–54.4)	166 (148–188)	113 (97–132)	207 (183–234)	31.5 (26.7–37.2)
PCB170	109 (95.1–124)	141 (92.2–215)	96.2 (87.7–106)	166 (144–192)	56.9 (50.2–64.5)	156 (137–177)	129 (109–153)	222 (196–252)	41.7 (35.5–48.9)
PCB180	(273–358)	(263–612)	(293–356)	(404–544)	(154–199)	(433–559)	(316–441)	(567–733)	(104–142)
PCB183	24.5 (22.1–27.1)	30.7 (23.3–40.5)	26.4 (24.3–28.7)	28.5 (25.5–31.7)	17.6 (15.7–19.6)	44.5 (39.9–49.5)	33 (29–37.6)	50.5 (45.8–55.6)	13.8 (11.5–16.4)
PCB187	125 (112–140)	147 (107–203)	126 (115–138)	120 (106–136)	74.5 (65.9–84.1)	205 (184–228)	130 (113–150)	225 (201–252)	54.2 (46–63.8)

[a]Qaanaq 2010; [b]Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik 2006; [c]Qaqortoq 2005–2006, Nanortalik 2007, Narsaq 2007, Maniitsoq 2007; [d]Tasiilaq 2008; [e]Nuuk 2007.

Table A3.4 Confidence intervals (95%) for data presented in Sect. 3.4.3.1, and geometric means of additional OC pesticides by region and residence in towns or villages, Greenland. POPs in µg/kg plasma lipid. Data from the Inuit Health in Transition study, 2005–2010. Source: Nielsen et al. (2012); Bjerregaard et al. (2013); Valera et al. (2013c).

	Avanersuaq[a]		North-west[b]		South-west[c]		East[d]		Nuuk[e]
	Town	Villages	Towns	Villages	Towns	Villages	Towns	Villages	Town
Sample size	n=246	n=30	n=330–331	n=185–187	n=346–350	n=250–251	n=171–172	n=180	n=154
Aldrin	1.34 (1.29–1.4)	1.3 (1.2–1.5)	1.67 (1.62–1.71)	1.6 (1.5–1.7)	1.48 (1.42–1.53)	1.45 (1.39–1.51)	1.47 (1.4–1.55)	1.64 (1.55–1.72)	2.2 (1.8–2.7)
α-Chlordane	1.38 (1.32–1.44)	1.5 (1.3–1.8)	1.4 (1.31–1.48)	1.6 (1.5–1.7)	1.47 (1.42–1.53)	1.54 (1.47–1.61)	1.5 (1.4–1.6)	1.65 (1.57–1.74)	2.2 (1.8–2.7)
γ-Chlordane	0.72 (0.7–0.74)	0.73 (0.69–0.78)	0.81 (0.78–0.84)	0.8 (0.78–0.82)	0.76 (0.74–0.78)	0.77 (0.75–0.79)	0.78 (0.75–0.79)	0.83 (0.79–0.87)	1.1 (0.9–1.3)
Oxychlordane	(301–400)	(334–742)	(217–269)	(384–528)	(69.6–92.5)	(253–329)	(158–218)	(339–436)	(49.4–72)
trans-Nonachlor	(507–649)	(504–950)	(405–498)	(417–552)	(157–203)	(460–573)	(281–374)	(508–632)	(112–161)
cis-Nonachlor	(88.2–112)	(92.5–164)	(68–82.1)	(68.3–89.3)	(32.4–41.3)	(84.7–104)	(53.9–70.7)	(99.2–122)	(22.7–32.7)
p,p'-DDT	(28.6–34.6)	(31–53.4)	(22.4–26.2)	(25.1–31.7)	(13.5–15.7)	(30.6–37.3)	(31.4–41.2)	(61.3–74.4)	(13.3–19.8)
p,p'-DDE	(1085–1339)	(1137–2030)	(1124–1339)	(1140–1445)	(534–672)	(1412–1717)	(1103–1430)	(1877–2297)	(416–567)
DDE:DDT	(36.2–40.5)	(31.8–43.7)	(48–53.2)	(42.6–48.6)	(38.4–44.5)	(43.5–48.8)	(32–38)	(28.9–32.7)	(25.7–35)
HCB	(232–292)	(256–461)	(291–347)	(230–293)	(96.8–120)	(184–222)	(125–159)	(250–301)	(81.1–116)
β-HCH	(43.1–55.1)	(52.7–101)	(28.2–32.8)	(41.3–52.7)	(13.9–16.9)	(28.6–34.9)	(19.8–26.1)	(38.2–47.6)	(12.8–18.1)
Mirex	(35.1–46.8)	(41.2–95.1)	(25.1–31.4)	(38.9–55)	(15.1–20)	(38.9–55)	(30.2–42.7)	(58.1–77.1)	(9.7–14.7)

[a]Qaanaq 2010; [b]Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik 2006; [c]Qaqortoq 2005–2006, Nanortalik 2007, Narsaq 2007, Maniitsoq 2007; [d]Tasiilaq 2008; [e]Nuuk 2007.

Table A3.5 Additional POPs in pregnant women from different regions in Greenland in 2010–2011 and 2013. Data presented as geometric means (range). Data in µg/kg plasma lipid. Source: Long et al. (2015).

	North[a]	Disko Bay[b]	West[c]	South[d]	East[e]	*p*	All[f]
Mean age (range)	28 (21–35)	27 (19–40)	27 (17–44)	28 (21–41)	33 (31–37)		27 (17–44)
No. individuals sampled	n=15	n=50	n=124	n=15	n=3		n=207
No. individuals measured	n=14	n=50	n=122	n=15	n=3		n=204
PFHpS	0.27 (0.06–1.44)	0.22 (0.06–0.63)	0.17 (0.06–1.15)	0.14 (0.06–0.34)	0.31 (0.11–0.58)	0.007	0.19 (0.06–1.44)
PFNA	1.85 (0.47–7.35)	1.37 (0.67–3.34)	1.23 (0.41–7.71)	1.0 (0.44–1.6)	2.0 (0.79–3.21)	0.006	1.29 (0.41–7.71)
PFHpA	0.03 (0.02–0.14)	0.04 (0.03–0.18)	0.03 (0.02–0.26)	0.03 (0.02–0.1)	0.02 (0.02–0.02)	0.367	0.03 (0.02–0.26)
PFUnA	2.88 (0.71–12.1)	2.34 (0.32–16.3)	1.44 (0.18–14.9)	1.25 (0.48–4.69)	3.11 (0.64–18.2)	0.001	1.68 (0.18–18.2)
PFDoA	0.45 (0.21–1.02)	0.35 (0.2–1.36)	0.29 (0.21–1.39)	0.32 (0.21–1.85)	0.27 (0.21–0.49)	0.074	0.31 (0.2–1.85)
PFTrA	0.21 (0.21–0.21)	0.21 (0.21–0.21)	0.21 (0.21–0.9)	0.21 (0.21–0.21)	0.21 (0.21–0.21)	0.76	0.21 (0.21–0.9)

The *p* value is the difference among five regions in Greenland (one-way ANOVA analysis). [a]Qaanaaq, Upernavik, Uummannaq; [b]Ilulissat, Qasigiannguit, Qeqertarsuaq, Aasiaat; [c]Sisimiut, Maniitsoq, Nuuk, Paamiut; [d]Nanortalik, Narsaq, Qaqortoq; [e]Tasiilaq; [f]Includes the 15 Greenland districts.

Table A3.6 Concentrations of additional PFCs (µg/L serum) in pregnant Inuit women from Denmark and Greenland. The district is given by where the Inuit lived for the longest time. Data presented as geometric means (range). Data from the ACCEPT project (2010–2011 and 2013). Source: Long et al. (2015).

	Denmark	Greenland	*p*	All[a]
Arithmetic mean age (range)	32 (29–41)	27 (17–44)		27 (17–44)
No. individuals sampled	n=5	n=207		n=212
No. individuals measured	n=5	n=204		n=209
PFHxS	0.64 (0.38–0.85)	0.69 (0.13–4.48)	0.33	0.68 (0.13–4.48)
PFNA	1.11 (0.8–1.93)	1.29 (0.41–7.71)	0.3	1.28 (0.41–7.71)
PFHpA	0.04 (0.03–0.09)	0.03 (0.02–0.26)	0.96	0.03 (0.02–0.26)
PFUnA	1.75 (0.68–6.63)	1.68 (0.18–18.2)	0.26	1.68 (0.18–18.2)
PFDoA	0.37 (0.21–0.66)	0.31 (0.2–1.85)	0.21	0.32 (0.2–1.85)
PFTrA	0.21 (0.21–0.21)	0.21 (0.21–0.9)	0.21	0.21 (0.21–0.9)

[a]Includes Denmark and the 15 Greenland districts.

Table A3.7 Unadjusted 95% confidence intervals of total Hg and Se (µg/L whole blood) by region and residence in towns or villages, Greenland. Data from the Inuit Health in Transition study 2005–2010. Source: Nielsen et al. (2012), Bjerregaard et al. (2013), Valera et al. (2013c).

	Avanersuaq[a]		North-west[b]		South-west[c]		East[d]		Nuuk[e]
	Town	Villages	Towns	Villages	Towns	Villages	Town	Villages	Town
	n=246	n=30	n=576–578	n=244	n=897–902	n=283	n=172	n=179	n=430–441
Total Hg	65.4–80.7	68.7–116	16.7–19.3	42.7–51.9	8.2–9.3	20.7–24.2	7.4–12	42.7–51.9	5.9–7.1
Se	682–814	1029–1720	229–249	298–338	250–275	357–449	174–193	251–279	199–220

[a]Qaanaaq 2010; [b]Aasiaat 2005–2006, Qasigiannguit 2005, Upernavik 2006; [c]Qaqortoq 2005–2006, Nanortalik 2007, Narsaq 2007, Maniitsoq 2007; [d]Tasiilaq 2008; [e]Nuuk 2007.

Table A3.8 Correction to AMAP (2009) data. Trends in contaminant concentrations (µg/kg plasma lipids for POPs, µg/L whole blood for metals) in pregnant Inuit women from Disko Bay, Greenland. Data show geometric means (range) for specified period of sampling. Statistical analysis a linear regression using log variables adjusted for age. Source: Deutch and Hansen (2000); Deutch et al. (2007a); Deutch unpubl. data; Krüger et al. (2012).

	1994	1995	1996	1997	1999	2006	*p*
Mean age (range)	25 (20–35)	27 (20–35)	27 (20–35)	25 (20–34)	25 (20–34)	27 (21–35)	
Sample size	n=9	n=94	n=63	n=12	n=21	n=20	
Oxychlordane	61 (8.5–289)	63 (2.7–417)	55 (2.5–241)	58 (4.0–190)	40 (1.9–148)	20 (3.8–67)	<0.0001
p,p'-DDE	477 (224–986)	408 (63–2216)	342 (61–1246)	453 (142–2023)	269 (75–692)	178 (34–481)	<0.0001
PCB153	143 (63–471)	193 (39–918)	169 (40–563)	204 (72–596)	118 (43–372)	69 (22–224)	<0.0001
Total Hg	14 (3.3–42)	14 (2.0–75)	11 (5.0–29)	na	13 (2.0–58)	12 (3.5–33)	ns
Pb	26 (13–81)	37 (15–389)	32 (9.0–98)	na	50 (25–135)	13 (2.8–48)	<0.0001

Table A3.9 Correction to AMAP (2009) data. Concentrations of POPs (µg/kg plasma lipids) in Inuit women of childbearing age from Greenland. Data show geometric means (range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch pers. comm. (2007); Krüger et al. (2012).

	Sisimiut	Qaanaaq	Nuuk	Qeqertarsuaq	Narsaq	All Greenland[a]
	2002–2003	2003	2005	2006	2006	1999–2006
Mean age (range)	33 (18–44)	33 (18–44)	36 (19–45)	34 (21–45)	35 (18–50)	33 (18–50)
Sample size	n=42	n=34	n=45	n=44	n=42	n=299
Oxychlordane	35 (2.0–290)	164 (5.4–1249)	25 (4.0–250)	45 (3.8–403)	69 (7.5–670)	82 (20–2132)
trans-Nonachlor	77 (7.7–564)	278 (19–1530)	62 (9.3–471)	100 (11–687)	144 (18–1158)	149 (7.7–1530)
p,p'-DDT	3.8 (1.3–56)	21 (1.7–131)	4.3 (1.1–24)	7.2 (2.7–48)	12 (3.0–143)	13 (1.1–359)
p,p'-DDE	250 (37–1453)	581 (28–3296)	283 (51–1617)	364 (34–2388)	596 (54–3148)	553 (28–5847)
DDE:DDT	65 (13–270)	28 (8.5–120)	66 (9.5–280)	51 (10–270)	50 (5.2–410)	42 (5.2–410)
HCB	68 (11–308)	152 (13–639)	52 (22–265)	99 (12–984)	95 (19–342)	102 (11–984)
β-HCH	7.1 (1.4–33)	29 (1.8–139)	4.1 (1.1–38)	7.1 (0.82–66)	10 (1.7–42)	14 (0.8–291)
Mirex	5.6 (1.4–24)	18 (1.8–99)	4.7 (1.0–49)	5.9 (0.82–63)	12 (0.83–77)	12 (0.8–234)
Total toxaphene	40 (6.8–218)	110 (9.2–614)	41 (5.5–200)	55 (5.3–391)	70 (5.0–707)	76 (5.0–941)
Parlar 26	13 (1.4–87)	40 (1.8–247)	8.9 (1.3–40)	20 (2.0–137)	27 (2.0–280)	26 (1.3–373)
Parlar 50	18 (1.4–126)	61 (1.8–362)	16 (1.8–81)	35 (3.3–254)	43 (3.0–427)	40 (1.4–528)
Aroclor 1260	950 (168–3824)	2819 (222–15858)	970 (272–6764)	1117 (184–6500)	2259 (253–10609)	2213 (168–36380)
PCB118	21 (3.1–114)	58 (3.0–263)	20 (2.2–119)	28 (3.0–258)	36 (5.7–204)	43 (2.2–575)
PCB138	54 (11–237)	155 (13–700)	59 (20–353)	69 (9.0–417)	146 (18–722)	139 (9.0–2125)
PCB153	128 (20–524)	385 (30–2350)	126 (33–926)	144 (22–896)	286 (31–1463)	283 (20–4870)
PCB180	54 (8.4–201)	171 (21–1268)	63 (13–500)	73 (8.0–583)	132 (15–605)	140 (8.0–3594)
ΣPCB_{14}	353 (67–1384)	1043 (99–5980)	358 (97–2427)	430 (58–2500)	807 (93–3571)	825 (58–13242)

[a]Includes Ittoqqortoormiit 1999, Uummannaq 1999, Tasiilaq 2000, Sisimiut 2002–2003, Qaanaaq 2003, Nuuk 2005, Qeqertarsuaq 2006 and Narsaq 2006.
ΣPCB_{14} includes PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187.

Table A3.10 Correction to AMAP (2009) data. Concentrations of POPs (µg/kg plasma lipid) in Inuit men from Nuuk, Greenland by age category. Data show geometric means (range) for 2005. Source: Deutch et al. (2007a), Deutch pers. comm. (2007).

Mean age (range)	36 (35–38)	46 (42–50)	61 (51–77)	All ages, 55 (35–77)
Sample size	n=3	n=16	n=31	n=50
Oxychlordane	98 (85–111)	193 (25–575)	446 (125–1724)	302 (25–1724)
trans-Nonachlor	199 (171–231)	449 (69–1220)	934 (338–3793)	657 (69–3793)
p,p'-DDT	14 (13–16)	18 (1.4–72)	31 (10–106)	25 (1.4–106)
p,p'-DDE	760 (442–1304)	919 (232–2352)	1818 (437–10344)	1351 (232–10344)
DDE:DDT	55 (28–104)	51 (19–170)	58 (28–101)	55 (19–170)
HCB	114 (81–159)	218 (40–647)	405 (146–1149)	302 (40–1149)
β-HCH	12 (9.7–16)	25 (1.4–65)	49 (22–149)	36 (1.4–149)
Mirex	20 (13–30)	32 (7.0–120)	88 (19–321)	56 (7.0–321)
Total toxaphene	103 (100–106)	219 (31–560)	347 (134–1413)	274 (31–1413)
Parlar 26	21 (20–22)	46 (6.2–119)	77 (31–310)	59 (6.2–310)
Parlar 50	41 (40–42)	87 (13–220)	135 (50–551)	107 (13–551)
Aroclor 1260	3083 (2429–3913)	4262 (1315–12083)	9163 (3728–27586)	6527 (1315–27586)
PCB118	57 (34–94)	76 (13–220)	170 (63–540)	119 (13–540)
PCB138	177 (135–232)	234 (68–680)	463 (203–1264)	342 (68–1264)
PCB153	422 (342–521)	585 (178–1666)	1290 (491–4022)	909 (178–4022)
PCB180	208 (157–275)	322 (106–875)	823 (260–2643)	542 (106–2643)
ΣPCB_{14}	1123 (875–1442)	1600 (490–4361)	3594 (1396–11112)	2509 (490–11112)

ΣPCB_{14} includes PCB28, PCB52, PCB99, PCB101, PCB105, PCB118, PCB128, PCB138, PCB153, PCB156, PCB170, PCB180, PCB183, PCB187.

Table A3.11 Correction to AMAP (2009) data. Concentrations of metals (µg/L whole blood) in Inuit women of childbearing age, Greenland. Data show geometric means (range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch pers. comm. (2007).

	Sisimiut	Qaanaaq	Nuuk	Qeqertarsuaq	Narsaq	All Greenland[a]
	2002–2003	2003	2005	2006	2006	1999–2006
Mean age (range)	32 (18–44)	33 (18–44)	36 (19–45)	34 (21–45)	34 (18–50)	33 (18–50)
Sample size	n=42	n=36	n=45	n=44	n=42	n=299
Total Hg	8.2 (1.2–33)	50 (5.7–164)	2.2 (0.5–10)	18 (3.5–65)	13 (4.1–60)	13 (0.5–164)
Pb	30.2 (8.0–118)	36 (18–164)	16 (5.0–101)	16 (2.8–84)	18 (2.0–404)	26.8 (2.0–404)
Cd	0.8 (0–5.3)	1.7 (0–11)	0.8 (0–2.5)	0.8 (0–2.1)	1.1 (0–6.4)	1.1 (0–11)
Se	158 (69–363)	502 (120–1910)	124 (58–428)	213 (86–798)	140 (85–409)	196 (58–1910)

[a]Includes Ittoqqortoormiit 1999, Uummannaq 1999, Tasiilaq 2000, Sisimiut 2002–2003, Qaanaaq 2003, Nuuk 2005, Qeqertarsuaq 2006 and Narsaq 2006.

Table A3.12 Correction to AMAP (2009) data. Concentrations of metals (µg/L whole blood) in Inuit men, Greenland. Data show geometric means (range) for specified period of sampling. Source: Deutch et al. (2004, 2007a), Deutch pers. comm. (2007).

	Sisimiut	Qaanaaq	Nuuk	Qeqertarsuaq	Narsaq	All Greenland[a]
	2002–2003	2003	2005	2006	2006	1999–2006
Mean age (range)	31 (18–46)	34 (19–45)	44 (35–50)	35 (20–45)	39 (23–50)	35 (18–50)
Sample size	n=52	n=43	n=19	n=35	n=29	n=314
Total Hg	6.5 (1.4–23)	54 (2.3–240)	16 (3.1–52)	22 (3.5–79)	10 (3.0–25)	20 (1.4–240)
Pb	39 (12–267)	42 (14–231)	52 (16–127)	23 (9.3–102)	20 (3.6–71)	43 (3.6–380)
Cd	1.2 (0–7.6)	1.4 (0–7.5)	1.4 (0.4–6.2)	0.7 (0–3.5)	0.8 (0–5.4)	1.4 (0–7.6)
Se	141 (59–1457)	468 (73–1379)	274 (95–1241)	255 (86–2258)	132 (72–397)	219 (59–2258)

[a]Includes Ittoqqortoormiit 1999, Uummannaq 1999, Tasiilaq 2000, Sisimiut 2002–2003, Qaanaaq 2003, Nuuk 2005, Qeqertarsuaq 2006 and Narsaq 2006.

Table A3.13 Blood concentrations of OCs and other POPs in pregnant women in their third trimester, from Reykjavik, Iceland. Data presented as geometric means (range). POPs are reported in µg/kg plasma.

	2009
Mean age; Median age (range)	30.4; 30 (21–43)
Sample size	n=33
Oxychlordane	0.021 (0.01–0.07)
trans-Nonachlor	0.041 (0.02–0.12)
p,p'-DDT	0.01 (<0.01–0.045)
p,p'-DDE	0.222 (0.06–1.1)
DDE:DDT	25.7 (11.2–62.2)
HCB	0.122 (0.06–0.21)
β-HCH	0.044 (0.02–0.13)
Toxaphene Parlar 26	<0.01 (<0.01–0.036)
Toxaphene Parlar 50	0.018 (<0.01–0.057)
PCB99	0.023 (0.01–0.078)
PCB118	0.052 (0.029–0.14)
PCB138	0.091 (0.03–0.31)
PCB153	0.208 (0.09–0.56)
PCB180	0.098 (0.04–0.41)
ΣPCB_{14}	0.654 (0.336–1.92)
PBDE47	0.011 (<0.01–0.164)
PBDE99	<0.01 (<0.01–0.029)
PBDE100	<0.01 (<0.01–0.039)
PBDE153	<0.01 (<0.01–0.031)

Table A3.14 Concentrations of additional PCBs in pregnant women (early pregnancy) from northern Norway (mean parity = 0.9 (0–4)). Average values presented for compounds with detection frequencies ≥70%. Data presented as geometric means (range), in µg/kg plasma lipid. Source: Hansen et al. (2010).

	2006–2008
Mean age (range)	30.6 (18–43)
Sample size	n=515
PCB156[a]	2.3 (<LOD–26.3)
PCB163	3.4 (0.7–24.6)
PCB170	6.4 (1.0–59.2)
PCB183[a]	1.5 (<LOD–20.6)
PCB187	4.3 (0.8–29.5)

[a]Detection frequency 50–69%. For statistical purposes, all values below the limit of detection (LOD) were replaced by LOD/√2.

Table A3.15 Concentrations of additional essential elements in pregnant women (early pregnancy) from northern Norway. Data presented as geometric mean [standard deviation] or geometric mean (range), in µg/L whole blood except for Cu and Zn which are in mg/L whole blood. Source: AMAP (1998), Hansen et al. (2011).

	Kirkenes	Hammerfest	Bergen	Tromsø	Northern Norway[a]
	1994	1994	1994	1995	2006–2008
Sample size	n=40	n=57	n=50	n=15	n=282
As	na	na	na	na	1.5 (0.1–12.8)
Co	na	na	na	na	0.1 (0.02–0.6)
Mo	na	na	na	na	0.7 (0.2–2.3)
Mn	na	na	na	na	10.6 (3.8–37.8)
Cu	2.2 [±0.3]	2.1 [±0.4]	2.1 [±0.4]	2.1 [±0.3]	1.6 (1.0–2.9)
Zn	0.7 [±0.1]	0.5 [±0.1]	0.8 [±0.2]	0.5 [±0.1]	5.2 (2.7–9.8)

[a]Mean age (range)=30.6 (18–43), mean parity (range)=0.9 (0–4).

Table A3.16 Concentrations of contaminants in the general population of Sweden, by region arranged south to north. Data presented as arithmetic mean (95% confidence interval), except for the collective Sweden data which are the median (maximum). Data from the Riksmaten 2010–2011 study. Data adjusted for age, sex and education. PFCs in µg/L and PBDEs in ng/kg.

	Lund	Gothenburg region	Linköping	Stockholm	Örebro	Uppsala	Umeå	Sweden (maximum)
PFHpA	na	na	na	na	na	na	na	0.02 (0.3)[a]
PFNA	0.6 (0.5–0.8)	0.6 (0.5–0.7)	0.6 (0.5–0.8)	0.7 (0.6–0.8)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.6 (0.5–0.7)	0.8 (4.6)[a]
PFUnDA	0.2 (0.2–0.3)	0.3 (0.2– 0.4)	0.2 (0.2–0.3)	0.3 (0.2–0.4)	0.2 (0.2–0.3)	0.2 (0.2–0.3)	0.2 (0.2–0.25)	0.3 (1.9)[a]
PFDoDA	na	na	na	na	na	na	na	0.04 (0.3)[a]
PBDE28	na	na	na	na	na	na	na	50 (2360)[b]
PBDE66	na	na	na	na	na	na	na	0 (296)[b]
PBDE138	na	na	na	na	na	na	na	0 (670)[b]
PBDE183	na	na	na	na	na	na	na	66.4 (758)[b]

[a]n=292; [b]n=170.

Table A3.17 Concentrations of contaminants in serum in the general population of Sweden, by region arranged south to north. Data presented as arithmetic mean (95% confidence interval), except for the collective Sweden data which are the median (maximum). Data from the Riksmaten 2010–2011 study. Data not lipid-adjusted, but adjusted for age, sex and education using a linear model. PCBs and OCs in ng/L, and PBDEs and HBCD in ng/kg. Source: Bjermo et al. (2013a,b,c).

	Lund	Gothenburg region	Linköping	Stockholm	Örebro	Uppsala	Umeå	Sweden (maximum)
Oxychlordane	12 (10–16)	9.3 (7.1–12)	11 (8.9–15)	12 (9.1–15)	11 (8.5–14)	11 (8.5–14)	10 (7.8–13)	16.6 (135)[a]
trans-Nonachlor	24 (19–31)	18 (14–23)	20 (16–25)	23 (18–30)	20 (16–26)	21 (17–27)	20 (16–26)	35.5 (267)[a]
p,p'-DDT	na	na	na	na	na	na	na	8.2 (152)[a]
p,p'-DDE	506 (353–724)	351 (238–517)	358 (249–515)	480 (329–701)	373 (256–543)	450 (312–650)	363 (252–524)	434 (15494)[a]
HCB	72 (61–85)	55 (46–65)	66 (56–79)	77 (65–92)	60 (50–71)	61 (51–72)	66 (56–78)	78.9 (780)[a]
β-HCH	30 (23–40)	16 (12–22)	23 (17–31)	26 (20–35)	19 (15–26)	18 (14–24)	20 (15–27)	26.3 (368)[a]
PCB118	33 (24–43)	22 (16–30)	28 (21–37)	34 (25–46)	27 (20–37)	27 (20–36)	34 (25–46)	37.3 (974)[a]
PCB138	184 (146–232)	118 (92–152)	140 (111–178)	151 (118–193)	140 (110–179)	143 (113–181)	159 (126–202)	189 (1452)[a]
PCB153	394 (320–486)	273 (218–343)	314 (254–388)	319 (255–398)	300 (241–374)	316 (255–392)	321 (259–398)	449 (2789)[a]
PCB180	247 (202–302)	183 (147–228)	204 (166–251)	195 (158–242)	185 (149–228)	203 (165–249)	183 (149–225)	364 (1574)[a]
PBDE47	na	na	na	na	na	na	na	493 (44600)[b]
PBDE99	na	na	na	na	na	na	na	94.2 (6070)[b]
PBDE100	na	na	na	na	na	na	na	206 (3700)[b]
PBDE153	1063 (812–1393)	1135 (850–1516)	1302 (973–1741)	966 (705–1324)	1036 (784–1370)	1061 (823–1368)	1005 (766–1320)	1235 (6990)[b]
PBDE154/BB 153	179 (131–244)	182 (130–254)	205 (146–286)	195 (135–280)	142 (103–196)	191 (142–256)	183 (134–250)	280 (5360)[b]
PBDE 209	1213 (717–2055)	1722 (972–3050)	1253 (711–2209)	1111 (601–2054)	1079 (626–1860)	1251 (762–2052)	1162 (684–1974)	948 (77900)[b]
HBCD	na	na	na	na	na	na	na	101 (76800)[b]

[a]n=267; [b]n=170.

Table A3.18 Trends in POPs concentrations in breast milk samples from Swedish first-time mothers (µg/kg lipid weight). Samples collected three weeks after delivery. Data presented as median concentrations. Source: Lignell et al. (2014).

Year	PCB28	n	PCB153	n	Total-TEQ[a,b]	n	HCB	n	*p,p'*-DDE	n	PBDE47	n	PBDE153	n
1996	2.5	26	74	26	16	15	17	26	131	26	1.3	19	0.38	19
1997	1.9	68	62	68	13	38	16	68	109	68	1.8	57	0.45	57
1998	1.8	88	56	88	16	29	15	88	104	88	1.7	63	0.49	63
1999	1.7	21	59	21	12	15	14	21	100	21	1.5	19	0.54	19
2000–2001	1.9	28	56	28	12	23	14	28	75	28	1.7	28	0.62	28
2002–2003	1.4	30	43	32	11	16	8.9	30	58	30	1.3	29	0.67	29
2004	1.9	32	35	32	8.6	15	10	32	62	32	1.4	29	0.68	29
2006	1.2	30	31	30	8.2	30	7.6	30	63	30	0.99	30	0.68	30
2008	1.2	31	32	31	6.7	30	7.9	31	39	31	0.76	31	0.57	31
2009	1.1	29	27	29	na	na	7.6	29	52	29	0.55	29	0.49	29
2010	0.98	30	24	30	5.2	30	na	na	na	na	0.46	30	0.45	30
2012	na	na	na	na	na	na	7.0	30	34	30	0.42	30	0.54	30

[a]PCDD/F TEQ+mono-ortho PCB TEQ+non-ortho PCB TEQ; [b]Data reported in pg/g lipid weight.

Table A3.19 Trend in PFC concentrations (µg/kg pooled serum) in blood drawn three weeks after delivery from nursing Swedish first-time mothers. Three pools per year analyzed, with serum from 5 to 25 individuals in each pool. Data presented as geometric means. Source: Glynn et al. (2011b, 2012).

Year	PFHxS	PFOS	PFOA	PFDA
1996	2.1	24.4	2.6	0.18
1997	1.8	21.8	2.6	0.23
1998	1.8	21.4	2.4	0.21
1999	2.2	21.5	2.6	0.15
2000-2001	2.4	22.6	2.7	0.2
2002	2.7	19.5	2.6	0.22
2004	2.5	15.3	2.1	0.28
2006	4.0	12.9	1.9	0.26
2007	4.1	13.4	2.0	0.26
2008	4.3	10.2	2.1	0.27
2009	4.8	8.2	1.9	0.32
2010	6.4	6.7	1.7	0.33

Table A3.20 Trends in Pb concentration (µg/L whole blood) in men and women grouped by age (25–35 years and 50–60 years) and smoking behavior from Västerbotten, Sweden from 1990–2009. Data show median (range) for specified period of sampling. Source: Sundkvist et al. (2011).

		1990		1994		1999		2004		2009	
			n		n		n		n		n
Men											
25–35	All	38.1 (15.5–112)	26	23.9 (6.1–56.3)	25	17.6 (8.9–190)	25	na		11 (3.5–35.6)	68
	Never smoked	38.1 (15.5–112)	16	25.1 (6.1–56.3)	20	15.7 (8.9–82.5)	17	na		10.8 (3.5–35.6)	57
50–60	All	31.1 (16.2–68.6)	25	39.8 (11.3–98.4)	15	24.1 (12.6–48.1)	25	na		13.3 (4.8–42)	82
	Never smoked	30.4 (16.2–62.8)	8	16.1 (11.3–39.8)	3	20.8 (13–41.6)	7	na		11.6 (6.0–35.2)	32
Women											
25–35	All	20 (10.3–48.2)	25	14.9 (7.9–37)	25	12.8 (6.7–315)	24	10.5 (4.8–70)	164	7.7 (3.3–88.2)	91
	Never smoked	19.6 (10.5–36.4)	12	16.4 (9.7–37)	15	11.2 (6.7–18.1)	13	10.8 (4.8–70)	111	7.4 (3.3–25.4)	64
50–60	All	24.4 (5.5–47.9)	29	22.5 (9.0–48.8)	24	17 (4.4–49.4)	24	14.8 (6.0–60.2)	123	12.8 (5.4–61)	86
	Never smoked	20.1 (5.5–47.9)	15	16.9 (12–48.8)	8	16.6 (4.4–49.4)	12	14.4 (6.0–44.6)	54	11.8 (5.9–32.5)	35

Table A3.21 Trends in Cd concentration (µg/L whole blood) in men and women grouped by age (25–35 years and 50–60 years) and smoking behavior from Västerbotten, Sweden from 1990–2009. Data show median (range) for specified period of sampling. Source: Sundkvist et al. (2011).

		1990		1994		1999		2004		2009	
			n		n		n		n		n
Men											
25–35	All	0.1 (0.02–2.9)	26	0.08 (0.02–2.2)	24	0.08 (0.02–0.7)	25	na		0.1 (0.04–0.8)	68
	Never smoked	0.1 (0.02–0.2)	16	0.07 (0.02–0.2)	20	0.08 (0.02–0.1)	17	na		0.1 (0.04–0.4)	57
50–60	All	0.2 (0.05–3.1)	25	0.2 (0.08–2.1)	15	0.2 (0.04–0.7)	25	na		0.2 (0.05–4.3)	82
	Never smoked	0.1 (0.05–0.2)	8	0.2 (0.1–0.7)	3	0.2 (0.04–0.2)	7	na		0.1 (0.05–0.4)	32
Women											
25–35	All	0.2 (0.07–3.0)	25	0.1 (0–1.7)	25	0.1 (0.06–1.6)	24	0.2 (0.07–3.0)	164	0.1 (0.05–3.4)	91
	Never smoked	0.1 (0.07–0.3)	12	0.1 (0–0.3)	15	0.1 (0.06–0.2)	13	0.1 (0.07–0.4)	111	0.1 (0.05–0.4)	64
50–60	All	0.2 (0.06–2.7)	29	0.2 (0.2–1.5)	24	0.4 (0.09–1.8)	24	0.3 (0.09–2.0)	123	0.2 (0.08–2.6)	86
	Never smoked	0.2 (0.1–0.4)	15	0.2 (0.2–0.3)	8	0.2 (0.09–0.6)	12	0.2 (0.09–0.7)	54	0.2 (0.08–0.5)	35

Table A3.22 Concentrations of POPs in pregnant women, non-pregnant women, men and the general population (men and non-pregnant women of all ages) in the Pechenga district of Murmansk Oblast, 2013–2014. Data from the Kolarctic Project (KO467). Data lipid-adjusted (µg/kg lipid weight) and presented as arithmetic mean (standard deviation). Source: Dudarev pers. comm. (2014).

	Pregnant women	Women	Men	General population
Mean age (range)	28.2 (16–41)	44.2 (26–65)	39.2 (27–54)	42.5 (26–65)
Sample size	n=50	n=17	n=33	n=50
p,p'-DDT	30.1 (±70)	24.8 (±26.5)	53.2 (±42.3)	35.4 (±35.6)
p,p'-DDE	159 (±206)	173 (±115)	216 (±205)	188 (±151)
HCB	24.5 (±34.9)	37.4 (±19.1)	49 (±39.8)	41.2 (±27.8)
β-HCH	18.4 (±29.7)	65.9 (±38)	49.3 (±21.3)	60.9 (±34.5)
PCB118	31.1 (±22.5)	41.2 (±22.7)	55.8 (±32.6)	45.8 (±26.7)
PCB138	13.1 (±10.6)	33.5 (±19.2)	49.5 (±23.6)	38.7 (±21.8)
PCB153	15.6 (±11.2)	32.2 (±17)	54.7 (±31.4)	39.4 (±24.6)

Table A3.23 Concentrations of POPs in pregnant women, non-pregnant women, men and the general population (men and non-pregnant women of all ages) in the Pechenga district of Murmansk Oblast, 2013–2014. Data from the Kolarctic Project (KO467). Data wet weight (µg/L serum) and presented as geometric means [arithmetic means] and (range). Source: Dudarev pers. comm. (2014).

	Pregnant women	Women	Men	General population
Mean age (range)	28.2 (16–41)	44.2 (26–65)	39.2 (27–54)	42.5 (26–65)
Sample size	n=50	n=17	n=33	n=50
p,p'-DDT	0.09 [0.24] (0.01–3.11)	0.14 [0.17] (0.07–0.57)	0.19 [0.27] (0.06–0.7)	0.16 [0.2] (0.06–0.7)
p,p'-DDE	0.82 [1.28] (0.14–8.56)	1.03 [1.36] (0.34–4.66)	0.85 [1.05] (0.27–3.36)	0.97 [1.25] (0.27–4.66)
HCB	0.15 [0.2] (0.04–2.22)	0.24 [0.27] (0.09–0.55)	0.21 [0.24] (0.06–0.74)	0.23 [0.26] (0.06–0.74)
β-HCH	0.07 [0.15] (0.01–1.31)	0.41 [0.48] (0.14–1.2)	0.24 [0.25] (0.14–0.54)	0.34 [0.41] (0.14–1.2)
PCB118	0.21 [0.25] (0.08–0.99)	0.26 [0.29] (0.13–0.64)	0.24 [0.27] (0.07–0.66)	0.26 [0.28] (0.07–0.66)
PCB138	0.07 [0.11] (0.01–0.46)	0.21 [0.25] (0.05–0.6)	0.23 [0.27] (0.08–0.72)	0.22 [0.26] (0.05–0.72)
PCB153	0.1 [0.13] (0.01–0.4)	0.2 [0.24] (0.06–0.54)	0.25 [0.28] (0.14–0.64)	0.22 [0.25] (0.06–0.64)

4. Health effects associated with measured levels of contaminants in the Arctic

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4.1 Introduction

The Human Health Assessment Group has over the past decade recommended that effect studies be conducted in the circumpolar area. Such studies examine the association between contaminant exposure in the Arctic populations and health effects. Because fetuses and young children are the most vulnerable, effect studies are often prospective child cohort studies. Chapter 2 provides an overview of the ongoing cohort and dietary studies in the Arctic and detailed exposure information is available in Ch. 3. The emphasis in this chapter is on a description of the effects associated with contaminant exposure in the Arctic. The main topics addressed are neurobehavioral (Sect. 4.2), immunological (Sect. 4.3), reproductive (Sect. 4.4), cardiovascular (Sect. 4.5), endocrine (Sect. 4.6) and carcinogenic effects (Sect. 4.7). For each topic, the association between exposure and effects is described and some results are reported for similar studies outside the Arctic.

4.2 Neurobehavioral effects

4.2.1 Mercury

One of the cohort studies established to determine the exposure levels and potential health effects of contaminants in an Arctic population group is Birth Cohort 1 in the Faroe Islands (see Chap. 2, Sect. 2.2.17). This cohort was established in 1986 and 1987 to investigate the effects of fetal exposure to mercury (Hg) owing to the frequent consumption of whale meat at that time by pregnant women. Follow-ups of the children in this cohort have indicated the serious and permanent neurobehavioral effects of fetal exposure to Hg even at low levels. As these findings are among the most important of the present assessment, a detailed summary of these results is given here.

In the first follow-up of the children in this cohort, at age 7 years, clinical examination and neurophysiological testing did not reveal any clear-cut Hg-related abnormalities. However, Hg-related neuropsychological dysfunctions were observed in language, attention, and memory, and to a lesser extent in visuospatial and motor functions. These associations remained after adjusting for covariates and after excluding children whose mothers had hair Hg concentrations over 10 μg/g (50 nmol/g). Effects on brain function associated with prenatal methylmercury (MeHg) exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe (Grandjean et al. 1997).

At age 14 years, 878 cohort members underwent detailed neurobehavioral examination (Debes et al. 2006). The neuropsychological test battery was designed based on the same criteria as applied at the examination at age 7 years (Grandjean et al. 1997, 2012d). Indicators of prenatal MeHg exposure were significantly associated with deficits in finger tapping speed, reaction time on a continued performance task, and cued naming. Postnatal MeHg exposure had no discernible effect. These findings are similar to those obtained at age 7 years, and the relative contribution of Hg exposure to the predictive power of the multiple regression models was also similar. An analysis of the test score difference between results at 7 and 14 years suggested that Hg-associated deficits had not changed between the two examinations. In structural equation model analyses, the neuropsychological tests were separated into five groups; MeHg exposure was significantly associated with deficits in motor, attention, and verbal tests. These findings are supported by independent assessment of neurophysiological outcomes. The effects on brain function associated with prenatal MeHg exposure therefore appear to be multi-focal and permanent.

As an objective measure of neurobehavioral toxicity in 14-year-olds, auditory evoked potential latencies (EVP; Murata et al. 2004) were recorded and compared with their cord blood Hg concentration at birth. Auditory evoked potentials are small electrical voltage potentials recorded in response to an auditory stimulus from electrodes placed on the scalp. They reflect neuronal activity seen as peaks in the recording from the electrodes. The response latency from auditory stimulus to the peaks is only a few milliseconds. Latencies of peaks III and V increased by about 0.012 ms when the cord blood Hg concentration doubled. As seen at age 7 years, this effect appeared mainly within the I-III interpeak interval. Despite lower postnatal exposures, hair Hg level at age 14 years was associated with prolonged III-V interpeak latencies. All benchmark dose results were similar to those obtained for dose-response relationships at age 7 years. Thus, the persistence of prolonged I-III interpeak intervals indicates that some neurotoxic effects from prenatal MeHg exposure are irreversible. A change in vulnerability to MeHg toxicity is suggested by the apparent sensitivity of the peak III-V component to recent MeHg exposure (Murata et al. 2004).

Methylmercury exposure was associated with decreased sympathetic and parasympathetic modulation of the heart rate variability. Parallel MeHg-related delays of brainstem auditory evoked potential (BAEP) latencies may be caused by underlying MeHg neurotoxicity to brainstem nuclei (Grandjean et al. 2004).

At age 22 years, 830 of the young adults were re-examined and administered an extended neuropsychological test battery, covering eight broad ability domains. Effects of MeHg exposure on single neuropsychological outcomes were tested in multiple regression analyses after correction for the same obligatory covariate model as applied in the 14-year-old study. Of the single test variables, six were adversely affected by MeHg to a statistically significant degree after correction for the covariate model: Boston Naming Test, without cues; Boston Naming Test, with cues; Synonyms, WJ III; Antonyms, WJ III; Block Design WAIS-R, Last 3 items (Grandjean pers. comm. 2014); California Verbal Learning Test, Trial 1, Correct (Debes et al. 2016).

The vast majority of the variables were affected in a negative direction, and for each broad ability domain the balance was also in a negative direction, possibly reflecting a weak negative effect in the dataset.

In accordance with traditions in psychometrics for a brief estimation of general mental ability, a structural equation model (SEM) was specified defining a higher-order measurement model with a superordinate latent variable for general intelligence affecting two subordinate latent variables, fluid intelligence and crystallized intelligence with seven manifest indicator variables in total. All manifest indicator variables were corrected for a preselected set of 11 covariates. Second, a measurement model was defined for a latent MeHg exposure variable with two logarithmically transformed manifest indicator variables and one logarithmically transformed manifest formative variable. Finally, a structural model was defined with the latent exposure variable affecting the latent variable for general intelligence (Debes et al. 2016). The fit of the model was acceptable to good as judged from three goodness-of-fit indexes. The standardized effect of the latent exposure variable on the latent variable for general intelligence was -0.145 and was significant (p=0.002). Transformed to the standard IQ-scale, with mean 100 and standard deviation 15, this signifies a loss of 2.2 IQ-points for a ten-fold increase in MeHg exposure.

An extended higher-order measurement model was subsequently specified with a broad definition of general intelligence specified to affect seven subordinate ability domains (Verbal comprehension, Visual-Spatial Processing, Short-Term Memory, Long-Term Storage and Retrieval, Cognitive Processing Speed, Timed Reaction and Decision Speed, Psychomotor Speed and Dexterity), with between two and seven manifest indicator variables each. The extended model also fitted the data well. The standardized effect of the latent exposure variable on the latent variable for general intelligence was -0.093 and was significant (p=0.041). Thus, the negative effect of prenatal exposure to MeHg on general intelligence was still statistically significant when broadly measured in young adulthood at age 22 years. Transformed to the standard IQ-scale, this signifies a loss of 1.4 IQ-points for a ten-fold increase in MeHg exposure. In models for the individual domains, all showed negative associations, with crystallized intelligence being highly significant.

These results demonstrate that the negative effect of MeHg is not limited to narrow, specific or circumscribed so-called differential abilities. It constitutes a significant adverse impact on general mental ability, the variance of which enters into all specific abilities to an often considerable degree. General mental ability is recognized as the strongest single most predictor in the social sciences for success in education and occupation, as well as in many other areas of life. The generality of the effect probably decreases the possibilities for neural or behavioral compensation as late as age 22 years, and thereby signifies a lasting impairment of the intellect with a probable adverse impact on the future life outcomes of the most highly exposed individuals. The results add to understanding of the extent and severity of prenatal exposure to MeHg.

Recent analyses (Debes, F., Ludvig, A., Budtz-Jørgensen, E., Weihe, P., Bellinger, D.C. Grandjean, P., pers. corresp. 2015) have demonstrated a significant indirect effect of latent prenatal MeHg on latent educational attainment in standardized examinations at the end of compulsory education at age 16 years when mediated by a latent factor for general cognitive ability at age 7 years and 14 years. This demonstrates that insofar as educational attainment is dependent on general cognitive ability, and insofar as general cognitive ability is negatively affected by MeHg, there is a highly significant mediated negative effect of MeHg on educational attainment. No direct effect or total effect was found. The same pattern is observed at the level of the individual school subjects, except for a significant independent negative effect of MeHg in mother's hair at delivery on her child's Danish spelling, a significant negative total (indirect + direct) effect of latent MeHg also on Danish spelling, and a significant positive direct effect on mathematical problem solving (the last two results are from models with a latent verbal factor at age 7 years as a mediating variable). The same pattern, with highly significant negative indirect effects, was seen for the subjects' educational status reached at age 22 years (if graduated from high school or had started advanced studies). In the mixed composition of determinants of educational attainment (Kraphol et al. 2014, Rimfeld et al. 2015), some are significantly negatively affected by MeHg (cognitive factors), while others may be less so (factors of personality and mental health), thereby attenuating the total effect of MeHg on educational attainment and status. Thus, whereas significant negative effects from prenatal exposure to MeHg have previously been found on several neuropsychological test results from various functional domains in the same birth cohort at age 7 years, 14 years and 22 years, no independent or direct effects were found on latent variables for educational attainment at age 16 years or educational status at age 22 years Still, recent analyses have demonstrated significant indirect negative effects of MeHg on educational attainment at both the latent and the manifest level at age 16 years and on educational status at age 22 years when mediated by latent variables of verbal or general cognitive ability at age 7 and age 14 years.

In another study, the Nunavik Child Development Study (NCDS; see also Chap. 2, Sect. 2.2.9), a prospective mother-child cohort study taking place in Nunavik (Arctic Quebec), results obtained through both neurobehavioral and electrophysiological testing with children aged 11 years suggested that prenatal Hg exposure is associated with poorer perceptual processing, attentional mechanisms, memory and intellectual function (Boucher et al. 2009, 2010, 2011, 2012a; Jacobson et al. 2015).

In the NCDS, behavioral assessments of 11-year old children were obtained from two questionnaires completed by the child's classroom teacher, which provided scores of attention and internalizing and externalizing problems, and four clinical

diagnoses. Cord blood Hg concentrations were significantly related to attention problems, with consistent results obtained with the two teacher-completed tests. Detailed results are presented by Boucher et al. (2012b). The NCDS was the first to demonstrate that prenatal Hg exposure constitutes a risk factor for attention deficit hyperactivity disorder (ADHD) symptomatology at school age. The increased incidence of teacher-reported ADHD symptoms indicates that the adverse effects on attention previously linked to prenatal Hg exposure in neuropsychological assessments in Nunavik and in the Faroe Islands (e.g. Grandjean et al. 1997; Debes et al. 2006; Julvez et al. 2010) are clinically significant and likely to interfere with learning and performance in the classroom. Likewise, cross-sectional evidence links MeHg exposure to autism spectrum disorder (Geier et al. 2012). However, the evidence available is limited and so conclusions regarding autism or ADHD must be drawn with caution.

The visual system can also be affected by exposure to Hg, and this has been shown in the adult exposed population in the Amazon. In AMAP countries, this has been studied in the NCDS and the Faroese birth cohorts. None of the environmental contaminants considered in the NCDS were associated with negative effects on visual acuity, color perception and contrast sensitivity. Electrophysiological testing was used to measure the integrity of the visual system, and to document subtle Hg effects. Detailed protocols and results were presented by Ethier et al. (2012) and Jacques et al. (2011). A significant association between cord blood Hg and event-related potential (ERP) amplitude at the highest contrast level suggests that a deficit may predominantly involve the parvocellular system, which is specialized in high-contrast vision, visual acuity and color vision. In support of this hypothesis, deficits in acuity and color vision have been reported in association with prenatal Hg exposure in other studies (Cavalleri et al. 1995; Ventura et al. 2004; Fillion et al. 2011). However, in a visual evoked potential (VEP) study involving school-age children from Greenland, no neurotoxic effect was seen on visual processing in relation to prenatal Hg exposure (Weihe et al. 2002). The lack of significant results in Greenlandic children may be due to differences in testing protocols. Similarly, VEP alterations were not observed in 7-year-old Faroese children (Grandjean et al. 1997; Murata et al. 1999) but VEPs were elicited using only checkerboard stimuli presented exclusively at high levels of visual contrast. By manipulating visual contrast levels, the NCDS protocol was designed to optimally detect subtle effects. Changes in VEP latency in association with cord Hg concentrations were previously reported in preschoolers from Nunavik (Saint-Amour et al. 2006). NCDS results at age 11 years show that this negative effect on latency persists at school age.

Overall, the Hg effects seen in the NCDS (Table 4.1) corroborate those reported in the Faroe Islands and New Zealand. Furthermore, results from the highest exposed Faroese and Nunavik cohorts are also observed in studies conducted in lower Hg exposed populations. For example, the Project Viva study in Boston, where fish consumption is higher than average for the United States, showed a mean maternal hair Hg concentration of 0.55 μg/g (Oken et al. 2005). Although these levels are lower than in the Faroe Islands and Nunavik, maternal hair Hg was associated with a reduction in children's cognition at six months of age and again at age 3 years. Comparable results were obtained in New York City at similar exposure levels (Lederman et al. 2008).

The evidence available thus suggests that cognitive impairment occurs at MeHg exposure levels prevalent in general populations elsewhere, and so constitutes a matter of public health concern. Since 2000, prevention efforts have relied on the recommendations of the US National Research Council to maintain MeHg exposure below a Reference Dose (RfD) of 0.1 μg/kg body weight per day (National Academy of Sciences 2000). However, prudent advice is to minimize exposure to the extent possible, because a threshold for adverse effects on brain development may not exist (Grandjean et al. 2012c).

Some of the adverse effects of MeHg on neurodevelopment may be masked by beneficial effects of seafood nutrients (Budtz-Jorgensen et al. 2007). On the other hand, the benefits from seafood nutrients may be offset by the Hg toxicity. Thus, full benefit from fish and seafood diets requires that MeHg exposure is minimized. This was already demonstrated by the studies in Boston and New York City above. Both showed that benefits

Table 4.1 Summary of findings from the 11-year follow-up (2005–2010) in the Nunavik Child Development Study (NCDS).

	Mercury (Hg)	Lead (Pb)	Polychlorinated biphenyls (PCBs)
Prenatal exposure			
	Poorer early processing of visual information	Smaller height	Poorer information processing when the information is being consciously evaluated
	Alteration of attentional mechanisms modulating processing of sensory information	Poorer early processing of visual information	
	Lower estimated IQ	Lower estimated IQ	
	Poorer comprehension and perceptual reasoning	Poorer working memory	
	Poorer immediate memory and recollection of information stored into memory		
	Increased risk of attention problems and ADHD behavior		
Childhood exposure			
	Decreased heart rate variability	Increased risk of ADHD behavior, especially the hyperactive-impulsive type	Reduced physical growth (height, weight, head circumference, BMI)
		Deficit in response inhibition	Non-optimal cognitive processes associated with error monitoring, which result in reduced efficiency during cognitive tasks
			Poorer immediate memory

from the mother's seafood diet to the child's brain development were less when Hg exposure was higher, that is, due to the seafood being contaminated with MeHg. Data from the NCDS showed that the prenatal Hg effect on intellectual function became stronger when cord docosahexaenoic acid (DHA) was also considered, indicating that the beneficial effect of prenatal DHA statistically suppresses the adverse effects of prenatal Hg exposure (Jacobson et al. 2015). Data from the Seychelles show that cognitive development in children is associated with neither maternal fish intake nor MeHg exposure, when examined one at a time. Only if maternal fish intake and Hg are accounted for simultaneously is fish intake clearly beneficial, while Hg has negative effects (Strain et al. 2008). Thus, in the Seychelles population, the positive and negative effects appeared to offset one another.

Given the continued development of the nervous system after birth, postnatal exposure to MeHg is also likely to cause adverse effects. However, the evidence is inconsistent, although this may be due to difficulties in characterizing the trajectory of postnatal exposure. Neurophysiological assessment of brain function supports the notion that postnatal exposure up to the teenage years can cause harm (Murata et al. 2004). Thus, both pregnant women and children should be considered populations at increased risk (Grandjean 2013).

Effects associated with MeHg exposure have been documented in humans at successively lower exposures. This tendency reflects the use of better study design, larger groups of subjects examined, more sensitive methodology and better control of confounding factors that may influence study outcome. From the evidence available, it is clear that the developing brain is the most vulnerable organ system. Given the complexity of brain development and the difficulties in determining detailed functions, especially in small children, it is likely that future studies will continue to identify effects at lower exposures than those considered safe today.

4.2.2 Lead

Few studies have examined the effects of mixed metal exposures in humans. In a Faroese birth cohort the effect of prenatal lead (Pb) exposure in the presence of similar molar-level exposure to MeHg was evaluated. A cohort of 1022 singleton births was assembled during 1986–1987 and Pb was measured in cord blood. A total of 896 cohort subjects participated in a clinical examination at age 7 years and 808 subjects in a follow up at age 14 years. The association between cord-blood Pb concentration and cognitive deficits (attention/working memory, language, visuospatial, memory) was evaluated using multiple regression models. Overall, the Pb concentration showed no clear pattern of association. However, in subjects with a low MeHg exposure, after including statistical interaction terms, Pb-associated adverse effects on cognitive function were observed. In particular, higher cord-blood Pb was associated with a lower digit span forward score on the Wechsler Intelligence Scale for Children-Revised (WISC-R) (β = -1.70, 95% confidence interval (CI): -3.12 to -0.28) at age 7 years and a lower digit span backward score on the WISC-R (β = -2.73, 95% CI: -4.32 to -1.14) at age 14 years. Some interaction terms between Pb and MeHg suggested that the combined effect of the exposures was less than additive (Yorifuji et al. 2011).

Classic IQ tests involving neurobehavioral testing can be complemented by cognitive electrophysiological assessments using event-related potentials (ERPs) to identify subclinical alterations and improve understanding of the impairment of cognitive processes by neurotoxicants. ERP protocols involved the presentation of standard visual or auditory stimuli and the recording of EEG waveforms obtained a few milliseconds after stimulus presentation. In the NCDS, results obtained with 5- and 11-year old children through both neurobehavioral and ERP testing suggested that prenatal Pb is related to poorer cognitive development and intellectual function (Boucher et al. 2009; Jacobson et al., 2015). Furthermore, 11-year old blood Pb concentrations were associated with externalizing problems, with consistent results obtained with two teacher-completed tests (Boucher et al. 2012b). NCDS results relating to postnatal Pb exposure and child behavior replicate those of several previous studies (reviewed by Eubig et al. 2010) although the main source of Pb exposure in Nunavik, lead shot, is unique in the Pb exposure literature.

4.2.3 Persistent organic pollutants

Grandjean et al. (2012d) analyzed banked cord blood from a Faroese birth cohort to determine the possible neurotoxic impact of prenatal exposure to polychlorinated biphenyls (PCBs). The subjects were born in 1986–1987, and 917 cohort members completed a series of neuropsychological tests at age 7 years. Major PCB congeners (PCB118, PCB138, PCB153, PCB180), the calculated total PCB concentration, and the PCB exposure estimated in a structural equation model showed weak associations with test deficits, with statistically significant negative associations only with the Boston Naming test. Likewise, neither hexachlorobenzene (HCB) nor *p,p'*-dichlorodiphenyldichloroethylene (*p,p'*-DDE) showed clear links with neurobehavioral deficits. Thus, these associations were much weaker than those associated with cord-blood Hg concentration, and adjustment for Hg substantially attenuated the regression coefficients for PCB exposure. When the outcomes were subdivided according to motor- and verbally-mediated functions in a structural equation model, the PCB effects remained weak and virtually disappeared after adjusting for MeHg exposure, while Hg remained statistically significant. Thus, in the presence of elevated MeHg exposure, PCB neurotoxicity may be difficult to detect, and PCB exposure does not explain the MeHg neurotoxicity previously reported in this cohort (Grandjean et al. 2012d).

Through electrophysiological testing and traditional neurobehavioral testing, results from the NCDS support the hypothesis of negative effects of prenatal PCB exposure on child cognitive development: prenatal PCB exposure affected processing of information when the information is being consciously evaluated. This effect was seen only in participants that had been breastfed for a short period. In addition, postnatal PCB exposure affects processes associated with error monitoring, an aspect of behavioral regulation required to adapt to the changing demands of the environment, thus resulting in reduced task efficiency (Boucher et al. 2011, 2012a). However, the NCDS failed to confirm the adverse effects of prenatal PCB exposure on IQ reported in Michigan (Jacobson and Jacobson 1996) and Oswego NY (Stewart et al. 2008) but

comparison of the congener profile in Nunavik with that in the Michigan cohort suggests that the PCB mixture to which the children were exposed was likely to be less neurotoxic than in the Michigan study.

4.3 Immunological effects

Certain environmental pollutants can adversely affect the development of the immune system (Dewailly et al. 1993; Weisglas-Kuperus et al. 1995, 2000; Chao et al. 1997; Dewailly et al. 2000; Vine et al. 2001; ten Tusscher et al. 2003; Jusko et al. 2010).

The high incidence of infectious diseases – particularly meningitis, bronchopulmonary infections, and middle ear infections – in young children from Nunavik has been known for many years (Dufour 1988). In view of the immunotoxic properties displayed by some organochlorines (OCs), in particular following perinatal exposure, it has been hypothesized that part of the high infection incidence among Inuit infants could be related to the relatively high maternal body burden of these contaminants, and their partial transfer to newborns during breastfeeding. To test this hypothesis, three epidemiological studies have been conducted during the past 20 years in Arctic Quebec to investigate the relationship between pre- or postnatal OC exposure, immune status, and the occurrence of infectious diseases among Inuit infants. Results in three different groups of Inuit children indicated that prenatal exposure to OCs increases susceptibility to infectious diseases, and in particular to otitis media (Dewailly et al. 2000; Dallaire et al. 2004, 2006). Although potential confounding factors were considered in the statistical analyses, residual confounding is still a possibility. Hence, to verify the plausibility of this association, a toxicological study was performed using the pig model and a relevant OC mixture. Several aspects of immune-system function were observed to alter following developmental exposure to the complex OC mixture (Bilrha et al. 2004). The decrease in the secondary vaccinal response noted in the high-dose group indicates that the OC mixture affected the production of antibodies by B cells and the memory response. This result increases the biological plausibility of associations noted in epidemiological studies between OC exposure during the developmental period and decreased humoral immunity.

Most experimental evidence (Holladay and Smialowicz 2000), although not all (Lyche et al. 2004), points to PCB-associated immunotoxicity being due to effects caused by dioxin-like PCB congeners. The perfluorinated compounds (PFCs) also constitute an immunotoxic hazard. The immune system in mice has been shown to be highly sensitive to perfluorooctane sulfonate (PFOS), with adverse effects on humoral immunity detected at blood concentrations similar to those occurring in humans (Fair et al. 2011). Effects on the immune system by PFOS are supported by several (Keil et al. 2008; Peden-Adams et al. 2008; Fair et al. 2011) although not all (Qazi et al. 2010) experimental studies on rodents, in which adverse effects of PFOS on humoral immune function were observed at serum concentrations similar to those reported in the Faroese study and at levels prevalent in the United States (Kato et al. 2009).

The Faroese studies are the first to provide epidemiological data on human immunotoxicity – as reflected by a reduction in serum antibody production after routine childhood immunizations – in relation to developmental exposures to environmental chemicals (Heilmann et al. 2006, 2010; Grandjean et al. 2012a). The studies showed that developmental and perinatal exposure to PCBs and PFCs from marine food and other sources may inhibit immune function, as indicated by deficient serum concentrations of antibodies against childhood vaccines. Results from the Faroe Islands show that the risk of having an antibody concentration below 0.1 IU/mL at age 7 years increased at higher levels of exposure to PCBs and PFCs. The results suggest that PFCs have an even stronger negative effect than PCBs on serum-antibody concentrations (Heilmann et al. 2006, 2010; Grandjean et al. 2012a). For PCBs, a doubling of the serum concentration at age 18 months was associated with a decline of 20% in the antibody level at age 7 years. After the completion of breastfeeding and associated transfer of PCBs, the child at age 18 months has an average serum-PCB concentration similar to that of the mother (Heilmann et al. 2010), after which the concentration declines as the body lipid compartment continues to expand. For PFCs, the recent accumulation was found to be the most important predictor of immunotoxicity: A doubling in serum-PFC concentration measured at age 5 years was linked to a decrease of up to 50% in the antibody concentration at age 7 years ($p<0.001$). Due to the long half-life of PFCs (Olsen et al. 2007), serum concentrations at early school age are expected to be relatively stable.

In conclusion, elevated exposure to PCBs and PFCs in Faroese children was associated with reduced humoral immune response to routine childhood immunizations (Heilmann et al. 2006, 2010; Grandjean et al. 2012a). The findings suggest a decreased effect of childhood vaccines and may reflect a more general immune system deficit. The clinical implications of insufficient antibody production emphasize the need to prevent immunotoxicant exposure and assessment of risk related to exposure to these contaminants. The Faroese study appears to be the first to epidemiologically link PCB and PFC exposure in children to deficits in immune system function. Follow-up studies of Cohort 1 and Cohort 5 are currently ongoing in the Faroe Islands with the aim to reexamine the effect of pollutants on the immune system on pre-school children and extend this research to adulthood. Studies in other populations and with other exposure levels than those in the Faroe Islands are needed to confirm the PCB and PFC effect on humoral immune responses.

4.4 Reproductive effects

In 1992, Carlsen and co-workers published a combined analysis of results from 61 papers published between 1939 and 1991 and showed a significant decline in sperm count over the 50-year period. A detailed reanalysis of the results found that their conclusion was supported by the underlying studies (Swan et al. 1997, 2000). Following the 1992 publication, many researchers retrospectively analyzed their historical data for temporal trends, some finding a decline and others not.

The causes of decreased semen quality are not clear, but it is feasible that many cases may have been caused by exposure to environmental factors *in utero*, during adolescence or in adulthood (Joensen et al. 2008); probably also acting against a backdrop of different genetic susceptibility to environmental exposure.

The median sperm concentration of fertile men in a semen quality study conducted in Greenland in 2004 was 53 million/mL, with a median sperm cell volume of 3.2 mL, a total sperm count of 186 million and a median motility of 60% (Toft et al. 2004). No regional difference was found in sperm count, but sperm cell motility differed among regions. In a following study, Toft et al. (2006) found that sperm concentration was not impaired by increasing serum PCB153 or *p,p'*-DDE levels in Greenlanders. Also, that there was no association between the proportion of morphologically normal sperm and either PCB153 or *p,p'*-DDE concentration in blood. However, sperm motility was inversely related to PCB153 concentration in this population.

Results concerning male reproductive toxicity in the CLEAR study (see Chap. 2) indicated that exposure to PFOS was associated with more abnormal sperm morphology (Toft et al. 2012) but that PFCs were not consistently associated with other markers of male reproductive function, including reproductive hormones and markers of sperm DNA damage (Specht et al. 2012). There was no observed change in male reproductive function at higher levels of PBDEs and Hg exposure (Mocevic et al. 2013; Toft et al. 2014). However, menstrual cycle characteristics were adversely affected at higher levels of exposure to PFCs as indicated by longer menstrual cycles in women in the highest tertile of PFOS exposure compared to the lowest (Lyngso et al. 2014).

In a recent study on testicular function in the Faroe Islands, Halling et al. (2013) found sperm concentrations for Faroese men to be lower than for Danish men (crude median 40 vs 48 million/mL, $p<0.0005$). However, because semen volume was higher in the Faroese men, the total sperm counts did not differ (159 vs 151 million, $p=0.2$). Similarly, there was no overall difference between the two populations in terms of sperm motility or morphology. Recent data have shown sperm count to be low in young men from several European countries, but slightly higher than among the Danes (Jorgensen et al. 2002; Punab et al. 2002; Richthoff et al. 2002). This indicates that semen quality for both Danish and Faroese men seems to be low compared to men from other European countries.

The inhibin B: follicle-stimulating hormone (FSH) ratios for the Faroese men were lower than for the Danes (64 vs 76, $p=0.001$). Similarly, a lower total testosterone:luteinizing hormone ratio (T:LH; 4.6 vs 6.0, $p<0.0005$) and a lower calculated free-testosterone:luteinizing hormone ratio (FT:LH; 94 vs 134, $p<0.0005$) were detected for the Faroese men (Halling et al. 2013). The low inhibin B:FSH ratio for the Faroese men corroborates the finding of low sperm count, and provides independent evidence of poorer testicular function in the Faroese men than in the Danes, although the medians were at a level where the association between sperm count and inhibin B is weakened (Jorgensen et al. 2010). The lower T:LH and FT:LH ratios indicate a lower Leydig cell capacity among Faroese men compared to Danes. Thus, the level of total testicular function among Faroese men may be the same or lower than for the Danes.

The reason for low testicular function in the Faroese young men is unclear, but could be due to high exposure to persistent organic pollutants (POPs). Studies have shown associations between high PCB levels and low semen quality, and since PCBs and *p,p'*-DDE have the potential to interfere with sex hormone function (Bonefeld-Jørgensen 2010; Bonefeld-Jørgensen et al. 2014), it could be assumed that these compounds can affect the function of the hormone producing organs (Elzanaty et al. 2006). Some reports on the effect of POPs on male reproduction in humans indicate weak negative effects on sperm motility (Hauser et al. 2002; Richthoff et al. 2003; Elzanaty et al. 2006). Among the Faroese men the present study found the percentage of motile cells to be significantly lower compared to Danish men, indicating that increased exposure to endocrine disruptors may be one explanation for the difference.

Serum steroid hormone-binding globulin (SHBG) levels for the Faroese men were much higher than for the Danes. One explanation could be the high PCB levels among the Faroese. Grandjean et al. (2012b) reported that SHBG increased at higher PCB exposure, both prenatally and postnatally. Because PCBs are known to affect a number of liver functions it may be that PCB-induced hepatic SHBG synthesis could play a role, although this remains to be confirmed (Grandjean et al. 2012b).

Studies of the association between previous exposure to PCB153 and *p,p'*-DDE and fetal loss showed the risk of ever experiencing a fetal loss to increase at higher levels of PCB153 and *p,p'*-DDE exposure (Toft et al. 2010). Lower birth weight and shorter gestational age also appear to be associated with higher POPs exposure (Wojtyniak et al. 2010). A large European meta-analysis of birth weight in relation to PCB and DDE exposure confirmed the negative association between PCB exposure and birth weight (Govarts et al. 2012), although it has been questioned as to whether the results could have been biased by maternal weight gain during pregnancy (Verner et al. 2013).

Contaminant effects have also been observed on fetal growth and growth during childhood. In the NCDS, weight, height and head circumference were measured at birth and during childhood. Path analyses were conducted to model the longitudinal relations between exposure variables and growth outcomes in newborns and children. Detailed results were presented by Dallaire et al. (2013). Prenatal exposure to PCB153 and Pb was not associated with fetal growth. However, prenatal exposure to Pb, but not childhood Pb exposure, was related to shorter height in childhood. Plasma PCB levels in 11-year olds were moderately related to smaller height, weight (controlled for height), head circumference and BMI at school-age. In the sample of children followed at 11 year of age, *in utero* exposure to PCB153 was not related to fetal growth but in another sample from the same population (n=248 pregnant women) cord PCB153 and Hg concentrations were related to shorter duration of pregnancy, a recognized determinant of fetal growth (Dallaire et al. 2013), and their associations with reduced fetal growth were mediated through their relation with a shorter gestation duration. PCBs are present in the environment as complex mixtures of different congeners, and the relative proportions of the congeners that comprise these mixtures can differ markedly between various geographic regions. Failure to detect direct effects on fetal growth, as observed in studies in Europe and elsewhere, suggests that the congeners forming the PCB mixture found in the Arctic might be less toxic. The NCDS results support findings from two other studies on children moderately exposed to PCBs, indicating that chronic exposure to PCBs during childhood can adversely

affect skeletal growth and body weight (Karmaus et al. 2002; Burns et al. 2011). Consistent with results from the NCDS, cord blood Pb concentrations are not related to fetal growth in most studies (Greene and Ernhart 1991; Gonzalez-Cossio et al. 1997; Hernandez-Avila et al. 2002; Gundacker et al. 2010), with one exception (Osman et al. 2000). The NCDS is the first study providing empirical evidence that prenatal Pb exposure is related to poorer growth in school-age children.

4.5 Cardiovascular effects

4.5.1 Mercury

Possible cardiovascular effects of Hg have recently emerged in the scientific literature (Roman et al. 2011). A growing body of evidence suggests that MeHg exposure can increase risk of adverse cardiovascular impacts in exposed populations. The link between MeHg and acute myocardial infarction or sudden cardiac death is still debated in low Hg exposed populations (Mozaffarian et al. 2011; Virtanen et al. 2012).

Contradictory results have been reported on Hg exposure and the risk of hypertension (Mozaffarian et al. 2012). In Nunavik adults, a retrospective analysis of the 1992 survey reported no association between Hg and high blood pressure (Valera et al. 2013b). Based on the 2004 data, however, Hg was associated with increased blood pressure and pulse pressure (Valera et al. 2008, 2009). In the Faroe Islands, high blood pressure was found to be associated with Hg exposure among male whale hunters (Choi et al. 2009). In Greenland, no association was found between Hg exposure and high blood pressure (Nielsen et al. 2012). Associations between Hg exposure and blood pressure were also studied in children. Associations were reported between prenatal Hg exposure and lower systolic blood pressure in 7-year-old Faroese children (Sorensen et al. 1999) and for lower diastolic blood pressure in the Seychelles (Thurston et al. 2007). In Nunavik children, no associations were found between blood pressure and either cord blood or contemporary Hg exposure at age 11 years (Valera et al. 2012).

Heart rate variability has also been studied in Arctic populations. An association was reported between Hg exposure and decreased heart rate variability in adults from Nunavik (Valera et al. 2008). Similar results were reported among James Bay Cree adults (Valera et al. 2011b). In children from Nunavik, cord blood Hg concentrations were not related to heart rate variability parameters at age 11 years, but child blood Hg levels were associated with decreased overall heart rate variability parameters, and these associations remained significant after adjusting for cord blood Hg, *n*-3 polyunsaturated fatty acids (PUFA) and selenium. In Faroese children, cord blood Hg concentrations were related to reduced low-frequency (LF) activities at age 7 years as well as with reduced LF, high frequency (HF), HF variation and coefficient of variation for the R-R interval of the electrocardiogram at age 14 years, and hair Hg at age 7 years was associated with LF and LF variation coefficient (Grandjean et al. 2004). A difference that is likely to explain discrepancies between findings with regard to cardiac autonomic activity in childhood is the consideration of cord *n*-3 PUFA and selenium in Nunavik: a significant negative association between cord blood Hg and NN (standard $\beta = -0.13$, $p = 0.05$) was observed after adjusting for most of the traditional risk factors used in the Faroe Islands studies (age, sex, birthweight, child body mass index, smoking during pregnancy), but these associations were no longer significant after adjusting for cord *n*-3 PUFA and selenium. This indicates that not adjusting for the nutrients found in abundance in fish could overestimate the prenatal Hg effect. Differences in study findings might also be attributable to differences in Hg exposure between cohorts. In fact, average cord blood Hg was about 1.5-fold higher among Faroese children (Grandjean et al. 1992) than those from Nunavik, and hair Hg at age 7 years was three times higher in the Faroese study than the Nunavik study. Prenatal Hg exposure was also higher in the Seychelles study than in Nunavik (Thurston et al. 2007).

The predictive value of heart rate variability parameters in healthy children and risk of chronic diseases is unknown. Nevertheless, results from the Faroese and Nunavik cohorts provide evidence that Hg exposure during childhood is related to changes in cardiac autonomic activity at school age.

4.6 Endocrine effects

Environmental chemicals have significant impacts on biological systems. Exposure during early stages of fetal and neonatal development is especially critical and can disrupt the normal pattern of development and thus dramatically alter disease susceptibility in later life. Endocrine-disrupting chemicals are those that interfere with the body's endocrine system and so result in adverse developmental, reproductive, neurological, cardiovascular, metabolic and immune effects in humans. An endocrine-disrupting chemical is defined as 'an exogenous substance or mixture, that alters the function(s) of the endocrine system, and consequently causes adverse health effects in an intact organism or its progeny or (sub)-population' (IPCS 2002). Thus they are compounds that can mimic, interfere with or block the function of endogenous hormones and thereby disrupt the normal hormone homeostasis of the body. Growing evidence shows that endocrine-disrupting chemicals may also modulate the activity and/or expression of steroidogenic hormone receptors and enzymes, having the ability to convert circulating precursors into active hormones as well as to affect hormone metabolism and transport through the body (Yang et al. 2006; Schug et al. 2011; Bonefeld-Jørgensen et al. 2014).

The previous AMAP human health assessment described endocrine-disrupting chemicals and their potential effects mediated via the aryl hydrocarbon receptor (AhR), the estrogen receptor (ER), and the androgen receptor (AR) in detail (Gilman et al. 2009). The present chapter provides an update on recent knowledge and studies since 2008.

4.6.1 Biomarkers of POPs exposure and their endocrine-disrupting effects

4.6.1.1 Legacy POPs and endocrine disruption

Levels and trends of legacy POPs in the Arctic have been assessed since 1997 by AMAP and reports on biomonitoring,

toxicological effects and health risks for Arctic populations were published in 1998 (AMAP 1998), 2003 (Bonefeld-Jørgensen and Ayotte 2003), and 2009 (Bonefeld-Jørgensen 2009). Since 2000, parallel studies have been undertaken in Greenland on the human monitoring of biomarkers for POPs exposure and biomarkers of POPs effects, focusing on hormone-disruptive potentials and genetic sensitivity biomarkers (Bonefeld-Jørgensen 2010; Bonefeld-Jørgensen et al. 2014).

Arctic populations have some of the highest body burdens of POPs globally (Van Oostdam et al. 2004). Levels of some POPs in Arctic Inuit are positively correlated with traditional food consumption (specifically fatty marine mammals), age, and smoking, and *n*-3 PUFA levels in plasma are strong indicators of the main source of POPs in traditional marine food (Deutch et al. 2003, 2004, 2007b; Cote et al. 2004; Bonefeld-Jørgensen 2010). In Greenland (Fig. 4.1), regional differences and sex differences (highest in men) are observed in serum POP levels. The highest levels are found in Inuit living on the east coast (Ittoqqortoormiit and Tasiilaq) and in the north-west (Qaanaaq, although at a lower level) (Deutch and Hansen 2000; Bonefeld-Jørgensen 2010; Krüger et al. 2012) (Fig. 4.2). Higher levels of PCBs, *p,p'*-DDE, and *p,p'*-DDT in marine species and birds on the east coast compared to the west coast (Riget et al. 2004; Vorkamp et al. 2004) might contribute to the differences observed. Some inhabitants in districts and settlements such as Ittoqqortoormiit (east coast) still rely on traditional foods, whereas in Qeqertarsuaq (west coast) and Narsaq (south) the diet is more westernized (Dewailly et al. 1999; Deutch and Hansen 2000; Bonefeld-Jørgensen 2010).

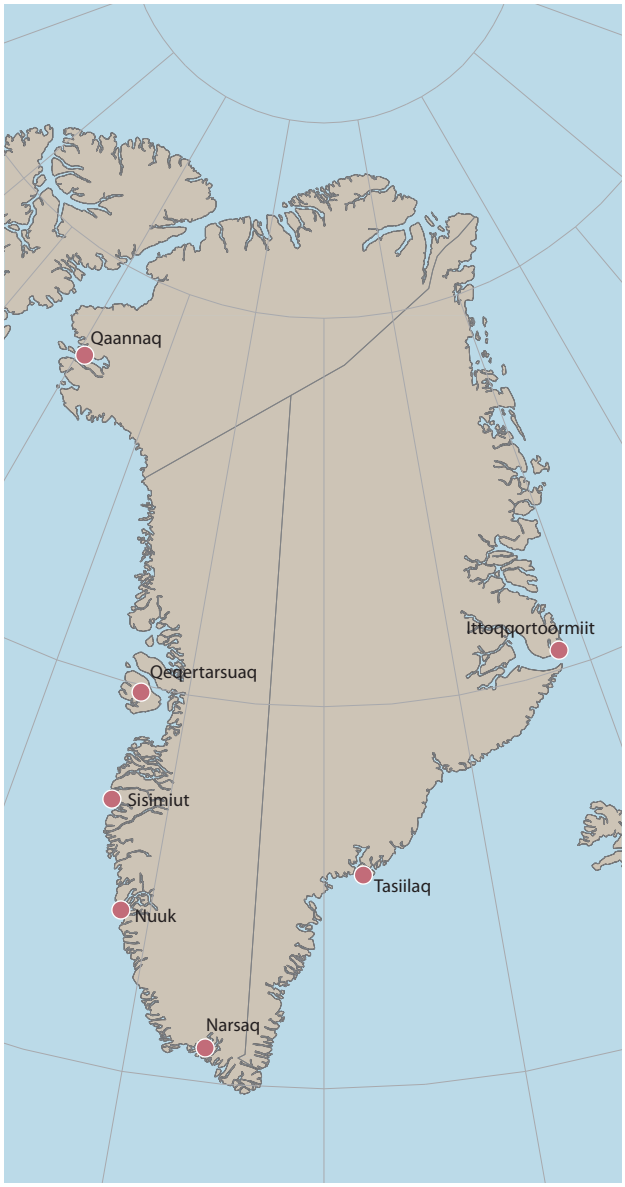

Figure 4.1 Districts for study of serum POP levels and serum POP biomarkers of effect in Greenlandic Inuit.

The legacy POPs, with half-lives of 5 to 15 years (Ritter et al. 2011), have been regulated by global and regional conventions with the aim of eliminating or reducing emissions (Stockholm Convention 2009–2014). The declining trend for many of these chemicals indicates that present-day contamination is largely a 'legacy' of past releases (Riget et al. 2010; Bjerregaard et al. 2013). A comparison of temporal trends for legacy POPs in Greenland revealed a decrease in atmospheric emissions (modeled), and ringed seal and human body burden between the late 1990s and 2010 (Bonefeld-Jørgensen pers. comm. 2015). For both ringed seals and humans the decline was greater on the west coast (Nuuk > Disko Bay) than the east coast (Ittoqqortoormiit), while the level of MeHg and selenium in humans although highest in the north-west (Qaanaaq) showed no decreasing trend. However, a significant increasing trend for selenium was seen in Disko Bay (humans) and Ittoqqortoormiit (seals) (Bonefeld-Jørgensen pers. comm. 2015). The decreasing trends in legacy POPs might reflect a combination of both legislation and change to a more western diet. To supplement the biomonitoring studies, Sonne et al. (2013) set up a physiologically-based pharmacokinetic model to examine the fate of POPs in the liver, blood, muscle and adipose tissue of Greenlandic Inuit, following long-term exposure to a traditional Greenlandic diet. The model described the metabolism, excretion and accumulation of POPs on the basis of their physicochemical properties and metabolic rates in the organisms concerned. Basic correlations between chemically analyzed blood POP concentrations and calculated daily POP intake from food questionnaires were conducted for Greenlandic Inuit from four cities in western Greenland (collected from 2003 to 2006). Significant correlations were found between blood POP concentrations and the calculated daily intake of POPs for Inuit from several districts. Despite the large variation in circulating blood POP concentrations, the model predicted blood concentrations of a factor of 2–3 within actual measured values. Moreover, the PBPK model showed that estimated blood POP concentration increased significantly after meals. As expected, for individuals with a high existing POPs body burden the model showed blood levels to be less influenced by recent meal intake. Of the POPs accumulated in the body, the model showed concentrations to be highest for PCB153. Furthermore, the model predicted that a significant internal body burden would continue to exist for several years after a dietary shift from traditional to western food; it also predicted that contaminant accumulation was 2 to 6 times faster than the decay following a shift to a diet low in contaminants (Sonne et al. 2013). This suggests that physiologically-based pharmacokinetic modelling should be used as a tool in future human health exposure and effect assessments in the Arctic.

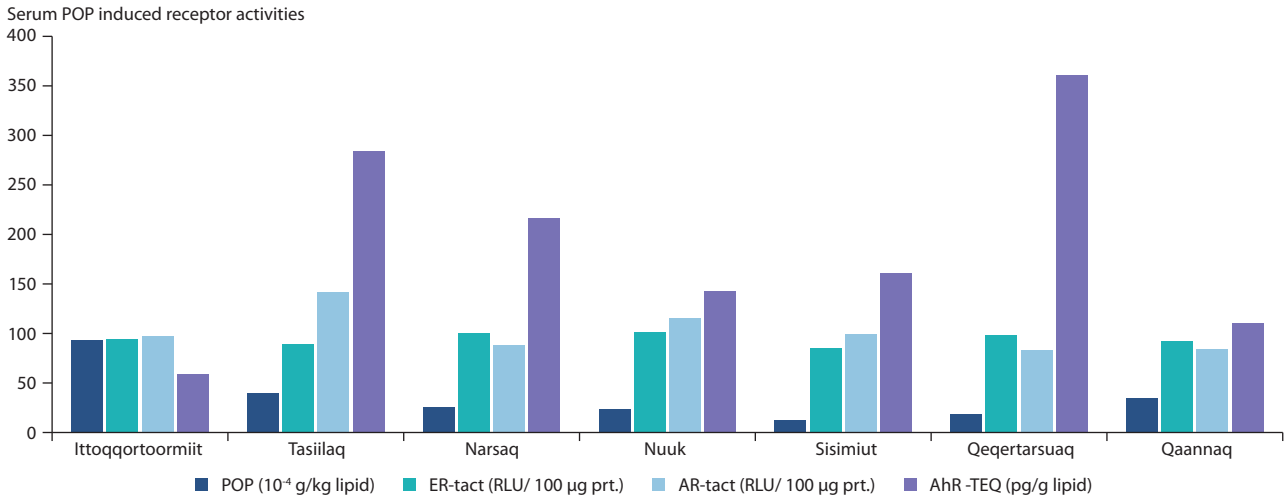

Figure 4.2 Serum POP levels and POP-related effects on receptor transactivities in Greenlandic Inuit (Bonefeld-Jørgensen et al. 2006; Long et al. 2006, 2007; Krüger et al. 2007, 2008, 2012; Bonefeld-Jørgensen 2010). POP: persistent organic pollutant, including PCBs and organochlorine pesticides. ER-tact; ER-transactivity: estrogen receptor transactivity induced by serum extract of lipophilic legacy POPs in the presence of the ER agonist 17β-estradiol (E2). AR-tact; AR-transactivity: androgenic receptor transactivation induced by serum extracts of lipophilic legacy POPs in the presence of the synthetic AR agonist methyltrienolone (R1881). RLU: Relative light unit. Prt: Cell Protein. AhR-TEQ: aryl hydrocarbon receptor –TCDD (2,3,7,8-tetrachlorodibenmzodioxin) toxic equivalent of serum extracts of lipophilic POPs.

4.6.1.2 Perfluoroalkyl acids and endocrine disruption

The perfluoroalkyl acids (PFAAs) include perfluorinated carboxylic acids (PFCAs) and perfluorinated sulfonic acids (PFSAs). The two most-studied PFAAs are perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS). These are the most studied because laboratory procedures in the past did not allow analyses of other PFAAs that in general exist at lower concentrations. PFOA and PFOS are persistent in the environment and occur in human blood, breast milk and liver with half-lives of 4 to 10 years (Olsen et al. 2008). The PFAAs are found globally and governmental regulations now exist in North America and Europe on the use and production of specific compounds such as PFOS and PFOA.

Biomarkers of PFAA: *in vivo* rodent studies

The biological effects of PFAAs have been studied in detail in rodents; few data are available for other species and humans (OECD 2002; Kennedy et al. 2004). Studies in animals have documented an array of toxicological outcomes including liver hypertrophy and tumors (Butenhoff et al. 2004), thyroid hormone alterations, decreased serum cholesterol and glucose, developmental toxicity, immunotoxicity, and carcinogenic potency (Lau et al. 2007; Andersen et al. 2008). Animal studies have also suggested that PFAAs may have potential geno- and neurotoxic effects (Fuentes et al. 2007; Johansson et al. 2009). The US EPA proposed that PFOA be deemed a rodent carcinogen of relevance to humans (US EPA 2006). Conflicting data for PFOA exposure in rats are reported for effects on reproductive tissues; an increase in mammary fibroadenomas and Leydig cell adenomas has been reported (Sibinski 1987), whereas two other rat studies did not find increased incidence of mammary-gland neoplasms (Hardisty et al. 2010; Butenhoff et al. 2012). However, in mice gestational exposure to PFOA compared to non-exposed controls was associated with altered mammary gland development in dams and female offspring, and a significant reduction in mammary differentiation among exposed dams was also evident affecting epithelial involution and altering milk protein gene expression (White et al. 2007). Because of these data, the US EPA Science Advisory Board recommended to reconsider the possible impact of PFOA on mammary tissues (Kropp and Houlihan 2005; US EPA 2006).

Biomarkers of PFAA: *in vitro* studies

In vitro studies have demonstrated endocrine-disrupting potentials of the PFAAs. Estrogenic properties of PFAAs were reported in human MCF-7 breast cancer cells (Maras et al. 2006) and the endocrine-disrupting potential of seven PFAAs was demonstrated in mammalian cell culture models (Kjeldsen and Bonefeld-Jørgensen 2013; Long et al. 2013). Three PFAAs elicited agonistic effects on ER transactivity (PFOS, PFOA, PFHxS) and five elicited antagonistic effects on AR transactivity (PFOS, PFOA, PFHxS, PFNA, PFDA) while the mixture including all seven PFAAs showed additive combined mixture effects (Box 4.1). PFDA also weakly decreased the aromatase activity at a high test concentration (Kjeldsen and Bonefeld-Jørgensen 2013). The seven PFAAs tested also affected thyroid-hormone function by inhibiting rat pituitary GH3 cell growth (Fig. 4.4); four PFAAs (PFOS, PFHxS, PFNA, PFUnA) also antagonized the T3-induced GH3 cell growth (Long et al. 2013). Only PFDoA and PFDA elicited an activating effect on AhR transactivation (Long et al. 2013). Moreover, perfluorinated compounds, and their metabolites present in food packaging materials, were reported to affect steroidogenesis in H295R human adrenal cortico-carcinoma cells, decreasing and increasing gene expression of *Bzrp* and *CYP19*, respectively, leading to lower androgen and higher estrogen levels (Rosenmai et al. 2013).

A smaller epidemiological case-control study showed for the first time a significant association between PFAA serum levels and risk of breast cancer in Greenlandic women (Bonefeld-Jørgensen et al. 2011). Moreover, in the same study population polymorphisms in *CYP1A1* (Val) and *CYP17* (A1) were shown to be risk factors for breast cancer among Inuit women and that risk increased with higher serum levels of PFOS and PFOA (Ghisari et al. 2014).

Box 4.1 Estrogenic and antiandrogenic effects of PFAAs in mammalian cell cultures

Estrogen receptor transactivity in human breast carcinoma (MVLN) cells

Seven PFAAs (PFOS, PFOA, PFHxS, PFNA, PFDA, PFUnA, PFDoA) were tested as individual compounds and in mixture upon co-exposure with 25 pM of the natural estrogen receptor ligand 17β-estradiol (E2) to mimic possible *in vivo* interactions between the test compounds and a natural estrogen hormone (Kjeldsen and Bonefeld-Jørgensen 2013).

Table 4.2 Estrogen receptor transactivity in human breast carcinoma (MVLN) cells

PFAAs tested with 25 pM E2	LOEC (M)	MOEC (M)	Percentage of solvent + 25 pM E2 ± SD
Solvent			100
PFHxS	4×10^{-5}	9×10^{-5}	187±24
PFOS	1×10^{-5}	5×10^{-5}	210±13
PFOA	3×10^{-5}	9×10^{-5}	145±15
Mix	3.5×10^{-5}	3.5×10^{-5}	150±25

LOEC: lowest tested concentration at which a significant effect ($p<0.05$) was detected; MOEC: lowest tested concentration causing the maximum effect (non-toxic); SD: standard deviation. Mix: equimolar mixture of all seven PFAAs. No effects were observed for PFNA, PFDA, PFUnA and PFDoA when these compounds were tested alone (data not shown).

Androgen receptor transactivity in Chinese hamster ovary (CHO-K1) cells

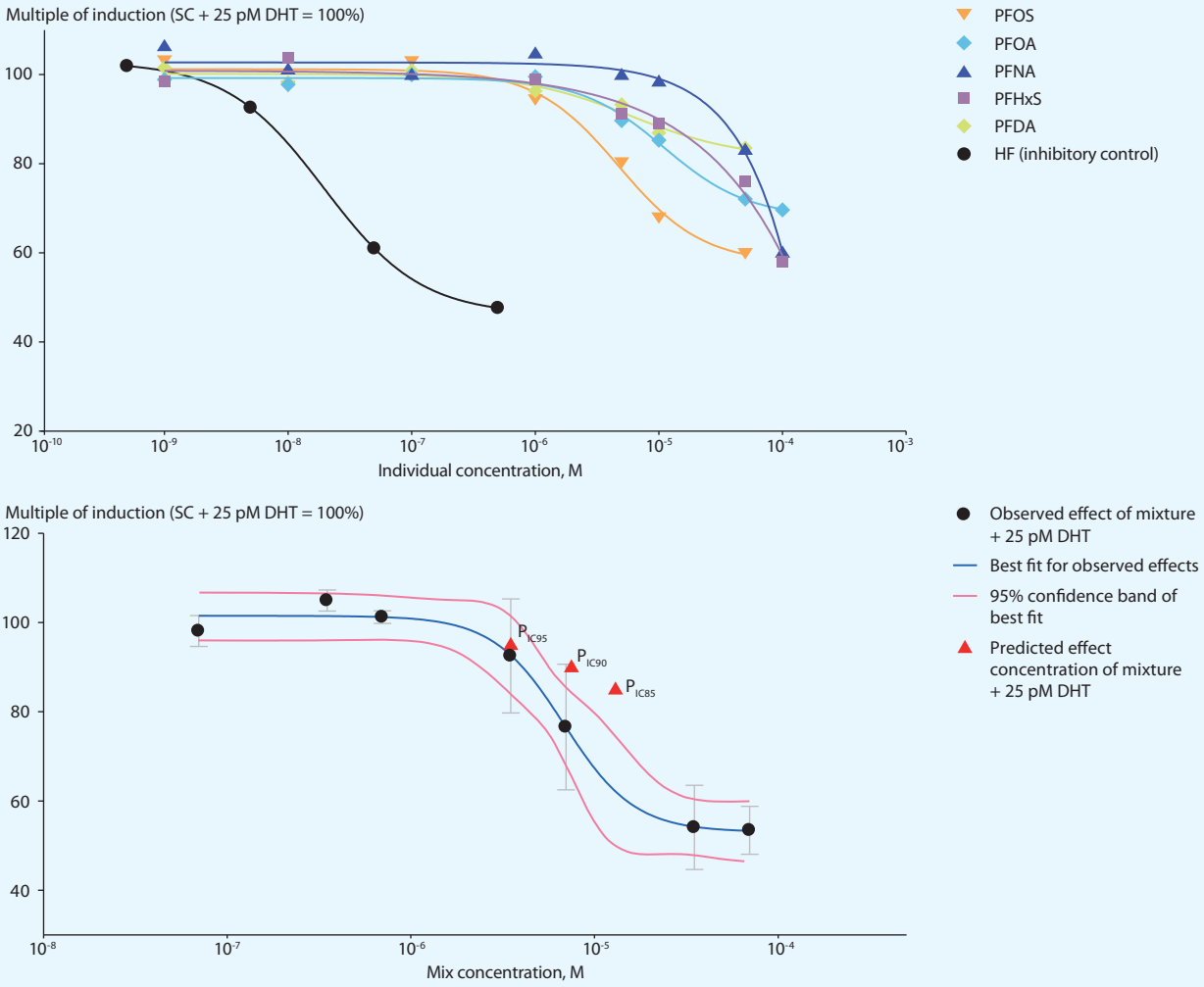

Figure 4.3 Seven PFAAs (PFOS, PFOA, PFHxS, PFNA, PFDA, PFUnA, PFDoA) were tested as individual compounds and in mixture upon co-exposure with 25 pM of the natural androgen receptor ligand dihydrotestosterone (DHT) to mimic possible *in vivo* interactions between the test compounds and a natural androgen hormone. No effects were observed for PFUnA and PFDoA when these compounds were tested alone (data not shown). Combined effects of the mixture were assessed using the principle of concentration addition (CA). HF: hydroxyflutamide (inhibitory control), SC: solvent control (Kjeldsen and Bonefeld-Jorgensen 2013).

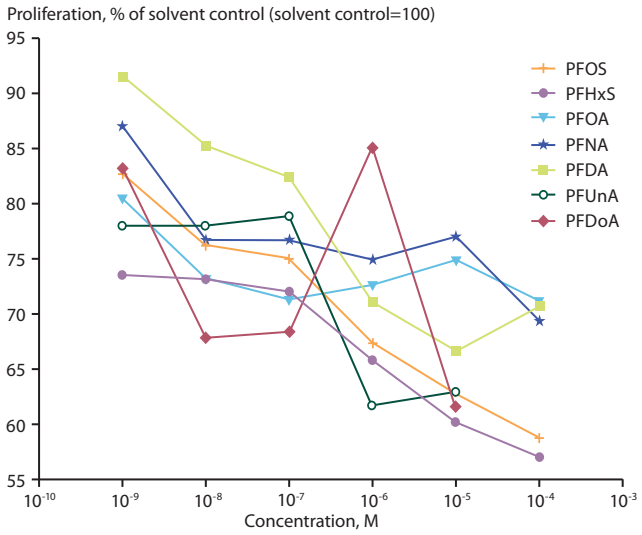

Figure 4.4 Effects of PFAAs on rat pituitary basal GH3 cell growth in the T-screen assay. GH3 cells were incubated with the given concentration (M) of compounds in the absence of 3,3',5-Triiodo-L-thyronine (T3). Data represent the mean of at least three independent experiments, each performed in four replicates per concentration. Exposure to each PFAA significantly decreased cell proliferation compared to the solvent control (0.02% dimethyl sulfoxide or 0.02% ethanol) ($p<0.05$). The results given refer only to effects observed at non-cytotoxic concentrations. Source: Long et al. (2013).

4.6.1.3 Contaminant exposure and hormone levels

Impact on the hypothalamo-pituitary-gonadal axis

Exposure to POPs may have a negative impact on reproductive function via impact on the hypothalamo-pituitary-gonadal axis.

A study of reproductive hormones in men from Greenland and three European cohorts (Swedish fishermen, Warsaw Poland, Kharkiv Ukraine) (Bonde et al. 2008) reported significant variation in associations between exposure to PCB153 and *p,p'*-DDE and the outcomes. For the Kharkiv group, statistically significant positive associations were found between levels of both PCB153 and *p,p'*-DDE and SHBG, as well as luteinizing hormone, while for the Greenlandic Inuit men there was a positive association between PCB153 exposure and luteinizing hormone. For the pooled data set from all four centers, there was a positive association between *p,p'*-DDE and FSH levels (β = 1.1 IU/L; 95% CI: 1.0–1.1 IU/L), whereas the association between PCB153 and SHBG was of borderline statistical significance (β = 0.90 nmol/L; 95% CI: -0.04 to 1.9 nmol/L). The authors concluded that gonadotropin levels and SHBG seem to be affected by POPs exposure, but that the pattern of endocrine response is the subject of considerable geographic variation (Giwercman et al. 2006).

Studying differences between men living south and north of the Arctic Circle in Norway, Haugen et al. (2011) found no geographical differences in either mean levels of PCB153 (50 vs 59 ng/g lipid; $p=0.27$) or sperm parameters. However, mean levels of *p,p'*-DDE were higher in the south than the north (81 vs. 66 ng/g lipid; $p=0.02$), as were levels of total and free testosterone. Moreover, FSH levels were lowest in the south. A strong relationship was observed between PCB153 and SHBG levels. The regional differences observed for *p,p'*-DDE, testosterone and FSH were not reflected in semen quality.

Ferguson et al. (2012) studied the relationship between PCB exposure and reproductive hormones in adult men from a US infertility clinic at low background exposure compared to Arctic populations. Several negative associations of PCBs and HCB with SHBG and total and free testosterone were observed in the crude regression models used. After adjusting for lipids, age and body mass index, nearly all significant associations were attenuated. However, a negative relationship remained between PCB118 and SHBG ($p<0.01$), and relationships between dioxin-like PCBs and SHBG and total testosterone, and between PCB118 and total testosterone were not significant. The results suggest a minimal relationship between PCB exposure at low background levels similar to those observed in the general U.S. population and circulating reproductive hormones.

In the Faroe Islands, where PCB exposure is elevated, Grandjean et al. (2012b) studied the possible endocrine disruption of PCBs on 438 adolescent boys from a birth cohort by measuring PCB and *p,p'*-DDE levels in cord blood and serum from clinical examination at age 14 years. Higher prenatal PCB exposure was associated with lower serum concentrations of both luteinizing hormone and testosterone. In addition, SHBG was positively associated with both prenatal and concurrent PCB exposure. The PCB–SHBG association was robust to covariate adjustment. In a structural equation model, a doubling in prenatal PCB exposure was associated with a decrease in luteinizing hormone of 6% ($p=0.03$). Prenatal exposure to PCB and DDE showed weak, non-significant inverse associations with testicular size and Tanner stage. DDE was highly correlated with PCB and showed slightly weaker associations with the hormone profile. The findings suggest that delayed puberty with low serum-LH concentrations associated with developmental exposure to non-dioxin-like PCBs may be due to a central hypothalamo-pituitary mechanism.

Impact on the hypothalamo-pituitary-thyroid axis

In experimental studies, it has frequently been observed that the homeostasis of thyroid hormones is affected by exposure to POPs, such as dioxins and PCBs, polybrominated flame retardants, OC pesticides, perfluorinated compounds and other compounds with endocrine-disrupting potentials such phthalates, bisphenol A, UV filters used in sunscreens, cosmetic products like night creams and anti-wrinkle remedies such as 4-methylbenzylidene-camphor, octyl-methoxycinnamate, and benzophenone 2 and 3, and perchlorate. There is substantial evidence that perinatal exposure to PCBs and their hydroxylated metabolites decrease thyroid hormone in the offspring. In man, similar effects have been indicated in several epidemiological studies (Boas et al. 2012).

In systematic review, Salay and Garabrant (2009) evaluated 22 studies to look for a possible association between PCB exposure and circulating thyroid hormones and thyroid-stimulating hormone (TSH) levels in adults. The review indicated that PCBs can interfere with thyroid hormone homeostasis but that the epidemiological evidence was not entirely clear. The authors suggested that rigorous study design, assessment of potential confounding factors and a full report of methods in future studies might help explain the association between PCB and changes in thyroid function.

Dalaire et al. (2008) investigated the potential impact of transplacental exposure to PCBs and HCB on thyroid hormone concentrations in neonates from two remote coastal populations in Canada; one in Nunavik (n=410) and one on the Lower North Shore of the St Lawrence River (n=260). Both populations were exposed to OCs through seafood consumption. Cord blood samples were analyzed for thyroid parameters (TSH; free T4, fT4; total T3, tT3; and thyroxine-binding globulin, TBG) and contaminants. PCB153 was not associated with thyroid hormone and TSH levels in either population. Prenatal exposure to HCB was positively associated with fT4 levels at birth in both populations (Nunavik, $\beta = 0.12$, $p = 0.04$; St. Lawrence, $\beta = 0.19$, $p < 0.01$), whereas TBG concentrations were negatively associated with PCB153 concentrations ($\beta = -0.13$, $p = 0.05$) in the St Lawrence cohort. Thus OC levels were not associated with a reduction in thyroid hormones in neonates from the two populations. Essential nutrients derived from seafood such as iodine may have prevented the negative effects of OCs on thyroid function during fetal development. Dallaire et al. (2009a,b) studied the relationship between exposure to potential thyroid hormone-disrupting toxicants and thyroid hormone status in pregnant Inuit women from Nunavik and their infants within the first year of life. In pregnant women, they found a positive association between hydroxylated metabolites of PCBs and total tT3 concentrations ($\beta = 0.57$, $p = 0.02$). In cord blood, PCB153 concentrations were negatively associated with TGB levels ($\beta = -0.26$, p=0.01). In a subsample analysis, a negative relationship was also found between maternal pentachlorophenol levels and cord fT4 concentrations in neonates ($\beta = -0.59$, p=0.02). No association was observed between contaminants and thyroid hormones at age 7 months. The authors concluded that there is little evidence that the environmental contaminants analyzed in their study affect thyroid hormone status in Inuit mothers and their infants. The possibility that pentachlorophenol may decrease thyroxine levels in neonates requires further investigation.

The relationship between exposure to several polyhalogenated compounds and thyroid hormone homeostasis was studied by Dallaire et al. (2009a) for Inuit adults from Nunavik. Thyroid parameters and PCBs and their metabolites, OC pesticides, polybrominated diphenyl ethers (PBDEs), PFOS, and dioxin-like compounds, were detected in plasma samples from Inuit adults (n=623). Negative associations were found between tT3 concentrations and levels of 14 PCBs, seven hydroxylated PCBs, all methylsulfonyl metabolites of PCBs (MeSO(2)-PCBs), and two OC pesticides. Moreover, negative associations between fT4 levels and HCB concentrations were observed. Thyroxine-binding globulin concentrations were inversely related to the levels of eight PCBs, five hydroxylated PCBs, and three OC pesticides. Exposure to BDE47 was positively related to tT3, whereas PFOS concentrations were negatively associated with TSH, tT3 and TBG and positively associated with fT4 concentrations. The authors concluded that exposure to several polyhalogenated compounds was associated with modifications of the thyroid parameters in adult Inuit, mainly by reducing tT3 and TBG circulating concentrations. The effects of PFOS and BDE47 on thyroid homeostasis require further investigation because other human populations display similar or even higher concentrations of these compounds.

Audet-Delage et al. (2013) studied whether exposure to POPs might decrease the circulating concentrations of T4 bound to transthyretin (TTR) in Inuit women of reproductive age in Nunavik Canada. Hydroxylated PCBs, pentachlorophenol and PFOS compete with T4 binding sites on TTR. The data suggested that circulating levels of TTR-binding compounds were not high enough to affect TTR-mediated thyroid hormone transport. However, the authors suggested that the possibility of increased delivery of these compounds to the developing brain requires further investigation.

As a tool to evaluate a possible thyroid dysfunction of POPs, 115 young adults of the Akwesasne Mohawk Nation, Canada were included in a study on the relationship between exposure to PCBs and OCs and the level of anti-thyroid peroxidase antibody (TPOAb) (Schell et al. 2009). Overall, 18 participants (15.4%) had TPOAb levels above the normal laboratory reference range (23% of females, 9% of males). Among participants that were breastfed (n=47), those with an elevated TPOAb level had significantly higher levels of all PCB groupings, with the exception of levels of non-persistent PCBs, which did not differ significantly. Levels of *p,p*'-DDE were also significantly elevated, while HCB and Mirex were not higher among those with elevated TPOAb. Also, after stratifying by breast-feeding status, participants who were breastfed showed significant, positive relationships between TPOAb levels and all PCB groupings, except groups comprising non-persistent PCBs, and with *p,p*'-DDE, HCB, and Mirex. No effects were evident among non-breastfed young adults. Further studies are necessary to elucidate the site and mechanism of action of these POPs and to establish thresholds for these effects, especially among populations with background levels of toxicant exposure.

Bloom et al. (2014) observed an association between POPs and thyroid hormones in aging residents of upper Hudson River communities (48 women, 66 men, age range 55–74 years). The POPs included 39 PCBs, DDT and DDE and nine PBDEs. Among women, DDT+DDE increased T4 by 0.34 µg/dL (p=0.04) and T3 by 2.78 ng/dL (p=0.05). Also in women, ΣPCBs in conjunction with PBDEs elicited increases of 24.39–80.85 ng/dL T3 (p<0.05), and ΣPCBs in conjunction with DDT+DDE elicited increases of 0.18–0.31 µg/dL T4 (p<0.05). For men, estrogenic PCBs were associated with a 19.82 ng/dL T3 decrease (p=0.003), and the sum of estrogenic PCBs in conjunction with DDT+DDE elicited an 18.02 ng/dL T3 decrease (p=0.04). The authors suggested that the influence of POPs on thyroid hormones in aging populations may have clinical implications and merits further investigation.

4.6.2 Combined effect of serum legacy POPs on hormone receptor transactivities *ex vivo*

Today it is well known that the levels and profiles for the various POP groups vary among Greenlandic districts (Fig. 4.2) (Bonefeld-Jørgensen 2010). Studies on biomarkers of toxicological effects have shown that individual POPs have very different biological potentials. For example, some PCB congeners possess an estrogenic potential (e.g. some hydroxy-PCBs) while others are antiestrogenic (e.g. PCB153, PCB180, PCB138) and antiandrogenic (PCB138); and some have dioxin-like potentials (e.g. PCB126). Likewise, for OC pesticides both estrogenic potentials (e.g. toxaphene, β-HCH, DDT and DDE)

and antiandrogenic effects (e.g. DDE) have been reported (Bonefeld-Jørgensen 2010), and an *in vitro* inhibitive effect of α-HCH on activated androgen receptor was shown to antagonize the androgen receptor (AR)-mediated effects of the natural ligand dihydrotestosterone, DHT (Roy et al. 2004). Enantioselective effects of α-HCH were demonstrated by Pavlikova et al. (2012) and data suggested an interaction with multiple regulatory events controlling AR activity. Furthermore, additive enhancement of hormone actions has been reported *in vitro* for xenoestrogen and xenoantiandrogen mixtures (Bonefeld-Jørgensen et al. 2001; Payne et al. 2001; Rajapakse et al. 2002) and *in vivo* for antiandrogens (Metzdorff et al. 2007).

Mechanistic studies in human adrenocortical carcinoma cells (H295R) demonstrated that PCB118, PCB153 and PCB126 decrease protein expression and alter steroidogenesis (Tremoen et al. 2014). Exposure to three PCB congeners with different chemical structure perturbed steroidogenesis and protein expression in the H295R *in vitro* model. Exposure to PCB118 increased estradiol and cortisol secretion, while exposure to PCB153 elevated estradiol secretion. PCB126 was the most potent congener, increasing estradiol, cortisol, and progesterone secretion in exposed H295R cells. The alterations in protein regulation and steroid hormone synthesis suggest that exposure to PCB disturbs several cellular processes, including protein synthesis, stress response, and apoptosis.

4.6.2.1 *Ex vivo* human studies in Greenland

In Greenland, district and gender differences were observed for POP exposure biomarkers and biomarkers of the combined effect of extracted lipophilic serum POPs on nuclear receptors (Fig. 4.2). A general inverse relationship was found between higher serum legacy POP concentrations and ER, AR and AhR transactivity. A higher frequency of serum samples with antagonistic ER and AR effects was observed for both sexes on the east (Ittoqqortoormiit, Tasiilaq) and north-west (Qaanaaq) coast of Greenland, whereas higher frequencies of serum samples with agonistic ER and AR effects were observed for both sexes on the west coast (Qeqertarsuaq, Narsaq, Nuuk, Sisimiut). However, for men in Nuuk and Sisimiut (two west Greenland districts), a tendency towards increased serum POP-induced AR activity was observed (Fig. 4.2) (Bonefeld-Jørgensen 2010; Krüger et al. 2012).

Using a more specific method for serum extraction of dioxin-like compounds than reported by AMAP in the previous human health assessment (AMAP 2009), more than 75% of the serum POP extracts from both sexes elicited AhR-mediated dioxin-like activities. As seen for hormone receptor transactivities, the tendency was the higher the serum legacy POP levels the lower the AhR transactivities (Fig. 4.2). The lowest medians of the AhR-TCDD toxic equivalence (AhR-TEQ) values were observed in Ittoqqortoormiit (East) and Qaanaaq (North-west), with higher AhR-TEQ levels for both sexes observed in Tasiilaq (only five individuals), Narsaq, Sisimiut, and Nuuk, and the highest in Disko Bay (Qeqertarsuaq) (Fig. 4.2) (Bonefeld-Jørgensen 2010; Krüger et al. 2012). A tendency towards an inverse relation between the dioxin-like-induced AhR and ER activity supports the perception that dioxins exert an antiestrogenic effect. The authors concluded that the actual mixtures of serum POPs in Greenlandic Inuit have a hormone disrupting potential.

Similar data for ER and AhR transactivity were observed by Erdmann et al. (2013) using the same method set up for extracting whole blood from East Greenlandic polar bears. However, compared to Inuit, a higher frequency of agonistic xenohormone activity was seen in polar bears. They suggested that differences in POPs metabolism resulting in higher levels of hydroxylated PCBs circulating in the blood of polar bears could be partly responsible but further investigation is needed. Although the frequency of serum POP agonisms towards the AhR activity in Inuit and polar bears was similar, higher AhR-TEQ levels were found in polar bears. This might be explained by a higher overall POPs burden in polar bears influenced by differences in the POPs mixture profile and the ratio of non-dioxin-like PCBs and dioxin-like PCBs compared to Inuit (Erdmann et al. 2013).

In a comparison of Inuit and young Danish women, Bonefeld-Jørgensen and Long (2010) found POPs levels in Inuit to be more than ten times higher than in Danes. Moreover, levels were positively associated with age in both study groups. The AhR-TEQ level was significantly higher in Inuit, and was positively associated with plasma POPs, whereas no correlations were found for the Danish samples (Bonefeld-Jørgensen and Long 2010; Long and Bonefeld-Jørgensen 2012). A recent study on AhR-TEQ in Danish subjects showed a higher level of AhR-TEQ for individuals living in urban areas than rural areas (Mørck et al. 2014) indicating higher exposure to dioxin-like compounds via food intake and traffic in urban areas.

Comparisons between European and Greenlandic male serum POP levels showed significantly higher levels in Inuit, and as a result lower ER and AhR transactivity and a tendency towards higher AR activity for the Greenlandic serum samples. However, in the same study, Inuit had significantly lower sperm DNA damage (Bonefeld-Jørgensen 2010).

Determinants and effects of AhR function

To obtain a measure of POPs in plasma that interact with the AhR signaling pathway, Medehouenou et al. (2010) used a luciferase reporter gene assay to assess the AhR-mediated transcriptional activity elicited by plasma sample extracts from 874 Inuit adults recruited in the course of a prospective epidemiological study in Nunavik. Several socio-demographic, anthropometric, dietary and lifestyle variables were considered as possible modulating factors in the AhR-mediated activity in multivariate statistical analyses. The geometric mean AhR-mediated activity expressed as 2,3,7,8-tetachlorodibenzo-*p*-dioxin (TCDD) equivalents was 8.9 µg/kg lipid (range: <5–144 pg/g lipid). PCB153 concentration moderately correlated with AhR-mediated activity (Pearson's r=0.53, $p<0.001$). Multiple linear regression analyses revealed that age and n-3 fatty acids in erythrocyte membranes (an index of marine food consumption) were positively associated with plasma AhR-mediated activity ($p<0.001$), whereas a negative association was noted with body fat mass ($p=0.037$). The authors suggested that AhR-mediated transcriptional activity of Inuit plasma extracts is linked to their OC body burden, probably that of dioxin-like PCBs, polychlorinated dibenzo-*p*-dioxins and polychlorodibenzofurans. AhR-mediated transcriptional activity measures may prove useful in investigating possible associations between exposure to AhR agonists and adverse health effects in this indigenous population (Medehouenou et al. 2010).

4.6.2.2 Dioxin-like PCBs in relation to bone quality/strength

Results from experimental and population studies suggest that some dioxin-like compounds can alter bone metabolism and increase bone fragility. Bone strength in Inuit appears to be lower than in non-indigenous people.

Paunescu et al. (2013b) conducted a descriptive cross-sectional study to investigate the relationship between plasma concentrations of dioxin-like compounds and bone quality in Cree women of Eastern James Bay (Canada). Total dioxin-like compound concentrations were measured in plasma samples of participants by the AhR-mediated transcriptional activity elicited by plasma sample extracts using a luciferase reporter gene assay. Plasma concentrations of mono-*ortho*-substituted dioxin-like PCB105, PCB118 and PCB156 were measured by gas chromatography-mass spectrometry.

PCB105 and PCB118 concentrations, but not the total dioxin-like compound concentration, were inversely associated with the stiffness index, even after adjusting for several confounding factors. Other factors, including age, height, smoking status, menopausal status and the percentage of *n*-6 PUFAs in erythrocyte membranes were negatively associated with one of the ultrasound parameters, while the percentage of *n*-3 PUFAs in these membranes and levels of physical activity and education were positively associated with them. Thus, increase in plasma concentrations of PCB105 and PCB118 was negatively associated with stiffness index, a measure of bone quality/strength, in women of this population. Future studies should consider whether PUFA intake is a factor which influences bone quality.

Inuit women from Nunavik were also assessed using the AhR-mediated transactivity for dioxin-like compounds and specific dioxin-like PCBs in plasma to determine whether lower bone strength observed in Inuit women might be explained by intake of dioxin-like compounds via their traditional diet (Paunescu et al. 2013a). Neither total plasma dioxin-like compounds nor specific dioxin-like PCBs were associated with stiffness index after adjusting for several confounding and co-varying factors. Thus, this study does not support a link between exposure to dioxin-like compounds and bone strength measured by ultrasonography in Inuit women of Nunavik.

4.6.3 Persistent organic pollutants and Type 2 diabetes

Several descriptive epidemiology studies suggest that certain POPs can contribute to the development of Type 2 diabetes (Carpenter 2008; Patel et al. 2010). Although many POPs have now been banned, exposure continues for the most persistent, such as the PCBs and the pesticide metabolite *p,p'*-DDE. Other persistent environmental chemicals still in current use are suspected to be diabetogenic, for example the brominated flame retardants and perfluorinated compounds. A causal relationship is supported by follow-up of subjects poisoned by PCBs and related substances (Wang et al. 2008). However, most of the recent epidemiological evidence is from cross-sectional case-control studies, where increased serum POP concentrations were found to be a major determinant of diabetes (Everett and Matheson 2010) and metabolic syndrome (Lee et al. 2007). Genetic predisposition to Type 2 diabetes seems to play a role, but most genetic variants so far identified are associated with β-cell function and account for no more than about 10% of the risk. Thus it is very likely that POP exposure may trigger gene–environment interactions with effects on insulin resistance and/or secretion.

In support of a POP-induced Type 2 diabetes etiology, experimental data have shown that certain POPs may increase insulin demand by decreasing insulin sensitivity in target tissues (Ruzzin et al. 2010). The findings related to physiological concentrations of the environmental chemicals showed effects of crude fish oil as compared to fish oil that had been cleaned of POPs. In addition, 2,3,7,8-tetradichlorobenzo-*p*-dioxin (TCDD) is known to cause toxicity to pancreatic β-cell lines, such as interference with mitochondrial membrane potential and induction of increased Ca^{2+} influx (Kim et al. 2009b). A scientific justification therefore exists for exploring the possible role of POP toxicity in Type 2 diabetes etiology and pathogenesis.

In the Faroe Islands, 713 septuagenarians with a high POP exposure owing to a traditional diet (including pilot whale blubber), were examined for indicators of glucose metabolism in subjects free of Type 2 diabetes and pre-diabetes (impaired fasting glycaemia). Results showed that the fasting insulin concentration decreased by about 8% for each doubling of the serum concentration of PCBs, and that a similar increase occurred in the fasting glucose level. Along with higher PCB exposure in subjects with Type 2 diabetes and impaired fasting glycaemia, the results suggest that PCB-induced β-cell deficiency may be involved in the disease pathogenesis. Impaired insulin secretion appears to constitute an important part of the Type 2 diabetes pathogenesis associated with exposure to persistent lipophilic food contaminants (Grandjean et al. 2011).

Individuals with vitamin D levels below 50 nmol/L doubled their risk of newly diagnosed Type 2 diabetes. Thus, in elderly subjects, vitamin D may provide protection against Type 2 diabetes (Dalgard et al. 2011). The high prevalence of low vitamin D levels among the elderly Faroese population (19% with <25 nmol/L) reflects the low skin synthesis during most months of the year, which is caused by limited sun exposure and insufficient intake of marine food (Dalgard et al. 2010).

4.7 Carcinogenic effects

Throughout the 20th century, the cancer patterns of the Inuit population have been characterized by a high risk of Epstein-Barr virus (EBV)-associated carcinomas of the nasopharynx and salivary glands, and a lower risk of tumors common in Caucasian populations, including cancer of the breast, prostate, testis, and hemopoietic system. Both genetic and environmental factors seem to be responsible for this pattern. Over the past 50 years, Inuit societies have undergone major changes in lifestyle and living conditions. The incidence of traditional Inuit cancers (nasopharynx and salivary glands cancer) has remained relatively constant, whereas the incidence of lifestyle-associated cancers, especially cancer of the lung, breast, stomach and colorectal has increased considerably following changes in lifestyle (smoking, alcohol), diet, and reproductive factors (Friborg and Melbye 2008).

A comparison of cancer incidence patterns between residents of Inuit Nunangat and the rest of Canada showed the age-standardized incidence rate for all cancer sites (1998–2007) to be 14% lower for the Inuit Nunangat male population and 29% higher for the female population compared to the rest of Canada (Carriere et al. 2012). Cancers of the nasopharynx, lung and bronchus, colorectal, stomach (males), and kidney and renal pelvis (females) were elevated in the Inuit Nunangat population compared to the rest of Canada, whereas prostate and female breast cancers were lower. As well as higher smoking prevalence within Inuit Nunangat, distinct socio-economic characteristics between the respective populations (including housing and income) may have contributed to the incidence differentials (Carriere et al. 2012).

Some cancer incidence in Greenland is several times higher compared to Denmark, such as nasopharyngeal, esophagus, biliary, ventricle, cervical, lung, liver, pancreas and colorectal cancer, respectively (The Danish National patient Register).

A study showed that the indigenous coastal Chukchi and Inuit living in Chukotka (Russia) were at higher risk of death from cancer during 1961–1990 than the Russian population nationally, with age-standardized cancer mortality among men twice that of Russia in general, and among women 3.5 times higher. The difference is due to the particularly high mortality from esophageal cancer and lung cancer in the indigenous people of coastal Chukotka. The mortality data from this study correspond to the pattern of incidence reported among other indigenous people of the Russian Arctic (Dudarev et al. 2013). The incidence of colorectal cancer is currently higher in Alaskan Inuit than in Caucasians living in the United States (Friborg and Melbye 2008). Cancer is now the leading cause of death among Alaska Native people, and cancer mortality rates in Alaska are significantly higher than in the mainland United States (Lanier et al. 2008).

According to epidemiological studies, about 80% of all cancers are suspected to be related to environmental factors such as contaminant exposure and lifestyle.

4.7.1 Contaminant exposure, oxidative stress and carcinogenicity

Oxidative stress, the imbalance between production of the oxidants such as free radicals and the radical scavengers including enzymes and antioxidants, plays an important role in carcinogenicity (Kuraoka et al. 2003). However, epigenetic mechanisms (see Sect. 4.8.7) that do not involve DNA attack or heritable genetic alteration have been shown for several chemicals which produced tumors in laboratory animals (Williams and Whysner 1996). These non-genotoxic carcinogens may target nuclear receptors, cause aberrant DNA methylation at the genomic level and induce post-translational modifications at the protein level, thereby affecting the stability or activity of key regulatory proteins, including oncoproteins and tumor suppressor proteins (Fukushima et al. 2005).

Overall, PCBs possess carcinogenicity through inducing formation of reactive oxygen species, genotoxic effects, immune suppression, an inflammatory response, and endocrine effects to various extents and via different pathways. The dioxin-like PCBs exert their effects mainly through AhR activation and the downstream cascade of related events; less-chlorinated PCBs act more readily through metabolic activation and the downstream effects of these metabolites. Thus, mixtures might have more than additive effects. Recently, PCBs and polybrominated biphenyls (PBBs) were classified by the International Agency for Research on Cancer as 'human carcinogen' and 'possible human carcinogen', respectively (Lauby-Secretan et al. 2013). Organochlorine pesticides elicit carcinogenicity mainly through non-genotoxic effects. Those such as *o,p'*-DDT, *p,p'*-DDE, and *p,p'*-DDD are able to modulate several cancer-related processes, namely in breast cancer cell lines, and underline the relevance of POP exposure to the risk of cancer development and progression and indicate the distinct pathways of action of these compounds on tumor cell biology (Pestana et al. 2015).

Synthetically produced perfluorinated chemicals are widely used in industrial products because of their anti-wetting and surfactant properties. Perfluorinated chemicals are suspected carcinogens and oxidative stress is a possible mechanism of action (O'Brien et al. 2005; Hu and Hu 2009; Eriksen et al. 2010; Wielsøe et al. 2015). Oxidative stress is also involved in the carcinogenetic effect of other contaminants such as PBDEs (Hu et al. 2007) and heavy metals including arsenic, cadmium, chromium, cobalt, lead, mercury and nickel (Shi et al. 2004; Kern and Jones 2006; Beyersmann and Hartwig 2008; Schwerdtle et al. 2010; Filipic 2012; Hartwig 2013). Cadmium can also mimic the *in vivo* effects of estrogen in reproductive tissues (Johnson et al. 2003), and these estrogen-mimicking effects may be mediated via the estrogen receptor. Thus, cadmium might be related to the development of hormone-dependent cancer such as breast cancer (Byrne et al. 2009).

To assess the DNA-damaging potential of PCBs in Inuit, 103 blood samples (70 women, 33 men) were collected for a population from Salluit (Canada). Their traditional diet mainly comprises marine mammal blubber and fatty fish, which both accumulate non-biodegradable PCBs to varying degrees. A wide range of potentially damaging DNA adducts, from highly polar to highly lipophilic were detected in the blood samples. The known oxidative lesion, 8-oxodG was predominant, with 51%, 54% and 57% of the total DNA adduct burden in the low, medium and high PCB exposure groups, respectively. Thus DNA damage might be associated with PCBs in the blood of Inuit. While some individual adducts appear to accumulate with increasing PCB level, a definitive association between PCBs and other newly detected DNA adducts could not be made (Ravoori et al. 2008).

In addition to POPs, the traditional Inuit foods also contain a number of important nutrients, such as trace elements/antioxidants and unsaturated fatty acids which have a favorable effect on health. Further investigation of 83 Inuit from Salluit (56 women, 27 men) showed the DNA adduct levels to be inversely associated with PCB and selenium (Se) levels. In the high Se:PCB ratio group, Se had a significantly negative effect on 8-oxodG ($r = -0.38$, $p=0.014$) and total adducts ($r = -0.41$, $p=0.009$) while there was no correlation within the low Se:PCB group, suggesting that increasing Se has a mitigating effect in reducing DNA adducts and therefore, possible negative effects of PCB were not seen. Thus there may be a protective effect of Se on the potentially damaging effect of PCB on DNA (Ravoori et al. 2010).

In addition to genetic alteration, epigenetic regulation (see Sect. 4.8.7) through promoter methylation and microRNA expression alters gene expression profiling leading to a genome more vulnerable and unstable to the cancer risk of arsenic (Bhattacharjee et al. 2013).

4.7.2 Contaminant exposure and cancer risk in Arctic regions

4.7.2.1 Lung cancer

The incidence of lung cancer has increased remarkably in all Inuit populations over the past 40 years. Lung cancer now constitutes about 20% of all cancers in Inuit (Friborg and Melbye 2008). In fact, lung cancer incidence in circumpolar Inuit is among the highest in the world, for men and women. The age-standardized incidence rate of lung and bronchus cancer during 1998–2007 of male Inuit from Nunangat was 113 per 100,000 which was double that for the rest of Canada (50.6 per 100,000) (Carriere et al. 2012). Greenland Inuit have double the standardized incidence rate of lung cancer in Denmark (NORDCAN). The smoking pattern among Inuit, possibly combined with co-factors related to environment and diet, are believed to be the relevant causal factors (Miller and Gaudette 1996). Although modern housing conditions have decreased exposure to fumes from lamps and open fires for cooking, many Inuit still spend substantial periods out on the land, cooking on open stoves inside tents. Marijuana smoking in 85% of adults (of Nunavik, Canada) might also play a role in the high incidence of lung cancer (Young 2008).

A cross-sectional study of Alaska Natives has demonstrated the importance of genetic variation in *CYP2A6* on the regulation of tobacco consumption behavior; pro-carcinogen exposure and metabolism in both light smokers and smokeless tobacco users (Zhu et al. 2013) (see Sect. 4.8).

4.7.2.2 Breast cancer

Breast cancer is the most common cancer for women in the western world. The established risk factors include genetic inheritance, for example mutations in the *BRCA-1* and *BRCA-2* genes (Ferla et al. 2007), lifelong exposure to estrogens (early menarche and late menopause increase risk), obesity after menopause, alcohol, smoking and high fat intake. Although breast cancer risk is influenced by genetics and reproductive history, the known risk factors explain less than a third of all cases and more than 70% of women diagnosed with breast cancer have no inherited or sporadic cancer. Risk is thought to be modified by lifestyle and environmental exposure (Madigan et al. 1995). Although still lower in the Arctic Inuit, incidence is now approaching incidences recorded in Western populations (Friborg et al. 2003) and today about 12 to 15 women are diagnosed every year in Greenland. From 1988 to 1997, the age-adjusted incidence rate for women in Greenland was 46.4 per 100,000. For comparison, the rate in the United States was 124 per 100,000 for 2001 to 2008 and in Denmark about 100 per 100,000 in 2010 (Fredslund and Bonefeld-Jørgensen 2012). The age-adjusted incidence rate for breast cancer in the Arctic Inuit Nunangat was lower than for the rest of Canada (45 vs 81 per 100,000) (Carriere et al. 2012).

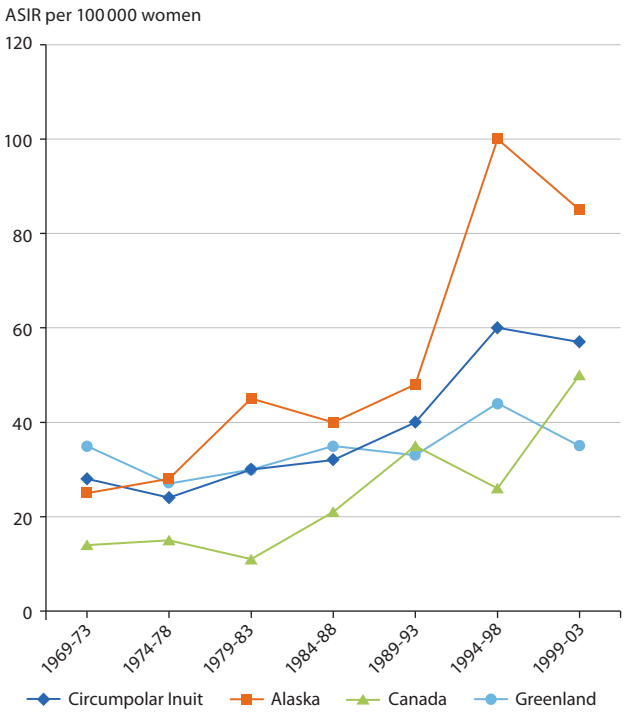

Figure 4.5 Trend in age-standard incidence rate (ASIR) of breast cancer in Inuit over the past 45 years (Fredslund and Bonefeld-Jørgensen 2012).

Although there is no significant difference in breast cancer rate between Alaska Native women and US white women, a significant increase in Alaska Native women was reported during 1974–2003 (Day et al. 2010).

Breast cancer incidence in the Arctic increased between 1969 and 2003 (Fredslund and Bonefeld-Jørgensen 2012) (Figs. 4.5 and 4.6). The enormous transition in health conditions and lifestyle in the Arctic might be contributing to the known risk factors. Previous data suggest that exposure to POPs including PFCs might contribute to breast cancer risk. PCBs have been associated with effects relevant to breast cancer development such as estrogenic tumor promotion (Moysich et al. 2002). Although conflicting data for PFOA exposure in rats an increase in mammary fibroadenomas and Leydig cell adenomas was reported (Sibinski 1987), and in mice gestational exposure to PFOA was associated with altered mammary gland development in dams and female offspring, and reduction in mammary differentiation among exposed dams (White et al. 2007). Bonefeld-Jørgensen et al. (2011) evaluated the association between serum levels of POPs/PFCs in 31 cases of breast cancer in Greenlandic Inuit and 115 controls during 2000–2003 to establish whether the combined POP-related effect on nuclear hormone receptors affects risk. Serum levels of POPs, PFCs, some metals and the combined serum POP-related effect on ER-, AR- and AhR-transactivity were determined. For the very first time a significant association between serum PFC levels and the risk of breast cancer was observed. The breast cancer cases also showed a significantly higher concentration of PCBs at the highest quartile. Also, for the combined serum legacy POP-induced agonistic AR transactivity a significant association with breast cancer risk was found, and cases elicited a higher frequency of samples with significant POP-related hormone-like agonistic ER transactivity. The AhR toxic

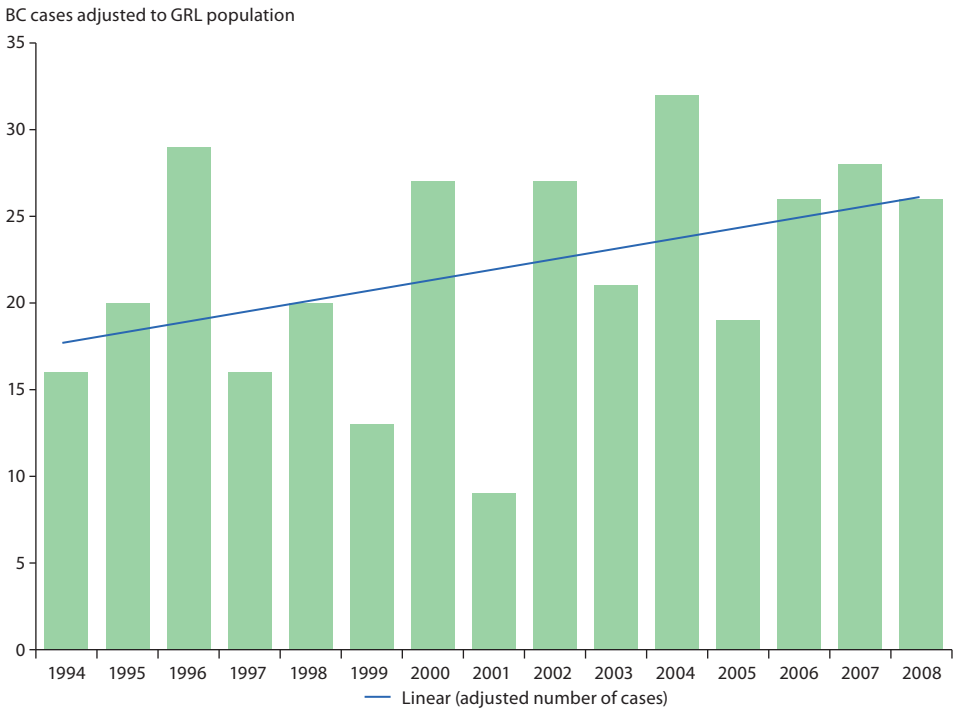

Figure 4.6 Increase in breast cancer incidence in Greenland for the period 1994–2008. The number of cases per year was adjusted for change in population size and then multiplied by 100,000 (Fredslund and Bonefeld-Jørgensen 2012).

equivalent was lowest in breast cancer cases possibly owing to receptor inhibition by non-dioxin-like POPs. The level of serum POPs, particularly PFCs, might be a risk factor in the development of breast cancer in Inuit. Hormone disruption by the combined serum POP-related xenoestrogenic and xenoandrogenic activities may contribute to the risk of developing breast cancer in Inuit (Bonefeld-Jørgensen et al. 2011). Moreover, genetic analyses showed that the *BRCA1* founder mutations and polymorphism in P450 1A1 and *CYP17* might increase risk among Greenlandic women (Ghisari et al. 2014) (see Sect. 4.6.1.2 and 4.8.2). A study in southern Quebec found an association between increased levels of PCBs, particularly PCB105, PCB118 and PCB156, and breast cancer (Demers et al. 2002).

4.7.2.3 Ovarian cancer and prostate cancer

The etiology of ovarian cancer is not fully understood. Previous results support the hypothesis of long-term elevated estrogen concentrations as etiologically important for this disease (Spillman et al. 2010). For Arctic populations, the age-standard incidence rate of ovarian cancer among Alaska Native women was significantly lower than for US white women (5.2 vs.10.5 per 100,000) in 1999–2003. No significant change in the rate of developing ovarian cancer was observed for Alaska Natives during 1973–2003 (Day et al. 2010).

Germ-line mutations in the tumor suppressor proteins BRCA1 and BRCA2 predispose individuals to breast and ovarian cancer. About 10% of all breast and ovarian cancers are dominantly inherited and mutations are mainly found in the *BRCA1* and *BRCA2* genes. Harboe et al. (2009) found three patients out of nine diagnosed with ovarian cancer (33%), and one out of ten breast cancer patients (10%) to be carrying the *BRCA1* mutation in Greenland.

Risk of prostate cancer in Inuit is 10–20% of the risk in the respective national white population (Friborg et al. 2003; Snyder et al. 2006). A recent study showed that the age-standard incidence rate for prostate cancer during 1998–2007 was lower in the Inuit Nunangat population than in the rest of Canada (17 vs. 85 per 100,000) (Carriere et al. 2012).

4.7.2.4 Pancreatic cancer

A comprehensive meta-analysis has suggested that tobacco smoking, obesity, Type 2 diabetes mellitus and chronic pancreatitis are risk factors for pancreatic cancer. Kirkegaard (2012) reported that the age-standardized incidence rate for pancreatic cancer is 138% higher in Greenland Inuit than in Denmark. This could be partly explained by a higher prevalence of smoking and Type 2 diabetes (Kirkegaard 2012).

4.7.2.5 Summary

The pattern of malignant diseases in Inuit in the Arctic region is characterized by high frequencies of cancers of the nasopharynx, salivary glands and esophagus and low frequencies of tumors common in Caucasians such as cancers of the testis, prostate, breast, and hematological system. However, during the latter half of the 20th century, cancer incidence increased substantially among all circumpolar Inuit in the Arctic region, especially for the lifestyle-associated lung, breast and colon cancers (Friborg and Melbye 2008; Carriere et al. 2012; Kelly et al. 2008; Fredslund and Bonefeld-Jørgensen 2012). Overall cancer rates now seem comparable to those of the United States, Canada and Denmark. The recent change in lifestyle and diet and thus environmental contaminant exposure of the Inuit might play a role in this. Risk characterization modelling based on blood concentrations of PCB153 in Inuit women during 1994–2005 at Disko Bay, 1999–2005 at Nuuk, and 1992–2007 at Nunavik resulted in an estimated cancer risk for the Arctic indigenous population upon exposure to PCB153 of 4.6×10^{-5} to 1.8×10^{-6} for the 90th percentile and 3.6×10^{-5} to 1.4×10^{-10} for the 50th percentile between 1930 and 2049 (Abass et al. 2013).

4.8 Genetic modifiers

4.8.1 Gene–Environment interactions in relation to cancer risk

Polymorphisms relevant in relation to environmental cancers are those that either modify the exposure dose or that modify the carcinogenic effect of a given exposure. A polymorphism may modify the correlation between environmental exposure and cancer risk, for example, by changing the metabolism and thereby the internal concentration of carcinogenic compounds. A functional effect of the polymorphism is a prerequisite for a biological effect. Much of the current molecular epidemiological research aims at identifying those functional polymorphisms and their interaction with environmental factors. The simplest model for the effect of polymorphisms in cancer is that they have additive effects in relation to cancer risk, and additive effects in combination with environmental factors. However, if polymorphisms interact with environmental factors in relation to cancer risk, it means that there are less-than-additive effects or more-than-additive effects. For instance, it could be that the rate of skin cancer formation after sun exposure is much higher among people with defective nucleotide excision repair than among people with proficient DNA repair. Therefore, there is interaction between genotype and sun exposure in relation to skin cancer risk. These differences in risk of cancer are often called 'genetic susceptibility'.

4.8.2 Genetic polymorphisms and contaminants in the Arctic

The indigenous Arctic population is of Asian descent, and their genetic background is different to that of the Caucasian populations. Relatively little is known about the specific genetic polymorphisms in genes involved in the activation and detoxification mechanisms of environmental contaminants in Inuit and their relation to health risk. The Greenlandic Inuit are highly exposed to legacy POPs such as PCBs and OC pesticides, and an elucidation of gene-environment interactions in relation to health risks is needed.

Ghisari et al. (2013) compared the genotype and allele frequencies of the cytochrome P450 CYP1A1 Ile462Val (rs1048943), CYP1B1 Leu432Val (rs1056836) and catechol-*O*-methyltransferase COMT Val158Met (rs4680) in Greenlandic Inuit (n=254) and Europeans (n=262) and explored the possible relation between the genotypes and serum levels of POPs. The genotype and allele frequency distributions of the three genetic polymorphisms differed significantly between the Inuit and Europeans. For Inuit, the genotype distribution was more similar to those reported for Asian populations. A significant difference in serum PCB153 and *p,p*'-DDE levels between Inuit and Europeans was found, and for Inuit associations were also found between POP levels and genotypes for *CYP1A1*, *CYP1B1* and *COMT*. Thus, the data provide new information on gene polymorphisms in Greenlandic Inuit that might support evaluation of susceptibility to environmental contaminants and warrant further studies (Ghisari et al. 2013).

Ghisari et al. (2014) investigated the main effect of polymorphisms in genes involved in xenobiotic metabolism and estrogen biosynthesis, *CYP1A1*, *CYP1B1*, *COMT* and *CYP17*, *CYP19* and the *BRCA1* founder mutation in relation to breast cancer risk, and possible interactions between the gene polymorphisms and serum POP levels on breast cancer risk in Greenlandic Inuit women. They found that the *BRCA1* founder mutation and polymorphisms in *CYP1A1* and *CYP17* can increase breast cancer risk among Inuit women and that risk increases with higher serum levels of PFOS and PFOA. Serum PFAS levels were a consistent risk factor for breast cancer, but inter-individual polymorphic differences might cause variations in sensitivity to the PFAS/POP exposure (Ghisari et al. 2014).

In the INUENDO study population, which includes proven-fertile men from Greenland, Warsaw (Poland), and Kharkiv (Ukraine) the effect of exposure to POPs on sperm concentration was seen only in men with a short AR gene nucleotide CAG sequence repeat. To investigate whether these effects could also be observed *in vitro*, the impact of PCB153 and 4,4'-DDE on 5α-dihydrotestosterone-activated ARs containing 16, 22 and 28 CAG repeats, respectively, was tested. Single exposure to 4,4'-DDE had the most pronounced effect on the AR activity containing 16 CAG repeats, whereas 28 CAG was the most sensitive variant when a mixture of the two compounds was added. Thus, the *in vitro* results confirmed the *in vivo* data indicating a CAG repeat length dependent effect of endocrine disrupters on AR activity (Bjork et al. 2011).

The view that there is an inverse linear association between AR CAG and nucleotide GGN sequence polymorphisms and receptor activity has been challenged. In a study population which includes proven-fertile men from Greenland, Warsaw, and Kharkiv the pattern of association was analyzed between 21 male reproductive phenotypes and AR CAG/GGN repeat lengths in 557 men. A linear association was found only between sperm DNA fragmentation index (DFI) and CAG length, and between inhibin B and GGN length. Men with longer CAG than the reference condition (22–24), had higher estradiol levels, whereas men with shorter CAG stretches had a higher DFI and a higher proportion of Fas-positive germ cells. Subjects with either short or long CAG had increased seminal levels of prostate-specific antigen and neutral α-glucosidase activity. Compared to men with the median GGN length of 23, those with shorter GGN repeats had higher inhibin B levels, higher proportions of normal and progressive sperm, and a higher fraction of Fas-positive sperm, while men with longer GGN repeats had higher estradiol levels. These data indicate that at least for some markers of male reproductive function the association with CAG or GGN repeat length is curvilinear (Brokken et al. 2013).

4.8.3 Genetics in relation to lifestyle factors in Arctic populations

Nicotine, the psychoactive ingredient in tobacco, is metabolically inactivated by *CYP2A6* to cotinine. *CYP2A6* also activates pro-carcinogenic tobacco-specific nitrosamines (TSNA). Genetic variation in *CYP2A6* is known to alter smoking quantity and lung cancer risk in heavy smokers. The study aimed to investigate how *CYP2A6* activity influences tobacco consumption and pro-carcinogen levels in light smokers and smokeless tobacco users. Cigarette smokers (n=141), commercial smokeless tobacco users (n=73) and *iqmik* (mixture of tobacco and ash) users (n=20) were recruited in a cross-sectional study of

Alaska Native people. The participants' *CYP2A6* activity was measured by both endophenotype and genotype, and their tobacco and pro-carcinogen exposure biomarker levels were also measured. Smokers, smokeless tobacco users and *iqmik* users with lower *CYP2A6* activity had lower urinary total nicotine equivalents and (methylnitrosamino)-1-(3)pyridyl-1-butanol (NNAL) levels (a biomarker of TSNA exposure). Levels of N-nitrosonornicotine (NNN), a TSNA metabolically bioactivated by *CYP2A6*, were higher in smokers with lower *CYP2A6* activities. Light smokers and smokeless tobacco users with lower *CYP2A6* activity reduce their tobacco consumption in ways (such as inhaling less deeply) that are not reflected by self-report indicators. Tobacco users with lower *CYP2A6* activity are exposed to lower pro-carcinogen levels (lower NNAL levels) and have lower pro-carcinogen bioactivation (as indicated by the higher urinary NNN levels suggesting reduced clearance), which is consistent with a lower risk of developing smoking-related cancers. This study demonstrates the importance of *CYP2A6* in the regulation of tobacco consumption behaviors, pro-carcinogen exposure and metabolism in light smokers and smokeless tobacco users (Zhu et al. 2013).

4.8.4 Genetic variability and hepatitis in the Arctic

Hepatitis B virus (HepB) infection is highly prevalent in circumpolar indigenous peoples. However, the clinical outcome is extremely variable, such that while hepatocellular carcinoma is uncommon in Canadian Inuit, its incidence is slightly higher in Greenlanders than in Danes, and it is especially high in Alaskan Native people infected with HepB genotypes F (HepB/F) and C (HepB/C). These differences may be associated with the genomic variability of the predominant HBV genotype in each group. Kowalec et al. (2013) examined the rate, nature and regional susceptibility of HepB genomic mutations among circumpolar indigenous individuals. Paired serum samples, separated by 5–6 years, were analyzed from Canadian and Greenlandic Inuit infected with HepB genotype B6 (HepB/B6) and HepB/D, respectively, and from Alaskan Native people infected with HepB/F, each having subsequently developed hepatocellular carcinoma. Mutations associated with severe outcomes predominated in HepB/F. HepB/B6 genomes exhibited higher diversity compared to HepB/D and HepB/F, particularly within the core coding region. Thus, differing mutational profiles and genetic variability were observed among different HepB genotypes predominating in circumpolar indigenous patients. The unusual observation of persistently high genetic variability with HepB/B6 despite clinical inactivity could be due to the evolution of a host-pathogen balance, but other possible factors also need to be explored (Kowalec et al. 2013).

4.8.5 Genetics in relation to hearing impairment in the Arctic

In a cross-sectional survey, the genetic causes of hearing impairment (HI) were investigated among the Inuit with a high prevalence. Mutations in the *GJB2* gene have been identified as a frequent cause of HI. *GJB2* encodes the gap junction protein connexin-26 (Cx26), involved in cochlear K^+ homeostasis and is important for mechano-sensory sound transduction. Cx26 mutations explain 15–50% of all non-syndromic HI, but apart from that gene there is huge genetic heterogeneity with more than 75 loci/genes for autosomal recessive HI now being identified. The study group comprised 45 patients selected from 166 East Greenlanders with hearing impairment, including 24 males and 21 females and with a median age of 35 years (range: 5–76). Controls were 108 East- and 109 West-Greenlanders. Connexin-26 GJB2 DNA sequence analyses were performed. The c.35delG allele frequency was 3.3%. One patient, homozygous for the c.35delG GJB2 mutation, had bilateral congenital profound hearing impairment. Another with mixed hearing impairment was heterozygous for the same mutation. Three were heterozygous for the p.V27I variant and one was heterozygous for the p.V153I variant. The frequency of the c.35delG mutation in the controls varied between 0.5% in West Greenland to 2.3% in East Greenland. In conclusion, the c.35delG GJB2 mutation occurs in Greenland with low frequency, and the main causes behind the prevalence of hearing impairment in this population are chronic otitis media, noise traumas, and/or unidentified genetic causes (Homoe et al. 2012).

4.8.6 Metabolism and contaminants: animal studies to mimic human exposures

Exposure to environmental contaminants induces the activation of cytochrome P450s (CYP) which leads to the hydroxylation of contaminants and endogenous hormones such as estrogens. The hydroxylation of estrogens forms catecholestrogens, one being the mutagenic 4-hydroxyestradiol-17β (4-OH-E2). Catecholestrogens are transformed by catechol-*O*-methyltransferases (COMTs) into nonreactive methoxyestrogens. To investigate the hepatic metabolism of estradiol-17β in female offspring at postnatal day 21, pregnant rats were dosed daily from gestation day 1 until postnatal day 21 with two dose levels of OC pesticides (0.019 or 1.9 mg/kg per d), MeHg (0.02 or 2 mg/kg per d), PCBs (0.011 or 1.1 mg/kg per d), or a mixture (0.05 or 5 mg/kg per d) including all three groups of chemicals, reflecting the concentrations of OCs in serum of the Canadian Arctic population. The low-dose treatments or the MeHg groups showed no effect. The high-dose OC pesticides, PCB, and the Mixture group increased the production of 2-OH-E2 and 6α-OH-E2, while only the PCB and Mixture groups increased the 2-OH-CE:methoxyestrogen ratio. In all groups, the cytosolic COMT activity exceeded the microsomal production rate of 4-OH-E2. Although the Mixture treatment included the PCB and OC pesticide mixtures, it did not modify the estrogen metabolism more than the PCB mixture alone. This endocrine-disruption information contributes to understanding of chemical interactions in the toxicology of chemical mixtures (Desaulniers et al. 2012).

Environmental contaminants are thought to be involved in the epidemic incidence of metabolic disorders, with food ingestion a primary route of exposure. It has been hypothesized that life-long consumption of a high-fat diet that contains low doses of pollutants will aggravate metabolic disorders induced by obesity itself. Mice dams were challenged from preconception throughout life with a high-fat diet containing pollutants commonly present in food (2,3,7,8-tetrachlorodibenzo-*p*-dioxin, PCB153, diethylhexyl phthalate, and bisphenol A), added at low doses in the tolerable daily intake range. Pollutant-

exposed mice exhibited significant sex-dependent metabolic disorders in the absence of toxicity and weight gain. In their male progeny, pollutants increased the expression of hepatic genes (from 36% to 88%) encoding proteins related to cholesterol biosynthesis and decreased (40%) hepatic total cholesterol levels. In female progeny, there was a marked deterioration of glucose tolerance, which may be related to the two-fold induction of estrogen sulfotransferase and reduced expression of estrogen receptor α (25%) and estrogen target genes (>34%). Owing to the very low doses of pollutants used in the mixture, these findings may have strong implications in understanding the potential role of environmental contaminants in food in the development of metabolic diseases (Naville et al. 2013).

The potential toxicity of PFOS, an environmentally persistent organic pollutant, is of great concern. A study by Yu et al. (2009) examined the ability of PFOS to disturb thyroid function and the possible mechanisms involved in PFOS-induced thyroid hormone alteration. Male Sprague-Dawley rats were exposed to 1.7, 5.0, and 15.0 mg/L of PFOS in drinking water for 91 consecutive days. Serum total T4 level decreased significantly at all dosages, whereas the total T3 level increased markedly only at 1.7 mg/L of PFOS. No statistically significant toxic effects of PFOS on serum TSH were observed. Hepatic uridine diphosphoglucuronosyl transferases (UGTIA1) mRNA was up-regulated at 5 and 15 mg/L of PFOS. Treatment with PFOS lowered hepatic type 1 deiodinase (DIO1) mRNA at 15 mg/L but increased thyroidal DIO1 mRNA dose-dependently. The activity of thyroid peroxidase, sodium iodide symporter, and TSH receptor mRNA in thyroid were unaffected by PFOS treatment. The results indicate that increased hepatic T4 glucuronidation via UGT1A1 and increased thyroidal conversion of T4 to T3 via DIO1 were responsible in part for PFOS-induced hypothyroxinemia in rats (Yu et al. 2009).

4.8.7 Epigenetics

The placenta and its myriad functions are central to successful reproductive outcomes. These functions can be influenced by the environment encountered throughout pregnancy, thereby altering the genetic programming needed to allow sustained pregnancy and appropriate fetal development. This altered programming may result from epigenetic alterations related to environmental contaminant exposure. Epigenetic alterations are now being linked to several important reproductive outcomes, including early pregnancy loss, intrauterine growth restriction, congenital syndromes, preterm birth, and preeclampsia. As research continues to enhance understanding of the molecular processes including epigenetic regulation that influence pregnancy, it will be critical to specifically examine how the environment, broadly defined, may play a role in altering these critical functions (Robins et al. 2011).

Rusiecki et al. (2008) analyzed the relationship between plasma POP concentrations and global DNA methylation (percent 5-methylcytosine) in DNA extracted from blood samples from 70 Greenlandic Inuit and used pyrosequencing to estimate global DNA methylation via Alu and LINE-1 assays of bisulfite-treated DNA to evaluate the correlations between plasma POP concentrations and global DNA methylation. They found an inverse correlation between methylcytosine percent and many of the POP concentrations. Linear regressions, adjusting for age and cigarette smoking, showed statistically significant inverse linear relationships mainly for the Alu assay for *p,p'*-DDT (β = -0.26), *p,p'*-DDE (β = -0.38), β-HCH (β = -0.48), oxychlordane (β = -0.32), α-chlordane (β = -0.75), Mirex (β = -0.27), ΣPCBs (β = -0.56) and ΣPOPs (β = -0.48). Linear regressions for the LINE-1 assay showed β estimates of similar magnitudes to those using the Alu assay; however, none was statistically significant. This first study investigating environmental exposure to POPs and DNA methylation levels in an Arctic population has shown that global methylation levels are inversely associated with blood plasma levels for several POPs and merit further investigation.

To evaluate changes in methylation associated with *n*-3 PUFA intake, Aslibekyan et al. (2014) undertook an epigenome-wide methylation association study of long-chain *n*-3 PUFA intake and the associations between the diabetes- and cardiovascular disease-related traits. DNA methylation was assessed at ~470,000 cytosine-phosphate-guanine (CpG) sites in a cross-sectional study of 185 Yup'ik Alaska Native individuals representing the top and bottom deciles of PUFA intake. Linear regression models were used to test for the associations of interest, adjusting for age, sex, and community group, and identified 27 differentially methylated CpG sites at biologically relevant regions that reached epigenome-wide significance ($p < 1 \times 10^{-7}$). Specifically, regions on chromosomes 3 (helicase-like transcription factor), 10 (actin α2 smooth muscle/Fas cell surface death receptor), and 16 (protease serine 36/C16 open reading frame 67) each harbored two significant correlates of *n*-3 PUFA intake. This indicates an association between several biologically relevant epigenetic markers and long-term intake of marine-derived *n*-3 PUFAs (Aslibekyan et al. 2014).

4.8.8 Genetic predisposition and methylmercury neurotoxicity

Cognitive consequences at school age associated with prenatal MeHg exposure may need to take into account nutritional and socio-demographic cofactors as well as relevant genetic polymorphisms. Julvez et al. (2013) selected a subsample (n=1311) of the Avon Longitudinal Study of Parents and Children (Bristol, UK) and measured Hg concentrations in freeze-dried umbilical cord tissue as a measure of MeHg exposure. A total of 1135 children had data on 247 single-nucleotide polymorphisms within relevant genes, as well as the Wechsler Intelligence Scale for Children IQ scores at age 8 years. Multivariate regression models were used to assess the associations between MeHg exposure and IQ and to determine possible gene-environment interactions. Mercury concentrations indicated low background exposure (mean = 26 ng/g, SD = 13). Log_{10}-transformed Hg concentration was positively associated with IQ, which attenuated after adjustment for nutritional and socio-demographic cofactors. In stratified analyses, a reverse association was found in higher social class families (for performance IQ, $p = 0.0013$) among which there was a wider range of MeHg exposure. Among 40 single-nucleotide polymorphisms showing nominally significant main effects, MeHg interactions were detected for rs662 (paraoxonase 1) and rs1042838 (progesterone receptor) ($p < 0.05$) and for rs3811647 (transferrin) and rs2049046 (brain-derived neurotrophic factor) ($p < 0.10$). Thus, in this

population with low MeHg exposure, associations between MeHg exposure and adverse neuropsychological outcomes were equivocal. Heterogeneities in several relevant genes suggest possible genetic predisposition to MeHg neurotoxicity in a substantial proportion of the population. Future studies should address this possibility (Julvez et al. 2013).

4.9 Effect modifiers

Most environmental research on the effects of chemicals focuses on single exposures. However, exposure to mixtures of chemicals is ubiquitous in real life (Bellinger 2009). Certain chemical substances may target the same organ and induce similar effects in an additive or non-additive way (Carpenter et al. 2002). Recent studies suggest a synergistic effect of metal mixtures with neuropsychological outcomes (Kim et al. 2009a) or kidney disease (Navas-Acien et al. 2009). However, studies that examine the effects of chemical mixtures remain limited in humans, and even in experimental animal studies (Carpenter et al. 2002).

Methylmercury, a worldwide contaminant of seafood, can cause adverse effects on the developing nervous system. However, long-chain *n*-3 PUFAs in seafood provide beneficial effects on brain development. Negative confounding is likely to result in underestimation of both Hg toxicity and nutrient benefits unless mutual adjustment is included in the analysis. In the Faroe Islands and NCDS cohort studies, associations between prenatal exposure to MeHg and neurobehavioral deficits at school age were strengthened after fatty acid adjustment, thus suggesting that n-3 fatty acids should be included in similar studies to avoid underestimating associations with MeHg exposure (Choi et al. 2014).

Yorifuji et al. (2011) examined the effects of prenatal Pb exposure on cognitive deficits in the presence of a similar molar concentration of a neurotoxic co-pollutant (MeHg) in 7- and 14-year-olds born in the Faroe Islands. Their analyses of the total cohort and those of cohort members without interaction terms among lower co-pollutant exposure categories showed equivocal results. However, when the subjects were restricted to a lower co-pollutant category, and statistical interaction terms were entered within the category, adverse effects of prenatal Pb exposure on cognitive function in childhood were observed, especially on attention, learning and memory. In the Faroe Islands it has been suggested that another co-pollutant, the PCBs, may affect human brain development through maternal ingestion of contaminated pilot whale blubber. However, Yorifuji et al. (2011) found that PCBs were only weakly associated with neuropsychological deficits (deficits on the Boston naming test – without cues p=0.09 and with cues p=0.03 – and long-term recall in CVLT-C – p=0.15), and not in the outcomes affected by Pb in the present study.

4.10 Conclusions

Neurobehavioral effects: Effects associated with MeHg exposure have been documented in humans at successively lower exposures and it is clear that the developing brain is the most vulnerable organ system. Prenatal exposure to MeHg has been associated with clear effects on the developing brain. Cohort studies in the Faroe Islands have demonstrated that children exposed to MeHg *in utero* exhibit decreased motor function, attention span, verbal abilities, memory and other mental functions. Follow-up of these children up to the age of 22 years indicates that these deficits appear to be permanent. Similarly, a study in Nunavik of child development at age 11 showed that Hg exposure was associated with poorer early processing of visual information, lower estimated IQ, poorer comprehension and perceptual reasoning, poorer memory functions, and increased risk of attention problems and ADHD behavior. Some of the adverse effects of MeHg on neurodevelopment may be masked by beneficial effects of seafood nutrients. Neurophysiological assessments of brain function also indicate that postnatal exposure up to the teenage years can cause harm. Thus, both pregnant women and children are at increased risk from MeHg exposure. New studies indicate that certain genetic factors may increase vulnerability to MeHg toxicity. Neurophysiological assessments of children from the Faroe Islands and Nunavik have been less clear with regard to the effects of prenatal exposure to PCBs.

Immunological effects: Certain environmental pollutants can adversely affect the development of the immune system. Young children in Nunavik have had a high incidence of infectious diseases (such as meningitis, bronchopulmonary infections, and middle ear infections) for many years. Recent studies to investigate the possibility that this could be partly due to maternal transfer of OCs with known immunotoxic properties during breastfeeding show that that prenatal exposure to OCs does increase susceptibility to infectious diseases (in particular otitis media). Most experimental evidence points to the role played by the dioxin-like PCB congeners. Immunotoxic effects have also been seen on routine childhood immunizations. Faroese children exhibiting elevated levels of PCBs and especially perfluorinated compounds showed reduced immune response to routine vaccinations. These findings suggest a decreased effect of childhood vaccinations and may indicate a more general immune system deficit. The implications of inadequate antibody production highlight the need to significantly reduce immunotoxicant exposure in Arctic populations, as well as the need for long-term assessments of the health risks associated with exposure to immunotoxic contaminants.

Reproductive effects: Many Danish and Faroese men have a low level of semen quality compared to men from other European countries, and there are also indications of lower capacity for testosterone production. Studies of semen quality did not show a relationship with PCB153 or *p,p*'-DDE levels in blood in Greenlanders; however, sperm motility was inversely related to PCB153 concentration in this population.

Cardiovascular effects: Conflicting results have been reported regarding the impact of prenatal Hg exposure on blood pressure, with 7-year-old Faroese children exhibiting elevated blood pressure and children from Nunavik showing no association between blood pressure and prenatal Hg exposure. However, elevated blood pressure was found to be associated with Hg exposure among adults from the Faroe Islands and Nunavik. Decreased heart rate variability was associated with cord blood Hg concentrations in Faroese children at ages 7 and 14 but not in 11-year-old children from Nunavik; however, contemporary blood Hg concentrations in these children from Nunavik were associated with decreased overall heart rate variability parameters. This was also the case for adults from Nunavik and for James Bay Cree adults.

Endocrine effects: Endocrine-disrupting chemicals can mimic, interfere or block the function of endogenous hormones and so cause adverse developmental, reproductive, neurological, cardiovascular, metabolic and immune effects in humans. Exposure during early stages of fetal and neonatal development is especially critical and can disrupt the normal pattern of development in later life. Higher prenatal PCB exposure was associated with lower serum concentrations of luteinizing hormone and testosterone in Faroese adolescent boys, while sex hormone-binding globulin was positively associated with both prenatal and concurrent PCB exposures. DDE was highly correlated with PCBs and showed slightly weaker associations with the hormone profile. These findings suggest that delayed puberty with low serum luteinizing hormone concentrations associated with development exposure to non-dioxin-like PCBs may be due to a central hypothalamo-pituitary mechanism

Exposure to several polyhalogenated compounds has been associated with modifications in thyroid hormone parameters in Inuit adults from Nunavik. An association between POPs levels and thyroid hormones has also been observed in aging residents in upper Hudson River communities. This influence of POPs on thyroid hormones in aging populations may have clinical significance and merits further investigation.

A potential influence of POPs on Type 2 diabetes pathogenesis has also been observed. An examination of septuagenarian Faroese with a high POPs exposure from the traditional diet but still free of Type 2 diabetes and pre-diabetes showed that the fasting insulin concentration decreased by about 8% for each doubling of the serum concentration of PCBs, and that a similar increase occurred in the fasting glucose level. Along with higher PCB exposures in persons with Type 2 diabetes and impaired fasting glycemia, these results suggest that PCB-induced β-cell deficiency may be involved in the disease pathogenesis. Impaired insulin secretion appears to constitute an important part of the Type 2 diabetes pathogenesis associated with dietary exposure to lipophilic POPs. The study of Faroese septuagenarians also found that a vitamin D status of less than 50 nmol/L doubled the risk of newly diagnosed Type 2 diabetes. Thus, vitamin D may provide protection against Type 2 diabetes in older persons.

Carcinogenic effects: During the latter half of the 20th century, cancer incidence increased substantially among all circumpolar Inuit in the Arctic region, especially for the lifestyle-associated lung, breast and colon cancers. Lung cancer now constitutes about 20% of all cancers in Inuit. Overall cancer rates now seem comparable to those of the United States, Canada and Denmark. The recent change in lifestyle and diet and thus environmental contaminant exposure of the Inuit might play a role in this.

Effect modifiers: Different chemical substances can interact and induce similar effects in an additive, synergistic or non-additive way and may target the same organ. Because most studies concern human exposure to single chemicals rather than chemical mixtures, negative confounding could cause underestimation of those chemicals causing toxicity (e.g. MeHg and PCBs in seafood) and those having benefits (e.g. long-chain *n*-3 PUFAs in seafood).

5. Approaches to describe risks and future needs

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5.1 Introduction

Previous AMAP assessments have reported that Arctic residents are exposed to many chemical pollutants that are emitted to the environment in countries south of the Arctic and then transported to the Arctic via air and ocean currents. Population exposure is primarily via the food chain, especially from seafood and marine mammals.

Studies on the precise impact of environmental pollutants on human health in the Arctic are difficult to undertake and interpret, because many factors influence health at the same time and to varying degrees. These include genetic and environmental factors. Environmental factors include the mixtures of chemical compounds to which individuals are commonly exposed (Humblet et al. 2013; Lam et al. 2014; Moltke et al. 2014). Understanding of the effects of mixtures is still at an early stage (Kortenkamp et al. 2007; Boobis et al. 2013). The incidence of many diseases in the Arctic has increased and it has been suggested that pollutants may have a contributory effect. This applies to many adverse effects on health, including cancer (see Chap. 4).

This chapter reports on the issues associated with risk assessment of single chemicals, and presents suggestions for future studies as well as a summary of lessons learned during the health-related parts of the EU-funded FP7 project ArcRisk (*Arctic Health Risks: Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling, 2009–2014*; www.arcrisk.eu).

5.2 Blood levels and biological guideline values for contaminants

Measurements of pollutants in human blood in the Arctic region obtained since the previous AMAP assessment on human health in the Arctic (AMAP 2009), indicate that concentrations of several contaminants are continuing to decrease (Table 5.1).

Humans are exposed to toxic substances from different sources within the environment, and the most significant routes of exposure are ingestion, inhalation and dermal absorption. The risk assessment process, which incorporates hazard identification, exposure assessment, dose–response assessment and risk characterizations is usually used to quantify the probability of harmful effects on human health. The United States Environmental Protection Agency (US-EPA) addresses the first two components, hazard identification and exposure assessment, through the Integrated Risk Information System (IRIS) databases. This scientific evidence-based methodology is currently used for evaluating non-cancer hazard and cancer risk in environmental and occupational settings. The objective of exposure assessment is to estimate the average

Table 5.1 Change over time in pollutant levels in human blood within the Arctic region. Data sources: AMAP (1998, 2003, 2009).

Contaminant	Media, source	Units	1996–2004	2004–2009	2009–2013
PCB153	Maternal blood, northern Norway	µg/kg plasma lipid	52 (25–130)	24.8 (5.3–201)	-
p,p'-DDT	Maternal blood, Faroe Islands	µg/kg plasma lipid	0.7 (0.1–139)	7.0 (0.1–110)	-
p,p'-DDE	Child's blood, Faroe Islands	µg/kg plasma lipid	613 (68–10265)	-	180 (15–4414)
HCB	Maternal blood, Alaska	µg/kg plasma lipid	14	22 (2.4–188)	15.9 (2.7–98.8)
β-HCH	Maternal blood, Iceland	µg/kg plasma lipid	24 (10–71)	9.0 (2.5–20)	7.1 (3.0–28)
Oxychlordane	Maternal blood, Iceland	µg/kg plasma lipid	4.7 (1.3–22)	6.5 (1.3–22)	3.5 (1.3–8.9)
Toxaphene Parlar 50	Maternal blood, Nunavik, Canada	µg/kg plasma lipid	-	17 (<LOD–133)	9.1 (<LOD–63)
Mirex	Child's blood, Nunavik, Canada	µg/kg plasma lipid	4.1 (1.1–72)[a]	2.3 (0.6–29)[b]	-
Pb	Maternal blood, Coastal Chukotka, Russia	µg/L whole blood	37.5 (18.3–76.8)	29.6 (4.9–137)	-
Hg	Maternal blood, Disko Bay, Greenland	µg/L whole blood	6.3 (1.4–46.5)	-	4.0 (1.0–10)
Cd	Maternal blood, Alaska	µg/L whole blood	0.57	0.44	0.20
PFOS	Maternal blood, Alaska	µg/L	-	0.9 (0.2–27.6)	2.2 (<LOD–9.0)
PFOA	Maternal blood (pooled), Sweden	µg/L	2.56	1.88	1.67
PFHxS	Maternal blood (pooled), Sweden	µg/L	2.7	4.78	6.39
PBDEs (BDE47, BDE99, BDE100, BDE153, BDE209)	Breast milk, northern Finland	µg/kg lipid	-	2.53 (1.38–6.33)	1.57 (0.65–3.79)
Bisphenol A	Maternal urine, Sweden	µg/g creatinine	-	-	1.23 (0.34–7.85)

LOD: limit of detection. [a]age 5 years; [b]age 11 years.

daily dose (ADD) and the lifetime average daily dose (LADD). With hazard identification the former is used to estimate the hazard quotient (HQ) for non-cancer effects and the latter to calculate excess lifetime cancer risk (CR). Traditional risk assessment considers each external source of contaminant uniquely with its own characteristics (Fjeld et al. 2007; US EPA 2014). The concentration of the contaminant in blood generally provides the sum of exposure from various exposure routes. How accurate it is depends on the elimination half-life of the contaminants in blood and accumulation in tissues. Several reference values have been published by different organizations to evaluate the exposure limit (see Tables 5.2, 5.3 and 5.4).

The health effects are most pronounced in sensitive groups like children, who are of special concern because many chemicals and metals are known to affect child development. There may be synergistic effects when more than one pollutant is present at the same time, and the composition of these pollutant mixtures varies from one region to another (Garçon et al. 2004, 2007; Cui et al. 2005; Pillai and Gupta 2005; Nampoothiri and Gupta 2008; Pillai et al. 2009). In humans, co-exposure

Table 5.2 Biological guideline values for contaminants in blood.

Contaminant	Media	Comments	Guideline value	Source
Total PCBs	Plasma lipids	For pregnant women, women of childbearing age, breastfeeding women	0.7 µg/g	ANSES 2010
		Young girls and teenage girls		
		Children under age three		
		In boys over age three, adult men and women beyond childbearing age	1.8 µg/g	ANSES 2010
Pb	Blood	Blood lead intervention level	100 µg/L	CEOH 1994
		Pregnant women intervention level	50 µg/L	CDC 2010
		Children (reference level)	50 µg/L	CDC 2012
MeHg	Blood	Reference dose	5.8 µg/L	Rice et al. 2003
		Intervention level for children, pregnant women and women of childbearing age	8 µg/L	Legrand et al. 2010
		Females (≥50 years) and males (>18 years) at increasing risk	≥20 µg/L	Health Canada 1999
		Females (≥50 years) and males (>18 years) at risk	≥100 µg/L	Health Canada 1999

Table 5.3 Reference values for cadmium and mercury in blood or urine (HBM Commission 2003, 2005). Reference values are statistically derived values that indicate the upper margin of background exposure to a given pollutant in a given population at a given time. Reference values are derived from the analytical data provided within the framework of the German Environmental Surveys (Seifert et al. 2000).

Contaminant	Media	Comments	Reference value
Cd	Urine	Children (6–12 years)	0.5 µg/L
		Non-smoking adults (18–69 years)	0.8 µg/L
Cd	Blood	Children (6–12 years)	0.5 µg/L
		Non-smoking adults (18–69 years)	1.0 µg/L
Hg	Urine	Children (6–12 years) without amalgam filling	0.7 µg/L
		Adults (18–69 years) without amalgam filling	1.0 µg/L
Hg	Blood	Children (6–12 years), fish consumption ≤3 times/month	1.5 µg/L
		Adults (18–69 years), fish consumption ≤3 times/month	2.0 µg/L

Table 5.4 Human biomonitoring values for cadmium and mercury in blood and urine (HBM Commission 1997, 1999). Human biomonitoring values (HBM) are derived on the basis of toxicological and epidemiological studies.

Contaminant	Media	Comments	HBM I	HBM II
Cd	Urine	Adults ≤25 years	1.0 µg/g creatinine	3.0 µg/g creatinine
		Adults >25 years	2.0 µg/g creatinine	5.0 µg/g creatinine
Hg	Blood	Children and adults	5 µg/L	15 µg/L
Hg	Urine	Children and adults	5µg/g creatinine, 7µg/L	20µg/g creatinine, 25µg/L

HBM I represents the concentration of a substance in humans below which there is no risk or adverse health effects and no need for action. HBM II represents the concentration of a substance in [add correct text from row above] above which there is an increased risk for adverse health effects and urgent need to reduce the exposure and to provide individual biomedical care (advice). This is considered as an intervention or action level.

to mixtures of cadmium (Cd) and lead (Pb) has been linked to renal dysfunction in people living in the contaminated area (Cui et al. 2005). Exposure to Cd, as well as affecting renal Pb concentrations, also altered renal concentrations of essential elements, such as copper (Cu) and zinc (Zn). Chronic occupational exposure to Pb and Cd has been shown to alter a number of oxidative stress markers such as α-glutathione-*S*-transferase, which is a useful biomarker for clinical renal disease (Garçon et al. 2004, 2007). For a few substances, a direct association has been documented between disease and exposure to a chemical in the Arctic, this is typically the case for chemicals that have been in use for a long time and are now banned or in the process of being banned.

5.3 Mercury levels in the Arctic and in Europe

One of the tasks in the ArcRisk project was to compare Hg levels measured in Arctic cohorts with those from the Mediterranean region, which belongs to the mercury belt area with Hg mines and where populations are exposed to low levels of Hg throughout their lifespan. The levels of Hg in people from Arctic Canada vary and have decreased since 1992 (see Chap. 3). However, there is very large inter-individual variation in Hg level in most of the cohort studies. Among the study groups in the ArcRisk project, participants in the Greek part of the PHIME project (Public Health Impact of long-term, low-level Mixed element Exposure in susceptible population strata, an EU-funded project) had higher blood Hg levels than those in the cohort in Slovenia. The PHIME cohorts were used to compare with the ArcRisk cohorts. The main reason for the difference between Hg levels in the Mediterranean and the central European regions is probably linked to the consumption of locally caught fish (Jenssen et al. 2012; Miklavčič et al. 2014; Veyhe et al. 2015). For example, fish consumption in Greece is mostly based on locally caught fish, while in Slovenia the fish are mostly from the fish market which is supplied by fish farms (Miklavčič et al. 2013; Zagar et al. 2014).

Blood Hg levels in pregnant women from Nunavik (see Chap. 3) were previously several-fold higher than those in the ArcRisk cohorts (see Brantsæter and Knutsen 2013), but have since declined to the same range as in the Norwegian high-fish consumers in the Norwegian Fish and Game Study and in Greece in the most recent samples. In the Russian study groups, Hg levels in adult males and females were in the same range but somewhat higher than in the high-fish consumers of the Norwegian Fish and Game study. However, Hg levels in pregnant women in all studied cohorts are falling, and at present are in the same range as maternal blood samples from Italy, Croatia, Arctic Norway, and Greece. The same values as in Arctic Norway were also reported in people from the Spanish islands (Menorca and Ribera d'Erbe), where predominantly local fish are consumed. Living in inland or coastal settlements in Norway also affected Hg levels in blood, being higher in coastal populations (Jenssen et al. 2012).

Within the framework of the European Union (EU), various projects have focused on the potential toxicity at low exposure levels of environmental contaminants to child development (e.g. ENRIECO, Environmental Health Risks in European Birth Cohorts; OBELIX, OBesogenic Endocrine disrupting chemicals: LInking prenatal eXposure to the development of obesity later in life; CLEAR, Climate change, Environmental contaminants and Reproductive health; INUENDO Biopersistent organochlorines in diet and human fertility. Epidemiological studies of time-of-pregnancy and semen quality in Inuit and European populations; ArcRisk; and PHIME), and several Arctic cohorts have formed part of this research focus.

5.4 Health outcomes and mercury exposure

Humans in Europe and in the Arctic are exposed to Hg mainly through fish consumption. Other sources, such as elemental Hg in air and inorganic Hg in food items are minor sources of exposure. Consequently, the highest exposure levels to methylmercury (MeHg) in Europe are found in coastal populations that consume more fish, particularly locally caught fish than people living inland. Mercury levels in fish vary greatly according to species and origin (Miklavčič et al. 2011a,b, 2013; Jenssen et al. 2012; Leino et al. 2013). Farmed fish generally contain less Hg than free-ranging fish from the open ocean. The highest values have been reported for wild fish catches in the Mediterranean region (Minganti et al. 2010; Pawlas et al. 2013; Akerblom et al. 2014; González-Estecha et al. 2014).

Neurodevelopment among children in the Mediterranean coastal regions of Italy, Slovenia, Croatia and Greece was investigated in the PHIME project. The study results showed that exposure to Hg was low in these Mediterranean populations and that the Hg levels measured did not significantly affect neurodevelopment by the age of 18 months. Exposure to the highest quartile of Hg levels during pregnancy did not cause lower performance in testing for cognitive, language or motor neurodevelopment (Valent et al. 2013). Instead, higher fish consumption in pregnancy was associated with higher cognitive and language (but not motor) neurodevelopmental performance at the age of 18 months (Bilić Čace et al. 2011; Miklavčič et al. 2011a, 2013; Valent et al. 2011; Visnjevec et al. 2014). The mean Hg levels in the ArcRisk study groups were in the same range (<100 μg/L) but there was high variation in measured Hg concentrations between individuals in all cohorts.

5.5 Levels of organohalogens and PCBs

The Tromsø study was established in 1979 and the same males were followed for almost 30 years. Blood levels of the persistent organic pollutants (POPs) analyzed declined over the follow-up period, although median concentrations of some compounds peaked in 1986 (e.g. PCB170, PCB180 and PCB194, see Chap. 3). Peak PCB153 concentrations were measured in 1979 and 1986, confirming this period as the years of highest human exposure (Nøst et al. 2013). However, in Russian indigenous peoples, there were no changes in geometric mean serum concentration of polychlorinated biphenyls (PCBs) in children and adults over the 10-year period (see Chap. 3).

Concentration levels and enantiomeric fractions for α-hexachlorocyclohexane (α-HCH) and *trans*-, *cis*-, and

oxychlordane in selected Greenlandic traditional food items (raw and smoked salmon and halibut, whale meat, seal meat and narwhal *mattak* – skin and blubber), collected at the local market in Nuuk in 2010 were below the tolerable daily intake (TDI) threshold (Carlsson et al. 2014a,b). Furthermore, daily exposure to PCBs, polybrominated diphenylethers (PBDEs), and perfluorinated alkylated substances (PFAS) from traditional Greenlandic seafood items was below the TDI for all compounds. Excluding local food items such as intestines and blubber from the diet has a strong positive effect on reduction of POPs levels in food while maintaining the health benefits of traditional food intake.

The median levels of PCB153 in serum were not statistically different between the ArcRisk cohorts. The highest levels were found among adults in the Norwegian Fish and Game Study (the oldest group in the study, median age 55 years; Jenssen et al. 2012). Lower levels were found in the Spanish INMA study groups (Valencia) and in the Norwegian MISA (Tromsø) study. (INMA is a research network for Spanish children's health in relation to environmental pollutants.) This may reflect differences in cumulative exposure and dietary patterns among birth cohorts, consistent with the associations between PCB153 and age or birth cohort that have been reported based on cross-sectional studies (Rylander et al. 1997; Bjerregaard et al. 2001; Perry et al. 2005; Wolff et al. 2005, 2007; Hardell et al. 2010).

In comparison with other European studies, the Mediterranean populations exhibit higher median concentrations of hexachlorobenzene (HCB), β-hexachlorocyclohexane (β-HCH), and DDT with its metabolites (Vizcaino et al. 2014). In contrast, PCB concentrations are lower in Mediterranean populations than in other European populations. For instance, studies in Slovakia and the Czech Republic show much higher PCB levels in their inhabitants than in the Mediterranean populations (Mikes et al. 2012). These specific pollution cases have been attributed to the presence of a PCB factory in Slovakia and to intensive industrial activity, particularly in the chemical sector, in the former Czechoslovakia (Holoubek et al. 2001).

5.6 Health outcomes and organohalogens

Several health effects have been identified in the ArcRisk project (see Grimalt et al. 2012; Odland et al. 2012). The results from the ArcRisk Arctic cohorts are discussed in Chap. 4, only the Mediterranean results are discussed in this section. Analysis of POPs in a large number of individuals is required to assess the possible health effects of long-term exposure to low concentrations of these compounds.

Fetuses and newborns are most sensitive to POPs because their organs and metabolic functions are still under development. In the Mediterranean cohorts, several adverse health effects have been related to exposure to organohalogens. For example, low birth size, low birth weight, low birth head circumference, poor social behavior, increased incidence of attention-deficit hyperactivity disorder (ADHD), decreased cognitive skills, overweight, and alterations of porphyrin, thyroid and liver metabolism (Table 5.5).

The health end points listed in Table 5.5 are the results of several studies conducted in different cohorts. The associations between prenatal exposure to a particular contaminant and children's social behavior or health outcomes should be considered when evaluating potential neurotoxicological effects.

5.7 Contaminants and placental transport

To reach the fetal circulation, contaminants must cross the placenta, the main interface between mother and fetus. Based on analyses of cord blood, it is known that the fetus is exposed to environmental contaminants present in the maternal circulation. The important properties determining placental transfer by passive diffusion are molecular weight, pKa (the pH at which a weak organic acid is 50% ionized), lipid solubility and protein binding. The placenta also expresses a large variety of

Table 5.5 Health outcomes in children related to exposure to organohalogens *in utero* and/or in early age in the ArcRisk Mediterranean cohorts.

Compound	Exposure	Health end point	Source
HCB	*In utero*	Small length for gestational age	Ribas-Fitó et al. 2002
		Poor social behavior at 4 years	Ribas-Fitó et al. 2007
		ADHD at 4 years	
		Overweight at 6 years	Smink et al. 2008
DDE	*In utero*	Prematurity	Ribas-Fitó et al. 2002
		Delay in mental and psychomotor development at 1 year	Ribas-Fitó et al. 2003
		Increase in urinary coproporphyrins	Sunyer et al. 2008
		Asthma at 4 and 6 years	Sunyer et al. 2005, 2006
DDT	*In utero*	Decrease of cognitive skills at 4 years	Ribas-Fitó et al. 2006; Morales et al. 2008
	4 years	Alteration of thyroid hormones	Álvarez-Pedrerol et al. 2008a
β-HCH	*In utero*	Alteration of thyroid hormones	Álvarez-Pedrerol et al. 2008b; Lopez-Espinosa et al. 2010
	4 years	Alteration of thyroid hormones	Álvarez-Pedrerol et al. 2008a
PCBs	4 years	Alteration of thyroid hormones	Álvarez-Pedrerol et al. 2008b
PBDEs	4 years	ADHD, Poor social behavior	Gascon et al. 2011

transporter proteins which modify placental transfer processes (Vähäkangas and Myllynen 2009).

In addition to their physiological substrates, transporter proteins may also transfer foreign compounds such as therapeutic agents, environmental pollutants and chemical carcinogens bearing structural resemblance to their physiological substrates. Depending on the localization and function of transporter proteins they may either increase or decrease fetal exposure to foreign compounds. ABCG2 (BCRP), a transporter protein highly expressed in the human placenta relative to any other organ, has been shown to protect the fetus from exposure to some toxicants. ABCC2 (MRP2) is likely to be important for preventing the passage of conjugated metabolites of toxicants while ABCC1 (MRP1) is proposed to prevent or limit the entry of organic anions into the fetal circulation.

There is evidence of placental transfer for POPs. The distribution of contaminants between maternal blood, cord blood and placenta are usually related. If compounds are metabolized in the fetus or placenta, metabolites may accumulate and cause toxic effects, and fetal and maternal serum levels may differ (Vizcaino et al. 2014). A strong correlation has been observed between concentrations in the maternal and fetal compartments for perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), PCB153, HCB, PCB180, and *p,p'*-DDE (Jaraczewska et al. 2006; Porpora et al. 2013). Thus, even if the placenta cannot prevent the transfer of foreign chemicals into the fetal circulation, it can at least modify their transfer and toxicity. The function of transporter proteins may cause person-to-person variation in fetal exposure to environmental contaminants, which may affect individual risk for adverse events after exposure to harmful compounds.

A significant number of protein carriers have been identified in the placenta and it has been suggested that they may play a role in the uptake and/or efflux of MeHg complexes (Leslie et al. 2005). The role of polymorphisms of ABC transporters as modifiers of prenatal exposure to MeHg has been studied (Llop et al. 2014). The study population comprised participants (n=1651) in two birth cohorts, one in Italy and Greece (PHIME) and the other in Spain (INMA). Total Hg concentrations were measured in cord blood samples while maternal fish intake during pregnancy was determined from questionnaires. Polymorphisms (n=5) in the ABC genes *ABCA1*, *ABCB1*, *ABCC1* and *ABCC2* were analyzed in both cohorts. The findings showed the role of ABC transporters in MeHg accumulation during early development.

Cadmium may modulate fetal exposure to other harmful compounds transported by ABCG2, one of the main efflux transporters in human placenta, by inhibiting its activity (Leslie et al. 2005). The metal salts methylmercury chloride (MeHgCl) and lead chloride ($PbCl_2$) were not found to affect mRNA or protein expression of ABCG2, cadmium chloride ($CdCl_2$) inhibited its function. Further studies are needed to clarify whether this leads to elevated placental transfer of ABCG2 substrates (Kummu et al. 2012).

5.8 Modelling

5.8.1 Toxicokinetic modelling of PCB153

Toxicokinetic modelling is increasingly employed to reconstruct past contaminant exposure and to relate exposure and body concentrations. Although systematic monitoring has usually been conducted for a relatively short period compared to the entire contamination history, it is possible to extrapolate body burden and exposure to the whole lifespan of the population under certain assumptions. These concern toxicokinetic model structure, weight, intake proportionality factor, total mass of the body adipose tissue, net gastrointestinal absorption, and elimination half-life of the contaminant in the human body. PCB153 is among the most prevalent of the PCB congeners found in human populations and so has been one of the most studied. Concentrations of PCB153 in pregnant Inuit women living in Nunavik (Quebec, Canada), Disko Bay (Greenland), and Nuuk (Greenland) are clearly declining in all three regions (Fig. 5.1). Inuit born in the 1960s and 1970s have a higher lifetime exposure (Fig. 5.2) than those born either earlier or later.

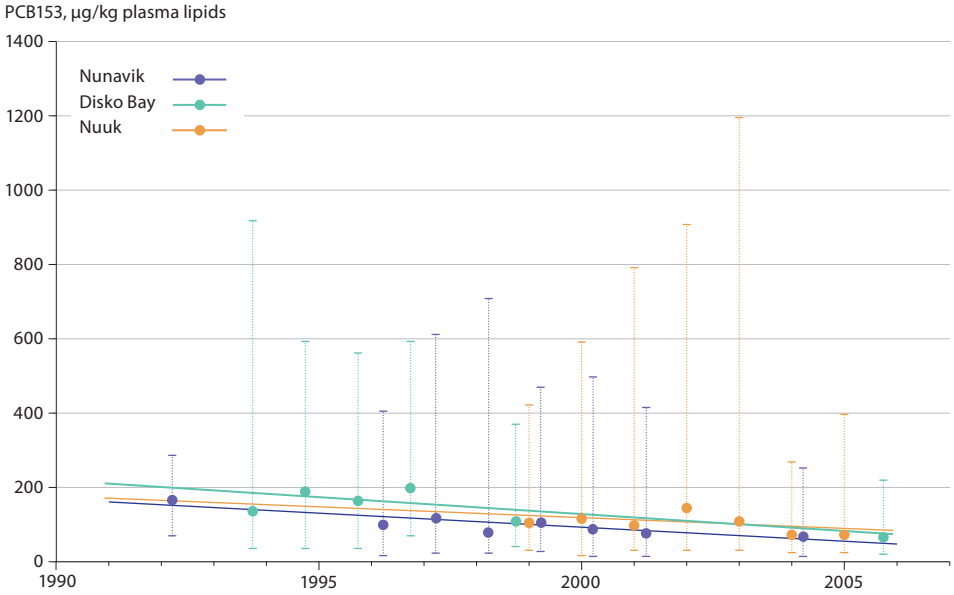

Figure 5.1 Trends in PCB153 concentration (geometric mean and range) in plasma lipids among pregnant Inuit women living in Nunavik (Quebec, Canada), Disko Bay (Greenland), and Nuuk (Greenland) during the years 1992 to 2007 (Abass et al. 2013).

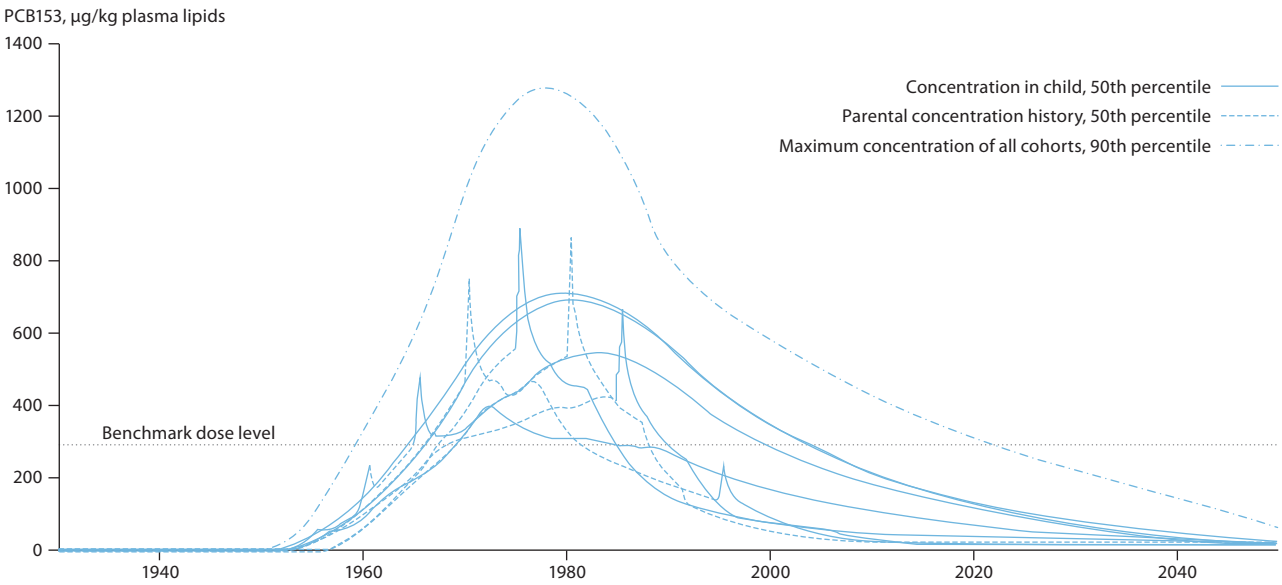

Figure 5.2 Extrapolated concentrations of PCB153 in pooled plasma lipids among pregnant Inuit women living in Nunavik (Quebec, Canada), Disko Bay (Greenland), and Nuuk (Greenland) (Abass et al. 2013).

In summary, the known disposition of PCBs in the human body combined with population toxicokinetic modelling makes extrapolation possible to an acceptable accuracy. Birth during the 1960s and 1970s has led to high lifelong exposure, and body burdens remain elevated. Although lifelong exposure is lower for generations born after the 1960s, contamination during early childhood and possibly during the fetal period has been extremely high due to the high contamination levels of mothers leading to large exposure of the fetus during pregnancy and from contaminated milk during breastfeeding. Currently, the health risk of PCB153 in Arctic populations is estimated by using a toxicological cut-off point in lipids, that is, a benchmark dose level (BMDL) of 300 µg/kg plasma lipid, at which it is considered to pose no appreciable risk or minimal risk to human health (see VKM 2008).

5.8.2 CoZMoMAN model

Studies on the health effects of PCBs require an understanding of past and present human exposure. Time-resolved models may supplement information on concentrations in individuals obtained from measurements and/or statistical approaches, if they can be shown to reproduce empirical data (Breivik et al. 2010; Nøst et al. 2013). The CoZMoMAN model was used in person-specific predictions of life course concentrations of PCBs in individual Norwegians (Nøst et al. 2013). The CoZMoMAN model was evaluated by reproducing measured time-variant concentrations of PCBs in environmental compartments, local food items, and human breast milk. Person-specific predictions of contaminant levels were also made using statistical models that linearly regressed PCB concentrations against dietary and lifestyle variables (Nøst et al. 2013). The rank correlation between measurements and predictions from both the CoZMoMAN model and regression analyses was strong (Spearman's r >0.67). Simulations indicated large inter-individual differences in concentrations experienced in the past. Agreement between measurements and predictions of concentrations, subject ranking and quartile assignment was good. Contamination histories for individuals predicted by the CoZMoMAN model revealed variation between study subjects, particularly in the timing of peak concentrations. Realistic *a priori* assessments of PCB exposure by mechanistic models provide individual PCB exposure metrics that could serve as valuable supplements to measurements. The time-variant model CoZMoMAN has been useful in estimating prenatal, postnatal and childhood exposure to PCB153 under scenarios of hypothetical and realistic maternal fish consumption (Binnington et al. 2014).

5.9 Literature review

5.9.1 Health outcomes – critical reviews

Reviews and meta-analyses of original scientific articles are needed to evaluate potential health effects and their magnitude. Literature reviews conducted during the ArcRisk project aimed to establish whether there are correlations between exposure to contaminants and detected health outcomes (Govarts et al. 2012; Nieminen et al. 2013a,b). Combining the published data was challenging: particularly concerning the use of different measurement scales of explanatory variables across studies and the lack of necessary information in the study reports. The publications included findings generated by multivariable analysis, for example, multiple regression, discriminate analysis, factor analysis and structural equation models. The presentation of the findings should not rely only on the coefficients of the estimated models.

Reporting on model results requires ancillary information such as tables that describe the basic data, to enable the results to be more understandable and more widely useful. Complexity and diversity across studies with regard to the selection of variables and reporting practices has made it difficult to combine and compare original studies. Studies should focus more on the reporting of descriptive statistics. Among other things, the distributions of response variables and explanatory variables are needed when summarizing and meta-analyzing the magnitude of effects. This is a prerequisite for other researchers to utilize the results in their work.

A new method, the synthesis of regression coefficients, was developed during the ArcRisk project to combine findings

across different published studies with different statistical content. This method helps in identifying significant findings from combined cohorts with identical variables (Nieminen et al. 2013b). In ArcRisk, critical reviews were prepared based on original articles describing studies on PCBs (as a total sum of PCBs, a sum of more than six congeners, or PCB153) and DDT and related compounds (DDTs) in relation to weight and sex ratio at birth. These critical reviews (Govarts et al. 2012; Nieminen et al. 2013a,b) showed the following: a weak correlation between birth weight and exposure to PCBs; no correlation between birth weight and exposure to DDTs; and no correlation between the sex ratio of newborns and exposure to PCBs. The results are supported by data collected from 27 circumpolar jurisdictions of the eight Arctic countries which showed that the contaminants present do not disrupt endocrine systems to the extent that sex ratios are affected (Bjerregaard et al. 2012). Findings from Arctic cohort studies have reported links between exposure to contaminants and human health outcomes (Table 5.6).

5.9.2 Problems identified in meta-analyses

In a systematic review of the association between PCB exposure levels and secondary sex ratio (Nieminen et al. 2013a), special attention was paid to methodological information and differences in study design, choice of study subjects, planning of measurements and presentation of findings. Meta-analysis were performed with the goal to estimate a pooled summary of the proportion of boys in the highly exposed families and internal exposure-outcome comparisons across studies. This identified several limitations (Nieminen et al. 2013a):

- the small number of publications with relevant epidemiological data for Arctic populations
- findings of epidemiological studies are analyzed and reported in many different ways
- results across repeated studies of the same phenomena are rarely identical (for reasons such as size of the study, differences in analytical methods, and genetic differences between study populations)
- although the principal aim of the epidemiological studies is identical, for example to measure the relationship between PCB exposure levels and health outcomes, different studies use different statistical methods
- the quality of reporting varies: detailed descriptive statistics of the variables under study are not given in all articles, and standard error for regression coefficients or the mean differences may not be available.

The observation of Taylor et al. (2013) confirmed this view. They studied POPs (organochlorine, organofluorine, and organobromine compounds) and health outcomes related to Type 1 and Type 2 diabetes, and childhood obesity with Type 2 diabetes. Only 43 studies were eligible in their meta-analysis out of 2752 publications. Collectively, the data used were not considered sufficient to establish causality and there was too much variation across studies to permit a detailed meta- or pooled analysis. Another recent article described similar problems when trying to pursue association between environmental contaminants and health effects in indigenous populations in the Arctic. Singh and coworkers (2014) tried to combine data from Arctic populations and various health outcomes. Difficulties in drawing conclusions included the small number of studies, studies restricted to a small number of regions, and mixed results. They recommended further studies on the association between environmental contaminants and health with a wider geographical coverage. Within the framework of the EU projects ENRIECO and OBELIX, the effects of PCBs and DDE on birth weight were studied (Govarts et al. 2012). This covered maternal and cord blood and breast milk samples of 7990 women enrolled in 15 study populations from 1990 through 2008. Using identical variable definitions, Govarts et al. (2012)

Table 5.6 Health outcomes reported in published Arctic cohort studies associated with exposure to contaminants.

Cohort	Health endpoint	Findings	Source
Nunavik and Greenland	Blood pressure	Risk age and congener dependent	Valera et al. 2013a,c
Arctic Québec	Gestation	Reduce gestation duration	Dallaire et al. 2013
Greenland	ER, AR, Ah-receptor functions	The serum POPs have hormone disruptive potentials	Krüger et al. 2012
Arctic Québec	Neurophysiological functions in children	Absence of clear evidence of adverse effects of PCB exposure on child behavior	Boucher et al. 2010, 2012a,b
		Postnatal PCB exposure appears to affect processes associated with error monitoring	
		Prenatal PCB exposure appears to affect information processing at later stages	
Norway	Reproductive effects in men	A strong relationship between PCB153 and the sex hormone binding globulin	Haugen et al. 2011
Faroe Islands	Effects on immune system	Serum PCB concentrations at 7 years of age were positively associated with total IgE concentrations	Grandjean et al. 2010
Greenland	DNA methylation	Global methylation levels were inversely associated with blood plasma levels for several POPs and merit further investigation	Rusiecki et al. 2008
Greenland	Parkinson's disease	The concentrations of PCBs did not differ between the Parkinson's disease cases and controls	Koldkjaer et al. 2004
Québec, Canada	Placental toxicity	Organochlorine exposure was positively associated with ethoxyresorufin-*O*-deethylase activity and DNA adducts levels when stratifying for smoking	Lagueux et al. 1999

performed a linear regression of birth weight on estimates of cord serum concentration of PCB153 and *p,p´*-DDE adjusted for gestational age and *a priori* selected covariates for each cohort. The meta-analysis including all cohorts indicated a birth weight decline of 150 g per 1 µg/L increase in PCB153, and DDE was associated with a 7 g decrease in birth weight (Govarts et al. 2012). The findings suggest that low-level exposure to PCB impairs fetal growth, but that exposure to DDE does not.

5.10 Toxicokinetic modelling and future risk prediction

There are several research-based methodologies on how environmental contaminants affect biological processes in humans and the implications for human health risk assessment. Risk assessment of environmental pollutants is an essential tool in protecting public health. This process requires data from different sources and methodology. For example, from *in vivo* toxicology, *in vitro* toxicology, mathematical modeling and quantitative methods, risk characterization of chemicals in food and diet, epidemiology, and the use of toxicogenomics. These may all form part of the multi-faceted framework of evidence-based toxicology leading to a well-documented overall risk assessment process (Fjeld et al. 2007; US EPA 2014). The main challenge in traditional risk assessment is how to link external and internal doses. To circumvent this problem, quantitative risk estimation is based on reverse dosimetry of average daily dose and life-long average daily dose by toxicokinetic modelling of the contaminant blood concentration trends. The data could be from external contamination sources or from concentrations measured in blood, and the normative methods to quantify the associated risk could be via relative comparisons or quantitative risk estimates. Relative comparison of blood concentrations is a way of comparing data from different biomonitoring studies on a scale for risk assesment. However, in many cases the scale is nonlinear when estimating human health risk. Quantitative risk estmates are a way of estimating hazard quotient (HQ) for non-cancer effects and the excess lifetime cancer risk (CR) from exposure to a particular contaminant.

A modified approch based on the traditional risk assessment process has been introduced for quantitative risk estmates (Abass et al. 2013). This comprises three stages: extrapolation of exposure by pharmacokinetic modelling; incorporation of the reference dose and cancer slope factor; and estimation of HQ and life-time cancer risk. The only deviation from the traditional exposure assessment procedure is that the average daily and average life-time doses are calculated based on the extrapolation of contaminant concentrations in blood by toxicokinetic modellling. In this model, the total dose is a sum of all exposure pathways: inhalation, ingestion, or dermal absorption, and these are all reflected in the total blood concentration of a chemical. Metabolism, excretion, and accumulation in tissues other than blood complicate the issue, that is, accumulation of organochlorines in fatty tissue, accumulation of Cd in liver and kidney and accumulation of Pb in bone. Thus it is important to know the toxicokinetics of the individual contaminants to get an accurate estimate.

To assess potential PCB153-associated human health effects and risks, it is necessary to model past exposure. Blood concentrations of PCB153 obtained from the AMAP biomonitoring program for Inuit women in the years 1994–2006 at Disko Bay (Greenland), 1999–2005 at Nuuk (Greenland), and 1992–2007 at Nunavik (Québec, Canada) were used to extrapolate body burden and exposure through the whole lifespan of the population using the one-compartment toxicokinetic model. By using risk characterization modelling, calculated HQs were higher than 1 between 1955 and 1987 for the 90th population percentile and during 1956 to 1984 for the 50th population percentile. HQ values provide a basis for estimating potential non-cancer adverse effects (US-EPA). It should be stressed that HQ is analogous to a margin of exposure concept, which could be used to estimate the potential of PCB153 to cause harmful effects. The HQ cannot be assumed to a probability that harmful health effects will occur and it is unlikely to be proportional to risk. Cancer risk was estimated based on an oral cancer slope factor (CSF) provided by US-EPA-IRIS for PCBs. The probability of carcinogenic effects was calculated with two CSFs. Probability of carcinogenic effect was determined by multiplying CSF and lifetime average daily dose of PCB153. Cancer risk (Fig. 5.3) for overall exposure to PCB153 ranged from 4.6×10^{-5} to 1.8×10^{-6} for the 90th percentile and 3.6×10^{-5} to 1.4×10^{-7} for the 50th percentile between 1930 and 2049, when central estimates or upper-bound CSFs were applied. Cancer

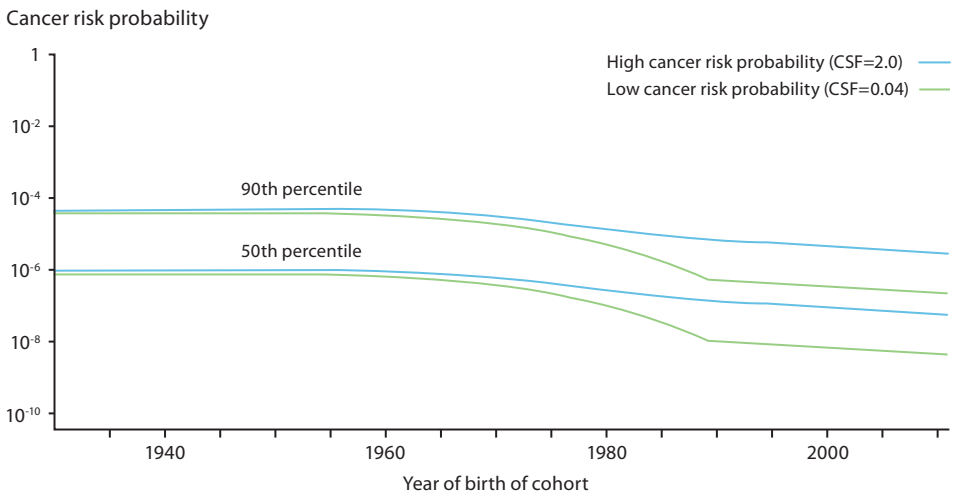

Figure 5.3 Cancer risk probability estimates for the high and low cancer slope factors (CSFs) for the 90th and 50th percentiles of the birth cohorts for pregnant Inuit women living in Disko Bay (Greenland), Nuuk (Greenland), and Nunavik (Québec, Canada). The year axis indicates the time of birth of the cohort (Abass et al. 2013).

risk was below 1×10^{-6} for the same period when a lower CSF was applied. Significant future research requirements to improve health risk characterization include larger sample sizes, better analytical accuracy, fewer assumptions in exposure assessment and, consequently a better choice of the toxicity benchmark used to develop the HQ.

The Abass et al. (2013) study relied on the dose-response values (reference dose and cancer slope factor) established by the USEPA-IRIS. Non-cancer hazard and cancer risk estimation are widely accepted and commonly used in the field of chemical risk assessment. The next step should include the incorporation of dietary information as well as potential residential and personal exposure trends. Studies should also examine cumulative risk assessment for PCBs and other contaminants measured in human blood. The answers to the important questions – what is the total contaminant burden people acquire over their lifespan and what are the long-term health effects – require more multidisciplinary research and the toxicokinetic modelling approaches presented above for PCB153 could be one means for estimating human health risk.

5.11 Toxicokinetic modelling and total risk estimation

Within the ArcRisk project, Čupr et al. (2011) presented an approach to estimate the total risk of POPs. Human biomonitoring of the concentration of POPs in breast milk in the Czech Republic has been carried out since 1994 by the National Institute of Public Health with the main aim being to evaluate long-term trends in selected POPs. Bioaccumulation of the lipid-soluble POPs leads to high levels in breast milk; so a new method was developed for the risk assessment of POPs for women (breastfeeding women). The method depends on the backward model for life-long POPs exposure of breastfeeding women only (Fig. 5.4). The human body is considered as a flux-through system.

This toxicokinetic model (PBPK model) used backward computation of chronic daily intake (CDI) POPs from human milk based on the model for organic compound accumulation in breastfeeding women (Čupr et al. 2011). The main backward-model results are the maternal dietary intake (i.e. CDI). Phase equilibrium is assumed within the body. The compound is eliminated from the body by excretion and metabolism ('outflux' in Fig. 5.4). In this case, human health risk from chronic daily intake was predicted using the reference dose approach.

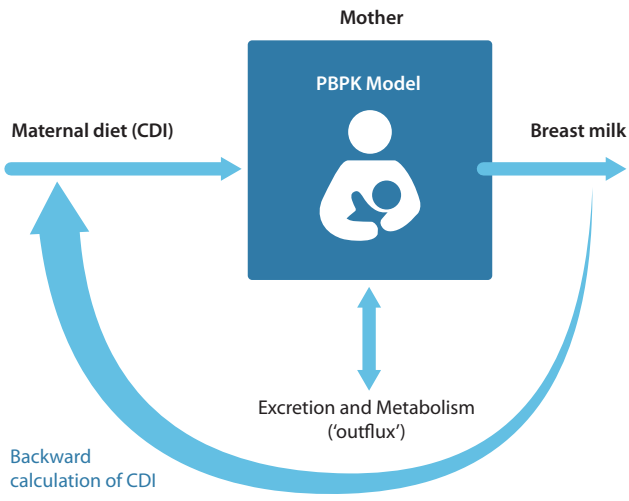

Figure 5.4 Schematic illustration of the PBPK model which uses backward computation of chronic daily intake (CDI) for estimating the health risk of persistent organic pollutants in breastfeeding women (Čupr et al. 2011).

The total human health risk of selected POPs in the form of a hazard index (HI) was calculated as the sum of individual HQs for selected POPs (according to the availability of reference dose values). The total risk (HI) shows that the main risk-posing group continues to be the PCBs (Fig. 5.5; Václavíková et al. 2014). Based on the total risk estimation approach, Václavíková et al. (2014) concluded as follows: the new method presented for human health risk assessment of breastfeeding women is a useful tool when data from long-term biomonitoring epidemiologic studies are available; biomonitoring of breast milk is useful in evaluating internal exposure of humans to different chemical substances; and estimated total intake can be compared with changes in 'food baskets' to predict the prevailing sources of exposure from different food types.

5.12 The incorporation of *in vitro* mechanistic studies in human health risk assessment

The aim of *in vitro* characterization is to produce relevant information on metabolism and interactions in order to anticipate and ultimately predict what could happen *in vivo* in humans. Numerous *in vitro* models are available and each model has advantages and disadvantages. To understand some of the factors related to environmental contaminant metabolism, there are several important points to consider. For example, the metabolic stability of the compound, reactive metabolites, variation between mammalian species, human cytochrome P450 enzymes (CYPs) and their isoforms involved in the activation or detoxification of the environmental contaminants, variation between individuals, individuals and subpopulations at increased risk, and the overall process of human risk assessment.

Examples of the incorporation of *in vitro* biotransformation studies into human health risk assessment were published by Abass et al. (2014a,b). *In vitro* metabolism of the pesticide benfuracarb was studied in liver microsomes from seven mammalian species in order to develop quantitative species-specific metabolic profiles and to enhance benfuracarb risk assessment by interspecies comparisons (Abass et al. 2014a). Using LC-MS/MS, a total of seven phase-I metabolites were detected from the extracted chromatograms and six were unequivocally identified. Benfuracarb was metabolized via two pathways, the sulfur oxidation pathway and nitrogen sulfur bond cleavage, yielding the highly toxic pesticide carbofuran, which is further metabolized. Analysis of the metabolic profiles showed that benfuracarb was extensively metabolized with roughly similar profiles in different mammalian species *in vitro*. The highest inter-species differences in hepatic clearance rates were for mouse and rat liver microsomes compared to human (4.8- and 4.1-fold higher), as illustrated by *in vivo* hepatic clearance of carbofuran. Overall, there are quantitative inter-

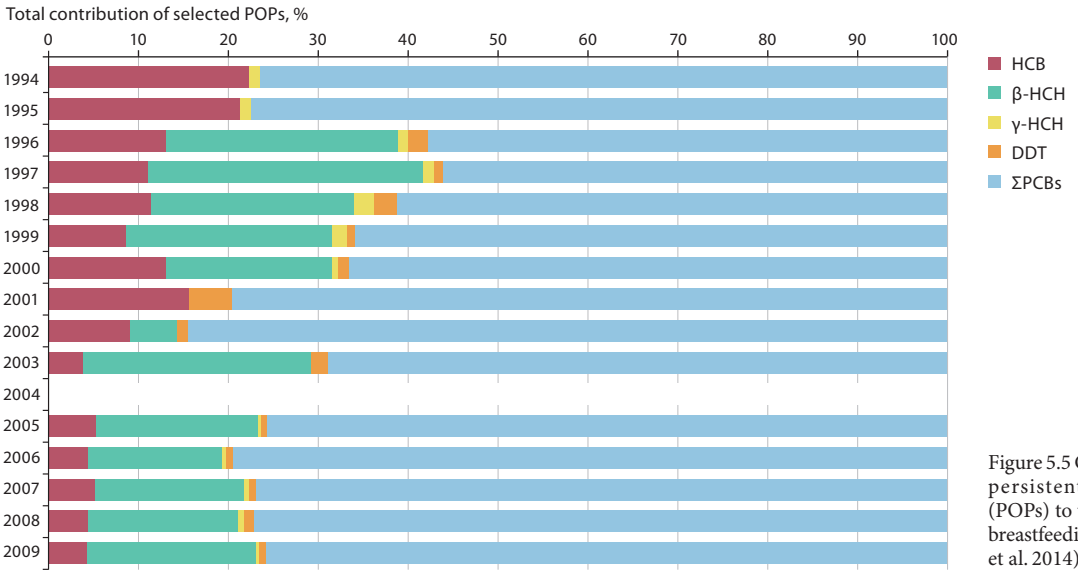

Figure 5.5 Contribution of selected persistent organic pollutants (POPs) to total health risk (HI) in breastfeeding women (Václavíková et al. 2014).

species differences in the metabolic profiles and kinetics of benfuracarb biotransformation.

Human responses to the toxicological effects of chemicals are often complicated by a substantial inter-individual variability in toxicokinetics, of which metabolism is often the most important factor. Human variation and the contributions of human-CYP isoforms to *in vitro* metabolism of benfuracarb were therefore investigated (Abass et al. 2014b). The Kinetic parameters (Km, Vmax and intrinsic clearance Clint) for carbofuran production in hepatic samples from ten individuals varied 7.3-, 3.4-, and 5.4-fold, respectively. Carbofuran formation represents 79–98% of the total metabolism of the parent compound, benfuracarb.

Several approaches have confirmed that human CYP3A4 is the major enzyme involved in benfuracarb activation and that CYP3A4-catalyzed metabolism is the primary source of inter-individual differences (Abass et al. 2014b).

For risk assessment, the quantitative *in vitro* chemical-specific data can then be scaled to determine the *in vivo* hepatic clearance. In the scale-up process, it is essential to determine scaling factors, such as the amount of microsomal protein per gram of liver, liver blood flow (L/min), and the size of the liver. This approach (Fig. 5.6) is used to extrapolate *in vitro* metabolic data to the *in vivo* situation and to translate inter-species and inter-individual *in vivo* hepatic clearances into risk assessment of chemicals.

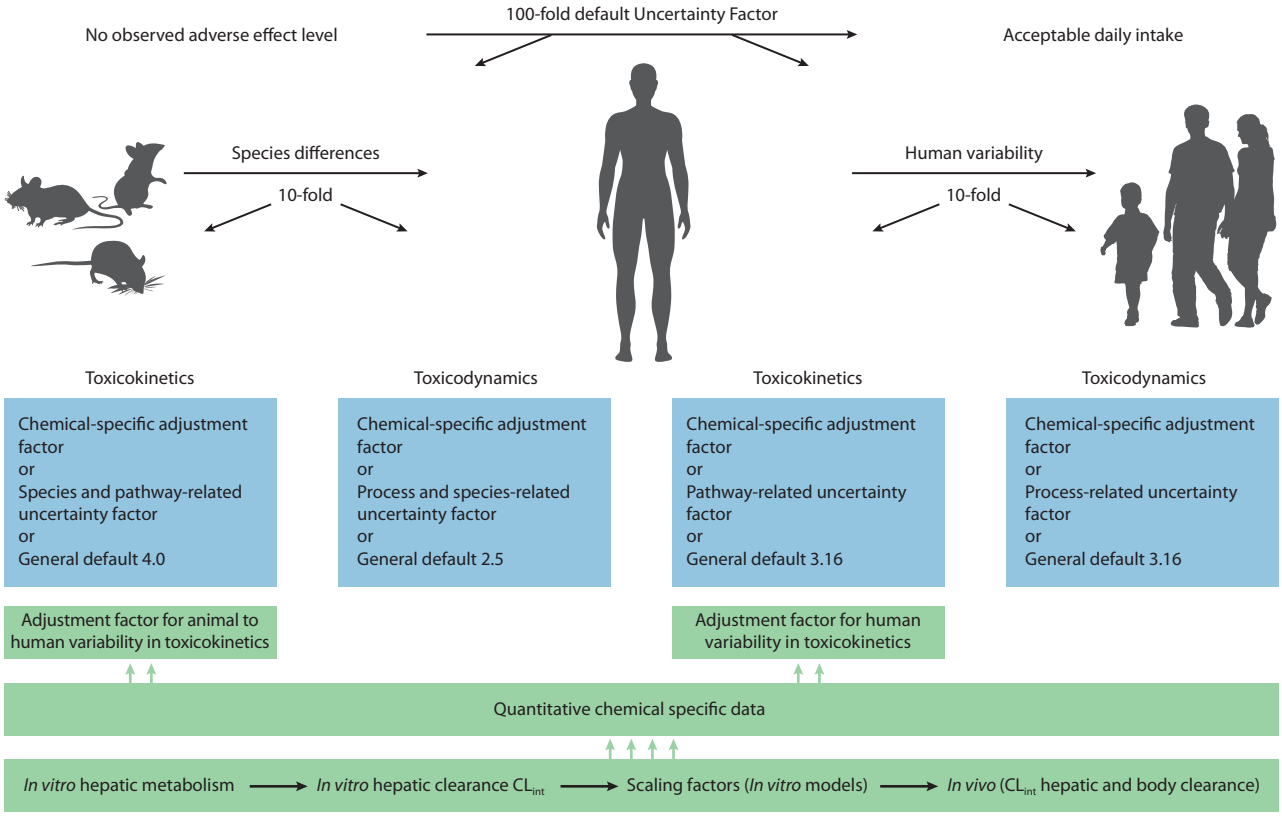

Figure 5.6 The subdivision of the 100-fold default uncertainty factor and the integration of *in vitro* data into human health risk assessment (Abass 2013).

5.13 Conclusions and recommendations

Although the environmental levels of legacy POPs are generally declining in the Arctic and Europe, concentrations of some (such as PCBs) have remained relatively stable in indigenous adults and children in Russia. This is because revolatilization from soils is now the main source, and this balances the overall decrease in primary emissions. Environmental levels of some organohalogen compounds, such as PBDEs, are even increasing. Current and future trends in contaminant concentrations may vary in different geographical areas of the Arctic and Europe (new hot spots may develop) and in different populations (especially indigenous populations). Extreme weather events associated with global climate change, such as tsunamis and flooding, might also affect food and water security, possibly increasing the incidence of contaminated food items.

The impact of climate change on future human exposure to POPs will largely depend on the amount and type of fish consumed (wild or farmed fish) and other seafood (Fig. 5.7). At present, it is not possible to draw final conclusions about future trends in exposure or the related trends in human health.

In relation to dietary exposure to Hg in the Arctic and Europe, ArcRisk concluded as follows:

- Humans in the Arctic are exposed to Hg mainly through fish consumption. Other sources such as elemental Hg in air and inorganic Hg in food are minor sources of exposure.
- Mercury levels in fish can vary greatly depending on the species and its origin; wild-caught fish generally have higher Hg levels than farmed fish. The highest Hg concentrations have been reported in wild fish from the Mediterranean and marine mammals in the Canadian Arctic.
- Current exposure assessments in Europe are based on information on the frequency of fish consumption and Hg concentrations measured in biomonitoring studies. Data quality and quantity are still insufficient, resulting in uncertainties in exposure assessments across Europe and the Arctic region.
- Further studies are needed to confirm whether the currently low levels of Hg exposure represent a health risk to Arctic and European populations, taking into consideration exposure to various Hg compounds and mixtures of stressors with similar end-points.
- Recent studies have indicated the importance of susceptibility to MeHg exposure, and this should be the focus of future studies.
- Research is required concerning the causes for the high inter-individual variations, other important sources of Hg exposure, and biological mechanisms behind MeHg.

Vulnerable subgroups exist owing to genetic background, exposure history, and age, among others. Although there are currently few data with which to draw conclusions about the implications of such vulnerabilities, it is already clear that the fetal stage is the most sensitive during human life and so fetal exposure deserves special attention. According to lifestyle factors, there are possibly more significant exposure scenarios than the oral route, but these are not considered in conventional risk assessment (such as dermal exposure).

In health risk characterization, better toxicokinetic models would require larger sample sizes, better analytical accuracy, fewer assumptions in exposure assessment, and thus a better choice of the toxicity benchmark used to develop the HQ. Human biomonitoring studies of environmental contaminants can be used together with the expected exposure routes to build up such models. The models can be further used to predict future levels of similar chemicals in blood or to predict changes in exposure, such as could result from changes in the levels of the chemicals in fish and game.

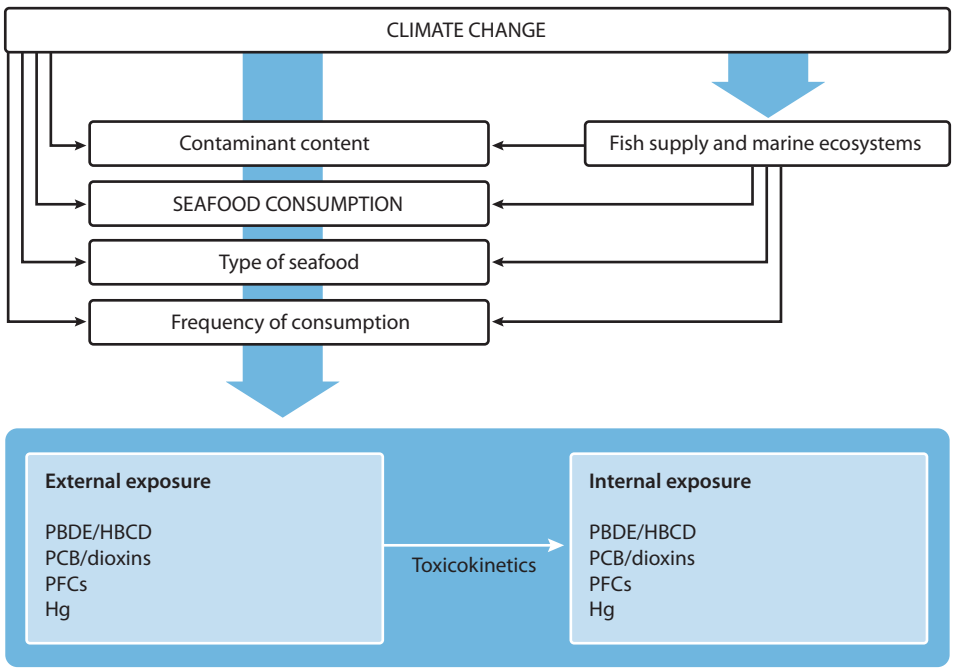

Figure 5.7 Interaction between climatic change and internal exposure to contaminants from seafood consumption. The role of other factors such as emissions and environmental fate and transport cannot be ignored (Brantsæter and Knutsen 2013).

6. Risk communication

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6.1 Introduction

This chapter provides an update on risk communication in the Arctic. It summarizes some of the historical and newer research on risk communication methodologies as well as approaches to an evaluation of the outcomes of risk communication initiatives. It updates information on specific initiatives in several Arctic countries and particularly those that were directed at indigenous populations. While an effort was made to include information for risk communication activities or experiences for all Arctic countries, there is a lack of information from the European Arctic. The chapter also summarizes some international *versus* local risk communication activities and the complexity of developing and delivering messages designed for different audiences. This chapter provides a description of the potential application of social media for risk communication and concludes with a summary of 'best practices' based on published literature, experience and a survey of Inuit in a few Arctic countries.

Risk Communication involves messages and advice designed to reduce harm and to maintain and improve health, delivered in a culturally and socially respectful manner. Risk communication has as its foundation good *Risk Assessment*, that is, evaluation of all the available science including epidemiological evidence, animal studies and a determination of 'safe levels' of exposure. *Risk Management* is based on risk assessment and considers the economic, social and cultural issues which interconnect to inform 'who' must be protected (the most vulnerable) and 'how' to best obtain the protection required (appropriate and effective exposure reduction strategies). A more detailed description of the risk assessment process, including risk communication, has been provided by Odland et al. (2009).

Arctic residents are exposed to a wide range of contaminants through consumption of traditional (country) foods (i.e., food from wild animals and plants that are hunted, caught or collected locally in the Arctic). Yet these same foods provide excellent nutrition, promote social cohesion, meet some spiritual needs for connectedness to the land and water, reinforce cultural ties, are economically important, and promote overall good health for many. The risk and benefit balance associated with consumption of traditional Arctic foods is complicated to communicate, and has been referred to as the *'Arctic Dilemma'* (AMAP 2009).

The complexity of communicating risk to northern communities was recognized in the first two health assessments published by the Arctic Monitoring and Assessment Programme (AMAP 1998, 2003), but while its importance was acknowledged and concrete examples provided, information about how to develop and evaluate risk communication initiatives was lacking.

It was not until the third AMAP health assessment (AMAP 2009) that the overall state of risk communication in the Arctic was discussed, as well as recommendations for more evaluation of risk communication initiatives and focused research on methodologies. The risk communication process requires communication and information sharing to take place between risk assessors, risk managers, the local community, news media and interest groups (Odland et al. 2009). Effective risk communication can be very complicated, especially in the Arctic region. Some key aspects which are relevant for risk communication especially in Arctic areas were described in the risk communication chapter of the 2009 AMAP health assessment report (Odland et al. 2009), and are summarized in Fig. 6.1. For example, the development of risk communication messages needs to take regional and cultural differences in diet into account, as well as the fact that multiple food types are consumed which contain mixtures of contaminants. Important aspects of delivering messages include interactions between the sender (e.g. a health official) and receiver (e.g. people in a community) of risk communication.

However, it can be argued that far less effort has so far been directed toward learning how best to inform or influence public decision making to protect health and culture in the Arctic, than has been invested in the identification, monitoring and assessment of effects of human exposure to these environmental contaminants. There has not been any apparent pattern to the production of publications on this topic over a 20-year period starting in 1992 (Furgal pers. comm. 2013). Three distinct peaks in publication occurred – in 1998, 2005 and 2009 – which may be associated with focused assessment efforts by AMAP and national programs such as the Canadian Northern Contaminants Program (NCP)(Jensen et al., 1997; Van Oostdam et al., 2003, 2009; Furgal et al., 2003). Much of the communication recommendations appearing in the peer-reviewed literature are not the result of communication research studies presenting empirical evidence on this topic in these regions, but are a component in discussions or recommendations arising from contaminant studies.

6.2 Approaches to risk communication

There are many theories on how behavior can be influenced to reduce risks to health. There are also models which describe how risk communication can be presented (framed) for greater uptake. These theories and models when combined with the specific challenges of communicating health-based messages may be instructive for developing and evaluating risk communication strategies in the Arctic.

Covello and Allen (1988) provided the following seven cardinal rules of risk communication over 25 years ago, which are still applicable today:

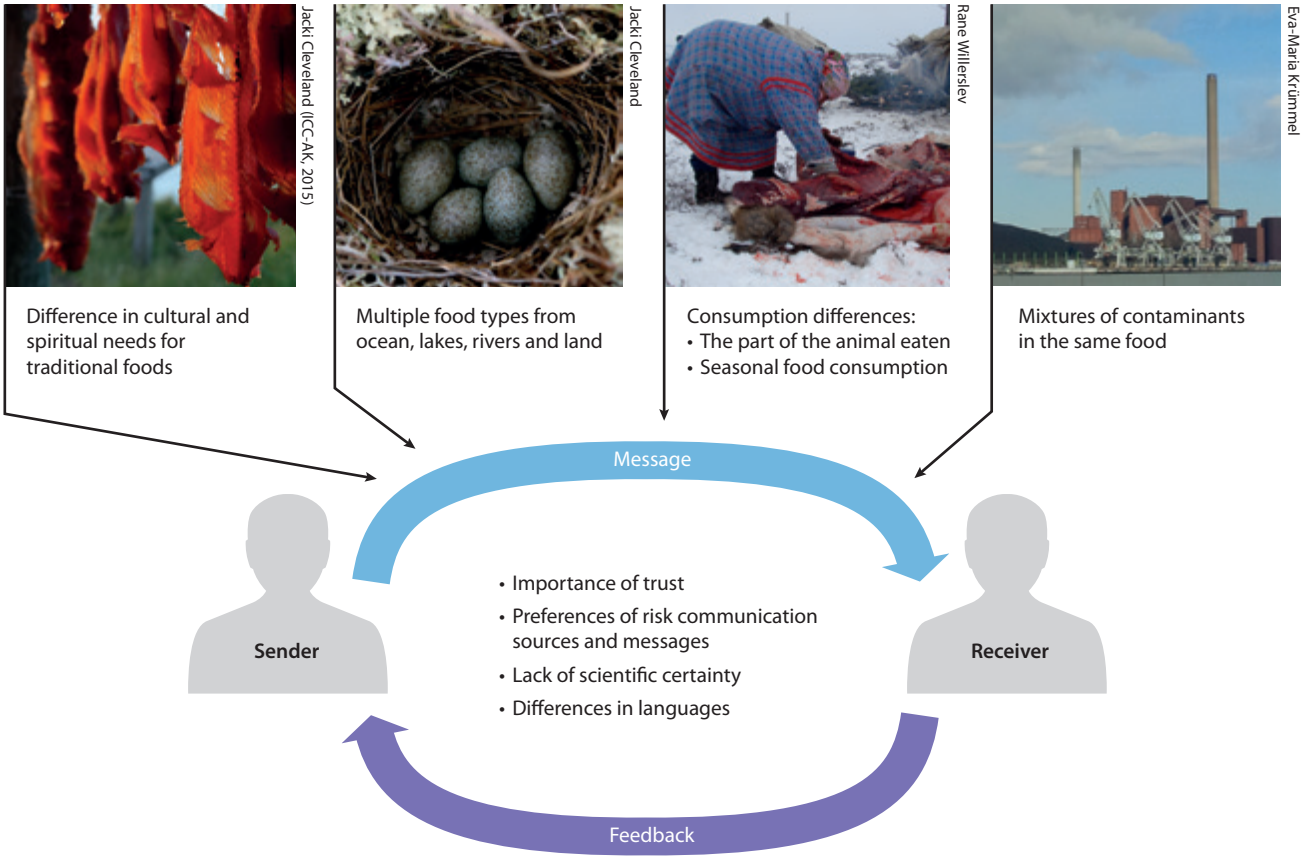

Figure 6.1 General aspects relevant for risk communication in the Arctic as described by Odland et al. (2009).

- Accept and involve the public as a legitimate partner
- Plan carefully and evaluate efforts
- Listen to the public's specific concerns
- Be honest, frank, and open
- Coordinate and collaborate with other credible sources
- Meet the needs of the media
- Speak clearly and with compassion.

Different risk communication theories offered by these and other authors (such as Becker 1974; Ajzen and Fishbein 1980; Bandura 1992; Prochaska et al. 1992; Weiss and Tschirhart 1994; Coffman 2002) address several key considerations that influence the uptake and effectiveness of risk communication messages. Effectiveness of a risk communication message is often modulated by personal beliefs and an understanding of the benefits of changing a behavior. A concern that the consumption behavior poses a personal health threat or a threat to people that are important to the individual are significant considerations when deciding to change a behavior. This includes a view that the cost of changing behavior outweighs the cost of adopting the behavior (e.g. in social, financial and conformity terms).

The different theories also distinguish between the origin and form of the risk communicated, and the receiver's understanding and ability to recognize the relevance and importance of the behavior change. The chosen form of communication must capture attention, support motivation, and affirm a belief in one's own skills to effect the change. And, over all, the message must speak to personal values and preferences in a way that is respectful and trustworthy. Also, Coffman (2002) described a difference between communication strategies concerning shifts in individual behavior and shifts in public will. Communication on a food advisory in the Arctic would be considered a strategy designed to address individual behavior or that of a family or community.

Weinstein (1999) argued that decisions made by individuals about changing their behavior are based upon their common understanding of information from a wide range of sources. In addition, there are considerable differences in what individuals perceive as 'correct' information. Where there are differences which matter in individual perceptions *versus* scientific fact, information and strategies that update perceptions may add significantly to the effectiveness of an advisory.

'Framing' refers to how risk communication is constructed, that is, its language, its visuals and its messengers (Shonkoff and Bales 2011). Sandman et al. (1994) examined how a risk is perceived depending on where it is located on a gradient of risks (risk ladder) well known by the population. They concluded that research into the formats used in risk communication (framing) were a significant element for designing effective advice. Connelly and Knuth (1998) studied framing with respect to fish advisories and concluded that a diversity of approaches is necessary for effective communication of risk, such as written material in a good and understandable language (not to be confused with simple language), videos, signs, maps, symbols and/or interpersonal contacts.

Good risk communication is best formed within an interdisciplinary frame and expertise is required in various fields such as program planning, evaluation, communications theory, marketing, and public health (Tinker 1996).

6.3 Evaluating the effectiveness of risk communication strategies

The notion that evaluation of effectiveness is an important component of any risk communication campaign is not new. Covello and Allen (1988) specifically stated the need for pretesting messages and evaluating communication efforts. The need to evaluate the results of risk communication initiatives was also supported by Tinker (1996). Coffman (2002) offered different evaluation approaches that can be considered at different stages of the risk communication: a *formative evaluation* which examines how the strategy is unfolding and where the message, delivery method or materials may need to be revised; a *process evaluation* which examines how materials such as brochures are being consumed or how many phone calls have been received on a help line; an *outcome evaluation* which looks at how people have adopted and understood the message and changed their behavior; and an *impact evaluation* which examines how personal or target population health has improved or how contaminant concentrations in human tissue have declined as a result of the risk communication initiative.

For most Arctic risk communication initiatives there appears to have been very little pretesting of risk messages. Only in the last 10 years have a few evaluative exercises been reported that help with an understanding of successes and challenges related to the delivery of risk information. Furgal et al. (2005) described how poor risk communication can lead to fear, confusion, undesirable changes in dietary behavior and traditional lifestyles, and impacts on society, economy and health in indigenous communities in the Canadian Arctic. Myers and Furgal (2006) reported that women of childbearing age in communities in Nunavut and Nunatsiavut (Labrador), Canada, did not appear to have understood, remembered, or acted upon the messages on contaminants in traditional foods and the potential health impacts for the developing fetus. It is difficult to assess if the target audience did not understand the messages or if they did not receive, register or remember the message. There is also the possibility that they could not comply with the message due to extenuating circumstances (i.e. food insecurity).

The difference in knowledge systems between the indigenous populations of the Arctic and the primarily non-indigenous populations outside the Arctic can also hinder a full understanding of risk communication messages on environmental contaminants. For some indigenous populations, it is difficult to understand the concept of 'invisible' risks such as contaminants, which have no equivalent word in their languages[2], may not have a direct effect on health in the immediate future, or may be considered a lower priority compared to other issues within Aboriginal societies (Usher et al. 1995; Furgal et al. 2005). It cannot be assumed that the views and concerns on risks held by researchers and government bodies outside the Arctic are shared by residents of the North (Myers and Furgal 2006). Perceptions of contaminant risk must be linked with a population's relationships with, and views of, traditional foods to develop effective risk communication messages that result in individual responses that reduce risk (Donaldson et al. 2010b).

Acceptance of information pertaining to levels of contaminants, potential risks and consumption guidelines for traditional foods is highly dependent on trust, that is, where there is little trust between an Inuit community and a federal agency or public health office, there is less likelihood that the community will believe the source, the message or take up the advice (see Sect. 6.6 and ICC 2012). More complete information on the benefits of consuming traditional foods and some of the issues associated with consuming store-bought foods which contain high levels of carbohydrates, especially sweeteners, and unhealthy fats may better enable Arctic residents to make appropriate choices about the foods they eat.

Binnington et al. (2014) examined the effectiveness of maternal fish advisories using a mathematical time-variant mechanistic model (CoZMoMAN). While they found that dietary fish substitution reduced maternal exposure for substances such as polychlorinated biphenyls (PCBs) if the advice was followed for at least five years, compliance with an advisory as structured in their model was essentially of no value if only followed for a year. These model estimates could be helpful in the future for determining whether both the length and nature of food advisories, designed to protect the fetus and developing infant from placental and breast milk exposures, respectively, will be effective.

6.4 Arctic-specific experiences in risk communication

This section provides some examples of risk communication experience from the Arctic. It describes different strategies and, if available, how effectiveness has been evaluated. However, it does not provide information about more general food and nutrition advice issued in each of the Arctic countries, such as those on fish consumption, environmental contaminants and pregnancy. These general advisories have been revised from time to time in all the Arctic nations based on scientific updates on health effects and benefits associated with consuming traditional foods as well as insights in risk communication.

6.4.1 Alaska, US

Fur seal (*Callorhinus ursinus*) is an important subsistence food for the Aleut of the Pribilof Islands, Alaska (St. Paul and St. George islands) as well as the Commander Islands (Kamchatka, Russia). Concern over the decline in fur seals from 2000 to 2010 led researchers to analyze fur seal placentas. Duncan et al. (2013) found 109 of 146 (75%) were positive for the bacterium *Coxiella burnetii*. In humans, this bacterium can cause the illness known as 'Q Fever'. Concern about exposure to *C. burnetii* and the safety of consuming fur seal resulted in an inclusive health consultation process with Pribilof residents (AHSS 2014).

Public health officials from the State of Alaska, Alaska Native Tribal Health Consortium and the Centers for Disease Control (CDC) consulted with regional and local tribal health authorities. CDC staff made site visits to meet public and local officials. Based on the consultation, tribal resolutions

[2] Efforts have been made in Nunavut to develop material that has Inuktitut terminology for contaminants.

were provided requesting that human serum samples collected from Pribilof Island residents (1980–2000) and stored at the Alaska Native Serum Bank be tested for *C. burnetii* antibodies. Analysis by CDC found a seroprevalence of 12% (56/470) for St. Paul samples and 11% (16/151) for St. George samples (AHSS 2014). For comparison, the seroprevalence of this antibody in the US all-races population is 3% (AHSS 2014). Subsequent health consultations explained that *C. burnetii* exposure occurs primarily through inhalation and not through ingestion and that fur seal was a safe traditional food. CDC offered community blood testing to determine whether there had been any change in exposure to *C. burnetii* and local health care providers incorporated Q Fever in the differential diagnosis for patients with unexplained febrile illness (especially prolonged fever and elevated liver enzymes). No locally acquired cases of Q Fever have been identified in Alaska (AHSS 2014). This could be due to the symptoms, described above, which are those of community-acquired pneumonia due to a large variety of infectious agents. Q Fever has only very recently become known to Alaska health care providers as a zoonotic infection common in any Alaskan animal species.

Owing to the migratory route of northern fur seals, Alaskans share this resource with communities in Kamchatka, Russia. Considering that rapid environmental change will result in further incidences of zoonotic diseases, improving communication with Russian health officials is seen as an important aspect of the risk evaluation and management process for Aleut health issues, as there are no active formal relationships with public health officials in Russia. Copies of the public health bulletins developed by the State of Alaska (AHSS 2014) were sent to the Aleut International Association which has formal ties with the Commander Islands. No formal analysis on the effectiveness of communication has been performed either with the Pribilof Island communities or with those in Kamchatka, Russia. However, the project was inclusive with active participation by U.S. federal, state, tribal and local officials. Project opportunities and options were presented and actions were taken based on local preference and with local permission. With expectations that rapid environmental change will result in new or changed patterns of zoonotic disease epidemiology, this case study provides an important example of how effective research and data evaluation, an inclusive consultation process and international cooperation can result in effective communication and outreach sensitive to the local needs and desires of Arctic indigenous peoples.

6.4.2 Canada

6.4.2.1 Risk communication in Nunavik

In Nunavik, elevated levels of contaminants in Inuit adults, newborns and pregnant women have been documented in various publications (Dewailly et al. 1994, 2007; Muckle et al. 1998, 2001, pers. comm. 2014; Lemire et al. 2015). Risk communication experiences due to findings from these studies were described by Couture et al. (2012) on lead (Pb) and Dallaire et al. (2013, 2014) on PCBs and mercury (Hg).

In 1992, a cross-sectional health survey in Nunavik (northern Quebec) found that mean blood Pb levels in Inuit were five times higher than levels in the general population in the United States. A study of Inuit newborns from 1992 to 1996 found that 7% of the blood Pb levels were above the blood guideline set by Canadian authorities, and approximately double the concentration of blood Pb levels in newborns in southern Quebec. The likely reason for the higher blood Pb levels was the use of lead shot for hunting. More recent data on blood Pb levels in the Canadian Arctic and other circumpolar countries can be found in Chapter 3.

In 1999, the Nunavik Regional Board of Health and Social Services, in cooperation with the Nunavik Hunting, Fishing and Trapping Association, the Kativik Regional Government (KRG) and Makivik Corporation, acted to remove lead shot from use and to replace it with steel shot or other alternatives. The resulting *Regional Coalition of the Banning of Lead Shot in Nunavik*, implemented an awareness campaign that included municipal officials and merchants, local radio announcements, articles in various periodicals, and posters and brochures in three languages (Inuktitut, French and English).

Couture et al. (2012) reported that blood Pb levels in Inuit from Nunavik had decreased significantly and particularly after the intervention in 1999, but remained higher than in southern populations. It is uncertain whether the changes in Pb levels were due only to the intervention, or also to a general shift in diet away from hunted waterfowl. The availability of lead shot has declined in many stores in Nunavik, but is still available in some. A survey of hunters in Inukjuak showed that only 31% of respondents were aware of the ban on the use of lead shot. While there is evidence that the concerted intervention in 1999 initiated a positive result (lower blood Pb levels), the effectiveness of the messaging and the role played by hunters who may have switched to steel shot *versus* those who prepare the meals so as to exclude lead shot, have not been assessed.

Exposure to PCBs and Hg in Nunavik is mainly due to consumption of marine mammal fat, especially beluga (*Delphinapterus leucas*) blubber for PCBs, or marine mammal meat, especially beluga muscle for Hg (Lemire et al. 2015). The Nunavik Child Development Study (NCDS) conducted from 2005 to 2010 found that exposure to contaminants was related to health and developmental effects.

The results of the NCDS led to a shift in risk communication where the public health messages were revised to focus mainly on pregnant women and women of childbearing age, and on how to reduce exposure to Hg and Pb while maintaining an intake of *n*-3 fatty acids. Since PCB exposures had declined significantly in the population between 1994 and 2001 (Dallaire et al. 2003) as well as in the environment, no individual recommendation for reducing exposure to PCB was included because children born recently would be much less exposed than those in the original NCDS cohort.

The primary public health message for Hg was as follows: "*… the main source of mercury exposure is beluga meat. Therefore, until we have evidence of a decrease of the mercury content in this specific country food, pregnant women and those of childbearing age should decrease their consumption of beluga meat.*" More detailed information was also made available on the internet for persistent organic pollutants (POPs), Hg and Pb.

The campaign to communicate the results from the NCDS was extensive: it included study participants (parents and children), the general population, employees of the regional health and

social services network, midwives, regional organizations, national and international organizations (Inuit Tapiriit Kanatami, ITK; Inuit Circumpolar Council, ICC Canada), regional contaminant committees, health officials from other northern regions of Canada, representatives of the Northern Contaminants Program (see Box 6.1), Health Canada, and the general public. The communication of results was carefully planned to ensure that information went to the Nunavik population before it was presented at scientific meetings and in peer-reviewed journal articles. An effectiveness evaluation component is underway and should be completed in 2015.

6.4.2.2 Risk communication in Nunavut

Inuit in Nunavut expressed a desire to have health information of practical relevance so that they could make informed decisions in the face of the rapid changes that are affecting all dimensions of life in their communities. In response to these concerns, a large and complex participatory health research project for those 18 years of age and above was developed and undertaken in 25 communities in Nunavut in 2007 and 2008 (Chan 2012a). The goal of the Nunavut Inuit Health Survey (NIHS) was to obtain an overview of the health status and living conditions of Inuit aged 18 and over in Nunavut. The results of the work led to the following key messages related to food and contaminants:

"Country foods provide many essential nutrients that can lower the risk of chronic diseases. Most Inuit adults in Nunavut need not be concerned about contaminant-related effects from country food consumption. Generally, the benefits of eating country foods outweigh the risks from contaminant exposure.

Inuit women of child-bearing age who may become pregnant, are planning to get pregnant, or are pregnant should avoid eating ringed seal liver due to its high mercury content. Instead, ringed seal meat is a great and healthy alternative…"

Box 6.1 History of risk communication in Arctic Canada

In response to accumulating evidence of contaminants in traditional (country) food, a project was carried out by Kinloch and Kuhnlein (1988) in the Inuit community of Qikiqtarjuaq (Broughton Island) in Nunavut, Canada. The communication of the Broughton Island results, that is, that breast milk had high levels of PCBs, caused alarm and confusion in communities (Usher et al. 1995). It was reported that many people ceased to eat traditional foods altogether, which led to more immediate health problems and undermined the nutritional benefits of a diet consisting of traditional food. Further contaminants research found that blood and breast milk of Inuit women from the Hudson Bay area also had elevated levels of POPs (Dewailly et al. 1989). PCB concentrations in blood of many individuals living in the Arctic, including two-thirds of those under 15 years of age, were above 5μg/L, which was considered to be an exceedance of tolerable blood levels at the time (Kinloch et al. 1992).

The alarm and confusion during the communication of the Broughton Island study results highlighted the need for work on contaminants and risk communication to be undertaken concurrently as well as the necessity of including Aboriginal representation when addressing health concerns. In response, a five-year plan for the NCP was developed by a technical committee of federal and territorial government experts and five Aboriginal parties: the Council of Yukon Indians (now Council of Yukon First Nations); the Dene Nation; the Metis Nation-Northwest Territories; the Inuit Tapirisat of Canada (now Inuit Tapiriit Kanatami, ITK); and the Inuit Circumpolar Conference (now Inuit Circumpolar Council, ICC).

The NCP was established in 1991, and its key objective is *"to work towards reducing and, where possible, eliminating contaminants in traditional/country foods, while providing information that assists individuals and communities in making informed decisions about their food use."* (INAC 2003). Unique to the NCP was the vision that the Aboriginal peoples most impacted by these contaminants would be central to the program's management. The focus of the NCP is on research and human tissue monitoring related to the impacts and risks of Arctic contaminants to human health, and the temporal trends of contaminants of concern in key Arctic food species. Since the early years of the program, benefit-risk communication was undertaken by the Aboriginal partners and territorial health departments. The messages focused on the amount of traditional food consumption as well on as the benefits of such consumption. The NCP is a best practice model which supports capacity building and ensures participation of Arctic indigenous peoples in management, research development and implementation, as well as information dissemination. However, the communication of research results and advisories to the community still remains a challenging task due to the complexity of balancing the nutritional importance of traditional foods while also warning of health risks associated with contaminant levels in those same foods. Further, regional health officials have noted gaps in the risk communication practices within Canada. For example, in some cases contaminant results have not been shared directly with communities, or levels of concern were not flagged to public health officials by researchers. Regions are typically lacking their own toxicologists to assess the information and rely on federal toxicologists instead. Regional health officials also often lack designated resources to communicate back to local communities and recommend that risk communication be made an integral part of contaminant research in the Canadian North, with dedicated funding and an understanding of roles and responsibilities. To promote the communication and dissemination of NCP-derived health risk information in a coordinated way that is effective, coherent, proactive, consistent, accurate and culturally relevant, the NCP therefore decided to develop an integrated risk communication group comprising federal experts including toxicologists, as well as researchers, community representatives, public health officials and northern Aboriginal organizations. This group's role is to recommend strategies and methodologies to aid risk communication and could also assist in evaluating the effectiveness of risk communication initiatives.

Over the course of 2013 and 2014, the NIHS Steering Committee undertook a project aimed at reviewing the efficacy of NIHS contaminants communication, covering three communities in Nunavut and over 1000 participants. Preliminary results were published in the 2014 NCP Synopsis Report (AANDC 2014). They show that fewer than half of the people surveyed remembered hearing the risk communication messages on avoiding certain traditional foods due to contaminants, while over 80% of participants reported hearing about the benefits of traditional food. One-third of participants stated that they had modified their eating habits after hearing about contaminants in traditional foods. The most popular sources of information were 'friends or family', radio and television. The authors of the study found that responses differed between the three communities, and emphasized the need to conduct evaluations after risk communication activities, to ensure that messages were released and received as planned and expected.

6.4.3 Faroe Islands: Dietary advice on consumption of pilot whale

Odland et al. (2009) provided a detailed history of risk communication activities in the Faroe Islands related to PCBs and Hg exposure. Figure 6.2 provides a graphical representation of levels of PCBs and Hg in pilot whale (*Globicephala* sp.) and Faroese adults and the associated timeline for risk communication advisories in the Faroe Islands.

High levels of Hg in meat and organs from pilot whales, which are an important traditional food source for the Faroese were first reported in 1977 (Weihe and Joensen 2012). This finding led to the first consumption advisory for the general Faroese population from the Chief Medical Officer to limit the consumption of pilot whale to one meal per week and to completely avoid pilot whale liver and kidney. Since 1980, pregnant women were specifically advised to limit their consumption of pilot whale meat and blubber. In 1989, additional information on high levels of organochlorine contaminants in the blubber of pilot whales led to the consumption advisory that not more than 200 g of whale meat and blubber (each) should be consumed per month, and that liver and kidney should be avoided completely. In 1998, another advisory followed due to demonstrated effects of Hg and PCB exposure on the health of the fetus and newborns. This advisory focused on adults and most specifically on young and pregnant women.

As shown in Chapters 3 and 4, the Faroese body burden of contaminants is still high in comparison with other populations, and is associated with adverse health effects. In 2008, the Faroese health authority concluded that pilot whales currently exceed limits for acceptable concentrations of toxic contaminants and can no longer be recommended for human consumption (Weihe and Joensen 2012).

In the case of the Faroe Islands, the risk communication efforts appears to have been successful in convincing pregnant women to consume less pilot whale than before (Odland et al. 2009; Weihe and Joensen 2012). While Hg levels in pilot whales have not decreased over the last three decades, concentrations in the blood of pregnant women have decreased significantly (Fig 6.2). While a dietary shift can be caused by several factors, it is likely that the risk communication undertaken in the Faroe Islands was the driving force for the decreases in human tissue levels of Hg and PCB for several reasons. For example, associated with the extensive cohort studies that have been ongoing since 1985, risk communication was continuous throughout the years and reached all areas of the islands (Odland et al. 2009). Further, risk communication messages were always restricted to pilot whale consumption, and several fish species with low contaminant concentrations were available and recommended as alternative dietary choices. However, as outlined in Chapter 4, health effects are still measurable even at these lower levels of exposure. Additionally, the success of the risk communication efforts and lower levels of contaminants in the Faroese population comes at a cost of loss of cultural identity for the Faroese people, who have relied on pilot whales as a staple part of their diet for hundreds of years (Weihe and Joensen 2012; Weihe pers. comm. 2014).

6.4.4 Greenland: Addressing conflicting evidence about diet and health

A country-wide population survey from 2005 to 2009 on adult Inuit in Greenland found that 78% exceeded 5.8 μg/L, an Hg blood guideline level established by the United States EPA (Environmental Protection Agency), and 98% exceeded 5 μg/L blood PCB concentrations (Bjerregaard and Mulvad 2012). At the same time, there was concern about a pronounced increase in overweight individuals and diabetes during the previous 15 years due to the dietary transition from a nutritious traditional diet to a less healthy diet based on store-bought food.

The Greenland Board of Nutrition is tasked with providing balanced information to the public about contaminants in the traditional marine food diet and general information about a healthy and nutritious diet. Recently, it was determined that obesity plays a greater role in adverse health outcomes than exposure to contaminants (Bjerregaard and Mulvad 2012). As a result, dietary advice to the general Greenlandic population has been revised and consists of ten simple recommendations (Bjerregaard and Mulvad 2012):

- Eat a variety of foods
- Eat local foods and eat fish often
- Eat fruit and vegetables daily
- Eat whole grains daily and eat potatoes, rice and pasta often
- Consider the fat you eat
- Eat less sugar, candy, chips and cakes
- Drink water and drink less fruit syrup and soda pop
- Eat frequently but not a lot
- Be physically active for at least one hour per day
- Think about what you eat.

There are also recommendations on physical activities and social aspects of preparing and eating meals. In addition, pregnant and nursing women[3], as well as children and young people are encouraged to continue to eat traditional marine food but to avoid or reduce consumption of older seals, toothed whales, seabirds

[3] A book in Danish and Greenlandic is provided to all pregnant women. It includes information about contaminants and dietary considerations.

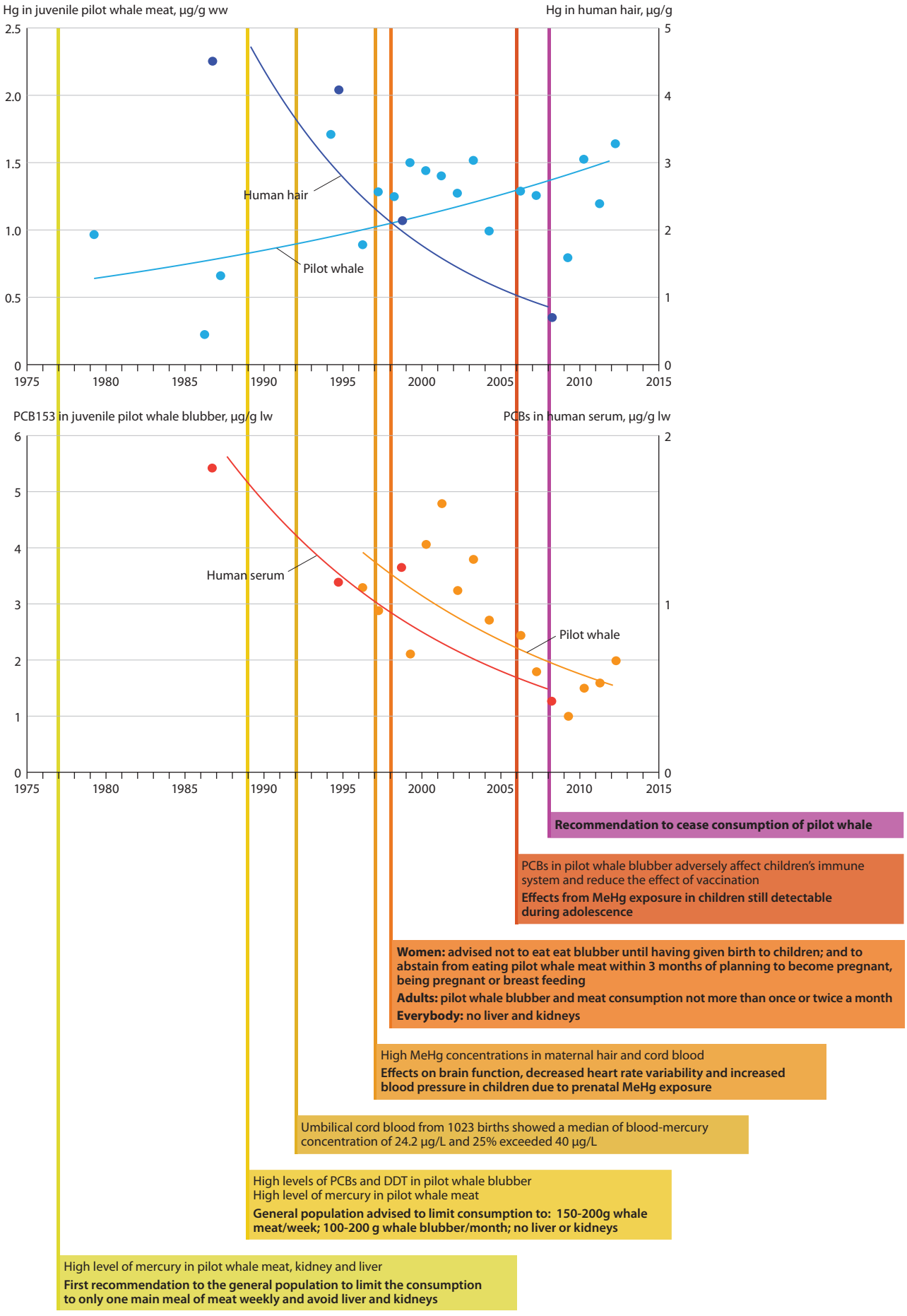

Figure 6.2 Timeline of risk communication for mercury (Hg) and polychlorinated biphenyls (PCBs) related to pilot whale consumption in the Faroe Islands (Dam, M., Environment Agency, Faroe Islands, unpublished, 2015).

and polar bear, due to high concentrations of contaminants. It is recommended that individuals substitute these foods with lean fish and terrestrial mammals. The specific focus in the recommendation is to promote availability and consumption of more fish known to have the lowest contaminant levels. The recommendation is directed at all parts of society (families, child care centers, schools, elder care facilities, hospitals, etc.) and commerce (fishermen, fish shops, sales and delivery, etc.).

Bjerregaard and Mulvad (2012) reported that in 2007 the Greenland Board of Nutrition evaluated the success of an information campaign on dietary recommendations. Their 'outcome' evaluation found that 43% of respondents knew about the campaign, mostly from television and brochures, and were familiar with recommendations regarding eating fruit and vegetables and traditional food. However, it was not known if these same respondents also followed the advice.

6.4.5 Russia: POPs and metals in Chukotka

The AMAP Russian Arctic Persistent Toxic Substances (PTS) study examined contaminants in food samples from Chukotka and undertook dietary surveys of the indigenous people living in inland Kanchalan and the coastal Uelen settlements (AMAP 2004). It was found that some marine wildlife exceeded Russian food safety limits. For example, livers of whales, walruses and seals exceeded the food safety limits for cadmium (Cd) by 5 to 15 times, and all species of seals exceeded limits for Hg by 3 to 100 times. Kidney and liver from walruses (*Odobenus rosmarus*) and grey whales (*Eschrichtius robustus*) exceeded the safety limits for Hg by 2 to 4 times. It was also suggested that houses and food containers were a source of POPs (e.g. through using insecticides in the home and preparing food and alcohol in contaminated containers). As a result, some prepared food items (such as fermented walrus meat) and homemade alcohol were highly polluted with PCBs and DDT.

Based on the PTS study findings, consumption restrictions were recommended for several species and tissues, and several risk communication measures were implemented to reduce contaminant exposure (Dudarev 2012). The Ministry of Health Care and Social Development of the Russian Federation approved systematic population health inspections, contaminant waste clean-up projects, and training sessions. Risk communication initiatives included brochures, a film, community meetings, non-technical summaries of the PTS, a school education program and broad media coverage of the issues. The risk communication initiatives were prepared and distributed to local indigenous communities; school teachers and pupils; managers of local administrative, maintenance, health and sanitary services; and other groups involved in decision-making on a wide range of quality of life issues.

Dudarev (2012) reported that the comprehensive study approach in Chukotka, and the thorough awareness campaign were very successful in producing desired 'outcomes', that is, implementation exercises and contaminant exposure reduction measures. However, to date there has been no follow-up study to investigate whether the measures taken have caused a desired 'impact', that is, a decrease in contaminant exposure.

6.4.6 Circumpolar Inuit perspectives

The ICC recently completed a report to address circumpolar perspectives on risk communication: views from Alaska, Canada, Chukotka, and Greenland (ICC 2012).

Information was obtained through a series of questions circulated to regional/local health officials, Inuit organizations, government officials and/or the general population. For example, in Alaska two teleconferences were held with a total of 15 participants. The participants were hunters, gatherers and professionals appointed by villages and regional organizations who were recognized to hold authority to speak on this topic and were specifically sought to be engaged in the survey. Overall, the representatives covered all rural areas home to Alaskan natives. In Greenland, a health official responsible for dietary advice was asked to provide input on the topic. Additionally, a survey lasting eight days was undertaken online and by mail to solicit views from Greenlandic civil society organizations (representing a broad spectrum of the Greenlandic population) and the Greenlandic public (which is approximately 80% Inuit). The survey was also broadcast by national and local media. A total of 66 people responded covering all four municipalities in Greenland, with the majority of people responding from the Greenland capital, Nuuk.

In Canada, regional organizations responsible for risk communication were contacted and provided their views on the topic. Additionally, views from local Inuit were sought and recorded at a workshop where contaminants and climate change were discussed.

In Russia, information was obtained by representatives of three civil society organizations and one Russian scientist who were involved in risk communication efforts, as well as one representative from a Chukotkan indigenous hunter organization.

In all cases (where it was possible), the information was summarized and sent back to the informing parties for their review to ensure that it reflected their input correctly.

While the report tried to reflect the views of all Arctic indigenous peoples as much as possible, the majority of views reflected Inuit perspectives. Because it was found that perspectives can vary widely between regions or even within one region, the findings should not be extrapolated to be considered representative of all indigenous peoples in the Arctic.

Responses to the key question *How is contaminant risk communicated in your region?* are summarized in Table 6.1. Two themes arise from the responses. First, most regions report that risk communication varies by issue and community, that is, there is no one-size-fits-all risk communication strategy for the Arctic. Second, two countries have no national strategic approach to risk communication (Alaska, Russia) while two others (Canada, Greenland) have an integrated national risk communication development and dissemination approach.

Most of the risk communication initiatives described in Sect. 6.4.1 to 6.4.5 indicate that there is only limited awareness of the outcome of risk communication messages. In some cases, risk communication efforts appear to have

Table 6.1 Inuit views on communicating contaminant risk (ICC 2012).

Region	*How is contaminant risk communicated in your region?*
Alaska, US	There are distinct approaches to risk communication within Federal and State agencies and within some regional organizations, such as the North Slope Borough and Maniilaq Association
	Perception exists that there is no overall organized State-wide risk communication strategy across multiple agencies or regional organizations
	Some reports of miscommunication, insufficient communication, no communication, or at times a distrust of the information being communicated
Canada	Risk communication is the responsibility of the health authorities in the Canadian Territories and sub-regions, and is carried out in collaboration with and/or organised through the NCP using a structure agreed to by most.
	Communication pathways, strategies and messages vary by issue and community
	The focus of risk communication is mostly on the benefit of traditional foods; occasionally, health advice is issued to limit consumption of certain traditional foods if contaminant exposures are of concern (see Sect. 6.4.2)
Russia (Chukotka)	No national or regional strategy or systematic approach
	Risk communication has been related to specific studies or projects such as the AMAP PTS study (see Sect. 6.4.5) and IPEN/Eco-Accord studies (Dudarev 2006a,b)
	Risk communication related to specific studies is often focused on how to cook/store foods (e.g. avoiding use of old, contaminated barrels)
Greenland	There is a national strategy in Greenland on promoting certain foods (like fish), but usually there are no direct warnings to avoid food items (see Sect. 6.4.4)
	Greenland has a one-for-all health system that is well integrated and unified, and there is a good rapport between doctors and communities
	Public responses to the ICC online questionnaire resulted in heightened interest in the topic and a need for more risk communication

Table 6.2 Inuit views on behavior change resulting from risk communication (ICC 2012).

Region	*Are changes in behavior observed due to the risk communication?*
Alaska, US	No long-term changes have taken place in hunting or consumption of traditional foods so far; however, there are anecdotal reports of some short-term changes due to fear or lack of information
	Concerns have been expressed in some communities about sick animals[1]
	Hunters have relied on indigenous knowledge to determine if sick animals are safe to eat, or if there is a risk
Canada	No particular strategy to assess the effectiveness of the risk communication in the regions
	One case study found a low level of message retention in the target group of women of childbearing age (Myers and Furgal 2006)
Russia (Chukotka)	No follow-up studies have been done on the effectiveness or retention of the messages, but there was a lot of interest to conduct such studies
	There is a need for more risk communication, but generally the priorities of the people in Chukotka are on other aspects of survival as life is very hard
Greenland	A range of responses to risk messaging with 55% of survey respondents (n=66) reporting that they would not change their behavior, 23% reporting changes in behavior due to risk messaging, 15% saying that behavior changes depended on a variety of factors, and 8% did not know or did not answer that question

[1] The ICC (2012) survey took place during the seal/walrus disease outbreak in the western Arctic, where many animals were visibly sick or died.

been successful, at least when effectiveness is measured in an indirect way – for example by lower contaminant levels. However, due to missing effectiveness evaluation studies, uncertainty remains as to whether a specific risk communication method had been particularly successful and could be clearly linked to behavioral changes that resulted in decreased contaminant exposure.

The ICC survey (ICC 2012) provided the following comments about the effectiveness of risk communication activities (Table 6.2). The responses from the recipients of the risk messages appear consistent in their view that there are few behavioral changes and few studies which indicate that the messages were effective.

6.5 International risk communication experiences related to the Arctic

Risk communications on contaminants are of importance on the international stage, for instance during international scientific and policy meetings related to contaminants and/or to support negotiations for multinational environmental agreements which may impact on the Arctic. However, sharing concerns about the risks posed by contaminants to the health of Arctic indigenous peoples, specific research findings and risk reduction messages can be a double edged sword. While some specific risk communication messages are intended for the protection of a local community or regional population from possible adverse health effects of contaminants found in parts of their diet, these same public health messages can spread to other communities, regions or countries through the global availability of media, and particularly via the internet. Rapid

dispersal of messages meant for one group or location can create anxiety and confusion in other areas where the scientific information or the advisory does not apply, or is not intended.

For example, an international conference in 2011 on Climate Change and Pollution included a presentation from the Faroe Islands about the inhibitory effects of PCBs on the efficacy of vaccinations (Heilmann et al. 2010). The conference presentation also explained that the findings of the research led to a health advisory in the Faroe Islands suggesting that local communities refrain from eating pilot whale (see Sect. 6.4.3). Subsequent media reporting by an Arctic newspaper that the same recommendation would be valid for the consumption of other toothed whales in other areas in the Arctic, including Canada, led to concerns there that the reports would discourage Canadian Inuit from eating their traditional foods.

The Faroe Island example underlines an inherent obstacle in sharing risk communication messages in international fora; news about research results and risk reduction strategies may be extrapolated to other regions, regardless of the relevance or validity of the advice. This can be a challenge for the development of trustworthy risk communication messages in other regions and for specific groups in specific locations where contaminant levels and food intakes have been measured and evaluated and have not been found to pose a similar risk.

The ICC had similar experiences during the negotiations for legally-binding instruments for implementing global action on POPs and Hg (Stockholm and Minamata Conventions, respectively, see Box 6.2).

For the POPs negotiations, several Canadian Aboriginal partners formed the coalition *Canadian Arctic Indigenous Peoples Against POPs* (CAIPAP), to advocate for consensus and urgency (Downie and Fenge 2003). CAIPAP was seen as a valuable source of relevant scientific information but also as a human face to the problem of contaminants that have reached the Arctic. The international messages throughout the POPs negotiations made their way back to Canada and into the Arctic regions through international media, and seemed to contradict the messages developed for local constituents at home (Myers and Furgal 2006). Examples are illustrated in Fig. 6.3.

Contrary to messages during the POPs negotiations, ICC interventions during the Hg negotiations 2010–2013 were able to draw directly from regional consumption advisories such as the beluga meat consumption advisory in Nunavik (Sect. 6.4.2.1) to highlight impacts of atmospheric Hg emissions on Inuit in the Canadian Arctic. However, while ICC took care to refrain from the sensationalistic wording used previously in international communication, subsequent media reporting by local media still misconstrued and distorted the international message in some cases.

For example, after the fifth negotiation session in January 2013, the ICC press release stated:

"*After a week with long negotiations that lasted throughout several nights, ICC participants were pleased to see the adoption of a global mercury treaty* […]. […] *the mercury treaty is expected to result in the reduction of mercury levels in the environment globally, however many years will pass before the first measures have to be implemented.* […] *Nevertheless, the fact that over 140 countries were able to agree on measures to reduce mercury in the environment has to be viewed as a success.*"

Box 6.2 Global conventions on POPs and mercury

The Stockholm Convention (Stockholm Convention 2014) on Persistent Organic Pollutants (POPs) now covers 23 POPs in its elimination and control annexes. It entered into force in 2004 and has more than 160 signatories/ratifications. The Minamata Convention on Mercury was opened for signature in October 2013 (Minamata Convention 2014); as of May 2015 it had been signed by 128 countries and ratified by 11.

Although there has not been a formal evaluation of the effectiveness of the international risk communication messages following the negotiations for either the Stockholm Convention or the Minamata Convention, both treaties contain preambular texts which reference indigenous communities and the vulnerability of indigenous people.

The preamble in the Stockholm Convention text acknowledges that … "*the Arctic ecosystems and indigenous communities are particularly at risk because of the biomagnification of persistent organic pollutants and that contamination of their traditional foods is a public health issue.*"

The preamble in the Minamata Convention notes … "*the particular vulnerabilities of Arctic ecosystems and indigenous communities because of the biomagnification of mercury and contamination of traditional foods*" and concern about … "*indigenous communities more generally with respect to the effects of mercury…*"

Figure 6.3 International versus community messaging on persistent organic pollutants (POPs). Comparison of messages communicated in 1998–2001 during the Stockholm Convention negotiations by Sheila Watt-Cloutier (ICC Vice-Chair at the time) with messages given locally in Canadian Inuit regions (Loring pers. comm. 2009).

It also included a quote from the ICC Canada President, Duane Smith:

"***Several Inuit regions currently have consumption advisories in effect due to high mercury levels in some traditional food items****, and the mercury in our foods is largely due to global mercury emissions, for example from coal-fired power plants in Asia. Consumption advisories are not an acceptable way for us to avoid health effects from mercury. Our environment needs to be healthy in order for us to be healthy.*"

One media outlet subsequently reported:

"*The Inuit Circumpolar Council says it is pleased with progress made in efforts to reduce global mercury levels. Early this week, more than 140 countries adopted a global mercury treaty at the United Nations Environment Programme meetings in Geneva, Switzerland. The treaty includes legally binding and voluntary measures to regulate mercury emissions, the related health aspects and other concerns. Mercury is a poison released into the air, water and land from small-scale artisanal gold mining, coal-powered plants, and from discarded electronic or consumer products such as thermostats, batteries and paints. Because mercury concentrates and accumulates in fish and goes up the food chain, it poses the greatest risk of nerve damage to pregnant women, women of childbearing age and young children.*

"*Over the years in the Arctic, mercury levels have been rising.* ***Inuit consume mercury when they eat country food like beluga and ringed seal****. The council has been pushing for tougher regulations in countries where mercury is coming from.*"

The highlighted text portions are added here for clarity. They illustrate that while ICC referred to food advisories due to high Hg levels in **some** traditional food items, the media just took a broad-brush approach saying that "*Inuit consume mercury when they eat country food*". Such generalized messages may cause anxiety and uncertainty in Northern regions, where the overall dietary advice given by health officials is that traditional food is healthy and should be consumed.

Overall, the experience of risk communication on the international scale shows that it is not desirable for one source to use messages with significantly different content for different audiences, since this message can reach a non-target audience through global media sources such as the internet. At the same time, it is likely that different messages are transmitted by different (global) sources and reach local non-target audiences, which can cause confusion in local populations. Therefore, continuous communication is required locally to reinforce the validity of messages to a local audience and prevent confusion through non-local information sources that may not be valid for a specific local audience.

6.6 Application of social media for risk communication in the Arctic

Use of social media (see Box 6.3) is becoming a potent tool for all forms of communication, including risk communication. However, use of social media for risk communication differs from more commonly used approaches for communicating health risk in as much as the former involves multi-way communication (between the originator and social media users) whereas the latter tends to rely more on the one-way flow of information (usually as a top-down approach from health experts to the target group). Using social media for a dynamic exchange of information rather than a more traditional passive communication, facilitates the development of a greater understanding of how health risk messages can elicit different responses based on who delivers the messages, how they are delivered, and how the public actively processes the information (Lemal and Merrick 2011).

Box 6.3 Social media

….*"the various electronic tools, technologies, and applications that facilitate interactive communication and content exchange, enabling the user to move back and forth easily between the roles of audience and content producers*" (Tinker and Fouse 2009).

Social media can be used to meet the objective of providing health information in an accessible, timely fashion, and can be used as a strategy to monitor the perceptions, reception and understanding of the message and contributions to the conversations (Schein et al. 2010; Rutsaert et al. 2013).

6.6.1 Social media for health risk communications: forms, practices and effectiveness

The form of social media used within a health communication strategy is largely dependent on the goals of the strategy, whether it is message dissemination and/or public engagement (US CDC 2011b).

The 'one-way' electronic-media based communication depicted in Fig. 6.4 is a form of information dissemination that is often more accessible now compared to traditional media forms (radio, television, letters, brochures and newspapers). Nevertheless, the accessibility of different forms of media and communication sources remains audience dependent. Internet-based content with graphics, color, text and audio can be updated rapidly but is still not fully enabled for discussion or rapid group interaction. *YouTube* is one of the best known content communities used for video sharing (NCSD 2009).

The 'two-way' communication category represents perhaps the greatest shift in risk messaging communication possibilities, especially when combined with access to information available online. Two-way media allow for an exchange of comments, feedback, and clarity. They are open to discussions on the disparity of views arising from the factors influencing risk perception and behavior in northern communities, such as cultural, social and demographic factors (Furgal et al. 2005; Rutsaert et al. 2013).

Social networking sites are websites used for building virtual communities, organizations or personal networks, allowing users to connect and socialize online (Mayfield 2008; NCSD 2009; US CDC 2011b). Social networking sites are another way for health messages or campaigns to be advertised and targeted to appropriate groups. However, people would need to be linked to the discussion group or organization's pages in order to receive the health messages.

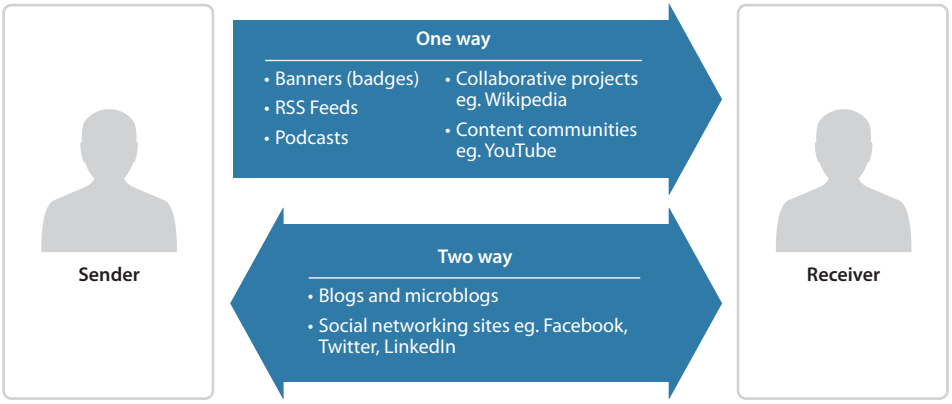

Figure 6.4 Schematic illustration of different communication forms within social media.

6.6.2 Social media as a tool and opportunity for risk communication in the Arctic

Social media as a tool for health risk communications can provide opportunities in the circumpolar North to enhance risk communication strategies. For communities with few resources to put towards the communication of health risks, social media could help overcome cost barriers as several social media tools offer a relatively cost-effective means of communication (Schein et al. 2010), especially for reaching out in-person to remote communities. Two-way communication and community engagement via social media is one means to build mutual trust among public health officials and community members; this is especially critical in the north where there is much health research underway related to contaminants and scientists and health officials are unable to make sufficiently frequent visits to communities to provide updates.

Health messages being delivered by northerners to northerners, can provide optimal trust in the message. For example, for the Nunavik Child Development Study (see Sect. 6.4.2.1), the Nunavik Assistant Director of Public Health was chosen as the spokesperson for the *YouTube* capsules. As an Inuk, she was considered by the communities as both a representative of the people and a credible professional (Muckle pers. comm. 2014). In this case, the *YouTube* capsules were included in an effort to increase messaging effectiveness to youth and young women of childbearing age. Videos were purposefully kept to less than two minutes and just provided the basic results of the study (Muckle pers. comm. 2014). Longer video clips may be useful for other target audiences for which more background information to the study would be valuable.

Not all communities in the Arctic have reliable access to broadband internet, an essential component for effective social media messaging. Among the circumpolar countries, Iceland, Alaska and Norway have the highest percentages of population using the internet, followed by Sweden, Finland, and northern Canada (Nordregio 2011). Greenland has over 90% of its population connected to internet (IWS 2014). Arctic Russia has the lowest percentage of the population using the internet. In those countries and regions with limited internet availability, radio may continue to be a better communication tool for widespread distribution of risk communication messages.

Three confounding factors make the evaluation of risk messaging in social media fora difficult: a general lack of understanding of how social connections impede or validate/support behavior change; whether or not to have confidence in forum moderators (in terms of how they might direct or influence the conversation); and knowing who might have joined a social networking group and why (e.g. their motivation and bias) (Bennett and Glasgow 2009; Schein et al. 2010). These factors need to be taken into account when considering the use of social media tools for undertaking research on disseminating risk messages, evaluating public perceptions of messages, or gathering research data on effectiveness of messaging.

6.6.3 Considerations for social media use in Arctic risk communications

There are several Arctic-specific considerations which would enhance risk communication through social media; many are common to the traditional one-way communication forms:

- Preservation of indigenous language in an online world that works primarily in English
- Risk message text which can be combined with audio, video and/or in-person communication and community workshops
- Establishing trustworthy and credible channels and sources for the social media tools available
- Monitoring and managing the communications online continuously (see Tinker and Fouse 2009)
- Avoiding anxiety and fear by providing correct and clear information on contaminants in traditional foods and the benefits of these foods
- Directing health messages to the correct target populations and consulting broadly on the messages prior to issuing a risk message
- Streamlining message approval processes to enable real time communications (see Schein et al. 2010)
- Avoiding information overload
- Enhancing staff knowledge of social media tools and promoting technological/IT capacity (see Tinker and Fouse 2009)
- Improving the availability of technical infrastructure and internet access/bandwidth to enable reliable use of some social media tools
- Recognizing that social media tools may not be as effective for reaching certain demographic groups, for example seniors.

There is very little published literature on the impact of social media on vulnerable populations. The social media practices of community organizations have yet to be formally evaluated (Taylor 2011). Therefore, given the fairly recent introduction of social media as a tool for risk communication, particularly in

the North, it is difficult to say whether such campaigns are or will be effective at reaching target audiences. Research aimed at examining the effectiveness of social media campaigns will assist health communicators in the future use of these tools.

6.7 Optimizing risk communication in the Arctic

Many authors have provided information on best practices for risk communication, and several have focused on indigenous populations. They point to the need to understand the target population and culture (DeWeese et al. 2009) and especially those groups most vulnerable to the impacts of the exposure event. For environmental contaminants those most at risk are elders, women of childbearing age, infants and children, residents with chronic diseases and those on medications that affect the immune system. Other authors highlight the importance of trust (DeWeese et al. 2009; Jardine et al. 2013) and the role of indigenous communities and indigenous knowledge in risk communication (Friendship and Furgal 2012). Friendship and Furgal (2012) proposed a set of common guiding principles rather than a prescriptive rigid framework for bringing people, different cultures and knowledge systems together.

The importance of the right language and tone of the message, good visualization of the message, and the advantages of framing have been highlighted by several authors (Connelly and Knuth 1998; Tan et al. 2011). Other authors particularly highlight the need for monitoring, evaluating and adjusting risk communication campaigns (Covello and Allen 1988; Wylie et al. 2001; Coffman 2002).

The ICC survey of Inuit in Alaska, Canada, Russia (Chukotka), and Greenland (see Sect. 6.4.6 and ICC 2012) provided the following comments about best practices for risk communication (Table 6.3). These comments are consistent with those reported above and also contain a summary of best practices (see the section on 'General Comments' in Table 6.3).

Consideration could be given to the following points when using and evaluating social media tools for risk communication in the Arctic:

- Provide messages in multiple formats, that is, use social media tools alongside more traditional forms of risk communication.
- Adopt low-risk social media tools first, that is, those which also allow a good entry point into the use of social media, and then expand into other tools.
- Make strategic choices and understand the level of effort needed to develop and maintain the social media tools selected.
- Understand the target group and their preferred social media sites; the most effective messages are those tailored to specific cultural or demographic groups. Choose communication tools that would enhance the receipt of information, for example, consider using video or audio tools for communities or target groups with low reading or computer literacy, consider short clips for youth who may be used to shorter bursts of information.
- Develop social media messages and tools in collaboration with the communities they are designed to assist.
- Make it easy for people to share the health messages by using social media tools with sharing features that can be

Table 6.3 Inuit views on effective risk communication (ICC 2012).

Region	*What are the most effective ways to do risk communication?*
Alaska, US	Input by Inuit into risk communication Good relationships between co-management entities is most important
Canada	Views and preferences on how to do risk communication can vary extensively between different regions and even within one region
Russia (Chukotka)	Visual digital messaging (e.g. in the form of a film and/or television program) is likely to be successful and efficient for distributing messages
Greenland	Use television and radio for messages and make messages available online for a more in-depth review afterward Have local face-to-face meetings with scientists Have a local perspective with clear messages Avoid 'scare' campaigns
General Comments	Recommendations from Inuit on best practices for risk communication include: • risk communication should be made by Inuit for Inuit • sources of data should be locally available, and if there is overall local involvement in the research, chances are higher that risk communication is being done properly • the trust factor is important; it matters very much who does the risk communication. A non-trusted source will create a lot of skepticism • messaging needs to be clear and consistent • workshops should be held with all groups involved in research (scientists, communicators, locals) • the use of social media in risk communication should be explored • the messages should not be just about 'doom and gloom' • there needs to be a higher frequency of risk communication – a single fact sheet or just one workshop is forgotten very quickly • the context of the message is important • it is important that there is enough time allocated to develop proper messaging

used by others on their organizational or personal websites or social networking pages.

- Evaluate the social media communication efforts throughout the full lifecycle of the communication campaign.
- Acquire feedback from community members to gather information on the effectiveness of the messages and social media tools. Feedback from the community can also help with message adaptation and can help build relationships and engagement with communities.
- Use a flexible framework to allow the risk communication strategy to move toward the most useful social media tools.

6.8 Conclusions, recommendations and knowledge gaps

6.8.1 Conclusions

There has been little growth in both the scientific activity and publication productivity on risk communication research and specifically on the evaluation of the effectiveness of risk communication initiatives. Modern advisories focus on changing behavior patterns by recommending an overall healthy diet and consumption of the safest (least contaminated) traditional (country) foods. Their overall objective is better health and social well-being for the individual and the family.

A diversity of approaches is necessary for effective communication of risk, for example, tone, presentation of information, reading level, balanced messages, a variety of ways to reduce risk, and messages targeted to particular groups. Optimal practices for risk communication in the Arctic include the following aspects:

- Full awareness of the most vulnerable groups in the community
- Involvement of Arctic indigenous peoples in research and communication
- Clear and consistent messages
- Balanced information delivered by trusted sources
- Multi-pronged approach using a variety of media realistic for the region
- Adapted use of social media
- Communicating risk more frequently and for sustained periods (years)
- Workshops with all stakeholders (scientists, communicators, locals)
- Evaluation of all risk communication before, during and after the risk communication period.

Insufficient effort has been directed toward learning how best to inform or influence public decision-making to protect health and culture in the Arctic compared to the identification, monitoring and assessment of effects of human exposure to the environmental contaminants. Evaluations of the outcomes or impacts of risk communication activities in the Arctic are rare.

While some authors have concluded that there was a successful outcome because human tissue levels declined after communication of a contaminant intake advisory, other factors unrelated to the advisory may be responsible for the declines reported.

Effectiveness evaluations also apply to risk messages used to heighten international awareness of contaminant–health issues in the Arctic. Risk messages have been effective in global negotiations related to contaminants (both the Stockholm and Minamata Conventions have been successfully launched and mention the particular vulnerability of the Arctic and indigenous communities); however, the same messages have sometimes resulted in confusion in some local areas where the message has been received through the mainstream media and may seem to conflict with local advice.

Social media tools can be a way to overcome some of the obstacles to communicating in the North by using appropriate language and literacy, enhancing reach to remote communities or particular target groups (e.g. youth), and engaging the communities in two-way communications without the physical presence of a health communicator. Health communicators and several Aboriginal organizations and governments targeting Aboriginal people in the circumpolar North have begun to incorporate social media tools into their communication strategies online.

6.8.2 Recommendations

- The previous AMAP human health assessment (AMAP 2009) called for more research on the effectiveness of communication initiatives. Little work appears to have been undertaken and published. **There is a need for a focused effort in risk communication research that includes the evaluation of how successful a risk communication strategy has been.** The measure of success of a risk communication initiative cannot be based solely upon declining contaminant levels in the target populations.
- AMAP (2009) recommended that **risk communication needs to be developed together with target communities, ensuring the use of culturally appropriate methods that are tailored to the communities' needs.** This recommendation is strongly endorsed. Dialogue with communities may include workshops with all stakeholders, use of traditional media such as radio messages and/or the adapted use of internet/social media.
- AMAP (2009) emphasized the importance of undertaking risk communication with great care and respect for the receiver culture. This remains a strong recommendation. **Communicators need to be aware of the possible spread of messages to audiences that were not originally targeted. Messages should be balanced and avoid possible conflicts with communications at local versus international levels.** Identifying vulnerable groups within communities (e.g. elders, women of childbearing age, infants and children, residents with chronic diseases and those on medications that affect the immune system) can improve adaptation strategies to reduce their risk of exposure to dietary contaminants and disease.
- Experience to date has shown that developing culturally appropriate messages, evaluating their effectiveness, as well as the overall coordination of risk communication are likely to be important components of successful risk communication. Therefore, good risk communication may require the establishment of a group of experts with a range

of backgrounds (toxicologists, researchers, community representatives, public health officials, etc.) who can work in a collaborative manner to balance varying perspectives and needs. Arctic countries should consider the creation of such groups in their respective regions, with the ultimate goal of connecting these groups to **form an overarching network for risk communication in the circumpolar Arctic**.

- Risk communication is not a solution to the Arctic contaminant issue. AMAP (2009) endorsed the need for strong support of international efforts to restrict the use and emission of substances which are persistent, toxic and able to accumulate in food chains. This strong support needs to continue globally to reduce levels of contaminants in the Arctic. It includes **supporting and ratifying global agreements to regulate contaminants, such as the Stockholm Convention on POPs and the Minamata Convention on Mercury**.

6.8.3 Knowledge gaps

This chapter highlights the clear lack of information on how risk communication on contaminants is practiced in several Arctic countries. For those countries where information about risk communication exists, further research on the evaluation of risk communication methods and messages is required to promote the development and deployment of more effective risk communication strategies. This research should focus on methodology for developing and deploying risk communication messages, understanding the types of messages and how they are received, and identifying methods for evaluating the effectiveness of the communication strategies.

7. Adaptation in Arctic circumpolar communities: Food and water security in a changing climate

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7.1 Introduction

This is the first AMAP human health assessment report to contain a chapter that focuses on adaptation to the environmental impact of climate change, with an emphasis on those small rural communities with a high dependence on local wildlife resources, stable permafrost, ice for winter subsistence hunting, and other temperature-critical environmental or ecosystem characteristics. Regardless of the Arctic nation in which these small communities are located, they share many of the same vulnerabilities. These include a small resident population; little or no wage-based economy; a remote location, often with dependence on air or water transport at great expense; unreliable and expensive power generation; susceptibility to forest fire, flooding, and coastal erosion of village sites by storms or flooding; and failure of key infrastructure owing to thawing permafrost, including loss of permafrost containment of tundra pond water sources and village sewage lagoons (Huntington and Fox 2005; AMAP 2011).

For the purposes of this chapter, *Adaptation* is defined as the ability of a small rural community to tolerate change imposed by climate regime change. The changes discussed in this chapter are major environmental changes, which directly threaten the security of subsistence food (traditional country food) and community water supply, and so threaten community sustainability. In this context, adaptation is the ability of the community to change, or adopt new behaviors, in order to avoid or minimize risk, and to be able to continue the most important cultural, economic and health-related benefits of the present way of living. The most recent assessment of the Intergovernmental Panel on Climate Change (IPCC) concluded with a major recommendation that all levels of government, in all regions, emphasize the development of Adaptation Strategies (IPCC 2014).

This chapter addresses climate-mediated impacts on remote rural communities. Some of these impacts are already occurring in parts of the Arctic, while other regions have experienced relatively few impacts. Adaptation activity is underway in some regions but is still at the planning stage in others. Examples of community-based adaptation strategies are used to illustrate the wide range of strategies currently in use. Because this chapter focuses on the impacts of environmental change, socio-economic impacts and changes in national policy are not addressed here. The often profound impacts on infrastructure, especially those related to permafrost and ice, are also beyond the scope of this assessment. Readers interested in this topic are referred to the relevant sections of the Arctic Climate Impact Assessment (Berner and Furgal 2005; McCarthy and Long Martello 2005).

Recent completion of the EU-funded project ArcRisk (www.arcrisk.eu; see also Sect. 7.5) has resulted in a number of findings concerning the influence of climate change on the long-range transport of contaminants to the Arctic, their accumulation in Arctic food webs, and ultimately human exposure through the consumption of Arctic wildlife species (fish and marine mammals). These findings have provided new insights for further work on modeling and estimating the impact of climate change on the accumulation of anthropogenic contaminants in the Arctic environment, and ultimate human exposure.

7.2 Categories of environmental threat

The major categories of environmental threat emerging in the Arctic are climate change (principally climate warming), anthropogenic contaminants, and zoonotic diseases (diseases of wildlife communicable to humans). These impacts, and the ways in which they interact, present an existential threat to small communities through their potential effects on subsistence food and community drinking water security. How communities are responding to such issues is important. Ideally, the response would include assessing the impacts of climate warming on infrastructure, food security and water security; prioritizing existing threats; identifying the most vulnerable residents; developing community-specific adaptation strategies designed to reduce risk to the most vulnerable subset of the population; and establishing metrics to monitor trends in established environmental threats and to detect emerging threats. Human biomonitoring is not addressed here as it is fully discussed in Chapter 3.

7.2.1 Climate change in the Arctic region

Climate regime change in the circumpolar north varies widely as it is greatly affected by proximity to the Arctic Ocean, the Bering Sea, the North Pacific Ocean, and the northern extensions of the Atlantic Ocean. In addition, seasonal variation in the strength of the stable low atmospheric pressure fields (the Aleutian Low in the North Pacific and the Icelandic Low in the North Atlantic) and high atmospheric pressure fields (over Siberia and Arctic Canada) gives rise to very different regional weather patterns. The northern extension of the North Atlantic thermohaline circulation (known as the Gulf Stream) warms the Labrador Sea, and an eastern extension (known as the North Atlantic Drift) warms western Europe. Changes in water temperature around the eastern shore of the North Pacific (known as the Pacific Decadal Oscillation) result in significant differences in air temperature over adjacent land masses. There are many other cyclical atmospheric and oceanic changes that also drive environmental and ecological change, but these are not described here further. The annual Arctic Report Card (NOAA 2014) provides a recent discussion of Arctic climate trends, while the Arctic Climate Impact Assessment (ACIA 2005) gave an in-depth discussion of many of the underlying mechanisms.

7.2.2 Anthropogenic contaminants

Environmental contaminants of anthropogenic origin are mostly produced and released by sources at lower latitudes and then transported to the Arctic by winds, ocean currents, and rivers. After entering the northern environment, toxic heavy metals (such as mercury and lead) and persistent organic pollutants (POPs) enter the Arctic food chain and bioaccumulate through successively higher trophic levels. Tissue concentrations of lipid-soluble POPs, which have a long half-life in fat tissue, may be many hundreds of times higher in top predators than in organisms at the lowest trophic level, putting consumers of these top predators at risk from toxic effects (see Chapter 4). Among the many toxic effects, a major concern is suppression of the immune system, making humans, and animals, more likely to develop an active infection.

7.2.3 Zoonotic diseases

A number of microbial infections occur in both humans and the animals with which they come into contact, and in healthy individuals are most often suppressed by the immune system, offering no health risk to the animal or human. However, under some circumstances, animals and humans can develop an infection that has been suppressed for many years. This is usually associated with the occurrence of factors that affect the immune system such as a decrease in natural immunity with age; an immature immune system in infancy; changes in immunity during pregnancy, or during treatment with a medication that suppresses the immune system such as cancer chemotherapy or steroid medications; and exposure to high tissue levels of immunosuppressive contaminants.

The most common zoonotic infections are caused by three types of bacteria – *Brucella*, *Toxoplasma*, and *Coxiella* – which are found in marine mammals, terrestrial mammals, birds and many other animals throughout the circumpolar north. There are many other similar infections, which are common in some regions, but more localized in their distribution. New zoonotic pathogens are spreading north as climate warming has made conditions more favorable. Examples include West Nile Virus in North America (which has reached the prairie provinces of Canada) and tick-borne encephalitis in northern Europe. Studies suggest that existing infectious threats may be present in greater numbers of subsistence animals and that pathogens new to the Arctic may continue to spread northward (Hueffer et al. 2013).

7.2.4 Combined effects of climate warming, anthropogenic contaminants and zoonotic disease

A change in temperature may directly affect community infrastructure (including water treatment and sewage treatment facilities, power supply, and runways, harbors, roads and schools) and community food and drinking water security (defined here as adequate supply, adequate access, and adequate information concerning food-borne threats such as contaminants and food-borne disease agents). However, the *combined effects* of climate warming, anthropogenic contaminants, and zoonotic diseases also represent a significant risk to the security of subsistence food and drinking water supplies. Many circumpolar communities, particularly small rural communities, will need to develop monitoring and adaptation strategies to deal with these interacting risks.

- The warming climate has resulted in changes in ocean and atmospheric contaminant transport, which may have increased the movement of organohalogens and mercury from lower latitudes to the Arctic (Kallenborn et al. 2012). Warmer water in freshwater lakes, tundra ponds and streams may result in greater bacterial methylation of mercury, and mercury released from thawing permafrost (Stern et al. 2012).
- Climate-mediated changes in the transport of anthropogenic contaminants to the circumpolar region may result in higher exposure in subsistence wildlife which could increase the risk of immunosuppression, and thus active zoonotic infection in these animals. This could result in risk to human consumers of infection and toxic effects from contaminant exposure (Fisk et al. 2005).
- The warming climate is enabling southern plant, insect and animal species to expand their ranges further north, in some cases, into Arctic regions. These species may bring new zoonotic diseases with them. Higher winter temperatures in the Arctic may increase the winter survival of infected animals, raising the risk of hunter/consumer exposure.
- The northward expansion of new species has brought new water-borne disease, such as tularemia (Rydén et al. 2009; Hueffer et al. 2013), and warmer waters in tundra ponds and estuaries and nearshore ocean waters can support toxin-producing cyanobacteria and toxin-producing algal blooms (Greene et al. 2011).
- Longer Arctic summers and warmer winters, with less sea-ice cover, may increase use of the Northern Sea Route by commercial shipping from northern Europe and western Russian ports (IPCC 2013), raising the possibility of new rat-borne infection from Europe to the North American Arctic. Tick-borne encephalitis is one such example (Revich et al. 2012).
- The warming climate may drive changes in the forage resources of subsistence species, and thus in the range, health and abundance of those subsistence species. The ecosystem changes could also impact on existing and newly emerging zoonotic pathogens of subsistence species.

7.3 Developing a community-based adaptation strategy

The environmental impacts of climate warming, anthropogenic contaminants and zoonotic disease on subsistence food species and rural drinking water represent direct threats to the sustainability of small rural communities and create the need for community-based adaptation planning. There are four steps in the development of a community-specific adaptation strategy.

1. An assessment of the known, and potential, environmental threats. This may require the assistance of regional tribal and/or government agencies, as well as academic institutions with this assessment capacity.

2. A community review of the data available and a community decision, taking into account traditional ecological knowledge (TEK), on prioritizing existing and potential threats and selecting the highest priority threats for further assessment. Communities rarely have in-depth information on the prevalence of zoonotic infections or tissue levels of contaminants in subsistence species and may require the assistance of regional wildlife managers to acquire the necessary data. Such as water quality data from regional authorities for use as a historical baseline, long-term weather observations, permafrost data, and other regional baseline data.

3. Once the relevant data have been obtained, adaptation planning can start. A critical part of adaptation planning involves identifying the subset of residents most at risk for the prioritized threats, which may require assistance from regional medical providers. The adaptation strategy should be directed at reducing risk for this group.

4. Plans for monitoring key indicators in order to follow the trends in threat development, and to identify newly emerging threats are the final step in developing a community-specific adaptation strategy. Community-based monitoring will give the community trend data on increasing or decreasing risk from the prioritized threats, and will allow the adaptation plan to be modified accordingly. This activity may benefit from assistance by regional agencies with relevant monitoring capacity and the ability to train residents and provide equipment and supplies.

   Data metrics in current use include long-term local weather data; environmental parameters, such as water temperature and water levels of nitrogen, mercury and phosphorus; permafrost temperature; river- and sea-ice data; filter paper sampling of animal blood by village hunters for the presence of antibodies to zoonotic infections (Curry et al. 2014), mercury (Hansen et al. 2014), and other contaminants (Burse et al. 1997); biological toxin levels (such as from harmful algal blooms) in subsistence marine species; shoreline changes; and insect vector sampling for the presence of pathogenic bacteria.

A useful component of any adaptation strategy, or monitoring plan, is to use residents as local environmental observers to link new environmental events or observations with networks of regional wildlife management agencies, health care providers, and academic consultants. This type of observer network has proved very useful for early detection of significant environmental events and conditions. In Alaska, the network of local environmental observers (LEO) often provides the first warning of a significant environmental event, such as a mass wildlife mortality event in an otherwise unobserved remote area. The LEO network of observers has also noted the appearance of new species, and signs of new wildlife disease events, and can quickly communicate each observation via a network of internet-connected LEOs (ANTHC 2014).

7.4 Managing the response to environmental threats

One of the most important benefits of the multi-step process used for developing community-based adaptation strategies is that it enables residents to help plan, contribute TEK, and participate in the investigation, and so build understanding of the most important environmental threats to their community. As part of the process, the entire community is involved in managing the response to the environmental threats. An equally important benefit is the recognition of vulnerable subsets of the population, and the development of strategies to reduce exposure, and thus risk, where exposure cannot be prevented. In terms of harvest plans, for example, this might involve harvesting younger and smaller seals to reduce the exposure of infants, children and pregnant women to mercury and organohalogens. It might involve changing food preparation practices for these populations, and for residents on chemotherapy, or those with chronic diseases, when a particular species is known to have a high prevalence of zoonotic exposure. Using informed adaptation plans, the health, cultural and economic benefits of the traditional diet can be preserved, and risk to the most vulnerable residents can be understood and reduced. The following sections provide examples of successful adaptation strategies (Sect. 7.4.1 and 7.4.2) and an example of the critical role of an LEO network (Sect. 7.4.3).

7.4.1 Seasonal changes to whale hunting in Wainwright, Alaska

Coastal communities in the Arctic have long-established expertise in traveling on the frozen sea and using sea ice as a platform from which to harvest a wide range of food resources. In the Iñupiat village of Wainwright in Alaska, this includes hunting for bowhead whale, walrus, seal, polar bear, fish, and birds. In Wainwright, a sustained west wind in winter will 'ground' the sea ice and cause it to build into large stacked sheets attached to the sea floor. An east wind during spring will then create a break between the shore-fast ice and the floating sea ice, known as a 'lead'. The lead provides a passage of open water through which whales pass on their northward migration. The grounded ice provides a platform from which to camp, launch boats, and haul out the enormous whales for processing. In recent years, however, conditions have been changing. Warming has resulted in a decline in sea ice, particularly in the thick multi-year ice, and there has been a breakdown of the historical wind regimes that are crucial for safe travel and hunting conditions on the sea ice. Winds from the northwest and south have prevented the grounding of the ice and the formation of an accessible lead. The result is new challenges for ice-based hunting in Wainwright and other parts of the Arctic.

Starting in the 1980s, hunters in Wainwright began to notice changes in the sea ice and to discuss the need for entirely new hunting methods. Traditionally, Wainwright hunters pursued bowhead during spring, working off the ice shelf on the edge of the open water; launching skin boats when a whale was sighted and paddling in pursuit to harpoon a passing whale. Only a limited number of harpoon strikes are currently allowed by the International Whaling Commission, so each attempt must be taken with great care. In recent years, unusual wind and poor

With climate change, a new whaling tradition is developing on the North Slope of Alaska. Early retreat of spring ice along the Alaskan Arctic coast is making a spring ice-based hunt impractical; traditional skin whaling boats (above) are being replaced by more modern boats (below) as ice in spring becomes unpredicatable. Photos: Mike Brubaker

ice conditions have combined to prevent hunting, sometimes for weeks. In some years, ice conditions only improved after the whales had passed Wainwright. So, in autumn 2011 with unused harpoon strikes available and open water across the Chukchi Sea, Wainwright hunters harvested their first autumn bowhead whale in the memory of current residents. It may even have been the first autumn bowhead harvested from Wainwright since the early American whaling era in the Arctic (late 1800s). To accomplish this, the hunters had had to acquire larger boats that could go further and handle the growing ocean swell generated by miles of wind across ice-free seas. If warming continues, boat-based hunting may also become common for spring hunting. The end result is a new and successful adaptation strategy, adding autumn sea-based hunting to the traditional spring ice-based hunting and increasing food security for one Arctic community.

7.4.2 Maintaining food security – an example from the Canadian Arctic

Caribou herds are currently declining in several regions of Arctic Canada. For example, the George River migratory caribou herd, whose range spans Quebec and Labrador was probably around 800,000 animals 25 years ago, was counted to around 74,000 animals and declining in 2010, and later estimated to be only 20,000 animals. The low numbers caused the Government of Newfoundland and Labrador to impose a five-year ban on harvesting in early 2013, and the Government of Quebec halted sports hunting indefinitely. Prior to the five-year ban, the Nunatsiavut Government called on all beneficiaries of the Labrador Inuit Land Claims Agreement to suspend harvesting immediately for a two-year period, and encouraged other aboriginal groups to do the same.

While the size of caribou herds appears to fluctuate as part of their population dynamics, climate change may represent an additional stress (www.caribou-ungava.ulaval.ca) that could weaken herds to the point of no recovery. A recent survey on Baffin Island caribou found that herds there are also severely reduced.

Inuit communities that rely on caribou as a staple country food are adapting in different ways. For example, Aboriginal groups in Quebec and Labrador formed the Ungava Caribou Aboriginal Roundtable to work on a conservation plan, while several Inuit populations are likely to be consuming more seal as a partial replacement for caribou in the diet. However, because contaminant levels in seals are generally higher than in caribou this could result in increased contaminant exposure for some populations, unless they switch to less contaminated foods such as musk ox and anadromous Arctic char. Various studies are underway on whether climate change is causing higher levels of contaminants in marine mammals such beluga and seals. Concerns around contaminants and human health in the Canadian North prompted the creation of the Northern Contaminant Program in 1991, which has regularly measured and reported levels, sources and transport of contaminants in environment, biota and subsistence species in this region for many years (NCP 2013)(See Box 6.1 on page 115).

7.4.3 Applying local observation in response to food safety concerns

Climate change in Alaska is causing a wide range of impacts on the environment and on the health of animals and people (Markon et al. 2012). But in this vast and sparsely populated state, systems for monitoring changes in weather, landscape, biota, and public health are limited. However, improvements in communications and local environmental capacity have led the Alaska Native Tribal Health Consortium (ANTHC) to develop a system for sharing information on environmental impacts and community health effects. This local environmental observer network (LEO; see also Sect. 7.3) documents time- and location-specific events and encourages communication between communities, academic institutions and resource agencies to increase understanding about climate and other drivers of change and to develop adaptation strategies. LEO applies traditional knowledge, western science, and modern technology to achieve a robust and effective environmental health surveillance system.

LEO is an association of environmental and wildlife managers and health professionals located in tribal organizations in Alaska and western Canada. There are LEO network members in about 140 communities. They share observations about unusual and unique environmental events, which are then posted on public Google maps. Since the program was initiated in January 2012, the network has compiled a database of observations on topics including extreme weather, floods, erosion, ice changes,

permafrost thaw, invasive species, infrastructure damage, environmental contamination and changes in the health, range and behavior of fish, insects, birds and wildlife. The utility of public observer networks for connecting remote communities with technical experts to help address food safety and other public health concerns is demonstrated in Box 7.1.

With the likelihood that climate change will continue to grow as a global public health challenge, it is important that communities have the capacity to monitor, respond, and adapt to new events, impacts and health effects. The LEO network provides one possible template for engaging communities to perform environmental monitoring, improve communication, and connect with technical experts and resources as required. It is a powerful tool for documenting local events and developing effective adaptation strategies for communities in the changing Arctic (Brubaker et al. 2013).

Village-based environmental monitoring data can also be used for broader applications. For example, data on contaminant levels in animal tissue can lead to a better understanding of the impact of climate change on the transport and fate of contaminants within the Arctic, and on regional trends in contaminant levels. Such information can be used to indicate the efficacy of national and international programs to reduce the production and release of contaminants. Another application of village-based environmental monitoring data concerns zoonotic diseases. Climate change is affecting the distribution of known pathogens within the Arctic and causing the emergence of pathogens new to the Arctic, and this is creating a need to make residents aware of the possible importance of modifying food preparation and storage methods. Regional public health and wildlife managers can then follow trends in pathogen prevalence in subsistence species. Archived biosamples should be preserved for baseline reference in identifying emergence of new pathogens or contaminants.

7.5 ArcRisk – key findings for community adaptation

One aim of the ArcRisk project (see Box 7.2) was to estimate the potential impact of climate change on the bioaccumulation of contaminants in an Arctic food web. Although there were sufficient data to model the basic structure of an Arctic marine food web near Svalbard (such as food web composition, feeding relationships, and species-specific properties), there were insufficient data, or the uncertainties were too great, to quantify, evaluate, and improve the model. This was basically due to a lack of good monitoring datasets for multiple species and abiotic media. For the bioaccumulation study, seawater samples were not taken when the biological sampling was done (2010) and species-specific properties such as growth and feeding rates were taken from a much earlier study (around 2000). These factors were considered largely responsible for the discrepancy

Box 7.1 A village LEO investigates an alarming color change in the village harbor water

In September 2012, the Environmental Program Manager for the tribal government of St. George Island (and also the LEO for St. George) was informed that the water in the harbor had turned red. On St. George Island, residents harvest food locally from the land and sea. Their intimate knowledge of the climate, environment, and biota translates into exceptional observational skills and a wealth of TEK. Consulting with local experts and elders, the LEO confirmed that there was no memory of this type of event ever having occurred in the past. Suspecting a harmful algal bloom and concerned about the safety of wild foods harvested from local waters for subsistence, he began to acquire information about the event. He collected surface and underwater photos (by placing his camera in a plastic bag and tying it to an oar), took a video of the harbor water, and collected water samples. He then used the only microscope on the island, his daughter's 'My First Microscope', to examine the samples and find that the cause of the red harbor water was a living organism. He then took photomicrographs using a point and shoot digital camera and posted the observations, images and video on the LEO Network website, including details of the event and comments about why the event was of local significance.

Once reviewed at the ANTHC Center for Climate and Health, the observation was transferred to a public, web-based Google map. The map link and a request for assistance was emailed to consultants at the University of Alaska Fairbanks (UAF) Institute of Marine Science and then by further referral, to consultants at the Woods Hole Oceanographic Institute (WHOI). Water samples collected by the LEO were sent to WHOI for genetic analysis and academic consultants used the data to provide a preliminary identification of the bloom source; not a dinoflagellate plankton such as is commonly associated with toxic red tides, but instead a harmless non-toxic ciliate called *Mesodinium rubrum*. Within a week of posting his observation, the LEO and the village had the answer and the findings were distributed to St. George Island residents. The outcome and guidance for future events were posted on the original Google map and shared with the LEO membership via webinar. Based on concerns about harmful algal blooms in Alaska, a topic-based web map was then developed by UAF, WHOI and LEO to track related future events posted by the network.

The LEO for the community of St. George, Alaska, with a home-made sample bottle, and his daughter's school microscope.

Box 7.2 Overview of the ArcRisk project

The ArcRisk project (Arctic Health Risks: Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling), an EU-funded project implemented between mid-2009 and 2014, aimed to investigate the potential influence of climate change on the exposure of humans to contaminants in the Arctic and, for comparison, several areas of Europe. The contaminants were mainly persistent organic pollutants (POPs) and mercury.

The project had three main components: modeling long-range transport of contaminants to the Arctic and the anticipated influence of climate change on these transport pathways; field and laboratory studies of contaminants in the Arctic environment and in fish and other animals consumed as traditional foods by indigenous peoples; and studies of contaminant levels in cohorts of human populations in the Arctic and northern Europe and, for comparison, in exposed populations in the Mediterranean area. Critical reviews of the effects of several contaminants on specific health outcomes were also conducted based on the results of studies published in the scientific literature.

The ArcRisk project has contributed to a better knowledge of climate change impacts on the transport pathways of contaminants to the Arctic, their transfer through abiotic Arctic ecosystems, and their accumulation in food webs, as well as to a better understanding of human exposure and the health effects of contaminants in the Arctic and selected populations in Europe. ArcRisk results indicate that the direct effects of warmer conditions on the transport of contaminants from source regions to the Arctic will not be large; however, climate change will increase the exposure risk for some contaminants and decrease it for others, depending on the specific physico-chemical properties of the contaminant. Future climate-mediated changes in the Arctic, such as altered biotopes and thus availability of fish and marine mammals used for human consumption, and increased exploitation of natural resources, may have a far greater influence on human exposure to contaminants than direct climate effects.

The project highlighted the need for better characterization of sources and more accurate quantification of POPs emissions in order to improve prediction of environmental exposure to these contaminants. More information is needed on the transformation products that may be formed under a warmer climate and on their impact on the health of Arctic ecosystems and humans. Improved modeling of contaminant bioaccumulation in ecosystems is also needed to reduce the large uncertainties involved in quantifying and evaluating human exposure to contaminants in the Arctic. More effort is needed to generate datasets in which multiple species and abiotic media are sampled at the same time and analyzed for organic pollutants.

The ArcRisk project has highlighted the importance of systematic and well-documented epidemiological research on the human health impacts of contaminants. Reviews of health outcomes in relation to several POPs were prepared within the project based on the screening of a large number of scientific studies in the literature. However, the complexity and diversity across studies in terms of variables selected and reporting practices made it difficult to combine and compare the original studies to obtain a coherent meta-analysis. To permit meta-analyses of results on health outcomes of contaminants to determine the magnitude of effects, reports should provide more background details, including tables of the basic data and descriptive statistics on the distributions of response and explanatory variables.

observed between measurements and model predictions. Given the difficulty of evaluating models of bioaccumulation in Arctic food webs under present-day climate conditions, it was considered almost impossible to predict how global climate change might affect bioaccumulation in the future, and thus human exposure, with any degree of certainty. Datasets are needed in which multiple species and abiotic media are sampled at the same time and analyzed for organic pollutants. Such datasets should enable improved understanding and more accurate bioaccumulation models for Arctic food webs. Basic research is also needed on how food webs, and ultimately human diets, are likely to respond to global climate change.

Dietary transitions, which may be partly a consequence of changes in the availability of local food items due to climate-mediated changes in habitats, are expected to play a greater role in future changes in POPs exposure (Armitage et al. 2011; Quinn et al. 2012; Gouin et al. 2013).

7.6 Conclusions and recommendations for addressing gaps in knowledge

The challenges posed by the combined impact of climate change, anthropogenic contaminants and zoonotic diseases on small, isolated Arctic communities will need to be met with adaptation strategies that aim to ensure effective responses to these challenges in order to maintain and enhance the stability of the community. Several examples of community-based responses have been presented in this chapter. Some conclusions based on these examples include the following:

- The community impacts of Arctic warming differ across the circumpolar region and tend to be more severe in regions with infrastructure dependent on permafrost stability and where ice is needed for travel, hunting and the protection of shoreline from coastal erosion during autumn and winter storms.
- Disruptive impacts on subsistence food species include changes in their range and a possible increase in the transport of some contaminants to the Arctic from source regions at more southerly latitudes and thus higher levels in top predators. This creates the potential for increased susceptibility of subsistence species to existing and emerging zoonotic pathogens.

- Disruptive climate-mediated impacts on rural drinking water systems and freshwater ponds and lakes include newly arriving species carrying potential waterborne pathogens, harmful algal blooms, and thawing permafrost containment of ponds used for community drinking water.
- Environmental threat assessment methods allow a community to establish existing and emerging threats, and to identify those residents that are most vulnerable to the prioritized threats. With appropriate technical support from the relevant agencies, communities can then develop adaptation strategies for responding to the threats identified. These strategies will focus on reducing exposure and risk. With the various elements of the strategy having been developed, metrics are selected to monitor trends in priority threats, recognize new threats as they emerge and evaluate the success of the adaptation strategy.
- Community-based environmental monitoring networks can help provide the data needed to better understand the effects of global climate change on movement of contaminants and pathogens through the Arctic region.

Gaps in knowledge concerning adaptation strategies for Arctic communities in a warming climate, particularly in terms of food and water security, may be addressed by:

- Continuing the development of culturally-specific risk communication.
- Developing regional models of contaminant transport, especially local release from thawing permafrost.
- Improving regional and circumpolar knowledge of the prevalence and trends in zoonotic pathogens in key subsistence species, and identifying intermediate and transport host species for key pathogens.
- Undertaking a systematic international circumpolar evaluation of pathogen and contaminant monitoring protocols, and basic public health adaptation strategies, to ensure the comparability of different monitoring data sets.

8. Key findings and recommendations

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The Arctic Monitoring and Assessment Programme (AMAP) 2015 human health assessment is an update of the previous human health assessment published by AMAP in 2009. The objectives of the 2015 assessment are two-fold. First, to report on recent AMAP human health-related work to fulfill requests from the Arctic Council Ministers at their meeting in Kiruna (Sweden) in 2013 regarding the health of Arctic peoples in relation to pollution, climate change and the combined effects of stressors. Second, to fulfill AMAP's commitments to support the Stockholm Convention on Persistent Organic Pollutants (POPs) and the Minamata Convention on Mercury, regarding human health-related issues. This report also provides further information and policy-relevant scientific recommendations for Arctic governments in their efforts to take remedial and preventive actions relating to contaminants. Moreover, the report addresses, for the first time, the effects of multiple stressors on small remote communities. Most of these communities are highly dependent on local wildlife resources for food, and are also highly impacted by environmental changes following a climate regime shift.

Evaluations of individual and population-based impacts of contaminants must be placed within the context of the general health status and vulnerability of indigenous and non-indigenous Arctic residents. Changing economies, climate, and social structures within the circumpolar region also play a significant role in health and well-being. In general, the conclusions and recommendations of the AMAP 2009 human health assessment are still valid. However, new monitoring data and scientific research, and the detection of emerging threats from zoonotic diseases (diseases of wildlife communicable to humans), have led to a strengthening of the previous conclusions as well as to several new conclusions.

The purpose of this chapter is to summarize the key findings and recommendations from the preceding chapters on human health in the Arctic. The ultimate goal is to identify clearly what has changed over the past six years in knowledge of contaminant-health interactions and to provide recommendations for consideration by public health practitioners, health and environment policy makers, and governments.

The main conclusions of the report are as follows:

- Human exposure to most POPs and metals is declining across many parts of the Arctic, but remains high among certain populations including some Inuit in Canada and Greenland. Even where levels of contaminants have declined significantly, current levels of several contaminants, such as mercury, are still a concern and still exceed blood guidance levels in some regions.
- Compounds such as certain brominated flame retardants and perfluorinated contaminants (PFCs) have been measured in human populations living in the Arctic. These and several other emerging contaminants can be transported to the Arctic from their source regions at lower latitudes, where they may not be internationally regulated, and thus can still be in widespread use.
- Dietary advice can be complex for several reasons: varying contaminant levels in different traditional foods and different areas of the Arctic; limited access to, or choice of, imported foods in remote communities; and shifting food preferences or availability of traditional foods among Arctic populations. Consumption of most traditional foods is still recommended as a healthy food choice, although preference is given to foods that are lower on the food chain, containing lower concentrations of contaminants.
- Several ongoing cohort studies in the Arctic and elsewhere provide increasing evidence for effects of contaminant exposure on fetal growth and development and cardiovascular effects and neurodevelopmental effects related to dietary mercury exposure. In addition, recent data indicate a reduced vaccine response in children associated with exposure to fluorinated substances.
- Interactions between climate change and contaminant transport have the potential to change human exposure in the Arctic significantly. Current understanding is inadequate to determine the likelihood and magnitude of the health impacts of these changes in exposure.

8.1 Key findings from the 2015 human health assessment

This human health assessment has documented several new findings that support previous conclusions as well as some that support new conclusions. These findings were drawn from research and monitoring activities that have taken place since the previous AMAP human health assessment report was released in 2009.

8.1.1 Biomonitoring

Biomonitoring is key to understanding past and current human exposure to contaminants, as well as for understanding whether levels are staying the same, increasing or decreasing spatially and/or temporally. This is important for tracking the effectiveness of international agreements such as the Stockholm Convention on Persistent Organic Pollutants and the Minamata Convention on Mercury. Biomonitoring can also aid in tracking the effectiveness of local dietary advice from health authorities intended to reduce human exposure to harmful substances.

- Levels of most POPs and metals measured in human tissues are declining in many regions of the circumpolar Arctic, although the decline is not uniform. Despite significant declines, certain sub-populations remain at risk.
    - Human tissue concentrations of many POPs, including polychlorinated biphenyls (PCBs) and dichlorodiphenyltrichloroethane (DDT), remain

elevated in some areas, particularly in eastern Canada and Greenland.

  - Human tissue concentrations of polybrominated diphenyl ethers (PBDEs) do not behave like most other POPs, which suggests an alternative exposure route. Baseline levels of several PFCs such as perfluorooctane sulfonate (PFOS) have been established in several Arctic regions; however there are insufficient data to describe trends.
  - Inuit continue to have the highest exposure levels of dietary mercury in the Arctic and their blood mercury concentrations are among some of the highest in the world. In Canada and Greenland, a substantial number of Inuit pregnant women and women of childbearing age still exceed some national blood guidelines.

- The results of the Tromsø Study, a population-based health survey in which POPs data were collected systematically between 1979 and 2008, indicated that human tissue concentrations followed calendar year dependent patterns. This trend and the changing composition of different POPs in serum over the past three decades, reflects the overall trends in production, use and release of the different POPs along with compound-specific persistence, bioaccumulation potential and global transport mechanisms.

8.1.2 Health effects

Different epidemiological studies in the circumpolar area have shown associations between contaminants and various health outcomes. It is important to note that associations are not the same as causal relationships between exposure to a single substance (or substances) and an effect. When finding an association between a contaminant and an effect, it is important to bear in mind the possibility that the studied substance is a proxy for other substances in the mixture of contaminants to which the study population has been exposed – both harmful and beneficial. The effects reported below are findings from different communities in the Arctic. However, due to differences in genetic composition, socio-cultural practices, local food consumption patterns and exposure mixtures, a finding in one population should not be extrapolated to another population without careful investigation and comparative information.

Neurobehavioral effects: Effects associated with methylmercury exposure have been documented in humans at successively lower exposures and it is clear that the developing brain is the most vulnerable organ system. Studies in the Faroe Islands and in Nunavik show that children exposed to methylmercury *in utero* exhibit a range of neurobehavioral effects (e.g. decreased motor function, attention span, verbal abilities, memory, and other cognitive functions including IQ, attention problems and hyperactive behavior) and that the effects are dose-dependent: the greater the mercury exposure, the greater the effect. Follow-up studies suggest that the deficits could be permanent. Given the continued development of the nervous system after birth, postnatal exposure to methylmercury is also likely to cause adverse effects, although the evidence is inconsistent. Some of the adverse effects of methylmercury on neurodevelopment may be masked by beneficial effects of seafood nutrients. Neurobehavioral effects of lead and PCB exposure are less clear.

Immunological effects: Certain environmental pollutants can adversely affect the development of the immune system. Young children in Nunavik have had a high incidence of infectious diseases (such as meningitis, bronchopulmonary infections, and middle ear infections) for many years. Recent studies to investigate the possibility that this could be partly due to maternal transfer of organochlorines with known immunotoxic properties during breastfeeding show that that prenatal exposure to organochlorines does increase susceptibility to infectious diseases (in particular otitis media). Most experimental evidence points to the role played by the dioxin-like PCB congeners. Perinatal exposure to PCBs and (especially) perfluorinated compounds in Faroese children has been associated with lower than expected antibody production after routine childhood immunizations. This decreased effect of childhood vaccines may indicate a more general immune system deficit through immunotoxicant exposure. The implications of inadequate antibody production highlight the need to significantly reduce immunotoxicant exposure in Arctic populations, as well as the need for long-term assessments of the health risks associated with exposure to immunotoxic contaminants.

Reproductive effects: There has been a significant and widespread decline in sperm count since at least the mid-20th century, with semen quality in Danish and Faroese men particularly low compared to men from other European countries. Although the causes of this decline are still unclear, high levels of PCBs have been linked to low semen quality. Other studies have found no consistent links between reproductive function in men and, for example, PFCs or high PBDE levels. Prenatal lead exposure is known to cause poorer growth in school-age children. Further study is needed on the influence of environmental exposure and genetic factors, particularly in relation to semen quality.

Cardiovascular effects: Studies show that the cardiovascular system may be vulnerable at high methylmercury exposures. Results are inconsistent, however. Some studies find a link between mercury and higher blood pressure (Nunavik adults and male whale hunters in the Faroe Islands) while others do not (Greenland adults). Heart rate variability is also affected, with decreased variability observed in mercury-exposed Nunavik adults and children, and James Bay Cree adults. The Faroese cohort study found prenatal mercury exposure affects cardiac autonomic activity in children. Whether this could be used as a predictor of chronic heart disease in adults is unknown.

Endocrine effects: Endocrine-disrupting chemicals can mimic, interfere with or block the function of endogenous hormones and so cause adverse developmental, reproductive, neurological, cardiovascular, metabolic and immune effects in humans. Exposure during early stages of fetal and neonatal development is especially critical and can disrupt the normal pattern of development and thus dramatically alter disease susceptibility in later life. The hormone disruptive effects of extracted lipophilic POPs from human serum have been demonstrated in epidemiological studies in Greenland. The combined effects of the POPs mixtures in serum was shown to include interference with steroid hormone receptor functions as well as the dioxin Ah-receptor. In addition, the combined effects of POPs mixtures in serum on the androgen receptor was a significant risk biomarker for breast cancer development in Inuit women.

Carcinogenic effects: During the latter half of the 20th century, cancer incidence increased substantially among all circumpolar Inuit in the Arctic region, especially for the lifestyle-associated lung, breast and colon cancers. Lung cancer now constitutes about 20% of all cancers in Inuit. Overall cancer rates now seem comparable to those of the United States, Canada and Denmark. The recent change in lifestyle and diet and thus environmental contaminant exposure of the Inuit might play a role in this.

Effect modifiers: Different chemical substances may target the same organ and induce similar effects in an additive or non-additive way. Because most studies concern human exposure to single chemicals rather than chemical mixtures, negative confounding could cause underestimation of those chemicals causing toxicity (e.g. methylmercury in seafood) and those having benefits (e.g. polyunsaturated omega-3 fatty acids in seafood).

8.1.3 Risk description

Risk assessment of the effects of environmental contaminants is an essential tool in the overall process for protecting the health of Arctic residents. A number of methods are available. One of the biggest challenges is how to translate contaminant concentrations measured in blood into information useful for risk characterization (i.e. the likelihood that specific effects will occur at these concentrations). Risk profiles are tools used in the Stockholm Convention review process for assessing whether particular chemicals are possible POPs. The risk profiles describe hazards, exposures and national/regional action on the substances under consideration.

ArcRisk was a project funded by the European Union and coordinated by AMAP. The health-related aspects of the project were implemented to compare diets, sources of exposure, blood contamination levels for mercury and POPs, and the influence of changing climate on human levels of contaminants in Arctic cohorts and, for comparison, cohorts from several areas of Europe.

- There was a large amount of inter-individual variation in mercury concentration within the ArcRisk study groups. Consumption of fish in the Mediterranean region and consumption of some species or parts of fish and marine mammals in the Arctic are the main sources of exposure to mercury in humans in both regions. Other sources of mercury exposure can also be important (dental amalgam, inhalation of elemental mercury in air, and ingestion of inorganic mercury in food particularly in highly contaminated areas) but their contribution is minor in comparison.
- ArcRisk results indicate that the direct effects of warmer conditions on the transport of contaminants from source regions to the Arctic will not be large; however, climate change will increase the exposure risk for some contaminants and decrease it for others, depending on the specific physico-chemical properties of the contaminant. Future climate-mediated changes in the Arctic, such as altered biotopes and thus availability of fish and marine mammals used for human consumption, and increased exploitation of natural resources, may have a far greater influence on human exposure to contaminants than direct climate effects.

8.1.4 Risk communication

The objective of risk communication activities is to inform individuals and communities of ways to improve their health and social well-being. Modern food advisories in the Arctic focus on changing behavior patterns by providing high quality information and recommendations for an overall healthy diet, including the consumption of the safest traditional foods.

- There has been little progress in evaluating the effectiveness of risk communication activities in the Arctic. While it is reported that declining human tissue levels are due to successful local food advisories, scientific evaluations which attempt to measure the success of risk communication activities and that take into account declining marine mammal and fish consumption and environmental concentrations, are lacking.
- While risk messages have been effective at several levels (including internationally during UN treaty negotiations), the messages can be misconstrued in subsequent media reporting. This can cause confusion in local areas where the messages are received through various mainstream media and can appear to conflict with local advice.
- The use of electronic two-way social media tools (e.g. blogs, tweets and social networking sites) is likely to increase in the Arctic over the next five years and may be suitable in some situations for providing and receiving messages related to risk reduction strategies. Social media tools may help overcome some of the obstacles to communicating in the North by using appropriate language and literacy, enhancing reach to remote communities or particular target groups (e.g. youth), and engaging the communities in two-way communications without the physical presence of a health communicator.
- Risk communication on contaminants is an important interim mechanism to reduce peoples' exposure to harmful chemicals. While there has been a significant reduction in exposure to contaminants in the Faroe Islands since the implementation of risk communication messaging regarding consumption of pilot whale, this has also had a considerable impact on Faroese cultural identity.

8.1.5 Climate change adaptation

Climate change is resulting in major environmental changes within the Arctic that directly threaten the security of traditional foods and community water supply and thus threaten community sustainability. In this context, climate change adaptation is defined as the ability of a community to change, or adopt new behaviors, in order to avoid or minimize risk, and to be able to continue the most important cultural, economic and health-related benefits of the present way of living.

- The most pronounced impacts of climate change in the Arctic occur in small communities in regions with infrastructure dependent on permafrost stability and where ice is needed for travel, hunting and the protection of the shoreline from coastal erosion.
- Climate change will have impacts on food species and contaminant transport as well as on existing and emerging zoonotic pathogens. A disruptive impact on drinking water systems is also likely.

8.2 Knowledge gaps

8.2.1 Biomonitoring

- Knowledge gaps remain for the main routes of human exposure in the Arctic for contaminants such as PBDEs. In addition, there are few data available for some new POPs, including contaminants newly listed under the Stockholm Convention, or those substances being considered for addition. Screening studies are needed to identify the presence and accumulation of these contaminants in the Arctic. Insufficient information is available on sources, health effects and exposure information.
- Studies suggest that climate-mediated environmental changes are occurring in the Arctic, affecting the safety of transport, hunting, trapping and fishing practices. The impact on wildlife health and availability/access of wildlife species as a traditional (country) food resource for Arctic residents is not fully understood. Information on contaminant transport and behavior in response to climate change is lacking, because many predictive models of contaminant transport and behavior do not account for a changing climate.

8.2.2 Health effects

- Follow-up studies on mother-child cohorts are needed to elucidate the impact of contaminant exposure during fetal life and the risk of disease later in life.
- Some studies have suggested potential effects of PCBs and PFCs on the immune system of children in the Arctic, however further studies are needed to improve understanding and quantify this relationship.
- Studies have suggested that exposure to certain POPs, such as PCBs, DDE, brominated flame retardants and perfluoroalkyl acids, are associated with an increased risk of developing Type 2 diabetes in Arctic populations. Despite recent studies, current knowledge remains limited.
- Cancer incidence has increased substantially among all circumpolar Inuit, especially for lung, breast and colon cancers, and the reasons for this are unclear, including the contribution of lifestyle changes and/or exposure to environmental contaminants. Studies are needed that focus on the relationship between cancer incidence, lifestyle changes and exposure to environmental contaminants in Arctic populations.
- Genetic predisposition to mercury neurotoxicity due to heterogeneities in relevant genes has been suggested, however studies in the Arctic are limited and are needed to explore this possibility.

8.2.3 Risk description

- Methodological approaches are lacking for estimating risks of single substances and mixtures of substances. These approaches could build on current toxicokinetic modelling (estimating exposure and risk from blood concentrations) and CoZMoMAN models (calculating human body burden from environmental emissions and exposures). Systematically collected monitoring data are essential for future risk estimation in Arctic populations. Further development of *in vitro/ex vivo* methods using serum POPs mixture extracts would also be useful for risk estimation and understanding the underlying cellular mechanisms.
- Most Arctic populations are living in large or medium-sized cities, and this trend will continue; for example, in Arctic Russia half the population is living in nine big cities. However, there are few studies or follow-up programs about Arctic urban environmental health risks.
- There is a lack of information about the genetic factors which could play a role in heightened health risks of some isolated populations in the Arctic.
- High inter-individual variations in mercury levels were identified in the ArcRisk project in some population groups; the reasons for this are unknown and further follow-up is needed on the causes, as well as on the underlying biological mechanisms.

8.2.4 Risk communication

- There is a lack of information on how risk communication on contaminants is practiced in several Arctic countries.
- For those countries where information about risk communication does exist, there is a lack of information on the success of the risk communication. The measure of success cannot be based solely on declining contaminant levels in the target populations.
- There is currently insufficient information on the possible use and effectiveness of electronic two-way social media tools in risk communication efforts.
- Research is needed on the development and deployment of risk communication messages, how they are received, understood and implemented, and methods for evaluating the effectiveness of the communication strategies, notably among different risk groups (elders, youth, pregnant women, and women of childbearing age).

8.2.5 Climate change adaptation

- Monitoring is lacking for early detection of climate-induced human health threats. Essential monitoring elements include contaminant levels in humans and consumed food species, zoonotic diseases in wildlife (i.e. animal-borne diseases communicable to humans), and observations of environmental parameters such as water quality, ice, permafrost, and weather.
    - Regional models of contaminant transport are lacking, especially concerning local release from thawing permafrost.
    - There is limited understanding of the prevalence and trends in zoonotic pathogens in key subsistence species, particularly at the regional level.
    - There is a lack of regional information on availability and accessibility of wildlife as traditional foods, and information on shifts in traditional foods consumed in relation to a changing environment.

8.3 Key recommendations

Based on the key findings of this assessment, recommendations for policy makers and for future research activities in the Arctic are as follows:

- **Further monitoring of contaminants is needed in all Arctic regions** to determine whether the declining trends of some POPs continue, and **monitoring of 'emerging' chemicals** is also needed. **Additional studies are needed to better understand recently observed health effects and risks** associated with current levels of exposure in the Arctic.
- **It is critical to continue to generate biomonitoring data in a coordinated, international approach**, as this is key to providing a globally comparable data set which will aid in understanding trends. This is important for tracking the effectiveness of international agreements such as the Stockholm Convention on Persistent Organic Pollutants and the Minamata Convention on Mercury.
- Biomonitoring studies show that mercury exposure is still very high among women of childbearing age and pregnant women in certain regions of the Arctic. Recent studies in Nunavik and the Faroe Islands confirm persistent, significant and multiple adverse neurodevelopmental outcomes in children and teenagers. **Strong international efforts should be made to reduce mercury emissions from all anthropogenic sources as quickly as possible.**
- Based on strengthened associations between prenatal exposure to methylmercury and neurobehavioral deficits at school age after adjustment for seafood nutrients such as polyunsaturated omega-3 fatty acids, **future studies on the effects of mercury should include and incorporate an analysis of seafood nutrients** to avoid underestimating the associations between childhood deficits and methylmercury exposure.
- Evaluation of the impacts of environmental contaminants on human health in the Arctic is complex, due to the many factors jointly influencing health. While many persistent substances have been regulated or banned and others are being phased out, new chemicals are being introduced that have not been studied adequately under the conditions of an Arctic ecosystem. **Precautionary approaches to chemical evaluation, introduction and general management are required for the 'emerging' chemicals** in the absence of full test data.
- Conclusions drawn in the literature about the effects of contaminant exposure on health outcomes are based on a variety of methods, study designs and techniques for analysis, which has made it very difficult to combine and compare original studies. **Studies should focus more on reporting descriptive statistics about the distributions of response variables and explanatory variables** which are needed when summarizing and meta-analyzing the magnitude of effects.
- During the past five years there have been several EU-funded research projects on the health risks of environmental contaminants which have included Arctic population data sets. **Study protocols should be harmonized wherever practical** to improve opportunities for comparing contaminant levels and effects data between different regions of the world.
- **Biomonitoring research that is linked to environmental change** is required to understand how climate change may influence contaminant levels in wildlife and humans as well as the availability/access of Arctic populations to traditional foods including wildlife food species.
- As environmental contaminants are not the only threat to Arctic populations, **adaptive strategies need to be developed at the community level that address contaminants, climate change and emerging zoonotic diseases, as well as interactions between these factors**. Development of comparable international and circumpolar monitoring protocols for pathogens and contaminants would simplify the development of generalized human and wildlife public health adaptation strategies. As the effects are not uniform across the Arctic, region-specific adaptation strategies will be required and could be built in part upon the general strategies.
- **Continued participation of analytical laboratories in an external QA/QC program is critical** to ensuring high quality and comparability of human biomonitoring data on POPs and metals across the Arctic. Small errors can have large impacts on interpretations of data, and therefore it is recommended that laboratory participation in an external QA/QC program is mandatory, in order for AMAP to demonstrate convincingly that spatial and temporal trends in exposure levels are real and not a result of analytical artifacts.
- **Communicating the risks and benefits associated with dietary choices of both traditional and imported foods must be done carefully and in partnership with affected communities**, taking into account a wide range of factors (social, economic, cultural), to ensure that advice is culturally appropriate.
- **Communicators need to be aware of the possible spread of messages to audiences that were not originally targeted**. Messages should be balanced and avoid, where possible, conflict with communications at regional versus international levels.
- **Vulnerable individuals in communities should be identified** as this can improve the development of population-specific adaptation strategies to reduce their risks of exposure to dietary contaminants and disease. Such individuals include elders, women of childbearing age, infants and children, residents with chronic diseases and those on medications that affect the immune system.
- Risk communication is not a solution to the Arctic contaminant issue. **Continued efforts globally are required to reduce levels of contaminants in the Arctic.** This includes ratifying and supporting global agreements to regulate contaminants, such as the Stockholm Convention and the Minamata Convention.

References

Personal communications

Ayotte, P. Université de Laval/INSPQ, Québec City, QC, Canada.

Berner, J. Alaska Native Tribal Health Consortium, Anchorage, Alaska, USA.

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Weihe, P. Department of Occupational Medicine and Public Health, The Faroese Hospital System, Torshavn, Faroe Islands.

General references

AANDC 2014. Synopsis of research conducted under the 2013-2014 Northern Contaminants Program. Ottawa: Aboriginal Affairs and Northern Development Canada (AANDC).

Abass, K., 2013. From *in vitro* hepatic metabolic studies towards human health risk assessment: Two case studies of diuron and carbosulfan. Pesticide Biochemistry and Physiology, 107:258-265.

Abass, K., A. Huusko, P. Nieminen, P. Myllynen, O. Pelkonen, K. Vahakangas and A. Rautio, 2013. Estimation of health risk by using toxicokinetic modelling: a case study of polychlorinated biphenyl PCB153. Journal of Hazardous Materials, 261:1-10.

Abass, K., P. Reponen, S. Mattila, A. Rautio and O. Pelkonen, 2014a. Comparative metabolism of benfuracarb in *in vitro* mammalian hepatic microsomes model and its implications for chemical risk assessment. Toxicology Letters, 224:290-299.

Abass, K., P. Reponen, S. Mattila, A. Rautio and O. Pelkonen, 2014b. Human variation and CYP enzyme contribution in benfuracarb metabolism in human in vitro hepatic models. Toxicology Letters, 224:300-309.

Achenbach, T.M. and L. Rescorla, 2001. Manual for the ASEBA School-Age Forms & Profiles. University of Vermont, Research Center for Children, Youth, & Families, Burlington, VT.

ACIA, 2005. Arctic Climate Impact Assessment. Cambridge University Press.

AHSS, 2014. Q Fever in Alaska – Update. State of Alaska Epidemiology Bulletin, Public Health Division, Alaska Health and Social Services (AHSS). 6 March 2014. Online: www.epi.alaska.gov/bulletins/docs/b2014_01.pdf

Ajzen, I. and M. Fishbein, 1980. Understanding Attitudes and Predicting Social Behavior. Prentice Hall.

Akerblom, S., A. Bignert, M. Meili, L. Sonesten and M. Sundbom, 2014. Half a century of changing mercury levels in Swedish freshwater fish. Ambio, 43(S1):91-103.

Alkazemi, D., G.M. Egeland, L.J. Roberts, H.M. Chan and S. Kubow, 2013. New insights regarding tissue Se and Hg interactions on oxidative stress from plasma IsoP and IsoF measures in the Canadian Inuit population. Journal of Lipid Research, 54:1972-1979.

Alvarez-Pedrerol, M., N. Ribas-Fitó, M. Torrent, D. Carrizo, J.O. Grimalt and J. Sunyer, 2008a. Effects of PCBs, *p,p'*-DDT, *p,p'*-DDE, HCB and β-HCH on thyroid function in preschool children. Occupational and Environmental Medicine, 65:452-457.

Álvarez-Pedrerol, M., N. Ribas-Fitó, M. Torrent, D. Carrizo, R. Garcia-Esteban, J.O. Grimalt and J. Sunyer, 2008b. Thyroid disruption at birth due to prenatal exposure to β-hexachlorocyclohexane. Environment International, 34:737-740.

AMAP, 1998. AMAP Assessment Report: Arctic Pollution Issues. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

AMAP, 2003. AMAP Assessment 2002: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo.

AMAP, 2004. Persistent Toxic Substances. Food Security and Indigenous Peoples of the Russian North. Final Report. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

AMAP, 2009. AMAP Assessment 2009: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

AMAP, 2011. Snow, Water, Ice and Permafrost in the Arctic (SWIPA): Climate Change and the Cryosphere. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

AMAP, 2014. Trends in Stockholm Convention Persistent Organic Pollutants (POPs) in Arctic Air, Human Media and Biota. By: S. Wilson, H. Hung, A. Katsoyiannis, D. Kong, J. van Oostdam, F. Riget and A. Bignert. AMAP Technical Report No. 7 (2014). Arctic Monitoring and Assessment Programme (AMAP), Oslo.

Anda, E.E., E. Nieboer, A.A. Dudarev, T.M. Sandanger and J.O. Odland, 2007. Intra- and intercompartmental associations between levels of organochlorines in maternal plasma, cord plasma and breast milk, and lead and cadmium in whole blood, for indigenous peoples of Chukotka, Russia. Journal of Environmental Monitoring, 9:884-893.

Andersen, M.E., J.L. Butenhoff, S.C. Chang, D.G. Farrar, G.L. Kennedy Jr., C. Lau, G.W. Olsen, J. Seed and K.B. Wallace, 2008. Perfluoroalkyl acids and related chemistries – toxicokinetics and modes of action. Toxicological Sciences, 102:3-14.

Anderson, D., T.E. Schmid and A. Baumgartner, 2014. Male-mediated developmental toxicity. Asian Journal of Andrology, 16:81-88.

Andreassen, J.W.P., 2014. Prevalence of diabetes and impaired glucose regulation in Faroe Islands. World Diabetes Congress 2104. Melbourn, Australia.

ANSES, 2010. Guidelines on PCB. French Agency for Food, Environmental and Occupational Health & Safety (ANSES). www.anses.fr/en/content/what-are-critical-blood-concentration-levels-pcbs (accessed December 2014).

ANTCH, 2014. Alaska Native Tribal Health Consortium. www.anthc.org/chs/ces/climate/leo

Armitage, J.M., U. Schenker, M. Scheringer, J.W. Martin, M. Macleod and I.T. Cousins, 2009. Modeling the global fate and transport of perfluorooctane sulfonate (PFOS) and precursor compounds in relation to temporal trends in wildlife exposure. Environmental Science and Technology, 43:9274-9280.

Armitage, J.M., C.L. Quinn and F. Wania, 2011. Global climate change and contaminants – an overview of opportunities and priorities for modelling the potential implications for long-term human exposure to organic compounds in the Arctic. Journal of Environmental Monitoring, 13:1532-1546.

Armstrong, B., K. Tofflemire, E. Myles, O. Receveur and L. Chan, 2007. Monitoring temporal trends of human environmental contaminants in the NWT study. Department of Health and Social Services, Government of the Northwest Territories.

Aslibekyan, S., H.W. Wiener, P.J. Havel, K.L. Stanhope, D.M. O'Brien, S.E. Hopkins, D.M. Absher, H.K. Tiwari and B.B. Boyer, 2014. DNA methylation patterns are associated with n-3 fatty acid intake in Yup'ik people. The Journal of Nutrition, 144:425-430.

Audet-Delage, Y., N. Ouellet, R. Dallaire, É. Dewailly and P. Ayotte, 2013. Persistent organic pollutants and transthyretin-bound thyroxin in plasma of Inuit women of childbearing age. Environmental Science and Technology, 47:13086-13092.

Aylward, L.L., S.M. Hays, J.S. Lakind and J.J. Ryan, 2003. Rapid Communication: Partitioning of persistent lipophilic compounds, including dioxins, between human milk lipid and blood lipid: an initial assessment. Journal of Toxicology and Environmental Health A, 66:1-5.

Ayotte, P., A. Carrier, N. Ouellet, V. Boiteau, B. Abdous, E.A. Sidi, M.L. Chateau-Degat and É. Dewailly, 2011. Relation between methylmercury exposure and plasma paraoxonase activity in Inuit adults from Nunavik. Environmental Health Perspectives, 119:1077-1083.

Bandura, A., 1992. Exercise of personal agency through the self-efficacy mechanism. In: Schwarzer, R. (Ed.), Self-efficacy: Thought Control of Action, pp. 3-38. Hemisphere.

Barregård, L. 2006. Hälsorelaterad miljöövervakning av exponering för metaller (kvicksilver) hos gravida. Arbets- och miljömedicin. Göteborgs Universitet, Göteborg. Rapport till Naturvårdsverket.

Becker, D., 1974. The health belief model and personal health behavior. Health Education Monographs, 2:324-508.

Bellinger, D.C., 2009. Interpreting epidemiologic studies of developmental neurotoxicity: conceptual and analytic issues. Neurotoxicology and Teratology, 31:267-274.

Bellinger, D.C., K.M. Stiles and H.L. Needleman, 1992. Low-level lead exposure, intelligence and academic achievement: a long-term follow-up study. Pediatrics, 90:855-861.

Bennett, G.G. and R.E. Glasgow, 2009. The delivery of public health interventions via the internet: Actualizing their potential. Annual Review of Public Health, 30:273-292.

Berg, V., T.H. Nøst, S. Huber, C. Rylander, S. Hansen, A.S. Veyhe, O.M. Fuskevåg, J.Ø. Odland and T.M. Sandanger, 2014. Maternal serum concentrations of per- and polyfluoroalkyl substances and their predictors in years with reduced production and use. Environment International, 69:58-66.

Bergdahl I.A., M. Svensson and T. Lundh, 2006. Metallmätningar hos gravida kvinnor i Västerbotten. Rapport till Naturvårdverket kontrakt nr: 215 0305.

Berner, J. and C. Furgal, 2005. Human health. In: Arctic Climate Impact Assessment, pp. 863-906. Cambridge University Press.

Beyersmann, D. and A. Hartwig, 2008. Carcinogenic metal compounds: recent insight into molecular and cellular mechanisms. Archives of Toxicology, 82:493-512.

Bhattacharjee, P., M. Banerjee and A.K. Giri, 2013. Role of genomic instability in arsenic-induced carcinogenicity. A review. Environment International, 53:29-40.

Bilić Čace, I., A. Milardović, I. Prpić, R. Krajina, O. Petrović, P. Vukelić, Z. Špirić, M. Horvat, D. Mazej and J. Snoj, 2011. Relationship between the prenatal exposure to low-level of mercury and the size of a newborn's cerebellum. Medical Hypotheses, 76:514-516.

Bilrha, H., R. Roy, E. Wagner, M. Belles-Isles, J.L. Bailey and P. Ayotte, 2004. Effects of gestational and lactational exposure to organochlorine compounds on cellular, humoral, and innate immunity in swine. Toxicological Sciences, 77:41-50.

Binnington, M.J., C.L. Quinn, M.S. McLachlan and F. Wania, 2014. Evaluating the effectiveness of fish consumption advisories: modeling prenatal, postnatal and childhood exposures to persistent organic pollutants. Environmental Health Perspectives, 122:178-186.

Bjermo, H., E. Ax, T. Cantillana, G. Glynn, P.O. Darnerud and A.K. Lindroos, 2013a. Miljöföroreningar i blod och urin och kopplingar till rapporterat matintag i Riksmaten 2010-11 – resultatsammanställning. Report from National Food Administration to the Swedish National Environmental Monitoring Programme. Contract 215 1108/219 1009.

Bjermo, H., P.O. Darnerud, S. Lignell, M. Pearson, P. Rantakokko, C. Nälsén, H. Enghardt Barbieri, H. Kiviranta, A.K. Lindroos and A. Glynn, 2013b. Fish intake and breastfeeding time are associated with serum concentrations of organochlorines in a Swedish population. Environment International, 51:88-96.

Bjermo, H., P.O. Darnerud, M. Pearson, H. Enghardt Barbieri, A.K. Lindroos, C. Nälsén, C.H. Lindh, B.A.G. Jönsson and A. Glynn, 2013c. Serum concentrations of perfluorinated alkyl acids and their associations with diet and personal characteristics among Swedish adults. Molecular Nutrition and Food Research, 57:2206-2215.

Bjermo, H., S. Sand, C. Nälsén, T. Lundh, H. Enghardt Barbieri, M. Pearson, A.K. Lindroos, B.A.G. Jönsson, L. Barregård, and P.O. Darnerud, 2013d. Lead, mercury, and cadmium in blood and their relation to diet among Swedish adults. Food and Chemical Toxicology, 57:161-169.

Bjerregaard, P., 2010. Inuit Health in Transition – Greenland survey 2005-2010. Population sample and survey methods. SIF Writings on Greenland vol. 19.

Bjerregaard, P. and C. Jeppesen, 2010. Inuit dietary patterns in modern Greenland. International Journal of Circumpolar Health, 69:13-24.

Bjerregaard, P. and G. Mulvad, 2012. The best of two worlds: how the Greenland Board of Nutrition has handled conflicting evidence about diet and health. International Journal of Circumpolar Health, 71:18588. http://dx.doi.org/10.3402/ijch.v71i0.18588

Bjerregaard, P., E. Dewailly, P. Ayotte, T. Pars, L. Ferron and G. Mulvad, 2001. Exposure of Inuit in Greenland to organochlorines through the marine diet. Journal of Toxicology and Environmental Health, 62:69-81.

Bjerregaard, P., S. Chatwood, B. Denning, L. Joseph and T.K. Young, 2012. Sex ratios in the Arctic – do man-made chemicals matter? American Journal of Human Biology, 24:165-169.

Bjerregaard, P., H.S. Pedersen, N.O. Nielsen and É. Dewailly, 2013. Population surveys in Greenland 1993–2009: temporal trend of PCBs and pesticides in the general Inuit population by age and urbanisation. Science of the Total Environment, 454-455:283-288.

Bjork, C., H. Nenonen, A. Giwercman, A. Bergman, L. Rylander and Y.L. Giwercman, 2011. Persistent organic pollutants have dose and CAG repeat length dependent effects on androgen receptor activity in vitro. Reproductive Toxicology, 32:293-297.

Blanchet, C. and L. Rochette, 2008. Nutrition and food consumption among the Inuit of Nunavik. Quebec: Institut national de santé publique du Québec (INSPQ) and Nunavik Regional Board of Health and Social Services (NRBHSS).

Bloom, M.S., R.L. Jansing, K. Kannan, R. Rej and E.F. Fitzgerald, 2014. Thyroid hormones are associated with exposure to persistent organic pollutants in aging residents of upper Hudson River communities. International Journal of Hygiene and Environmental Health, 217:473-482.

Boas, M., U. Feldt-Rasmussen and K.M. Main, 2012. Thyroid effects of endocrine disrupting chemicals. Molecular and Cellular Endocrinology, 355:240-248.

Bonde, J.P., G. Toft, L. Rylander, A. Rignell-Hydbom, A. Giwercman, M. Spano, G.C. Manicardi, D. Bizzaro, J.K. Ludwicki, V. Zvyezday, E.C. Bonefeld-Jørgensen, H.S. Pedersen, B.A. Jonsson and A.M. Thulstrup, 2008. Fertility and markers of male reproductive function in Inuit and European populations spanning large contrasts in blood levels of persistent organochlorines. Environmental Health Perspectives, 116:269-277.

Bonefeld-Jørgensen, E.C., 2009. Genetics and contaminants. In: AMAP Assessment 2009: Human Health in the Arctic, pp. 111-130. Arctic Monitoring and Assessment Programmme (AMAP).

Bonefeld-Jørgensen, E.C., 2010. Biomonitoring in Greenland: human biomarkers of exposure and effects – a short review. Rural and Remote Health, 10:1362.

Bonefeld-Jørgensen, E.C. and P. Ayotte, 2003. Toxicological properties of persistent organic pollutants and related health effects of concern for the Arctic populations. In: AMAP Assessment 2002: Human Health in the Arctic, pp 57-74. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

Bonefeld-Jørgensen, E.C. and M. Long, 2010. Dioxin-like activity in the blood of Greenlandic Inuit and Danish women: a pilot study. International Journal of Circumpolar Health, 69:181-194.

Bonefeld-Jørgensen, E.C., H.R. Andersen, T.H. Rasmussen and A.M. Vinggaard, 2001. Effect of highly bioaccumulated polychlorinated biphenyl congeners on estrogen and androgen receptor activity. Toxicology, 158:141-153.

Bonefeld-Jørgensen, E.C., P.S. Hjelmborg, T.S. Reinert, B.S. Andersen, V. Lesovoy, C.H. Lindh, L. Hagmar, A. Giwercman, M. Erlandsen, G.C. Manicardi, M. Spano, G. Toft and J.P. Bonde, 2006. Xenoestrogenic activity in blood of European and Inuit populations. Environmental Health, 5:12. doi:10.1186/1476-069X-5-12.

Bonefeld-Jørgensen, E.C., M. Long, R. Bossi, P. Ayotte, G. Asmund, T. Krüger, M. Ghisari, G. Mulvad, P. Kern, P. Nzulumiki and É. Dewailly, 2011. Perfluorinated compounds are related to breast cancer risk in Greenlandic Inuit: a case control study. Environmental Health, 10:88. doi:10.1186/1476-069X-10-88.

Bonefeld-Jørgensen, E.C., M. Ghisari, M. Wielsøe, C. Bjerregaard-Olesen, L. Stigaard Kjeldsen and M. Long, 2014. Biomonitoring and hormone-disrupting effect biomarkers of Persistent Organic Pollutants *in vitro* and *ex vivo*. Basic and Clinical Pharmacology and Toxicology, 115:118-128.

Boobis, A., A. Chiodini, J. Hoekstra, P. Lagiou, H. Przyrembel, J. Schlatter, K. Schutte, H. Verhagen and B. Watzl, 2013. Critical appraisal of the assessment of benefits and risks for foods, 'BRAFO Consensus Working Group'. Food and Chemical Toxicology, 55:659-675.

Boucher, O., G. Muckle, D. Saint-Amour, É. Dewailly, P. Ayotte, S.W. Jacobson, J.L. Jacobson and C.H. Bastien, 2009. The relation of lead neurotoxicity to the event-related potential P3b component in Inuit children from Arctic Quebec. Neurotoxicology, 30:1070-1077.

Boucher, O., C.H. Bastien, D. Saint-Amour, É. Dewailly, P. Ayotte, J.L. Jacobson, S.W. Jacobson and G. Muckle, 2010. Prenatal exposure to methylmercury and PCBs affects distinct stages of information processing: an event-related potential study with Inuit children. Neurotoxicology, 31:373-384.

Boucher, O., M.J. Burden, G. Muckle, D. Saint-Amour, P. Ayotte, É. Dewailly, C.A. Nelson, S.W. Jacobson and J.L. Jacobson, 2011. Neurophysiologic and neurobehavioral evidence of beneficial effects of prenatal omega-3 fatty acid intake on memory function at school age. American Journal of Clinical Nutrition, 93:1025-1037.

Boucher, O., M.J. Burden, G. Muckle, D. Saint-Amour, P. Ayotte, É. Dewailly, C.A. Nelson, S.W. Jacobson and J.L. Jacobson, 2012a. Response inhibition and error monitoring during a visual go/no-go task in Inuit children exposed to lead, polychlorinated biphenyls, and methylmercury. Environmental Health Perspectives, 120:608-615.

Boucher, O., S.W. Jacobson, P. Plusquellec, É. Dewailly, P. Ayotte, N. Forget-Dubois, J.L. Jacobson and G. Muckle, 2012b. Prenatal methylmercury, postnatal lead exposure, and evidence of attention deficit hyperactivity disorder among Inuit children in Arctic Quebec. Environmental Health Perspectives, 120:1456-1461.

Brantsæter, A.L. and H.K. Knutsen (lead authors), 2013. Effects of Climate/Global Change on Future Dietary Exposure in ArcRisk Study Groups. ArcRisk Deliverable Number: D39. Norwegian Institute of Public Health, Oslo, Norway.

Braune, B.M., P.M. Outridge, A.T. Fisk, D.C.G. Muir, P.A. Helm, K. Hobbs, P.F. Hoekstra, Z.A. Kuzyk, M. Kwan, R.J. Letcher, W.L. Lockhart, R.J. Norstrom, G.A. Stern and I. Stirling, 2005. Persistent organic pollutants and mercury in marine biota of the Canadian Arctic: An overview of spatial and temporal trends. Science of the Total Environment, 351-352:4-56.

Breivik, K., G. Czub, M.S. McLachlan and F. Wania, 2010. Towards an understanding of the link between environmental emissions and body burdens of PBCs using CoZMoMAN. Environment International, 36:85-91.

Brokken, L.J.S., L. Rylander, B.A. Jonsson, M. Spano, H.S. Pedersen, J.K. Ludwicki, V. Zviezdai, D. Bizzaro, G.C. Manicardi, G. Toft, J.P. Bonde, A. Giwercman and Y. Lundberg Giwercman, 2013. Non-linear association between androgen receptor CAG and GGN repeat lengths and reproductive parameters in fertile European and Inuit men. Molecular and Cellular Endocrinology, 370:163-171.

Brubaker, M., J. Berner and M. Tchefipanoff, 2013. LEO, the Local Environmental Observer Network: a community-based system for surveillance of climate, environment, and health events. International Journal of Circumpolar Health, 72:22447.

Budtz-Jorgensen, E., P. Grandjean and P. Weihe, 2007. Separation of risks and benefits of seafood intake. Environmental Health Perspectives, 115:323-327.

Burns, J.S., P.L. Williams, O. Sergeyev, S. Korrick, M.M. Lee, B. Revich, L. Altshul, J.T. Del Prato, O. Humblet, D.G. Patterson Jr., W.E. Turner, L.L. Needham, M. Starovoytov and R. Hauser, 2011. Serum dioxins and polychlorinated biphenyls are associated with growth among Russian boys. Pediatrics, 127:e59-68.

Burse, V., M. Deguzman, K. Korver, A. Najam, C. Williams, B. Hannon and R. Therell, 1997. Preliminary investigation of the use of dried blood spots for the assessment of in-utero exposure to environmental pollutants. Biochemical and Molecular Medicine, 61:236-239.

Butenhoff, J.L., D.W. Gaylor, J.A. Moore, G.W. Olsen, J. Rodricks, J.H. Mandel and L.R. Zobel, 2004. Characterization of risk for general population exposure to perfluorooctanoate. Regulatory Toxicology and Pharmacology, 39:363-380.

Butenhoff, J.L., G.L. Kennedy Jr., S.C. Chang and G.W. Olsen, 2012. Chronic dietary toxicity and carcinogenicity study with ammonium perfluorooctanoate in Sprague-Dawley rats. Toxicology, 298:1-13.

Byrne, C., S.D. Divekar, G.B. Storchan, D.A. Parodi and M.B. Martin, 2009. Cadmium - a metallohormone? Toxicology and Applied Pharmacology, 238:266-271.

Carlsen, E., A. Giwercman, N. Keiding and N.E. Skakkebaek, 1992. Evidence for decreasing quality of semen during past 50 years. BMJ, 305:609-613.

Carlsson, P., D. Herzke and R. Kallenborn, 2014a. Enantiomer-selective and quantitative trace analysis of selected persistent organic pollutants (POP) in traditional food from western Greenland. Journal of Toxicology and Environmental Health, 77:616-627.

Carlsson, P., D. Herzke and R. Kallenborn, 2014b. Polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and perfluorinated alkylated substances (PFASs) in traditional seafood items from western Greenland. Environmental Science and Pollution Research, 21:4741-4750.

Carpenter, D.O., 2008. Environmental contaminants as risk factors for developing diabetes. Reviews on Environmental Health, 23:59-74.

Carpenter, D.O., K. Arcaro and D.C. Spink, 2002. Understanding the human health effects of chemical mixtures. Environmental Health Perspectives, 110(S1):25-42.

Carrie, J., F. Wang, H. Sanei, R.W. Macdonald, P.M. Outridge and G.A. Stern, 2010. Increasing contaminant burdens in an Arctic fish, burbot (*Lota lota*) in a warming climate. Environmental Science and Technology, 44:316-322.

Carriere, G.M., M. Tjepkema, J. Pennock and N. Goedhuis, 2012. Cancer patterns in Inuit Nunangat: 1998-2007. International Journal of Circumpolar Health, 71:18581. http://dx.doi.org/10.3402/ijch.v71i0.18581.

Cavalleri, A., L. Belotti, F. Gobba, G. Luzzana, P. Rosa and P. Seghizzi, 1995. Colour vision loss in workers exposed to elemental mercury vapour. Toxicology Letters, 77:351-356.

CDC, 2010. Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women. Centers for Disease Control and Prevention, Atlanta. www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf.

CDC, 2012. Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention. Centers for Disease Control and Prevention (CDC), Atlanta. www.cdc.gov/nceh/lead/acclpp/final_document_030712.pdf.

CDC, 2015. NHANES, 1999-2000. National Health and Nutrition Examination Survey. Centers for Disease Control and Prevention, Atlanta. wwwn.cdc.gov/nchs/nhanes/search/nhanes99_00.aspx [accessed July 2015]

CEC, 2011. Trinational Biomonitoring Study: Assessment of Persistent Organic Pollutants and Selected Metals in the Blood of First-Birth Mothers in Southern Canada and Mexico and in Women of Reproductive Age in the United States. Commission for Environmental Cooperation (CEC), Montreal.

CEOH, 1994. Update of evidence for low-level effects of lead and blood-lead intervention levels and strategies – final report of the working group. Federal–Provincial Committee on Environmental and Occupational Health (CEOH). Environmental Health Directorate, Health Canada, Ottawa, Canada.

Chan, L., 2012a. Inuit Health Survey 2007-2008, Contaminant Assessment in Nunavut. Nunavut Steering Committee.

Chan, L., 2012b. Inuit Health Survey 2007-2008, Contaminant Assessment in Nunatsiavut. Nunatsiavut Steering Committee.

Chan, L., 2012c. Inuit Health Survey 2007-2008, Contaminant Assessment in the Inuvialuit Settlement Region. Inuvialuit Settlement Region Steering Committee.

Chao, W.Y., C.C. Hsu and Y.L. Guo, 1997. Middle-ear disease in children exposed prenatally to polychlorinated biphenyls and polychlorinated dibenzofurans. Archives of Environmental Health, 52:257-262.

Chateau-Degat, M.L., É. Dewailly, R. Louchini, E. Counil, M. Noel, A. Ferland, M. Lucas, B. Valera, J.M. Ekoe, R. Ladouceur, S. Dery and G. Egeland, 2010a. Cardiovascular burden and related risk factors among Nunavik (Quebec) Inuit: insights from baseline findings in the circumpolar Inuit health in transition cohort study. Canadian Journal of Cardiology, 26:190-196.

Chateau-Degat, M.L., É. Dewailly, M. Noel, B. Valera, A. Ferland, E. Counil, P. Poirier and G.M. Egeland, 2010b. Hypertension among the Inuit from Nunavik: should we expect an increase because of obesity? International Journal of Circumpolar Health, 69:361-372.

Chateau-Degat, M.L., D. Pereg, R. Dallaire, P. Ayotte, S. Dery and É. Dewailly, 2010c. Effects of perfluorooctanesulfonate exposure on plasma lipid levels in the Inuit population of Nunavik (Northern Quebec). Environmental Research, 110:710-717.

Chateau-Degat, M.L., D.A. Dannenbaum, G.M. Egeland, E. Nieboer, E.A. Laouan Sidi, B. Abdous and É. Dewailly, 2011a. A comparison of the metabolic response to abdominal obesity in two Canadian Inuit and First Nations population. Obesity, 19:2254-2260.

Chateau-Degat, M.L., É. Dewailly, G. Charbonneau, E.A. Laouan-Sidi, A. Tremblay and G.M. Egeland, 2011b. Obesity risks: towards an emerging Inuit pattern. International Journal of Circumpolar Health, 70:166-177.

Choi, A.L., P. Weihe, E. Budtz-Jorgensen, P.J. Jorgensen, J.T. Salonen, T.P. Tuomainen, K. Murata, H.P. Nielsen, M.S. Petersen, J. Askham and P. Grandjean, 2009. Methylmercury exposure and adverse cardiovascular effects in Faroese whaling men. Environmental Health Perspectives, 117:367-372.

Choi, A.L., U.B. Mogensen, K.S. Bjerve, F. Debes, P. Weihe, P. Grandjean and E. Budtz-Jorgensen, 2014. Negative confounding by essential fatty acids in methylmercury neurotoxicity associations. Neurotoxicology and Teratology, 42:85-92.

Coffman, J., 2002. Public communication campaign evaluation: An environmental scan of challenges, criticisms, practice, and opportunities. Harvard Family Research Project. Communications Consortium Media Center, Washington, DC.

Connelly, N.A. and B.A. Knuth, 1998. Evaluating risk communication: examining target audience perceptions about four presentation formats for fish consumption health advisory information. Risk Analysis, 18:649-659.

Cote, S., S. Dodin, C. Blanchet, G. Mulvad, H.S. Pedersen, B.J. Holub and É. Dewailly, 2004. Very high concentrations of n-3 fatty acids in peri- and postmenopausal Inuit women from Greenland. International Journal of Circumpolar Health, 63(S2):298-301.

Couture, A., B. Lévesque, É. Dewailly, G. Muckle, S. Déry and J.-F. Proulx, 2012. Lead exposure in Nunavik: From research to action. International Journal of Circumpolar Health, 71:1-8.

Covello, V.T. and F.W. Allen, 1988. Seven Cardinal Rules of Risk Communication. US Environmental Protection Agency, Washington, DC.

Crump, K.S., C. Van Landingham, T.S. Bowers, D. Cahoy and J.K. Chandalia, 2013. A statistical reevaluation of the data used in the Lanphear et al. (2005) pooled-analysis that related low levels of blood lead to intellectual deficits in children. Critical Reviews in Toxicology, 43:785-799.

Cui, Y., Y.G. Zhu, R. Zhai, Y. Huang, Y. Qiu and J. Liang, 2005. Exposure to metal mixtures and human health impacts in a contaminated area in Nanning, China. Environment International, 31:784-790.

Čupr, P., O. Mikeš, A. Krsková and M. Černá, 2011. Long-term trends of POPs in human milk in Czech Republic and application for human health risk assessment. Environmental Health Perspectives. 23th ISEE Annual Meeting, 13-16 September 2011, Barcelona, Spain, Abstract Book: P-0472.

Curren, M.S., K. Davis, C.L. Liang, B. Adlard, W.G. Foster, S.G. Donaldson, K. Kandola, J. Brewster, M. Potyrala and J. Van Oostdam, 2014. Comparing plasma concentrations of persistent organic pollutants and metals in primiparous women from northern and southern Canada. Science of the Total Environment, 479-480:306-318.

Curren, M.S, C.L. Liang, K. Davis, K. Kandola, J. Brewster, M. Potyrala and H.M. Chan, 2015. Assessing determinants of maternal blood concentrations for persistent organic pollutants and metals in the Eastern and Western Canadian Arctic. Science of the Total Environment, 527-528:150-158.

Curry, P., C. Ribble, W. Sears, W. Hutchins, K. Orsel, D. Godson, R. Lindsay, A. Dibernardo and S. Kutz, 2014. Blood collected on filter paper for wildlife serology: Detecting antibodies to *Neospora caninum*, West Nile virus, and five bovine viruses in reindeer. Journal of Wildlife Diseases, 50:297-307.

Dalgard, C., M.S. Petersen, A.V. Schmedes, I. Brandslund, P. Weihe and P. Grandjean, 2010. High latitude and marine diet: vitamin D status in elderly Faroese. British Journal of Nutrition, 104:914-918.

Dalgard, C., M.S. Petersen, P. Weihe and P. Grandjean, 2011. Vitamin D status in relation to glucose metabolism and type 2 diabetes in septuagenarians. Diabetes Care, 34:1284-1288.

Dallaire, F., É. Dewailly, G. Muckle and P. Ayotte, 2003. Time trends of persistent organic pollutants and heavy metals in umbilical cord blood of Inuit infants born in Nunavik (Quebec, Canada) between 1994 and 2001. Environmental Health Perspectives, 111:1660-1664.

Dallaire, F., É. Dewailly, G. Muckle, C. Vezina, S.W. Jacobson, J.L. Jacobson and P. Ayotte, 2004. Acute infections and environmental exposure to organochlorines in Inuit infants from Nunavik. Environmental Health Perspectives, 112:1359-1365.

Dallaire, F., É. Dewailly, C. Vezina, G. Muckle, J.P. Weber, S. Bruneau and P. Ayotte, 2006. Effect of prenatal exposure to polychlorinated biphenyls on incidence of acute respiratory infections in preschool Inuit children. Environmental Health Perspectives, 114:1301-1305.

Dallaire, R., É. Dewailly, D. Pereg, S. Dery and P. Ayotte, 2009a. Thyroid function and plasma concentrations of polyhalogenated compounds in Inuit adults. Environmental Health Perspectives, 117:1380-1386.

Dallaire, R., G. Muckle, É. Dewailly, S.W. Jacobson, J.L. Jacobson, T.M. Sandanger, C.D. Sandau and P. Ayotte, 2009b. Thyroid hormone levels of pregnant Inuit women and their infants exposed to environmental contaminants. Environmental Health Perspectives, 117:1014-1020.

Dallaire, R., É. Dewailly, P. Ayotte, N. Forget-Dubois, S.W. Jacobson, J.L. Jacobson and G. Muckle, 2013. Exposure to organochlorines and mercury through fish and marine mammal consumption: associations with growth and duration of gestation among Inuit newborns. Environment International, 54:85-91.

Dallaire, R., É. Dewailly, P. Ayotte, N. Forget-Dubois, S.W. Jacobson, J.L. Jacobson and G. Muckle, 2014. Growth in Inuit children exposed to polychlorinated biphenyls and lead during fetal development and childhood. Environmental Research, 134:17-23.

Day, G.E., A.P. Lanier, L. Bulkow, J.J. Kelly and N. Murphy, 2010. Cancers of the breast, uterus, ovary and cervix among Alaska Native women, 1974-2003. International Journal of Circumpolar Health, 69:72-86.

Debes, F., E. Budtz-Jorgensen, P. Weihe, R.F. White and P. Grandjean, 2006. Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years. Neurotoxicology and Teratology, 28:536-547.

Debes, F., P. Weihe and P. Grandjean, 2016. Cognitive deficits at age 22 years associated with prenatal exposure to methylmercury. Cortex, 74:358-369.

Delbès, G., B.F. Hales and B. Robaire, 2010. Toxicants and human sperm chromatin integrity. Molecular Human Reproduction, 16:14-22.

Delis, D.C., J.H. Kramer, E. Kaplan and B.A. Ober, 1994. The California Verbal Learning Test for Children. Psychological Corporation, San Antonio, TX.

Demers, A., P. Ayotte, J. Brisson, S. Dodin, J. Robert and É. Dewailly, 2002. Plasma concentrations of polychlorinated biphenyls and the risk of breast cancer: a congener-specific analysis. American Journal of Epidemiology, 155:629-635.

Democophes, 2014. www.imm.ki.se/Democophes/Urval.htm (accessed 28 November 2014). (In Swedish).

Democophes-Cophes, 2014. www.eu-hbm.info/democophes (accessed 17 December 2014).

Desaulniers, D., K. Leingartner, G. Pelletier, G.H. Xiao and W.J. Bowers, 2012. Effects of developmental exposure to mixtures of environmental contaminants on the hepatic metabolism of estradiol-17beta in immature female Sprague Dawley rats. International Journal of Toxicology, 31:454-466.

Després, C., A. Beuter, F. Richer, K. Poitras, A. Veilleux, P. Ayotte, É. Dewailly, D. Saint-Amour and G. Muckle, 2005. Neuromotor functions in Inuit preschool children exposed to Pb, PCBs, and Hg. Neurotoxicology and Teratology, 27:245-257.

Deutch, B. and J.C. Hansen, 2000. High human plasma levels of organochlorine compounds in Greenland. Regional differences and lifestyle effects. Danish Medical Bulletin, 47:132-137.

Deutch, B., H.S. Pedersen, E.C. Jorgensen and J.C. Hansen, 2003. Smoking as a determinant of high organochlorine levels in Greenland. Archives of Environmental Health, 58:30-36.

Deutch, B., H.S. Pedersen and J.C. Hansen, 2004. Dietary composition in Greenland 2000, plasma fatty acids and persistent organic pollutants. Science of the Total Environment, 331:177-188.

Deutch, B., H.S. Pedersen, G. Asmund and J.C. Hansen, 2007a. Contaminants, diet, plasma fatty acids and smoking in Greenland 1999-2005. Science of the Total Environment, 372:486-496.

Deutch, B., J. Dyerberg, H.S. Pedersen, E. Aschlund and J.C. Hansen, 2007b. Traditional and modern Greenlandic food - Dietary composition, nutrients and contaminants. Science of the Total Environment, 384:106-119.

Dewailly, É., A. Nantel, J.P. Weber and F. Meyer, 1989. High levels of PCBs in breast milk of Inuit women from Arctic Quebec. Bulletin of Environmental Contamination and Toxicology, 43:641-646.

Dewailly, É., S. Bruneau, C. Laliberte, M. Belles-Isles, J.P. Weber, P. Ayotte and R. Roy, 1993. Breast milk contamination by PCBs and PCDDs/PCDFs in Arctic Quebec: preliminary results on the immune status of Inuit infants. Organohalogen Compounds, 13:403-406.

Dewailly É., J.J. Ryan, C. Laliberté, S. Bruneau, J.-P. Weber, S. Gingras and G. Carrier, 1994. Exposure of remote maritime populations to coplanar PCBs. Environmental Health Perspectives, 102:S205-S209.

Dewailly, É., G. Mulvad, H. Pedersen, P. Ayotte, A. Demers, J. Weber and J. Hansen, 1999. Concentration of organochlorines

in human brain, liver, and adipose tissue autopsy samples from Greenland. Environmental Health Perspectives, 107:823-828.

Dewailly, É., P. Ayotte, S. Bruneau, S. Gingras, M. Belles-Isles and R. Roy, 2000. Susceptibility to infections and immune status in Inuit infants exposed to organochlorines. Environmental Health Perspectives, 108:205-211.

Dewailly, É., R. Dallaire, D. Pereg, P. Ayotte, J. Fontaine and S. Dery, 2007. Qanuippitaa? How are we? Exposure to environmental contaminants in Nunavik: persistent organic pollutants and new contaminants of concern. Nunavik Regional Board of Health and Social Services, Institut national de santé publique.

DeWeese, A.D., N.E. Kmiecik, E.D. Chiriboga and J.A. Foran, 2009. Efficacy of risk-based, culturally sensitive Ogaa (walley) consumption advice for Anishinaabe tribal members in the Great lakes Region. Risk Analysis, 29:729-742.

Dietrich, K.N., K.M. Krafft, R.L. Bornschein, P.B. Hammond, O. Berger, P.A. Succop and M. Bier, 1987. Low-level fetal lead exposure effect on neurobehavioral development in early infancy. Pediatrics, 80:721-730.

Donaldson, S.G., J. van Oostdam, C. Tikhonov, M. Feeley, B. Armstrong, P. Ayotte, O. Boucher, W. Bowers, L. Chan, F. Dallaire, R. Dallaire, É. Dewailly, J. Edwards, G.M. Egeland, J. Fontaine, C. Furgal, T. Leech, E. Loring, G. Muckle, T. Nancarrow, D. Pereg, P. Plusquellec, M. Potyrala, O. Receveur and R.G. Shearer, 2010a. Environmental contaminants and human health in the Canadian Arctic. Science of the Total Environment, 408:5165-5234.

Donaldson, S.G., J. Van Oostdam, C. Tikhonov, M. Feeley, B. Armstrong, P. Ayotte, O. Boucher, W. Bowers, L. Chan, F. Dallaire, R. Dallaire, É. Dewailly, J. Edwards, G.M. Egeland, J. Fontaine, C. Furgal, T. Leech, E. Loring, G. Muckle, T. Nancarrow, D. Pereg, P. Plusquellec, M. Potyrala, O. Receveur and R.G. Shearer, 2010b. Environmental contaminants and human health in the Canadian Arctic. Science of the Total Environment, 408:5165-5234. Corrigendum to "Environmental contaminants and human health in the Canadian Arctic" Science of the Total Environment, Corrigendum to "Environmental contaminants and human health in the Canadian Arctic" [Sci. Total Environ. 408 (2010) 5165–5234]431:437-438.

Downie, D.L. and T. Fenge (Eds.), 2003. Northern Lights against POPs: Combatting Toxic Threats in the Arctic. Published for the Inuit Circumpolar Conference (ICC) Canada by McGill-Queens University Press.

Dudarev, A.A., 2006a. Reproductive Health Effects Associated with Exposure to PCBs Among Natives of the Russian Arctic. Study of the Impacts of Some Congeners of Polychlorinated Biphenyls (PCBs) on the Reproductive Health of Indigenous Peoples of the Russian Arctic. International POPs Elimination Project (IPEN). Online: www.ipen.org.

Dudarev, A.A., 2006b. DDT and DDE in the Russian Arctic and Reproductive Health of Indigenous Peoples. International POPs Elimination Project (IPEN). Online: www.ipen.org.

Dudarev, A., 2012. Dietary exposure to persistent organic pollutants and metals among Inuit and Chukchi in Russian Arctic Chukotka. International Journal of Circumpolar Health, 71:18592. http://dx.doi.org/10.3402/ijch.v71i0.18592.

Dudarev A.A. and V.S. Chupakhin, 2014. Influence of exposure to persistent toxic substances (PTS) on pregnancy outcomes, gender ratio and menstrual status in indigenous females of Chukotka. Gigiena i Sanitariia, 1: 35-39. [In Russian].

Dudarev, A.A., V. Chupakhin, J.O. Odland, L-O. Reiersen and V. Chashchin, 2010. A follow-up study of blood levels of persistent toxic substances (PTS) among indigenous peoples of the coastal Chukotka, Russia, 2001–2007. Journal of Circumpolar Health Supplements, 7:263-268.

Dudarev, A.A., V.S. Chupachin, Z.S. Ivanova and G.B. Lebedev, 2011. The blood levels of stable toxic substances in the native dwellers of coastal Chukotka and their children's infection morbidity. Gigiena i Sanitariia, 4:26-30. [In Russian].

Dudarev, A.A., V.S. Chupachin, Z.S. Ivanova and G.B. Lebedev, 2012a. Specificity of exposure of the indigenous dwellers of coastal and inland Chukotka to polychlorinated biphenyls. Gigiena i Sanitariia, 4:22-28. [In Russian].

Dudarev, A.A., V.S. Chupachin, Z.S. Ivanova and G.B. Lebedev, 2012b. Specificity of exposure of the indigenous dwellers of coastal and inland Chukotka to dichlorodiphenyltrichloroethane. Gigiena i Sanitariia, 2:15-20. [In Russian].

Dudarev, A.A., V.N. Mizernyuk and A.N. Nikanov, 2012c. Persistent organic pollutants and diabetes mellitus in the indigenous population and newcomers to Kola Lapland. Toxicol Vesnik, 4: 7-13. [In Russian].

Dudarev, A.A., V.S. Chupakhin and J.O. Odland, 2013. Cancer mortality in the indigenous population of coastal Chukotka, 1961-1990. International Journal of Circumpolar Health, 72:20471.

Dufour, R., 1988. The otitis media among Inuit children. Proposal for a new approach. Arctic Medical Research, 47(S1):659-665.

Duncan, C., K. Savage, M. Williams, B. Dickerson, A.V. Kondas, K.A. Fitzpatrick, J.L. Guerrero, T. Spraker and G.J. Kersh, 2013. Multiple strains of *Coxiella burnetii* are present in the environment of St. Paul Island, Alaska. Transboundary and Emerging Diseases, 60:345-350.

Egeland, J. and I. Kovalik-Gran, 2010. Validity of the factor structure of Conners' CPT. Journal of Attention Disorders, 13:347-357.

Elzanaty, S., A. Rignell-Hydbom, B.A. Jonsson, H.S. Pedersen, J.K. Ludwicki, M. Shevets, V. Zvyezday, G. Toft, J.P. Bonde, L. Rylander, L. Hagmar, E. Bonefeld-Jørgensen, M. Spano, D. Bizzaro, G.C. Manicardi and A. Giwercman, 2006. Association between exposure to persistent organohalogen pollutants and epididymal and accessory sex gland function: multicentre study in Inuit and European populations. Reproductive Toxicology, 22:765-773.

Erdmann, S.E., R. Dietz, C. Sonne, T.O. Bechshoft, K. Vorkamp, R.J. Letcher, M. Long and E.C. Bonefeld-Jørgensen, 2013. Xenoestrogenic and dioxin-like activity in blood of East Greenland polar bears (*Ursus maritimus*). Chemosphere, 92:583-591.

Eriksen, K.T., O. Raaschou-Nielsen, M. Sorensen, M. Roursgaard, S. Loft and P. Moller, 2010. Genotoxic potential of the perfluorinated chemicals PFOA, PFOS, PFBS, PFNA and PFHxA in human HepG2 cells. Mutatation Research, 700:39-43.

Ethier, A.A., G. Muckle, C. Bastien, É. Dewailly, P. Ayotte, C. Arfken, S.W. Jacobson, J.L. Jacobson and D. Saint-Amour, 2012. Effects of environmental contaminant exposure on visual brain development: a prospective electrophysiological study in school-aged children. Neurotoxicology, 33:1075-1085.

Eubig, P.A., A. Aguiar and S.L. Schantz, 2010. Lead and PCBs as risk factors for attention deficit/hyperactivity disorder. Environmental Health Perspectives, 118:1654-1667.

Everett, C.J. and E.M. Matheson, 2010. Biomarkers of pesticide exposure and diabetes in the 1999-2004 national health and nutrition examination survey. Environment International, 36:398-401.

Fair, P.A., E. Driscoll, M.A. Mollenhauer, S.G. Bradshaw, S.H. Yun, K. Kannan, G.D. Bossart, D.E. Keil and M.M. Peden-Adams, 2011. Effects of environmentally-relevant levels of perfluorooctane sulfonate on clinical parameters and immunological functions in B6C3F1 mice. Journal of Immunotoxicology, 8:17-29.

Fei, C., J.K. McLaughlin, R.E. Tarone and J. Olsen, 2007. Perfluorinated chemicals and fetal growth: a study within the Danish National Birth Cohort. Environmental Health Perspectives, 115:1677-1682.

Ferguson, K.K., R. Hauser, L. Altshul and J.D. Meeker, 2012. Serum concentrations of *p,p'*-DDE, HCB, PCBs and reproductive hormones among men of reproductive age. Reproductive Toxicology, 34:429-435.

Ferla, R., V. Calo, S. Cascio, G. Rinaldi, G. Badalamenti, I. Carreca, E. Surmacz, G. Colucci, V. Bazan and A. Russo, 2007. Founder mutations in BRCA1 and BRCA2 genes. Annals of Oncology, 18(S6):vi93-98.

Filipic, M., 2012. Mechanisms of cadmium induced genomic instability. Mutatation Research, 733:69-77.

Fillion, M., A. Philibert, F. Mertens, M. Lemire, C.J. Passos, B. Frenette, J.R. Guimaraes and D. Mergler, 2011. Neurotoxic sequelae of mercury exposure: an intervention and follow-up study in the Brazilian Amazon. Ecohealth, 8:210-222.

Fillion, M., J.M. Blais, E. Yumvihoze, M. Nakajima, P. Workman, G. Osborne and H.M. Chan, 2014. Identification of environmental sources of lead exposure in Nunavut (Canada) using stable isotope analyses. Environment International, 71:63-73.

Fisk, A., C. DeWit, M. Wayland, Z. Kuzyk, N. Burgess, R. Letcher, B. Braune, S. Blum, R. Norstrom, E. Lie, N. Larson, J. Skaare and D. Muir, 2005. An assessment of the toxicological significance of anthropogenic contaminants in Canadian Arctic wildlife. Science of the Total Environment, 351-353:57-93.

Fjeld, R., N. Esienberg and K. Compton (Eds.), 2007. Quantitative Environmental Risk Analysis for Human Health. Wiley Interscience.

Fraser, S., G. Muckle and C. Despres, 2006. The relationship between lead exposure, motor function and behaviour in Inuit preschool children. Neurotoxicology and Teratology, 28:18-27.

Fredslund, S.O. and E.C. Bonefeld-Jørgensen, 2012. Breast cancer in the Arctic – changes over the past decades. International Journal of Circumpolar Health, 71:19155.

Friborg, J.T. and M. Melbye, 2008. Cancer patterns in Inuit populations. The Lancet Oncology, 9:892-900.

Friborg, J., A. Koch, J. Wohlfarht, H.H. Storm and M. Melbye, 2003. Cancer in Greenlandic Inuit 1973-1997: a cohort study. International Journal of Cancer, 107:1017-1022.

Friendship, K.A. and C.M. Furgal, 2012. The role of Indigenous knowledge in environmental health risk management in Yukon, Canada. International Journal of Circumpolar Health, 71:19003. http://dx.doi.org/10.3402/ijch.v71i0.19003.

Fuentes, S., P. Vicens, M.T. Colomina and J.L. Domingo, 2007. Behavioral effects in adult mice exposed to perfluorooctane sulfonate (PFOS). Toxicology, 242:123-129.

Fukushima, S., A. Kinoshita, R. Puatanachokchai, M. Kushida, H. Wanibuchi and K. Morimura, 2005. Hormesis and dose-response-mediated mechanisms in carcinogenesis: evidence for a threshold in carcinogenicity of non-genotoxic carcinogens. Carcinogenesis, 26:1835-1845.

Furgal, C., S. Kalhok, E. Loring and S. Smith, 2003. Knowledge in action: northern contaminants program structures, processes and products. Canadian Arctic Contaminants Assessment Report II, Department of Indian Affairs and Northern Development, Ottawa, Ontario, Canada.

Furgal, C.M., S. Powell and H. Myers, 2005. Digesting the message about contaminants and country foods in the Canadian North: A review and recommendations for future research and action. Arctic, 58:103-114.

Gagne, D., R. Blanchet, J. Lauziere, E. Vaissiere, C. Vezina, P. Ayotte, S. Dery and H. Turgeon O'Brien, 2012. Traditional food consumption is associated with higher nutrient intakes in Inuit children attending childcare centres in Nunavik. International Journal of Circumpolar Health, 71:18401.

Gamberg, M., B. Braune, E. Davey, B. Elkin, P.F. Hoekstra, D. Kennedy, C. Macdonald, D. Muir, A. Nirwal, M. Wayland and B. Zeeb, 2005. Spatial and temporal trends of contaminants in terrestrial biota from the Canadian Arctic. Science of the Total Environment, 351/352:148-164.

Garçon, G., B. Leleu, F. Zerimech, T. Marez, J. Haguenoer, D. Furon and P. Shirali, 2004. Biologic markers of oxidative stress and nephrotoxicity as studied in biomonitoring of adverse effects of occupational exposure to lead and cadmium. Occupational and Environmental Medicine, 46:1180-1186.

Garçon, G., B. Leleu, T. Marez, F. Zerimech, J. Haguenoer, D. Furon and P. Shirali, 2007. Biomonitoring of the adverse effects induced by the chronic exposure to lead and cadmium on kidney function: usefulness of alpha-glutathione-*S*-transferase. Science of the Total Environment, 3771:65-72.

Garmash, O., M.H. Hermanson, E. Isaksson, M. Schwikowski, D. Divine, C. Teixeria and D.C.G. Muir, 2013. Deposition history of polychlorinated biphenyls to the Lomonosovfonna glacier, Svalbard: a 209 congener analysis. Environmental Science and Technology, 47:12064-12072.

Gascon, M., M. Vrijheid, D. Martínez, J. Forns, J.O. Grimalt, M. Torrent and J. Sunyer, 2011. Effects of pre- and postnatal exposure to low levels of polybromodiphenyl ethers on neurodevelopment and thyroid hormone levels at 4 years of age. Environment International, 37:605-611.

Geier, D.A., J.K. Kern, P.G. King, L.K. Sykes and M.R. Geier, 2012. Hair toxic metal concentrations and autism spectrum disorder severity in young children. International Journal of Environmental Research and Public Health, 9:4486-4497.

Ghisari, M., M. Long and E.C. Bonefeld-Jørgensen, 2013. Genetic polymorphisms in CYP1A1, CYP1B1 and COMT genes in Greenlandic Inuit and Europeans. International Journal of Circumpolar Health, 72:21113. doi.org/10.3402/ijch.v72i0.21113.

Ghisari, M., H. Eiberg, M. Long and E.C. Bonefeld-Jørgensen, 2014. Polymorphisms in Phase I and Phase II genes and breast cancer risk and relations to persistent organic pollutant exposure: a case-control study in Inuit women. Environmental Health, 13:19. doi:10.1186/1476-069X-13-19.

Gilman, A., P. Ayotte, J. Berner, E. Dewailly, A.A. Dudarev, E.C. Bonefeld-Jørgensen, G. Muckle, J. Øyvind Odland and C. Tikhonov, 2009. Public health and the effects of contaminants. In: AMAP Assessment 2009: Human Health in the Arctic, pp. 143-189. Arctic Monitoring and Assessment Programme (AMAP), Oslo.

Giwercman, A.H., A. Rignell-Hydbom, G. Toft, L. Rylander, L. Hagmar, C. Lindh, H.S. Pedersen, J.K. Ludwicki, V. Lesovoy, M. Shvets, M. Spano, G.C. Manicardi, D. Bizzaro, E.C. Bonefeld-Jørgensen and J.P. Bonde, 2006. Reproductive hormone levels in men exposed to persistent organohalogen pollutants: a study of Inuit and three European cohorts. Environmental Health Perspectives, 114:1348-1353.

Glynn, A.W., A. Wolk, M. Aune, S. Atuma, S. Zettermark, M. Mæhle-Schmid, P.O. Darnerud, W. Becker, B. Vessby and H.O. Adami, 2000. Serum concentrations of organochlorines in men: a search for markers of exposure. Science of the Total Environment, 263:197-208.

Glynn, A., S. Lignell, P.O. Darnerud, M. Aune, E. Halldin Ankarberg, I.A. Bergdahl, L. Barregård and I. Bensryd, 2011a. Regional differences in levels of chlorinated and brominated pollutants in mother's milk from primiparous women in Sweden. Environment International, 37:71-79.

Glynn, A., U. Berger, A. Bignert, S. Ullah, S. Lignell, M. Aune and P.O. Darnerud, 2011b. Perfluoroalkyl substances in serum from first-time mothers in Uppsala – temporal trend 1996-2010. Report to the Swedish Environmental Protection Agency.

Glynn, A., U. Berger, A. Bignert, S. Ullah, M. Aune, S. Lignell and P.O. Darnerud, 2012. Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: serial sampling during pregnancy and nursing, and temporal trend 1996-2010. Environmental Science and Technology, 46:9071-9079.

Gonzalez-Cossio, T., K.E. Peterson, L.H. Sanin, E. Fishbein, E. Palazuelos, A. Aro, M. Hernandez-Avila and H. Hu, 1997. Decrease in birth weight in relation to maternal bone-lead burden. Pediatrics, 100:856-862.

González-Estecha, M., A. Bodas-Pinedo, M.Á. Rubio-Herrera, M. Martell-Claros, E.M. Trasobares-Iglesias, J.M. Ordóñez-Iriarte, J.J. Guillén-Pérez, M.Á. Herráiz-Martínez, J.A. García-Donaire, R. Farré-Rovira, E. Calvo-Manuel, J.R. Martínez-Álvarez, M.T. Llorente-Ballesteros, M. Sáinz-Martín, T. Martínez-Astorquiza, M.J. Martínez-García, I. Bretón Lesmes, M.Á. Cuadrado-Cenzual, S. Prieto-Menchero, C. Gallardo-Pino, R. Moreno-Rojas, P. Bermejo-Barrera, M. Torres-Moreno, M. Arroyo-Fernández and A. Calle-Pascual, 2014. The effects of methylmercury on health in children and adults; national and international studies. Nutricion Hospitalaria, 30:989-1007.

Gouin, T., J.M. Armitage, I.T. Cousins, D.C. Muir, C.A. Ng, L. Reid and S. Tao, 2013. Influence of global climate change on chemical fate and bioaccumulation: the role of multimedia models. Environmental Toxicology and Chemistry, 32:20-31.

Govarts, E., M. Nieuwenhuijsen, G. Schoeters, F. Ballester, K. Bloemen, M. de Boer, C. Chevrier, M. Eggesbø, M. Guxens, U. Krämer, J. Legler, D. Martínez, L. Palkovicova, E. Patelarou, U. Ranft, A. Rautio, M. Skaalum Petersen, R. Slama, H. Stigum, G. Toft, T. Trnovec, S. Vandentorren, P. Weihe, N. Weisglas Kuperus, M. Wilhelm, J. Wittsiepe, J.P. Bonde and OBELIX/ENRIECO, 2012. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): a meta-analysis within 12 European Birth Cohorts. Environmental Health Perspectives, 120:162-170.

Grandjean, P., 2013. Only One Chance: How Environmental Pollution Impairs Brain Development – and How to Protect the Brains of the Next Generation. Oxford University Press.

Grandjean, P. and K.T. Herz, 2011. Methylmercury and brain development: imprecision and underestimation of developmental neurotoxicity in humans. Mount Sinai Journal of Medicine, 78:107-118.

Grandjean, P., P. Weihe, P.J. Jorgensen, T. Clarkson, E. Cernichiari and T. Videro, 1992. Impact of maternal seafood diet on fetal exposure to mercury, selenium, and lead. Archives of Environmental Health, 47:185-195.

Grandjean, P., P. Weihe, R.F. White, F. Debes, S. Araki, K. Yokoyama, K. Murata, N. Sorensen, R. Dahl and P.J. Jorgensen, 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicology and Teratology, 19:417-428.

Grandjean, P., K. Murata, E. Budtz-Jorgensen and P. Weihe, 2004. Cardiac autonomic activity in methylmercury neurotoxicity: 14-year follow-up of a Faroese birth cohort. Journal of Pediatrics, 144:169-176.

Grandjean, P., E. Budtz-Jørgensen, D.B. Barr, L.L. Needham, P. Weihe and B. Heinzow, 2008. Elimination half-lives of polychlorinated biphenyl congeners in children. Environmental Science and Technology, 42:6991-6996.

Grandjean, P., L.K. Poulsen, C. Heilmann, U. Steuerwald and P. Weihe, 2010. Allergy and sensitization during childhood associated with prenatal and lactational exposure to marine pollutants. Environmental Health Perspectives, 118:1429-1433.

Grandjean, P., J.E. Henriksen, A.L. Choi, M.S. Petersen, C. Dalgard, F. Nielsen and P. Weihe, 2011. Marine food pollutants as a risk factor for hypoinsulinemia and type 2 diabetes. Epidemiology, 22:410-417.

Grandjean, P., E.W. Andersen, E. Budtz-Jorgensen, F. Nielsen, K. Molbak, P. Weihe and C. Heilmann, 2012a. Serum vaccine antibody concentrations in children exposed to perfluorinated compounds. Journal of the American Medical association, 307:391-397.

Grandjean, P., C. Gronlund, I.M. Kjaer, T.K. Jensen, N. Sorensen, A.M. Andersson, A. Juul, N.E. Skakkebaek, E. Budtz-Jorgensen and P. Weihe, 2012b. Reproductive hormone profile and pubertal development in 14-year-old boys prenatally exposed to polychlorinated biphenyls. Reproductive Toxicology, 34:498-503.

Grandjean, P., C. Pichery, M. Bellanger and E. Budtz-Jorgensen, 2012c. Calculation of mercury's effects on neurodevelopment. Environmental Health Perspectives, 120(12):author reply A452.

Grandjean, P., P. Weihe, F. Nielsen, B. Heinzow, F. Debes and E. Budtz-Jorgensen, 2012d. Neurobehavioral deficits at age 7 years associated with prenatal exposure to toxicants from maternal seafood diet. Neurotoxicology and Teratology, 34:466-472.

Greene, T. and C.B. Ernhart, 1991. Prenatal and preschool age lead exposure: relationship with size. Neurotoxicology and Teratology, 13:417-427.

Greene, C., C. Hadley, G. Magdanz and G. Sampson, 2011. Hotham Inlet cyanobacterial blooms: Cyanobacterial blooms in the Arctic and their potential effects. Alaska Oceans Sciences Bowl high school competition. http://seagrant.uaf.edu/nosb/papers/2011/kotzebue-bullheads.php.

Grimalt, J.O., M. Horvat, O. Mikes, P. Cupr and A. Rautio, 2012. Health outcomes in relation to contaminant exposure in Mediterranean cohorts. ArcRisk Deliverable Number: 36.

Gundacker, C., S. Frohlich, K. Graf-Rohrmeister, B. Eibenberger, V. Jessenig, D. Gicic, S. Prinz, K.J. Wittmann, H. Zeisler, B. Vallant, A. Pollak and P. Husslein, 2010. Perinatal lead and mercury exposure in Austria. Science of the Total Environment, 408:5744-5749.

Gyllenhammar, I., U. Berger, M. Sundström, S. Lignell, M. Aune, P.O. Darnerud, N. Kotova and A. Glynn, 2013. Perfluoralkyl acids in serum from nursing women living in an area in Sweden with drinking water contamination. Report from the Swedish National Food Agency and Stockholm University to the Swedish National Environmental Monitoring Programme. Contract 219 1202.

Halling, J., M.S. Petersen, N. Jorgensen, T.K. Jensen, P. Grandjean and P. Weihe, 2013. Semen quality and reproductive hormones in Faroese men: a cross-sectional population-based study of 481 men. BMJ Open 3: e001946. doi:10.1136/bmjopen-2012-001946.

Hansen, J.C., U. Tarp, J. Bohm, 1990. Prenatal exposure to methyl mercury among Greenlandic polar Inuits. Archives of Environmental Health, 45:355-358.

Hansen, J.C., A. Gilman, V. Klopov and J. Odland (Eds.), 1998. Pollution and human health. In: AMAP Assessment Report: Arctic Pollution Issues, pp. 775-844. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

Hansen, S., E. Nieboer, J.Ø. Odland, T. Wilsgaard, A.S. Veyhe and T.M. Sandanger, 2010. Levels of organochlorines and lipids across pregnancy, delivery and postpartum periods in women from northern Norway. Journal of Environmental Monitoring, 12:2128-2137.

Hansen, S., E. Nieboer, T.M. Sandanger, T. Wilsgaard, Y. Thomassen, A.S. Veyhe and J.Ø. Odland, 2011. Changes in maternal blood concentrations of selected essential and toxic elements during and after pregnancy. Journal of Environmental Monitoring, 13:2143-2152.

Hansen, C., K. Hueffer, F. Gulland, R. Wells, B. Balmer, M. Castellini and T. O'Hara, 2014. Use of cellulose filter paper to quantify whole-blood mercury in two marine mammals: Validation study. Journal of Wildlife Diseases, 50:271-278.

Harboe, T.L., H. Eiberg, P. Kern, B. Ejlertsen, L. Nedergaard, V. Timmermans-Wielenga, I.M. Nielsen and M.L. Bisgaard, 2009. A high frequent BRCA1 founder mutation identified in the Greenlandic population. Familial Cancer, 8:413-419.

Hardell, E., M. Carlberg, M. Nordström and B. van Bavel, 2010. Time trends of persistent organic pollutants in Sweden during 1993–2007 and relation to age, gender, body mass index, breast-feeding and parity. Science of the Total Environment, 408:4412-4419.

Hardisty, J.F., G.A. Willson, W.R. Brown, E.E. McConnell, S.R. Frame, D.W. Gaylor, G.L. Kennedy and J.L. Butenhoff, 2010. Pathology Working Group review and evaluation of proliferative lesions of mammary gland tissues in female rats fed ammonium perfluorooctanoate (APFO) in the diet for 2 years. Drug and Chemical Toxicology, 33:131-137.

Hartwig, A., 2013. Cadmium and cancer. Metal Ions in Life Sciences, 11:491-507.

Haugen, T.B., T. Tefre, G. Malm, B.A. Jonsson, L. Rylander, L. Hagmar, C. Bjorsvik, T. Henrichsen, T. Saether, Y. Figenschau and A. Giwercman, 2011. Differences in serum levels of CB-153 and *p,p'*-DDE, and reproductive parameters between men living south and north in Norway. Reproductive Toxicology, 32:261-267.

Hauser, R., L. Altshul, Z. Chen, L. Ryan, J. Overstreet, I. Schiff and D.C. Christiani, 2002. Environmental organochlorines and semen quality: results of a pilot study. Environmental Health Perspectives, 110:229-233.

Hays, S.M., R.A. Becker, H.W. Leung, L.L. Aylward and D.W. Pyatt, 2007. Biomonitoring equivalents: A screening approach for interpreting biomonitoring results from a public health risk perspective. Regulatory Toxicology and Pharmacology, 47:96-109.

Hays, S.M., L.L. Aylward, J.S. Lakind, M.J. Bartels, H.A. Barton, P.J. Boogaard, C. Brunk and S. Dizio, 2008. Guidelines for the derivation of biomonitoring equivalents: Report from the Biomonitoring Equivalents Expert Workshop. Regulatory Toxicology and Pharmacology, 51:S4-15.

HBM Commission, 1997. Stoffmonographie Pentachlorphenol - Referenz- und Human-Biomonitoring-Werte (HBM). German Human Biomonitoring Commission. Bundesgesundheitsblatt; 40:212-222.

HBM Commission, 1999. Stoffmonographie Quecksilber – referenz – und human-biomonitoring-werte (HBM). German Human Biomonitoring Commission. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 42:522-532.

HBM Commission, 2003. Aktualisierung der Referenzwerte fur Blei, Cadmium, und Quecksilber im Blut und im Urin von Erwachsenen. German Human Biomonitoring Commission. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 46:1112-1113.

HBM Commission, 2005. Neue und aktualisierte Referenzwerte fur Schadstoffgehalte in Blut und Urin von Kindern – Arsen, Blei,

Cadmium und Quecksilber. German Human Biomonitoring Commission. Bundesgesundheitsblatt - Gesundheitsforschung - Gesundheitsschutz, 48:1308-1312.

Health Canada, 1999. Methylmercury in Canada. III. Medical Services Branch, Health Canada, Minister of Public Works and Government Services Canada, Ottawa.

Health Canada, 2010. Report on Human Biomonitoring of Environmental Chemicals in Canada. Results of the Canadian Health Measures Survey Cycle 1 (2007-2009).

Health Canada, 2013. Second Report on Human Biomonitoring of Environmental Chemicals in Canada. Canadian Health Measures Survey: Cycle 2 Data Tables (2009-2011). www.statcan.gc.ca/pub/82-626-x/82-626-x2012002-eng.htm.

Heilmann, C., P. Grandjean, P. Weihe, F. Nielsen and E. Budtz-Jorgensen, 2006. Reduced antibody responses to vaccinations in children exposed to polychlorinated biphenyls. PLoS Med, 3(8):e311.

Heilmann, C., E. Budtz-Jorgensen, F. Nielsen, B. Heinzow, P. Weihe and P. Grandjean, 2010. Serum concentrations of antibodies against vaccine toxoids in children exposed perinatally to immunotoxicants. Environmental Health Perspectives, 118:1434-1438.

Hernandez-Avila, M., K.E. Peterson, T. Gonzalez-Cossio, L.H. Sanin, A. Aro, L. Schnaas and H. Hu, 2002. Effect of maternal bone lead on length and head circumference of newborns and 1-month-old infants. Archives of Environmental Health, 57:482-488.

Holladay, S.D. and R.J. Smialowicz, 2000. Development of the murine and human immune system: differential effects of immunotoxicants depend on time of exposure. Environmental Health Perspectives, 108(S3):463-473.

Holoubek, I., A. Kocan, I. Holoubkova, K. Hilscherova, J. Kohoutek, J. Falandysz and O. Roots, 2001. Persistent, bioaccumulative, and toxic compounds in the central and eastern European countries – the state-of-the-art report – human exposure. Archives of Industrial Hygiene and Toxicology, 52:181-215.

Homoe, P., A. Koch, N.D. Rendtorff, M. Lodahl, T. Andersen, S. Andersen, H. Eiberg, I.-M. Nielsen and L. Tranebjarg, 2012. GJB2 (Connexin-26) mutations are not frequent among hearing impaired patients in east Greenland. International Journal of Audiology, 51:433-436.

Hu, X.Z. and D.C. Hu, 2009. Effects of perfluorooctanoate and perfluorooctane sulfonate exposure on hepatoma Hep G2 cells. Archives of Toxicology, 83:851-861.

Hu, X.Z., Y. Xu, D.C. Hu, Y. Hui and F.X. Yang, 2007. Apoptosis induction on human hepatoma cells Hep G2 of decabrominated diphenyl ether (PBDE-209). Toxicology Letters, 171:19-28.

Hueffer, K., A. Parkinson, R. Gerlach and J. Berner, 2013. Zoonotic infections in Alaska: Disease prevalence, potential impact of climate change and recommended action for earlier disease detection, research, prevention and control. International Journal of Circumpolar Health, 72:19562. http://dx.doi.org/10.3402/inch.72i0.19562.

Humblet, O., S.A. Korrick, P.L. Williams, O. Sergeyev, C. Emond, L.S. Birnbaum, J.S. Burns, L.M. Altshul, D.G. Patterson, Jr., W.E. Turner, M.M. Lee, B. Revich and R. Hauser, 2013. Genetic modification of the association between peripubertal dioxin exposure and pubertal onset in a cohort of Russian boys. Environmental Health Perspectives, 121:111-117.

Huntington, H. and S. Fox, 2005. The changing Arctic: Indigenous perspectives. In: Arctic Climate Impact Assessment, pp. 61-99. Cambridge University Press.

ICC, 2012. Inuit: Circumpolar Perspectives of Risk Communication. Contract report by Inuit Circumpolar Council (ICC) Canada submitted to Health Canada, Ottawa. 30 March 2012. www.inuitcircumpolar.com/uploads/3/0/5/4/30542564/iccreport_circumpperspectivesriskcomm_finalx.pdf.

ICC-AK, 2015. Inuit Circumpolar Council-Alaska. Alaskan Inuit Food Security Conceptual Framework: How to Assess the Arctic From an Inuit Perspective. Technical Report. Anchorage, AK.

INAC, 2003. Canadian Arctic Contaminants Assessment Report II: Highlights. Indian and Northern Affairs Canada (INAC). Ottawa.

IPCC, 2013. Climate Change 2013: The Physical Science Basis. Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Stocker, T.F., D. Qin, G.-K. Plattner, M. Tignor, S.K. Allen, J. Boschung, A. Nauels, Y. Xia, V. Bex and P.M. Midgley (eds.). Cambridge University Press.

IPCC, 2014. Summary for policymakers. In: Field, C.B., V.R. Barros, D.J. Dokken, K.J. Mach, M.D. Mastrandrea, T.E. Bilir, M. Chatterjee, K.L. Ebi, Y.O. Estrada, R.C. Genova, B. Girma, E.S. Kissel, A.N. Levy, S. MacCracken, P.R. Mastrandrea and L.L. White (eds.), Climate Change 2014: Impacts, Adaptation and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press.

IPCS, 2002. Global Assessment of the State-of-the-Science of Endocrine Disruptors. Damstra, T., S. Barlow, A. Bergman, R. Kavlock, and G. van der Kraak (Eds). International Programme on Chemical Safety, World Health Organization, Geneva.

IWS, 2014. Internet World Stats: Usage and Population Statistics – Greenland. www.internetworldstats.com/am/gl.htm.

Jacobson, J.L. and S.W. Jacobson, 1996. Intellectual impairment in children exposed to polychlorinated biphenyls *in utero*. New England Journal of Medicine, 335:783-789.

Jacobson, J.L., G. Muckle, P. Ayotte, É. Dewailly and S.W. Jacobson, 2015. Relation of prenatal methylmercury exposure from environmental sources to childhood IQ. Environmental Health Perspectives, 123:827-833.

Jacques, C., E. Levy, G. Muckle, S.W. Jacobson, C. Bastien, É. Dewailly, P. Ayotte, J.L. Jacobson and D. Saint-Amour, 2011. Long-term effects of prenatal omega-3 fatty acid intake on visual function in school-age children. Journal of Pediatrics, 158:83-90.

Jaraczewska, K., J. Lulek, A. Covaci, S. Voorspoels, A. Kaluba-Skotarczak, K. Drews and P. Schepens, 2006. Distribution of polychlorinated biphenyls, organochlorine pesticides and polybrominated diphenyl ethers in human umbilical cord

serum, maternal serum and milk from Wielkopolska region, Poland. Science of the Total Environment, 372:20-31.

Jardine, C.G., L. Banfield, S.M. Driedger and C.M. Furgal, 2013. Risk communication and trust in decision-maker action: a case study of the Giant Mine Remediation Plan. International Journal of Circumpolar Health, 72:21184. http://dx.doi.org/10.3402/ijch.v72i0.21184.

Jensen, J., L. Adare and R. Shearer (eds.), 1997. Canadian Arctic Contaminants Assessment Report. Department of Indian Affairs and Northern Development, Ottawa, Ontario, Canada.

Jensen, R.G., A. Koch, P. Homoe and P. Bjerregaard, 2013. Tobacco smoke increases the risk of otitis media among Greenlandic Inuit children while exposure to organochlorines remain insignificant. Environment International, 54:112-118.

Jenssen, M.T.S., A.L. Brantsäter, M. Haugen, H.M. Metzer, T. Larssen, H.E. Kvalem, B.E. Birgisdottir, Y. Thomassen, D. Ellingsen, J. Alexander and H.K. Knutsen, 2012. Dietary mercury exposure in a population with a wide range of fish consumption – Self-capture of fish and regional differences are important determinants of mercury in blood. Science of the Total Environment, 439:220-229.

Jeppesen, C., 2008. Kost [Diet]. In: Bjerregaard, P. and I.K. Dahl-Petersen (Eds.), Befolkningsundersøgelsen i Grønland 2005-2007 [Writings on Greenland], pp.104-105. National Institute of Public Health, Copenhagen.

Jeppesen, C., M.E. Jørgensen and P. Bjerregaard, 2012. Assessment of consumption of marine food in Greenland by a food frequency questionnaire and biomarkers. International Journal of Circumpolar Health, 71:18361. http://dx.doi.org/10.3402/ijch.v71i0.18361.

Jeppesen, C., P. Bjerregaard and M.E. Jørgensen, 2013. Dietary patterns in Greenland and their relationship with type 2 diabetes mellitus and glucose intolerance. Public Health Nutrition, 11:1-9.

Joensen, U.N., N. Jorgensen, E. Rajpert-De Meyts and N.E. Skakkebaek, 2008. Testicular dysgenesis syndrome and Leydig cell function. Basic and Clinical Pharmacology and Toxicology, 102:155-161.

Johansson, N., P. Eriksson and H. Viberg, 2009. Neonatal exposure to PFOS and PFOA in mice results in changes in proteins which are important for neuronal growth and synaptogenesis in the developing brain. Toxicological Sciences, 108:412-418.

Johnson, M.D., N. Kenney, A. Stoica, L. Hilakivi-Clarke, B. Singh, G. Chepko, R. Clarke, P.F. Sholler, A.A. Lirio, C. Foss, R. Reiter, B. Trock, S. Paik and M.B. Martin, 2003. Cadmium mimics the *in vivo* effects of estrogen in the uterus and mammary gland. Nature Medicine, 9:1081-1084.

Jones, L., J.D. Parker and P. Mendola, 2010. Blood lead and mercury levels in pregnant women in the United States, 2003-2008. NCHS Data Brief No. 52. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics (NCHS).

Jönsson, B.A.G., L. Rylander, C. Lindh, A. Rignell-Hydbom, A. Giwercman, G. Toft, H.S. Pedersen, J.K. Ludwicki, K. Góralczyk, V. Zvyezday, M. Spanò, D. Bizzaro, E.C. Bonefeld-Jörgensen, G.C. Manicardi, J.P. Bonde, L. Hagmar and INUENDO, 2005. Inter-population variations in concentrations, determinants of and correlations between 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) and 1,1-dichloro-2,2-bis (*p*-chlorophenyl)-ethylene (*p,p*'-DDE): a cross-sectional study of 3161 men and women from Inuit and European populations. Environmental Health, 4:27. doi:10.1186/1476-069X-4-27.

Jorgensen, N., E. Carlsen, I. Nermoen, M. Punab, J. Suominen, A.G. Andersen, A.M. Andersson, T.B. Haugen, A. Horte, T.K. Jensen, O. Magnus, J.H. Petersen, M. Vierula, J. Toppari and N.E. Skakkebaek, 2002. East-West gradient in semen quality in the Nordic-Baltic area: a study of men from the general population in Denmark, Norway, Estonia and Finland. Human Reproduction, 17:2199-2208.

Jorgensen, N., F. Liu, A.M. Andersson, M. Vierula, D.S. Irvine, J. Auger, C.K. Brazil, E.Z. Drobnis, T.K. Jensen, P. Jouannet, J.W. Overstreet, J.B. Redmon, A. Sparks, J. Toppari, C. Wang, N.E. Skakkebaek and S.H. Swan, 2010. Serum inhibin-b in fertile men is strongly correlated with low but not high sperm counts: a coordinated study of 1,797 European and US men. Fertility and Sterility, 94:2128-2134.

Julvez, J. and P. Grandjean, 2013. Genetic susceptibility to methylmercury developmental neurotoxicity matters. Frontiers in Genetics, 4:278. doi:10.3389/fgene.2013.00278.

Julvez, J., F. Debes, P. Weihe, A. Choi and P. Grandjean, 2010. Sensitivity of continuous performance test (CPT) at age 14 years to developmental methylmercury exposure. Neurotoxicology and Teratology, 32:627-632.

Julvez, J., G.D. Smith, J. Golding, S. Ring, B.S. Pourcain, J.R. Gonzalez and P. Grandjean, 2013. Prenatal methylmercury exposure and genetic predisposition to cognitive deficit at age 8 years. Epidemiology, 24:643-650.

Jusko, T.A., A.J. De Roos, S.M. Schwartz, B.P. Lawrence, L. Palkovicova, T. Nemessanyi, B. Drobna, A. Fabisikova, A. Kocan, D. Sonneborn, E. Jahnova, T.J. Kavanagh, T. Trnovec and I. Hertz-Picciotto, 2010. A cohort study of developmental polychlorinated biphenyl (PCB) exposure in relation to post-vaccination antibody response at 6-months of age. Environmental Research, 110:388-395.

Kallenborn, R., C. Halsall, M. Dellong and P. Carlsson, 2012. The influence of global distribution on fate processes and distribution of anthropogenic persistent organic pollutants. Journal of Environmental Monitoring, 14:2854-2869.

Karmaus, W., S. Asakevich, A. Indurkhya, J. Witten and H. Kruse, 2002. Childhood growth and exposure to dichlorodiphenyl dichloroethene and polychlorinated biphenyls. Journal of Pediatrics, 140:33-39.

Kärrman, A., I. Ericson, B. van Bavel, P.O. Dernerud, M. Aune, A. Glynn, S. Lignell and G. Lindström, 2007. Exposure of perfluorinated chemicals through lactation: levels of matched human milk and serum and a temporal trend, 1996-2004, in Sweden. Environmental Health Perspectives, 115:226-230.

Kato, K., A.M. Calafat, L.Y. Wong, A.A. Wanigatunga, S.P. Caudill and L.L. Needham, 2009. Polyfluoroalkyl compounds in pooled sera from children participating in the National Health and Nutrition Examination Survey 2001-2002. Environmental Science and Technology, 43:2641-2647.

Keil, D.E., T. Mehlmann, L. Butterworth and M.M. Peden-Adams, 2008. Gestational exposure to perfluorooctane sulfonate suppresses immune function in B6C3F1 mice. Toxicological Sciences, 103:77-85.

Kellett, S., P. Poirier, É. Dewailly, H. Sampasa and M.L. Chateau-Degat, 2012. Is severe obesity a cardiovascular health concern in the Inuit population? American Journal of Human Biology, 24:441-445.

Kelly, J., A. Lanier, M. Santos, S. Healey, R. Louchini, J. Friborg, K. Young and C. Ng, 2008. Cancer among the circumpolar Inuit, 1989-2003. II. Patterns and trends. International Journal of Circumpolar Health, 67:408-420.

Kennedy, G.L., Jr., J.L. Butenhoff, G.W. Olsen, J.C. O'Connor, A.M. Seacat, R.G. Perkins, L.B. Biegel, S.R. Murphy and D.G. Farrar, 2004. The toxicology of perfluorooctanoate. Critical Reviews in Toxicology, 34:351-384.

Kern, J.K. and A.M. Jones, 2006. Evidence of toxicity, oxidative stress, and neuronal insult in autism. Journal of Toxicology and Environmental Health B, 9:485-499.

Kim, Y., B.N. Kim, Y.C. Hong, M.S. Shin, H.J. Yoo, J.W. Kim, S.Y. Bhang and S.C. Cho, 2009a. Co-exposure to environmental lead and manganese affects the intelligence of school-aged children. Neurotoxicology, 30:564-571.

Kim, Y.H., Y.J. Shim, D. Sul, E. Lee and B.H. Min, 2009b. 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) induces calcium influx through T-type calcium channel and enhances lysosomal exocytosis and insulin secretion in INS-1 cells. International Journal of Toxicology, 28:151-161.

Kinloch, D. and H.V. Kuhnlein, 1988. Assessment of PCBs in Arctic foods and diets. A pilot study in Broughton Island, Northwest Territories, Canada. Arctic Medical Research, 47(S1):159-162.

Kinloch, D., H.V. Kuhnlein and D.C.G. Muir, 1992. Inuit foods and diet: A preliminary assessment of benefits and risks. Science of the Total Environment, 122:247-278.

Kirkegaard, J., 2012. Incidence of pancreatic cancer in Greenland 2000-2010. International Journal of Circumpolar Health, 71:18368.

Kirman, C.R., L.L. Aylward, S.M. Hays, K. Krishnan and A. Nong, 2011. Biomonitoring equivalents for DDT/DDE. Regulatory Toxicology and Pharmacology, 60:172-80.

Kiviranta, H., R. Purkunen and T. Vartiainen, 1999. Levels and trends of PCDD/Fs and PCBs in human milk in Finland. Chemosphere, 38:311-323.

Kiviranta IV, H., A. Hallikainen, M.-L. Ovaskainen, J. Kumpulainen and T. Vartiainen, 2001. Dietary intakes of polychlorinated dibenzo-*p*-dioxins, dibenzofurans and polychlorinated biphenyls in Finland. Food Additives and Contaminants, 18:945-953.

Kjeldsen, L.S. and E.C. Bonefeld-Jørgensen, 2013. Perfluorinated compounds affect the function of sex hormone receptors. Environmental Science and Pollution Research (international), 20:8031-8044.

Knudsen, A.-K., M. Long, H.S. Pedersen and E.C. Bonefeld-Jørgensen, 2015. Lifestyle, reproductive factors and food intake in Greenlandic pregnant women: The ACCEPT - sub study. International Journal of Circumpolar Health, 74:29469.

Koldkjaer, O.G., L. Wermuth and P. Bjerregaard, 2004. Parkinson's disease among Inuit in Greenland: organochlorines as risk factors. International Journal of Circumpolar Health, 63(S2):366-368.

Kortenkamp, A., M. Faust, M. Scholze and T. Backhaus, 2007. Low-level exposure to multiple chemicals: Reason for human health concerns? Environmental Health Perspectives, 115:106-114.

Kowalec, K., G.Y. Minuk, M.L. Borresen, A. Koch, B.J. McMahon, B. Simons and C. Osiowy, 2013. Genetic diversity of hepatitis B virus genotypes B6, D and F among circumpolar indigenous individuals. Journal of Viral Hepatitis, 20:122-130.

Krapohl, E., K. Rimfeld, N.G. Shakeshaft, M. Trzaskowski, A. McMillan, J-B. Pingault, K. Asbury, N. Harlaard, Y. Kovas, P.S. Dale and R. Plomin, 2014. The high heritability of educational achievement reflects many genetically influenced traits, not just intelligence. PNAS, 42:15273-15278.

Krishnan, K., T. Adamou, L.L. Aylward, S.M. Hays, C.R. Kirman and A. Nong, 2011. Biomonitoring equivalents for 2,2',4,4',5-pentabromodiphenylether (PBDE-99). Regulatory Toxicology and Pharmacology, 60:165-171.

Kropp, T. and J. Houlihan, 2005. Evaluating human health risks from exposure to perfluorooctanoic acid (PFOA): Recommendations to the Science Advisory Board's PFOA Review Panel. Presented 10 February 2005 to the US EPA Science Advisory Board's PFOA Review Panel, in Washington, D.C.

Krüger, T., P.S. Hjelmborg, B.A.G. Jönsson, L. Hagmar, A. Giwercman, G.-C. Manicardi, D. Bizzaro, M. Spanò, A. Rignell-Hydbom, H.S. Pedersen, G. Toft, J.P. Bonde and E.C. Bonefeld-Jørgensen, 2007. Xeno-androgenic activity in serum differs across European and Inuit populations. Environmental Health Perspectives 115:S21-S27.

Krüger, T., M. Ghisari, P.S. Hjelmborg, B. Deutch and E.C. Bonefeld-Jørgensen, 2008. Xenohormone transactivities are inversely associated to serum POPs in Inuit. Environmental Health, 7:38. doi:10.1186/1476-069X-7-38.

Krüger, T., M. Long, M. Ghisari and E.C. Bonefeld-Jørgensen, 2012. The combined effect of persistent organic pollutants in the serum POP mixture in Greenlandic Inuit: xenoestrogenic, xenoandrogenic and dioxin-like transactivities. Biomarkers, 17:692-705.

Kummu, M., K. Wallin, E. Sieppi, A. Rautio, K. Vähäkangas and P. Myllynen, 2012. Cadmium inhibits ABCG2 transporter function in BeWo and MCF-7/MTX cells. Placenta, 33:859-865.

Kuraoka, I., M. Endou, Y. Yamaguchi, T. Wada, H. Handa and K. Tanaka, 2003. Effects of endogenous DNA base lesions on transcription elongation by mammalian RNA polymerase II. Implications for transcription-coupled DNA repair and transcriptional mutagenesis. Journal of Biological Chemistry, 278:7294-7299.

Labonte, M.E., É. Dewailly, M.L. Chateau-Degat, P. Couture and B. Lamarche, 2012. Population-based study of high plasma C-reactive protein concentrations among the Inuit of Nunavik. International Journal of Circumpolar Health, 71. doi:10.3402/ijch.v71i0.19066.

Labonte, M.E., É. Dewailly, M. Lucas, M L. Chateau-Degat, P. Couture and B. Lamarche, 2014. Traditional dietary pattern is associated with elevated cholesterol among the Inuit of Nunavik. Journal of the Academy of Nutrition and Dietetics, 114:1208-1215.

Lagueux, J., D. Pereg, P. Ayotte, E. Dewailly and G.G. Poirier, 1999. Cytochrome P450 CYP1A1 enzyme activity and DNA adducts in placenta of women environmentally exposed to organochlorines. Environmental Research, 80:369-382.

Laird, B.D., A.B. Goncharov and H.M. Chan, 2013a. Body burden of metals and persistent organic pollutants among Inuit in the Canadian Arctic. Environment International, 59:33-40.

Laird, B.D., A.B. Goncharov, G.M. Egeland and H.M. Chan, 2013b. Dietary advice on Inuit traditional food use needs to balance benefits and risks of mercury, selenium and n3 fatty acids. Journal of Nutrition, 143:923-930.

Lakind, J.S., C.M. Berlin Jr., A. Sjodin, W. Turner, R.Y. Wang, L.L. Needham, I.M. Paul, J.L. Stokes, D.Q. Naiman and D.G. Patterson Jr., 2009. Do human milk concentrations of persistent organic chemicals really decline during lactation? Chemical concentrations during lactation and milk/serum partitioning. Environmental Health Perspectives, 117:1625-1631.

Lam, T., P.G. Williams, M.M. Lee, S.A. Korrick, L.S. Birnbaum, J.S. Burns, O. Sergeyev, B. Revich, L.M. Altshul, D.G. Patterson, Jr., W.E. Turner and R. Hauser, 2014. Prepubertal organochlorine pesticide concentrations and age of pubertal onset among Russian boys. Environmental International, 73:135-142.

Lanier, A.P., G.E. Day, J.J. Kelly and E. Provost, 2008. Disparities in cancer mortality among Alaska Native people, 1994-2003. Alaska Medicine, 49:120-125.

Lanphear, B.P., R. Hornung, J. Khoury, K. Yolton, P. Baghurst, D.C. Bellinger, R.L. Canfield, K.N. Dietrich, R. Bornschein, T. Greene, S.J. Rothenburg, H.L. Needleman, L. Schnaas, G. Wasserman, J. Graziano and R. Roberts, 2005. Low-level environmental exposure and children's intellectual function: An international pooled analysis. Environmental Health Perspectives, 113:894-899.

Larsson, K., K.L. Björklund, B. Palm, M. Wennberg, L. Kaj, C.H. Lindh, B.A.G. Jönsson and M. Berglund, 2014. Exposure determinants of phthalates, parabens, bisphenol A and triclosan in Swedish mothers and their children. Environment International, 73:323-333.

Lau, C., K. Anitole, C. Hodes, D. Lai, A. Pfahles-Hutchens and J. Seed, 2007. Perfluoroalkyl acids: a review of monitoring and toxicological findings. Toxicological Sciences, 99:366-394.

Lauby-Secretan, B., D. Loomis, Y. Grosse, F. El Ghissassi, V. Bouvard, L. Benbrahim-Tallaa, N. Guha, R. Baan, H. Mattock, K. Straif and L.F. International Agency for Research on Cancer Monograph Working Group IARC, 2013. Carcinogenicity of polychlorinated biphenyls and polybrominated biphenyls. The Lancet Oncology, 14:287-288.

Lederman, S.A., R.L. Jones, K.L. Caldwell, V. Rauh, S.E. Sheets, D. Tang, S. Viswanathan, M. Becker, J.L. Stein, R.Y. Wang and F.P. Perera, 2008. Relation between cord blood mercury levels and early child development in a World Trade Center cohort. Environmental Health Perspectives, 116:1085-1091.

Lee, D.H., I.K. Lee, M. Porta, M. Steffes and D.R. Jacobs, Jr., 2007. Relationship between serum concentrations of persistent organic pollutants and the prevalence of metabolic syndrome among non-diabetic adults: results from the National Health and Nutrition Examination Survey 1999-2002. Diabetologia, 50:1841-1851.

Legrand, M., M. Feeley, C. Tikhonov, D. Schoen and A. Li-Muller, 2010. Methylmercury blood guidance values for Canada. Canadian Journal of Public Health, 101:28-31.

Leino, O., A.K. Karjalainen and J.T. Tuomisto, 2013. Effects of docosahexaenoic acid and methylmercury on child's brain development due to consumption of fish by Finnish mother during pregnancy: A probabilistic modeling approach. Food and Chemical Toxicology, 54:50-58.

Lemal, M. and J. Merrick, 2011. Health risk communication. International Journal of Public Health, 3:3-5.

Lemire, M., M. Kwan, A.E. Laouan-Sidi, G. Muckle, C. Pirkle, P. Ayotte and É. Dewailly, 2015. Local country food sources of methylmercury, selenium and omega-3 fatty acids in Nunavik, Northern Quebec. Science of the Total Environment, 509-510:248-259.

Lenters, V., C. Thomsen, L.A.M. Smit, B.A.G. Jonsson, H.S. Pedersen, J.K. Ludwicki, V. Zviezdai, A.H. Piersma, G. Toft, J.P. Bonde, G. Becher, R. Vermeulen and D. Heederik, 2013. Serum concentrations of polybrominated diphenyl ethers (PBDEs) and a polybrominated biphenyl (PBB) in men from Greenland, Poland and Ukraine. Environment International, 61:8-16.

Lenters, V., L. Portengen, A.M.S. Lidwien, B.A.G. Jönsson, A. Giwercman, L. Rylander, C.H. Lindh, M. Spanò, H.S. Pedersen, J.K. Ludwicki, L. Chumak, A.H. Piersma, G. Toft, J.P. Bonde, D. Heederik, R. Vermeulen, 2015. Phthalates, perfluoroalkyl acids, metals and organochlorines and reproductive function: a multipollutant assessment in Greenlandic, Polish and Ukrainian men. Occupational Environmental Medicine, 72:385-393.

Leslie, E.M., R.G. Deeley and S.P. Cole, 2005. Multidrug resistance proteins: role of P-glycoprotein, MRP1, MRP2, and BCRP (ABCG2) in tissue defense. Toxicology and Applied Pharmacology, 204:216-237.

Lignell, S., M. Aune, A. Glynn, C. Cantillana and U. Fridén, 2012. Levels of persistent halogenated organic pollutants (POP) in mother's milk from first-time mothers in Uppsala, Sweden – results from 2008/2010 and temporal trends 1996-2010. Report to the Swedish Environmental Protection Agency. Report No. 2012-09-27.

Lignell, S., M. Aune, A. Glynn, T. Cantillana and M. Isaksson, 2013. Polybrominated diphenylethers (PBDE) and hexabromocyclododecane (HBCD) in paired samples of blood serum and breast milk – a correlation study. Report to the Swedish Environmental Protection Agency. Report No. 2013-03-28.

Lignell, S., M. Aune, A. Glynn, T. Cantillana and U. Fridén, 2014. Levels of persistent halogenated organic pollutants (POP) in mother's milk from first-time mothers in Uppsala, Sweden – results from year 2012 and temporal trends for the time period 1996-2012. Report to the Swedish Environmental Protection Agency. Report No. 2014-05-06.

Lindh, C.H., L. Rylander, G. Toft, A. Axmon, A. Rignell-Hydbom, A. Giwercman, H.S. Pedersen, K. Góalczyk, J.K. Ludwicki, V. Zvyezday, R. Vermeulen, V. Lenters, D. Heederik, J.P. Bonde and B.A.G. Jönsson, 2012. Blood serum concentrations of perfluorinated compounds in men from Greenlandic Inuit and European populations. Chemosphere, 88:1269-1275.

Llop, S., K. Engström, F. Ballester, E. Franforte, A. Alhamdow, F. Pisa, J.S. Tratnik, D. Mazej, M. Murcia, M. Rebagliato, M. Bustamante, J. Sunyer, A. Sofianou-Katsoulis, A. Prasouli, E. Antonopoulou, I. Antoniadou, S. Nakou, F. Barbone, M. Horvat and K. Broberg, 2014. Polymorphisms in ABC transporter genes and concentrations of mercury in newborns – evidence from two Mediterranean birth cohorts. PLoS One, 9:e97172.

Long, M. and E.C. Bonefeld-Jørgensen, 2012. Dioxin-like activity in environmental and human samples from Greenland and Denmark. Chemosphere, 89:919-928.

Long, M., B.S. Andersen, C.H. Lindh, L. Hagmar, A. Giwercman, G.C. Manicardi, D. Bizzaro, M. Spano, G. Toft, H S. Pedersen, V. Zvyezday, J.P. Bonde and E.C. Bonefeld-Jørgensen, 2006. Dioxin-like activities in serum across European and Inuit populations. Environmental Health, 5:14. doi:10.1186/1476-069X-5-14.

Long, M., B. Deutch and E.C. Bonefeld-Jørgensen, 2007. AhR transcriptional activity in serum of Inuits across Greenlandic districts. Environmental Health, 6:1-17.

Long, M., R. Bossi and E.C. Bonefeld-Jørgensen, 2012. Level and temporal trend of perfluoroalkyl acids in Greenlandic Inuit. International Journal of Circumpolar Health, 71:17998. doi:10.3402/ijch.v71i0.17998.

Long, M., M. Ghisari and E.C. Bonefeld-Jørgensen, 2013. Effects of perfluoroalkyl acids on the function of the thyroid hormone and the aryl hydrocarbon receptor. Environmental Science and Pollution Research (international), 20:8045-8056.

Long, M., A-K.S. Knudsen, H.S. Pedersen and E.C. Bonefeld-Jørgensen, 2015. Food intake and serum persistent organic pollutants in the Greenlandic pregnant women of the ACCEPT sub-study. Science of the Total Environment, 529:198-212.

Lopez-Espinosa, M.-J., E. Vizcaino, M. Murcia, V. Fuentes, A-M. Garcia, M. Rebagliato, J.O. Grimalt and F. Ballester, 2010. Prenatal exposure to organochlorine compounds and neonatal thyroid stimulating hormone levels. Journal of Exposure Science and Environmental Epidemiology, 20:579-588.

Lucas, M., L.J. Kirmayer, S. Dery and É. Dewailly, 2010a. Erythrocyte n-3 is inversely correlated with serious psychological distress among the Inuit: data from the Nunavik health survey. Journal of the American College of Nutrition, 29:211-221.

Lucas, M., F. Proust, C. Blanchet, A. Ferland, S. Dery, B. Abdous and É. Dewailly, 2010b. Is marine mammal fat or fish intake most strongly associated with omega-3 blood levels among the Nunavik Inuit? Prostaglandins, Leukotrienes and Essential Fatty Acids, 83:143-150.

Lyche, J., H. Larsen, J.U. Skaare, A. Tverdal, E. Dahl, G. Johansen and E. Ropstad, 2004. Effects of perinatal exposure to low doses of PCB 153 and PCB 126 on lymphocyte proliferation and hematology in goat kids. Journal of Toxicology and Environmental Health A, 67:889-904.

Lye, E., M. Legrand, J. Clarke and A. Probert, 2013. Blood total mercury concentrations in the Canadian population: Canadian Health Measures Survey Cycle 1, 2007-2009. Canadian Journal of Public Health, 104:e246-e251.

Lyngso, J., C.H. Ramlau-Hansen, B.B. Hoyer, H. Stovring, J.P. Bonde, B.A. Jonsson, C.H. Lindh, H.S. Pedersen, J.K. Ludwicki, V. Zviezdai and G. Toft, 2014. Menstrual cycle characteristics in fertile women from Greenland, Poland and Ukraine exposed to perfluorinated chemicals: a cross-sectional study. Human Reproduction, 29:359-367.

Madigan, M.P., R.G. Ziegler, J. Benichou, C. Byrne and R.N. Hoover, 1995. Proportion of breast cancer cases in the United States explained by well-established risk factors. Journal of the National Cancer Institute, 87:1681-1685.

Mannetje, A., J. Coakley, J.F. Mueller, F. Harden, L.M. Toms and J. Douwes, 2012. Partitioning of persistent organic pollutants (POPs) between human serum and breast milk: a literature review. Chemosphere, 89:911-918.

Maras, M., C. Vanparys, F. Muylle, J. Robbens, U. Berger, J.L. Barber, R. Blust and W. De Coen, 2006. Estrogen-like properties of fluorotelomer alcohols as revealed by mcf-7 breast cancer cell proliferation. Environmental Health Perspectives, 114:100-105.

Markon, C.J., S.F. Trainor and F.S. Chapin III (Eds.), 2012. The United States National Climate Assessment: Alaska Technical Regional Report. U.S. Geological Survey Circular 1379.

Mayfield, A, 2008. What is Social Media? Icrossing, UK. Online at: www.icrossing.co.uk/ebooks.

McCarthy, J.J. and M. Long Martello, 2005. In: Arctic Climate Impact Assessment, pp. 945-988. Cambridge University Press.

McMichael, A.J., P.A. Baghurst, N.R. Wigg, G.V. Vimpani, E.F. Robertson and R.J. Roberts, 1988. Port Pirie Cohort Study: environmental exposure to lead and children's abilities at the age of four years. New England Journal of Medicine, 319:468-475.

Medehouenou, T.C., C. Larochelle, P. Dumas, É. Dewailly and P. Ayotte, 2010. Determinants of AhR-mediated transcriptional activity induced by plasma extracts from Nunavik Inuit adults. Chemosphere, 80:75-82.

Messier, V., B. Levesque, J.F. Proulx, L. Rochette, B. Serhir, M. Couillard, B.J. Ward, M.D. Libman, É. Dewailly and S. Dery, 2012. Seroprevalence of seven zoonotic infections in Nunavik, Quebec (Canada). Zoonoses and Public Health, 59:107-117.

Metzdorff, S.B., M. Dalgaard, S. Christiansen, M. Axelstad, U. Hass, M.K. Kiersgaard, M. Scholze, A. Kortenkamp and A.M. Vinggaard, 2007. Dysgenesis and histological changes of genitals and perturbations of gene expression in male rats after in utero exposure to antiandrogen mixtures. Toxicological Sciences, 98:87-98.

Mikes, O., P. Cupr, L. Kohut, A. Krskova and M. Cerna, 2012. Fifteen years of monitoring of POPs in the breast milk, Czech Republic, 1994-2009: trends and factors. Environmental Science and Pollution Research, 19:1936-1943.

Miklavčič, A., P. Cuderman, D. Mazej, J. Snoj Tratnik, M. Krsnik, P. Planinšek, J. Osredkar and M. Horvat, 2011a. Biomarkers

of low-level mercury exposure through fish consumption in pregnant and lactating Slovenian women. Environmental Research, 111:129-127.

Miklavčič, A., V. Stibilj, E. Heath, T. Polak, J. Snoj Tratnik, J. Klavž, D. Mazej and M. Horvat, 2011b. Mercury, selenium, PCBs and fatty acids in fresh and canned fish available on the Slovenian market. Food Chemistry, 124:711-720.

Miklavčič, A., A. Casetta, J.S. Tratnik, D. Mazej, M. Krsnik, M. Marius, K. Sofianou, Z. Spiric, F. Barbone and M. Horvat, 2013. Mercury, arsenic and selenium exposure levels in relation to fish consumption in the Mediterranean area. Environmental Research, 120:7-17.

Miklavčič, A., D. Kocman and M. Horvat, 2014. Human mercury exposure and effects in Europe. Environmental Toxicology and Chemistry, 33:1259-1270.

Miller, A.B. and L.A. Gaudette, 1996. Cancer of the respiratory system in Circumpolar Inuit. Acta Oncologica, 35:571-576.

Minganti, V., G. Drava, R. De Pellegrini and C. Siccardi, 2010. Trace elements in farmed and wild gilthead seabream, *Sparus aurata*. Marine Pollution Bulletin, 60:2022-2025.

Minimata Convention, 2014. The Minimata Convention on Mercury (accessed April 2014). www.mercuryconvention.org.

Mocevic, E., I.O. Specht, J.L. Marott, A. Giwercman, B.A. Jonsson, G. Toft, T. Lundh and J.P. Bonde, 2013. Environmental mercury exposure, semen quality and reproductive hormones in Greenlandic Inuit and European men: a cross-sectional study. Asian Journal of Andrology, 15:97-104.

Möller, A., R. Sturm, Z. Xie, M. Cai, J. He and R. Ebinghaus, 2012. Organophosphorus flame retardants and plasticizers in airborne particles over the northern Pacific and Indian Ocean toward the polar regions: evidence for global occurrence. Environmental Science and Technology, 46:3127-3134.

Moltke, I., N. Grarup, M.E. Jorgensen, P. Bjerregaard, J.T. Treebak, M. Fumagalli, T.S. Korneliussen, M.A. Andersen, T.S. Nielsen, N.T. Krarup, A.P. Gjesing, J.R. Zierath, A. Linneberg, X. Wu, G. Sun, X. Jin, J. Al-Aama, J. Wang, K. Borch-Johnsen, O. Pedersen, R. Nielsen, A. Albrechtsen and T. Hansen, 2014. A common Greenlandic TBCD4 variant confers muscle insulin resistance and type 2 diabetes. Nature, 512:190-193.

MONICA, 2014. MONICA-study in northern Sweden. www9.umu.se/phmed/medicin/monica/index.php?content=inenglish (accessed 3 September 2014).

Morales, E., J. Sunyer, F. Castro-Giner, X. Estivill, J. Julvez, N. Ribas-Fitó, M. Torrent, J.O. Grimalt and R. de Cid, 2008. Influence of glutathione *S*-transferase polymorphisms on cognitive functioning effects induced by *p,p′*-DDT among pre-schoolers. Environmental Health Perspectives, 116:1581-1585.

Mørck, T.A., S.E. Erdmann, M. Long, M. Mathiesen, F. Nielsen, V.D. Siersma, E.C. Bonefeld-Jørgensen and K.E. Knudsen, 2014. PCB concentrations and dioxin-like activity in blood samples from Danish school children and their mothers living in urban and rural areas. Basic and Clinical Pharmacology and Toxicology, 115:134-144.

Mortensen, M.E., S.P. Caudill, K.L. Caldwell, C.D. Ward, R.L. Jones, 2014. Total and methyl mercury in whole blood measured for the first time in the U.S. population: NHANES 2011-2012. Environmental Research, 134:257-264.

Moysich, K.B., R.J. Menezes, J.A. Baker and K.L. Falkner, 2002. Environmental exposure to polychlorinated biphenyls and breast cancer risk. Reviews on Environmental Health, 17:263-277.

Mozaffarian, D., P. Shi, J.S. Morris, D. Spiegelman, P. Grandjean, D.S. Siscovick, W.C. Willett and E.B. Rimm, 2011. Mercury exposure and risk of cardiovascular disease in two U.S. cohorts. New England Journal of Medicine, 364:1116-1125.

Mozaffarian, D., P. Shi, J.S. Morris, P. Grandjean, D.S. Siscovick, D. Spiegelman, W.C. Willett, E.B. Rimm, G.C. Curhan and J.P. Forman, 2012. Mercury exposure and risk of hypertension in US men and women in 2 prospective cohorts. Hypertension, 60:645-652.

Muckle, G., É. Dewailly and P. Ayotte, 1998. Prenatal exposure of Canadian children to polychlorinated biphenyls and mercury. Canadian Journal of Public Health, 89(S1):22-27.

Muckle, G., P. Ayotte, É. Dewailly, S.W. Jacobson and J.L. Jacobson, 2001. Prenatal exposure of the northern Quebec Inuit infants to environmental contaminants. Environmental Health Perspectives, 109:1291-1299.

Muir, D., B. Braune, D. DeMarch, R. Norstrom, R. Wagemann, L. Lockhart, B. Hargrave, D. Bright, R. Addison, J. Payne and K. Reimer, 1999. Spatial and temporal trends and effects of contaminants in the Canadian Arctic marine ecosystem: a review. Science of the Total Environment, 230:83-144.

Murata, K., P. Weihe, S. Araki, E. Budtz-Jorgensen and P. Grandjean, 1999. Evoked potentials in Faroese children prenatally exposed to methylmercury. Neurotoxicology and Teratology, 21:471-472.

Murata, K., P. Weihe, E. Budtz-Jorgensen, P.J. Jorgensen and P. Grandjean, 2004. Delayed brainstem auditory evoked potential latencies in 14-year-old children exposed to methylmercury. Journal of Pediatrics, 144:177-183.

Myers, H. and C. Furgal, 2006. Long-range transport of information: Are Arctic residents getting the message about contaminants? Arctic, 59:47-60.

Nampoothiri, L.P. and S. Gupta, 2008. Biochemical effects of gestational coexposure to lead and cadmium on reproductive performance, placenta, and ovary. Journal of Biochemical and Molecular Toxicology, 22:337-344.

National Academy of Sciences, 2000. Toxicological Effects of Methylmercury, National Academy Press.

Naturvårdsverket, 2007. Hälsorelaterad miljöövervakning – mätningar av miljöns effecter på mönniskors hälsa. Report 5635.

Navas-Acien, A., M. Tellez-Plaza, E. Guallar, P. Muntner, E. Silbergeld, B. Jaar and V. Weaver, 2009. Blood cadmium and lead and chronic kidney disease in US adults: a joint analysis. American Journal of Epidemiology, 170:1156-1164.

Naville, D., C. Pinteur, N. Vega, Y. Menade, M. Vigier, A. Le Bourdais, E. Labaronne, C. Debard, C. Luquain-Costaz, M. Begeot, H. Vidal and B. Le Magueresse-Battistoni, 2013. Low-dose food contaminants trigger sex-specific, hepatic metabolic

changes in the progeny of obese mice. Journal of the American Societies for Experimental Biology, 27:3860-3870.

NCP, 2013. Canadian Arctic Contaminant Assessment Report On Persistent Organic Pollutants – 2013. Muir D., P. Kurt-Karakus and J. Stow (Eds). Northern Contaminants Program (NCP), Aboriginal Affairs and Northern Development Canada, Ottawa.

NCSD, 2009. Guidelines for Internet-based health communications. National Coalition of STD Directors. www.ncsddc.org/Internet_Guidelines.

Needham, L.L., O. Grandjean, B. Heinzow, P.J. Jørgensen, F. Nielsen, D.G. Patterson Jr., A. Sjödin, W.E. Turner and P. Weihe, 2011. Partition of environmental chemicals between maternal and fetal blood and tissues. Environmental Science and Technology, 45:1121-1126.

Ng, S., C.C. Lin, Y.H. Hwang, W.S. Hsieh, H.F. Liao and P.C. Chen, 2013. Mercury, APOE, and children's neurodevelopment. Neurotoxicology, 37:85-92.

Nielsen, A.B., M. Davidsen and P. Bjerregaard, 2012. The association between blood pressure and whole blood methylmercury in a cross-sectional study among Inuit in Greenland. Environmental Health, 11:44. doi:10.1186/1476-069X-11-44.

Nieminen, P., H. Lehtiniemi, A. Huusko, K. Vähäkangas and A. Rautio, 2013a. Polychlorinated biphenyls (PCBs) in relation to secondary sex ratio – a systematic review of published studies. Chemosphere, 91:131-138.

Nieminen, P., H. Lehtiniemi, K. Vähäkangas, A. Huusko and A. Rautio, 2013b. Summarizing the reported findings between quantitative exposure and outcome variables from epidemiologic studies in a consistent form: The effect of exposure to polychlorinated biphenyls (PCBs) on birth weight as an example. Epidemiology Biostatistics and Public Health, 10:e8854.

NOAA, 2014. Arctic Report Card: Update for 2014. National Oceanic and Atmospheric Administration (NOAA). www.arctic.noaa.gov/reportcard.

Noel, M., É. Dewailly, M.L. Chateau-Degat, E. Counil, E.A. Laouan-Sidi and E. Lonn, 2012. Cardiovascular risk factors and subclinical atherosclerosis among Nunavik Inuit. Atherosclerosis, 221:558-564.

Nordregio, 2011. Internet in the Arctic: Share of internet users as percentage of population. Nordic Centre for Spatial Development (Nordregio). www.nordregio.se/en/Maps--Graphs/09-Other/Internet-in-the-Arctic.

Nøst, T.H., K. Breivik, O-M. Fuskevåg, E. Nieboer, J.Ø. Odland and T.M. Sandanger, 2013. Persistent organic pollutants in Norwegian men from 1979 to 2007: Intraindividual changes, age-period-cohort effects, and model predictions. Environmental Health Perspectives, 121:1292-1298.

Nøst, T.H., R. Vestergren, V. Berg, E. Nieboer, J.Ø. Odland and T.M. Sandanger, 2014. Repeated measurements of per- and polyfluoroalkyl substances (PFASs) from 1979 to 2007 in males from northern Norway: Assessing time trends, compound correlations and relations to age/birth cohort. Environment International, 67:43-53.

O'Brien, M.L., B.T. Spear and H.P. Glauert, 2005. Role of oxidative stress in peroxisome proliferator-mediated carcinogenesis. Critical Reviews in Toxicology, 35:61-88.

Odland, J.O. (lead author), 2012. Health outcomes in relation to contaminant exposure in Arctic cohorts. ArcRisk Deliverable Number: D35.

Odland, J.Ø. and E. Nieboer, 2012. Human biomonitoring in the Arctic: Special challenges in a sparsely populated area. International Journal of Hygiene and Environmental Health, 215:159-167.

Odland J.Ø., A. Carlsen, S.G. Donaldson, A. Dudarev, C. Furgal and P. Weihe, 2009. Risk communication. In: AMAP Assessment 2009: Human Health in the Arctic, pp. 191-204. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

OECD, 2002. Hazard Assessment of Perfluorooctane Sulfonate and its Salts. Organisation for Economic Co-operation and Development (OECD). ENV/JM/EXCH, 8, Paris, France.

Official Statistics of Sweden, 2014. Mercury in hair 1996-2013. Naturvårdsverket. www.imm.ki.se/datavard/tidsserier/kvicksilver%20i%20har_ENG.htm (accessed 3 September 2014).

Oken, E., R.O. Wright, K.P. Kleinman, D. Bellinger, C.J. Amarasiriwardena, H. Hu, J.W. Rich-Edwards and M.W. Gillman, 2005. Maternal fish consumption, hair mercury, and infant cognition in a U.S. Cohort. Environmental Health Perspectives, 113:1376-1380.

Olsen, G.W., J.M. Burris, D.J. Ehresman, J.W. Froehlich, A.M. Seacat, J.L. Butenhoff and L.R. Zobel, 2007. Half-life of serum elimination of perfluorooctanesulfonate, perfluorohexanesulfonate, and perfluorooctanoate in retired fluorochemical production workers. Environmental Health Perspectives, 115:1298-1305.

Olsen, G.W., D.C. Mair, T.R. Church, M.E. Ellefson, W.K. Reagen, T.M. Boyd, R.M. Herron, Z. Medhdizadehkashi, J.B. Nobiletti, J.A. Rios, J.L. Butenhoff and L.R. Zobel, 2008. Decline in perfluorooctanesulfonate and other polyfluoroalkyl chemicals in American Red Cross adult blood donors, 2000-2006. Environmental Science and Technology, 42:4989-4995.

Oskarsson, A., A. Schütz, S. Skerfving, I.P. Hallén, B. Ohlin, B.J. Lagerkvist, 1996. Total and inorganic mercury in breast milk and blood in relation to fish consumption and amalgam fillings in lactating women. Archives of Environmental Health, 51:234-241.

Osman, K., A. Akesson, M. Berglund, K. Bremme, A. Schutz, K. Ask and M. Vahter, 2000. Toxic and essential elements in placentas of Swedish women. Clinical Biochemistry, 33:131-138.

Patel, C.J., J. Bhattacharya and A.J. Butte, 2010. An Environment-Wide Association Study (EWAS) on type 2 diabetes mellitus. PLoS One, 5:e10746.

Paunescu, A.C., P. Ayotte, É. Dewailly and S. Dodin, 2013a. Dioxin-like compounds are not associated with bone strength measured by ultrasonography in Inuit women from Nunavik (Canada): results of a cross-sectional study. International Journal of Circumpolar Health, 72: 20843. http://dx.doi.org/10.3402/ijch.v72i0.20843.

Paunescu, A.C., É. Dewailly, S. Dodin, E. Nieboer and P. Ayotte, 2013b. Dioxin-like compounds and bone quality in Cree

women of Eastern James Bay (Canada): a cross-sectional study. Environmental Health, 12:54. doi:10.1186/1476-069X-12-54.

Pavlikova, N., L. Blahova, P. Klan, S.R. Bathula, V. Sklenar, J.P. Giesy and L. Blaha, 2012. Enantioselective effects of alpha-hexachlorocyclohexane (HCH) isomers on androgen receptor activity in vitro. Chemosphere, 86:65-69.

Pawlas, N., U. Strömberg, B. Carlberg, M. Cerna, F. Harari, R. Harari, M. Horvat, F. Hruba, K. Koppova, A. Krskova, M. Krsnik, Y.F. Li, L. Löfmark, T. Lundh, N.G. Lundström, B. Lyoussi, I. Markiewicz-Górka, D. Mazej, J. Osredkar, K. Pawlas, G. Rentschler, V. Spevackova, Z. Spiric, A. Sundkvist, J.S. Tratnik, D. Vadla, S. Zizi, S. Skerfving and I.A. Bergdahl, 2013. Cadmium, mercury and lead in the blood of urban women in Croatia, the Czech Republic, Poland, Slovakia, Slovenia, Sweden, China, Ecuador and Morocco. International Journal of Occupational Medicine and Environmental Health, 26:58-72.

Payne, J., M. Scholze and A. Kortenkamp, 2001. Mixtures of four organochlorines enhance human breast cancer cell proliferation. Environmental Health Perspectives, 109:391-397.

Peden-Adams, M.M., J.M. Keller, J.G. Eudaly, J. Berger, G.S. Gilkeson and D.E. Keil, 2008. Suppression of humoral immunity in mice following exposure to perfluorooctane sulfonate. Toxicological Sciences, 104:144-154.

Pelham, W.E., E. Gnagy, K.E. Greenslade and R. Milich, 1992. Teacher ratings of DSM-III-R symptoms for the disruptive behavior disorders. Journal of the American Academy of Child and Adolescent Psychiatry, 31:210-218.

Perry, M.J., F. Ouyang, S. Korrick, S.A. Venners, L. Altshul, X. Xu and X. Wang, 2005. Body mass index and serum 1,1,1-trichloro-2,2-bis(*p*-chlorophenyl) ethane in nulliparous Chinese women. Cancer Epidemiology Biomarkers and Prevention, 14:2433-2438.

Pestana, D., D. Teixeira, A. Faria, V. Domingues, R. Monteiro and C. Calhau, 2015. Effects of environmental organochlorine pesticides on human breast cancer: Putative involvement on invasive cell ability. Environmental Toxicology, 30:168-176.

Petersen, M.S., J. Halling, S. Bech, L. Wermuth, P. Weihe, F. Nielsen, P.J. Jorgensen, E. Budtz-Jorgensen and P. Grandjean, 2008. Impact of dietary exposure to food contaminants on the risk of Parkinson's disease. Neurotoxicology, 29:584-590.

Pillai, A. and S. Gupta, 2005. Effect of gestational and lactational exposure to lead and/or cadmium on reproductive performance and hepatic oestradiol metabolising enzymes. Toxicology Letters, 155:179-186.

Pillai, P., R. Patel, C. Pandya and S. Gupta, 2009. Sex-specific effects of gestational and lactational coexposure to lead and cadmium on hepatic phase I and phase II xenobiotic/steroid-metabolizing enzymes and antioxidant status. Journal of Biochemical and Molecular Toxicology, 23:419-431.

Plusquellec, P., É. Dewailly, G. Muckle, P. Ayotte, G. Bégin, C. Desrosiers, C. Després, D. Saint-Amour and K. Poitras, 2010. The relation of environmental contaminants exposure to behavioral indicators in Inuit preschoolers in Arctic Quebec. Neurotoxicology, 31:17-25.

Porpora, M.G., R. Lucchini, A. Abballe, A.M. Ingelido, S. Valentini, E. Fuggetta and E.D. Felip, 2013. Placental transfer of persistent organic pollutants: A preliminary study on mother-newborn pairs. International Journal of Environmental Research and Public Health, 10:699-711.

Potyrala, M., J. Brewster, K. Tofflemire, O. Receveur, H.M. Chan and I. Sobol, 2008. The Anaana Project (Inuit prenatal health survey). Department of Health and Social Services, Government of Nunavut.

Prochaska, J.O., C.C. DiClemente and J.C. Norcross, 1992. In search of how people change: Applications to addictive behaviors. American Psychologist, 47:1102-1114.

Proust, F., M. Lucas and É. Dewailly, 2014. Fatty acid profiles among the Inuit of Nunavik: Current status and temporal change. Prostaglandins, Leukotrienes and Essential Fatty Acids, 90:159-167.

Punab, M., B. Zilaitiene, N. Jorgensen, A. Horte, V. Matulevicius, A. Peetsalu and N.E. Skakkebaek, 2002. Regional differences in semen qualities in the Baltic region. International Journal of Andrology, 25:243-252.

Qazi, M.R., M.R. Abedi, B.D. Nelson, J.W. DePierre and M. Abedi-Valugerdi, 2010. Dietary exposure to perfluorooctanoate or perfluorooctane sulfonate induces hypertrophy in centrilobular hepatocytes and alters the hepatic immune status in mice. International Immunopharmacology, 10:1420-1427.

Quinn, C.L., F. Wania, G. Czub and K. Breivik, 2011. Investigating intergenerational differences in human PCB exposure due to variable emissions and reproductive behaviors. Environmental Health Perspectives, 119:641-646.

Quinn, C.L., J.M. Armitage, K. Breivik and F. Wania, 2012. A methodology for evaluating the influence of diets and intergenerational dietary transitions on historic and future human exposure to persistent organic pollutants in the Arctic. Environment International, 49:83-91.

Rajapakse, N., E. Silva and A. Kortenkamp, 2002. Combining xenoestrogens at levels below individual no-observed-effect concentrations dramatically enhances steroid hormone action. Environmental Health Perspectives, 110:917-921.

Ravoori, S., P. Ayotte, C. Srinivasan, D. Pereg, L.W. Robertson, G.K. Russell, J. Jeyabalan and R.C. Gupta, 2008. DNA damage associated with PCBs in the whole blood cells of Inuit. Environmental Toxicology and Pharmacology, 25:273-276.

Ravoori, S., C. Srinivasan, D. Pereg, L.W. Robertson, P. Ayotte and R.C. Gupta, 2010. Protective effects of selenium against DNA adduct formation in Inuit environmentally exposed to PCBs. Environment International, 36:980-986.

Rawn, D.F.K., J.J. Ryan, A.R. Sadler, W.F. Sun, D. Weber, P. Laffey, D. Haines, K. Macey and J. Van Oostdam, 2014. Brominated flame retardant concentrations in sera from the Canadian Health Measures Survey (CHMS) from 2007 to 2009. Environment International, 63:26-34.

Revich, B., N. Tokarevich and A. Parkinson, 2012. Climate change and zoonotic disease in the Russian Arctic. International Journal of Circumpolar Health, 71:18792 http:// dx.doi.org/10.3402/ijch.v71i0:i0.18792.

Ribas-Fitó, N., M. Sala, E. Cardo, C. Mazón, M.E. De Muga, A. Verdú, E. Marco, J.O. Grimalt and J. Sunyer, 2002. Association of hexachlorobenzene and other organochlorine compounds with anthropometric measures at birth. Pediatric Research, 52:163-167.

Ribas-Fitó, N., E. Cardo, M. Sala, M.E. De Muga, C. Mazón, A. Verdú, M. Kogevinas, J.O. Grimalt and J. Sunyer, 2003. Breastfeeding, exposure to organochlorine compounds, and neurodevelopment in infants. Pediatrics, 111:e580–5.

Ribas-Fitó, N., M. Torrent, D. Carrizo, L. Munoz-Ortiz, J. Júlvez, J.O. Grimalt and J. Sunyer, 2006. In utero exposure to background concentrations of DDT and cognitive functioning among preschoolers. American Journal of Epidemiology, 164:955-962.

Ribas-Fitó, N., M. Torrent, D. Carrizo, J. Júlvez, J.O. Grimalt and J. Sunyer, 2007. Exposure to hexachlorobenzene during pregnancy and children's social behavior at 4 years of age. Environmental Health Perspectives, 115:447-450.

Rice, D.C., R. Schoeny and K. Mahaffey, 2003. Methods and rationale for derivation of a reference dose for methylmercury by the U.S. EPA. Risk Analysis, 23:107-115.

Richthoff, J., L. Rylander, L. Hagmar, J. Malm and A. Giwercman, 2002. Higher sperm counts in Southern Sweden compared with Denmark. Human Reproduction, 17:2468-2473.

Richthoff, J., L. Rylander, B.A. Jonsson, H. Akesson, L. Hagmar, P. Nilsson-Ehle, M. Stridsberg and A. Giwercman, 2003. Serum levels of 2,2',4,4',5,5'-hexachlorobiphenyl (CB-153) in relation to markers of reproductive function in young males from the general Swedish population. Environmental Health Perspectives, 111:409-413.

Riget, F., R. Dietz, K. Vorkamp, P. Johansen and D. Muir, 2004. Levels and spatial and temporal trends of contaminants in Greenland biota: an updated review. Science of the Total Environment, 331:29-52.

Riget, F., A. Bignert, B. Braune, J. Stow and S. Wilson, 2010. Temporal trends of legacy POPs in Arctic biota, an update. Science of the Total Environment, 408:2874-2884.

Rimfeld, K., Y. Kovas, P.S. Dale and R. Plomin, 2015. Pleiotropy across academic subjects at the end of compulsory education. Nature, 5:11713.

Ritter, R., M. Scheringer, M. MacLeod, C. Moeckel, K.C. Jones and K. Hungerbuhler, 2011. Intrinsic human elimination half-lives of polychlorinated biphenyls derived from the temporal evolution of cross-sectional biomonitoring data from the United Kingdom. Environmental Health Perspectives, 119:225-231.

Robins, J.C., C.J. Marsit, J.F. Padbury and S.S. Sharma, 2011. Endocrine disruptors, environmental oxygen, epigenetics and pregnancy. Frontiers in Bioscience (Elite edn.), 3:690-700.

Roman, H.A., T.L. Walsh, B.A. Coull, É. Dewailly, E. Guallar, D. Hattis, K. Marien, J. Schwartz, A.H. Stern, J.K. Virtanen and G. Rice, 2011. Evaluation of the cardiovascular effects of methylmercury exposures: current evidence supports development of a dose-response function for regulatory benefits analysis. Environmental Health Perspectives, 119:607-614.

Rosenmai, A.K., F.K. Nielsen, M. Pedersen, N. Hadrup, X. Trier, J.H. Christensen and A.M. Vinggaard, 2013. Fluorochemicals used in food packaging inhibit male sex hormone synthesis. Toxicology and Applied Pharmacology, 266:132-142.

Roy, P., H. Salminen, P. Koskimies, J. Simola, A. Smeds, P. Saukko and I.T. Huhtaniemi, 2004. Screening of some anti-androgenic endocrine disruptors using a recombinant cell-based in vitro bioassay. Journal of Steroid Biochemistry and Molecular Biology, 88:157-166.

Rudkowska, I., É. Dewailly, R.A. Hegele, V. Boiteau, A. Dube-Linteau, B. Abdous, Y. Giguere, M.L. Chateau-Degat and M.C. Vohl, 2013. Gene-diet interactions on plasma lipid levels in the Inuit population. British Journal of Nutrition, 109:953-961.

Rusiecki, J.A., A. Baccarelli, V. Bollati, L. Tarantini, L.E. Moore and E.C. Bonefeld-Jørgensen, 2008. Global DNA hypomethylation is associated with high serum-persistent organic pollutants in Greenlandic Inuit. Environmental Health Perspectives, 116:1547-1552.

Rutsaert, P., A. Regan, Z. Pieniak, A. McConnon, A. Moss, P. Wall and W. Verbeke, 2013. The use of social media in food risk and benefit communication. Trends in Food Science and Technology, 30:84-91.

Ruzzin, J., R. Petersen, E. Meugnier, L. Madsen, E.J. Lock, H. Lillefosse, T. Ma, S. Pesenti, S.B. Sonne, T.T. Marstrand, M.K. Malde, Z.Y. Du, C. Chavey, L. Fajas, A.K. Lundebye, C.L. Brand, H. Vidal, K. Kristiansen and L. Froyland, 2010. Persistent organic pollutant exposure leads to insulin resistance syndrome. Environmental Health Perspectives, 118:465-471.

Rydén, P., A. Sjöstedt and A. Johansson, 2009. Effects of climate change on tularemia activity in Sweden. Global Health Action 2009. doi:103402/ghav2i0.2063.

Rylander, L., E. Dyremark, U. Strömberg, C. Östman and L. Hagmar, 1997. The impact of age, lactation and dietary habits on PCB in plasma in Swedish women. Science of the Total Environment, 207:55-61.

Rylander, C., T.M. Sandanger, N. Petrenya, A. Konoplev, E. Bojko and J.Ø. Odland, 2011. Indications of decreasing human PTS concentrations in North West Russia. Global Health Action, 4: 8427. doi:10.3402/gha.v4i0.8427.

Saint-Amour, D., M.S. Roy, C. Bastien, P. Ayotte, É. Dewailly, C. Despres, S. Gingras and G. Muckle, 2006. Alterations of visual evoked potentials in preschool Inuit children exposed to methylmercury and polychlorinated biphenyls from a marine diet. Neurotoxicology, 27:567-578.

Salay, E. and D. Garabrant, 2009. Polychlorinated biphenyls and thyroid hormones in adults: a systematic review appraisal of epidemiological studies. Chemosphere, 74:1413-1419.

Sandman, P.M., N.D. Weinstein and P. Miller, 1994. High risk or low: How location on a 'Risk Ladder' affects perceived risk. Risk Analysis, 14:35-45.

Saudny, H., D. Leggee and G. Egeland, 2012. Design and methods of the Adult Inuit Health Survey 2007-2008. International Journal of Circumpolar Health, 71:19752. doi.org/10.3402/ijch.v71i0.19752.

Schein, R., K. Wilson and J. Keelan, 2010. Literature Review on Effectiveness of the Use of Social Media. A report for Peel Public Health. www.peelregion.ca.

Schell, L.M., M.V. Gallo, J. Ravenscroft and A.P. DeCaprio, 2009. Persistent organic pollutants and anti-thyroid peroxidase levels in Akwesasne Mohawk young adults. Environmental Research, 109:86-92.

Shonkoff, J.P. and S.N. Bales, 2011. Science does not speak for itself: Translating child development research for the public and its policymakers. Child Development, 82:17-32.

Schug, T.T., A. Janesick, B. Blumberg and J.J. Heindel, 2011. Endocrine disrupting chemicals and disease susceptibility. Journal of Steroid Biochemistry and Molecular Biology, 127:204-215.

Schwerdtle, T., F. Ebert, C. Thuy, C. Richter, L.H. Mullenders and A. Hartwig, 2010. Genotoxicity of soluble and particulate cadmium compounds: impact on oxidative DNA damage and nucleotide excision repair. Chemical Research in Toxicology, 23:432-442.

Seifert, B., K. Becker, K. Hoffmann, C. Krause and C. Schulz, 2000. The German Environmental Survey 1990/92 (GerES II): a representative population study. Journal of Exposure Analysis and Environmental Epidemiology, 10:103-114.

Shi, H., X. Shi and K.J. Liu, 2004. Oxidative mechanism of arsenic toxicity and carcinogenesis. Molecular and Cellular Biochemistry, 255:67-78.

Sibinski, L.J., 1987. Final report of a two year oral (diet) toxicity and carcinogenicity study of fluorochemical FC-143 (perfluorooctanane ammonium carboxylate) in rats. 3M Company/RIKER Exp. No. 0281CR0012; 8EHQ-1087-0394 1–4.

Singh, K., P. Bjerregaard and H.M. Chan, 2014. Association between environmental contaminants and health outcomes in Indigenous populations of the Circumpolar North. International Journal of Circumpolar Health, 73:25808. http://dx.doi.org/10.3402/ijch.v73.25808.

Smink, A., N. Ribas-Fitó, R. Garcia, M. Torrent, M.A. Mendez, J.O. Grimalt and J. Sunyer, 2008. Exposure to hexachlorobenzene during pregnancy increases the risk of overweight in children aged 6 years. Acta Pædiatrica, 97:1465-1469.

Smith, J.D., K. Cianflone, É. Dewailly, M.L. Chateau-Degat, M.C. Vohl and P. Julien, 2009. Acylation stimulating protein is higher in Inuit from Nunavik compared to a southern Quebec population. International Journal of Circumpolar Health, 68:421-432.

Snyder, O.B., J.J. Kelly and A.P. Lanier, 2006. Prostate cancer in Alaska Native men, 1969-2003. International Journal of Circumpolar Health, 65:8-17.

Sonne, C., K. Gustavson, F.F. Riget, R. Dietz, T. Krüger and E.C. Bonefeld-Jørgensen, 2013. Physiologically based pharmacokinetic modeling of POPs in Greenlanders. Environment International, 64C:91-97.

Sørensen, M., 2013. Kohorte opfølgning: Vækst og sundhed hos 6-10-årige børn i Grønland [Cohort follow-up: growth and health among 6-10 year old children in Greenland]. Master Thesis. University of Southern Denmark.

Sorensen, N., K. Murata, E. Budtz-Jorgensen, P. Weihe and P. Grandjean, 1999. Prenatal methylmercury exposure as a cardiovascular risk factor at seven years of age. Epidemiology, 10:370-375.

Specht, I.O., K.S. Hougaard, M. Spano, D. Bizzaro, G.C. Manicardi, C.H. Lindh, G. Toft, B.A. Jonsson, A. Giwercman and J.P. Bonde, 2012. Sperm DNA integrity in relation to exposure to environmental perfluoroalkyl substances - a study of spouses of pregnant women in three geographical regions. Reproductive Toxicology, 33:577-583.

Specht, I.O., J.P. Bonde, G. Toft, A. Giwercman, M. Spanò, D. Bizzaro, G.C. Manicardi, B.A. Jönsson, W.A. Robbins, 2015. Environmental hexachlorobenzene exposure and human male reproductive function. Reproductive Toxicology, 58:8-14.

SPFO, 2005. Kartlegging av miljøgifter i humane blodprøver fra Taimyr, Russland og Bodø, Norge – en pilotstudie av 'nye' miljøgifter. SPFO-rapport: 930/2005, TA-2103/2005.

Spillman, M.A., N.G. Manning, W.W. Dye, C.A. Sartorius, M.D. Post, J.C. Harrell, B.M. Jacobsen and K.B. Horwitz, 2010. Tissue-specific pathways for estrogen regulation of ovarian cancer growth and metastasis. Cancer Research, 70:8927-8936.

Stern, G., R. Macdonald, P. Outridge, S. Wilson, J. Chetelat, A. Cole, H. Hintleman, L. Losoto, A. Steffens, F. Wang and P. Zdanowicz, 2012. How does climate change influence Arctic mercury? Science of the Total Environment, 414:22-42.

Steuerwald, U., P. Weihe, P.J. Jorgensen, K. Bjerve, J. Brock, B. Heinzow, E. Budtz-Jorgensen and P. Grandjean, 2000. Maternal seafood diet, methylmercury exposure, and neonatal neurologic function. Journal of Pediatrics, 136:599-605.

Stewart, P.W., E. Lonky, J. Reihman, J. Pagano, B.B. Gump and T. Darvill, 2008. The relationship between prenatal PCB exposure and intelligence (IQ) in 9-year-old children. Environmental Health Perspectives, 116:1416-1422.

Stockholm Convention, 2009-2014. Fourth Meeting of the Conference of the Parties of the Stockholm Convention. Stockholm Convention on Persistent Organic Pollutants Retrieved February 2014, http://chm.pops.int/.

Stockholm Convention, 2014. The Stockholm Convention on Persistent Organic Pollutants (POPs) (accessed April 2014 at http://chm.pops.int).

Strain, J.J., P.W. Davidson, M.P. Bonham, E.M. Duffy, A. Stokes-Riner, S.W. Thurston, J.M. Wallace, P.J. Robson, C.F. Shamlaye, L.A. Georger, J. Sloane-Reeves, E. Cernichiari, R.L. Canfield, C. Cox, L.S. Huang, J. Janciuras, G.J. Myers and T.W. Clarkson, 2008. Associations of maternal long-chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development Nutrition Study. Neurotoxicology, 29:776-782.

Sturludottir, E., H. Gunnlaugsdottir, H.O. Jorundsdottir, E.V. Magnusdottir, K. Olafsdottir and G. Stefansson, 2014. Temporal trends of contaminants in cod from Icelandic waters. Science of the Total Environment, 476-477:181-188.

Sundkvist, A., M. Wennberg, G. Rentschler, T. Lundh, B. Carlberg, I. Rodushkin and I.A. Bergdahl, 2011. Time trends of cadmium, lead and mercury in the population of Northern

Sweden 1990-2009 and blood levels of rhodium and platinum in 2009. Rapport 2011-03-31. Från Yrkes- och miljömedicin.

Sunyer, J., M. Torrent, L. Muñoz-Ortiz, N. Ribas-Fitó, D. Carrizo, J.O. Grimalt, J.M. Antó and P. Cullinan, 2005. Prenatal dichlorodiphenyldichloroethylene (DDE) and asthma in children. Environmental Health Perspectives, 113:1787-1790.

Sunyer, J., M. Torrent, R. Garcia-Esteban, N. Ribas-Fitó, D. Carrizo, I. Romieu, J.M. Antó and J.O. Grimalt, 2006. Early exposure to dichlorodiphenyldichloroethylene, breastfeeding and asthma at age six. Clinical and Experimental Allergy, 36:1236-1241.

Sunyer, J., M. Álvarez-Pedrerol, J. To-Figueras, N. Ribas-Fitó, J.O. Grimalt and C. Herrero, 2008. Urinary porphyrin excretion in children is associated with exposure to organochlorine compounds. Environmental Health Perspectives, 116:1407-1410.

Swan, S.H., E.P. Elkin and L. Fenster, 1997. Have sperm densities declined? A reanalysis of global trend data. Environmental Health Perspectives, 105:1228-1232.

Swan, S.H., E.P. Elkin and L. Fenster, 2000. The question of declining sperm density revisited: an analysis of 101 studies published 1934-1996. Environmental Health Perspectives, 108:961-966.

Tan, M.L., A. Ujihara, L. Kent and I. Hendrickson, 2011. Communicating fish consumption advisories in California: What works, what doesn't. Risk Analysis, 31:1095-1106.

Tang-Péronard, J.L., B.L. Heitmann, H.R. Andersen, U. Steuerwald, P. Grandjean, P. Weihe and T.K. Jensen, 2014. Association between prenatal polychlorinated biphenyl exposure and obesity development at ages 5 and 7y: a prospective cohort study of 656 children from the Faroe Islands. The American Journal of Clinical Nutrition, 99:5-13.

Taylor, A., 2011. Social Media as a Tool for Inclusion. Stiles Associates Inc. www.homelesshub.ca/ResourceFiles/Taylor_Social%20Media_feb2011%20(1)_1_2.pdf.

Taylor, K.W., R.F. Novak, H.A. Anderson, L.S. Birnbaum, C. Blystone, M. Devito, D. Jacobs, J. Köhrle, D.H. Lee, L. Rylander, A. Rignell-Hydbom, R. Tornero-Velez, M.E. Turyk, A.L. Boyles, K.A. Thayer and L. Lind, 2013. Evaluation of the association between persistent organic pollutants (POPs) and diabetes in epidemiological studies: a national toxicology program workshop review. Environmental Health Perspectives, 121:774-783.

ten Tusscher, G.W., P.A. Steerenberg, H. van Loveren, J.G. Vos, A.E. von dem Borne, M. Westra, J.W. van der Slikke, K. Olie, H.J. Pluim and J.G. Koppe, 2003. Persistent hematologic and immunologic disturbances in 8-year-old Dutch children associated with perinatal dioxin exposure. Environmental Health Perspectives, 111:1519-1523.

Thurston, S.W., P. Bovet, G. Myers, P.W. Davidson, L.A. Georger, C. Shamlaye and T.W. Clarkson, 2007. Does prenatal methylmercury exposure from fish consumption affect blood pressure in childhood? Neurotoxicology, 28:924-930.

Tinker, T.L., 1996. Recommendations to improve health risks communication: Lessons learned from the US Public Health Service. Journal of Health Communication, 1:197-217.

Tinker, T. and D. Fouse (Eds.), 2009. Special Report: Expert Round Table on Social Media and Risk Communication During times of Crisis: Strategic Challenges and Opportunities. www.boozallen.com/media/file/Risk_Communications_Times_of_Crisis.pdf.

Toft, G., H.S. Pedersen and J.P. Bonde, 2004. Semen quality in Greenland. International Journal of Circumpolar Health, 63 Suppl 2:174-178.

Toft, G., A. Axmon, A. Giwercman, A-M. Thulstrup, A. Rignell-Hydbom, H.S. Pedersen, J.K. Ludwicki, V. Zvyezday, A. Zinchuk, M. Spano, G.C. Manicardi, E.C. Bonefeld-Jörgensen, L. Hagmar, J.P. Bonde and INUENDO, 2005. Fertility in four regions spanning large contrasts in serum levels of widespread persistent organochlorines: a cross-sectional study. Environmental Health, 4:26. doi:10.1186/1476-069X-4-26.

Toft, G., A. Rignell-Hydbom, E. Tyrkiel, M. Shvets, A. Giwercman, C.H. Lindh, H.S. Pedersen, J.K. Ludwicki, V. Lesovoy, L. Hagmar, M. Spano, G.C. Manicardi, E.C. Bonefeld-Jørgensen, A.M. Thulstrup and J.P. Bonde, 2006. Semen quality and exposure to persistent organochlorine pollutants. Epidemiology, 17:450-458.

Toft, G., A.M. Thulstrup, B.A. Jonsson, H.S. Pedersen, J.K. Ludwicki, V. Zvezday and J.P. Bonde, 2010. Fetal loss and maternal serum levels of 2,2',4,4',5,5'-hexachlorbiphenyl (CB-153) and 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (*p,p'*-DDE) exposure: a cohort study in Greenland and two European populations. Environmental Health, 9:22. doi:10.1186/1476-069X-9-22.

Toft, G., B.A. Jonsson, C.H. Lindh, A. Giwercman, M. Spano, D. Heederik, V. Lenters, R. Vermeulen, L. Rylander, H.S. Pedersen, J.K. Ludwicki, V. Zviezdai and J.P. Bonde, 2012. Exposure to perfluorinated compounds and human semen quality in Arctic and European populations. Human Reproduction, 27:2532-2540.

Toft, G., V. Lenters, R. Vermeulen, D. Heederik, C. Thomsen, G. Becher, A. Giwercman, D. Bizzaro, G.C. Manicardi, M. Spano, L. Rylander, H.S. Pedersen, P. Strucinski, V. Zviezdai and J.P. Bonde, 2014. Exposure to polybrominated diphenyl ethers and male reproductive function in Greenland, Poland and Ukraine. Reproductive Toxicology, 43:1-7.

Tremoen, N.H., P.A. Fowler, E. Ropstad, S. Verhaegen and A. Krogenaes, 2014. Exposure to the three structurally different PCB congeners (PCB 118, 153, and 126) results in decreased protein expression and altered steroidogenesis in the human adrenocortical carcinoma cell line H295R. Journal of Toxicology and Environmental Health A, 77:516-534.

US CDC, 2009. Fourth National Report on Human Exposure to Environmental Chemicals, 2009. United States Department of Health and Human Services, Centers for Disease Control and Prevention (US CDC).

US CDC, 2011a. Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, February 2011. United States Department of Health and Human Services, Centers for Disease Control and Prevention (US CDC).

US CDC, 2011b. The health communicator's social media toolkit. United States Department of Health and Human Services, Centers for Disease Control and Prevention (US CDC).

US CDC, 2014a. Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables, August 2014. United States Department of Health and Human Services, Centers for Disease Control and Prevention (US CDC).

US CDC, 2014b. CDC – Lead – New Blood Lead Information. United States Department of Health and Human Services, Centers for Disease Control and Prevention (US CDC). www.cdc.gov/nceh/lead/acclpp/blood_lead_levels.htm (accessed 3 September 2014).

US EPA, 2006. Draft risk assessment of potential human health effects associated with PFOA and its salts. United States Environmental Protection Agency (US EPA). EPA-SAB-06-006, Washington, DC.

US EPA, 2013. Trends in blood mercury concentrations and fish consumption among US women of childbearing age NHANES, 1999-2010. Final Report. EPA-823-R-13-002. United States Environmental Protection Agency (US EPA).

US EPA, 2014. USEPA-IRIS, United State Environmental Protection Agency – Integrated Risk Information System (IRIS). www.epa.gov/iris (accessed December 2014).

US EPA, 2015. Mercury. United States Environmental Protection Agency (US EPA). www.epa.gov/mercury/resources-mercury-science-and-research (last updated on 21 October 2015, accessed 6 January 2016).

Usher, P., M. Baikie, M. Demmer, D. Nakashima, M. Stevenson and M. Stiles, 1995. Communicating about contaminants in country food: The experience in aboriginal communities. Inuit Tapiriit Kanatami / INAC (Indian and Northern Affairs Canada) publication.

Václavíková, J., O. Mikeš, M. Černá and P. Čupr, 2014. Toxicokinetic modeling of selected POPs in human breast milk: Prediction of chronic daily intake and health risks for Czech women in 1994-2009. Arctic Frontiers Conference, Tromsø, Abstract. Part II: Health & Environment in the Arctic.

Vähäkangas, K. and P. Myllynen, 2009. Drug transporters in the human blood-placental barrier. British Journal of Pharmacology, 158:665-678.

Valent, F., M. Horvat, D. Mazej, V. Stibilj and F. Barbone, 2011. Maternal diet and selenium concentration in human milk from an Italian population. Journal of Epidemiology, 21:285-292.

Valent, F., M. Mariuz, M. Bin, D. Little, D. Mazej, V. Tognin, J. Tratnik, A.J. McAfee, M.S. Mulhern, M. Parpinel, M. Carrozzi, M. Horvat, G. Tamburlini and F. Barbone, 2013. Associations of prenatal mercury exposure from maternal fish consumption and polyunsaturated fatty acids with child neurodevelopment: a prospective cohort study in Italy. Journal of Epidemiology, 5:360-370.

Valera, B., É. Dewailly and P. Poirier, 2008. Cardiac autonomic activity and blood pressure among Nunavik Inuit adults exposed to environmental mercury: a cross-sectional study. Environmental Health, 7:29. doi:10.1186/1476-069X-7-29.

Valera, B., É. Dewailly and P. Poirier, 2009. Environmental mercury exposure and blood pressure among Nunavik Inuit adults. Hypertension, 54:981-986.

Valera, B., É. Dewailly, E. Anassour-Laouan-Sidi and P. Poirier, 2011a. Influence of n-3 fatty acids on cardiac autonomic activity among Nunavik Inuit adults. International Journal of Circumpolar Health, 70:6-18.

Valera, B., É. Dewailly and P. Poirier, 2011b. Impact of mercury exposure on blood pressure and cardiac autonomic activity among Cree adults (James Bay, Quebec, Canada). Environmental Research, 111:1265-1270.

Valera, B., G. Muckle, P. Poirier, S.W. Jacobson, J.L. Jacobson and É. Dewailly, 2012. Cardiac autonomic activity and blood pressure among Inuit children exposed to mercury. Neurotoxicology, 33:1067-1074.

Valera, B., P. Ayotte, P. Poirier and É. Dewailly, 2013a. Associations between plasma persistent organic pollutant levels and blood pressure in Inuit adults from Nunavik. Environment International, 59:282-289.

Valera, B., É. Dewailly and P. Poirier, 2013b. Association between methylmercury and cardiovascular risk factors in a native population of Quebec (Canada): a retrospective evaluation. Environmental Research, 120:102-108.

Valera, B., M.E. Jørgensen, C. Jeppesen and P. Bjerregaard, 2013c. Exposure to persistent organic pollutants and risk of hypertension among Inuit from Greenland. Environmental Research, 122:65-73.

Van Oostdam, J. and S. Donaldson, 2009. Human tissue levels of environmental contaminants. In: AMAP Assessemnt 2009: Human Health in the Arctic. Arctic Monitoring and Assessment Programme (AMAP).

Van Oostdam, J., S. Donaldson, M. Feeley and N. Tremblay (eds.), 2003. Canadian Arctic Contaminants Assessment Report II (CACAR II) Northern Contaminants program.

Van Oostdam, J.C., É. Dewailly, A. Gilman, J.C. Hansen, J.O. Odland, V. Chashchin, J. Berner, J. Butler-Walker, B.J. Lagerkvist, K. Olafsdottir, L. Soininen, P. Bjerregard, V. Klopov and J.P. Weber, 2004. Circumpolar maternal blood contaminant survey, 1994-1997 organochlorine compounds. Science of the Total Environment, 330:55-70.

Van Oostdam, J., S. Donaldson, M. Feeley and C. Tikhonov (eds.), 2009. Canadian Arctic Contaminants and Health Assessment Report (CACAR III): Human Health 2009. Department of Indian Affairs and Northern Development, Ottawa, Ontario, Canada.

Vartiainen, T., S. Saarikoski, J. Jaakkola and J. Tuomisto, 1997. PCDD, PCDF and PCB concentrations in human milk from two areas of Finland. Chemosphere 34:2571-2583.

Ventura, D.F., M.T. Costa, M.F. Costa, A. Berezovsky, S.R. Salomao, A.L. Simoes, M. Lago, L.H. Pereira, M.A. Faria, J.M. De Souza and L.C. Silveira, 2004. Multifocal and full-field electroretinogram changes associated with color-vision loss in mercury vapor exposure. Visual Neuroscience, 21:421-429.

Verner, M.A., R. McDougall, A. Glynn, M.E. Andersen, H.J. Clewell, 3rd and M.P. Longnecker, 2013. Is the relationship between prenatal exposure to PCB-153 and decreased birth weight attributable to pharmacokinetics? Environmental Health Perspectives, 121:1219-1224.

Veyhe, A.S., S. Hansen, T.M. Sandanger, E. Nieboer and J.O. Odland, 2012. The Northern Norway mother-and-child contaminant cohort study: implementation, population characteristics and summary of dietary findings. International Journal of Circumpolar Health, 71:18644. http://dx.doi.org/10.3402/ijch.v71i0.18644.

Veyhe, A.S., T.H. Nost, T.M. Sandanger, S. Hansen, J.O. Odland and E. Nieboer, 2013. Is meconium useful to predict fetal exposure to organochlorines and hydroxylated PCBs? Environmental Science: Processes and Impacts, 15:1490-1500.

Veyhe, A.S., D. Hofoss, S. Hansen, Y. Thomassen, T.M. Sandanger, J.O. Odland and E. Nieboer, 2015. The northern Norway mother- and child contaminant cohort (MISA) Study: PCA analyses of environmental contaminants in maternal sera and dietary intake in early pregnancy. International Journal of Hygiene and Environmental Health, 218:254-264.

Vine, M.F., L. Stein, K. Weigle, J. Schroeder, D. Degnan, C.K. Tse and L. Backer, 2001. Plasma 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE) levels and immune response. American Journal of Epidemiology, 153:53-63.

Virtanen, J.K., J.A. Laukkanen, J. Mursu, S. Voutilainen and T.P. Tuomainen, 2012. Serum long-chain n-3 polyunsaturated fatty acids, mercury, and risk of sudden cardiac death in men: a prospective population-based study. PLoS One, 7:e41046.

Visnjevec, A.M., D. Kocman and M. Horvat, 2014. Human mercury exposure and effects in Europe. Environmental Toxicology and Chemistry, 33:1259-1270.

Vizcaino, E., J.O. Grimalt, A. Fernandez-Somoano and A. Tardon, 2014. Transport of persistent organic pollutants across the human placenta. Environment International, 65:107-115.

VKM, 2008. Risk assessment of non dioxin-like PCBs in Norwegian food: Opinion of the Panel on Contaminants of the Norwegian Scientific Committee for Food Safety (VKM). www.vkm.no/dav/c29e178d9c.pdf.

Vorkamp, K., J.H. Christensen, M. Glasius and F.F. Riget, 2004. Persistent halogenated compounds in black guillemots (*Cepphus grylle*) from Greenland - levels, compound patterns and spatial trends. Marine Pollution Bulletin, 48:111-121.

Wang, S.L., P.C. Tsai, C.Y. Yang and Y.L. Guo, 2008. Increased risk of diabetes and polychlorinated biphenyls and dioxins: a 24-year follow-up study of the Yucheng cohort. Diabetes Care, 31:1574-1579.

Watkins, D.J., M.D. McClean, A.J. Fraser, J. Weinberg, H.M. Stapleton, A. Sjödin and T.F. Webster, 2012. Impact of dust from multiple microenvironments and diet on pentaBDE body burden. Environmental Science and Technology, 46:1192-1200.

Weber, J.P., 2002. The AMAP Ring Test: A laboratory intercomparison program for POPs in human serum. Presented at the AMAP conference and workshop: Impacts of POPs and Mercury on Arctic environments and humans, Tromsø, Norway.

Wechsler, D., 2003. Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV). San Antonio, TX, The Psychological Corporation.

Weihe, P. and H.D. Joensen, 2012. Dietary recommendations regarding pilot whale meat and blubber in the Faroe Islands. International Journal of Circumpolar Health, 71:18594. http://dx.doi.org/10.3402/ijch.v71i0.18594.

Weihe, P., J.C. Hansen, K. Murata, F. Debes and P.J. Jorgensen, 2002. Neurobehavioral performance of Inuit children with increased prenatal exposure to methylmercury. International Journal of Circumpolar Health, 61:41-49.

Weinstein, N.A., 1999. What does it mean to understand a risk? Evaluating risk comprehension. Journal of the National Cancer Institute Monographs, 25:15-20.

Weisglas-Kuperus, N., T.C. Sas, C. Koopman-Esseboom, C.W. van der Zwan, M.A. De Ridder, A. Beishuizen, H. Hooijkaas and P.J. Sauer, 1995. Immunologic effects of background prenatal and postnatal exposure to dioxins and polychlorinated biphenyls in Dutch infants. Pediatric Research, 38:404-410.

Weisglas-Kuperus, N., S. Patandin, G.A. Berbers, T.C. Sas, P.G. Mulder, P.J. Sauer and H. Hooijkaas, 2000. Immunologic effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. Environmental Health Perspectives, 108:1203-1207.

Weiss, J.A. and M. Tschirhart, 1994. Public information campaigns as policy instruments. Journal of Policy Analysis and Management, 13:82-119.

Wennberg, M., T. Lundh, I.A. Bergdahl, G. Hallmans, J-H. Jansson, B. Stegmayr, H.M. Bustodio and S. Skerfving, 2006. Time trends in burdens of cadmium, lead, and mercury in the population of northern Sweden. Environmental Research, 100:330-338.

Wennberg, M, G. Rentschler, T. Lundh, L. Löfmark, B. Stegmayr, I. Bergdahl and S. Skerfving, 2007. Kadmium, bly och kvicksilver i blod samt kadmium och bly i urin hos unga och medelålders kvinnor i Skåne samt Norr- och Västerbotten. Report from Umeå University and Lund University to the Swedish National Environmental Monitoring Programme. Contract 215 0404.

White, S.S., A.M. Calafat, Z. Kuklenyik, L. Villanueva, R.D. Zehr, L. Helfant, M.J. Strynar, A.B. Lindstrom, J.R. Thibodeaux, C. Wood and S.E. Fenton, 2007. Gestational PFOA exposure of mice is associated with altered mammary gland development in dams and female offspring. Toxicological Sciences, 96:133-144.

Whitehead, T.P., S.C. Smith, J.S. Park, M.X. Petreas, S.M. Rappaport and C. Metayer, 2015. Concentrations of persistent organic pollutants in California women's serum and residential dust. Environmental Research, 135:57-66.

WHO, 2007. Health risks of heavy metals from long-range transboundary air pollution. Copenhagen, Denmark. World Health Organization (WHO).

Wielsøe, M., M. Long, M. Ghisari and E.C. Bonefeld-Jørgensen, 2015. Perfluoroalkylated substances (PFASs) affect oxidative stress biomarkers in vitro. Chemosphere, 129:239-245.

Williams, G.M. and J. Whysner, 1996. Epigenetic carcinogens: evaluation and risk assessment. Experimental and Toxicologic Pathology, 48:189-195.

Wojtyniak, B.J., D. Rabczenko, B.A. Jonsson, V. Zvezday, H.S. Pedersen, L. Rylander, G. Toft, J.K. Ludwicki, K. Goralczyk, A. Lesovaya, L. Hagmar and J.P. Bonde, 2010. Association of maternal serum concentrations of 2,2', 4,4'5,5'-hexachlorobiphenyl (CB-153) and 1,1-dichloro-2,2-bis (*p*-chlorophenyl)-ethylene (*p,p*'-DDE) levels with birth weight, gestational age and preterm births in Inuit and European populations. Environmental Health, 9:56. doi:10.1186/1476-069X-9-56.

Wolff, M.S., A. Zeleniuch-Jacquotte, N. Dubin and P. Toniolo, 2000. Risk of breast cancer and organochlorine exposure. Cancer Epidemiology, Biomarkers and Prevention, 9:271-277.

Wolff, M.S., J.A. Britton, S.L. Teitelbaum, S. Eng, E. Deych, K. Ireland, Z. Liu, A.I. Neugut, R.M. Santella and M.D. Gammon, 2005. Improving organochlorine biomarker models for cancer research. Cancer Epidemiology Biomarkers and Prevention, 14:2224-2236.

Wolff, M.S., H.A. Anderson, J.A. Britton and N. Rothman, 2007. Pharmacokinetic variability and modern epidemiology – the example of dichlorodiphenyltrichloroethane, body mass index, and birth cohort. Cancer Epidemiology Biomarkers and Prevention, 16:1925-1230.

Wong, S.L. and E.J.D. Lye, 2008. Lead, mercury and cadmium levels in Canadians. Statistics Canada, Catalogue no. 82-003-XPE. Health Reports, Vol. 19.

Wylie, J., S. Ouboter, L. Reijerkerk, A. Weenk and R. Weterings, 2001. Risk communication for contaminated land: Developing guidelines from observations and case studies. Land Contamination and Reclamation, 9:164-169.

Yaginuma-Sakurai, K., K. Murata, M. Shimada, K. Nakai, N. Kurokawa, S. Kameo and H. Satoh, 2010. Intervention study on cardiac autonomic nervous effects of methylmercury from seafood. Neurotoxicology and Teratology, 32:240-245.

Yaginuma-Sakurai, K., K. Murata, M. Iwai-Shimada, K. Nakai, N. Kurokawa, N. Tatsuta and H. Satoh, 2012. Hair-to-blood ratio and biological half-life of mercury: experimental study of methylmercury exposure through fish consumption in humans. Journal of Toxicological Sciences, 37:123-130.

Yang, M., M.S. Park and H.S. Lee, 2006. Endocrine disrupting chemicals: human exposure and health risks. Journal of Environmental Science and Health C, 24:183-224.

Yorifuji, T., F. Debes, P. Weihe and P. Grandjean, 2011. Prenatal exposure to lead and cognitive deficit in 7- and 14-year-old children in the presence of concomitant exposure to similar molar concentration of methylmercury. Neurotoxicology and Teratology, 33:205-211.

Yorifuji, T., K. Murata, K.S. Bjerve, A.L. Choi, P. Weihe and P. Grandjean, 2013. Visual evoked potentials in children prenatally exposed to methylmercury. Neurotoxicology, 37:15-18.

Young, B.M., 2008. Cancer patterns in Inuit populations. The Lancet Oncology, 9:1124. doi:10.1016/S1470-2045(08)70295-X.

Young, K. and P. Bjerregaard (Eds.), 2008. Health Transitions in Arctic Populations. University of Toronto Press.

Yu, W.-G., W. Liu and Y.-H. Jin, 2009. Effects of perfluorooctane sulfonate on rat thyroid hormone biosynthesis and metabolism. Environmental Toxicology and Chemistry (SETAC), 28:990-996.

Zagar, D., N. Sirnik, M. Cetina, M. Horvat, J. Kotnik, N. Ogrinc, I.M. Hedgecock, S. Cinnirella, F. DeSimone, C.N. Gencarelli and N. Pirrone, 2014. Mercury in the Mediterranean. Part 2: processes and mass balance. Environmental Science and Pollution Research, 21:4081-4094.

Zhang, Y., S. Beesoon, L. Zhu and J.W. Martin, 2013. Biomonitoring of perfluoroalkyl acids in human urine and estimates of biological half-life. Environmental Science and Technology, 47:10619-10627.

Zhu, A.Z., M.J. Binnington, C.C. Renner, A.P. Lanier, D.K. Hatsukami, I. Stepanov, C.H. Watson, C.S. Sosnoff, N.L. Benowitz and R.F. Tyndale, 2013. Alaska Native smokers and smokeless tobacco users with slower CYP2A6 activity have lower tobacco consumption, lower tobacco-specific nitrosamine exposure and lower tobacco-specific nitrosamine bioactivation. Carcinogenesis, 34:93-101.

Acronyms and Abbreviations

5-cx-MEPP	Mono(2-ethyl-5-carboxypentyl) phthalate;
5-OH-MEHP	Mono(2-ethyl-5-hydroxyhexyl) phthalate
5-oxo-MEHP	Mono(2-ethyl-5-oxohexyl) phthalate;
7-cx-MMeHP	Mono-(4-methyl-7-carboxyheptyl)phthalate
7-OH-MMeOP	Mono-(4-methyl-7-hydroxy-octyl)phthalate;
7-oxo-MMeOP	Mono-(4-methyl-7-oxo-octyl)phthalate;
ACCEPT	Adaptation to Climate Change, Environmental Pollution, and Dietary Transition (project)
ADHD	Attention-deficit hyperactivity disorder
AhR	Aryl hydrocarbon receptor
AMAP	Arctic Monitoring and Assessment Programme
ArcRisk	Arctic Health Risks: Impacts on health in the Arctic and Europe owing to climate-induced changes in contaminant cycling
As	Arsenic
BFR	Brominated flame retardant
BMI	Body mass index
BPA	Bisphenol A
Cd	Cadmium
CDC	Centers for Disease Control (US)
CHMS	Canadian Health Measures Survey
CSF	Cancer slope factor
cx-MiNP	monocarboxylated mono-isononylphthalate
DDD	*p,p*'-Dichlorodiphenyldichloroethane
DDE	*p,p*'-Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
DHA	Docosahexaenoic acid
EPA	Environmental Protection Agency (US)
EQAS	External quality assessment scheme
FOSA	Perfluorooctanesulfonamide
FSH	Follicle-stimulating hormone
HBCD	Hexabromocyclodecane
HCB	Hexachlorobenzene
HCH	Hexachlorocyclohexane
Hg	Mercury
HQ	Hazard quotient
ICC	Inuit Circumpolar Council
IHS	Inuit Health Survey
IPCC	Intergovernmental Panel on Climate Change
LEO	Local environmental observer
LOD	Limit of detection
MBzP	Monobenzyl phthalate
MeHg	Methylmercury
MEHP	Mono(2-ethylhexyl) phthalate
MEP	Mono-ethyl phthalate
MISA	Northern Norway mother-and-child contaminant cohort study
Mn	Manganese
MnBP	Mono-*n*-butyl phthalate
MONICA	Monitoring of Trends and Determinants in Cardiovascular Disease Study
NCP	Northern Contaminants Program (Canada)
NCDS	Nunavik Child Development Study (Canada)
NHANES	National Health and Nutrition Examination Survey (US)
NHS	Nunavik Health Survey
NIHS	Nunavut Inuit Health Survey
OC	Organochlorine pesticide
OH-MiNP	Monohydroxylated mono-isononylphthalate
oxo-MiNP	Monooxidated mono-isononylphthalate
Pb	Lead
PBDEs	Polybrominated diphenyl ethers
PCB	Polychlorinated biphenyl
PCP	Pentachlorophenol
PFASs	Per-and polyfluoroalkyl substances
PFC	Perfluorinated compound
PFDA	Perfluorodecanoate
PFDoDA	Perfluorododecanoate
PFAAs	Perfluoroalkyl acids / polyfluoroalkyl substances
PFHpA	Perfluoroheptanoate
PFHpS	Perfluoroheptane sulfonate
PFHxS	Perfluorohexane sulfonate
PFNA	Perfluorononanoate
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonate
PFTrDA	Perfluorotridecanoate
PFUnDA	Perfluoroundecanoate
POP	Persistent organic pollutant
PTS	Persistent toxic substance
QA	Quality assessment
QC	Quality control
Se	Selenium
SHBG	Steroid hormone-binding globulin
TBBPA	Tetrabromobisphenol A
TBG	Thyroxine-binding globulin
TEK	Traditional ecological knowledge
TSH	Thyroid-stimulating hormone
US EPA	United States Environmental Protection Agency
WCBA	Woman of child-bearing age

Arctic Monitoring and Assessment Programme

The Arctic Monitoring and Assessment Programme (AMAP) was established in June 1991 by the eight Arctic countries (Canada, Denmark, Finland, Iceland, Norway, Russia, Sweden and the United States) to implement parts of the Arctic Environmental Protection Strategy (AEPS). AMAP is now one of six working groups of the Arctic Council, members of which include the eight Arctic countries, the six Arctic Council Permanent Participants (indigenous peoples' organizations), together with observing countries and organizations.

AMAP's objective is to provide 'reliable and sufficient information on the status of, and threats to, the Arctic environment, and to provide scientific advice on actions to be taken in order to support Arctic governments in their efforts to take remedial and preventive actions to reduce adverse effects of contaminants and climate change'.

AMAP produces, at regular intervals, assessment reports that address a range of Arctic pollution and climate change issues, including effects on health of Arctic human populations. These are presented to Arctic Council Ministers in 'State of the Arctic Environment' reports that form a basis for necessary steps to be taken to protect the Arctic and its inhabitants.

This report has been subject to a formal and comprehensive peer review process. The results and any views expressed in this series are the responsibility of those scientists and experts engaged in the preparation of the reports.

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