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Mechanistic modeling of persistent organic pollutant exposure among Indigenous Arctic populations: motivations, challenges, and benefits

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Complete List of Authors:	Wania, Frank; University of Toronto at Scarborough, Binnington, Matthew; University of Toronto at Scarborough Curren, Meredith; Health Canada, Environmental Health Science and Research Bureau
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1 **Title:**
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4
5 **Authors:**
6 Wania F¹, Binnington MJ¹, Curren MS².
7 ¹Department of Physical and Environmental Sciences, University of Toronto Scarborough, 1065
8 Military Trail, Toronto, Ontario, Canada, M1C 1A4
9 ²Environmental Health Science and Research Bureau, Health Canada, 4908D - 269 Laurier Avenue
10 West, Ottawa, Ontario, Canada, K1A 0K9
11
12 **Corresponding Author:**
13 Frank Wania
14 Department of Physical and Environmental Sciences
15 University of Toronto Scarborough
16 1065 Military Trail
17 Toronto, ON
18 M1C 1A4
19 (t): (416) 287-7225
20 (e): frank.wania@utoronto.ca

21 **Abstract:**

22 Indigenous Arctic populations experience elevated exposures to many environmental
23 contaminants compared to groups residing in southern Canada. This is largely due to consumption of
24 traditional foods, some of which (ringed seals, beluga whales, narwhals, etc.) have relatively high
25 concentrations of persistent organic pollutants. Models of contaminant fate, transport, and
26 bioaccumulation represent powerful tools to explore this exposure issue, wherein combined models can
27 be used to mechanistically and dynamically describe the entire sequence of events linking chemical
28 emissions into the environment to ultimate contaminant concentrations in indigenous Arctic
29 populations. In this review, various approaches adapted and applied to understanding indigenous Arctic
30 contaminant exposure are explored, including early models describing body burdens in single
31 traditional food species to more recent approaches holistically examining uptake and bioaccumulation
32 in entire food chains. The applications of these models are also discussed, including attempts to i)
33 identify chemical properties favouring transport to, and bioaccumulation in, the Arctic, ii) clarify the
34 main determinants of temporal trends observed in indigenous Arctic biomonitoring, iii) explore the
35 impacts of permanent and temporary dietary transitions on current and future indigenous Arctic
36 contaminant exposures, and iv) correlate modeled early-life pollutant exposures with measured health
37 impacts. The review demonstrates the effectiveness of mechanistic model approaches in investigating
38 indigenous Arctic contaminant exposure, and confirms their utility in continued improvements to
39 understanding associated risk in this unique population context.

40 *Key words:* mechanistic models, indigenous Arctic Canadians, persistent organic pollutants, food chain
41 bioaccumulation, traditional foods,

42 **Introduction to mechanistic modeling of human exposure to POPs**

43 For more than 40 years, scientists have sought to mechanistically describe the bioaccumulation
44 of environmental contaminants in different organisms (Neely et al. 1974). These models integrate
45 mechanistic descriptions of the processes that lead to chemical uptake in, and chemical loss from, an
46 organism in the form of a mass balance equation (Mackay and Fraser 2000). The process of building a
47 mechanistic bioaccumulation model involves the formulation of mathematical expressions for chemical
48 uptake and loss processes such as the exchange across respiratory surfaces in lungs and gills, or the
49 exchange of chemicals between the gastrointestinal tract and internal body tissues. These expressions
50 are then parameterised based on chemical partitioning and degradation properties and the physiological
51 characteristics of the organism, such as rates of breathing, feeding, growth and reproduction. The
52 models range in complexity from those that treat the organism as a single compartment, to
53 physiologically based pharmacokinetic (PBPK) models that distinguish different organs and tissues
54 (e.g. Nichols et al. 1990). When several of these single organism models are combined, it is possible to
55 simulate the transfer and accumulation of contaminants in entire food chains. Such food chain
56 bioaccumulation models were first developed for aquatic food chains (Thomann 1989; Thomann et al.
57 1992; Gobas 1993; Campfens and Mackay 1997; Arnot and Gobas 2004), followed later by models for
58 terrestrial food chains (Armitage and Gobas 2007).

59 Similar model approaches can also be used to simulate human dietary exposure to
60 environmental contaminants. Models describing contaminant bioaccumulation in food chains that
61 provide for human food were developed (McLachlan 1994) and integrated with models of
62 bioaccumulation in humans (Moser and McLachlan 2002). ACC-Human, the first such human food
63 chain bioaccumulation model by Czub and McLachlan (2004a, 2004b) included both an agricultural
64 and an aquatic food chain. It is possible to further expand these approaches to include environmental

fate models that calculate contaminant concentrations in environmental media (e.g., air, water, soil, sediment) from chemical emissions rates (Mackay 1991), and input these concentrations into human food chain calculations. Such models or model combinations may then mechanistically simulate the entire sequence of events that link contaminant emissions into the environment with residue levels in humans. Examples of such models are the steady-state RAIDAR model (Arnot et al. 2006) and the dynamic CoZMoMAN model (Breivik et al. 2010), the latter allowing for time-variant emission inputs and therefore also time-variant exposure estimates.

However, not all models of human dietary contaminant exposure seek to include the contaminant transfer throughout food chains in the simulation. Some describe dietary exposure using transfer or exposure factors (Vermeire et al. 1997). Other models are essentially single organism models that require the contamination of food to be supplied as an input parameter; in certain cases these input data may be time-variant. Like any single organism model, the complexity of these models can range from simple single compartment models (e.g. Alcock et al. 2000; Lorber 2002; Ritter et al. 2009) to complex PBPK models (Carrier et al. 1995a, 1995b; Kreuzer et al. 1997; Beaudouin et al. 2010).

Over the past 10 years a number of mechanistic models have been developed that aim to specifically simulate the exposures of human populations indigenous to the Arctic to environmental contaminants (Kelly et al. 2007; Czub et al. 2008; Verner et al. 2009, 2013; Undeman et al. 2010; Quinn et al. 2012, Binnington et al. 2016a, Binnington et al. 2016b). These pursuits are largely motivated by exposures to many pollutants among indigenous Arctic people that substantially exceed those of southern populations (Donaldson et al. 2010; Laird et al. 2013; Curren et al. 2014; Arctic Monitoring and Assessment Programme 2015; Northern Contaminants Program 2016). For this reason, indigenous Arctic populations were identified as a population in need of improved contaminant

88 exposure estimation tools. Resultant models have been employed in a diverse range of applications,
89 including studies seeking to:

- 90 • Identify the properties of contaminants capable of accumulating in Arctic human food chains,
91 and to identify chemicals used in commerce that may have such properties.
- 92 • Enhance the understanding of human biomonitoring studies conducted in the Canadian Arctic
93 by trying to reconcile measured concentrations of persistent organic pollutants (POPs) with
94 recall estimates of dietary intake.
- 95 • Understand the impact of dietary change on human contaminant exposures, including dietary
96 transitions that may either be permanent or temporary.
- 97 • Characterize infant exposure to POPs during epidemiological studies and identify age periods of
98 increased susceptibility to adverse effects.

99 These applications will be presented and discussed in detail below.

100 **Environmental pollutant exposures among indigenous Canadian and Circumpolar Arctic**
101 **populations**

102 Human biomonitoring studies first documented appreciable POP concentrations in indigenous
103 Canadian Arctic populations in the mid-1980s (Kinloch and Kuhnlein 1988; Dewailly et al. 1989), even
104 though POP contamination in the Arctic environment is generally lower than in temperate locations
105 (McNeely and Gummer 1984). Similarly, unexpectedly high levels of organochlorine pesticides and
106 polychlorinated biphenyls (PCBs) were recorded in marine mammal traditional foods (Addison and
107 Smith 1974; Wagemann and Muir 1984). Shortly thereafter, in 1991, the Department of Indian and
108 Northern Affairs Canada, now Indigenous and Northern Affairs Canada (INAC), established the
109 Northern Contaminants Program (NCP), which continues to oversee issues related to indigenous Arctic
110 traditional food contamination from POPs and heavy metals in northern Canada (Donaldson et al.

2013). As part of its mandate, the NCP has funded numerous human biomonitoring studies in the Canadian Arctic (Van Oostdam et al. 1999, 2005; Donaldson et al. 2010; Arctic Monitoring and Assessment Programme 2015; Northern Contaminants Program 2016).

Indigenous populations in northern Canada have experienced elevated exposures to POPs and some metals due to the high proportion of marine mammals, fish, terrestrial animals, and birds in the traditional food component of their diet. Differences in traditional food preferences amongst indigenous populations across the eastern and western Canadian Arctic have resulted in differences in measured blood concentrations. Inuit living in eastern Canadian Arctic coastal communities in Nunavut and Nunavik (in northern Quebec) tend to exhibit higher POP concentrations than indigenous populations from inland communities in the Northwest Territories, based on lower prevalence of marine mammal traditional food consumption in the latter (Muckle et al. 2001a; Butler Walker et al. 2003, 2006; Dewailly et al. 2007; Donaldson et al. 2010; Curren et al. 2014).

Although exposures to many contaminants in northern Canada have been declining since the mid-1990s by as much as 10-fold (Donaldson et al. 2010, Arctic Monitoring and Assessment Programme 2015; Northern Contaminants Program 2016), indigenous Arctic Canadians continue to have higher levels of several POPs than southern Canadians (Laird et al. 2013; Curren et al. 2014; Arctic Monitoring and Assessment Programme 2015; Northern Contaminants Program 2016). Specifically, a comparison of blood concentrations for pregnant women from the Inuvik region of the Northwest Territories and the Baffin region of Nunavut (Armstrong et al. 2007; Potyrala et al. 2008) with those in major population centers across southern Canada (Commission for Environmental Corporation 2011) demonstrated that Arctic mothers possessed significantly higher levels of PCB-118 and PCB-180, for example, during the time period 2005-2007, even after age adjustment (Curren et al. 2014). Statistical analyses of these northern datasets reaffirmed the importance of traditional foods;

134 Arctic mothers' concentrations of several chemicals (trans-nonachlor, oxychlordane, PCB-153, PCB-
135 180) was significantly associated with traditional food consumption frequency, even after controlling
136 for other known exposure determinants (age, nursing duration, parity, smoking, indigenous group -
137 Curren et al. 2015). This study also observed that greater marine mammal traditional food consumption
138 by Inuit mothers from eastern coastal communities in Nunavut was likely the main reason for greater
139 POP concentrations than for western communities, even though Inuit participants from the Northwest
140 Territories consumed more traditional foods in general (Curren et al. 2015).

141 Declining temporal trends of some POP exposures have also been observed in the circumpolar
142 Arctic. For example, in the Disko Bay area of Greenland, significantly decreasing concentrations of all
143 quantified organochlorines in pregnant Inuit women were documented between 1994 and 2006 (Deutch
144 and Hansen 2000; Deutch et al. 2007; Arctic Monitoring and Assessment Programme 2009), which
145 Deutch et al. (2007) attributed partly to dietary transition behaviour away from traditional foods. Blood
146 concentrations of oxychlordane, *p,p'*-DDE, and PCB-153 among pregnant Inuit women in Disko Bay
147 continued to decrease during the period of 2006-2011 (Long et al. 2015; Arctic Monitoring and
148 Assessment Programme 2015). A study by Dudarev et al. (2010) determined that from 2001 to 2007
149 blood concentrations of several POPs in a sample of indigenous mothers from coastal Chukotka in
150 Russia showed declines ranging from 19-73%. Oxychlordane concentrations exhibited maximal
151 reductions during this period, reaching 73%, while *p,p'*-DDE and total PCBs decreased 70% and 44%,
152 respectively.

153 More moderate declines in POP exposure observed in populations from Finland, Norway, and
154 Sweden align with temporal trends of contamination in commercially available foods and local fish
155 species following legacy POP bans (Arctic Monitoring and Assessment Programme 2009). Also,
156 similar temporal POP exposure declines have not been observed in all indigenous Arctic populations,

as evidenced by work in Nuuk, Greenland during 1999-2005 (Bjerregaard et al. 2007). Annual changes in human exposure to oxychlordan, DDE, and PCB-153 varied in this town, and were theorized to fluctuate rather than decline over time due to lower marine mammal intakes than elsewhere in Greenland (Bjerregaard et al. 2007; Arctic Monitoring and Assessment Programme 2009).

Mechanistic models of contaminant exposure for indigenous Arctic populations

The elevated exposure of indigenous Arctic populations to POPs, and associated concerns over potential health outcomes related to these exposures, create a strong incentive for developing models to mechanistically simulate contaminant exposures in the North. The northern diet requires human bioaccumulation models that include a mechanistic description of contaminant bioaccumulation in aquatic and terrestrial Arctic food chains that lead to important traditional food species (e.g. Arctic char, beluga whale, caribou, ringed seal, etc.). Over the last decade, considerable progress has been made toward the development of such models. Figure 1 shows the structure of various models and model combinations that have been developed for describing organic chemical transport through Arctic food chains. Current model approaches are described below, beginning with a description of strategies to estimate bioaccumulation in key traditional food species.

Modeling contaminant bioaccumulation in Arctic food chains

The building blocks for models of Arctic food chains that extend to indigenous humans can be found in modeling studies of aquatic Arctic food webs. The earliest example comes from work by Borgå and Di Guardo (2005), who adapted an earlier aquatic food chain model for a temperate environment (Campfens and Mackay 1997) to simulate PCB bioaccumulation in a spring Barents Sea food chain consisting of seawater-zooplankton-polar cod (*Boreogadus saida*). Borgå et al. (2010) then extended their modeled food chain to include a predatory bird, the kittiwake (*Rissa tridactyla*), building upon another earlier temperate food web bioaccumulation model (Arnot and Gobas 2004). The

180 Campfens and Mackay (1997) model used by Borgå and colleagues served as the basis for another
181 aquatic food chain model, this one adapted for landlocked Arctic char (*Salvelinus alpinus*) residing in
182 Ellasjön, a lake on Bear Island, Norway (Gandhi et al. 2006). Finally, de Laender et al. (2010) similarly
183 adapted an earlier temperate model (Hendriks et al. 2001) to focus on trophic PCB transfer in a
184 southern Barents Sea food web consisting of seawater-zooplankton-herring (*Clupea harengus*)/capelin
185 (*Mallotus villosus*)-cod (*Gadus morhua*).

186 The unique physiological adaptations of Arctic organisms (e.g. seasonally variable lipid
187 reserves, longevity) to the characteristics of the physical environment in which they live (extreme
188 seasonality, low temperatures, ice cover, permafrost) may influence the bioaccumulation potential of
189 chemicals in Northern food chains. Thus, it is necessary to assess whether bioaccumulation models
190 developed for temperate organisms and food chains are suitable when modelling northern species
191 (Borgå et al. 2004). Applying the temperate fish bioaccumulation model by Gobas et al. (Gobas 1993;
192 Arnot and Gobas 2004) to northern Arctic char and southern lake trout, Gewurtz et al. (2006)
193 concluded that it is suitable for Arctic environments if water temperature and fish lipid content are
194 adjusted. This conclusion was echoed by Sobek et al. (2010), who suggested that ecological adaptations
195 in Arctic food webs do not systematically amplify bioaccumulation compared to temperate regions.
196 Consequently, existing mechanistic models can be used to describe aquatic Arctic food chain
197 bioaccumulation given appropriate system parameterization of water temperature and salinity (Sobek et
198 al. 2010). Further support was provided by de Laender et al. (2010), whose Barents Sea model included
199 several unique Arctic parameterizations (primary productivity, extensive migration, lipid dynamics).
200 Ultimately, only lipid dynamics appreciably affected fish PCB concentration estimates (de Laender et
201 al. 2010).

202 Traditional food from marine mammals is routinely identified as the dominant human POP
203 exposure vectors, due to high trophic level, longevity, and lipid content. To holistically simulate
204 indigenous Arctic POP exposure, food web models therefore also need to include marine mammal
205 species such as seals, walruses, and whales. Several attempts at modeling Arctic marine mammal
206 bioaccumulation via single compartment and/or PBPK approaches have been documented. The earliest
207 example is a PBPK model for estimating lifetime hydrophobic contaminant exposure in a generic
208 marine mammal that was applied to PCB intake among St. Lawrence estuary beluga whales
209 (*Delphinapterus leucas*) (Hickie et al. 1999). Model results for lifetime beluga exposure periods of 30
210 years satisfactorily replicated measured values, with female beluga simulations illustrating the key role
211 of milk as a PCB elimination route for mothers, and exposure source for offspring (Hickie et al. 1999).
212 Hickie et al. (2000) subsequently refined their model of POP accumulation, accurately reproducing the
213 impacts of age, growth, sex, and reproduction on lifetime PCB exposure trends observed in beluga
214 whales. A similar approach was adapted for pinnipeds, such as a harp seal (*Phoca groenlandica*) model
215 developed by Fraser et al. (2002), and two separate models for ringed seal (*Pusa hispida*) described by
216 Hickie et al. (2005) and Czub and McLachlan (2007). These ringed seal models were both notable in
217 that the assumption of simple equilibrium partitioning determining POP distribution, used previously in
218 models for other mammalian species (Czub and McLachlan 2004a), was insufficient to accurately
219 estimate contaminant concentrations in seal blubber, non-blubber tissues, and milk. The authors
220 deduced that the lipid-rich external blubber layer of seals, and the ambient temperature of their
221 surrounding seawater environment, necessitated assumptions of either an empirically-based
222 milk/blubber partition coefficient (K_{MB} - Hickie et al. 2005), or separating the core and blubber
223 compartments during calculations, with the latter requiring an assumed temperature gradient from
224 ambient seawater to core values (Czub and McLachlan 2007). Based on this work, additional models

were developed estimating contaminant uptake by bowhead whales (*Balaena mysticetus*) (Binnington and Wania 2014), and narwhals (*Monodon monoceros*) (Binnington et al. 2016a).

Terrestrial organisms such as caribou (*Rangifer tarandus*) often provide the traditional foods that are most frequently consumed in many indigenous Arctic communities (e.g. Zotor et al. 2012). Although such organisms are not typically dominant POP sources, a comprehensive exposure model should still account for important traditional food organisms. Kelly and Gobas (2003) were the first to mechanistically model POP bioaccumulation in an Arctic terrestrial food web, specifically the lichen-caribou-wolf food chain. They demonstrated that chemicals possessing octanol-air partition coefficient (K_{OA}) values greater than 100,000 and octanol-water partition coefficient (K_{OW}) values above 100 are likely to bioaccumulate in caribou. K_{OA} and K_{OW} are thermodynamic equilibrium properties that indicate a chemical's relative affinity for the gas phase, the aqueous solution and the octanol phase, whereby the latter is seen as a surrogate for organism lipids. Thus, terrestrial traditional foods may result in human exposure to more hydrophilic groups of chemicals than their aquatic counterparts. Based on its importance to indigenous Arctic traditional food consumers, the caribou is also included in the Arctic food chain model by Binnington et al. (2016a).

Integrating Arctic food chain bioaccumulation and human exposure models

Model frameworks to estimate environmental pollutant exposure among indigenous Arctic groups vary widely in their complexity. For example, existing stand-alone human bioaccumulation models can be directly applied to indigenous populations (Verner et al. 2009, 2013; Sonne et al. 2014), possibly adjusting model parameterization to reflect population-specific physiological or demographic characteristics. In this regard, Ayotte et al. (1996) allowed for a longer nursing period when applying the PBPK model by Carrier et al. (1995a, 1995b) to an Inuit population from Nunavik.

Expanding the above approaches, there have now been several studies where Arctic food chain models have been integrated with a human exposure model. The first such effort by Kelly et al. (2007) is only documented in the most rudimentary fashion, but describes exposure of an “Arctic indigenous human (Inuit)” calculated assuming a combined diet of “Arctic fish and wildlife (meat from caribou, ringed seals, walrus, and beluga whales) and agricultural products originating from southern Canada such as grains, beef, dairy” (Kelly et al. 2007 - Supporting Online Material). Czub et al. (2008) created an Arctic version of the ACC-Human food chain bioaccumulation model by adding the Arctic ringed seal model from Czub and McLachlan (2007), and thereby creating a zooplankton/amphipod–polar cod–ringed seal-Inuit food chain model. Quinn et al. (2012) modified this model by including southern agricultural food chain calculations. Binnington et al. (2016a) further expanded ACC-Human Arctic by adding three whale species (beluga, narwhal, bowhead), caribou, and Canada goose, and also adding Arctic char, which is more important for human consumption than Arctic cod (Sheehy et al. 2013). Figure 2 summarizes the flow of PCBs from the Arctic and southern environments to Inuit through the various food chains considered within the expanded ACC-Human Arctic model.

Applications of indigenous Arctic contaminant exposure models

Models of contaminant exposure for indigenous Arctic people have been applied for a wide range of studies, which are described in the following sections.

Predicting contaminants that will bioaccumulate in Arctic food chains

The first two studies relying on an Arctic human food chain bioaccumulation model used it for the same purpose: to identify the chemical partitioning properties that allow persistent organic chemicals to accumulate in indigenous populations consuming a traditional diet that includes marine mammals (Kelly et al. 2007; Czub et al. 2008). Both studies also presented their findings in a similar

way, calculating and plotting the potential for bioaccumulation in a two dimensional space defined by the equilibrium partitioning properties of chemicals between air, water and octanol (Figure 3).

The results are highly consistent, even though Czub et al. (2008) assumed exposure to be exclusively due to the consumption of seal blubber, while Kelly et al. (2007) assumed a more varied indigenous diet that included a number of traditional food species (seal, walrus, beluga, caribou), in addition to imported Southern food. Both studies identified chemicals that are not too volatile [octanol-air partitioning coefficients above 10^7] and high, but not extreme, hydrophobicities [octanol-water partitioning coefficients between 10,000 and 10^9] as particularly susceptible to accumulation in Inuit. Maximum bioaccumulation in either study was predicted for substances with an octanol-water partitioning coefficient of 10^6 to 10^7 (Figure 3). (Czub et al. 2008) explained the thresholds: marine mammals and humans efficiently exhale volatile compounds with an octanol-air partitioning coefficient below 10^7 , whereas compounds with an octanol-water partitioning coefficient below 10^4 and above 10^9 do not bioaccumulate because of rapid gill elimination by fish and inefficient dietary absorption by fish and mammals, respectively. The area of elevated bioaccumulation potential described by Kelly et al. (2007) extends to somewhat lower octanol-water partitioning coefficients due to the inclusion of dietary items from terrestrial organisms.

A contaminant not only has to be capable of efficient Arctic food chain bioaccumulation to achieve elevated levels in Arctic indigenous populations, but also needs to be able to reach the Arctic from its site of release in the global environment by means of long-range transport. Mechanistic model calculations of global transport and distribution had indicated that compounds require both intermediate volatility (Wania, 2003) and considerable persistence in air and surface media (Wania, 2006) in order to not only reach high latitudes, but also to be deposited there in sufficient quantities for notable uptake in food chains. Czub et al. (2008) therefore combined calculations of human food chain accumulation

with calculations of global scale fate and transport. Those calculations revealed that “a chemical’s potential to bioaccumulate has a stronger impact on the overall potential to become an Arctic contaminant in humans than its potential for long-range transport” (Czub et al. 2008).

Identifying new commercial chemicals of concern in Arctic food chains

Kelly et al. (2007) and Czub et al. (2008) both also recognized that their studies’ results could serve in the identification of potentially bioaccumulative substances among the large number of chemicals in commerce. Brown and Wania (2008) built upon the model results presented in Czub et al. (2008) to screen a set of more than 100,000 commercial chemicals for compounds that have predicted partitioning properties favouring long-range transport to the Arctic and accumulation in the local human food chain. After eliminating chemicals predicted to be readily degradable in the atmosphere, only about 2% of the screened compounds had predicted properties similar to known Arctic contaminants. Of these, only a subset had production volumes sufficiently high to warrant concern as global contaminants. Gawor and Wania (2013) used a similar approach to identify constituents in complex halogenated substance mixtures that have properties favouring global long-range transport and accumulation in Arctic food chains. For example, short-chain chlorinated paraffins with 5-6 chlorines and medium-chain chlorinated paraffins with 6-7 chlorines were identified as having the highest potential for accumulating in Inuit relying on a traditional diet. However, Zhang et al. (2010) noted that such a screening process can be susceptible to errors; for example, uncertain property predictions represent one limitation when relying on the comparisons of predicted chemical partitioning properties to a threshold value.

Comparing Arctic and temperate contaminant exposures

Kelly et al. (2007) and Czub et al. (2008) both highlighted the high magnitude of bioaccumulation calculated for the Arctic human food chains. Using the ratio between concentrations

315 in indigenous Arctic humans and in primary producers (e.g. plants and phytoplankton) as a measure,
316 Kelly et al. (2007) predicted chemical amplification up to 4000-fold. Using the environmental
317 bioaccumulation potential that relates the amount of chemical in one human to the size of the human's
318 environment that contains the same amount of chemical, Czub et al. (2008) noted a bioaccumulation
319 potential for Inuit that exceeded that estimated for a southern Swedish population by two orders of
320 magnitude. According to Czub et al. (2008) this "can, to a large extent, be attributed to the presence of
321 a marine mammal in the food web".

322 Undeman et al. (2010) expanded on these findings, by explicitly comparing several hypothetical
323 human populations in terms of their capability to accumulate organic chemicals from the environments
324 in which they live and from which they source their food. These populations, which included an Inuit
325 group, differed both in terms of the living environment and in terms of their dietary habits. By
326 expressing the accumulation potential relative to a southern Swedish reference population eating a
327 mixed diet of beef, dairy, and fish, Undeman et al. (2010) calculated an exposure susceptibility index.
328 An index value above 1 implies that, given identical emissions, a human living in an ecosystem of
329 interest and sourcing food locally can accumulate a higher body burden of a contaminant than a typical
330 Southern Swede. Again, Undeman et al. (2010) calculated and plotted this parameter in a two
331 dimensional space defined by the equilibrium partitioning properties between air, water, and octanol
332 (Figure 5).

333 This analysis by Undeman et al. (2010) suggested that Inuit exposure susceptibilities to most
334 persistent organic pollutants exceed those of the reference population by a factor of 100 (red area in
335 Figure 4). Further, for some chemical property combinations (with an octanol-water partitioning
336 coefficient around 10^6 and an octanol-air partitioning coefficient around 10^{11}) exposure susceptibility
337 was even up to a factor of 1000 greater than in the reference population. Only substances with very low

volatilities (octanol-air partition coefficients above 10^{10}) and a high bioaccumulation potential in agricultural food chains (octanol-water partitioning coefficient around 10^3 and octanol-air partitioning coefficient around 10^4) were characterized by Inuit exposure susceptibilities within the same order of magnitude as those for the Swedish reference population. Undeman et al. (2010) concluded that this high susceptibility of the Inuit to persistent organic pollutant exposure could not be explained by the characteristics of the physical environment in which they live, but rather by the presence of a seal in the marine food web. They wrote: “A long lifetime and high body temperature, ingestion rate, and dietary absorption efficiency combined with a slow depuration rate makes the seal a highly potent magnifier of persistent organic contaminants.”

Interestingly, the presence of a marine mammal in the human food chain had a markedly different impact on the exposure susceptibility of Inuit to degradable organic chemicals. When simulations were performed assuming that hypothetical contaminants had a degradation half-life in humans and mammals of 30 days, strong exposure susceptibility among Inuit was no longer predicted (Undeman et al. 2010). Instead of the ringed seal biomagnifying contaminants, as was estimated for persistent chemicals, the marine mammal acted as a filter that eliminated degradable contaminants before they could reach the Inuit.

Clarifying the reasons behind indigenous Arctic contaminant exposure declines

One of the key advantages of a human exposure model that includes contaminant transfer through the food chain is the possibility to explore the impact of permanent or temporary dietary shifts on contaminant exposure. As long as the dietary items that are being substituted are also part of the model, there is no need to provide empirical data on contamination levels in alternative foods. A major dietary shift is currently occurring in Arctic indigenous populations, characterized by an intergenerational transition from diets dominated by traditional food to replacement diets dominated by

361 food imported from the South (Kuhnlein et al. 2004; Young and Bjerregaard 2008; Bjerregaard and
362 Jeppsen 2010; Sharma et al. 2010; Nielsen et al. 2014). Because of differences in contaminant loads
363 between traditional and imported food, this transition is expected to influence long-term trends in the
364 exposure of indigenous Arctic populations. Specifically, because marine mammals have generally
365 higher contamination levels than store-bought foods from the South, and they also tend to have to
366 higher contaminant loads than other traditional foods frequently consumed by northerners (such as
367 Arctic char or caribou), a transition away from traditional diets including marine mammals may have
368 contributed to the observed decline in exposure to a number of POPs during the last two decades.

369 Quinn et al. (2012) demonstrated how a mechanistic modelling approach including both
370 traditional and imported diets could be used to quantify the independent contributions of
371 intergenerational dietary transition behaviours and the declining environmental contamination levels to
372 reductions in Inuit POP exposure. The calculations for the Arctic marine food chain [based on the
373 Arctic version of the ACC-Human model by Czub et al. (2008)] and the southern agricultural food
374 chain [based on the original ACC-Human model by Czub and McLachlan (2004a)] were both driven by
375 concentration data generated by a global distribution and fate model [GloboPOP by Wania and Mackay
376 (1995)] which, in turn, was fed with global-scale historical PCB emissions. The decline of PCB
377 emissions over time was predicted to decrease the PCB-153 body burden of 30-year old female Inuit 6
378 to 13-fold from 1980 to 2020. The degree to which dietary transitions away from marine mammal
379 traditional foods accelerated this rate of decline depended on the extent, timing, and rate of the
380 transition, and also on the foods that were substituted for marine mammals.

381 As the parameters describing current indigenous dietary transitions are not well-characterized
382 and also vary within different Canadian Arctic regions, communities, and even families, Quinn et al.
383 (2012) performed calculations assuming a number of hypothetical, yet realistic, transition scenarios,

which suggested that the dietary transition may be responsible for another 2 to 50-fold decline in PCB-153 exposure from 1980-2020. Even though these estimations were based on hypothetical scenarios, they clearly indicated that a dietary transition from traditional to market food is bound to have a notable effect on temporal trends in human contaminant exposure in the Arctic.

Binnington et al. (2016b) attempted to take these calculations out of the realm of the hypothetical by adopting the approach of Quinn et al. (2012), but using temporal data on dietary composition and PCB body burden derived from two separate pairs of baseline and follow-up studies in pregnant women from the Inuvik (Northwest Territories) and Baffin (Nunavut) regions of Arctic Canada. Contrary to expectations (e.g. Sharma et al., 2010), the data on dietary composition suggested a strong increase in the intake of marine mammal traditional foods between baseline (1996-1997) and follow-up (2005-2007) studies in these communities. As a result, the dietary composition data was judged as not sufficiently reliable to serve in the quantitative assessment of the impact of the dietary transition on declining PCB levels. While not satisfying, it implies that an analysis based on hypothetical, yet plausible dietary transition data (Quinn et al. 2012) is currently preferable to one using empirical data judged to be unreliable (Binnington et al. 2016a).

Exploring the effect of dietary change on human contaminant exposures

While Quinn et al. (2012) and Binnington et al. (2016a) explored the effect of population-level dietary transitions on PCB exposure, Binnington et al. (2016b) used the same model approach to study the impact of temporary dietary transitions on the exposure of women of childbearing age to PCBs. Specifically, the following dietary substitution scenarios were investigated: 1) decreased consumption of marine mammal traditional foods in order to reduce contaminant exposures, 2) increased consumption of marine mammal traditional foods in order to improve nutrient intake, and 3) replacement of caribou traditional foods with marine mammal alternatives due to diminishing caribou

407 availability. The impact of dietary change on mercury and nutrient intakes were also estimated,
408 although only PCB exposure predictions were based on mechanistic model calculations.

409 This study revealed the markedly different effects that increasing and decreasing marine
410 mammal intake may exert on PCB body burdens: Because of the very long elimination half-life of
411 PCBs from the human body, temporary reductions in marine mammal lipid consumption were largely
412 ineffective in lowering concentration levels, confirming earlier results of simulations that explored the
413 effectiveness of temperate fish consumption advisories (Binnington et al. 2014). On the other hand,
414 temporary increases in marine mammal intake can lead to rapidly rising PCB concentrations. However,
415 the study also showed that women of childbearing age with low baseline traditional food consumption
416 may supplement their diet with modest amounts of marine mammals to improve nutrition without
417 necessarily causing undue risk from greater contaminant exposure.

418 *Make sense and use of biomonitoring data*

419 Human exposure models are also increasingly used to understand and explain trends observed
420 in biomonitoring data, e.g. statistical associations between contaminant concentrations in study
421 participants and parameters such as age (Quinn and Wania 2012), body mass index (Wood et al.
422 2016a), parity, and breastfeeding (Quinn et al. 2011). While statistical associations do not confirm
423 causal relationships, reproducing an observed trend with a mechanistic model can lend support to an
424 explanation. While much of this work has not been done explicitly with Arctic human biomonitoring
425 data, the findings are directly applicable to indigenous groups from Canada's North.

426 For example, Quinn and Wania (2012) used the CoZMoMAN model to explain why PCB levels
427 tend to increase with age in cross-sectional human biomonitoring studies. Higher PCB levels in older
428 individuals are due to these individuals having experienced high PCB exposure in the past and having
429 retained much of that body burden over time; in other words, the body has a "memory" of elevated

430 exposure that occurred in the past. The main determinant of the body burden-age relationship is the
431 length of time elapsed since the peak in exposure (Lorber 2002; Ritter et al. 2011; Quinn and Wania
432 2012). Among Arctic populations, this age trend is even more pronounced, as older generations tend to
433 have a higher traditional food consumption than younger ones (Kuhnlein et al. 2004; Bjerregaard and
434 Jeppesen 2010; Sharma et al. 2010), implying a higher intake of PCBs throughout life (Quinn et al.
435 2012). During times of increasing environmental concentrations, such as the 1950s and 1960s for most
436 POPs, and the more recent past for newer POPs such as polybrominated diphenyl ethers (PBDEs), one
437 would expect younger study participants to have higher body burdens (Quinn and Wania 2012). A key
438 finding in this analysis was the realization that body burden–age relationships for population cross-
439 sections taken at one point in time versus those for individuals monitored at several points over time
440 are not equivalent, as demonstrated by various models (Ritter et al. 2011; Quinn and Wania 2012; Nøst
441 et al. 2013). Interestingly, the same is true for such relationships observed in long-lived wildlife,
442 including many of the marine mammals that are part of Arctic traditional diets (Binnington and Wania
443 2014).

444 It is also possible to use human exposure models to derive additional information from human
445 biomonitoring data, specifically to estimate the intake of a contaminant and its elimination half-life
446 from the human body (Ritter et al. 2009, 2011). The model essentially serves in the selection of values
447 for these parameters that best reproduce the observed human concentration trends with age and time.
448 Sometimes such studies confirm the elimination half-lives from earlier studies (Ritter et al. 2009; Bu et
449 al. 2015; Wood et al., 2016b) while at other times they reveal inconsistencies in the data. Specifically,
450 neither for North America (Ritter et al. 2009; Wong et al. 2013) nor for Australia (Gyalpo et al. 2015)
451 was it possible to reconcile contaminant intake estimates (accounting for both dietary and dust intakes),
452 measured body burdens, and reported elimination half-lives for PBDEs. In both cases, the intake

estimates were judged to be too low, suggesting the existence of an unrecognized exposure pathway. Human exposure models have not been applied in this way to biomonitoring data from Arctic indigenous populations. One reason may be that the intergenerational dietary transition occurring in Arctic communities is profoundly influencing contamination trends with time and age (Kuhnlein et al. 2004; Bjerregaard and Jeppesen 2010; Sharma et al. 2010). While accounting for this transition in a model simulation is possible in principle (Quinn et al. 2012), the input data required to describe it will need to be of sufficient quality (Binnington et al. 2016a).

Understanding associations between childhood exposures and health outcomes

Studies that have applied stand-alone human exposure models within the context of indigenous populations from the Canadian Arctic (Verner et al. 2009, 2010, 2013, 2015) almost exclusively aimed to improve the characterization of exposure among Inuit participating in the Nunavik Child Development Study (Muckle et al. 1998; Muckle et al. 2001b; Dallaire et al. 2003). The models essentially serve in the interpolation or extrapolation of measured concentrations with age, thereby allowing for the estimation of exposure during windows of developmental susceptibility even if no measurements were made during these periods.

Two papers evaluate the performance of two models when applied to the Nunavik cohort. In the first of these papers, Verner et al. (2009) expanded an existing PBPK model through inclusion of a nursing infant, and then tested the model's capability to predict various POP concentrations in breast milk, cord blood, and infant blood when supplied with maternal blood levels measured at the time of delivery. Four years later, Verner et al. (2013) presented a simplified version of the model that considered the lipid compartments of mother and child only, and was parameterized using individual physiologic variables (maternal age at birth, child birth weight, breastfeeding duration, etc.) alongside POP levels measured in maternal blood at delivery, cord blood, or breast milk. The model was then

used to calculate infants' exposure at 6 months of age. Simulated levels explained three quarters of PCB levels measured in blood at 6 months of age when based on maternal or cord blood values, and somewhat less when based on breast milk concentrations. Haddad et al. (2015) further used the model by Verner et al. (2013) to derive infant-to-mother ratios of external dose and body concentration for different POPs, and at distinct maternal ages. Haddad et al. (2015) also used the data from the Nunavik cohort by Muckle et al. (2001b) to evaluate model performance.

These models were then used in epidemiological studies to predict the exposure of Inuit infants from the Nunavik cohort to PCB-153 during every month of their first year of life, in order to relate exposure to the outcomes of various behavioural tests (attention, activity) performed at 11 months, (Verner et al. 2010) and 5 years of age (Verner et al. 2015).

Evaluating mechanistic contaminant exposure models for indigenous Arctic populations

Many of the human food chain modeling studies introduced in the previous sections did not attempt to predict actual POP concentrations in indigenous Arctic populations and individuals, but investigated hypothetical scenarios and/or hypothetical contaminants (Kelly et al. 2007; Czub et al. 2008; Undeman et al. 2010) to explore various features of Arctic human food chain bioaccumulation. Nevertheless, Czub et al. (2008) confirmed that their simulation results are reasonable by comparing estimated ratios of POP body burden in one Inuit over cumulative modeled global emissions (i.e., the fraction of global emissions found in one indigenous Arctic individual eating ringed seal) to equivalent empirical ratios. The modeled ratio of 3×10^{-12} person⁻¹ estimated for entirely persistent contaminants with an octanol-air partition coefficient of $10^{9.5}$ and an air-water partition coefficient of 10^{-2} , using the combination of GloboPOP and ACC-Human Arctic, was identical to the ratio obtained by dividing measured body burdens of PCB-153 in women of childbearing age from Western Greenland by the total global emissions of this congener (Breivik et al. 2007). While such perfect agreement is almost

499 certainly fortuitous to some extent, it “lends confidence to the model’s ability to predict chemical
500 transfer to the Arctic and bioaccumulation in humans” (Czub et al. 2008).

501 Binnington et al. (2016a) directly predicted the exposure arising from historical, global
502 emissions of PCBs using dietary intake data reported for young mothers in the Inuvik and Baffin
503 regions ($n = 33$ -101). Individual predicted PCB concentrations ranged quite substantially in accuracy,
504 wherein many estimates were within an order of magnitude of measurements, while some exceeded
505 empirical data by over 2 orders of magnitude (Binnington et al. 2016a). These predictions were very
506 sensitive to the assumed intake of marine mammal lipids, and because this intake was rather uncertain,
507 so were the predicted concentrations. The study by Nøst et al. (2016) predicting PCB exposure in
508 individual Norwegian women may indicate that better model-measurement agreement can be expected
509 with more reliable dietary intake data.

510 Because of the large number of participants ($n > 2000$), mean dietary data collected as part of
511 the Inuit Health Survey (IHS) may be more representative than the Inuvik and Baffin values. Laird et
512 al. (2013) reported a geometric mean total PCB concentration of $13.0 \mu\text{g L}^{-1}$ in all IHS participants and
513 $5.34 \mu\text{g L}^{-1}$ in all IHS female participants between 18 and 40 years of age. Binnington et al. (2016b)
514 calculated total PCB concentrations between 21.5 and $41.3 \mu\text{g L}^{-1}$ for women of childbearing age
515 eating the average reported diet of all participants in the Inuit Health Survey. For women of
516 childbearing age, the average diet of all IHS participants likely overestimated their marine mammal
517 intake because it included subgroups with higher marine mammal consumption: men and older women
518 (Kuhnlein et al. 2004; Egeland et al. 2011). If it was more realistically assumed that women of
519 childbearing age ate one third of the traditional food amount reported by all IHS participants, calculated
520 total PCB concentration ranged from 4.2 to $8.3 \mu\text{g L}^{-1}$. This level of model-measurement agreement,
521 although again likely to some extent fortuitous, is very encouraging.

Outlook

Simulation of Indigenous Arctic exposure to environmental contaminants represents a growing area of mechanistic modeling research. Largely motivated by the elevated exposure susceptibility to environmental contaminants experienced by indigenous Arctic populations, based on traditional food consumption, these pursuits have accomplished a diverse range of goals. Based on our review, there are a number of gaps and future opportunities that we have identified with respect to the mechanistic modelling of the POP exposure of indigenous Arctic populations. A lot of the work presented in this review has been done on PCBs. For example, evaluations of Arctic food chain models for substances other than PCBs are rare, because historical, global scale emissions are not available for many persistent organic chemicals. Looking forward, it would be desirable to achieve similar mechanistic capabilities to predict and characterize exposures of other contaminants of concern in indigenous Arctic communities.

In the case of traditional lipophilic POPs, achieving these capabilities should be feasible, if reliable global scale historical emissions can be defined. In the case of ionic persistent substances, such as the perfluorinated carboxylic and sulfonic alkyl acids, as well as the type of substances identified in Table 1, more substantial modifications to how bioaccumulation is described in the models will be required (Armitage et al., 2012; Ng and Hungerbuehler 2014). The limitations of current bioaccumulation modelling tools for such substances are, however, not restricted to Arctic organisms and food chains. Considering the concern elicited by exposure to methylmercury among indigenous Arctic populations, the development and application of simulation models of mercury exposure should also be a priority (Carrier et al. 2001, Knightes et al. 2009).

As the work by Verner et al. (2010, 2015) exemplifies, exposure characterisation in epidemiological studies can benefit from mechanistic modelling of longitudinal contaminant concentrations in individuals, including the reconstruction of cumulative exposure as well as exposure

546 during age brackets of susceptibility. While in the case of breast-feeding infants, parameterising dietary
547 contaminant uptake is rather straightforward, doing the same for older children and adults would
548 require reliable information on dietary composition and weight gain/loss, in addition to the parameters
549 typically collected for epidemiological studies (age, weight, height, reproductive characteristics, etc.).
550 It appears that data on traditional food intake on the individual level may be insufficient to allow
551 predictions of individual exposure that would be suitable for epidemiologic investigations. Therefore,
552 novel methods should be developed and applied to complement dietary recall and food frequency
553 questionnaires in efforts to establish reliable traditional food consumption rates during human
554 biomonitoring studies. These methods could rely on chemical tracers and/or on improved recording of
555 dietary intake and composition.

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559 **References**

- 560 Aboriginal Affairs and Northern Development Canada. 2013. Northern Contaminants Program -
561 Background [online]. Available from
562 <http://www.science.gc.ca/default.asp?lang=En&n=2917BAA6-1> [accessed 3 August 2016].
- 563 Addison, R.F., and Smith, T.G. 1974. Organochlorine residue levels in Arctic ringed seals: variation
564 with age and sex. *Oikos*. **25**(3): 335-337. DOI:10.2307/3543952.
- 565 Alcock, R.E., Sweetman, A.J., Juan, C.Y., and Jones, K.C. 2000. A generic model of human lifetime
566 exposure to persistent organic contaminants: development and application to PCB-101. *Environ.*
567 *Pollut.* **110**(2): 253-265. DOI:10.1016/S0269-7491(99)00298-5.
- 568 Arctic Monitoring and Assessment Programme (AMAP). 2015. AMAP Assessment 2015: Human
569 Health in the Arctic. Oslo, Norway. vii + 165 pp.
- 570 Arctic Monitoring and Assessment Programme (AMAP). 2009. AMAP Assessment 2009: Human
571 Health in the Arctic. Oslo, Norway. xiv + 256 pp.
- 572 Arctic Monitoring and Assessment Programme (AMAP). 2003. AMAP Assessment 2002: Human
573 Health in the Arctic. Oslo, Norway. xiv + 137 pp.
- 574 Arctic Monitoring and Assessment Programme (AMAP). 1998. AMAP Assessment Report 1998:
575 Arctic Pollution Issues. Oslo, Norway. xii + 859 pp.
- 576 Armitage, J.M., and Gobas, F.A.P.C. 2007. A terrestrial food-chain bioaccumulation model for POPs.
577 *Environ. Sci. Technol.* **41**(11): 4019-4025. DOI:10.1021/es0700597.
- 578 Armitage, J.M., Arnot, J.A. and F. Wania, F. 2012. The potential role of phospholipids in determining
579 the internal tissue distribution of perfluoroalkyl acids in biota. *Environ. Sci. Technol.* 2012, 46,
580 12285-12286. DOI:10.1021/es304430r.

- 581 Armstrong, B., Tofflemire, K., Myles, E., Receveur, O., and Chan, H.M. 2007. Monitoring temporal
582 trends of human environmental contaminants in the NWT. Department of Health and Social
583 Services, Government of the Northwest Territories, Yellowknife, NT.
- 584 Arnot, J.A., and Gobas, F.A.P.C. 2004. A food web bioaccumulation model for organic chemicals in
585 aquatic ecosystems. *Environ. Toxicol. Chem.* **23**(10): 2343-2355. DOI:10.1897/03-438.
- 586 Arnot, J.A., Mackay, D., Webster, E., and Southwood, J. 2006. Screening level risk assessment model
587 for chemical fate and effects in the environment. *Environ. Sci. Technol.* **40**(7): 2316-2323.
588 DOI:10.1021/es0514085.
- 589 Arnot, J.A., Brown, T.N., and Wania, F. 2013. Estimating screening-level organic chemical half-lives
590 in humans. *Environ. Sci. Technol.* **48**(1): 723-730. DOI:10.1021/es4029414.
- 591 Ayotte, P., Carrier, G., and Dewailly, É. 1996. Health risk assessment for Inuit newborns exposed to
592 dioxin-like compounds through breast feeding. *Chemosphere.* **32**(3): 531-542.
593 DOI:10.1016/0045-6535(96)00003-3.
- 594 Beaudouin, R., Micallef, S., and Brochot, C. 2010. A stochastic whole-body physiologically based
595 pharmacokinetic model to assess the impact of inter-individual variability on tissue dosimetry
596 over the human lifespan. *Regul. Toxicol. Pharmacol.* **57**(1): 103-116.
597 DOI:10.1016/j.yrtph.2010.01.005.
- 598 Binnington, M.J., and Wania, F. 2014. Clarifying relationships between persistent organic pollutant
599 concentrations and age in wildlife biomonitoring: individuals, cross-sections, and the roles of
600 lifespan and sex. *Environ. Toxicol. Chem.* **33**(6): 1415-1426. DOI:10.1002/etc.2576.
- 601 Binnington, M.J., Quinn, C.L., McLachlan, M.S., and Wania, F. 2014. Evaluating the effectiveness of
602 fish consumption advisories: modeling prenatal, postnatal, and childhood exposures to persistent
603 organic pollutants. *Environ. Health Persp.* **122**(2): 178-186. DOI:10.1289/ehp.1206380.

- 604 Binnington, M.J., Curren, M.S., Quinn, C.L., Armitage, J.M., Arnot, J.A., Chan, H.M., and Wania, F.
605 2016a. Mechanistic polychlorinated biphenyl exposure modeling of mothers in the Canadian
606 Arctic: the challenge of reliably establishing dietary composition. *Environ. Int.* **92-93**: 256-268.
607 DOI:10.1016/j.envint.2016.04.011.
- 608 Binnington, M.J., Curren, M.S., Chan, H.M., and Wania, F. 2016b. Balancing the benefits and costs of
609 traditional food substitution by indigenous Arctic women of childbearing age: Impacts on
610 persistent organic pollutant, mercury, and nutrient intakes. *Environ. Int.* **94**: 554-566. DOI:
611 10.1016/j.envint.2016.06.016.
- 612 Bjerregaard, P., Holm, A.L., Olesen, I., Schnor, O., Niclasen B. 2007. IVAAQ - The Greenland Inuit
613 child cohort: A preliminary report. Denmark National Institute of Public Health, Copenhagen,
614 Denmark. ISSN 1607-7765. Available from [http://www.si-folkesundhed.dk/upload/2671_-](http://www.si-folkesundhed.dk/upload/2671_-_ivaag_-_the_greenland_inuit_child_cohort_-_a_preliminary_report.pdf)
615 [_ivaag_-_the_greenland_inuit_child_cohort_-_a_preliminary_report.pdf](http://www.si-folkesundhed.dk/upload/2671_-_ivaag_-_the_greenland_inuit_child_cohort_-_a_preliminary_report.pdf) [accessed 19
616 September 2016]
- 617 Bjerregaard, P., and C. Jeppesen, 2010. Inuit dietary patterns in modern Greenland. *Int. J. Circumpol.*
618 Heal, **69**(1):13-24. Available from
619 <http://www.circumpolarhealthjournal.net/index.php/ijch/article/view/17387> [accessed 22
620 September 2016].
- 621 Borgå, K., and Di Guardo, A. 2005. Comparing measured and predicted PCB concentrations in Arctic
622 seawater and marine biota. *Sci. Total Environ.* **342**(1-3): 281-300. DOI:
623 10.1016/j.scitotenv.2004.12.043.
- 624 Borgå, K., Fisk, A.T., Hoekstra, P.F., and Muir, D.C.G. 2004. Biological and chemical factors of
625 importance in the bioaccumulation and trophic transfer of persistent organochlorine contaminants
626 in Arctic marine food webs. *Environ. Toxicol. Chem.* **23**(10): 2367-2385. DOI:10.1897/03-518.

- 627 Borgå, K., Saloranta, T.M., and Ruus, A. 2010. Simulating climate change-induced alterations in
628 bioaccumulation of organic contaminants in an Arctic marine food web. *Environ. Toxicol. Chem.*
629 **29**(6): 1349-1357. DOI:10.1002/etc.159.
- 630 Breivik, K., Sweetman, A., Pacyna, J.M., and Jones, K.C. 2007. Towards a global historical emission
631 inventory for selected PCB congeners - a mass balance approach 3. An update. *Sci. Total*
632 *Environ.* **377**(2-3): 296-307. DOI:10.1016/j.scitotenv.2007.02.026.
- 633 Breivik, K., Czub, G., McLachlan, M.S., and Wania, F. 2010. Towards an understanding of the link
634 between environmental emissions and human body burdens of PCBs using CoZMoMAN.
635 *Environ. Int.* **36**(1): 85-91. DOI:10.1016/j.envint.2009.10.006.
- 636 Brown, T.N., and Wania, F. 2008. Screening chemicals for the potential to be persistent organic
637 pollutants: A case study of Arctic contaminants. *Environ. Sci. Technol.* **42**(14): 5202-5209.
638 DOI:10.1021/es8004514.
- 639 Bu, Q., MacLeod, M., Wong, F., Toms, L.-M.L., Mueller, J.F., and Yu, G. 2015. Historical intake and
640 elimination of polychlorinated biphenyls and organochlorine pesticides by the Australian
641 population reconstructed from biomonitoring data. *Environ. Int.* **74**: 82-88.
642 DOI:10.1016/j.envint.2014.09.014.
- 643 Butler Walker, J., Seddon, L., McMullen, E., Houseman, J., Tofflemire, K., Corriveau, A., et al. 2003.
644 Organochlorine levels in maternal and umbilical cord blood plasma in Arctic Canada. *Sci. Total*
645 *Environ.* **302**(1-3): 27-52. DOI:10.1016/S0048-9697(02)00319-4.
- 646 Butler Walker, J., Houseman, J., Seddon, L., McMullen, E., Tofflemire, K., Mills, C., et al. 2006.
647 Maternal and umbilical cord blood levels of mercury, lead, cadmium, and essential trace elements
648 in Arctic Canada. *Environ. Res.* **100**(3): 295-318. DOI:10.1016/j.envres.2005.05.006.
- 649 Campfens, J., and Mackay, D. 1997. Fugacity-based model of PCB bioaccumulation in complex
650 aquatic food webs. *Environ. Sci. Technol.* **31**(2): 577-583. DOI:10.1021/es960478w.

- 651 Carrier, G., Brunet, R.C., and Brodeur, J. 1995a. Modeling of the toxicokinetics of polychlorinated
652 dibenzo-p-dioxins and dibenzofurans in mammals, including humans. I. Nonlinear distribution
653 of PCDD/PCDF body burden between liver and adipose tissues. *Toxicol. Appl. Pharmacol.*
654 **131**(2): 253-266. DOI:10.1006/taap.1995.1068.
- 655 Carrier, G., Brunet, R.C., and Brodeur, J. 1995b. Modeling of the toxicokinetics of polychlorinated
656 dibenzo-p-dioxins and dibenzofurans in mammals, including humans. II. Kinetics of
657 absorption and disposition of PCDDs/PCDFs. *Toxicol. Appl. Pharmacol.* **131**(2): 267-276.
658 DOI:10.1006/taap.1995.1069.
- 659 Carrier, G., Bouchard, M., Brunet, R.C., Caza, M. 2001. A toxicokinetic model for predicting the tissue
660 distribution and elimination of organic and inorganic mercury following exposure to methyl
661 mercury in animals and humans. II. Application and validation of the model in humans.
662 *Toxicology and Applied Pharmacology* **171**(1), 50-60. <https://doi.org/10.1006/taap.2000.9113>
- 663 Commission for Environmental Cooperation. 2011. Trilateral Biomonitoring Study: Assessment of
664 Persistent Organic Pollutants and Selected Metals in the Blood of First-Birth Mothers in Southern
665 Canada and Mexico and in Women of Reproductive Age in the United States [online]. Available
666 from [http://www3.cec.org/islandora/en/item/10143-trilateral-biomonitoring-study-assessment-](http://www3.cec.org/islandora/en/item/10143-trilateral-biomonitoring-study-assessment-persistent-organic-pollutants-and-selected-en)
667 [persistent-organic-pollutants-and-selected-en](http://www3.cec.org/islandora/en/item/10143-trilateral-biomonitoring-study-assessment-persistent-organic-pollutants-and-selected-en) [accessed 2 August 2016].
- 668 Curren, M.S., Davis, K., Liang, C.L., Adlard, B., Foster, W.G., Donaldson, S.G., et al. 2014.
669 Comparing plasma concentrations of persistent organic pollutants and metals in primiparous
670 women from northern and southern Canada. *Sci. Total Environ.* **479-480C**: 306-318.
671 DOI:10.1016/j.scitotenv.2014.01.017.
- 672 Curren, M.S., Liang, C.L., Davis, K., Kandola, K., Brewster, J., Potyralski, M., et al. 2015. Assessing
673 determinants of maternal blood concentrations for persistent organic pollutants and metals in the

- 674 eastern and western Canadian Arctic. *Sci. Total Environ.* **527-528C**: 150-158.
675 DOI:10.1016/j.scitotenv.2015.04.079.
- 676 Czub, G., and McLachlan, M.S. 2004a. A food chain model to predict the levels of lipophilic organic
677 contaminants in humans. *Environ. Toxicol. Chem.* **23**(10): 2356-2366. DOI:10.1897/03-317.
- 678 Czub, G., and McLachlan, M.S. 2004b. Bioaccumulation potential of persistent organic chemicals in
679 humans. *Environ. Sci. Technol.* **38**(8): 2406-2412.
- 680 Czub, G., and McLachlan, M.S. 2007. Influence of the temperature gradient in blubber on the
681 bioaccumulation of persistent lipophilic organic chemicals in seals. *Environ. Toxicol. Chem.*
682 **26**(8): 1600-1605. DOI:10.1021/es034871v.
- 683 Czub, G., Wania, F., and McLachlan, M.S. 2008. Combining long-range transport and bioaccumulation
684 considerations to identify potential Arctic contaminants. *Environ. Sci. Technol.* **42**(10): 3704-
685 3709. DOI:10.1021/es7028679.
- 686 Dallaire, F., Dewailly, É., Muckle, G., and Ayotte, P. 2003. Time trends of persistent organic pollutants
687 and heavy metals in umbilical cord blood of Inuit infants born in Nunavik (Québec, Canada)
688 between 1994 and 2001. *Environ. Health. Perspect.* **111**(13): 1660-64. DOI:10.1289/ehp.6269
- 689 de Laender, F., Oevelen, D.V., Frantzen, S., Middelburg, J.J., and Soetaert, K. 2010. Seasonal PCB
690 bioaccumulation in an arctic marine ecosystem: a model analysis incorporating lipid dynamics,
691 food-web productivity and migration. *Environ. Sci. Technol.* **44**(1): 356-361.
692 DOI:10.1021/es902625u.
- 693 Deutch, B., and Hansen, J.C. 2000. High human plasma levels of organochlorine compounds in
694 Greenland. Regional differences and lifestyle effects. *Danish. Med. Bull.* **47**(2): 132-137.

- 695 Deutch, B., Pedersen, H.S., Asmund, G., and Hansen, J.C. 2007. Contaminants, diet, plasma fatty
696 acids, and smoking in Greenland 1999-2005. *Sci. Total Environ.* **372**(2-3): 486-496.
697 DOI:10.1016/j.scitotenv.2006.10.043.
- 698 Dewailly, É., Nantel, A., Weber, J.P., and Meyer, F. 1989. High levels of PCBs in breast milk of Inuit
699 women from arctic Quebec. *Bull. Environ. Contam. Toxicol.* **43**(5): 641-646.
700 DOI:10.1007/BF01701981.
- 701 Dewailly, É., Dallaire, R., Pereg, D., Ayotte, P., Fontaine, J., and Dery, S. 2007. Nunavik Inuit Health
702 Survey 2004. Qanuippitaa? How are we? Exposure to environmental contaminants in Nunavik:
703 persistent organic pollutants and new contaminants of concern. Institute National de Santé
704 Publique du Québec (INSPQ) and Nunavik Regional Board of Health and Social Services.
705 Québec City, QC.
- 706 Donaldson, S. G., Curren, M. S., Adlard, B., Provost, J., Leech, T., Tikhonov, C., et al. 2013. Future
707 human health research directions for the Canadian northern contaminants program. *Int. J.*
708 *Circumpol. Heal.* **72**(1): 23049. DOI:10.3402/ijch.v72i0.23049
- 709 Donaldson, S.G., Van Oostdam, J., Tikhonov, C., Feeley, M., Armstrong, B., Ayotte, P., et al. 2010.
710 Environmental contaminants and human health in the Canadian Arctic. *Sci. Total Environ.*
711 **408**(22): 5165-5234. DOI:10.1016/j.scitotenv.2010.04.059.
- 712 Dudarev, A.A., Konoplev, A.V., Sandanger, T.M., Vlasov, S.V., Miretsky, G.I., Samsonov, D.P., et al.
713 2004. Blood concentrations of persistent toxic substances in the indigenous communities of the
714 Russian Arctic. *Int. J. Circumpol. Heal.* **63**(Suppl 2): 179-182. Available from
715 <http://www.circumpolarhealthjournal.net/index.php/ijch/article/view/17895> [accessed 19
716 September 2016].
- 717 Dudarev, A.A., Chupakhin, V., Odland, J.O., Reiersen, L.-O., and Chashchin, V. 2010. A follow-up
718 study of blood levels of persistent toxic substances (PTS) among indigenous peoples of the

- 719 coastal Chukotka, Russia, 2001-2007. *Int. J. Circumpol. Heal. Suppl.* **7**: 263-268. Available from
720 http://www.circumpolarhealthjournal.net/public/journals/32/chs/CHS_2010_7_ICCH14.pdf
721 [accessed 19 September 2016].
- 722 Egeland, G.M., Johnson-Down, L., Cao, Z.R., Sheikh, N., and Weiler, H. 2011. Food insecurity and
723 nutrition transition combine to affect nutrient intakes in Canadian arctic communities. *J. Nutr.*
724 **141**(9): 1746-1753. DOI:10.3945/jn.111.139006.
- 725 Fraser, A.J., Burkow, I.C., Wolkers, H., and Mackay, D. 2002. Modeling biomagnification and
726 metabolism of contaminants in harp seals of the Barents Sea. *Environ. Toxicol. Chem.* **21**(1): 55-
727 61. DOI:10.1002/etc.5620210108.
- 728 Gandhi, N., Bhavsar, S.P., Gewurtz, S.B., Diamond, M.L., Evenset, A., Christensen, G.N., et al. 2006.
729 Development of a Multichemical Food Web Model: Application to PBDEs in Lake Ellasjøen,
730 Bear Island, Norway. *Environ. Sci. Technol.* **40**(15): 4714-4721. DOI:10.1021/es052064l.
- 731 Gawor, A., and Wania, F. 2013. Using quantitative structural property relationships, chemical fate
732 models, and the chemical partitioning space to investigate the potential for long range transport
733 and bioaccumulation of complex halogenated chemical mixtures. *Environ. Sci.: Processes*
734 *Impacts.* **15**(9): 1671-1684. DOI:10.1039/c3em00098b.
- 735 Gewurtz, S.B., Laposa, R., Gandhi, N., Christensen, G.N., Evenset, A., Gregor, D., et al. 2006. A
736 comparison of contaminant dynamics in arctic and temperate fish: A modeling approach.
737 *Chemosphere.* **63**(8): 1328-1341. DOI:10.1016/j.chemosphere.2005.09.031.
- 738 Gobas, F.A.P.C. 1993. A model for predicting the bioaccumulation of hydrophobic organic chemicals
739 in aquatic food-webs: application to Lake Ontario. *Ecol. Model.* **69**(1-2): 1-17.
740 DOI:10.1016/0304-3800(93)90045-T.

- 741 Government of Canada. 2011. Canada Gazette, Part 1. **145**(41): 107 pp. Available from
742 <http://www.gazette.gc.ca/rp-pr/p1/2011/2011-10-08/pdf/g1-14541.pdf> [accessed 22 September
743 2016].
- 744 Gyalpo, T., Toms, L.-M., Mueller, J.F., Harden, F.A., Scheringer, M., and Hungerbühler, K. 2015.
745 Insights into PBDE uptake, body burden, and elimination gained from Australian age-
746 concentration trends observed shortly after peak exposure. *Environ. Health Persp.* **123**(10): 978-
747 984. DOI:10.1289/ehp.1408960.
- 748 Haddad, S., Ayotte, P., and Verner, M.-A. 2015. Derivation of exposure factors for infant lactational
749 exposure to persistent organic pollutants (POPs). *Regul. Toxicol. Pharmacol.* **71**(2): 135-140.
750 DOI:10.1016/j.yrtph.2014.12.003.
- 751 Hendriks, A.J., van der Linde, A., Cornelissen, G., and Sijm, D.T. 2001. The power of size. 1. Rate
752 constants and equilibrium ratios for accumulation of organic substances related to octanol-water
753 partition ratio and species weight. *Environ. Toxicol. Chem.* **20**(7): 1399-1420.
754 DOI:10.1002/etc.5620200703.
- 755 Hickie, B.E., Mackay, D., and de Koning, J. 1999. Lifetime pharmacokinetic model for hydrophobic
756 contaminants in marine mammals. *Environ. Toxicol. Chem.* **18**(11): 2622-2633.
757 DOI:10.1002/etc.5620181132.
- 758 Hickie, B.E., Kingsley, M.C.S., Hodson, P.V., Muir, D.C.G., Béland, P., and Mackay, D. 2000. A
759 modelling-based perspective on the past, present, and future polychlorinated biphenyl
760 contamination of the St. Lawrence beluga whale (*Delphinapterus leucas*) population. *Can. J.*
761 *Fish. Aquat. Sci.* **57**(S1): 101-112. DOI:10.1139/f99-242.
- 762 Hickie, B.E., Muir, D.C.G., Addison, R.F., and Hoekstra, P.F. 2005. Development and application of
763 bioaccumulation models to assess persistent organic pollutant temporal trends in arctic ringed

- 764 seal (*Phoca hispida*) populations. *Sci. Total Environ.* **351-352**: 413-426.
765 DOI:10.1016/j.scitotenv.2004.12.085.
- 766 Kelly, B.C., and Gobas, F.A.P.C. 2003. An arctic terrestrial food-chain bioaccumulation model for
767 persistent organic pollutants. *Environ. Sci. Technol.* **37**(13): 2966-2974.
768 DOI:10.1021/es021035x.
- 769 Kelly, B.C., Ikonomou, M.G., Blair, J.D., Morin, A.E., and Gobas, F.A.P.C. 2007. Food web-specific
770 biomagnification of persistent organic pollutants. *Science*. **317**(5835): 236-239.
771 DOI:10.1126/science.1138275.
- 772 Kinloch, D., and Kuhnlein, H. 1988. Assessment of PCBs in Arctic foods and diets. A pilot study in
773 Broughton Island, Northwest Territories, Canada. *Arctic. Med. Res.* **47**(Suppl 1): 159-162.
- 774 Knightes, C.D., Sunderland, E.M., Barber, M.C., Johnston, J.M., Ambrose Jr, R.B. 2009. Application
775 of ecosystem-scale fate and bioaccumulation models to predict fish mercury response times to
776 changes in atmospheric deposition. *Environ. Toxicol. Chem.* **28**(4), 881-893. DOI: 10.1897/08-
777 242R.1
- 778 Kreuzer, P.E., Csanády, G.A., Baur, C., Kessler, W., Pöpke, O., Greim, H., and Filser, J.G. 1997.
779 2,3,7,8-Tetrachlorodibenzo- p -dioxin (TCDD) and congeners in infants. A toxicokinetic model
780 of human lifetime body burden by TCDD with special emphasis on its uptake by nutrition. *Arch.*
781 *Toxicol.* **71**(6): 383-400. DOI:10.1007/s002040050402.
- 782 Kuhnlein, H.V., Receveur, O., Soueida, R., and Egeland, G.M. 2004. Arctic indigenous peoples
783 experience the nutrition transition with changing dietary patterns and obesity. *J. Nutr.* **134**(6):
784 1447-1453.
- 785 Laird, B.D., Goncharov, A.B., and Chan, H.M. 2013. Body burden of metals and persistent organic
786 pollutants among Inuit in the Canadian Arctic. *Environ. Int.* **59**: 33-40.
787 DOI:10.1016/j.envint.2013.05.010.

- 788 Long, M., Knudsen, A.-K.S., Pedersen, H.S., and Bonefeld-Jørgensen, E.C. 2015. Food intake and
789 serum persistent organic pollutants in the Greenlandic pregnant women of the ACCEPT sub-
790 study. *Sci. Total. Environ.* **529**: 198-212. DOI:10.1016/j.scitotenv.2015.05.022.
- 791 Lorber, M. 2002. A pharmacokinetic model for estimating exposure of Americans to dioxin-like
792 compounds in the past, present, and future. *Sci. Total. Environ.* **288**(1-2): 81-95.
793 DOI:10.1016/S0048-9697(01)01119-6
- 794 Mackay, D. 1991. *Multimedia Environmental Models: The Fugacity Approach*. Lewis Publishers/CRC
795 Press, Boca Ration, FL. 272 pp.
- 796 Mackay, D., and Fraser, A. 2000. Bioaccumulation of persistent organic chemicals: mechanisms and
797 models. *Environ. Pollut.* **110**(3): 375-391. DOI:10.1016/S0269-7491(00)00162-7
- 798 McLachlan, M.S. 1994. Model of the fate of hydrophobic contaminants in cows. *Environ. Sci. Technol.*
799 **28**(13): 2407-2414. DOI:10.1021/es00062a028.
- 800 McNeely, R., and Gummer, W.D. 1984. A reconnaissance survey of the environmental chemistry in
801 east-central Ellesmere Island, N.W.T. *Arctic.* **37**(3): 210-223. DOI:10.14430/arctic2194
- 802 Moser, G., and McLachlan, M.S. 2002. Modeling digestive tract absorption and desorption of lipophilic
803 organic contaminants in humans. *Environ. Sci. Technol.* **36**(15): 3318-3325.
804 DOI:10.1021/es015853l.
- 805 Muckle, G., Dewailly, É., and Ayotte, P. 1998. Prenatal exposure of Canadian children to
806 polychlorinated biphenyls and mercury. *Can. J. Public. Health.* **89**(Suppl 1):S20-25. Available
807 from <http://journal.cpha.ca/index.php/cjph/article/view/1396/1585> [accessed 22 September 2016].
- 808 Muckle, G., Ayotte, P., Dewailly, É., Jacobson, S.W., and Jacobson, J.L. 2001a. Determinants of
809 polychlorinated biphenyls and methylmercury exposure in Inuit women of childbearing age.
810 *Environ. Health Persp.* **109**(9): 957-963. DOI:10.2307/3454999

- 811 Muckle, G., Ayotte, P., Dewailly, É., Jacobson, S.W., and Jacobson, J.L. 2001b. Prenatal exposure of
812 the northern Québec Inuit infants to environmental contaminants. *Environ. Health Persp.*
813 **109**(12): 1291-1299. Available from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1240513/>
814 [accessed 19 September 2016].
- 815 Neely, W.B., Branson, D.R., and Blau, G.E. 1974. Partition coefficient to measure bioconcentration
816 potential of organic chemicals in fish. *Environ. Sci. Technol.* **8**(13): 1113-1115.
817 DOI:10.1021/es60098a008.
- 818 Ng C.A., and Hungerbühler, K. 2014. Bioaccumulation of perfluorinated alkyl acids: Observations and
819 models. *Environ. Sci. Technol.* **48**(9), 4637-4648, DOI:10.1021/es404008g
- 820 Nichols, J.W., McKim, J.M., Andersen, M.E., Gargas, M.L., Clewell, H.J., and Erickson, R.J. 1990. A
821 physiologically based toxicokinetic model for the uptake and disposition of waterborne organic
822 chemicals in fish. *Toxicol. Appl. Pharmacol.* **106**(3): 433-447. DOI:10.1016/0041-
823 008X(90)90338-U.
- 824 Nielsen, N.O., Jørgensen, M.E., Friis, H., Melbye, M., Soborg, B., Jeppesen, C., et al. 2014. Decrease
825 in vitamin D status in the Greenlandic adult population from 1987-2010. *PLoS ONE* **9**(12):
826 e112949. DOI: 10.1371/journal.pone.0112949.
- 827 Northern Contaminants Program 2016 – *reference to be updated when CACAR publication becomes*
828 *available*
- 829 Nøst, T.H., Breivik, K., Fuskevåg, O.-M., Nieboer, E., Odland, J.Ø., and Sandanger, T.M. 2013.
830 Persistent organic pollutants in Norwegian men from 1979 to 2007: intraindividual changes, age-
831 period-cohort effects, and model predictions. *Environ. Health Persp.* **121**(11-12): 1292-1298.
832 DOI:10.1289/ehp.1206317.
- 833 Nøst, T.H., Breivik, K., Wania, F., Rylander, C., Odland, J.Ø., Sandanger, T.M. 2016. Estimating time-
834 varying PCB exposures using person-specific predictions to supplement measured values: A

- 835 comparison of observed and predicted values in two cohorts of Norwegian women. *Environ.*
836 *Health Persp.* **124**(3): 299-305. DOI:10.1289/ehp.1409191
- 837 Potyrala, M., Brewster, J., Tofflemire, K., Receveur, O., Chan, H.M., and Sobol, I. 2008. The Anaana
838 Project - Inuit prenatal health survey. Department of Health and Social Services, Government of
839 Nunavut. Iqaluit, NU.
- 840 Quinn, C.L., and Wania, F. 2012. Understanding differences in the body burden-age relationships of
841 bioaccumulating contaminants based on population cross sections versus individuals. *Environ.*
842 *Health Persp.* **120**(4): 554-559. DOI:10.1289/ehp.1104236.
- 843 Quinn, C.L., Wania, F., Czub, G., and Breivik, K. 2011. Investigating intergenerational differences in
844 human PCB exposure due to variable emissions and reproductive behaviors. *Environ. Health*
845 *Persp.* **119**(5): 641-646. DOI:10.1289/ehp.1002415.
- 846 Quinn, C.L., Armitage, J.M., Breivik, K., and Wania, F. 2012. A methodology for evaluating the
847 influence of diets and intergenerational dietary transitions on historic and future human exposure
848 to persistent organic pollutants in the Arctic. *Environ. Int.* **49**(C): 83-91.
849 DOI:10.1016/j.envint.2012.08.014.
- 850 Ritter, R., Scheringer, M., MacLeod, M., Schenker, U., and Hungerbühler, K. 2009. A multi-individual
851 pharmacokinetic model framework for interpreting time trends of persistent chemicals in human
852 populations: application to a postban situation. *Environ. Health Persp.* **117**(8): 1280-1286.
853 DOI:10.1289/ehp.0900648.
- 854 Ritter, R., Scheringer, M., MacLeod, M., Moeckel, C., Jones, K.C., and Hungerbühler, K. 2011.
855 Intrinsic human elimination half-lives of polychlorinated biphenyls derived from the temporal
856 evolution of cross-sectional biomonitoring data from the United Kingdom. *Environ. Health*
857 *Persp.* **119**(2): 225-231. DOI:10.1289/ehp.1002211.

- 858 Sharma, S., Cao, X., Roache, C., Buchan, A., Reid, R., and Gittelsohn, J. 2010. Assessing dietary
859 intake in a population undergoing a rapid transition in diet and lifestyle: the Arctic Inuit in
860 Nunavut, Canada. *Br J Nutr* **103**(5): 749-759. DOI:10.1017/S0007114509992224.
- 861 Sheehy, T., Roache, C., and Sharma, S. Eating habits of a population undergoing a rapid dietary
862 transition: portion sizes of traditional and non-traditional foods and beverages consumed by Inuit
863 adults in Nunavut, Canada. *Nutr. J.* **12**: 70. DOI:10.1186/1475-2891-12-70.
- 864 Sobek, A., McLachlan, M.S., Borgå, K., Asplund, L., Lundstedt-Enkel, K., Polder, A., et al. 2010. A
865 comparison of PCB bioaccumulation factors between an arctic and a temperate marine food web.
866 *Sci. Total Environ.* **408**(13): 2753-2760. DOI:10.1016/j.scitotenv.2010.03.013.
- 867 Sonne, C., Gustavson, K., Rigét, F.F., Dietz, R., Krüger, T., and Bonefeld-Jorgensen, E.C. 2014.
868 Physiologically based pharmacokinetic modeling of POPs in Greenlanders. *Environ. Int.* **64**: 91-
869 97. DOI:10.1016/j.envint.2013.12.006.
- 870 Thomann, R.V. 1989. Bioaccumulation model of organic chemical distribution in aquatic food chains.
871 *Environ. Sci. Technol.* **23**(6): 699-707. DOI:10.1021/es00064a008.
- 872 Thomann, R.V., Connolly, J.P., and Parkerton, T.F. 1992. An equilibrium model of organic chemical
873 accumulation in aquatic food webs with sediment interaction. *Environ. Toxicol. Chem.* **11**(5):
874 615-629. DOI:10.1002/etc.5620110505.
- 875 Undeman, E., Brown, T.N., Wania, F., and McLachlan, M.S. 2010. Susceptibility of human
876 populations to environmental exposure to organic contaminants. *Environ. Sci. Technol.* **44**(16):
877 6249-6255. DOI:10.1021/es1009339.
- 878 Van Oostdam, J., Donaldson, S.G., Feeley, M., Arnold, D., Ayotte, P., Bondy, G., et al. 2005. Human
879 health implications of environmental contaminants in Arctic Canada: A review. *Sci. Total*
880 *Environ.* **351-352**: 165-246. DOI:10.1016/j.scitotenv.2005.03.034.

- 881 Van Oostdam, J., Gilman, A., Dewailly, É., Usher, P., Wheatley, B., Kuhnlein, H., et al. 1999. Human
882 health implications of environmental contaminants in Arctic Canada: a review. *Sci. Total*
883 *Environ.* **230**(1-3): 1-82. DOI:10.1016/S0048-9697(99)00036-4.
- 884 Vermeire, T.G., Jager, D.T., Bussian, B., Devillers, J., Den Haan, K., Hansen, B., Lundberg, I.,
885 Niessen, H., Robertson, S., Tyle, H., Van Der Zandt, P.T.J. 1997. European Union System for the
886 Evaluation of Substances (EUSES). Principles and structure. *Chemosphere* 34 (8): 1823-1836.
887 DOI: 10.1016/S0045-6535(97)00017-9
- 888 Verner, M.-A., Ayotte, P., Muckle, G., Charbonneau, M., and Haddad, S. 2009. A physiologically
889 based pharmacokinetic model for the assessment of infant exposure to persistent organic
890 pollutants in epidemiologic studies. *Environ. Health Persp.* **117**(3): 481-487.
891 DOI:10.1289/ehp.0800047.
- 892 Verner, M.A., Plusquellec, P., Muckle, G., Ayotte, P., Dewailly, É., Jacobson, S.W., et al. 2010.
893 Alteration of infant attention and activity by polychlorinated biphenyls: Unravelling critical
894 windows of susceptibility using physiologically based pharmacokinetic modeling.
895 *Neurotoxicology.* **31**(5): 424-431. DOI:10.1016/j.neuro.2010.05.011.
- 896 Verner, M.-A., Sonneborn, D., Lancz, K., Muckle, G., Ayotte, P., Dewailly, É., et al. 2013.
897 Toxicokinetic modeling of persistent organic pollutant levels in blood from birth to 45 months of
898 age in longitudinal birth cohort studies. *Environ. Health Persp.* **121**(1): 131-137.
899 DOI:10.1289/ehp.1205552.
- 900 Verner, M.-A., Plusquellec, P., Desjardins, J.L., Cartier, C., Haddad, S., Ayotte, P., et al. 2015. Prenatal
901 and early-life polychlorinated biphenyl (PCB) levels and behavior in Inuit preschoolers. *Environ.*
902 *Int.* **78**: 90-94. DOI:10.1016/j.envint.2015.02.004.

- 903 Wagemann, R., and Muir, D.C.G. 1984. Concentrations of heavy metals and organochlorines in marine
904 mammals of northern waters: overview and evaluation. Canadian Technical Report of Fisheries
905 and Aquatic Sciences 1279. Department of Fisheries and Oceans, Winnipeg, MB.
- 906 Wania, F., and Mackay, D. 1995. A global distribution model for persistent organic chemicals. *Sci.*
907 *Total Environ.* **160-61**: 211-232. DOI:10.1016/0048-9697(95)04358-8.
- 908 Wania, F. 2003. Assessing the potential of persistent organic chemicals for long-range transport and
909 accumulation in polar regions. *Environ. Sci. Technol.* **37**: 1344-1351. DOI: 10.1021/es026019e.
- 910 Wania, F. 2006. The potential of degradable organic chemicals for absolute and relative enrichment in
911 the Arctic. *Environ. Sci. Technol.* **40**: 569-577. DOI 10.1021/es051406k
- 912 Wong, F., Cousins, I.T., and MacLeod, M. 2013. Bounding uncertainties in intrinsic human elimination
913 half-lives and intake of polybrominated diphenyl ethers in the North American population.
914 *Environ. Int.* **59C**: 168-174. DOI:10.1016/j.envint.2013.05.004.
- 915 Wood, S.A., Xu, F., Armitage, J.M., and Wania, F. 2016a. Unravelling the relationship between body
916 mass index and polychlorinated biphenyl concentrations using a mechanistic model. *Environ. Sci.*
917 *Technol.* (In press). DOI:10.1021/acs.est.6b01961.
- 918 Wood, S.A., Armitage, J.M., Binnington, M.J., and Wania, F. 2016b. Deterministic modeling of the
919 exposure of individual participants in the National Health and Nutrition Examination Survey
920 (NHANES) to polychlorinated biphenyls. *Environ. Sci.: Processes Impacts.* **18**(9): 1157-1168.
921 DOI:10.1039/C6EM00424E.
- 922 Young, T.K., and Bjerregaard, P. 2008. Health Transitions in Arctic Populations. *Edited by* T.K. Young
923 and P. Bjerregaard. University of Toronto Press, Toronto, ON. 496 pp.
- 924 Zhang, X., Brown, T.N., Wania, F., Heimstad, E.S., and Goss, K.-U. 2010. Assessment of chemical
925 screening outcomes based on different partitioning property estimation methods. *Environ. Int.*
926 **36**(6): 514-520. DOI:10.1016/j.envint.2010.03.010.

927 Zotor, F., Sheehy, T., Lupu, M., Kolahdooz, F., Corriveau, A., and Sharma, S. 2012. Frequency of
928 consumption of foods and beverages by Inuvialuit adults in Northwest Territories, Arctic Canada.
929 Int. J. Food Sci. Nutr. **63**(7): 782-789. DOI:10.3109/09637486.2012.676029.

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930 **Figure Captions**

931 **Figure 1.** Illustration of how various environmental fate, food chain and single organism models have
932 been combined to describe the accumulation of persistent organic pollutants in Arctic food chains and
933 indigenous people.

934 **Figure 2.** Schematic representation of the dietary relationships considered within the Arctic version of
935 the ACC-human model. Reprinted with permission from Binnington et al. 2016a (Copyright 2016
936 Elsevier).

937 **Figure 3.** Results of human food chain calculations by Kelly et al. (2007) (left) and Czub and
938 McLachlan (2004b) (middle), indicating with red colors the combination of partitioning properties
939 [namely the logarithm of the equilibrium partitioning coefficients between octanol and water ($\log K_{OW}$)
940 and octanol and air ($\log K_{OA}$)] that allow for efficient accumulation of an organic contaminant in the
941 Inuit food chain. The parameters displayed are the ratio between concentrations in indigenous Arctic
942 humans and in primary producers (left panel) and the percentage of the highest calculated
943 environmental bioaccumulation potential (middle panel). The plot on the right (Czub and McLachlan
944 2004b) identifies the location of a number of chemicals in the partitioning space defined by $\log K_{OW}$
945 and $\log K_{OA}$. Reprinted with permission from Kelly et al. 2007 (Copyright 2007 The American
946 Association for the Advancement of Science) and from Czub and McLachlan 2004 (Copyright 2004
947 American Chemical Society).

948 **Figure 4.** Exposure susceptibility index (ESI) indicating the relative bioaccumulation capability of an
949 Inuit eating a traditional diet relative to a southern Swede eating a mixed temperate diet, calculated by a
950 combination of an environmental fate and a human food chain bioaccumulation model for hypothetical,
951 persistent chemicals across a range of octanol-water and octanol-air equilibrium partitioning

952 coefficients (Undeman et al. 2010). Reprinted with permission from Undeman et al. 2010 (Copyright
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Single Species Environmental Reviews Single Food Chains

Beluga Whale

Hickie et al. 1999, 2000

Harp Seal

Fraser et al. 2002

Ringed Seal

Hickie et al. 2005;

Czub and McLachlan 2007

Marine
Mammal

Aquatic

Zooplankton-Polar Cod

Borgå et al. 2005

Zooplankton-Polar Cod-Kittiwake

Borgå et al. 2010

Zooplankton/Insect-Arctic Char

Gandhi et al. 2006

Zooplankton-Capelin/Herring-Cod

de Laender et al. 2010

Aboriginal
Human

Verner et al. 2009, 2013

Terrestrial

Lichen-Caribou-Wolf

Kelly and Gobas 2003

Integrated Human Food Web Models

1

Kelly et al. 2007

2

Czub et al. 2008

Undeman et al. 2010

3

Quinn et al. 2012

<https://mc.manuscriptcentral.com/er-pubs>

ACC-Human Arctic & ACC-Human Temperate food chain calculations

Environmental Reviews

PCB exposure estimates in Aboriginal Arctic mothers.

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HUMAN FOOD CHAIN

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