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Abstract

Ecotoxicology evolved as a scientific field as the awareness of the unintended effects of anthropogenic pollutants in biota increased. Polar bears (Ursus maritimus) are often the focus of contaminant exposure studies because they are apex predators with high contaminant loads. While early studies focused on describing and quantifying pollutants, present-day polar bear toxicological studies often incorporate ecological variables. This systematic literature review investigates the ecological, physiological, and morphological variables that have been integrated in such studies. The systematic literature search resulted in 207 papers, published 1970-2016. Representation of each of the 19 polar bear subpopulations varied from 0 to 72 papers, with East Greenland, Barents Sea, Southern Beaufort Sea, and Lancaster Sound being the most well represented with > 30 papers each. Mean number of samples analyzed per paper overall was 76 (range 1-691). Samples were collected from 1881 to 2015, with the large majority from the 1990s and 2000s, primarily from harvested bears (66%). Adipose, liver, and blood were the most common tissues examined. On average, papers investigating temporal trends did so using samples from 61 bears over a time period of 6 years.

The frequencies with which ecological variables were integrated into the toxicological papers varied. Notably, 51% included age and/or sex as the only ecological variable(s) in relation to contaminant concentrations. Further, 98% dealt with toxicology at the individual level, leaving population level effects largely unstudied. Solitary subadult and adult polar bears were included in 57% and 79% of the papers, respectively. Younger bears were included in fewer studies: yearlings in 20% and cubs-of-the-year in 13%. Only 12% of the papers examined reproduction relative to contaminants. Finally, body condition was included in 26% of the research papers, while variables related to polar bear diet were included in ≤ 9%.

Knowledge gaps were identified in the polar bear ecotoxicology literature. Based on our findings, we suggest future polar bear ecotoxicology studies increase sample sizes, include more ecological variables, increase studies on family groups, and increase the applicability of studies to management and conservation by examining pollution effects on reproduction and survival.

Key words:

Bibliometrics, contaminants, ecology, polar bear, systematic review, toxicology

Introduction

Ecotoxicology is the multidisciplinary study of chemical contaminants in the environment and their effects on biota (Newman, 2010). The field includes studies of chemistry, ecology, toxicology, physiology, immunology, endocrinology, developmental biology, genetics, and others. Ecology and toxicology both consider multiple scales in three primary areas: biological scales of organization, time, and space (AMAP, 1998; Graham et al., 2013). Ecology was defined as the "relation of the animal both to its organic as well as inorganic environment" (Haeckel, 1866), and as such encompasses a range of disciplines including physiology, evolution, genetics, behavior, energetics, population dynamics, and relationships with other species. In contrast, toxicology focuses on the detection, properties, exposure concentrations, and effects of toxic compounds (Newman, 2010). Ecological and toxicological aspects can be applied to any level of biology, from cell to biosphere. However, in wildlife, ecology typically focuses on the individual, population, or species, whereas toxicology usually focuses on the molecular, cellular, and organ level of the individual. Thus, ecology often begins at the level of the individual, which is where toxicology usually ends (AMAP, 1998; Chapman, 2002). Furthermore, ecology examines the larger-scale effects (Johnson, 1980; Mayor et al., 2009), while toxicology tells us that variables are changing, but rarely what the larger-scale effects may be. The interdisciplinary perspective of combining the two fields in an ecotoxicological approach provides greater insight into factors influencing the bioaccumulation and toxicological effects of pollutants in wildlife.

Anthropogenic chemicals in the environment predate concerns of their effects on wildlife or humans. For example, polychlorinated biphenyls (PCBs) were first synthesized in 1881 and while their use in industry emerged about 50 years later (Cairns and Siegmund, 1981), they were not reported as persistent and bioaccumulated contaminants in biota until 1966 (Jensen, 1966). Generally, other environmental pollutants have a shorter history and new, emerging environmental pollutants are frequently discovered, including in the Arctic (Dietz et al., 2013a; Gebbink et al., 2016; Trumble et al., 2012). Persistent organic pollutants (POPs) cover a diversity of compounds including legacy compounds (defined as those that remain in the environment long after they were introduced) such as PCBs, DDTs, and chlordanes, as well as new chemicals of emerging concern (CECs), such as brominated flame retardants (BRFs) and some current-use pesticides (AMAP, 2016; Bidleman et al., 2010; Butt et al., 2010; Gebbink et al., 2016; Warner et al., 2010). Heavy metals, especially methylmercury (MeHg), are another group of toxic compounds of concern in Arctic biota (Dietz et al., 2013b; Eaton and Farant, 1982; Norstrom et al., 1986).

Ecotoxicology evolved as a scientific field in the 1950s and 1960s as the emergence of unintended effects of anthropogenic chemicals in biota became apparent (Newman, 2010; Rattner, 2009). Although DDT had been detected in wildlife in the 1950s (Rattner, 2009), it was eggshell thinning in birds of prey that provided evidence of the detrimental effects of environmental pollution (Ratcliff, 1967). The first Arctic ecotoxicological studies were reported in the 1970-80s at which time long-range transport of pollutants became apparent (Barrie et al., 1992; Kerr, 1979). The first paper on chlorinated organic chemicals in an Arctic marine mammal was published by Holden (1970), who detected PCBs, DDT, and dieldrin in ringed seals (*Pusa* *hispida*). More detailed reports on PCBs and DDT-related compounds in the Arctic were published in the early 1970s on ringed seal and beluga (*Delphinapterus leucas*) (Addison and Brodie, 1973; Addison and Smith, 1974; Clausen et al., 1974). Studies on heavy metals in the Arctic occurred about the same time on harp seals (*Pagophilus groenlandicus*) and hooded seals (*Cystophora cristata*) (Sergeant and Armstrong, 1973). The first paper on POPs in polar bears (*Ursus maritimus*) was published in 1975, when high concentrations of PCBs were reported in their milk (Bowes and Jonkel, 1975). Similar to the legacy contaminants, heavy metals were first quantified in polar bears several decades ago (Eaton et al., 1982; Norstrom et al., 1986). Once it became clear that polar bears were subjected to high concentrations of these compounds, they soon became a focal species for contaminant exposure studies in the Arctic.

Polar bear ecotoxicology has been a growing field of research since the 1970s (Fig. 1). Expanding our knowledge on the exposure and the effects of contaminants in relation to polar bear ecology is of particular concern because polar bears are apex predators with a high lipid diet and, as such, carry high loads of contaminants due to biomagnification (Atwell et al., 1998; Hobson et al., 2002). POPs are generally lipophilic compounds as exemplified by PCBs and PBDEs, as well as some forms of metals such as methylmercury (AMAP, 1998; Dietz et al., 2013b; McKinney et al., 2011; Sonne, 2010). Although subpopulation specific, polar bears are at risk as a consequence of the effects of climate change (Stirling and Derocher, 2012), pollution (Sonne, 2010), harvest (Taylor et al., 2006), and the synergistic effects of these stressors (Holmstrup et al., 2010; Hooper et al., 2013; Jenssen et al., 2015). In addition, polar bears are harvested for human consumption (Ostertag et al., 2009; Sonne et al., 2013b). Thus, knowledge of contaminants and their effects on polar bears may aid our understanding of the extent and nature of their potential effects in humans.

Collecting data on widely dispersed and solitary wildlife species, such as polar bears, is challenging. Thus, there is a need to coordinate and optimize available resources to maximize the scientific output contributing to the conservation of the species (Jenssen et al., 2015; Patyk et al., 2015; Vongraven et al., 2012). Despite identification of environmental contaminants as a key threat to polar bears (Amstrup et al., 2007; Patyk et al., 2015), there has been no systematic overview of their ecotoxicology across all subpopulations.

The primary aim of this systematic review was to examine polar bear ecotoxicology in the peer-reviewed literature, the patterns over time, and how ecological variables have been integrated in these studies. The secondary aim was to identify knowledge gaps within the field of polar bear ecotoxicology and provide recommendations on how to fill those knowledge gaps through future research within the field.

Methods

A systematic review of peer-reviewed literature was performed based on searches in the comprehensive database Web of Science^{TM} (WoS, Thompson Reuters, 2016). “All databases” were searched (see Table S1 for an overview of the included publication databases) on WoS using polar bear- and contaminant-relevant search terms to generate an initial list of potential papers. This list was then refined, retaining papers where polar bears were the focal species. Date of publication was unrestricted but only peer-reviewed papers in English were included. The resulting papers were then divided into two categories:

- research papers – original ecotoxicological studies (e.g., Basu et al., 2009; Derocher et al., 2003) or
- review papers - overview of published studies (e.g., Letcher et al., 2010; McKinney et al., 2015).

A number of ecological and toxicological variables were documented for each paper included in the systematic review (Table 1, core ecological and toxicological variables; Table S2, full list of all variables and their definitions). Refining the list of papers from the initial literature search and scoring the variables on those papers that were included in the review was done by co-author M. Viengkone.

Further, an index was created, consisting of ecotoxicology publications for a selection of marine and terrestrial mammal species relative to those published for polar bears. The index was created using the raw, unfiltered results from literature searches for each species in connection with the contaminant-related search terms outlined above.

Search terms

Two "TOPIC" search terms were combined using the Boolean operator "AND". The asterisk (*) indicated wildcard truncation in the specific terms.

- "polar bear" OR "ursus maritimus" OR "thalarctos maritimus"
- pollut* OR contamin* OR metal* OR flame* OR PCB* OR organo* OR cadmium* OR mercur* OR lead* OR pestic* OR PFOS OR PFAS OR PFOA OR PFCA OR PFC* OR

hydrox* OR OH-* OR bromin* OR perfluor* OR fluor* OR chlor* OR halogen* OR legacy OR emerg* OR metabolit*

Statistical analyses

Linear regression analyses were used to investigate temporal relationships in number of authors and number of samples used in research papers. In addition, a Kruskal-Wallis rank sum test was used to examine temporal patterns in the research papers. Statistical analyses were conducted using Microsoft Excel 2010. “The last decade” of papers included in the present systematic review was defined as those papers published between January 2006 and December 2015. Results were considered statistically significant at $p \leq 0.05$, with $0.05 < p \leq 0.1$ considered as approaching significance.

Results and discussion

Literature

The literature search was conducted August 17, 2016 and yielded 207 publications published between 1970 and 2016 (Fig. 1); 176 research papers, 27 reviews, and 4 papers that were both research and review (Dietz et al., 2015; Henriksen et al., 2001; Pavlova et al., 2016; Sonne et al., 2009a). For our purposes, these four papers were subsequently included in both the research and the review paper categories. Research papers were published in 43 different journals, with 19% published in Environmental Science & Technology and 16% in Science of the Total Environment. Review papers were published in 16 different journals, with 42% in Science of the

Total Environment. For perspective on how well researched polar bears are, we created an index of toxicology publications for a selection of marine and terrestrial mammal species relative to those published for polar bears (Fig. 2). This index showed that polar bears, along with beluga whales, were one of the more well-published Arctic marine mammal species within this field and had a similar number of published papers to mink (*Mustela lutreola* and *Neovison vison*), which are often used as a mammalian model species in toxicology studies (Folland et al., 2016; Pavlova et al., 2016; Wang et al., 2014). Ringed seals, the main prey species of polar bears (Thiemann et al., 2008), were also well studied.

There is a temporal trend to include more authors on publications in complex, collaborative fields of research such as ecotoxicology (Mindeli and Markusova, 2015; Subramanyam, 1983). While this trend was not found in the review papers (1992-2016; Fig. 3a; $F_{1,29} = 2.00$, $p = 0.17$, $r^2 = 0.06$), there was an increasing trend towards larger authorship for research paper published 1970-2016 (Fig. 3b; $F_{1,178} = 48.36$, $p < 0.001$, $r^2 = 0.21$). However, over the past decade, these results switched: review papers, perhaps due to the growing complexity, had an increasing number of authors (2006-2015; Fig. 3c; $F_{1,17} = 5.97$, $p = 0.03$, $r^2 = 0.26$), while research papers had an average of 7-8 authors per paper published in the period 2006-2015 (Fig. 3d; $F_{1,87} = 0.11$, $p = 0.74$, $r^2 = 0.001$). Although the number of authors varies between natural science fields, 7-8 authors in total is at the higher end of the range (Newman, 2001). International collaboration is common in polar bear ecotoxicology (Table 2). Institutions within Canada and Denmark have been the most prolific followed by Norway and the United States (Table 2). Greenland and Russia are largely represented as coauthors on research publications from other countries. Low contributions from these two countries may be related to our focus on publications in English only. The low number of papers from Greenland reflects that most research on Greenland polar bear subpopulations were conducted by Denmark-based scientists.

The ratio of polar bear ecotoxicology research to review papers was 6:1 (Fig. 1). The high frequency of review papers highlights two aspects about polar bear ecotoxicology: 1) it is a complex research field encompassing a large number of chemicals and ecological variables, 2) due to the often limited sample size, each individual study only takes a limited number of possible ecological variables into account. Review papers present a means to reduce these restrictions by integrating insights from individual papers, thereby facilitating incorporation and interpretation of a wider range of variables.

Toxicology

Samples

Results of ecotoxicology research have been published for all recognized polar bear subpopulations (mean ± S.E.: 21 ± 4 papers/subpopulation, range: 0-72), except the Arctic Basin (Fig. 4a-b; IUCN PBSG, 2010). The subpopulations of East Greenland, Barents Sea, Southern Beaufort Sea, and Lancaster Sound were the most published with > 30 papers each. Bears in East Greenland and Barents Sea have high contaminant loads and ecotoxicological research has been a priority in these areas (AMAP, 1998; Dietz et al., 2015; Norstrom et al., 1998; Sonne, 2010). The number of polar bears harvested varies widely across Canadian subpopulations (IUCN PBSG, 2010) and the access to samples from a large harvest in Lancaster Sound may have facilitated ecotoxicological studies. Finally, the high number of papers including the Southern Beaufort Sea subpopulation is likely due to it being a shared subpopulation and thus having publications from both Canada and USA, its long history of population assessment, and monitoring in relation to hydrocarbon exploration (Amstrup, 2000; Stirling, 2002).

For those subpopulations where research has occurred, Kane Basin, Laptev Sea, Kara Sea, and Norwegian Bay were the least studied (<10 papers each), likely because they are less accessible and have low or no harvest (Vongraven et al., 2012). Limited resources and varying priorities for the different subpopulations affect research intensity. However, ecotoxicological studies should optimally form part of polar bear research programs, in particular due to the adverse interactions that exist between climate change and contaminants (AMAP, 2011; Jenssen et al., 2015), but also due to the direct sub-lethal effects that contaminant exposure may have on the bears' reproduction and health (Dietz et al., 2015; Letcher et al., 2010; Sonne, 2010; Sonne et al., 2015). Without the ability to include ecologically relevant data as input in predictive toxicological models, the effects of potentially important variables influencing the health status and survival of polar bears is missing (also see Atwood et al., 2016).

Polar bears were the only species studied in 65% (117) of research papers, whereas in 35% (63), they were studied along with other species including fish, turtles, pinnipeds, cetaceans, sled dogs, and humans (Giesy and Kannan, 2001; Sonne, 2010). The mean number of sampled polar bears per paper was 76 (S.E. = 8.4, range: 1-691). Although the positive trend in number of samples/paper over time approached significance (Fig. 5a; $F_{1,171} = 3.16$, $p = 0.08$, $r^2 = 0.02$), the mean was stable over the last decade (2006-2015; mean ± S.E.: 96 ± 14.53; Fig. 5b; $F_{1,85} = 1.61$, $p = 0.21$, $r^2 = 0.02$). The three largest sample sizes came from studies that included museum specimens (Bechshoft et al., 2008; Bechshoft et al., 2009; range n = 510-691; Sonne et al., 2007b). Larger sample sizes allow for parsing of the data into homogenous groups (e.g., sex/age categories), while maintaining statistical robustness. It also better facilitates investigation of interactions between variables without overfitting or otherwise compromising the data analyses (Crawley, 2007; Hair et al., 2006). Ecotoxicological studies with small sample sizes (e.g., $n \leq 30$) were often investigative (e.g., Sacco, 2005; Verreault et al., 2006), experimental (e.g., Lie et al., 2005; Lie et al., 2004), or focused on new analytical method development for chemical contaminants and biomarker endpoints of effects pathways and mechanisms (e.g., Letcher and Norstrom, 1995; Simon et al., 2011). Developing new methods using only a small number of samples is advantageous with regards to cost, time, and optimal usage of the limited tissue samples available. The number of samples available for ecotoxicological polar bear research depends on a number of factors such as subpopulation(s) investigated and sampling methods. Of the 180 papers, 66% (119) used samples from harvested bears, 25% (45) samples from live bears, and 6% (10) with samples from both harvested and live bears. The remaining 3% (6) of papers did not specify how tissues were obtained. The most common tissues examined were adipose, liver, and blood, incorporated in 40% (72), 38% (69) and 26% (46) of the papers, respectively (Fig. 6). While tissue samples such as kidney, liver, and reproductive organs are useful in determining histopathological toxicological and functional endpoints (Beland et al., 1993; Bergman, 1999; Gabrielsen et al., 2015; Letcher et al., 2010; Sonne, 2010), they are only available from dead polar bears. As climate change induced habitat loss and, to some degree, pollution are expected to have increasingly adverse effects on the abundance of polar bears, the availability of invasive samples may decline long-term (Amstrup et al., 2007; Derocher et al., 2013). Thus, it is increasingly important to examine relationships between ecotoxicological results based on invasive versus minimally- or non-invasive samples. Such samples include those that can be collected without any direct contact with the animal, e.g., fecal samples collected opportunistically (Iversen et al., 2013) or hair samples collected using hair snags (de Groot et al., 2013). Born et al. (1991) found concentrations of mercury in polar bear hair to be positively correlated to mercury concentrations in muscle, liver, and kidney tissue. However, the types of samples and how these are collected will be dependent on the research questions: minimally- or non-invasive sampling will not be applicable in all studies.

Temporally, the research papers were based on samples collected from 1881 to 2015, with the 1990s and 2000s being more prevalent (Fig. 7; Kruskal-Wallis rank sum test, $H = 7.75$, $p < 0.01$). Ten papers analyzing hair or bones from museums spanned > 100 years (e.g., Horton et al., 2009; Sonne et al., 2013a). Including these 10 papers, the mean time span covered was 12 years (S.E. = 2.1; range 1-119), but excluding them reduced the mean to 6 years (S.E. = 0.8, range 1-71). Six years is a brief period considering the interannual variation in ecological as well as contaminant-related variables and the lifespan of polar bears (see Riget et al., 2010; Riget et al., 2011). The years included in these time spans, however, were not necessarily contiguous. Many papers listed only a range of years within which the bears were sampled, while 9 studies included no information of sampling year(s). Removing the 10 papers where the time series > 100 years, the mean sample size was 61 bears (S.E. = 6.0, range 1-378) or only 10 individuals/year, which is at the low end of the 10-25 annual samples recommended for monitoring time trends of PCBs in polar bears (Henriksen et al., 2001). Determining adequate annual sample size depends on degree of interannual variability, statistical tests used, number of years of sampling, and demographic composition of the sample (Bignert et al., 2004). While a sample of 10 bears/year may seem numerically reasonable, samples are often a mixture of bears of different age- and sex-class, reproductive status, body condition, geographical location, and contaminant load, which are all important factors that can have significant influence on exposure and physiology (Letcher et al., 2010; Polischuk et al., 2002; Sonne, 2010). Therefore, the annual sample size for any one demographic group is often significantly smaller. Coordinated sampling across years and polar bear subpopulations could help address sample size issues and provide statistical power to temporal studies.

Twenty-eight percent (50) of research papers reported on the analysis of tissues collected in one season: 19% spring (34; March-May), 4% summer (7; June-August), 3% fall (5; September-November), and 2% winter (4; December-February). The remaining papers incorporated samples collected in two (16%, 28), three (7%, 13), or all four (6%, 10) seasons. Two papers (1%) combined spring samples with samples of unknown season, while the remaining 43% (77) were entirely based on samples of unknown collection season. Overall, regardless of number of seasons represented, spring was the most prevalent sampling season (44% [79]), compared to summer 18% (32), fall 21% (38), and winter 21% (38). For most polar bear subpopulations, spring samples dominate because it is the season with most harvest, stable sea ice enables on-ice sampling of bears, and all sex/age groups are accessible. Although season can have a significant influence on polar bear contaminant load (Dietz et al., 2004; Dietz et al., 2007; Polischuk et al., 2002), it is rarely considered in polar bear ecotoxicology studies.

Contaminants

Chlorinated compounds and pesticides were included in 55% (99) and 41% (74) of the polar bear ecotoxicology papers, respectively. Heavy metals, metabolites, and brominated and fluorinated compounds were each included in 17-28% (30-50) of the papers (Fig. 8). Although the choice of compounds studied is rarely explained, the most commonly investigated are those included in the 2001 Stockholm Convention; a continuously updated, global treaty with the purpose of protecting humans and the environment against persistent organic pollutants (Hung et al., 2016; Muir and Howard, 2006; UNEP, 2001). Finally, our understanding of contaminant metabolites is still rudimentary. As our knowledge on the relationship between exposure and effects of parent compounds and metabolites increases, metabolites may be included in more studies. However, the study of metabolites and other new compounds continues to be challenged by the lack of analytical methods and pure chemical standards (Gebbink et al., 2016; Keith, 1976; Wiener, 2013).

Contaminants in research papers were examined in relation to biology (those listed in Table 3 as well as age and/or sex; see definition under "Effects" in Table S2), concentration, space, and time (Fig. 9). Most studies examined either contaminant concentrations (29%, 53) or contaminant concentrations and biology (32%, 57). However, 67% (38) of the latter only included age and/or sex in their analyses. Thus, 51% (53 + 38) of the papers included no, or only the most basic, biological information on their study animals. One explanation for this could be that the objectives of earlier studies focused on identifying and quantifying contaminants, essential information which formed the educated basis for studies on their effects. However, contaminant concentrations alone tell us little about the toxicity mechanisms and potential adverse effects. Controlled studies in other mammals have shown that even low concentrations of specific contaminants may have physiological and/or morphological effects (Kirkegaard et al., 2010; Martin et al., 2006; Sonne et al., 2009b; Voltura and French, 2000; Zimmer et al., 2009). Further, the potential mixture effects between the hundreds of different contaminants in polar bears requires additional consideration (Dietz et al., 2015; Letcher et al., 2010; Sonne, 2010; Sonne et al., 2012); these effects could furthermore differ depending on whether the exposure is acute or chronic (Chapman, 2002). Biology (as defined above) was investigated relative to concentrations and spatial, temporal, or spatial and temporal issues in 28% (49) of the papers. Finally, concentrations were investigated relative to spatial, temporal, or spatial and temporal issues in 9% (16) of the papers.

Of the physiological and morphological effects that were studied in relation to contaminant concentrations, pathology was the most prevalent (9%, 17; Table 3). Morphometrics, enzymes, and hormones were each studied in 4-6% of all papers ($7 \leq n \leq 11$), whereas immune system, protein levels, reproductive potential, vitamins, receptor levels, and transport proteins each were the focus of 2-3% ($3 \leq n \leq 5$) of the studies. Altogether, 37% (66) of the papers included in the review investigated physiological and morphological effects in relation to contaminant concentrations (Table 3).

Notably, 98% (176) of all papers dealt with toxicology at the individual level. The four exceptions were Bernhoft et al. (1997), who investigated population level effects by assessing the relationship between contaminants and reproductive success in female polar bears, and Sonne et al. (2009a), Dietz et al. (2015), and Pavlova et al. (2016), who all modelled potential for population level effects due to reproductive impairment. Modeling is likely to become increasingly applied in polar bear ecotoxicology in order to take the results of individual level studies and apply these at the population level (Dietz et al., 2015; Pavlova et al., 2016).

Ecology

The frequencies with which ecological variables were integrated into toxicological papers varied (Table 1). Age and sex were the most common: age to nearest month or year was used in 82% (148) of the papers, whereas sex was used in 72-74% (130 for males, 134 for females). Eighteen percent (32) did not include age, 16% (29) did not discuss gender, and 10.5% (19) overlapped in that they investigated neither sex nor age in relation to contaminants. Life history traits such as age and sex are primary variables determining vulnerability to contaminant exposure because they reflect the animal's life stage and physiological (dietary) requirements (Diamanti-Kandarakis et al., 2009; Letcher et al., 2010; McKinney et al., 2013; Thiemann et al., 2008). Further, inter-sexual differences in diet and hormones influence how a contaminant may affect an individual (Pilsner et al., 2010; Sonne, 2010). Bears of unknown sex were included in 14% of the studies, generally as a smaller percentage (< 15%) of the total number of individuals (e.g., Routti et al., 2011). In most of the studies where gender was unknown, it was the result of using inadequately labeled, museum specimens (e.g., Sonne et al., 2004).

Solitary subadult and adult polar bears were included in 57% (102) and 79% (142) of the papers, respectively. Younger bears were included in fewer studies: yearlings in 20% (36) and cubs-of-the-year in 13% (24). The category subadults here predominantly consists of independent immature individuals > 2 year old (Rosing-Asvid et al., 2002). From a conservation perspective, studying contaminants in adult polar bears is relevant to their reproductive success and would include variables such as epigenetics, reproductive organ deformation, and behavior (Jenssen et al., 2015; Pilsner et al., 2010; Sonne et al., 2007a; Sonne et al., 2015). Furthermore, effects of contaminants may reduce survival and thus reproductive output (Derocher et al., 2003; Dietz et al., 2015). However, developing young are more sensitive to the effects of contaminants (Domingo, 1994; Hamlin and Guillette, 2011), while also being subjected to high concentrations via maternal transfer (Bernhoft et al., 1997; Bytingsvik et al., 2012). Given the risk of lifelong consequences (Colborn et al., 1993; Hamlin et al., 2011), developing young are underrepresented in the polar bear ecotoxicology literature.

Presence of dependent offspring can have a profound influence on maternal contaminant load in polar bears (Lie et al., 2000; Polischuk et al., 2002). In addition, information on reproductive success, including sex, age, and survival of cubs, is essential to population assessments. However, only 12% (21) of the research papers examined reproduction in relation to contaminants. Lack of linkages to reproduction could be due, in part, to the large number of ecotoxicological studies where samples are collected from harvested animals, which generally excludes family groups because they are protected from harvest (Naalakkersuisut, 2005; Sonne, 2010). Data on family groups is more readily obtainable for frequently monitored subpopulations (e.g., Barents Sea, Western Hudson Bay, and Southern Beaufort Sea). Of the studies that incorporated offspring variables in the contaminant analysis, 9% (16) included offspring age, 4% (7) offspring sex, and 2% (4) litter size. In addition to the 12% of papers that included some measure of reproduction, another 7% reported on contaminants in dependent young, but without any further statistical analysis (e.g., Derocher et al., 2003; Dietz et al., 2000). Dependent young differ in contaminant exposure and physiological variables such as hormone concentrations, not only from adults, but also due to sex and age (Bechshoft et al., 2016a; Bernhoft et al., 1997; Knott et al., 2012; Oskam et al., 2003; Oskam et al., 2004). Differences in physiological response to contaminants is expected between offspring life stages (e.g., when shifting from milk to solids) as well as between the sexes, as these differ in their endocrine, morphological, and overall physiological profile already at the fetal stage (Derocher et al., 2005; Hamlin et al., 2011; Maekawa et al., 2014).

The amount of lipophilic contaminants biologically available to a bear is closely linked with that individual bear's body condition (size of adipose tissue store): the leaner the bear, the more of the contaminants will be released into the blood stream (Polischuk et al., 2002). However, body condition was included in the contaminant analyses in only 26% (46) of the research papers. In addition, adult female polar bear body condition is related to reproductive success (Derocher et al., 2004; Robbins et al., 2012), indicating a potential link between body condition, contaminant load, and reproductive success in polar bears. Investigating contaminants in relation to body condition is also interesting in that they are associated with altered metabolism in other species (van Ginneken et al., 2009; Verreault et al., 2007; Voltura et al., 2000). Finally, measures of polar bear diet were included in ≤ 9% (≤ 17) of the contaminant analyses. As the contaminant concentration and composition in prey species varies widely (McKinney et al., 2013; McKinney et al., 2010; Routti et al., 2012; St Louis et al., 2011), diet information could be a variable that warrants further investigation. For example, integrating information on the diet of a polar bear could help elucidate dietary reasons that baseline contaminant concentrations may differ between demographic groups such as males and females or subadults and adults.

Genetics, size of home range, and climate variables were each examined in ≤ 1% (≤ 2) of the research papers, while the variable behavior (which in this review is separate from movement, see Table S2) was never used. Given the relationship between these variables and toxicology, they could be an area for future studies. Investigating individual and geographical differences in the animals' exposure to contaminants is a relevant conservation topic (Bickham et al., 2000; Brown et al., 2009). Further, larger home range sizes have been linked to higher contaminant exposures in polar bears (Olsen et al., 2003), while climate variables have been linked to the abundance and behavior of the contaminants in their ecosystem (AMAP, 2011; Derocher et al., 2004; Ma et al., 2011). Finally, alteration of behavior has been observed in other mammal species (Clotfelter et al., 2004; Patisaul and Adewale, 2009; Zimmer et al., 2009). Therefore, combining contaminant concentration information with behavioral observations of wild polar bears may be useful given that the contaminants can affect vitamin and endocrine levels (Bechshoft et al., 2015; Bechshoft et al., 2016b; Pedersen et al., 2015; Villanger et al., 2011), which may affect behavior. Similarly, a change in feeding behavior could affect contaminant exposure (McKinney et al., 2013; McKinney et al., 2015).

Conclusions

Summary: Key knowledge gaps

Although our systematic review of the published literature found polar bears to be one of the better studied Arctic marine mammal species in the field of toxicology, few of the studies incorporated polar bear ecology. The increased integration of toxicology and ecology has particular relevance to polar bear conservation given concerns of contaminants as a threat to the species. Vongraven et al. (2012) and Patyk et al. (2015) noted the need for multidisciplinary projects that include a broad range of ecological variables. Our review identified existing knowledge gaps in polar bear ecotoxicology. Based on our findings, we suggest that polar bear researchers consider the following recommendations when designing future ecotoxicology studies:

(1) Subpopulation(s)

While it would be interesting to have ecotoxicological data for all polar bear subpopulations, logistical restraints require prioritization. Furthermore, the choice of which polar bear subpopulation to focus on in future ecotoxicology studies will depend on the nature of the scientific questions being investigated. For example, if family group data is required, relying on a hunter harvest will be of little value because family groups are protected from harvest. Similarly, studies on temporal trends would benefit from previous investigations of the variables of interest in the same geographical area. Our recommendation for focal subpopulations in future ecotoxicology studies are all included in those suggested as appropriate for high or medium intensity monitoring under the circumpolar polar bear monitoring framework outlined by Vongraven et al. (2012): Barents Sea, Chukchi Sea, East Greenland, Northern Beaufort Sea, Southern Beaufort Sea, and Western Hudson Bay (see Table 4 for an overview). Results from disparate subpopulations, differing with regards to ecological data or availability of invasive tissue samples, would complement each other, thereby providing a greater understanding of the relationship between ecology and toxicology.

(2) Exposure assessments and temporal trends

Assessing change in the contaminant exposure of polar bears, or temporal exposure trend studies, would benefit from increased sample set sizes as well as an increase in the range of years covered. Depending on collection protocols for a study, increased use of polar bear specimens from museums as well as those stored in tissue banks would help alleviate both of these problems, and at low cost. In addition, the continued collection and archiving of samples is recommended. Finally, larger and more homogenous sample sizes may allow for the incorporation of additional ecological variables in the temporal trend studies.

(3) Family groups

Developing young are underrepresented in the polar bear ecotoxicology literature. Hence,family groups and dependent young, including those < 2 years of age, should be included in ecotoxicology studies whenever possible (keeping in mind that samples from the youngest bears should be limited to those obtainable through minimally invasive methods).If sample size allows, dependent young should be split into sex/age groups before analyses. Furthermore, polar bear ecotoxicological studies should include measures of reproduction (e.g., lactation, number/age/sex/weight/body condition of offspring) in analyses whenever possible. Such detail may be more difficult to incorporate in studies based on hunter-gathered samples, as the harvest is often male biased (Derocher et al., 1997), but should be more readily obtainable in studies based on observational and/or researcher-gathered data.

(4) Ecological variables

Body condition is an essential variable to consider in ecotoxicological studies, especially with respect to lipophilic compounds, and should be among the data collected on all bears, regardless of the origin of the samples. Developing an understanding of the relationship between various methods of measuring body condition would also be helpful in facilitating inter-study comparisons (Cattet et al., 2002; McKinney et al., 2014; Stirling et al., 2008). Furthermore, we recommend increased incorporation of ecological variables such as diet, climate, reproduction, and survival in ecotoxicological studies. In addition to following up on the existing studies on hormone response and immune function (Bechshoft et al., 2012; Bernhoft et al., 2000; Lie et al., 2004; Macbeth et al., 2012; Oskam et al., 2004; Weisser et al., 2016), hitherto uninvestigated health and immune system variables such as parasitic load may also be of interest in relation to ecotoxicological polar bear studies. Finally, behavior may have the potential to be an important, yet largely uninvestigated, variable in polar bear ecotoxicological research.

(5) Conservation implications

Essentially all polar bear ecotoxicological data published investigate the impacts of contaminants at the individual level. If ecotoxicology is to be considered in population assessments, results must be applicable to the population level, which could be achieved through meta-analyses (e.g., Nuijten et al., 2016), modeling, or reviews based on already existing data. In new contaminant studies, an understanding of population-level effects can be achieved by incorporating more variables directly related to reproduction and survival.

Polar bear ecotoxicology has helped shape our understanding of the detrimental effects of anthropogenic contaminants in the Arctic. It is our hope that the knowledge gaps identified in this review will influence research planning, thus increasing the research impact, especially with regards to population assessments, management, and conservation of polar bears.

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References

Addison R. F. & Brodie, P. F. (1973). Occurence of DDT residues in beluga whales (*Delphinapterus leucas*) from Mackenzie Delta, NWT. *Journal of the Fisheries Research Board of Canada* **30,** 1733-1736.

Addison R. F. & Smith, T. G. (1974). Organochlorine residue levels in Arctic ringed seals - variation with age and sex. *Oikos* **25,** 335-337.

AMAP. (1998). *AMAP assessment report: Arctic pollution issues*. Arctic Monitoring and Assessment Programme (AMAP), Oslo, Norway.

AMAP. (2011). Combined effects of selected pollutants and climate change in the Arctic environment. In *AMAP Technical Report No. 5*, pp. 108. Arctic Monitoring and Assessment Programme (AMAP), Oslo.

AMAP. (2016). AMAP Chemical of Emerging Concern report.

Amstrup S. C. (2000). Polar bear. In *The Natural History of an Arctic Oil Field: Development and Biota* (ed. J. J. Truett and S. R. Johnson), pp. 133-157, New York, New York.

Amstrup S. C., Marcot, B. G. & Douglas, D. C. (2007). Forecasting the range-wide status of polar bears at selected times in the 21st century. In *USGS Science Strategy to Support U.S. Fish and Wildlife Service Polar Bear Listing Decision, U. S. Department of the Interior*, pp. 126 pp.

Atwell L., Hobson, K. A. & Welch, H. E. (1998). Biomagnification and bioaccumulation of mercury in an arctic marine food web: Insights from stable nitrogen isotope analysis. *Canadian Journal of Fisheries and Aquatic Sciences* **55,** 1114-1121.

Atwood T. C., Marcot, B. G., Douglas, D. C., Amstrup, S. C., Rode, K. D., Durner, G. M. & Bromaghin, J. F. (2016). Forecasting the relative influence of environmental and anthropogenic stressors on polar bears. *Ecosphere* **7,** e01370. 10.1002/ecs2.1370.

Barrie L. A., Gregor, D., Hargrave, B., Lake, R., Muir, D., Shearer, R., Tracey, B. & Bidleman, T. (1992). Arctic contaminants - sources, occurrence and pathways. *Science of the Total Environment* **122,** 1-74.

Basu N., Scheuhammer, A. M., Sonne, C., Letcher, R. J., Born, E. W. & Dietz, R. (2009). Is dietary mercury of neurotoxicological concern to wild polar bears (*Ursus maritimus*)? *Environmental Toxicology and Chemistry* **28,** 133-140.

Bechshoft T., Derocher, A. E., Richardson, E., Lunn, N. J. & St Louis, V. L. (2016a). Hair mercury concentrations in western Hudson Bay polar bear family groups. *Environmental Science & Technology* **50,** 5313-5319.

Bechshoft T., Derocher, A. E., Richardson, E., Mislan, P., Lunn, N. J., Sonne, C., Dietz, R., Janz, D. M. & Louis, V. L. S. (2015). Mercury and cortisol in Western Hudson Bay polar bear hair. *Ecotoxicology* **24,** 1315-1321.

Bechshoft T., Sonne, C., Dietz, R., Born, E. W., Muir, D. C. G., Letcher, R. J., Novak, M. A., Henchey, E., Meyer, J. S., Jenssen, B. M. & Villanger, G. D. (2012). Associations between complex OHC mixtures and thyroid and cortisol hormone levels in East Greenland polar bears. *Environmental Research* **116,** 26-35.

Bechshoft T., Sonne, C., Jakobsen, J., Rigét, F. F., Born, E. W., Letcher, R. J., Jenssen, B. M. & Dietz, R. (2016b). Vitamins A and E in liver, kidney, and whole blood of East Greenland polar bears sampled 1994–2008: reference values and temporal trends. *Polar Biology* **39,** 743-754.

Bechshoft T., Wiig, O., Sonne, C., Riget, F. F., Dietz, R., Letcher, R. J. & Muir, D. C. G. (2008). Temporal and spatial variation in metric asymmetry in skulls of polar bears

(*Ursus maritimus*) from East Greenland and Svalbard. *Annales Zoologici Fennici* **45,** 15-31.

BECHSHOFT T. O., RIGÉT, F. F., SONNE, C., DIETZ, R. & LETCHER, R. J. (2009). Skull foramina asymmetry in East Greenland and Svalbard polar bears (*Ursus maritimus*) in relation to stressful environments. *Annales Zoologici Fennici* **46,** 181-192.

BELAND P., DEGUISE, S., GIRARD, C., LAGACE, A., MARTINEAU, D., MICHAUD, R., MUIR, D. C. G., NORSTROM, R. J., PELLETIER, E., RAY, S. & SHUGART, L. R. (1993). Toxic compounds and health and reproductive effects in St. Lawrence beluga whales. *Journal of Great Lakes Research* **19,** 766-775.

BERGMAN A. (1999). Health condition of the Baltic grey seal (*Halichoerus grypus*) during two decades - Gynaecological health improvement but increased prevalence of colonic ulcers. *Apmis* **107,** 270-282.

BERNHOFT A., SKAARE, J. U., WIIG, O., DEROCHER, A. E. & LARSEN, H. J. S. (2000). Possible immunotoxic effects of organochlorines in polar bears (*Ursus maritimus*) at Svalbard. *Journal of Toxicology and Environmental Health* **59,** 561-574.

BERNHOFT A., WIIG, O. & SKAARE, J. U. (1997). Organochlorines in polar bears (*Ursus maritimus*) at Svalbard. *Environmental Pollution* **95,** 159-175.

BICKHAM J. W., SANDHU, S., HEBERT, P. D. N., CHIKHI, L. & ATHWAL, R. (2000). Effects of chemical contaminants an genetic diversity in natural populations: implications for biomonitoring and ecotoxicology. *Mutation Research* **463,** 33-51.

BIDLEMAN T. F., HELM, P. A., BRAUNE, B. M. & GABRIELSEN, G. W. (2010). Polychlorinated naphthalenes in polar environments - A review. *Science of the Total Environment* **408,** 2919-35.

BIGNERT A., RIGET, F., BRAUNE, B., OUTRIDGE, P. & WILSON, S. (2004). Recent temporal trend monitoring of mercury in Arctic biota - how powerful are the existing data sets? *Journal of Environmental Monitoring* **6,** 351-5.

BORN E. W., RENZONI, A. & DIETZ, R. (1991). Total mercury in hair of polar bears (*Ursus maritimus*) from Greenland and Svalbard. *Polar Research* **9,** 113-120.

BOWES G. W. & JONKEL, C. J. (1975). Presence and distribution of polychlorinated biphenyls (PCB) in Arctic and Subarctic marine food chains. *Journal of the Fisheries Research Board of Canada* **32,** 2111-2123.

BROWN A. R., HOSKEN, D. J., BALLOUX, F., BICKLEY, L. K., LEPAGE, G., OWEN, S. F., HETHERIDGE, M. J. & TYLER, C. R. (2009). Genetic variation, inbreeding and chemical exposure - combined effects in wildlife and critical considerations for ecotoxicology. *Philosophical Transactions of the Royal Society B* **364,** 3377-90.

BUTT C. M., BERGER, U., BOSSI, R. & TOMY, G. T. (2010). Levels and trends of poly- and perfluorinated compounds in the arctic environment. *Sci Total Environ* **408,** 2936-65.

BYTINGSVIK J., LIE, E., AARS, J., DEROCHER, A. E., WIIG, O. & JENSSEN, B. M. (2012). PCBs and OH-PCBs in polar bear mother-cub pairs: a comparative study based on plasma levels in 1998 and 2008. *Science of the Total Environment* **417-418,** 117-28.

CAIRNS T. & SIEGMUND, E. G. (1981). PCBs: regulatory history and analytical problems. *Analytical Chemistry* **53,** 1183A-1193A.

CATTET M. R. L., CAULKETT, N. A., OBBARD, M. E. & STENHOUSE, G. B. (2002). A body condition index for ursids. *Canadian Journal of Zoology* **80,** 1156-1161.

CHAPMAN P. M. (2002). Integrating toxicology and ecology: putting the ‘‘eco’’ into ecotoxicology. *Marine Pollution Bulletin* **44,** 7-15.

CLAUSEN J., BRAESTRU, L. & BERG, O. (1974). Content of polychlorinated hydrocarbons in Arctic mammals. *Bull. Environ. Contam. Toxicol.* **12,** 529-534.

CLOTFELTER E. D., BELL, A. M. & LEVERING, K. R. (2004). The role of animal behaviour in the study of endocrine-disrupting chemicals. *Animal Behaviour* **68,** 665-676.

COLBORN T., SAAL, F. S. V. & SOTO, A. M. (1993). Developmental effects of endocrine-disrupting chemicals in wildlife and humans. *Environmental Health Perspectives* **101,** 378-384.

CRAWLEY M. J. (2007). *The R book*. John Wiley & Sons Ltd, Chichester, West Sussex, England.

DE GROOT P. V., WONG, P. B. Y., HARRIS, C., DYCK, M. G., KAMOOKAK, L., PAGES, M., MICHAUX, J. & BOAG, P. T. (2013). Toward a non-invasive Inuit polar bear survey: Genetic data from polar bear hair snags. *Wildl. Soc. Bull.* **37,** 394-401.

DEROCHER A. E., AARS, J., AMSTRUP, S. C., CUTTING, A., LUNN, N. J., MOLNÁR, P. K., OBBARD, M. E., STIRLING, I., THIEMANN, G. W., VONGRAVEN, D., WIIG, Ø. & YORK, G. (2013). Rapid ecosystem change and polar bear conservation. *Conservation Letters* **6,** 368-375.

DEROCHER A. E., ANDERSEN, M. & WIIG, Ø. (2005). Sexual dimorphism of polar bears. *Journal of Mammalogy* **86,** 895-901.

DEROCHER A. E., LUNN, N. J. & STIRLING, I. (2004). Polar bears in a warming climate. *Integrative and Comparative Biology* **44,** 163-176.

DEROCHER A. E., STIRLING, I. & CALVERT, W. (1997). Male-biased harvesting of polar bears in Western Hudson Bay. *Journal of Wildlife Management* **61,** 1075-1082.

DEROCHER A. E., WOLKERS, H., COLBORN, T., SCHLABACH, M., LARSEN, T. S. & WIIG, Ø. (2003). Contaminants in Svalbard polar bear samples archived since 1967 and possible population level effects. *Science of the Total Environment* **301,** 163-174.

DIAMANTI-KANDARAKIS E., BOURGUIGNON, J.-P., GIUDICE, L. C., HAUSER, R., PRINS, G. S., SOTO, A. M., ZOELLER, R. T. & GORE, A. C. (2009). Endocrine-disrupting chemicals: An Endocrine Society scientific statement. *Endocrine Reviews* **30,** 293-342.

DIETZ R., GUSTAVSON, K., SONNE, C., DESFORGES, J. P., RIGET, F. F., PAVLOVA, V., MCKINNEY, M. A. & LETCHER, R. J. (2015). Physiologically-based pharmacokinetic modelling of immune, reproductive and carcinogenic effects from contaminant exposure in polar bears (*Ursus maritimus*) across the Arctic. *Environmental Research* **140,** 45-55.

DIETZ R., RIGET, F. & BORN, E. W. (2000). Geographical differences of zinc, cadmium, mercury and selenium in polar bears (*Ursus maritimus*) from Greenland. *Science of the Total Environment* **245,** 25-47.

DIETZ R., RIGET, F. F., SONNE, C., BORN, E. W., BECHSHOFT, T., MCKINNEY, M. A., DRIMMIE, R. J., MUIR, D. C. G. & LETCHER, R. J. (2013a). Three decades (1983-2010) of contaminant trends in East Greenland polar bears (Ursus maritimus). Part 2: Brominated flame retardants. *Environment International* **59,** 494-500.

DIETZ R., RIGET, F. F., SONNE, C., LETCHER, R., BORN, E. W. & MUIR, D. C. (2004). Seasonal and temporal trends in polychlorinated biphenyls and organochlorine pesticides in East Greenland polar bears (*Ursus maritimus*), 1990-2001. *Science of the Total Environment* **331,** 107-24.

DIETZ R., RIGET, F. F., SONNE, C., LETCHER, R. J., BACKUS, S., BORN, E. W., KIRKEGAARD, M. & MUIR, D. C. (2007). Age and seasonal variability of polybrominated diphenyl ethers in free-ranging East Greenland polar bears (*Ursus maritimus*). *Environ Pollut* **146,** 166-73.

DIETZ R., SONNE, C., BASU, N., BRAUNE, B., O'HARA, T., LETCHER, R. J., SCHEUHAMMER, T., ANDERSEN, M., ANDREASEN, C., ANDRIASHEK, D., ASMUND, G., AUBAIL, A., BAAGOE, H.,

BORN, E. W., CHAN, H. M., DEROCHER, A. E., GRANDJEAN, P., KNOTT, K., KIRKEGAARD, M., KREY, A., LUNN, N., MESSIER, F., OBBARD, M., OLSEN, M. T., OSTERTAG, S., PEACOCK, E., RENZONI, A., RIGET, F. F., SKAARE, J. U., STERN, G., STIRLING, I., TAYLOR, M., WIIG, O., WILSON, S. & AARS, J. (2013b). What are the toxicological effects of mercury in Arctic biota? *Science of the Total Environment* **443,** 775-90.

DOMINGO J. L. (1994). Metal-induced developmental toxicity in mammals: A review. *Journal of Toxicology and Environmental Health* **42,** 123-141.

EATON R. D. P. & FARANT, J. P. (1982). The polar bears as a biological indicator of the environmental mercury burden. *Arctic* **35,** 422-425.

FOLLAND W. R., NEWSTED, J. L., FITZGERALD, S. D., FUCHSMAN, P. C., BRADLEY, P. W., KERN, J., KANNAN, K., REMINGTON, R. E. & ZWIERNIK, M. J. (2016). Growth and reproductive effects from dietary exposure to Aroclor 1268 in mink (*Neovison vison*), a surrogate model for marine mammals. *Environmental Toxicology and Chemistry* **35,** 604-618.

GABRIELSEN K. M., KROKSTAD, J. S., OBREGON, M.-J., VILLANGER, G. D., SONNE, C., DIETZ, R. & JENSSEN, B. M. (2015). Thyroid hormones and deiodinase activities in plasma and tissues from East Greenland polar bears (*Ursus maritimus*) during winter season. *Polar Biology*.

GEBBINK W. A., BOSSI, R., RIGET, F. F., ROSING-ASVID, A., SONNE, C. & DIETZ, R. (2016). Observation of emerging per- and polyfluoroalkyl substances (PFASs) in Greenland marine mammals. *Chemosphere* **144,** 2384-2391.

GIESY J. P. & KANNAN, K. (2001). Global distribution of perfluorooctane sulfonate in wildlife. *Environmental Science and Technology* **35,** 1339-1342.

GRAHAM M. L., RENNER, V. E. & BLUKACZ-RICHARDS, E. A. (2013). Ecological risk assessment. In *Encyclopedia of Aquatic Ecotoxicology* (ed. J. F. Férard and C. Blaise). Springer, Dordrecht, Netherlands.

HAECKEL E. (1866). *Generelle morphologie der organismen*. Ceorg Riemer, Berlin.

HAIR J. F. J., BLACK, W. C., BABIN, B. J., ANDERSON, R. E. & TATHAM, R. L. (2006). *Multivariate data analysis*, 6 edition. Pearson Education, Upper Saddle RIver, New Jersey 07458, USA.

HAMLIN H. J. & GUILLETTE, L. J., JR. (2011). Embryos as targets of endocrine disrupting contaminants in wildlife. *Birth Defects Research Part C* **93,** 19-33.

HENRIKSEN E. O., WIIG, O., SKAARE, J. U., GABRIELSEN, G. W. & DEROCHER, A. E. (2001). Monitoring PCBs in polar bears: lessons learned from Svalbard. *Journal of Environmental Monitoring* **3,** 493-498.

HOBSON K. A., FISK, A., KARNOVSKY, N., HOLST, M., GAGNON, J. M. & FORTIER, M. (2002). A stable isotope (delta C-13, delta N-15) model for the North Water food web: implications for evaluating trophodynamics and the flow of energy and contaminants. *Deep-Sea Research Part Ii-Topical Studies in Oceanography* **49,** 5131-5150.

HOLDEN A. V. (1970). Monitoring organochlorine contamination of the marine environment by the analysis of residues in seals. . In *Marine pollution and sea life* (ed. M. Ruivo), pp. 266-272. Fishing News Books Ltd., England.

HOLMSTRUP M., BINDESBOL, A. M., OOSTINGH, G. J., DUSCHL, A., SCHEIL, V., KOHLER, H. R., LOUREIRO, S., SOARES, A. M., FERREIRA, A. L., KIENLE, C., GERHARDT, A., LASKOWSKI, R., KRAMARZ, P. E., BAYLEY, M., SVENDSEN, C. & SPURGEON, D. J. (2010). Interactions between effects of environmental chemicals and natural stressors: a review. *Science of the Total Environment* **408,** 3746-62.

HOOPER M. J., ANKLEY, G. T., CRISTOL, D. A., MARYOUNG, L. A., NOYES, P. D. & PINKERTON, K. E. (2013). Interactions between chemical and climate stressors: a role for mechanistic toxicology in assessing climate change risks. *Environmental Toxicology and Chemistry* **32,** 32-48.

HORTON T. W., BLUM, J. D., XIE, Z., HREN, M. & CHAMBERLAIN, C. P. (2009). Stable isotope food-web analysis and mercury biomagnification in polar bears (*Ursus maritimus*). *Polar Research* **28,** 443-454.

HUNG H., KATSOYIANNIS, A. A. & GUARDANS, R. (2016). Ten years of global monitoring under the Stockholm Convention on Persistent Organic Pollutants (POPs): Trends, sources and transport modelling. *Environmental Pollutution* **217,** 1-3.

IUCN PBSG. vol. 2016, pp. Polar bear population map.

IUCN PBSG. (2010). Polar Bears: Proceedings of the 15th Working Meeting of the IUCN/SSC Polar Bear Specialist Group, Copenhagen, Denmark, 29 June–3 July 2009 (ed. M. E. Obbard, G. W. Thiemann, E. Peacock and T. D. DeBruyn), pp. vii + 235 pp. IUCN, Gland, Switzerland and Cambridge, UK.

IVERSEN M., AARS, J., HAUG, T., ALSOS, I. G., LYDERSEN, C., BACHMANN, L. & KOVACS, K. M. (2013). The diet of polar bears (Ursus maritimus) from Svalbard, Norway, inferred from scat analysis. *Polar Biology* **36,** 561-571.

JENSEN S. K. (1966). Report of a new chemical hazard. *New Scientist* **36,** 612.

JENSSEN B. M., VILLANGER, G. D., GABRIELSEN, K. M., BYTINGSVIK, J., BECHSHØFT, T., CIESIELSKI, T. M., SONNE, C. & DIETZ, R. (2015). Anthropogenic flank attack on polar bears: interacting conseqiences of climate warming and pollutant exposure. *Frontiers in Ecology and the Evolution* **3**.

JOHNSON D. H. (1980). The comparison of usage and availability measurements for evaluating resource preference. *Ecology* **61,** 65-71.

KEITH L. H. (1976). Recent advances in the identification and analysis of organic pollutants in water. *Life Sciences* **19,** 1631-1635.

KERR R. A. (1979). Global pollution - is the Arctic haze actually industrial smog? *Science* **205,** 290-293.

KIRKEGAARD M., SONNE, C., JAKOBSEN, J., JENSSEN, B. M., LETCHER, R. J. & DIETZ, R. (2010). Organohalogens in a whale-blubber-supplemented diet affects hepatic retinol and renal tocopherol concentrations in greenland sled dogs (*Canis familiaris*). *Journal of Toxicology and Environmental Health, Part A* **73,** 773-86.

KNOTT K. K., BOYD, D., YLITALO, G. M. & O'HARA, T. M. (2012). Lactational transfer of mercury and polychlorinated biphenyls in polar bears. *Chemosphere* **88,** 395-402.

LETCHER R. J., BUSTNES, J. O., DIETZ, R., JENSSEN, B. M., JORGENSEN, E. H., SONNE, C., VERREAULT, J., VIJAYAN, M. M. & GABRIELSEN, G. W. (2010). Exposure and effects assessment of persistent organohalogen contaminants in arctic wildlife and fish. *Science of the Total Environment* **408,** 2995-3043.

LETCHER R. J. & NORSTROM, R. J. (1995). An integrated analytical method for determination of polychlorinated aryl methyl sulfone metabolites and polychlorinated hydrocarbon contaminants in biological matrices. *Analytical Chemistry* **67,** 4155-4163.

LIE E., DEROCHER, A. E., WIIG, O. & SKAARE, J. U. (2000). Polychlorinated biphenyls in mother/offspring pairs of polar bears (*Ursus maritimus*) at Svalbard. *Organohalogen Compounds* **49,** 457-460.

LIE E., LARSEN, H. J. S., LARSEN, S., JOHANSEN, G. M., DEROCHER, A. E., LUNN, N. J., NORSTROM, R. J., WIIG, O. & SKAARE, J. U. (2005). Does high organochlorine (OC) exposure impair the resistance to infection in polar bears (*Ursus maritimus*)? Part II: Possible effect of OCs on mitogen- and antigen-induced lymphocyte proliferation. *Journal of Toxicology and Environmental Health, Part A* **68,** 457-484.

LIE E., LARSEN, H. J. S., LARSEN, S., JOHNSEN, G. M., DEROCHER, A. E., LUNN, N. J., NORSTROM, R. J., WIIG, O. & SKAARE, J. U. (2004). Does high organochlorine (OC) exposure impair the resistance to infection in polar bears (*Ursus maritimus*)? Part I: Effect of OCs on the humoral immunity. *Journal of Toxicology and Environmental Health, Part A* **67,** 555-582.

MA J., HUNG, H., TIAN, C. & KALLENBORN, R. (2011). Revolatilization of persistent organic pollutants in the Arctic induced by climate change. *Nature Climate Change* **1,** 255-260.

MACBETH B. J., CATTET, M. R. L., OBBARD, M. E., MIDDEL, K. & JANZ, D. M. (2012). Evaluation of hair cortisol concentration as a biomarker of long-term stress in free-ranging polar bears. *Wildl. Soc. Bull.* **36,** 747-758.

MAEKAWA F., TSUKAHARA, S., KAWASHIMA, T., NOHARA, K. & OHKI-HAMAZAKI, H. (2014). The mechanisms underlying sexual differentiation of behavior and physiology in mammals and birds: relative contributions of sex steroids and sex chromosomes. *Frontiers in Neuroscience* **8**.

MARTIN P. A., MAYNE, G. J., BURSIAN, S., PALACE, V. & KANNAN, K. (2006). Changes in thyroid and vitamin A status in mink fed polyhalogenated-aromatic-hydrocarbon-contaminated carp from the Saginaw River, Michigan, USA. *Environmental Research* **101,** 53-67.

MAYOR S. J., SCHNEIDER, D. C., SCHAEFER, J. A. & MAHONEY, S. P. (2009). Habitat selection at multiple scales. *Ecoscience* **16,** 238-247.

MCKINNEY M. A., ATWOOD, T., DIETZ, R., SONNE, C., RIGET, F., BORN, E. & PEACOCK, E. (2014). Validation of adipose lipid content as a body condition index for polar bears. *Ecology and Evolution* **4,** 516-527.

MCKINNEY M. A., IVERSON, S. J., FISK, A. T., SONNE, C., RIGET, F. F., LETCHER, R. J., ARTS, M. T., BORN, E. W., ROSING-ASVID, A. & DIETZ, R. (2013). Global change effects on the long-term feeding ecology and contaminant exposures of East Greenland polar bears. *Global Change Biology* **19,** 2360-2372.

MCKINNEY M. A., LETCHER, R. J., AARS, J., BORN, E. W., BRANIGAN, M., DIETZ, R., EVANS, T. J., GABRIELSEN, G. W., PEACOCK, E. & SONNE, C. (2011). Flame retardants and legacy contaminants in polar bears from Alaska, Canada, East Greenland and Svalbard, 2005-2008. *Environment International* **37,** 365-74.

MCKINNEY M. A., PEDRO, S., DIETZ, R., SONNE, C., FISK, A. T., ROY, D., JENSSEN, B. M. & LETCHER, R. J. (2015). A review of ecological impacts of global climate change on persistent organic pollutant and mercury pathways and exposures in arctic marine ecosystems. *Current Zoology* **61,** 617-628.

MCKINNEY M. A., STIRLING, I., LUNN, N. J., PEACOCK, E. & LETCHER, R. J. (2010). The role of diet on long-term concentration and pattern trends of brominated and chlorinated contaminants in western Hudson Bay polar bears, 1991-2007. *Science of the Total Environment* **408,** 6210-22.

MINDELI L. E. & MARKUSOVA, V. A. (2015). Bibliometric studies of scientific collaboration: International trends. *Automatic Documentation and Mathematical Linguistics* **49,** 59-64.

MUIR D. C. G. & HOWARD, P. H. (2006). Are there other persistent organic pollutants? A challenge for environmental chemists. *Environmental Science & Technology* **40,** 7157-7166.

NAALAKKERSUISUT. (2005). Executive Order no. 21 of 22 September 2005 on the Protection and Hunting of Polar Bears, http://lovgivning.gl/lov?rid={699D9C77-D0A7-42D9-B90F-F9F04FA99E3D}.

NEWMAN M. C. (2010). *Fundamentals of ecotoxicology*. CRC Press, Taylor & Francis Group, Boca Raton, Florida.

NEWMAN M. E. (2001). The structure of scientific collaboration networks. *PNAS* **98,** 404-409.

NORSTROM R. J., BELIKOV, S. E., BORN, E. W., GARNER, G. W., MALONE, B., OLPINSKI, S., RAMSAY, M. A., SCHLIEBE, S., STIRLING, I., STISHOV, M. S., TAYLOR, M. K. & WIIG, Ø. (1998). Chlorinated hydrocarbon contaminants in polar bears from Eastern Russia, North America, Greenland, and Svalbard: biomonitoring of Arctic pollution. *Archives of Environmental Contamination and Toxicology* **35,** 354-367.

NORSTROM R. J., SCHWEINSBERG, R. E. & COLLINS, B. T. (1986). Heavy metals and essential elements in livers of the polar bear (*Ursus maritimus*) in the Canadian Arctic. *Science of the Total Environment* **48,** 195-212.

NUIJTEN R. J., HENDRIKS, A. J., JENSSEN, B. M. & SCHIPPER, A. M. (2016). Circumpolar contaminant concentrations in polar bears (Ursus maritimus) and potential population-level effects. *Environ Res* **151,** 50-57.

OLSEN G. H., MAURITZEN, M., DEROCHER, A. E., SORMO, E. G., SKAARE, J. U., WIIG, O. & JENSSEN, B. M. (2003). Space-use strategy is an important determinant of PCB concentrations in female polar bears in the Barents Sea. *Environmental Science and Technology* **37,** 4919-4924.

OSKAM I. C., ROPSTAD, E., DAHL, E., LIE, E., DEROCHER, A. E., WIIG, O., LARSEN, S., WIGER, R. & SKAARE, J. U. (2003). Organochlorines affect the major androgenic hormone, testosterone, in male polar bears (*Ursus maritimus*) at Svalbard. *Journal of Toxicology and Environmental Health, Part A* **66,** 2119-2139.

OSKAM I. C., ROPSTAD, E., LIE, E., DEROCHER, A. E., WIIG, O., DAHL, E., LARSEN, S. & SKAARE, J. U. (2004). Organochlorines affect the steroid hormone cortisol in free-ranging polar bears (*Ursus maritimus*) at Svalbard, Norway. *Journal of Toxicology and Environmental Health, Part A* **67,** 959-977.

OSTERTAG S. K., TAGUE, B. A., HUMPHRIES, M. M., TITTLEMIER, S. A. & CHAN, H. M. (2009). Estimated dietary exposure to fluorinated compounds from traditional foods among Inuit in Nunavut, Canada. *Chemosphere* **75,** 1165-1172.

PATISAUL H. B. & ADEWALE, H. B. (2009). Long-term effects of environmental endocrine disruptors on reproductive physiology and behavior. *Frontiers in Behavioral Neuroscience* **3,** 18.

PATYK K. A., DUNCAN, C., NOL, P., SONNE, C., LAIDRE, K., OBBARD, M., WIIG, Ø., AARS, J., REGEHR, E., GUSTAFSON, L. L. & ATWOOD, T. (2015). Establishing a definition of polar bear (*Ursus maritimus*) health: A guide to research and management activities. *Science of the Total Environment* **514,** 371-378.

PAVLOVA V., GRIMM, V., DIETZ, R., SONNE, C., VORKAMP, K., RIGET, F. F., LETCHER, R. J., GUSTAVSON, K., DESFORGES, J. P. & NABE-NIELSEN, J. (2016). Modeling population-level consequences of polychlorinated biphenyl exposure in East Greenland polar bears. *Archives of Environmental Contamination and Toxicology* **70,** 143-54.

PEDERSEN K. E., BASU, N., LETCHER, R., GREAVES, A. K., SONNE, C., DIETZ, R. & STYRISHAVE, B. (2015). Brain region-specific perfluoroalkylated sulfonate (PFSA) and carboxylic acid (PFCA) accumulation and neurochemical biomarker responses in East Greenland polar Bears (*Ursus maritimus*). *Environmental Research* **138,** 22-31.

PILSNER J. R., LAZARUS, A. L., NAM, D. H., LETCHER, R. J., SONNE, C., DIETZ, R. & BASU, N. (2010). Mercury-associated DNA hypomethylation in polar bear brains via the LUminometric Methylation Assay: a sensitive method to study epigenetics in wildlife. *Molecular Ecology* **19,** 307-14.

POLISCHUK S. C., NORSTROM, R. J. & RAMSAY, M. A. (2002). Body burdens and tissue concentrations of organochlorines in polar bears (*Ursus maritimus*) vary during seasonal fasts. *Environmental Pollution* **118,** 29-39.

RATCLIFF D. A. (1967). Decrease in eggshell weight in certain birds of prey. *Nature* **215,** 208-210.

RATTNER B. A. (2009). History of wildlife toxicology. *Ecotoxicology* **18,** 773-83.

RIGET F., BIGNERT, A., BRAUNE, B., STOW, J. & WILSON, S. (2010). Temporal trends of legacy POPs in Arctic biota, an update. *Science of the Total Environment* **408,** 2874-84.

RIGET F., BRAUNE, B., BIGNERT, A., WILSON, S., AARS, J., BORN, E., DAM, M., DIETZ, R., EVANS, M., EVANS, T., GAMBERG, M., GANTNER, N., GREEN, N., GUNNLAUGSDOTTIR, H., KANNAN, K., LETCHER, R., MUIR, D., ROACH, P., SONNE, C., STERN, G. & WIIG, O. (2011). Temporal trends of Hg in Arctic biota, an update. *Science of the Total Environment* **409,** 3520-6.

ROBBINS C. T., BEN-DAVID, M., FORTIN, J. K. & NELSON, O. L. (2012). Maternal condition determines birth date and growth of newborn bear cubs. *Journal of Mammalogy* **93,** 540-546.

ROSING-ASVID A., BORN, E. W. & KINGSLEY, M. C. S. (2002). Age at sexual maturity of males and timing of the mating season of polar bears (*Ursus maritimus*) in Greenland. *Polar Biology* **25,** 878-883.

ROUTTI H., LETCHER, R. J., BORN, E. W., BRANIGAN, M., DIETZ, R., EVANS, T. J., FISK, A. T., PEACOCK, E. & SONNE, C. (2011). Spatial and temporal trends of selected trace elements in liver tissue from polar bears (*Ursus maritimus*) from Alaska, Canada and Greenland. *Journal of Environmental Monitoring* **13,** 2260-2267.

ROUTTI H., LETCHER, R. J., BORN, E. W., BRANIGAN, M., DIETZ, R., EVANS, T. J., MCKINNEY, M. A., PEACOCK, E. & SONNE, C. (2012). Influence of carbon and lipid sources on variation of mercury and other trace elements in polar bears (*Ursus maritimus*). *Environmental Toxicology and Chemistry* **31,** 2739-47.

SACCO J. C. J., M.O. (2005). Sulfonation of environmental chemicals and their metabolites in the polar bear (*Ursus maritimus*). *Drug Metabolism and Disposition* **33,** 1341-1348.

SERGEANT D. E. & ARMSTRONG, F. A. (1973). Mercury in seals from eastern Canada. *Journal of the Fisheries Research Board of Canada* **30,** 843-846.

SIMON E., BYTINGSVIK, J., JONKER, W., LEONARDS, P. E., DE BOER, J., JENSSEN, B. M., LIE, E., AARS, J., HAMERS, T. & LAMOREE, M. H. (2011). Blood plasma sample preparation method for the assessment of thyroid hormone-disrupting potency in effect-directed analysis. *Environmental Science and Technology* **45,** 7936-44.

SONNE C. (2010). Health effects from long-range transported contaminants in Arctic top predators: An integrated review based on studies of polar bears and relevant model species. *Environment International* **36,** 461-491.

SONNE C., BECHSHOFT, T., RIGET, F. F., BAAGOE, H. J., HEDAYAT, A., ANDERSEN, M., BECH-JENSEN, J. E., HYLDSTRUP, L., LETCHER, R. J. & DIETZ, R. (2013a). Size and density of East Greenland polar bear (*Ursus maritimus*) skulls: Valuable bio-indicators of environmental changes? *Ecological Indicators* **34,** 290-295.

SONNE C., DIETZ, R., BORN, E. W., RIGET, F. F., KIRKEGAARD, M., HYLDSTRUP, L., LETCHER, R. J. & MUIR, D. C. G. (2004). Is bone mineral composition disrupted by organochlorines in East Greenland polar bears (*Ursus maritimus*)? *Environmental Health Perspectives* **112,** 1711-1716.

SONNE C., DIETZ, R., BORN, E. W., RIGET, F. F., LEIFSSON, P. S., BECHSHOFT, T. O. & KIRKEGAARD, M. (2007a). Spatial and temporal variation in size of polar bear (*Ursus maritimus*) sexual organs and its use in pollution and climate change studies. *Science of the Total Environment* **387,** 237-246.

SONNE C., DIETZ, R. & LETCHER, R. J. (2013b). Chemical cocktail party in East Greenland: A first time evaluation of human organohalogen exposure from consumption of ringed seal and polar bear tissues and possible health implications. *Toxicological and Environmental Chemistry* **95,** 853-859.

SONNE C., DYCK, M., RIGET, F. F., BECK JENSEN, J. E., HYLDSTRUP, L., LETCHER, R. J., GUSTAVSON, K., GILBERT, M. T. & DIETZ, R. (2015). Penile density and globally used chemicals in Canadian and Greenland polar bears. *Environmental Research* **137,** 287-91.

SONNE C., GUSTAVSON, K., RIGET, F. F., DIETZ, R., BIRKVED, M., LETCHER, R. J., BOSSI, R., VORKAMP, K., BORN, E. W. & PETERSEN, G. (2009a). Reproductive performance in East Greenland polar bears (*Ursus maritimus*) may be affected by organohalogen contaminants as shown by physiologically-based pharmacokinetic (PBPK) modelling. *Chemosphere* **77,** 1558-68.

SONNE C., LETCHER, R. J., BECHSHØFT, T. Ø., RIGÉT, F. F., MUIR, D. C. G., LEIFSSON, P. S., BORN, E. W., HYLDSTRUP, L., BASU, N., KIRKEGAARD, M. & DIETZ, R. (2012). Two decades of biomonitoring polar bear health in Greenland: a review. *Acta Veterinaria Scandinavica* **54,** S15.

SONNE C., RIGET, F. F., DIETZ, R., WIIG, O., KIRKEGAARD, M. & BORN, E. W. (2007b). Skull pathology in East Greenland and Svalbard polar bears (*Ursus maritimus*) during 1892 to 2002 in relation to organochlorine pollution. *Science of the Total Environment* **372,** 554-561.

SONNE C., WOLKERS, H., LEIFSSON, P. S., IBURG, T., JENSSEN, B. M., FUGLEI, E., AHLSTROM, O., DIETZ, R., KIRKEGAARD, M., MUIR, D. C. & JORGENSEN, E. H. (2009b). Chronic dietary exposure to environmental organochlorine contaminants induces thyroid gland lesions in Arctic foxes (*Vulpes lagopus*). *Environmental Research* **109,** 702-11.

ST LOUIS V. L., DEROCHER, A. E., STIRLING, I., GRAYDON, J. A., LEE, C., JOCKSCH, E., RICHARDSON, E., GHORPADE, S., KWAN, A. K., KIRK, J. L., LEHNHERR, I. & SWANSON, H. K. (2011). Differences in mercury bioaccumulation between polar bears (*Ursus maritimus*) from the Canadian high- and sub-Arctic. *Environmental Science & Technology* **45,** 5922-8.

STIRLING I. (2002). Polar bears and seals in the eastern Beaufort Sea and Amundsen Gulf: A synthesis of population trends and ecological relationships over three decades. *Arctic* **55,** 59-76.

STIRLING I. & DEROCHER, A. E. (2012). Effects of climate warming on polar bears: a review of the evidence. *Global Change Biology* **18,** 2694-706.

STIRLING I., THIEMANN, G. W. & RICHARDSON, E. (2008). Quantitative support for a subjective fatness index for immobilized polar bears. *Journal of Wildlife Management* **72,** 568-574.

SUBRAMANYAM K. (1983). Bibliometric studies of research collaboration: A review. *Journal of Information Science* **6,** 33-38.

TAYLOR M. K., LAAKE, J., MCLOUGHLIN, P. D., CLUFF, H. D. & MESSIER, F. (2006). Demographic parameters and harvest-explicit population viability analysis for polar bears in M'Clintock Channel, Nunavut, Canada. *Journal of Wildlife Management* **70,** 1667-1673.

THIEMANN G. W., IVERSON, S. J. & STIRLING, I. (2008). Polar bear diets and Arctic marine food webs: insights from fatty acid analysis. *Ecological Monographs* **78,** 591-613.

THOMPSON REUTERS. (2016). Web of Science, New York, USA.

TRUMBLE S. J., ROBINSON, E. M., NOREN, S. R., USENKO, S., DAVIS, J. & KANATOUS, S. B. (2012). Assessment of legacy and emerging persistent organic pollutants in Weddell seal tissue (*Leptonychotes weddellii*) near McMurdo Sound, Antarctica. *Science of the Total Environment* **439,** 275-83.

UNEP. (2001). The Stockholm Convention.

VAN GINNEKEN V., PALSTRA, A., LEONARDS, P., NIEVEEN, M., VAN DEN BERG, H., FLIK, G., SPANINGS, T., NIEMANTSVERDRIET, P., VAN DEN THILLART, G. & MURK, A. (2009). PCBs and the energy cost of migration in the European eel (*Anguilla anguilla* L.). *Aquatic Toxicology* **92,** 213-220.

VERREAULT J., BECH, C., LETCHER, R. J., ROPSTAD, E., DAHL, E. & GABRIELSEN, G. W. (2007). Organohalogen contamination in breeding glaucous gulls from the Norwegian Arctic: Associations with basal metabolism and circulating thyroid hormones. *Environmental Pollution* **145,** 138-145.

VERREAULT J., NORSTROM, R. J., RAMSAY, M. A., MULVIHILL, M. & LETCHER, R. J. (2006). Composition of chlorinated hydrocarbon contaminants among major adipose tissue depots of polar bears (*Ursus maritimus*) from the Canadian high Arctic. *Science of the Total Environment* **370,** 580-7.

VILLANGER G. D., JENSSEN, B. M., FJELDBERG, R. R., LETCHER, R. J., MUIR, D. C. G., KIRKEGAARD, M., SONNE, C. & DIETZ, R. (2011). Exposure to mixtures of organohalogen contaminants and associative interactions with thyroid hormones in East Greenland polar bears (*Ursus maritimus*). *Environment International* **37,** 694-708.

VOLTURA M. B. & FRENCH, J. B. J. (2000). Effects of dietary polychlorinated biphenyl exposure on energetics of white-footed mouse, *Peromyscus leucopus*. *Environmental Toxicology and Chemistry* **19,** 2757-2761.

VONGRAVEN D., AARS, J., AMSTRUP, S. C., ATKINSON, S. N., BELIKOV, S. E., BORN, E. W., DEBRUYN, T. D., DEROCHER, A. E., DURNER, G. M., GILL, M., LUNN, N., OBBARD, M. E., OMELAK, J., OVSYANIKOV, N., PEACOCK, E., RICHARDSON, E., SAHANATIEN, V., STIRLING, I. & WIIG, Ø. (2012). A circumpolar monitoring framework for polar bears. *Ursus Monographs* **5,** 1-66.

WANG W., EVANS, R. D., HICKIE, B. E., ROUVINEN-WATT, K. & EVANS, H. E. (2014). Methylmercury accumulation and elimination in mink (*Neovison vison*) hair and blood: results of a controlled feeding experiment using stable isotope tracers. *Environmental Toxicology and Chemistry* **33,** 2873-2880.

WARNER N. A., EVENSET, A., CHRISTENSEN, G., GABRIELSEN, G. W., BORGA, K. & LEKNES, H. (2010). Volatile siloxanes in the European Arctic: Assessment of sources and spatial distribution. *Environmental Science & Technology* **44,** 7705-7710.

WEISSER J. J., HANSEN, M., BJORKLUND, E., SONNE, C., DIETZ, R. & STYRISHAVE, B. (2016). A novel method for analysing key corticosteroids in polar bear (*Ursus maritimus*) hair using liquid chromatography tandem mass spectrometry. *Journal of Chromatography B* **1017-1018,** 45-51.

WIENER J. G. (2013). Mercury exposed: advances in environmental analysis and ecotoxicology of a highly toxic metal. *Environmental Toxicology and Chemistry* **32,** 2175-8.

ZIMMER K. E., GUTLEB, A. C., LYCHE, J. L., DAHL, E., OSKAM, I. C., KROGENAES, A., SKAARE, J. U. & ROPSTAD, E. (2009). Altered stress-induced cortisol levels in goats exposed to polychlorinated biphenyls (PCB 126 and PCB 153) during fetal and postnatal development. *Journal of Toxicology and Environmental Health, Part A* **72,** 164-72.

Tables

Table 1. Core ecological variables (biological and physical-chemical parameters) included in the present systematic review of polar bear ecotoxicology literature. The full list of all variables and their definitions can be found under Supporting information (Table S2).

Ecological variables included in the contaminant analysis in the 180 analyzed research papers	Number	Percent
Age		
- Specific age (months/years)	148	82
Class		
- Cub-of-the-year	24	13
- Yearling	36	20
- Subadult	102	57
- Adult	142	79
- Unknown	25	14
Behavior	0	0
Body condition (any metric)	46	26
Climate		
- Climate index	1	< 1
- Season	1	< 1
- Temperature	1	< 1
Diet		
- Fatty acid	6	3
- Stable isotopes	17	9
Genetics	2	1
Home range size (movement)	2	1
Reproductive history	21	12
Offspring		
- Litter size	4	2
- Sex	7	4
- Age	16	9
Sex		
- Male	130	72
- Female	134	74
- Unknown	43	24

Table 2. Authorship by country of the 207 papers included in the present systematic review of the status of polar bear ecotoxicology literature; 31reviews and 180 research papers (four publications were in both categories, see text for details).

	Review paper		Research paper	
Authorship	First author	Coauthor	First author	Coauthor
Canada	9	19	60	104
Denmark	10	9	43	70
Greenland	0	1	1	22
US	5	7	24	45
Norway	4	8	34	59
Russia	0	0	0	12
Other	3	7	18	31

Table 3. Biological (physiological and morphological) variables investigated in relation to contaminants in the research papers included in the present systematic review of polar bear ecotoxicology literature. The table is based on 66 papers, some of which analyzed multiple of the listed variables.

Physiological/morphological variable	Number	Percent
Enzymes	9	5
Hormones		
• Steroid	11	6
• Thyroid	10	6
Immune system	4	2
Morphometrics	7	4
Other	3	2
Parasites/zoonosis	0	0
Pathology	17	9
Protein levels	4	2
Receptor levels	5	3
Reproductive effects		
• Litter size	0	0
• Potential	4	2
Transport proteins	5	3
Vitamins	4	2

Table 4. Recommendation for which polar bear subpopulations to focus on in future ecotoxicology studies, based on their respective strengths with regards to available data.

		Barents Sea	Chukchi Sea	East Greenland	Northern and Southern Beaufort Sea	Western Hudson Bay
Data available on	life history (e.g., fatness, tooth wear)	X	X		X	X
	family groups	X	X		X	X
Samples available	maximally invasive (e.g., inner organs)			X		
	high number/consistent sampling efforts	X	X	X	X	X
	potential repeat captures and sampling of the same individual	X	X		X	X
Contaminant	high concentrations	X		X	X	
	previously investigated (i.e. potential for investigating temporal trends)	X		X	X	X

Figure legends

Fig. 1. Frequency of polar bear (*Ursus maritimus*) focused ecotoxicological papers (n=207) based on the year of publication and categorized by type (i.e. review or research) included in the present systematic review.

Fig. 2. Index of toxicology publications for a selection of marine and terrestrial mammal species relative to those published for polar bears. The index was created using the raw, unfiltered results from literature searches for each species in connection with the contaminant-related search terms outlined in the text. The dashed line represents the polar bear, here a value of 1 on the index scale.

Fig. 3a-d. Number of authors on the papers included in the present systematic review of the status of polar bear ecotoxicology literature: a) review papers, 1992-2016, b) research papers, 1970-2016, c) review papers, 2006-2015, d) research papers, 2006-2015.

Fig. 4a. Map indicating the 19 currently recognized polar bear subpopulations (map from IUCN PBSG). GB: Gulf of Boothia, KB: Kane Basin, LS: Lancaster Sound, MC: M'Clintock Channel, NB: Northern Beaufort Sea, NW: Norwegian Bay, SB: Southern Beaufort Sea, VM: Viscount Melville Sound, WH: Western Hudson Bay.

Fig. 4b. Number of times each of 19 polar bear subpopulations were incorporated in ecotoxicological research papers (n = 180).

Fig. 5a-b. Sample size (individual bears) in polar bear (*Ursus maritimus*) ecotoxicology research papers (n = 180), as included in the present systematic review, published a) over the investigated period as a whole (1970-2016) and b) over the past decade (2006-2015; see text for details).

Fig. 6. Percentage of published polar bear ecotoxicology research papers (n = 180) in relation to type of tissue(s) analyzed. As more than one tissue type may have been analyzed in a single paper, the combined percentages of all tissue types could exceed 100%.

Fig. 7. Percentage of published polar bear ecotoxicology research papers (n=180) in relation to year of sample collection. As more than one year bin may have been covered in a single paper, the combined percentages of all year bins could exceed 100%.

Fig. 8. Percentage of published polar bear ecotoxicology research papers (n=180) in relation to contaminant groups studied. As more than one contaminant group may have been analyzed in a single paper, the combined percentages of all contaminant groups could exceed 100%.

Fig. 9. Percentage of published polar bear ecotoxicology research papers (n = 180) in relation to contaminant-related issues studied. B: Biological (here: sex and/or age), C: Contaminant concentration(s), S: Spatial issues, T: Temporal issues, O: Other.

Figures

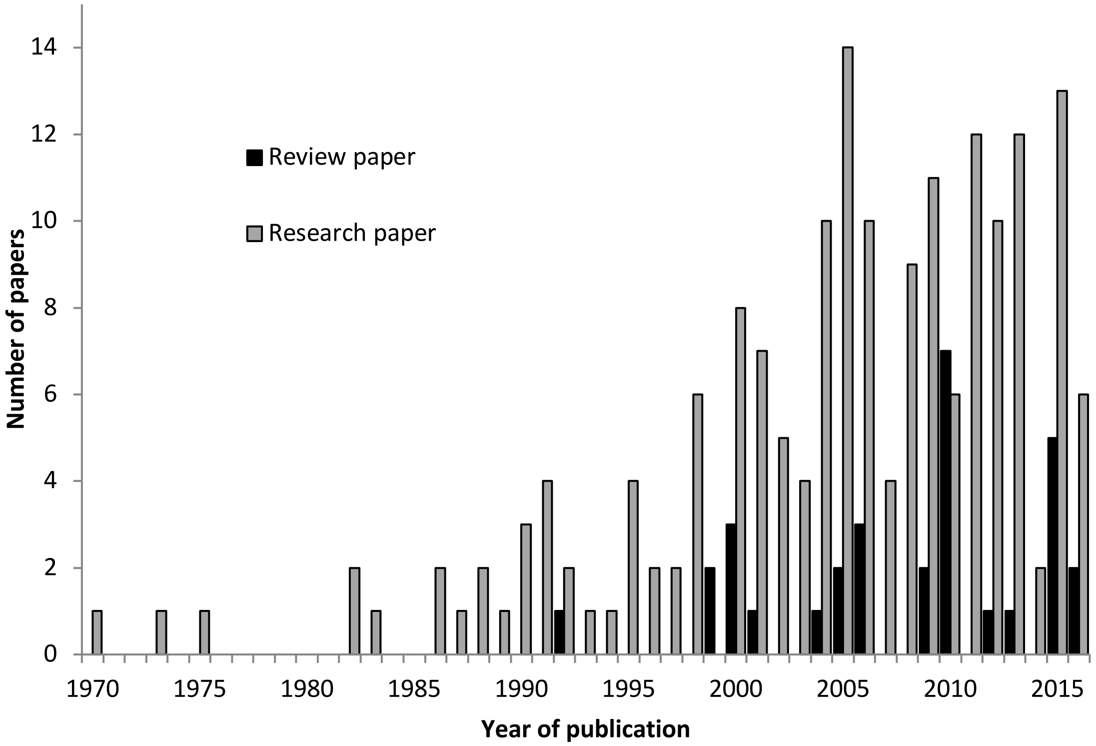
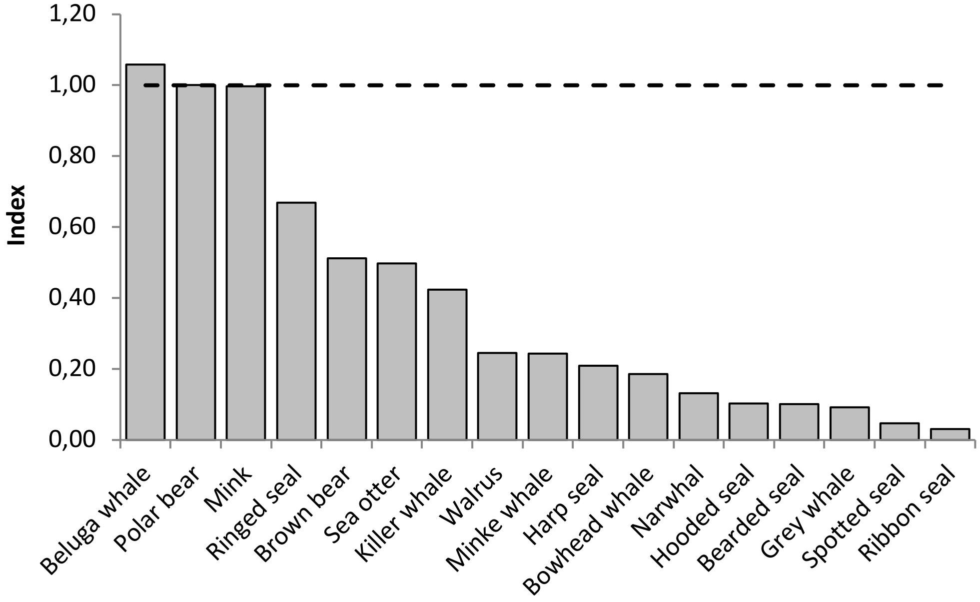


Fig. 1.



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0,60
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Index
Beluga whale
Polar bear
Mink
Ringed seal
Brown bear
Sea otter
Killer whale
Walrus
Minke whale
Harp seal
Bowhead whale
Narwhal
Hooded seal
Bearded seal
Grey whale
Spotted seal
Ribbon seal

Fig. 2.

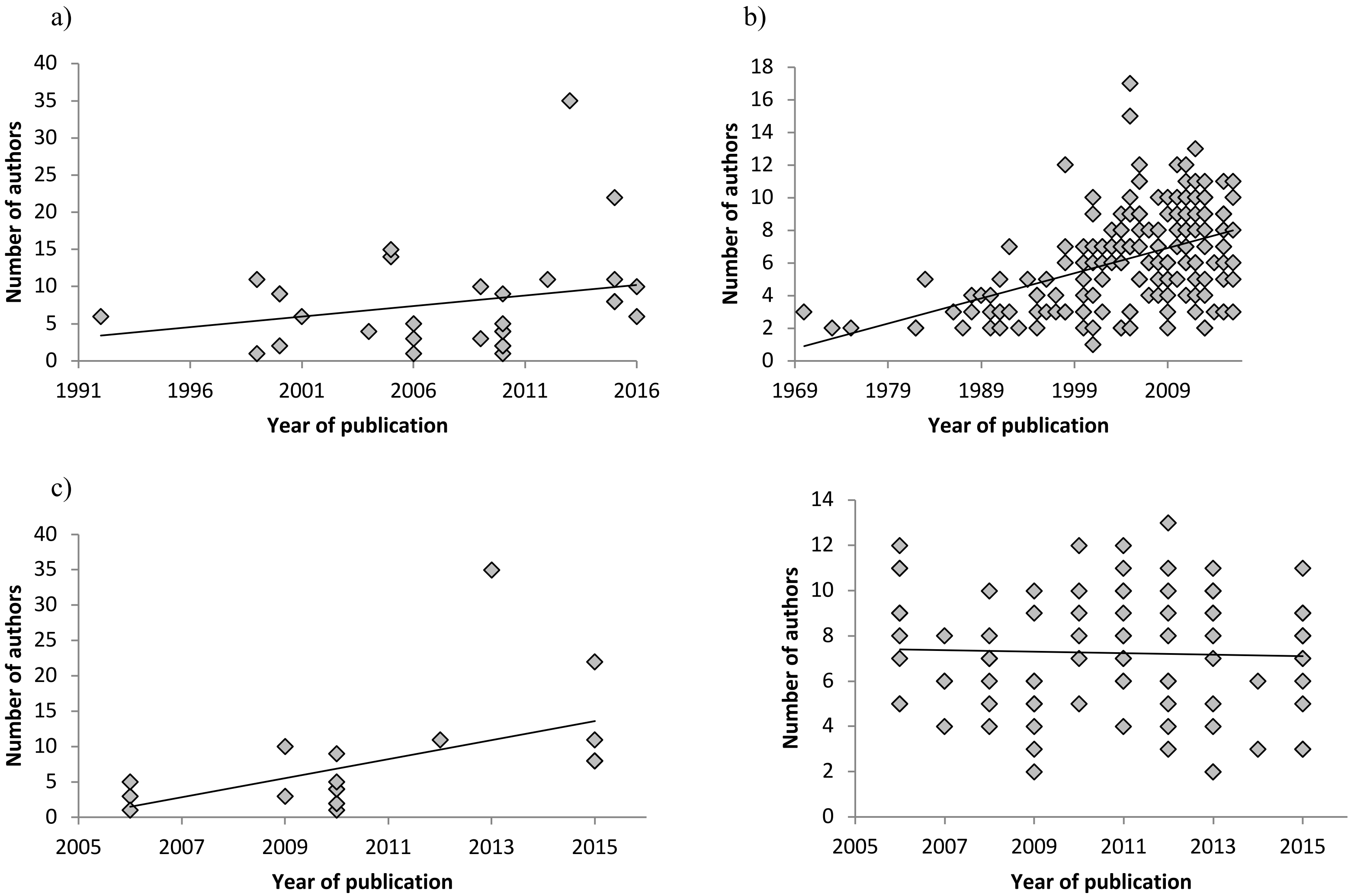

a)
Number of authors
40
35
30
25
20
15
10
5
0
1991
1996
2001
2006
2011
2016
Year of publication
b)
Number of authors
18
16
14
12
10
8
6
4
2
0
1969
1979
1989
1999
2009
Year of publication
c)
Number of authors
40
35
30
25
20
15
10
5
0
2005
2007
2009
2011
2013
2015
Year of publication
Number of authors
14
12
10
8
6
4
2
0
2005
2007
2009
2011
2013
2015
Year of publication

Fig. 3a-d.

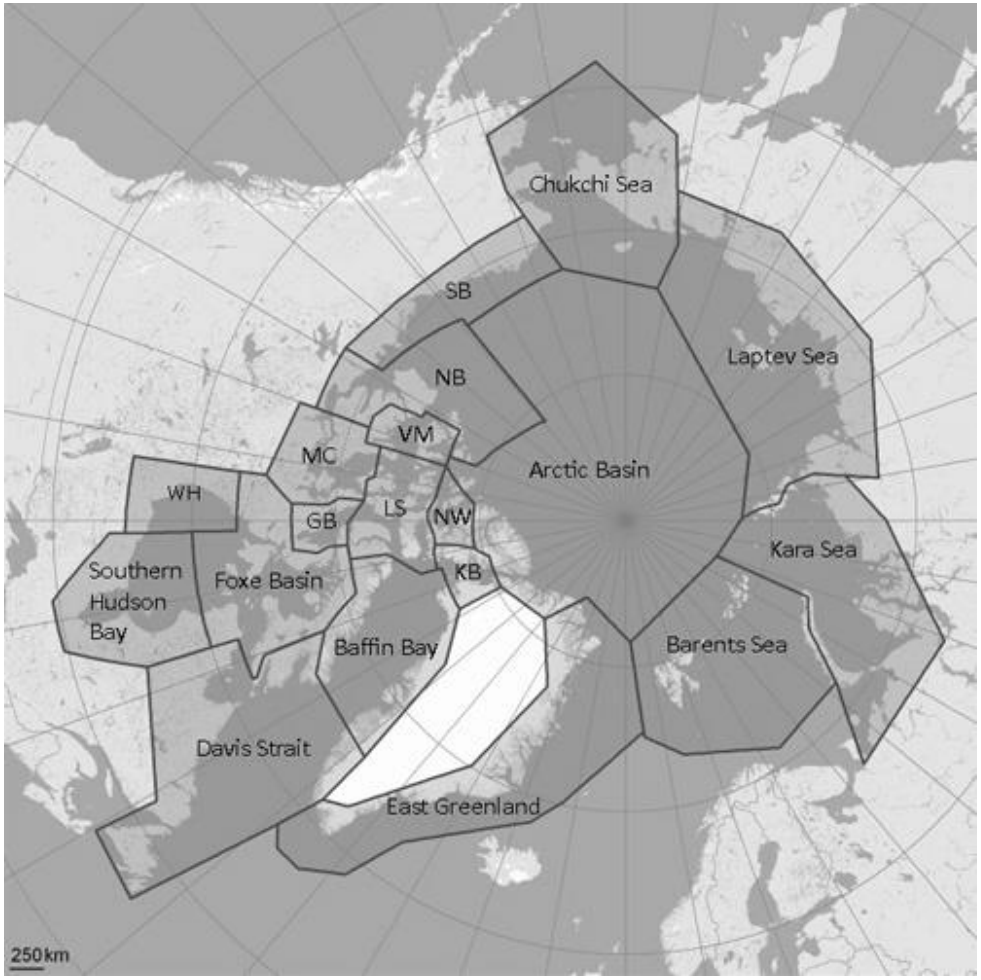
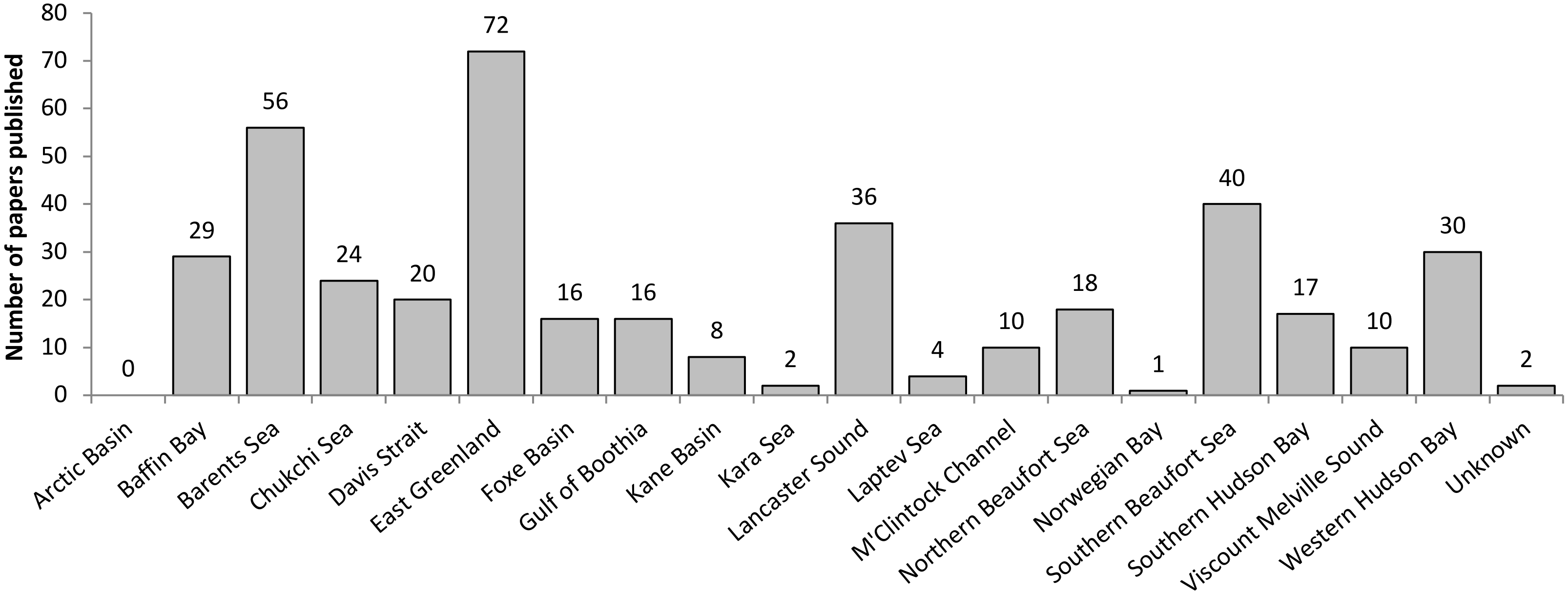

Chukchi Sea
SB
NB
Laptev Sea
VM
MC
Arctic Basin
WH
LS
NW
GB
Kara Sea
Southern Hudson Bay
Foxe Basin
KB
Baffin Bay
Barents Sea
Davis Strait
East Greenland
250 km

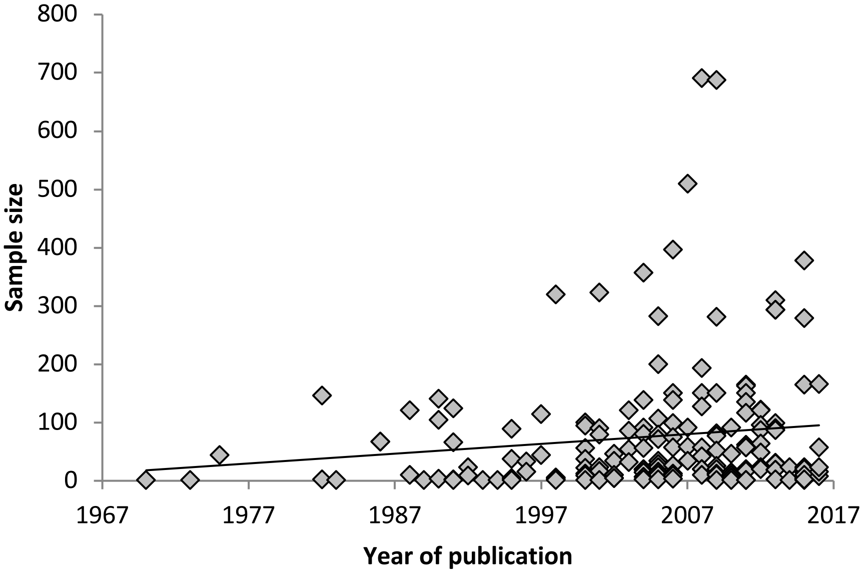
Fig. 4a.



Number of papers published
0
10
20
30
40
50
60
70
80
0
29
56
24
20
72
16
16
8
2
36
4
10
18
1
40
17
10
30
2
Arctic Basin
Baffin Bay
Barents Sea
Chukchi Sea
Davis Strait
East Greenland
Foxe Basin
Gulf of Boothia
Kane Basin
Kara Sea
Lancaster Sound
Laptev Sea
M'Clintock Channel
Northern Beaufort Sea
Norwegian Bay
Southern Beaufort Sea
Southern Hudson Bay
Viscount Melville Sound
Western Hudson Bay
Unknown

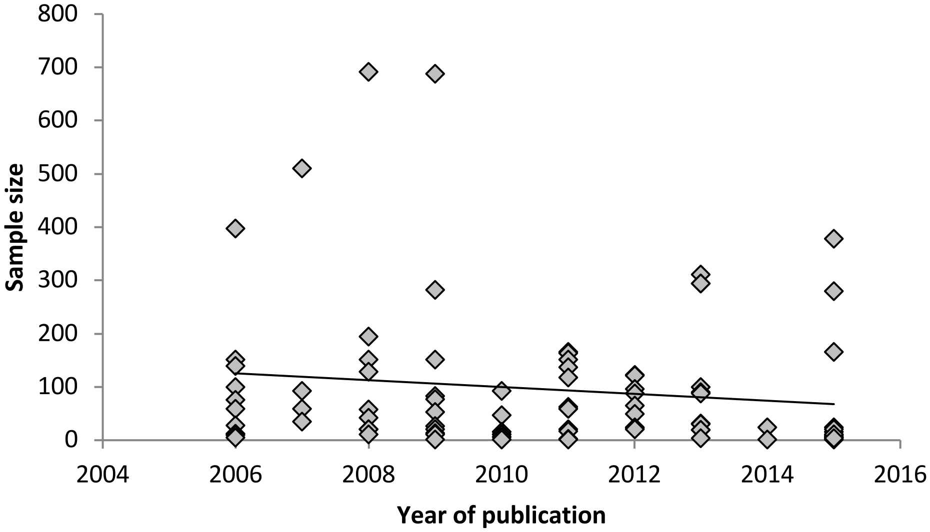
Fig. 4b.

a)



800
700
600
500
400
300
200
100
0
Sample size
1967
1977
1987
1997
2007
2017
Year of publication

b)



800
700
600
500
400
300
200
100
0
Sample size
2004
2006
2008
2010
2012
2014
2016
Year of publication

Fig. 5a-b.

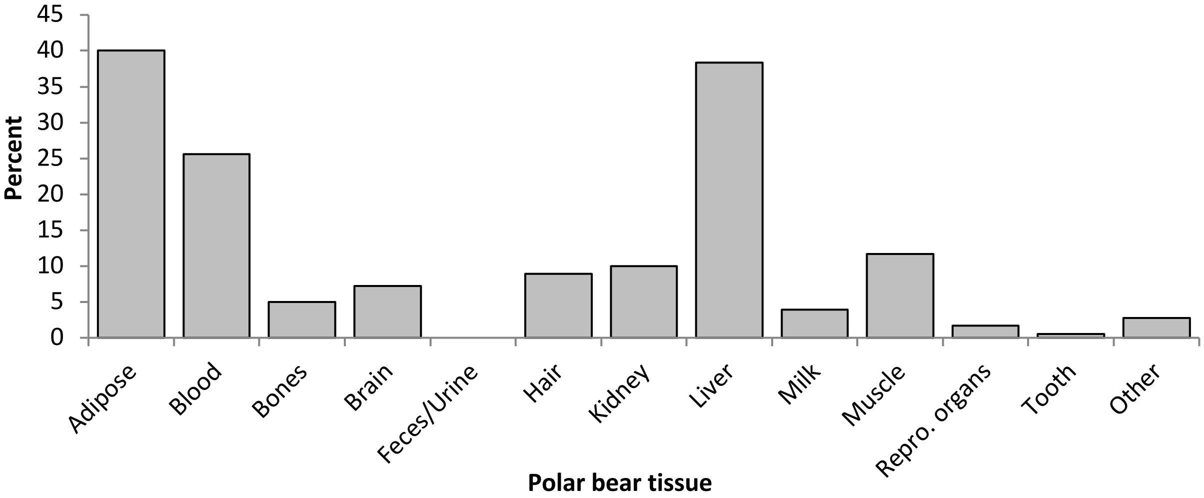

45
40
35
30
25
20
15
10
5
0
Percent
Adipose
Blood
Bones
Brain
Feces/Urine
Hair
Kidney
Liver
Milk
Muscle
Repro. organs
Tooth
Other
Polar bear tissue

Fig. 6.

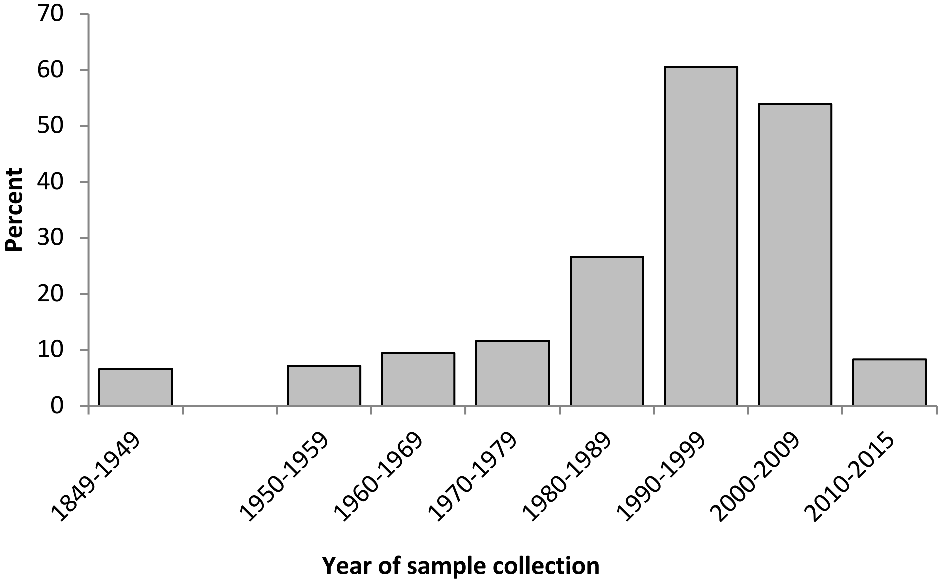
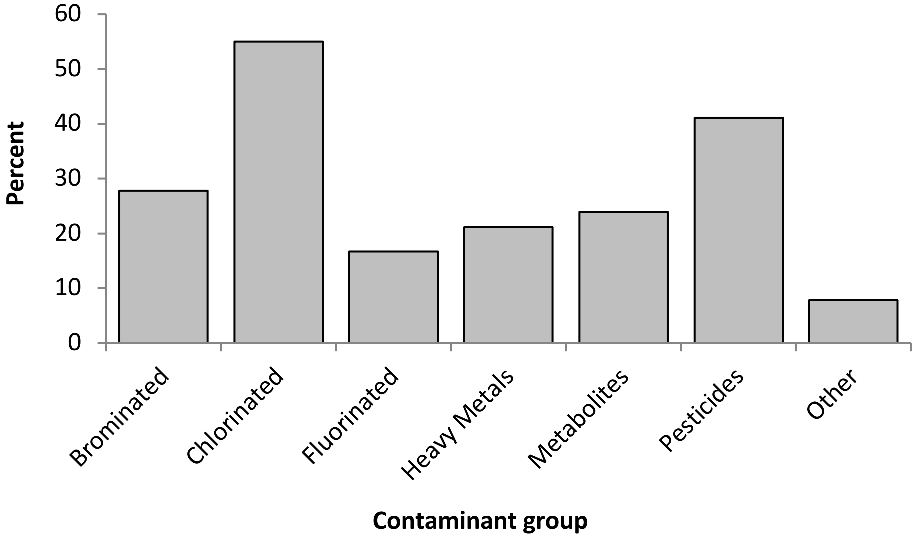

70
60
50
40
30
20
10
0
Percent
1849-1949
1950-1959
1960-1969
1970-1979
1980-1989
1990-1999
2000-2009
2010-2015
Year of sample collection

Fig. 7.



60
50
40
30
20
10
0
Percent
Brominated
Chlorinated
Fluorinated
Heavy Metals
Metabolites
Pesticides
Other
Contaminant group

Fig. 8.

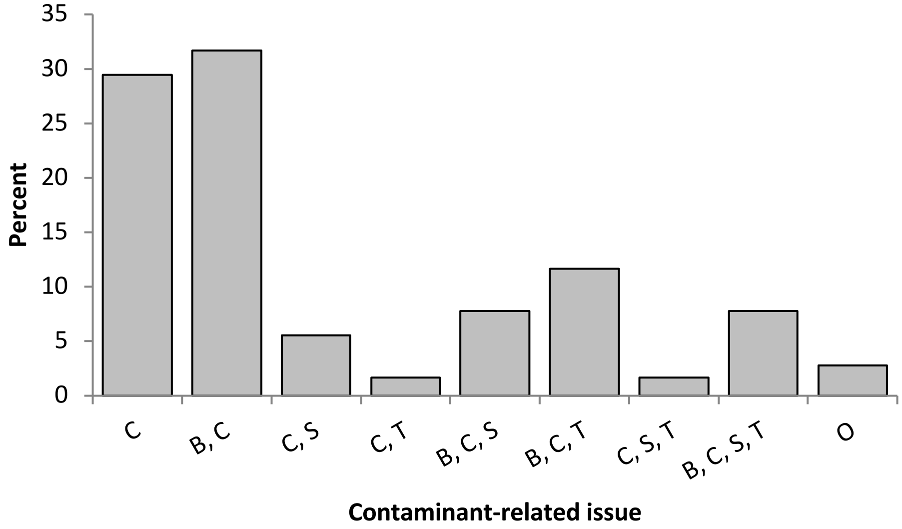

35
30
25
20
15
10
5
0
Percent
C
B, C
C, S
C, T
B, C, S
B, C, T
C, S, T
B, C, S, T
O
Contaminant-related issue

Fig. 9.

Supporting information

Table S1. The literature search for the present systematic review was done using Web of Science, which included the publication databases listed below.

Publication databases
Web of Science Core Collection
BIOSIS Citation Index
BIOSIS previews
CABI: CAB Abstracts
Current Contents Connect
Data Citation Index
Derwent Innovations Index
FSTA – the food science resource
KCI – Korean Journal Database
MEDLINE
SciELO Citation Index
Zoological Record

Table S2. Definition of all variables considered for every paper included in the present systematic review of polar bear ecotoxicology studies.

Source	Entry no.	Unique identifier assigned to each paper
	Journal	-
	Original research or review paper	-
	Publication year	-
	Total no. of authors	-
Affiliation, first author	Canada	-
	Denmark	-
	Greenland	-
	US	-
	Norway	-
	Russia	-
	Other	-

Affiliation, co-authors	Canada		-
	Denmark		-
	Greenland		-
	US		-
	Norway		-
	Russia		-
	Other		-
Subpopulation	Arctic Basin		Geographical location of polar bears included in older papers (pre-PBSG maps) were estimated and assigned following the subpopulation delineation maps available at http://pbsg.npolar.no/en/status/population-map.html Polar bears from Iceland were assumed to be part of the East Greenland subpopulation.
	Baffin Bay		
	Barents Sea		
	Chukchi Sea		
	Davis Strait		
	East Greenland		
	Foxe Basin		
	Gulf of Boothia		
	Kane Basin		
	Kara Sea		
	Lancaster Sound		
	Laptev Sea		
	M'Clintock Channel		
	Northern Beaufort Sea		
	Norwegian Bay		
	Southern Beaufort Sea		
	Southern Hudson Bay		
	Viscount Melville Sound		
	Western Hudson Bay		
Sample	Size (total)		Total number of bears included in the contaminant analyses. Where samples of multiple tissues were used / number of unique individuals was not given, we used the highest number of samples reported as the total number of samples
	Year of sampling		Year of sampling included in the contaminant analyses
	Species	Single species paper	Analyzed polar bear samples only
		Multiple species paper	Analyzed samples from polar bears and ≥1 other species

	Source	Live	Samples came from live bears (collected during capture-release studies)
		Dead	Samples came from hunter-harvested bears
Eco variables taken into account	Age	Aged	Each bear was assigned a specific age (months or years) based on tooth growth layers or skull characteristics
		Not Aged	Bears were not assigned specific ages (months or years) Bears were also classified as “not aged” if there was no indication of their age in the paper
	Age class	Cub-of-the-year	≥1 bear included in the contaminant analysis was classified as cub of the year (< 12 months old)
		Yearling	≥1 bear included in the contaminant analysis was classified as yearling (≥ 12 months and <2 years old)
		Subadult	≥1 bear included in the contaminant analysis was classified as subadult
		Adult	≥1 bear included in the contaminant analysis was classified as adult
	Sex	Male	≥1 bear identified as male was included in the contaminant analysis
		Female	≥1bear identified as female was included in the contaminant analysis
		Unknown	≥1 bear of unknown sex was included in the contaminant analysis
	Home range size		A measure of home range size was included in the contaminant analysis
	Distance traveled		A measure of distance traveled was included in the contaminant analysis
	Offspring	Y/N	Did the adult bears in the contaminant analysis have dependent offspring
		Litter size (1/0)	Litter size included in the contaminant analysis
		Sex (1/0)	Sex of the offspring included in the contaminant analysis

		Age (1/0)	Age (months, years) of offspring included in the contaminant analysis
		Other	-
	Reproductive history (1/0)		Some measure of reproductive history included in the contaminant analysis
	Body condition	Fat index	Fat index scores (category 1-5) included in the contaminant analysis
		Weight (any metric)	Bear weight (scale or by use of equation) included in the contaminant analysis
		Length (any metric)	Bear length (of skull, head or body) included in the contaminant analysis
		Other	-
	Diet	Fatty acid	Information on fatty acids included in the contaminant analysis
		Stable isotopes	Information on stable isotopes included in the contaminant analysis (N15, C13)
		Other	-
	Genetics		Genetic information included in the contaminant analysis (genealogy; any measure of DNA or RNA)
	Parasites		Parasite load included in the contaminant analysis
	Behavior		Some measure of bear behavior included in the contaminant analysis, e.g., the bear's behaviour before/during darting procedure; info from a time budget analyses; level of curiosity/avoidance
	Season	Spring (Mar-May)	Season of sampling included in the contaminant analysis. If bears were sampled over the course of multiple seasons, each individual season was registered
		Summer (June-Aug)	
		Fall (Sept-Nov)	
		Winter (Dec-Feb)	
	Climate variables	Sea ice	Was any measure of sea ice included in the contaminant analysis. e.g., sea ice extent, sea ice thickness
		Climate index	At least one climate index was included in the contaminant analysis e.g., Arctic oscillation index (AO, AOI), North Atlantic Oscillation index (NAO, NAOI, winter NAO)

		Temperature	Was any measure of temperature included in the contaminant analysis. e.g., surface temperature
		Other	-
Reporting on tox-related:	Levels		Reported on levels of contaminants
	Temporal trends		Reported on temporal trends of contaminant levels
	Spatial issues		Reported on contaminant(s) in relation to spatial issues. e.g., compared contaminant loads between polar bears from different populations/geographical areas; compared bears on land with bears on ice
	Biological response		Reported on any of the topics mentioned under "Effects" in this spreadsheet. “Biological response” also noted if age and/or sex were used as variables in the contaminant analysis
	Other		-
Effects level	Individual		-
	Population		-
	Other		-
Food web	Prey		The contaminant analysis included data on the bear's prey (direct link between food item and polar bear). e.g., ringed seal, bearded seal, kelp, berries.
	Food web approach		The contaminant analysis included data on the bear's prey as well as other food web species (direct as well as indirect links from food item to polar bear). e.g., fish + seal + polar bear
	Other		-
Tissue	Liver		-
	Kidney		-
	Adipose		-
	Repro. organs		Inner or outer
	Brain		-
	Hair		-
	Blood/plasma		-
	Bones		-
	Tooth		-

	Milk		-
	Feces/urine		-
	Other		-
Contaminants	Pesticides		e.g., Mirex, Dieldrin, DDT, DDE, DDD, HCH, α-HCH, β-HCH, OCS, CHL, oxy-CHL, ClBz, HCB, nonachlor (cis and trans), heptachlor epoxide
	Flourinated		e.g., PFOS, PFAS, PFOA, PFCA
	Chlorinated		e.g., PCDD, PCDF, PCB (For clarification: The compounds included in “Pesticides” can be chlorinated. At the same time, no compounds defined as “Chlorinated” are pesticides).
	Brominated		e.g., PBDE, HBCD, BTBPE, PBEB, EH-TBB, DBDPE, TBP-AE, TBCT, PBT, HBB, PBB-Acr, TBX, DBE-DBCH, HBCDD, OBTMPI, BB-101, BB-153, PBP_AE, DBHCTD, TBP-DPTE, PBPB-dbpe, BEH-TEBP, syn-DDC-CO, anti-DCC-CO
	Metabolites		e.g., OH- (or HO-), MeSO-, MeO-
	Heavy metals		e.g., cadmium, lead, mercury
	Other		e.g., crude oil, anti-freeze
Effects	Hormones	Steroid	Effect was measured on one or more steroid hormones <u>Progestagens:</u> pregnenolone, 17α-hydroxy pregnenolone, progesterone, 17α-hydroxy progesterone <u>Corticoids:</u> aldosterone, deoxy-corticosterone, corticosterone, 11-deoxycortisol, cortisol <u>Androgens:</u> dehydroepiandrosterone (DHEA), androstenedione, androstenediol, testosterone, dihydrotestosterone (DHT). <u>Estrogens:</u> estrone, estradiol, estriol
		Thyroid	Effect was measured on one or more thyroid hormones

			triiodothyronine (= 3.3',5-triiodothyronine = T3 = TT3 or FT3 or rT3) , thyroxine (= 3.3',5.5'-tetraiodothyronine = T4 or TT4 or FT4)
	Vitamins		Effect was measured on one or more vitamins e.g., vitamin A (retinol and derivatives), vitamin E (α-tocopherol), vitamin D (Cholecalciferol = D(3) and 25-OH vitamin D-3 (25(OH)D(3))
	Enzymes		Effect was measured on one or more enzymes e.g., deiodinase (D1 and/or D2)
	Pathology		Effect was measured on one or more pathology variables Any kind of tissue damage to any organ (to brain, repro. organs, teeth, kidney, liver, and others)
	Immune system		Effect was measured on one or more immune system variables e.g., immunoglobulin G (IgG), lymphocytes, antibodies
	Protein levels		Effect is measured on one or more protein variables e.g., CYP450
	Receptor levels		Effect was measured on one or more receptor level variables e.g., estrogen receptor (ER), aryl hydrocarbon receptor (AhR)
	Parasites/zoonosis		Effect was measured on one or more variables related to parasite/zoonosis infections *Toxoplasma*, *Brucella*, *Trichinella*
	Transport proteins		Effect was measured on one or more transport protein variables e.g., thyroxine-binding globulin (TBG), transthyretin (TTR or TBPA), albumin, retinol-binding protein (RBP)
	Morphometrics		Effect was measured on one or more morphometric variables.

			e.g., skull length or width, body length or mass
	Reproduction	Litter size	Effect was measured on litter size
		Potential	Effect was measured on variable directly related to reproductive potential. e.g., sperm quality, changes in reproductive organs (inner and outer)
		Other	-
	Other		e.g., thermoregulation