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On the integration of ecological and physiological variables in polar bear toxicology research: a systematic review

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Abstract

Ecotoxicology evolved as a scientific field as awareness of the unintended effects of anthropogenic pollutants in biota increased. Polar bears (*Ursus maritimus*) are often the focus of Arctic 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 papers often incorporate ecological variables. This systematic literature review investigates the ecological and physiological variables that have been integrated in such studies. The systematic literature search resulted in 207 papers, published between 1970-2016. Representation of each of the 19 polar bear subpopulations varied from 0 to 72 papers; East Greenland, Barents Sea, Southern Beaufort Sea, and Lancaster Sound had the most published research, with over 30 papers each. Samples were collected between 1881 and 2015, primarily from harvested bears (66%); most from the 1990s and 2000s. Adipose tissue, liver, and blood were the most common tissues examined, and mean number of bears analyzed per paper was 76 (range 1-691). Papers investigating temporal trends did so using a mean sample of 61 bears over a 6-year period.

The frequency with which ecological and physiological variables were integrated into toxicological papers varied. Age and/or sex was the only ecological variable(s) considered in 51% of papers. Further, a total of 37% of the papers included in the review investigated physiological effects in relation to contaminant concentrations. 98% dealt with contaminant exposure 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 papers: 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, whereas variables related to polar bear diet were included in $\leq 9\%$.

Based on our findings, we suggest future polar bear toxicology 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

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Background

Ecotoxicology is the multidisciplinary study of chemical contaminants in the environment and their effects on biota (Newman, 2010), including aspects of ecology, toxicology, chemistry, physiology, immunology, endocrinology, developmental biology, and genetics. 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 first defined as the “relation of the animal both to its organic as well as inorganic environment” (Haeckel, 1866) and later as “interactions that determine the distribution and abundance of organisms” (Krebs, 1972). As such, ecology 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 studies, ecology typically focuses on the individual, population, or species, whereas toxicology usually focuses on the molecular, cellular, and organ level of the individual. Thus, ecological studies in wildlife often begin at the individual level, which is where toxicology studies usually end (AMAP, 1998, Chapman, 2002). Furthermore, wildlife 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 and impacts may be. Taking an interdisciplinary approach by combining the two fields 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 ones are frequently discovered, including in the Arctic (Trumble et al., 2012, Dietz et al., 2013a, Gebbink et al., 2016). 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 (Bidleman et al., 2010, Butt et al., 2010, Warner et al., 2010, Gebbink et al., 2016, AMAP, In review). Heavy metals, especially methylmercury (MeHg), are another group of toxic compounds of concern in Arctic biota (Eaton and Farant, 1982, Norstrom et al., 1986, Dietz et al., 2013b).

Ecotoxicology evolved as a scientific field in the 1950s and 1960s as the emergence of unintended effects of anthropogenic chemicals in biota became apparent (Rattner, 2009, Newman, 2010). 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 toxicological papers were published in the 1970-80s at which time long-range transport of pollutants became apparent (Kerr, 1979, Barrie et al., 1992). 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 whales (*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 by Bowes and Jonkel (1975), who reported high concentrations of PCBs in the bears' milk. Similar to legacy contaminants, heavy metals were first quantified in polar bears several decades ago (Eaton and Farant, 1982, Norstrom et al., 1986). Once it became clear that high concentrations of these compounds were found in polar bears, they became a focal species for studies of contaminant exposure in the Arctic.

Publications in polar bear toxicology have been increasing since the 1970s (Fig. 1). Expanding our knowledge on the exposure and effects of contaminants on polar bears is of particular concern because they 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, Sonne, 2010, McKinney et al., 2011, Dietz et al., 2013b). 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). Since polar bears are harvested for human consumption (Ostertag et al., 2009, Sonne et al., 2013b), knowledge of contaminants and their effects on polar bears may also 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 (Vongraven et al., 2012, Jenssen et al., 2015, Patyk et al., 2015). 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 the integration of ecological and physiological variables in the polar bear toxicology peer-reviewed literature. The secondary aim was to identify knowledge gaps within the field of polar bear ecotoxicology and provide recommendations on how to fill those gaps through future research within the field.

The systematic review process

A systematic review of peer-reviewed literature was performed based on searches in the comprehensive database Web of Science™ (Reuters, 2016). “All databases” were searched (see Table S1 for an overview of the included publication databases) using polar bear- and contaminant-related search terms to generate an initial list of potential papers. This list was then refined, retaining papers where polar bears were the focal species. The 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 contaminant exposure or toxicological studies (e.g., Derocher et al., 2003, Basu et al., 2009) or

- review papers - overview of already published contaminant exposure or toxicological studies (e.g., Letcher et al., 2010, McKinney et al., 2015).

Please note that in this paper, “toxicology” and “toxicological” encompasses studies of contaminant exposure as well as studies of toxicology.

A number of biological, ecological, and contaminant related variables were registered for each paper included in the systematic review (see Table 1 for core ecological variables and Table S2, full list of all variables and their definitions). Refining the list of papers from the initial literature search (as described above) and registering the variables (Table S2) on those papers that were included in the review was done by co-author M. Viengkone.

To assess number of polar bear toxicology research publications relative to other species, we created an index of such publications for a selection of marine and terrestrial mammal species. 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 bears sampled in research papers. In addition, a Kruskal-Wallis rank sum test was used to examine temporal patterns in polar bear sample collection. Statistical analyses were conducted using Microsoft Excel 2010. Results were considered statistically significant at $p \leq 0.05$.

Literature review findings and considerations

Literature

The literature search was conducted on 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 (i.e., Henriksen et al., 2001, Sonne et al., 2009a, Dietz et al., 2015, Pavlova et al., 2016). These four papers were 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. The index of toxicology publications for a selection of marine and terrestrial mammal species (Fig. 2) 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 mammal model species in

toxicology studies (Wang et al., 2014, Folland et al., 2016, Pavlova et al., 2016). 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 toxicology (Subramanyam, 1983, Mindeli and Markusova, 2015). 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 more authors for research papers published 1970-2016 (Fig. 3b; $F_{1,178} = 48.36$, $p < 0.001$, $r^2 = 0.21$). Although the number of authors per paper varies between natural science fields, the 7-8 authors we found to be the average for polar bear toxicology papers (research as well as review) is at the higher end of the range (Newman, 2001). International collaboration is common in polar bear toxicology (Table 2). First authors based at 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 with first authors from other countries. Low contributions from these two countries may be related to our choice of search engine and focus on publications in English only. The low number of papers from Greenland reflects that most research on Greenland polar bear subpopulations was conducted by Denmark-based scientists.

The ratio of polar bear toxicology research papers to review papers was 6:1 (Fig. 1). The high frequency of review papers highlights two aspects about polar bear toxicology: 1) it is a complex field encompassing a large number of chemicals and ecological variables, 2) due to the often limited sample size, each study only considered a limited number of ecological variables. 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 exposure and toxicology research have been published for all recognized polar bear subpopulations (mean $\pm$ S.E.: 21 ± 4 papers/subpopulation, range: 0-72), except the Arctic Basin (Fig. 4a-b; IUCN PBSG, 2010). East Greenland, Barents Sea, Southern Beaufort Sea, and Lancaster Sound subpopulations were the most studied with > 30 papers each. Toxicological research has been a priority in East Greenland and Barents Sea because of high contaminant loads (AMAP, 1998, Norstrom et al., 1998, Letcher et al., 2010, Sonne, 2010, Dietz et al., 2015). 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 this research (Vongraven et al., 2012). Finally, the high number of papers including the Southern Beaufort Sea subpopulation is likely due to it being a shared subpopulation with 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 been undertaken, Kane Basin, Laptev Sea, Kara Sea, and Norwegian Bay were the least studied (<10 papers each), likely because they are less accessible (Fig. 4a) 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 monitoring and 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 (Letcher et al., 2010, Sonne, 2010, Dietz et al., 2015, 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 (e.g., Giesy and Kannan, 2001, Sonne, 2010). The mean number of polar bears sampled per paper was 76 (S.E. = 8.4, range: 1-691), with a positive trend in number of samples/paper over time that approached significance (Fig. 5; $F_{1,171} = 3.16$, $p = 0.08$, $r^2 = 0.02$). The three papers with the largest number of samples included museum specimens (range $n = 510$ -691; Sonne et al., 2007b, Bechshoft et al., 2008, Bechshoft et al., 2009). Larger sample sizes allow for parsing of data into homogenous groups (e.g., sex/age categories), while maintaining statistical robustness. It also facilitates investigation of interactions between variables without overfitting or otherwise compromising the data analyses (Hair et al., 2006, Crawley, 2007). Toxicological papers with small sample sizes (e.g., $n \leq 30$) were often exploratory (e.g., Sacco, 2005, Verreault et al., 2006), experimental (e.g., Lie et al., 2004, Lie et al., 2005), 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 regard to cost, time, and optimal usage of the limited tissue samples available. The number of polar bear

samples available for toxicological research depends on a number of factors such as subpopulation(s) investigated and sampling methods. The origin of samples used in the 180 papers were 66% (119) harvested bears, 25% (45) live bears, 6% (10) both harvested and live bears, and 3% (6) unknown. The most common tissues examined were adipose tissue, 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, Letcher et al., 2010, Sonne, 2010, Gabrielsen et al., 2015), they are only available from dead animals. 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 samples, especially invasive samples such as e.g. liver and kidney tissue, may decline long-term (Amstrup et al., 2007, Derocher et al., 2013). Thus, it is increasingly important to establish relationships between toxicological results based on invasive versus minimally- or non-invasive samples. Such samples include those that can be collected without direct contact with the animal, e.g., fecal samples (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 they are collected will be dependent on the research objectives.

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), while 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). Further, the years included in these time spans were not necessarily contiguous. Many papers listed only a range of years within which the bears were sampled, while 9 papers 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 mix of bears of different age- and sex-classes, reproductive status, body condition, geographical location, and contaminant load, which are all important factors that can affect exposure and physiology (Polischuk et al., 2002, Letcher et al., 2010, 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 only: 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 was the most prevalent sampling period because it is the season with the most harvest, the stable sea ice facilitates sampling of bears, and all sex/age classes are accessible during this time. Although season can have a significant influence on polar bear contaminant load (Polischuk et al., 2002, Dietz et al., 2004, Dietz et al., 2007), it was rarely considered in polar bear toxicology studies.

Contaminants

Chlorinated compounds and pesticides were included in 55% (99) and 41% (74) of the polar bear toxicology 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 specific 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 (UNEP, 2001, Muir and Howard, 2006, Hung et al., 2016). Our understanding of contaminant metabolites is still rudimentary. As our knowledge of 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 CECs continues to be challenged by the lack of analytical methods and pure chemical standards (Keith, 1976, Wiener, 2013, Gebbink et al., 2016).

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), space, and time (Fig. 9). Most papers 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 papers 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 effects (Voltura and French, 2000, Martin et al., 2006, Sonne et al., 2009b, Zimmer et al., 2009, Kirkegaard et al., 2010). Further, the potential mixture effects between the hundreds of different contaminants in polar bears requires additional consideration (Letcher et al., 2010, Sonne, 2010, Sonne et al., 2012, Dietz et al., 2015); these effects could furthermore differ depending on whether the exposure is acute or chronic (Chapman, 2002).

Of the biological 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 papers. Altogether, 37% (66) of the papers included in the review investigated biological effects in relation to contaminant concentrations (Table 3).

Notably, 98% (176) of all papers dealt with contaminant exposure 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 to extrapolate individual level studies to the population level.

Ecology

The frequencies with which ecological and physiological 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). Finally, 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 (Thiemann et al., 2008, Diamanti-Kandarakis et al., 2009, Letcher et al., 2010, McKinney et al., 2013). 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 papers, generally as a smaller percentage (< 15%) of the total number of individuals (e.g., Routti et al., 2011). In most of the papers where gender was unknown, it was the result of using inadequately labeled, museum specimens (e.g., Sonne et al., 2004).

376
377 Solitary subadult and adult polar bears were included in 57% (102) and 79% (142) of the papers,
378 respectively. Younger bears were included in fewer papers: yearlings in 20% (36) and cubs-of-
379 the-year in 13% (24). From a conservation perspective, studying contaminants in adult polar
380 bears is relevant to their reproductive success and would include variables such as epigenetics,
381 reproductive organ deformation, and behavior (Sonne et al., 2007a, Pilsner et al., 2010, Jenssen
382 et al., 2015, Sonne et al., 2015). Furthermore, effects of contaminants may reduce survival and
383 thus reproductive output (Derocher et al., 2003, Dietz et al., 2015). However, developing young
384 are more sensitive to the effects of contaminants (Domingo, 1994, Hamlin and Guillette, 2011),
385 while also being subjected to high concentrations via maternal transfer (Bernhoft et al., 1997,
386 Bytingsvik et al., 2012). Given the risk of lifelong consequences (Colborn et al., 1993, Hamlin
387 and Guillette, 2011), dependent and developing young are underrepresented in the polar bear
388 toxicology literature.

389
390 Presence of dependent offspring can have a profound influence on maternal contaminant load in
391 polar bears (Lie et al., 2000, Polischuk et al., 2002). In addition, information on reproductive
392 success, including sex, age, and survival of cubs, is essential for population assessments.
393 However, only 12% (21) of the research papers examined reproduction in relation to
394 contaminants. Lack of linkages to reproduction could be due, in part, to the large number of
395 toxicological papers where samples are collected from harvested animals, which generally
396 excludes family groups because they are protected from harvest (Naalakkersuisut, 2005, Sonne,
397 2010). Data on family groups is more readily obtainable for frequently monitored subpopulations
398 (e.g., Barents Sea, Western Hudson Bay, and Southern Beaufort Sea). Of the papers 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., Dietz et al., 2000, Derocher et al., 2003). Dependent young differ in contaminant exposure and physiological variables such as hormone concentrations, not only from adults, but also due to sex and age (Bernhoft et al., 1997, Oskam et al., 2003, Oskam et al., 2004, Knott et al., 2012, Bechshoft et al., 2016a). 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 and Guillette, 2011, Maekawa et al., 2014).

The amount of lipophilic contaminants biologically available to a bear is closely linked to its body condition (size of adipose tissue store): the leaner the bear, the higher the contaminant concentration in its 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. Investigating contaminants in relation to body condition is also interesting in that they are associated with altered metabolism in other species (Voltura and French, 2000, Verreault et al., 2007, van Ginneken et al., 2009), and, as shown in a paper published after and thus not included in our systematic literature review, may have the potential to modulate polar bear energy metabolism (Routti et al., 2016). Finally, measures of polar bear diet were included

in $\leq 9\%$ (≤ 17 ; Table 3) of the contaminant analyses. As the contaminant concentration and composition in prey species varies widely (McKinney et al., 2010, St Louis et al., 2011, Routti et al., 2012, McKinney et al., 2013), diet information is a variable that warrants further investigation. For example, information on diet could help explain differences in contaminant concentrations between demographic groups such as males and females or subadults and adults. Genetics, size of home range, and climate variables were each examined in $\leq 1\%$ (≤ 2 ; Table 3) 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 (Derocher et al., 2004, AMAP, 2011, Ma et al., 2011). Finally, alteration of behavior caused by contaminant exposure has been observed in other mammals (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 (Villanger et al., 2011, Bechshoft et al., 2015, Pedersen et al., 2015, Bechshoft et al., 2016b), which in turn may affect behavior. Similarly, a change in feeding behavior could affect contaminant exposure (McKinney et al., 2013, McKinney et al., 2015).

Conclusions and recommendations

Summary: Key knowledge gaps

Although our systematic review of the published literature found polar bears to be one of the better studied Arctic marine mammals in the field of toxicology, few of the papers incorporated variables related to their ecology and physiology (as outlined in Table 1 and Table 3): 51% of the research papers included merely the most basic of ecological variables in their analysis, while only 37% of the research papers investigated physiological effects in relation to contaminant concentrations. The increased integration of such variables in exposure and toxicology studies 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 beneficial to have ecotoxicological data for all polar bear subpopulations, logistical restraints require prioritization. Furthermore, the choice of which polar bear subpopulation to focus on 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 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 regard to ecological data or availability of 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, increased use of polar bear specimens from museums as well as those stored in tissue banks would help address 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 temporal trend studies.

(3) Family groups

Dependent and developing young are underrepresented in the polar bear toxicology literature. Hence, family groups and dependent young should be included in ecotoxicology studies whenever logistically and ethically possible. 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 sample origin. 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, Stirling et al., 2008, McKinney et al., 2014). 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 (Bernhoft et al., 2000, Lie et al., 2004, Oskam et al., 2004, Bechshoft et al., 2012, Macbeth et al., 2012, 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 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 at 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

512 studies, an understanding of population-level effects could be achieved by incorporating more
513 variables directly related to reproduction and survival.

514

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

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1019 **Tables**

1020

1021 **Table 1.** Core ecological variables included in the present systematic review of polar bear
1022 toxicology literature. The full list of all variables and their definitions can be found under
1023 Supporting information (Table S2).

1024

1025 **Table 2.** Authorship by country of the 207 papers included in the present systematic review of
1026 the status of polar bear toxicology literature; 31 reviews and 180 research papers (four
1027 publications were in both categories, see text for details).

1028

1029 **Table 3.** Biological (physiological and morphological) variables investigated in relation to
1030 contaminants in the research papers included in the present systematic review of polar bear
1031 toxicology literature. The table is based on 66 papers, some of which analyzed multiple of the
1032 listed variables.

1033

1034 **Table 4.** Recommendation for focal polar bear subpopulations for future ecotoxicology research
1035 based on their respective strengths with regard to available data.

1036

Figure legends

Fig. 1. Frequency of polar bear focused toxicological papers (n=207) based on the year of publication and categorized by type (i.e. review or research) included in the 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-b. The number of authors on the papers included in the present systematic review of the status of polar bear toxicology literature for: a) review papers, 1992-2016, b) research papers, 1970-2016.

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 toxicological research papers (n = 180).

Fig. 5. Sample size (individual bears) in polar bear toxicology research papers ($n = 180$), as included in the present systematic review, published over the investigated period (1970-2016).

Fig. 6. Percentage of published polar bear toxicology 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 toxicology 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 toxicology 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 toxicology 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

Fig. 1.

Fig. 2.

Fig. 3a-b.

Fig. 4a.

Fig. 4b.

Fig. 5

Fig. 6.

Draft

Fig. 7.

Fig. 8.

Draft

Fig. 9.

Ecological variables included in the contaminant analysis in the 180 analyzed research papers	Number	Percent
Age <ul style="list-style-type: none">• Specific age (months/years)	148	82
Class <ul style="list-style-type: none">• Cub-of-the-year• Yearling• Subadult• Adult• Unknown	24 36 102 142 25	13 20 57 79 14
Behavior	0	0
Body condition (any metric)	46	26
Climate <ul style="list-style-type: none">• Climate index• Season• Temperature	1 1 1	< 1 < 1 < 1
Diet <ul style="list-style-type: none">• Fatty acid• Stable isotopes	6 17	3 9
Genetics	2	1
Home range size (movement)	2	1
Reproductive history	21	12
Offspring <ul style="list-style-type: none">• Litter size• Sex• Age	4 7 16	2 4 9
Sex <ul style="list-style-type: none">• Male• Female• Unknown	130 134 43	72 74 24

Table 1.

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

Table 2

Draft

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 3.

		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

Table 4.