Diet and metabolic state are the main factors determining concentrations of perfluoroalkyl substances in female polar bears from Svalbard

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ABSTRACT

Perfluoroalkyl substances (PFASs) have been detected in organisms worldwide, including Polar Regions. The polar bear (*Ursus maritimus*), the top predator of Arctic marine ecosystems, accumulates high concentrations of PFASs, which may be harmful to their health. The aim of this study was to investigate which factors (habitat quality, season, year, diet, metabolic state [i.e. feeding/fasting], breeding status and age) predict PFAS concentrations in female polar bears captured on Svalbard (Norway). We analyzed two perfluoroalkyl sulfonates (PFSAs: PFHxS and PFOS) and C_8-C_{13} perfluoroalkyl carboxylates (PFCAs) in 112 plasma samples obtained in April and September 2012-2013. Nitrogen and carbon stable isotope ratios ($\delta^{15}N$, $\delta^{13}C$) in red blood cells and plasma, and fatty acid profiles in adipose tissue were used as proxies for diet. We determined habitat quality based on movement patterns, capture position and resource selection functions, which are models that predict the probability of use of a resource unit. Plasma urea to creatinine ratios were used as proxies for metabolic state (i.e. feeding or fasting state). Results were obtained from a conditional model averaging of 42 general linear mixed models. Diet was the most important predictor of PFAS concentrations. PFAS concentrations were positively related to trophic level and marine diet input. High PFAS concentrations in females feeding on the eastern part of Svalbard, where the habitat quality was higher than on the western coast, were likely related to diet and possibly to abiotic factors. Concentrations of PFSAs and C_8-C_{10} PFCAs were higher in fasting than in feeding polar bears and PFOS was higher in females with cubs of the year than in solitary females. Our findings suggest that female polar bears that are exposed to the highest levels of PFAS are those 1) feeding on high trophic level sea ice-associated prey, 2) fasting and 3) with small cubs.

42 **Capsule:** PFAS concentrations are driven by diet and metabolic state (feeding/fasting) in
43 female polar bears; decreasing sea ice extent is likely to modify PFAS exposure in polar bears.

44 **Keywords:** Ursus maritimus; PFAS; breeding status; habitat quality; fasting; stable isotope

45

INTRODUCTION

Perfluoroalkyl substances (PFASs) are a group of anthropogenic chemicals that have been manufactured for more than 50 years. PFASs are commonly used in the production of stain repelling agents, fluoropolymers, pesticides, lubricants, paints, medicines and fire-fighting foams due to their ability to repel both water and oils (Key et al., 1997; Prevedouros et al., 2006). PFAS are thermally and chemically stable, have no route of degradation and cannot be metabolized under normal environmental conditions, which makes them extremely persistent in the environment (Muir and de Wit, 2010). PFASs have been detected in blood and tissues of wildlife and humans worldwide, including remote regions such as the Arctic (Haukås et al., 2007; Houde et al., 2011; Lau et al., 2007; Martin et al., 2004).

In contrast to persistent lipophilic pollutants, such as polychlorinated biphenyls (PCBs), PFASs have a high affinity towards plasma proteins, in particular albumin, and tend to accumulate in protein-rich compartments such as blood, liver and kidneys (Buck et al., 2011). Retention of PFASs in these organs and tissues may be toxicologically significant. In laboratory mammals, the effects of PFAS include disrupted steroid hormone and lipid homeostasis, reduced body weight, increased liver weight and a steep dose–response curve for mortality (Guruge et al., 2006; Jensen and Leffers, 2008; Lau et al., 2007).

The degree of bioaccumulation of PFASs generally increases with chain length (Martin et al., 2003a, 2003b). For instance, perfluorooctanesulfonic acid (PFOS) and C_9-C_{13} perfluoroalkyl carboxylate (PFCA, C_n refers to the carbon chain length) concentrations increase with trophic position thus, several PFASs can reach very high levels in top predators (Martin et al., 2004; Tomy et al., 2009; Van de Vijver et al., 2003). In addition, PFAS are transported by air and ocean currents to remote Arctic regions (Armitage et al., 2009; Shoeib et al., 2006; Wania,

2007). Polar bears (*Ursus maritimus*), as Arctic top predators are therefore highly exposed to PFASs (Kelly et al., 2009; Tomy et al., 2004).

Polar bears are among the most polluted species in the Arctic (Letcher et al., 2010). Quantitatively, PFAS is the most important contaminant group found in polar bear blood in wet weight concentrations (Bytingsvik et al., 2012a, 2012b). Among polar bears subpopulations, the concentrations of both lipophilic and proteinophilic pollutants are higher in the Barents Sea (i.e. Svalbard) than in most other subpopulations (McKinney et al., 2011; Smithwick et al., 2005a). Polar bears are seasonal feeders, their preferred prey being ringed (*Pusa hispida)* and bearded seals (*Erignathus barbatus*) especially in spring and early summer. Polar bears also feed opportunistically on a large range of land-based and marine species (Iversen et al., 2013; Tartu et al., 2016; Thiemann et al., 2008). Because of bioaccumulation up the food chain, bears feeding on seals may have higher pollutant concentrations than bears that feed on species lower in the food web. Moreover, pollutant exposure may also be affected by life history traits, during prolonged fasts, which can last up to 6-8 months for pregnant females (Andersen et al., 2012; Ramsay and Stirling, 1988) polar bears can lose over 40% of their body mass and the energy is drawn primarily from fat tissue (Atkinson and Ramsay, 1995).

Information on the effects of PFAS in polar bears is scarce. Modelling and correlative field studies suggest that concentrations of PFASs in polar bears are associated with increased steroid hormone concentrations in the brain, impaired reproduction and immunity (Dietz et al., 2015; Pedersen et al., 2016). There is currently little knowledge of the intrinsic or extrinsic factors that determine individual variation in PFAS concentrations in Arctic wildlife. For example, trophic level is a likely factor to influence PFAS exposure in marine mammals (Van de Vijver et al., 2003). Furthermore, PFAS concentrations have been related to body condition in Arctic

92 foxes (*Vulpes lagopus*), harbor seals (*Phoca vitulina*) and Arctic breeding black-legged
93 kittiwakes (*Rissa tridactyla*) (Aas et al., 2014; Tartu et al., 2014; Van de Vijver et al., 2003).

94 Breeding status in mammals may also be a source of variation as PFAS can be transferred from
95 mother to young during pregnancy and lactation. Placental transfer is the dominant pathway
96 for PFASs in hooded seals (*Cystophora cristata*) and polar bears (Bytingsvik et al., 2012b;
97 Grønnestad et al., 2016). In polar bears, maternal transfer of PFASs is relatively low
98 (Bytingsvik et al., 2012b). Finally, space-use patterns may also influence exposure to PFAS
99 and other contaminants in polar bears through abiotic or biotic factors (Olsen et al., 2003; van
100 Beest et al., 2015). The aim of this study was to investigate which factors (habitat quality,
101 season, year, diet, metabolic state [i.e. feeding/fasting], breeding status and age) predict PFAS
102 concentrations in female polar bears from Svalbard. This information is highly valuable for
103 management to identify which individuals are the most vulnerable to PFAS exposure and how
104 ongoing climate change might alter PFAS exposure in polar bears.

105 **MATERIAL AND METHODS**

106 FIELD SAMPLING

107 Adult female polar bears (age 4-28 years) from the Barents Sea subpopulation were captured
108 non-selectively throughout Svalbard in April and September 2012 and 2013. The 112 samples
109 collected (April 2012, n=33, age: 12.9 ± 1.1 years (mean ± standard deviation), September
110 2012, n=24, 13.2 ± 1.4 years, April 2013, n=29, 13.4 ± 1.0 years and September 2013, n=26,
111 12.8 ± 1.2 years) represented 78 females. Twenty-six females were captured more than once,
112 specifically, we captured 19 females twice, six females three times and one female four times.
113 However, females were not recaptured within the same fieldwork season.

Females were immobilized by remote injection of tiletamine hydrochloride and zolazepam hydrochloride (Zoletil Forte Vet ®; Virbac, France), delivered by a dart fired from a helicopter (Eurocopter AS350 Ecureuil). We collected 50-100 ml of blood from the femoral vein using vacutainers (9-10 ml) with Lithium-Heparine to avoid clotting. We kept samples cool and out of sunlight until centrifuged within 10 h (3500 rpm, 10 minutes). Red blood cells and plasma were transferred to two separate cryotubes and frozen at -20ºC. Adipose tissue samples were collected using an 8 mm biopsy punch taken approximately 15 cm lateral to the base of the tail. In the field, adipose tissue samples were stored in a dry-shipper then kept at -80 ºC until analyses. Immobilization and handling procedures followed standard protocols (Derocher and Wiig, 2002; Stirling et al., 1989), and were approved by the National Animal Research Authority (Norwegian Animal Health Authority, P.O. Box 8147 Dep., N-0033 Oslo, Norway).

Females were classified in three groups according to their breeding status: solitary (i.e., alone or together with a male in spring), with 1 or 2 cubs of the year (COYs; cubs younger than 1 year old) or with 1 or 2 yearlings (cubs aged between 1 and 2 years). No females with older cubs were captured as part of the current project. Female polar bears were aged using a vestigial premolar tooth (P1) following a method described previously (Calvert and Ramsay, 1998). The age of the females was not significantly different between groups ($p>0.25$). Body condition index (BCI) was calculated as described for polar bears (Cattet et al., 2002) based on body mass (BM) and straight-line body length (SL): $BCI=(\ln BM-3.07 \times \ln SL+10.76) / (0.17+0.009 \times \ln SL)$.

ANALYSIS OF PFASs

Plasma samples (n=112) were analysed for PFASs at the Laboratory of Environmental Toxicology at the Norwegian University of Life Sciences (NMBU), Oslo, Norway. The plasma

137 samples were analysed for six perfluoroalkyl carboxylic acids (PFCAs: perfluorooctanoate
138 PFOA, perfluorononanoate PFNA, perfluorodecanoate PFDA, perfluoroundecanoate
139 PFUnDA, perfluorododecanoate PFDoDA and perfluorotridecanoate PFTrDA) and two
140 perfluoroalkyl sulfonic acids (PFSAs: perfluorohexane sulfonate PFHxS and PFOS). The
141 methods were described in another study (Grønnestad et al., 2016).

142 Plasma samples (1 ml) were weighed in 15 ml Falcon centrifuge tubes (VWR International,
143 LLC Radnor, USA). All tubes and pipettes used were made of plastic. Internal standards (^{13}C-
144 labeled equivalents, 20 ng/ml) and 5 ml methanol (Rathburn chemicals, Walkerburn, Scotland)
145 were added to the samples. The samples were mixed for 10 seconds on a Whirlymixer (MS2
146 Minishaker, IKA®, MA, USA) followed by 30 minutes of mixing in a Vibrax machine (Vibrax
147 VXR, IKA®, MA, USA). The samples were centrifuged at 3000 rpm for 10 minutes (Allegra®
148 X-12R, Beckman Coulter, CA, USA). The supernatant was extracted and transferred it to new
149 Falcon tubes. The extraction was repeated with 3 ml methanol. The supernatant was evaporated
150 to a volume of 2 ml using a zymark instrument (TurboVap® LV, Zymark Corporation
151 Hopkinton, MA, USA) with water bath (40°C) and a gentle flow of nitrogen gas (N_2) (Purity:
152 99.6%, Aga AS, Oslo, Norway). The samples were cleaned-up by adding approximately 0.2 -
153 0.3 g active coal (ENVI-Carb™, Sigma-Aldrich, Oslo, Norway) to each sample. The samples
154 were mixed on the Whirlymixer (10 seconds) and then centrifuged (3000 rpm, 10 minutes). The
155 supernatant was transferred quantitatively to new Falcon tubes calibrated to 0.5 ml. The extract
156 was evaporated to a final volume of 0.5 ml and the samples were centrifuged (3000 rpm, 10
157 minutes) and transferred to vials with plastic inserts (200 µl).

158 The final extracts were separated on a high-performance liquid chromatograph (HPLC) with a
159 Discovery C18 column (15 cm × 2.1 mm × 5 µm, Supelco, Sigma-Aldrich, Oslo, Norway),

160 connected to a pre-column; Supelguard Discovery C18 column (2 cm × 2.1 mm × 5 µm,
161 Supelco, Sigma-Aldrich, Oslo, Norway). Detection and quantification was accomplished with
162 a tandem mass spectrometry (MS-MS) system (API 3000, LC/MS/MS System). The injected
163 volume was 5 µl. Calculation was performed using MassHunter Quantitative analysis Version
164 B.05.02 (Agilent Technologies). LOD were three times signal to noise ratio found in the
165 samples and are given in **Table 1**.

166 For each series of approximately 30 samples, three procedural blank without matrix, one blind
167 and two recovery samples were analysed. The relative recovery rate ranged from 86% to 103%
168 for the PFCAs and 99% to 110% for the PFSAs. The results were corrected for recoveries. The
169 laboratory participates in several international ring tests per year, one of the series included
170 three samples of human serum as part of the ring test by Arctic Monitoring and Assessment
171 Program (www.amap.no) and the results were satisfactory.

172 STABLE ISOTOPES IN PLASMA AND FATTY ACIDS IN ADIPOSE TISSUE

173 Determination methods of δ^{15}N and δ^{13}C in red blood cells and plasma (n=112) and fatty acids
174 (FA) composition in adipose tissue (n=83) have been previously described (Tartu et al., 2016).
175 Briefly, δ^{15}N values change in a predictable fashion between trophic levels and thus reflect
176 trophic position of the individual polar bears (Hobson, 1999; Hobson et al., 1996). In contrast,
177 δ^{13}C remains little changed according to trophic position and thus can indicate sources of
178 primary productivity for example marine vs. terrestrial, pelagic vs. benthic, inshore vs. offshore
179 (Hobson, 1999; Hobson et al., 1996). Therefore, stable isotopes can be used as proxies for diet.
180 In polar bear red blood cells, half-life for δ^{13}C is ~1.5 months whereas half-life for δ^{15}N is at
181 least twice as long (Rode et al., 2016). In polar bear plasma, half-lives for δ^{13}C and δ^{15}N are
182 10 and 18 days, respectively (Rode et al., 2016). Thus, once acquired, polar bear red blood cells

183 and plasma can provide a retrospective record of diet sources over months to days' time periods,
184 respectively (Rogers et al., 2015; Tartu et al., 2016).

185 Dietary FAs are predictably incorporated into a consumer's tissues and can thus provide insight
186 into an organism's diet over the preceding weeks to months (Iverson et al., 2004), and perhaps
187 longer in some species (Budge et al., 2006). Seventy-five different FAs were determined in the
188 fat samples. As suggested by Budge et al. (2012), for further analyses we selected 33 FAs that
189 were ≥ 0.2% of total FAs and collectively accounted for 96.9% of total FAs. FA data were
190 transformed by calculating the log of the ratio of each FA to c18:0 prior to principal component
191 analysis (PCA) (Budge et al., 2006). Since the log of 0 cannot be taken, 0 values were replaced
192 with a small constant (0.005%) prior to transformation. The 32 FAs (without 18:0) used in the
193 present study included iso-14:0, 14:0, 14:1n-5, 15:0, 16:0, 16:1n-11, 16:1n-9, 16:1n-7, 16:1n-
194 5, iso-17:0, 16:2n-4, c17:0, 18:1n-11, 18:1n-9, 18:1n-7, 18:1n-5, 18:2n-6, 18:3n-4, 18:3n-3,
195 18:4n-3, 20:1n-11, 20:1n-9, 20:1n-7, 20:2n-6, 20:4n-6, 20:4n-3, 20:5n-3, 22:1n-11, 22:1n-9,
196 21:5n-3, 22:5n-3 and 22:6n-3. We generated FA principal components (PCs) for further
197 analysis from the first, second and third axis of the PCA (projected inertia: PC1: 31.6, PC2:
198 16.7, PC3:12.7%, respectively). Using PCA scores enables to summarize FA composition into
199 three continuous variables. The three first axes accounted for 61.0% of the total variance of the
200 data cloud. Individual FAs that contributed most (>5%) to PC1 were: 15:0, 16:1n-11, 16:1n-7,
201 16:1n-5, 16:2n-4, 18:4n-3, 20:1n-11, 20:1n-9, 20:5n-3, 22:1n-9; to PC2: 16:0, iso-17:0, 17:0,
202 18:1n-7, 18:3n-4, 20:1n-9, 20:4n-6, 22:1n-11 and to PC3: iso-14:0, 14:0, 14:1n-5, 16:1n-9,
203 18:1n-7, 22:1n-11, 21:5n-3, 22:5n-3.

204 METABOLIC STATE DETERMINATION

The ratio of urea to creatinine (urea:creatinine) is indicative of the metabolic state (feeding/fasting state) of polar bears, low values indicating a fasting state (Derocher et al., 1990; Nelson et al., 1984). Molar concentrations of urea and creatinine were analysed in plasma (n=111), the samples were stored at -20 ºC for 1-2 years and thawed before being analysed in autumn 2014. The analyses were performed using a "dry" clinical-chemical analyzer, Reflotron® (Model IV, Boehringer-Mannheim GmhB, Mannheim, Germany). The system is composed of a reagent carrier (test strip) and a microprocessor controlled reflectance photometer. The system uses individual strips for each parameter, and each strip uses a specific reaction to produce a dye that is measured and evaluated by the reflectance photometer. All samples were analysed in duplicates, if high variation was observed between the duplicates, an additional replicate was analysed. Limits of detection (LOD) are given in **Table 1**. Previous studies have reported a threshold value of urea:creatinine <10 to report a fasting state (Cherry et al., 2009; Nelson et al., 1984). This calculation was performed on urea and creatinine concentrations in mg/dl, if converted to molar concentrations as used in the present study we obtain a threshold value of 47.5. We therefore considered that females with urea:creatinine ≤ 47.5 were in a fasting state.

HABITAT QUALITY

Polar bears movements follow a circannual pattern with season-specific area fidelity (Mauritzen et al., 2001), for example female polar bears show fidelity to denning and spring feeding areas (Mauritzen et al. 2001; Lone, Aars & Ims 2012). We categorized the quality of habitat available to bears based on their movement patterns or capture positions. A resource selection function (RSF) for bears in the Barents Sea subpopulation (Lone et al., under review) was used to predict the distribution of high quality habitat during four periods preceding each capture effort

228 (September 2011-March 2012, April 2012-August 2012, September 2012-March 2013, April
229 2013-August 2013). The seasonal RSF models, which are based on telemetry data from 224
230 females between 1991 and 2015, predict the probability of use of a habitat based on sea ice
231 concentration, distance to the ice edge and ocean depth (Lone et al., under review). Daily
232 predictions were classified as habitat or non-habitat using a cut-off corresponding to 70% of all
233 polar bear positions occurring in pixels classified as habitat, and these daily maps were summed
234 across each period of interest. According to these maps produced using RSF, the western coast
235 of Svalbard has fewer habitat days in all four periods compared to the eastern side (**Figure S1**).
236 Therefore, we divided Svalbard into two relative habitat categories with the western side
237 considered as a poor quality habitat and the eastern side as a good quality habitat (**Figure S1**).
238 Among the 78 individual bears used in this study, 59 were equipped with satellite telemetry
239 collars during the study period or previous years. For these bears, we used location data to
240 determine whether they used the good or poor habitats (**Figure S1**). For the bears without
241 collars, we used the capture position during the study period to determine if they were using
242 good or poor habitats. Seventy-nine females were assigned to the "eastern good quality habitat"
243 and 33 to the "western poor quality habitat".

244 STATISTICS

245 PFAS concentrations were log transformed (*ln*) because of left-skewed distributions, and
246 continuous predictor variables such as stable isotopes in plasma and red blood cells,
247 urea:creatinine, BCI, age and FA PCs were standardized (mean = 0, SD = 1) before analysis to
248 facilitate the comparison of effect sizes (Gelman and Hill, 2006). Values below LOD were
249 replaced by ½ LOD. Creatinine was above LOD in all samples, whereas urea values were below
250 LOD in 26 samples (**Table 1**). Except for PFDoDA, PFASs in the 112 samples were above

LOD (**Table 1**). We conducted statistical analyses using R version 3.2.1 (R Core Team, 2016). We used generalized linear mixed models (GLMMs; R-package *nlme* version 3.1-121, Pinheiro *et al.*, 2015) with female identity (female ID) as a random factor to test whether plasma concentrations of PFASs were affected by individual characteristics and environmental factors. To do so, we selected 42 biologically relevant models (**Table S1**). We used an information-theoretic approach (Burnham and Anderson, 2004) based on Akaike's information criterion corrected for small sample size (AICc, R package *MuMIn,* Barton, 2016). We calculated the number of parameters (K), the difference in AICc values between the "best" model and the model at hand (ΔAICc) and a normalized weight of evidence in favor of the specific model, relative to the whole set of candidate models, derived by $e^{(-0.5(\Delta AICc))}$ (AICc weights). We used model averaging to make inference from all the models. This method produces averaged estimates of all predictor variables in the candidate model list (**Table S1**), weighted using the AICc weights (Burnham and Anderson, 2003; Lukacs et al., 2009). From this, we obtained conditional parameter-averaged estimates (β) and 95% confidence intervals (CIs) for all the predictors included in the models. We used 95% CI of the model averaged estimates to determine if parameters were significantly different from 0 at the 5% level, 95% CI provide information about a range in which the true value lies with a certain degree of probability, as well as about the direction and strength of the demonstrated effect (du Prel et al., 2009). If the 95% CI does not include the value of zero effect, it can be assumed that there is a statistically significant result. We used Redundancy analysis (RDA, R-package *ade4* version 1.7-4, Dray and Dufour, 2007) to illustrate the relationship between response variables (individual PFASs) and predictors (stable isotopes in plasma and red blood cells, urea:creatinine, BCI, age and FA PCs). RDA is a method to extract and summarize the variation in a set of response variables (PFAS concentrations) that can be explained by a set of explanatory variables (Legendre and

275 Anderson, 1999; Ramette, 2007). More specifically, it summarizes the response variables'
276 variance explained by a set of explanatory variables using linear relationships (Legendre and
277 Anderson, 1999; Ramette, 2007). To investigate the overlapping effect of habitat quality and
278 season on PFAS concentrations we used least squares means method (LSM, R-package
279 *lsmeans,* Lenth and Hervé, 2015).

280 **RESULTS AND DISCUSSION**

281 ***PFAS concentrations***

282 On average, PFOS accounted for 67.6% of total plasma PFAS concentration in female polar
283 bears of the present study. Then followed by decreasing order: 9.9% PFNA, 8.8% PFHxS, 6.4%
284 PFUnDA, 3.1% PFDA, 2.1% PFTrDA, 1.3% PFOA and 0.8% PFDoDA. PFAS concentrations
285 (ng/g wet weight) are presented in **Table 1**.

286 In the same females, plasma concentrations of PCBs and their metabolites (OH-PCBs) were
287 recently reported (Tartu et al., 2017). In comparison, plasma PFOS concentrations were 5.8-
288 and 3.6-fold higher than plasma Σ_{16}PCBs and Σ_{8}OH-PCBs (39.9 and 56.1 ng/g ww,
289 respectively; see Tartu et al. (2017) for a detailed list of the congeners included in the sums
290 above). In most polar bear subpopulations, including the Barents Sea, previous studies have
291 reported the dominance of PFOS among PFASs (Bytingsvik et al., 2012b; Smithwick et al.,
292 2005a). Svalbard female polar bears sampled in 2008 had similar proportions of PFASs (PFOS
293 > PFNA > PFHxS > PFUnDA > PFDA > PFTrDA > PFOA > PFDoDA) (Bytingsvik et al.,
294 2012b).

295 ***PFASs increase with trophic level and proportion of marine diet***

296 Concentrations of all PFASs increased with the trophic level of the female polar bears, as
297 inferred from $\delta^{15}N$ values in red blood cells and plasma (**Figure 1A-2, Table 2**). This is in
298 accordance with previous studies showing biomagnification of PFASs in Arctic marine
299 ecosystems (Haukås et al., 2007; Kelly et al., 2009; Tomy et al., 2004). In our study, PFAS
300 concentrations were positively related to sources of primary productivity (i.e. $\delta^{13}C$ values) in
301 red blood cells but not in plasma (**Figure 1A-2, Table 2**). In polar bears the half-lives of $\delta^{15}N$
302 and $\delta^{13}C$ in red blood cells and plasma $\delta^{15}N$ (weeks to months) are longer than those of plasma
303 $\delta^{13}C$ (~10 days) (Rode et al., 2016). Considering that, our results indicate that plasma PFAS
304 concentrations in polar bears reflect exposure over the past weeks/months rather than over the
305 past days. The higher PFAS exposure in female polar bears from Svalbard having a more
306 marine based diet is in accordance with previous studies that report higher PFAS concentrations
307 in marine than in terrestrial prey (Kelly et al., 2009; Müller et al., 2011). Prior to capture, several
308 of the females from the present study were observed feeding on whale carcasses, walruses,
309 seabirds, geese or reindeers (Tartu et al., 2016), which is also in accordance with previous
310 studies showing the opportunistic and highly variable diet of polar bears (Aars et al., 2015;
311 Dyck and Romberg, 2007; Gormezano and Rockwell, 2015, 2013; Iversen et al., 2013; Iverson
312 et al., 2014; Prop et al., 2015, 2013; Rogers et al., 2015; Smith et al., 2010; Stempniewicz, 2006,
313 1993; Stempniewicz et al., 2014).

314 The FA composition as inferred by FA PC2 and FA PC3, correlated positively and negatively,
315 respectively with PFUnDA, PFDoDA and PFTrDA (**Figure 3, Table 2**). These results were
316 expected as FA PC2 and FA PC3 respectively correlated positively and negatively with stable
317 isotopes (**Table S2**). Yet, for FA PC2, the significance of the relationships with PFCAs were
318 driven by two outliers, and the correlation was not significant when the outliers were removed

(PFUnDA: β=0.28, 95% CI [-0.09, 0.66], PFDoDA: β=0.33, 95% CI [-0.05, 0.70] and PFTrDA: β=0.27, 95% CI [-0.08, 20.62]). We should therefore remain cautious when interpreting the FA PC2 results. The individual FAs that contributed most to FA PC3 were mainly saturated and monounsaturated FAs (see list in the method section). This suggests that C_{11}-C_{13} PFASs could be in lower proportion in prey with larger proportions of saturated and monounsaturated FAs. In polar bears, FA composition is a product of both diet and lipid metabolism so both factors may affect PFASs (Iverson et al., 2004). In addition, longer chained PFCAs possess higher log K_{ow} (octanol-water partition coefficient) values, indicating that they have an increased solubility in lipid-soluble environments (Greaves et al., 2012). It has been suggested that long-chain PFCAs greatly resemble saturated FAs (Greaves et al., 2012), this could explain the relationships between PFASs and FA composition.

There is a great uncertainty regarding future temporal trends in polar bears PFAS concentrations in relation to the ongoing climate change and its effects on polar bears diet and energetic metabolism. While a diet shift towards more land-based lower trophic level (Gormezano and Rockwell, 2013; Prop et al., 2015) is likely to diminish their exposure to PFAS, the increasing proportion of fasting bears due to melting sea ice (Cherry et al., 2009) may lead to increased PFAS concentrations in plasma.

High PFAS concentrations in fasting polar bears

In this study, urea:creatinine ratios were negatively related to plasma PFHxS, PFOS, PFOA, PFNA and PFDA concentrations (**Figure 4, Table 2**). Low values of urea:creatinine indicate a fasting state (i.e. urea:creatinine ≤ 47.5 using molar concentrations), females in a fasting state had PFAS concentrations that were 1.18-1.47 fold higher than in feeding females (urea:creatinine > 47.5) . When fasting, bears can conserve their protein pool by recycling urea

342 nitrogen into plasma proteins (Nelson et al., 1975) and previous studies in polar bears have
343 reported increased concentrations of β-globulins in plasma of fasting polar bears (Cattet, 2000).
344 Considering that PFAS bind to proteins, an increased proportion of proteins in blood could
345 explain the higher PFHxS, PFOS, PFOA, PFNA and PFDA concentrations in fasting female
346 polar bears. Yet, in hooded seals and human, protein concentrations in plasma were not an
347 explanatory factor for PFAS variation (Butenhoff et al., 2012; Grønnestad et al., 2016). An
348 alternative explanation could be that metabolic rate and contaminant excretion are reduced in
349 fasting animals (Aas et al., 2014). In female polar bears we observed no significant relationships
350 between BCI and PFASs although BCI was selected among the best models (ΔAICc<2) for
351 PFHxS, PFOA, PFDoDA and PFTrDA (**Table S3**). While body condition was a stronger
352 predictor than diet for the concentrations of lipophilic pollutants (Tartu et al., 2017), PFAS
353 concentrations were not affected by body condition. Noticeably, BCI was not related to
354 urea:creatinine (β=0.38, 95% CI [-2.95, 2.19]) which could result from a mismatch between
355 blood parameters (e.g. urea and creatinine) and the lag for adipose tissue accumulation. Indeed,
356 in spring, polar bears are on average thinner after a winter period with low prey availability but
357 they are also feeding as ringed seal pups are abundant (Cattet, 2000; Derocher et al., 1990;
358 Lønø, 1970). In contrast, in autumn, polar bears still have large fat reserves after the intensive
359 feeding period in spring and early summer, but a larger proportion of individuals may be fasting
360 due to the absence of sea ice and thus less access to seals (Cattet, 2000; Derocher et al., 1990;
361 Lønø, 1970). These seasonal variations in body fat and metabolic state were also observed in
362 the females from the present study; females were fatter and a larger proportion were fasting in
363 September compared to April (BCI: β= 0.55, 95%CI [0.32; 0.79] and urea:creatinine: β= -0.45,
364 95%CI [-0.75; -0.15]).

365 ***PFASs in relation to sea ice condition***

366 Concentrations of PFOS and C_9-C_{13} PFCAs were higher in polar bears from eastern part of
367 Svalbard, where habitat quality was higher than in females from the western part of Svalbard,
368 where the habitat quality was poorer (**Figure 1B-S1, Table 2**). These results support previous
369 findings showing that PFAS concentrations in polar bears increased as home ranges covered
370 areas more eastwards of Svalbard (van Beest et al., 2015). This pattern could result from the
371 combination of differences in energy need, prey availability and abiotic factors affecting PFAS
372 cycling (e.g. sea ice extent). The eastern coast of Svalbard experiences large amplitude of sea
373 ice retreat during summer in comparison to the western coast that is often ice free year-long
374 (Hop et al., 2000; Pavlova et al., 2014; Vinje and Kvambekk, 1991). The home range size might
375 also influence contaminant intake, as a larger home range requires greater energy expenditure
376 and thus higher food intake leading to a higher total intake of contaminants (Mauritzen et al.,
377 2001; Olsen et al., 2003).

378 Diet variation in polar bears from different areas from Svalbard may also affect their PFAS
379 uptake. In a previous study using the same data set (Tartu et al., 2016), the authors divided
380 captured females into three groups according to the geographical area they were captured in
381 (see Figure 1 in Tartu et al., 2016). In Svalbard, large variations in sea-ice cover occur between
382 the north-west (poor sea-ice cover) and the south-east (large amplitude of sea-ice cover),
383 whereas sea ice around Nordauslandet and south Spitsbergen is extended and stable. Variations
384 in diet proxies according to the three geographical areas in Svalbard have been described in
385 details previously (Tartu et al., 2016). In this study, we used habitat quality based on RSF to
386 divide geographically the captured females (**Figure S1**). Our results indicate that females using
387 the eastern, high quality habitat had higher δ^{15}N values in red blood cells (LSM, β=0.51, 95%CI

[0.17; 0.85]) and were in better body condition (LSM, β=0.47, 95%CI [0.18; 0.76]) than females using the western, lower quality habitat. Hence, our findings indicate that females using the eastern habitat could have access to a higher quantity of preferred prey such as ringed and bearded seals. Ringed and bearded seals are more contaminated than terrestrial prey thought to be consumed in larger proportions by females using the poorer quality western habitat (Müller et al., 2011; Tartu et al., 2016). An access to different type of prey between females using different habitats could explain the higher concentration of more bioaccumulative PFASs such as PFOS and C_9-C_{13} PFCAs in eastern females (Kelly et al., 2009). These geographic differences present an ecological and physiological conundrum: bears that choose to use regions where the prey base is of higher quality-seals in eastern Svalbard, are inadvertently assimilating prey that are highly contaminated; thus, although they are fatter, their vulnerability to being contaminated is dramatically different.

Interestingly, we observed higher concentrations of PFNA and PFDA in autumn compared to spring (**Table 2**). Yet, this result only appeared significant in females captured in the eastern habitat (LSM, PFNA: β= -0.27, 95%CI [-0.45; -0.09] and PFDA: β= -0.23, 95%CI [-0.41; -0.06], **Figure 5A**) and not in females captured in the western habitat (LSM, PFNA: β= -0.01, 95%CI [-0.27; 0.25] and PFDA: β= 0.10, 95%CI [-0.14; 0.33], **Figure 5A**). Although δ^{15}N values in red blood cells were not season dependent in females from the eastern habitat (LSM, β= 0.08, 95%CI [-0.26; 0.41]), plasma δ^{15}N and δ^{13}C values were higher in spring compared to autumn (LSM, β= 0.60, 95%CI [0.22; 0.98] and β=1.32, 95%CI [0.94; 1.69], respectively, **Figure 5B**). Consequently, in summer, female polar bears from eastern Svalbard could ingest a larger proportion of lipid rich terrestrial food source such as waterfowl eggs (Tartu et al., 2016). Feeding on terrestrial species would result in a decrease in δ^{13}C values and a

411 modification of PFAS composition as PFAS proportions in terrestrial prey (e.g waterfowl eggs)
412 are likely different from those in seal species (Eriksson et al., 2016; Tomy et al., 2004).

413 In female polar bears, relationships between PFAS concentrations, habitat quality and season
414 may also be influenced by other abiotic factors. PFASs are generally more concentrated in
415 surface snow than in seawater, due to a dilution effect (Kwok et al., 2013). In addition, the
416 surface load (ng/m^2) of C_6-C_8 PFSAs and C_{10}-C_{12} PFCAs increases in the snowpack during snow
417 melting (Codling et al., 2014). In areas where sea ice cover is more extended, PFASs and their
418 precursors that are transported in the atmosphere are deposited on the sea ice from which they
419 are released into the seawater during melting periods. Pollutants released in seawater are then
420 assimilated by the food web. The sea ice melt is followed by a sharp increase in phytoplankton
421 biomass. Once the pollutants are assimilated by phytoplankton, the latter are consumed by the
422 copepod *Calanus glacialis*, a key Arctic planktonic herbivore, which is an important food item
423 for higher trophic levels (Leu et al., 2011; Søreide et al., 2010). In contrast, in areas with less
424 or no sea ice, PFAS deposition will more rapidly be diluted into seawater. Concentrations of
425 several PFAS are therefore expected to be higher in food webs from areas where sea ice extent
426 is subjected to a larger amplitude, such as the eastern habitat. This could also contribute to the
427 observed seasonal variation in PFAS concentrations between females using the eastern versus
428 those using the western habitats.

429 ***PFOS and breeding status***

430 Breeding status predicted PFOS concentrations in plasma (**Table 2**). We observed higher PFOS
431 concentrations in females with cubs of the year (COYs) than in solitary females (**Table 2**).
432 Although the other PFASs did not vary between breeding statuses, C_{10}-C_{13} PFCAs tended to be

433 higher in females with COYs than in solitary ones. PFAS concentrations in females with
434 yearlings were not different from any of the latter two groups (**Table 2**).

435 The high plasma PFOS concentrations in females with COYs could be related to an increased
436 protein synthesis for milk production coupled to a low metabolic state. Indeed, female polar
437 bears produce large quantities of milk for COYs (Arnould and Ramsay, 1994) and during
438 lactation, the activity of some lipoproteins, such as the lipoprotein lipase (LPL) increases
439 (Iverson et al., 1995; McBride and Korn, 1963; Mellish et al., 1999). LPL is critical for the
440 uptake and secretion of FA in milk (Hamosh et al., 1970). We therefore postulate that increased
441 lipoprotein synthesis related to lactation will increase the protein pool in females' body, which
442 will result in a higher proportion of PFOS bound proteins in plasma. In addition, females with
443 COYs may have been fasting for up to 6 months when they emerge from their dens in March
444 to April (Andersen et al., 2012) and as observed from the present results, a fasting state is related
445 to higher PFAS concentrations (**Table 2**). The high PFOS concentrations in females with COYs
446 are unlikely related to differences in feeding patterns between the females of different breeding
447 statuses. Indeed, females with COYs rather feed at a lower trophic level than solitary females,
448 although results were not statistically significant (Tartu et al., 2016). According to numerous
449 studies on murine and simian models, PFOS is highly toxic to mammals (Lau et al., 2004).
450 Consequently, females with COYs could be more at risk considering they have an increased
451 energy demand and are in poorer body condition compared to solitary females (data not shown).

452 ***PFOA and age***

453 In the present study, the age of female polar bears predicted a decrease of 1.14 ng/g ww per
454 year in PFOA concentrations whereas other PFASs were not related to age (**Table 2**). The
455 relationships between PFAS and age are inconsistent across wildlife. In polar bears from four

other subpopulations, hepatic concentrations of PFOS and C_8-C_{14} PFCAs increased with age (Smithwick et al., 2005a, 2005b), blood PFOA concentrations and age were not related in southern Beaufort Sea polar bears (Bentzen et al., 2008) and blood PFSA increased with increasing age in East Greenland polar bears (Greaves et al., 2012). In other marine mammals, such as ringed seals and beluga whales (*Delphinapterus leucas*), plasma PFAS concentrations were not related to age (Butt et al., 2008; Kelly et al., 2009; Routti et al., 2016), whereas in bottlenose dolphins (*Tursiops truncatus*), plasma concentrations of PFSAs decreased with age (Fair et al., 2012). The reason for age-PFOA relationships in polar bears is unclear and may be related to other confounding factors (e.g. age-related hormonal changes) not taken into account in this study.

CONCLUSIONS

Considering all the potential health effects of PFAS, it is important to increase knowledge on the underlying drivers of PFAS concentrations in polar bears. This study demonstrates that diet is the strongest predictor for circulating PFAS concentrations in Svalbard female polar bears, with individuals feeding at a higher trophic level and more marine prey being more exposed to PFASs. Diet is also a likely factor explaining seasonal and spatial differences in plasma PFAS concentrations in polar bears from Svalbard. PFAS concentrations were higher in fasting than in feeding female polar bears. The higher PFOS levels in females with COYs are likely related to both metabolic state and milk production. In conclusion, our findings suggest that feeding on high trophic level marine prey, fasting and having COYs are all factors that may lead to high PFAS exposure among adult female polar bears. The health effects of PFAS are numerous, but considering their disruption potential on lipid metabolism and the importance of storage and utilization of lipids in Arctic wildlife, further studies should focus on the relationships between

PFAS and energetic metabolism of polar bears and whether climate changes reinforces or not these relationships.

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Table 1: Biological parameters, PFAS concentrations, proxies for diet and metabolic state in 112 female polar bears representing 78 individuals sampled in Svalbard (2012-2013). We show averages and median values followed by the range (min-max). Limits of detection (LOD) and the number of samples for which values were below LOD (n<LOD) are given for PFASs, urea and creatinine. PFASs' abbreviations are followed by their carbon chain length. Metabolic state proxies were measured in 111 females representing 77 individuals. [a]The ratio is in molar concentration, ratios ≤ 47.5 correspond to fasting individuals.

	Spring		Autumn		LOD (n<LOD)
	n	average/median (min; max)	n	average/median (min; max)	
Age	62	13.2/12 (4;28)	50	12.7/10.5 (5;28)	
Body condition index	62	-1.46/-1.42 (-3.09;0.08)	50	-1.17/-0.93 (-2.61;-0.03)	
PFSAs (ng/g wet weight)					
PFHxS (C_6)	62	28.6/27.6 (5.5;65.3)	50	32.4/31.3 (11.0;70.7)	0.200 (0)
PFOS (C_8)	62	221/196.8 (54;593.2)	50	248.7/243.6 (40.1;622.2)	0.200 (0)
PFCAs (ng/g wet weight)					
PFOA (C_8)	62	4.6/4.2 (1;12.4)	50	4.8/4.4 (0.8;13)	0.050 (0)
PFNA (C_9)	62	30.4/27.2 (10;78.8)	50	38.8/35.3 (9.3;90.5)	0.160 (0)
PFDA (C_{10})	62	9.7/8.5 (2.8;25.9)	50	12.2/10.8 (2.2;31.3)	0.200 (0)
PFUnDA (C_{11})	62	20.8/18.4 (7;51.8)	50	24.1/23.6 (3.4;58.1)	0.250 (0)
PFDoDA (C_{12})	62	2.6/2.5 (0.9;6.3)	50	2.8/3 (LOD;7.2)	0.400 (1)
PFTrDA (C_{13})	62	6.9/5.8 (2.2;23.2)	50	7.4/7 (1.3;17.4)	0.500 (0)
Diet proxies					
$\delta^{15}N$ plasma	62	17.9/18 (15.1;19.2)	50	16.7/16.9 (12.4;20.1)	
$\delta^{13}C$ plasma	62	-20.3/-20.2 (-22.3;-19)	50	-21.2/-21 (-23.9;-17.6)	
$\delta^{15}N$ rbc	62	16.0/16.3 (12.7;18.3)	50	15.5/15.7 (12.2;17.6)	
$\delta^{13}C$ rbc	62	-20.0/-19.8 (-22.3;-19)	50	-20.0/-19.9 (-21.8;-18.9)	
Metabolic state					
Urea (mmol/l)	61	6.7/6.5 (LOD; 16.4)	50	5.0/4.12 (LOD;18.7)	3.33 (26)
Creatinine (µmol/l)	61	86.5/82.3 (54.9;159.0)	50	135.2/131.0 (59.3;221.0)	44.50 (0)
Urea:Creatinine[a]	61	83.4/76.3 (11.4;241.3)	50	43.5/27.7 (8.4;145.6)	

Table 2: Relationships between PFAS concentrations and diet proxies as stable nitrogen and carbon isotopes (δ^{15}N and δ^{13}C, respectively) in plasma and red blood cells (rbc), metabolic state (urea:creatinine), habitat quality, sampling season and year, body condition, age and breeding status (defined as solitary females (solitary), females with cubs of the year (with COYs) or females with yearlings (YRLs)). Adult female polar bears were capture in Svalbard (2012-2013). As urea and creatinine concentrations were not available for one female, conditional model averaging analyses were run on 111 samples from 77 individuals except in models including fatty acid principal components (FA PCs: 82 samples from 63 individuals). Values are parameter estimates and 95% confidence intervals derived from conditional model averaging of general linear mixed models that included female identity as a random factor. Values in bold are significantly different from 0 at the 5% level. COYs: cubs of the year.

	PFHxS	PFOS	PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA
Intercept (n=111)	**3.30 [3.2; 3.41]**	**5.38 [5.27; 5.49]**	**1.41 [1.32; 1.5]**	**3.45 [3.36; 3.54]**	**2.31 [2.22; 2.41]**	**3.02 [2.91; 3.13]**	**0.91 [0.8; 1.02]**	**1.83 [1.72; 1.94]**
δ^{15}N plasma	**0.11 [0.02; 0.19]**	**0.11 [0.03; 0.19]**	**0.20 [0.10; 0.29]**	0.08 [0; 0.16]	**0.12 [0.04; 0.20]**	**0.22 [0.13; 0.3]**	**0.27 [0.18; 0.36]**	**0.31 [0.22; 0.4]**
δ^{15}N rbc	**0.15 [0.05; 0.24]**	**0.17 [0.08; 0.27]**	**0.26 [0.17; 0.35]**	**0.13 [0.05; 0.22]**	**0.18 [0.09; 0.27]**	**0.28 [0.18; 0.37]**	**0.32 [0.22; 0.42]**	**0.37 [0.27; 0.47]**
δ^{13}C plasma	0.01 [-0.08; 0.10]	-0.03 [-0.11; 0.06]	0 [-0.11; 0.11]	-0.05 [-0.13; 0.04]	-0.03 [-0.12; 0.05]	-0.04 [-0.14; 0.06]	0.01 [-0.09; 0.11]	0.04 [-0.07; 0.15]
δ^{13}C rbc	**0.15 [0.06; 0.25]**	**0.14 [0.05; 0.22]**	**0.23 [0.14; 0.32]**	**0.16 [0.08; 0.24]**	**0.18 [0.10; 0.26]**	**0.20 [0.10; 0.30]**	**0.22 [0.12; 0.32]**	**0.25 [0.14; 0.36]**
Urea:Creatinine	**-0.10 [-0.18; -0.02]**	**-0.11 [-0.18; -0.04]**	**-0.12 [-0.21; -0.04]**	**-0.14 [-0.21; -0.06]**	**-0.12 [-0.19; -0.04]**	-0.07 [-0.15; 0.01]	-0.03 [-0.11; 0.06]	-0.03 [-0.11; 0.06]
Habitat (West vs East)	-0.08 [-0.34; 0.18]	**-0.41 [-0.67; -0.14]**	-0.15 [-0.41; 0.12]	**-0.30 [-0.53; -0.06]**	**-0.38 [-0.65; -0.1]**	**-0.36 [-0.63; -0.09]**	**-0.47 [-0.78; -0.16]**	**-0.51 [-0.86; -0.16]**
Season (Autumn vs Spring)	0.13 [-0.09; 0.34]	0.05 [-0.13; 0.22]	0.15 [-0.21; 0.51]	**0.28 [0.07; 0.49]**	**0.22 [0.02; 0.41]**	0.13 [-0.05; 0.31]	-0.05 [-0.26; 0.17]	-0.04 [-0.26; 0.19]
Year (2013 vs 2012)	0.09 [-0.13; 0.32]	-0.01 [-0.19; 0.17]	**0.22 [0.01; 0.44]**	**0.27 [0.06; 0.48]**	0.15 [-0.06; 0.36]	0.10 [-0.13; 0.34]	0.08 [-0.2; 0.35]	0.19 [-0.07; 0.46]
Body condition index	-0.06 [-0.14; 0.02]	-0.01 [-0.09; 0.06]	-0.03 [-0.11; 0.06]	0.03 [-0.04; 0.11]	0.02 [-0.06; 0.10]	-0.02 [-0.09; 0.06]	-0.04 [-0.13; 0.04]	-0.03 [-0.12; 0.05]
Age	-0.05 [-0.16; 0.05]	0.06 [-0.05; 0.18]	**-0.13 [-0.22; -0.04]**	0.01 [-0.08; 0.11]	0.04 [-0.06; 0.14]	0.05 [-0.06; 0.16]	0.04 [-0.07; 0.16]	0.01 [-0.11; 0.13]
Breeding status (with COYs vs solitary)	0.10 [-0.09; 0.30]	**0.20 [0.03; 0.38]**	0.16 [-0.27; 0.58]	0.09 [-0.11; 0.30]	0.13 [-0.05; 0.32]	0.17 [-0.03; 0.36]	**0.22 [0.005; 0.428]**	0.22 [-0.001; 0.441]
Breeding status (with YRLs vs solitary)	-0.07 [-0.32; 0.18]	0.06 [-0.16; 0.28]	-0.02 [-0.40; 0.36]	0.09 [-0.16; 0.34]	0.10 [-0.12; 0.33]	0.09 [-0.15; 0.33]	0.11 [-0.14; 0.37]	0.08 [-0.19; 0.36]
Intercept (n=82)	**3.29 [3.15; 3.42]**	**5.35 [5.22; 5.49]**	**1.40 [1.27; 1.53]**	**3.42 [3.31; 3.54]**	**2.27 [2.15; 2.4]**	**2.98 [2.85; 3.11]**	**0.87 [0.74; 1]**	**1.8 [1.67; 1.93]**
FA PC1	0.01 [-0.07; 0.09]	-0.02 [-0.1; 0.07]	0.01 [-0.11; 0.13]	-0.08 [-0.18; 0.03]	-0.05 [-0.15; 0.05]	0 [-0.11; 0.10]	0.03 [-0.08; 0.15]	0.03 [-0.08; 0.15]
FA PC2	-0.01 [-0.11; 0.09]	0.04 [-0.07; 0.15]	0.10 [-0.02; 0.23]	0.03 [-0.08; 0.15]	0.03 [-0.08; 0.15]	**0.12 [0.003; 0.239]**	**0.17 [0.05; 0.29]**	**0.18 [0.06; 0.3]**
FA PC3	-0.05 [-0.15; 0.05]	-0.06 [-0.17; 0.04]	-0.09 [-0.22; 0.03]	-0.06 [-0.17; 0.05]	-0.11 [-0.22; 0]	**-0.20 [-0.31; -0.08]**	**-0.23 [-0.35; -0.12]**	**-0.26 [-0.38; -0.15]**

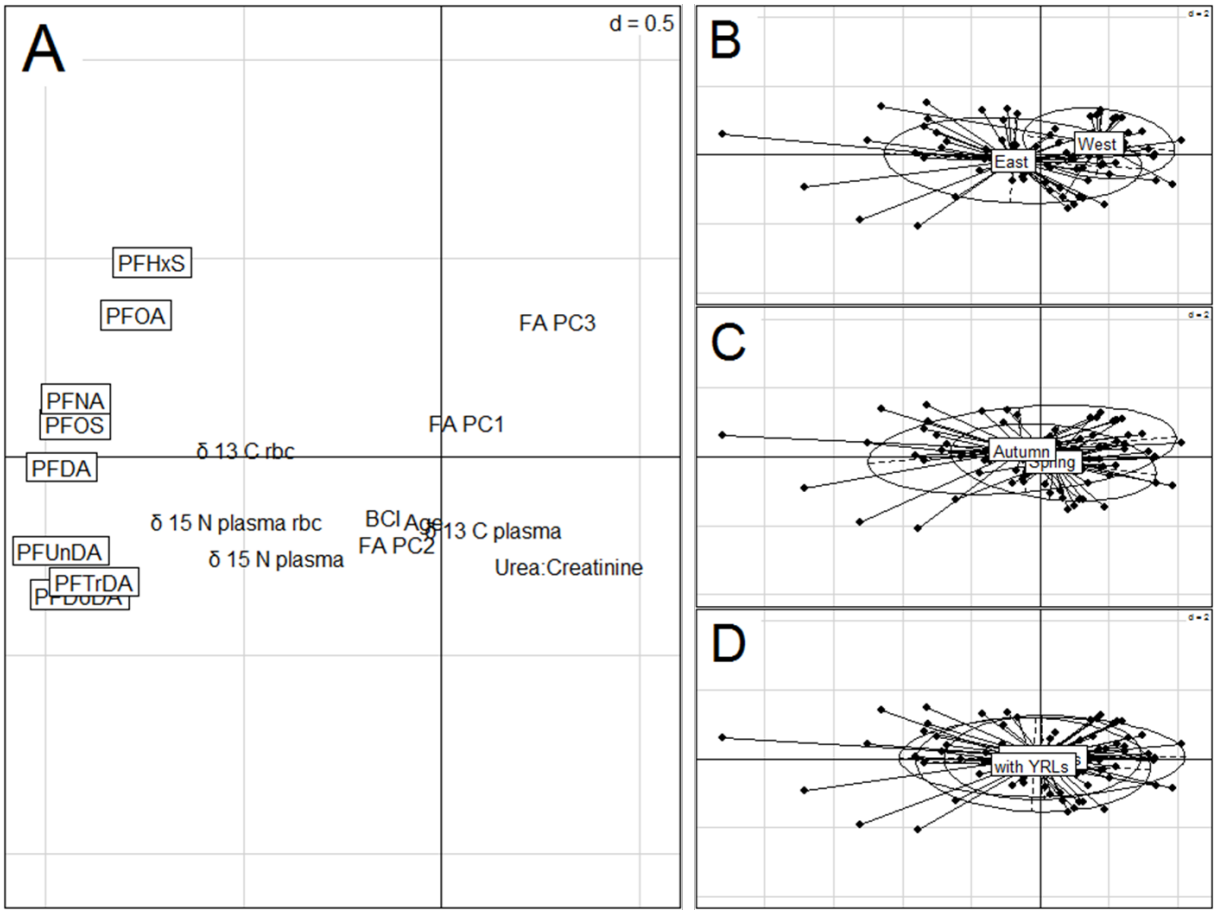


Figure 1: A-Correlation plot from redundancy analysis (RDA) illustrating relationships between plasma concentrations of PFAS, proxies for diet, body condition, metabolic state and age in female polar bears sampled in Svalbard in spring and autumn 2012-2013 (n=82). Boxed labels (PFAS) represent response variables and unboxed labels explanatory variables. In ordination plots grouped by B- habitat, C- season and D- breeding status. Each dot represents an individual. Individuals with similar PFAS concentrations are near each other and individuals with dissimilar PFAS concentrations are farther from each other. Explanatory variables are age; body condition index (BCI); diet proxies defined as nitrogen (δ^{15}N) and carbon (δ^{13}C) stable isotope values in plasma and red blood cells (rbc), fatty acid principal component scores (FA PC1, 2 and 3) in adipose tissue; metabolic state proxy is defined as urea to creatinine ratio (Urea:Creatinine).

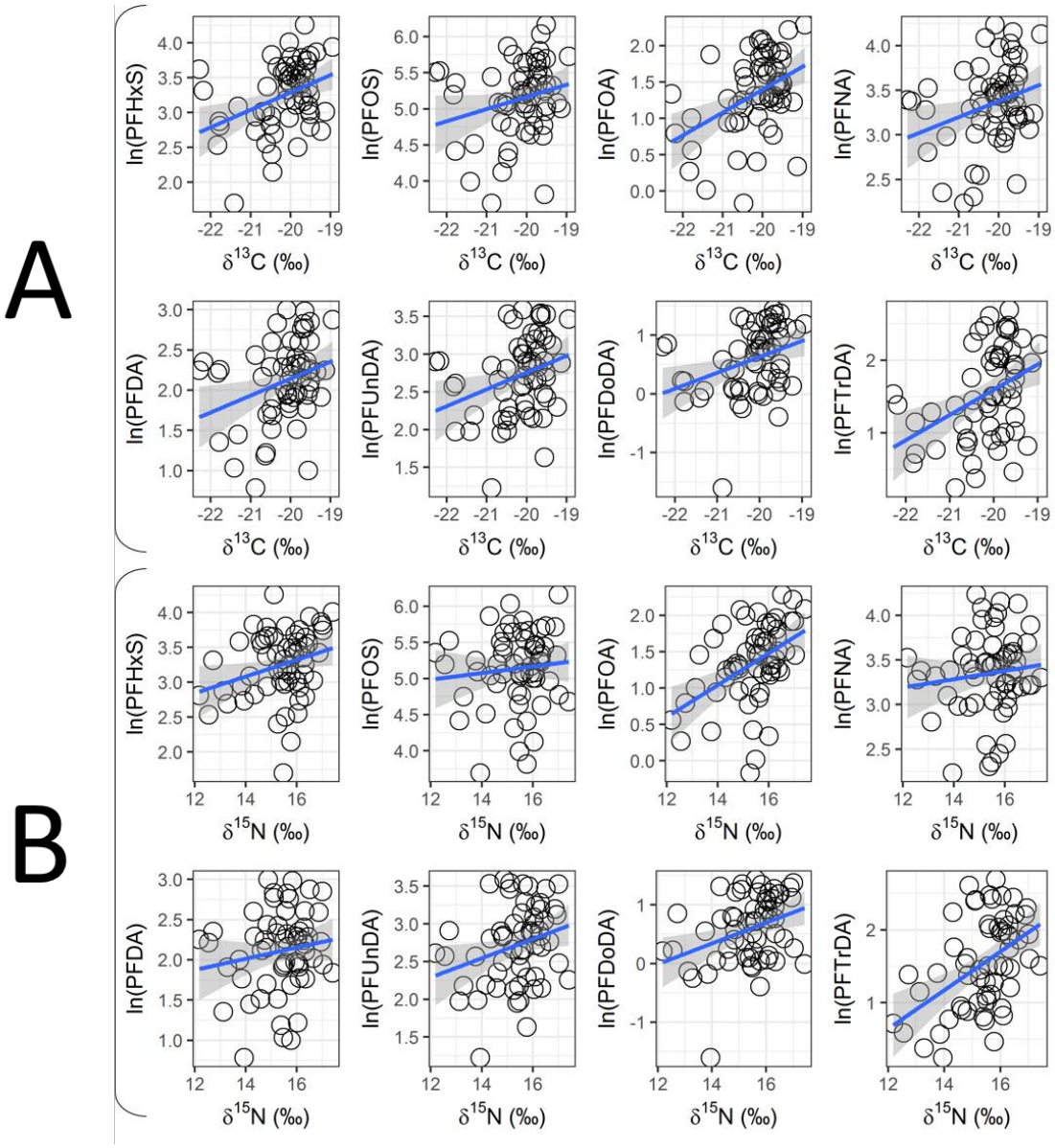
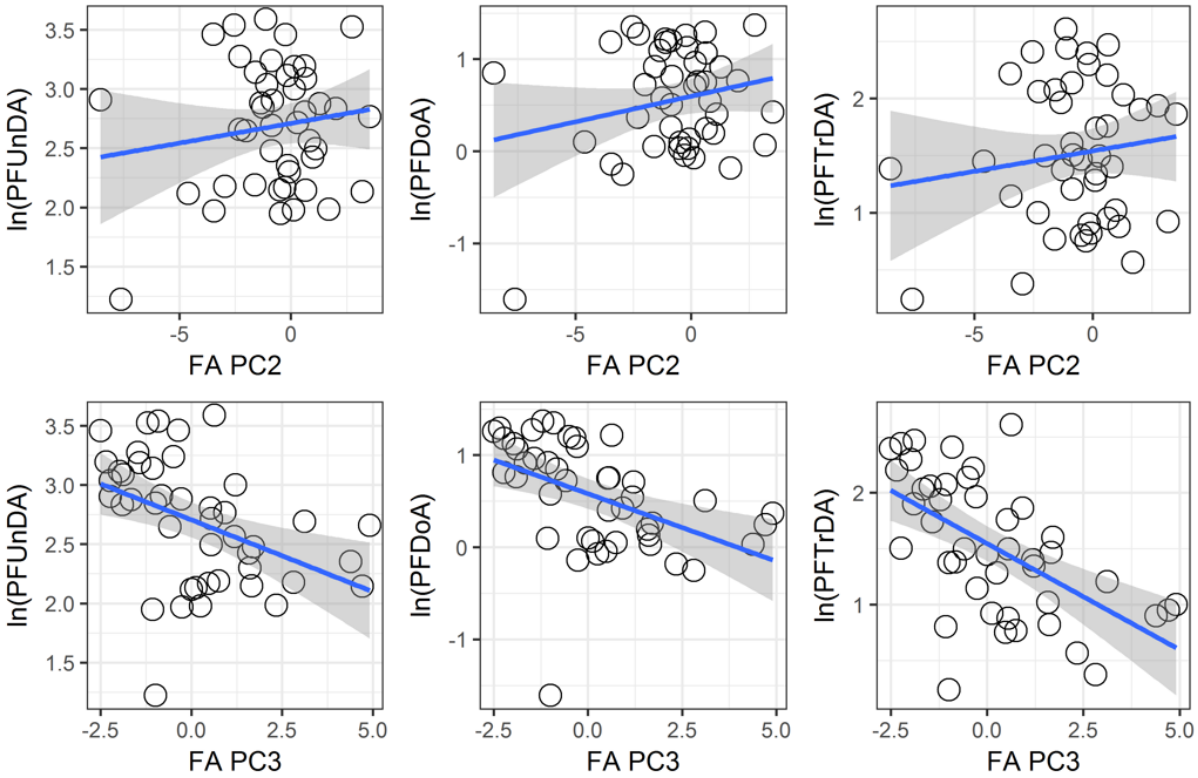


Figure 2: Relationship between PFAS (ng/g wet weight) in plasma and A- carbon ($\delta^{13}C$) and B- nitrogen ($\delta^{15}N$) stable isotope values (‰) in red blood cells. Female polar bears were sampled in Svalbard in 2012-2013. Plots show individuals (n=112), regression lines and shaded area 95% confidence interval.



18

19 **Figure 3:** Relationships between PFAS in plasma (ng/g ww) and the fatty acid principal

20 component scores 2 and 3 (FA PC2, FA PC3). Fatty acids were measured in adipose tissue,

21 female polar bears were sampled in Svalbard in 2012-2013. Plots show individuals (n=83),

22 regression lines and shaded area 95% confidence interval.

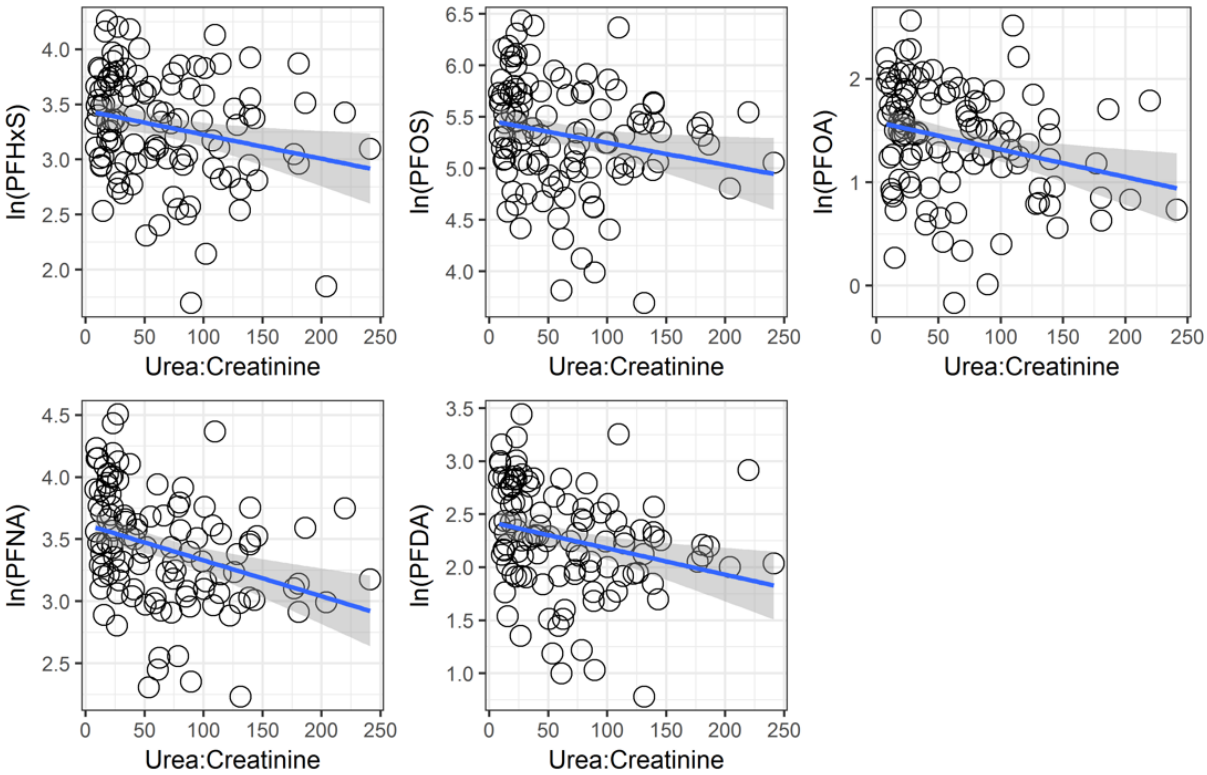


Figure 4: Relationship between plasma PFAS (ng/g wet weight) and plasma urea to creatinine ratio (urea:creatinine). Female polar bears were sampled in Svalbard in 2012-2013. Plots show individuals (n=111), regression lines and shaded area 95% confidence interval.

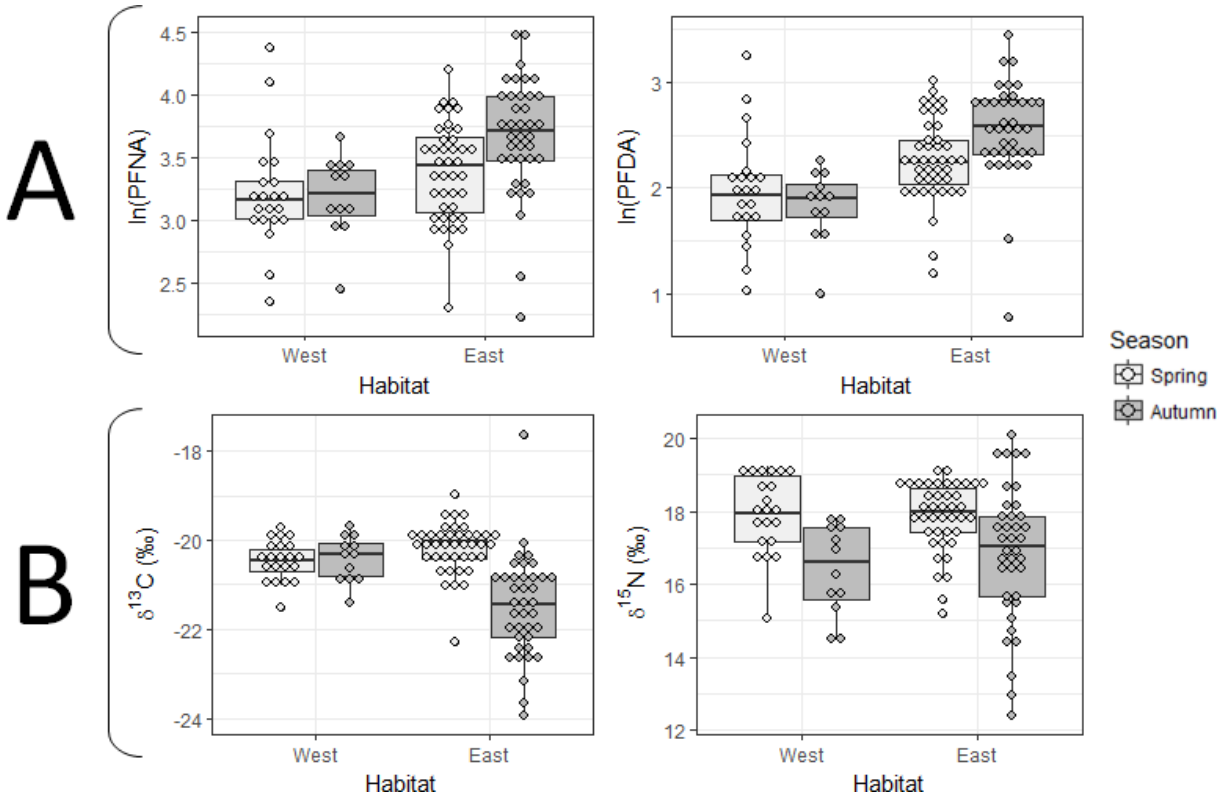


Figure 5: Plasma concentrations of A- PFNA and PFDA and B- stable isotope values according to season and habitat. PFAS are in ng/g wet weight, female polar bears (n=112) were sampled in Svalbard in 2012-2013. Light grey boxes and dots represent females captured in spring (April) and dark grey boxes and dots represent females captured in autumn (September).

SUPPORTING INFORMATION

Diet and metabolic state are the main factors determining concentrations of perfluoroalkyl substances in female polar bears from Svalbard

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Table S1: List of candidate models to explain PFASs variations in Svalbard female polar bears in 2012-2013. Except for models with fatty acids* (n=82), 111 females were included in the models.

Candidate models	Variables
1	Habitat
2	Season
3	Year
4	Status
5	Habitat + Season
6	Habitat + Status
7	Habitat + Year
8	Season + Status
9	Body condition
10	δ^{15}N plasma
11	δ^{13}C plasma
12	δ^{15}N rbc
13	δ^{13}C rbc
14	Body condition + δ^{15}N plasma
15	Body condition + δ^{13}C plasma
16	Body condition + δ^{15}N rbc
17	Body condition + δ^{13}C rbc
18	Age
19	Age + Body condition
20	Age + δ^{15}N plasma
21	Age + δ^{13}C plasma
22	Age + δ^{15}N rbc
23	Age + δ^{13}C rbc
24	Age + δ^{15}N plasma + Body condition
25	Age + δ^{13}C plasma + Body condition
26	Age + δ^{15}N rbc + Body condition
27	Age + δ^{13}C rbc + Body condition
28	Urea:Creatinine
29	Urea:Creatinine + Body condition
30	Urea:Creatinine + Age
31	Urea:Creatinine + δ^{15}N plasma
32	Urea:Creatinine + δ^{13}C plasma
33	Urea:Creatinine + δ^{15}N rbc
34	Urea:Creatinine + δ^{13}C rbc
35	Age + Urea:Creatinine + Body condition + δ^{15}N plasma
36	Age + Urea:Creatinine + Body condition + δ^{13}C plasma
37	Age + Urea:Creatinine + Body condition + δ^{15}N rbc
38	Age + Urea:Creatinine + Body condition + δ^{13}C rbc
39	Fatty acids PC1*
40	Fatty acids PC2*
41	Fatty acids PC3*
42	Null model

Table S2: Relationships between the fatty acid principal components scores (FA PCs) and stable isotope in plasma and red blood cells in female polar bears from Svalbard (2012-2013). Values are parameter estimates and 95% confidence intervals derived from conditional model averaging of general linear mixed models that included female identity as a random factor. Values in bold are significantly different from 0 at the 5% level.

	$\delta^{15}N$		$\delta^{13}C$	
	Plasma	Red blood cells	Plasma	Red blood cells
FA PC1	-0.01 [-0.24; 0.22]	0.11 [-0.16; 0.38]	0.05 [-0.2; 0.3]	0.18 [-0.09; 0.46]
FA PC2	**0.66 [0.45; 0.88]**	**0.53 [0.31; 0.75]**	0.18 [-0.08; 0.45]	**0.33 [0.08; 0.58]**
FA PC3	**-0.45 [-0.7; -0.21]**	-0.45 [-0.69; -0.22]	0.12 [-0.15; 0.38]	-0.1 [-0.37; 0.16]

Table S3: Variables included (×) in the five models with the lowest AICc explaining the concentration of individual PFAS compounds in plasma. All models (linear mixed models) include female identity as a random factor. "ΔAICc" is the difference in AICc between each candidate model and the model with the lowest AICc and "AIC wt" the Akaike weights.

	Explanatory variables						AICc	ΔAICc	AICc wt
Response variables	Age	BCI	δ^{13}C rbc	δ^{15}N rbc	δ^{15}N plasma	Urea: Creatinine			
PFHxS			×			×	130.24	0	0.25
	×	×	×			×	130.62	0.38	0.21
				×		×	130.63	0.4	0.21
	×	×		×		×	132.78	2.54	0.07
					×	×	133.42	3.18	0.05
PFOS				×		×	126.92	0	0.62
	×	×		×		×	130.08	3.17	0.13
					×	×	131.32	4.41	0.07
			×			×	131.37	4.45	0.07
	×	×	×			×	133.34	6.42	0.02
PFOA	×	×		×		×	140.57	0	0.76
				×		×	144.31	3.74	0.12
	×			×			145.42	4.84	0.07
	×	×		×			147.39	6.81	0.03
	×	×	×			×	149.12	8.54	0.01
PFNA			×			×	110.63	0	0.8
				×		×	114.38	3.75	0.12
							116.18	5.55	0.05
	×	×		×		×	118.51	7.88	0.02
			×				121.88	11.25	0
PFDA			×			×	117.68	0	0.65
				×		×	120.55	2.87	0.15
	×	×	×			×	121.47	3.79	0.1
	×	×		×		×	123.19	5.51	0.04
			×				125.08	7.4	0.02
PFUnDA				×		×	131.52	0	0.42
				×			132.88	1.36	0.21
	×			×			134.27	2.75	0.11
		×		×			134.95	3.43	0.08
	×	×		×		×	135.2	3.67	0.07
PFDoDA				×			141.54	0	0.33
		×		×			142.77	1.23	0.18
	×			×			143.28	1.74	0.14
				×		×	143.35	1.81	0.13
	×	×		×			144.52	2.98	0.07
PFTrDA				×			147.32	0	0.36
		×		×			148.91	1.59	0.16
				×		×	149.24	1.92	0.14
	×			×			149.52	2.19	0.12
	×	×		×			151.14	3.82	0.05

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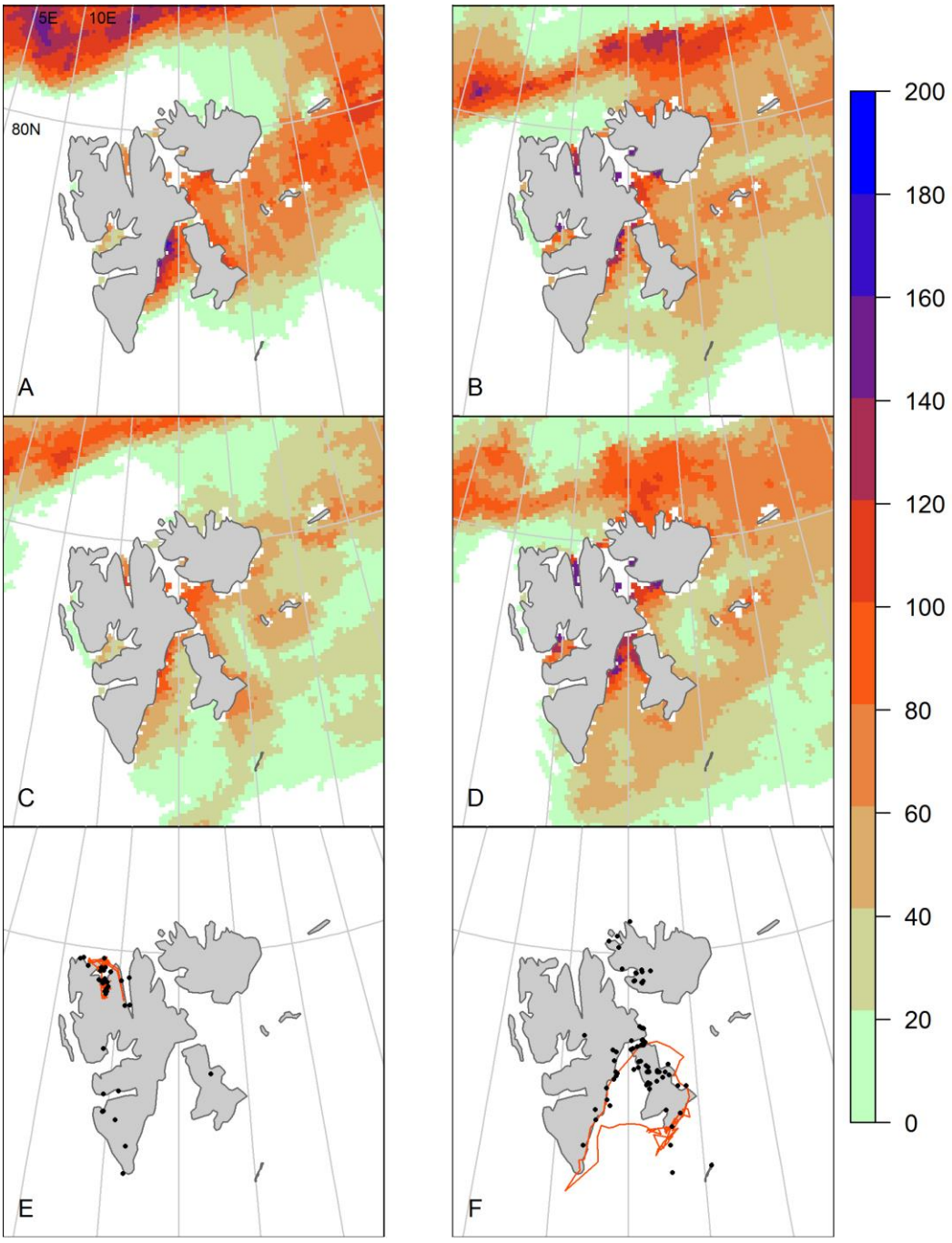

Figure S1: Days with polar bear habitat in the period preceding the four sampling periods, predicted from a resource selection function. The panels for the April sampling periods (A- April 2012, C- April 2013) sum up the days of habitat during the preceding 7 months (September-March), while the panels for the September sampling periods (B- September 2012 and D- September 2013) cover the preceding 5 months (April-August). Triangles represent location of captured females using E- the Western habitat and F- the Eastern habitat, red lines represent telemetry tracks for E- one female using the Western habitat and F- one female using the Eastern habitat. The color scale represents the number of days with optimal polar bear habitat (from 0-20 in green to 180-200 in blue).