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Predictors of human PBDE body burdens for a UK cohort

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1 Abstract

2   Human exposure to polybrominated diphenyl ethers (PBDEs) was investigated in a cohort 3of 20 UK adults along with their anthropometric covariates and relevant properties such as room 4surveys, lifestyle, diet and activity details. Selected PBDE congeners were measured in matched 5samples of indoor dust, (n=41), vehicles (n=8), duplicate diet (n=24), serum (n=24) and breast 6milk (n=6).

7   Combined exposure estimates via dust and diet revealed total PBDE intakes of 104 to 81,440 pg kg^{-1} bw d^{-1} for ΣBDEs$_{3-7}$ and 1,170 to 17,000 pg kg^{-1} bw d^{-1} for BDE-209. These adult 9intakes are well within health reference doses suggested by the European Food Safety Authority 10(EFSA) and the US EPA. For this cohort diet was the primary source of intake of BDE$_{3-7}$ congeners 11for the majority of the cohort, with dust the primary source of BDE-209. Primary sources of PBDE 12exposure vary between countries and regions with differing fire prevention regulations. 13Estimated infant exposures (ages 1.5 to 4.5 years) showed that BDE-99 intake for one of the 14households did not meet EFSA's recommended margin of exposure, a further two households 15were borderline for high level dust and diet intake.

16Males and those having a lower body fat mass had higher serum BDE-153. Higher meat consumption 17was significantly correlated with higher BDEs$_{3-7}$ in serum. A reduction in dietary BDEs$_{3-7}$ would 18therefore result in the greatest reduction in BDE-99 exposure. Rooms containing PUF sofas or 19armchairs over 20 years old had higher BDEs$_{3-7}$ in their dust, and rooms with carpets or rugs of that 20age had higher dust BDE-209. Dusting rooms more frequently resulted in significantly lower 21concentrations of all major congeners in their dust. Correlation between BDE-209 body burden and 22dust or diet exposure was limited by its low bioaccessibiliy. Although vehicle dust contained the 23highest concentrations of BDEs$_{3-7}$ and BDE-209, serum BDEs$_{3-7}$ correlated most strongly with 24bedroom dust.

25

26 1 Introduction

27UK residents are still exposed to a class of potentially harmful brominated flame retardants,
28polybrominated diphenyl ethers (PBDEs), even though European Union regulations
29restricting their manufacture, use and importation came into force in 2004 and 2008. Since
30the 1970s PBDEs have been incorporated into fabrics, foam cushioning and plastics used in
31everyday items such as vehicles, soft furnishings and electronics. PBDEs slow the rate of
32ignition and fire growth in petroleum based polymers and resins. PBDEs are not chemically
33bonded to these materials and are emitted into indoor dust and air through use and
34volatilisation (Rauert and Harrad, 2015; Sjödin et al., 2003). They can then move into the
35wider environment where they have been found in sewage sludge, soils and river and lake
36sediments (Allchin et al., 1999; De Boer et al., 2003; Eljarrat et al., 2008; Harrad et al., 2009).
37They are persistent organic pollutants as defined by the United Nations Environment
38Programme's Stockholm Convention and have an environmental half-life of several years.
39They can travel long distances in the atmosphere and are lipophilic, concentrating in animal
40and marine fats. These qualities and their wide usage have led them to permeate
41environments and food chains around the world (Fromme et al., 2016).

42A recent systematic review of human health consequences of exposure to PBDEs concluded
43health effects may include thyroid disorders, reproductive health effects, and
44neurobehavioral and developmental disorders (Kim et al., 2014). Evidence of these effects
45has been seen in animal and *in vitro* research, where the mechanism appears to be altered
46hormone regulation (endocrine disruption) (Linares et al., 2015; Marchesini et al., 2008;
47Meerts et al., 2000; Viberg et al., 2006). Exposure during key developmental stages in
48infancy is most damaging as this is the time when altered hormone regulation will have the
49greatest impact. Recent estimates of the economic cost of just the intelligence quotient (IQ)
50points loss and intellectual disability due to PBDE exposure was $266 billion in the USA and
51$12·6 billion in the EU (Attina et al., 2016). These figures must be balanced against amounts
52saved due to fire prevention resulting from furnishing flammability standards e.g. £140
53million annual savings in the UK estimated by prevention of death, injury and damage to
54property as a result of Furniture and Furnishings Fire Safety Regulations 1988 that require

55use of flame retardant chemicals. (BIS, 2009). PBDEs were only one group of flame retardant
56chemicals from the several BFR groups commonly used to meet such regulations.

57In 2004, use of two commercial PBDE products, Penta-BDE and Octa-BDE, were restricted
58within the EU (European Council Directive 2003/11/EC) and voluntarily phased out in the
59USA. In 2009, they were added to the Stockholm Convention list of POPs for elimination.
60Penta-BDE had been primarily used in polyurethane foam (PUF) in soft furnishings, vehicles
61and printed circuit boards, in greatest amounts in the USA. Furnishings could contain one to
62four percent Penta-BDE to comply with fire safety regulations (Hammel et al., 2017). The
63Octa-BDE commercial product has been produced and used less widely than Penta-BDE. Its
64major use has been in acrylonitrile-butadiene-styrene (ABS) plastics, such as electronics and
65resin casings of office equipment. The Deca-BDE commercial product has been added to
66furnishing textiles, and in high impact polystyrene (HIPS) for cables, sockets, mobile phones,
67fridges and TV housings.

68Concentrations of BDE-209 are higher in UK indoor dusts than in dusts from mainland
69Europe (Frederiksen et al., 2009; Harrad et al., 2008b) as a result of the UK's more stringent
70fire safety regulations (Furniture and Furnishings Fire Safety Regulations 1988/1989, 1993
71and 2010). Deca-BDE has been restricted from use in electrical and electronic equipment in
72the EU since 2008 and was added to Annex A of the Stockholm Convention list of POPs in
732017. Both diet and contact with indoor dust constitute important exposure pathways for
74PBDEs (Abdallah and Harrad, 2014). Foods from higher up the food chain, of animal origin,
75with a higher fat content (i.e. fish), meat and dairy have higher PBDE concentrations (EFSA,
762011). PBDEs will be circulating in our food chains for many years to come (Harrad and
77Diamond, 2006), and will be re-circulated back into homes as a result of plastics recycling
78(Samsonek and Puype, 2013) .

79Whether dust or diet is the primary exposure source for an individual depends on a number
80of factors; loading of PBDE in dust or food items and the amounts ingested, whether and
81when PBDE technical products have been phased out in that country and on the age of the
82individual (Bramwell et al., 2016a). PBDE intake via ingestion and inhalation of dust is the
83major exposure route for young children in the USA that have frequent hand to mouth
84behaviours and spend lots of time on floors and carpets (Stapleton et al., 2012). Foetal
85exposure in the womb and transfer of PBDEs from mother to child during breastfeeding are

86key exposures for children during important developmental periods. For countries outside

87of the US and Canada, the largest contribution to tri-hepta BDE body burden is thought to

88be from diet, especially in regions where Penta-BDE use has been restricted for longer. Dust

89is likely to be most important contributor to exposure to higher brominated congeners in all

90regions (Sahlström et al., 2015).

91The aim of this study was to determine the major dust and diet sources of PBDEs for a north

92east England cohort and to consider any potential health risks. The five specific objectives

93were: (a) to measure PBDE concentrations in dust from homes, work places and vehicles, (b)

94to calculate relative intake of PBDE via dust in the microenvironments, (c) to evaluate the

95relative importance of PBDE exposure via indoor dust versus dietary PBDE exposure, (d) to

96compare intake estimates with reference health values, (e) to investigate relationships

97between matched environmental and biomonitoring data, and (f) to determine the most

98effective means of reducing PBDE exposure for the cohort.

99

1002 Materials and Methods

101We used a cross sectional and purposive sampling strategy to provide a snap shot of PBDE

102exposures and body burdens for individuals with expected high, average and low exposures.

103By comparing individuals with expected divergent exposures, we aimed to reveal the factors

104influencing body burdens.

1052.1 Volunteer recruitment

106We targeted individuals with a range of occupations and diets; such as workers in

107electronics, soft furnishings, transport, office workers, outdoor workers, oily fish eaters,

108omnivores and vegetarians. In 2010/11, following ethical approval for the study, volunteers

109over 18 years of age and with six months or more of domestic and occupational stability

110were recruited via local authorities, universities, businesses, hospitals, playgroups and

111breast-feeding groups. A short pre-screening questionnaire was used to identify volunteers

112that could provide the optimum range of exposures. 79 couples completed the pre-

113screening questionnaires, 10 couples were invited, and agreed, to participate in the full

114study week. Further description of the cohort is provided in the Supplementary Information.
115Volunteers gave written informed consent prior to participation.

116**2.2   Timing of sample collection**

117Participants undertook a 'sampling week' during which they completed an exposure and
118food frequency questionnaire (FFQ), food- and activity-diaries, room surveys including
119contents, usage and cleaning information and they were asked not to vacuum or dust their
120home. We adapted the validated WHO-IARC EPIC semi-quantitative dietary questionnaire
121for the study. On the seventh day of their sampling week, participants collected their
122duplicate diet samples (DD), and the researcher visited that evening to collect the DD
123samples, home and vehicle dust samples, questionnaires and surveys. The participants then
124fasted until their blood sample collection appointment the following morning where
125anthropometric measurements were also taken. Two couples repeated the full sampling
126week, with sampling points 6.5 and 7.5 months apart. This provided a longitudinal
127dimension to the study and an element of validation. All sampling weeks took place
128between April 1st 2011 and 28th February 2012.

129

130**2.3   Serum, breast milk and duplicate diets**

131Study participants collected an equal amount of whatever food they ate throughout the day
132in a contaminant free (verified by tests carried out prior to sampling) lidded polypropylene
133container for the 24 hour duplicate diet collection. The next day they provided a fasted 60
134ml blood sample at the Clinical Research Facility of the Royal Victoria Infirmary in Newcastle.
13550 ml breastmilk samples were collected by either pump or manual expression up to 12 h
136before and 24 h after provision of the blood sample and kept in pre-cleaned Nalgene
137containers. Samples were stored at -18°C until transfer to the laboratory for analysis. Details
138of the serum, human milk and duplicate diet sample collection and analysis have been
139published previously (Bramwell et al., 2014; Bramwell et al., 2017).

140**2.4   Dust samples**

141Participants were requested not to vacuum or dust their home or vehicle during the
142sampling week. Dust samples from main living areas (n=11), bedrooms (n=12), and vehicles

143(n=8) were collected by a researcher following a standard sampling protocol to allow direct 144comparison with previous studies (Abdallah and Harrad, 2009; Coakley et al., 2013; Harrad 145et al., 2008a; Harrad et al., 2008b). Samples from workplaces (n=10) were collected during 146the sampling week at the participants' (and their employers') convenience. Dust samples 147were extracted and analysed at the University of Birmingham, UK, using previously 148published methods for preparation, extraction, clean up, analysis and quality control 149(Abdallah et al., 2009; Harrad et al., 2008a; Harrad et al., 2008b). Further details of the dust 150sample collection, preparation, extraction and analysis are provided in the Supplementary 151Information.

152**2.5   QA/QC**

153For the analysis of serum, breast milk and duplicate diet samples, the performance 154characteristics of the methodology, including quality assurance parameters such as limits of 155detection (LODs), precision, linear range of measurement, recoveries etc. are included in the 156previous reports (Fernandes et al., 2008; Fernandes, 2004). Further confidence in the data 157is provided by regular and successful participation in laboratory proficiency testing and 158inter-comparison schemes such as POPs in Food 2011 and 2012. PBDEs with IUPAC 159numbers 17, 28, 47, 49, 66, 71, 77, 85, 99, 100, 119, 126, 138, 153, 154, 183 and 209 were 160measured. The congeners selected for analysis are those for which reference standards are 161available. Typical LODs were 1 to 20 ng kg^{-1} lipid for PBDEs.

162For the dust sample analysis the average blank (including field blanks) plus 3 standard 163deviations was used for the limit of detection giving an average 0.7 ng g^{-1} for $BDEs_{3-7}$ (range 1640.2-1.7) and 52 ng g^{-1} for BDE-209. The PBDE ^{13}C labelled internal standard recoveries were: 165^{13}C-BDE 47 = 69 ± 20%, ^{13}C-BDE 99 = 70 ± 20%, ^{13}C-BDE 153 = 69 ± 20% and ^{13}C-BDE 209 = 17 166± 6%. The low recovery for BDE-209 indicates uncertainties in its measurement which are 167presented here with that caveat. Measurement of SRM NIST 2585 had range 78% (BDE-47) 168to 122% (BDE-49) and mean 100% of the certified contents.

169**2.6   Exposure Assessment**

170Concentrations of the PBDEs detected in milk and serum samples were lipid-adjusted to 171allow comparison with the literature. PBDE intake for the 24 hrs of the duplicate diet 172collection was measured using whole weight duplicate diet PBDE concentrations multiplied

173by the mass of DD collected and divided by the weight of the participant to give pg kg^{-1} body

174weight day^{-1}.

175PBDE intakes via dust were estimated by combining measured dust PBDE concentrations

176with occupation time for individual's various microenvironments (taken from their activity

177diary) using both average (20 mg/ day) and high (50 mg/day) adult dust intake rates average

178and high adult dust ingestion as estimated by Jones-Otazo et al. (2005). Although dust

179ingestion rates may differ between microenvironments and activities (as well as individuals),

180for the purpose of this study, we have assumed that that dust ingestion occurred pro-rata to

181the proportion of time spent in each microenvironment during the study week. This was

182considered the only practical approach in the absence of data to confirm any differences

183(Abdallah and Harrad, 2009). For time periods when participants were in their home but

184not in one of the microenvironments measured, the median of their home dust PBDE

185concentration was used. For time periods when they were in an indoor environment but not

186in their own home the median of all dusts collected for the study was used. Time spent

187outside was not assigned a PBDE concentration. Intake rates via dust were divided by the

188participant's weight to give pg PBDE intake kg^{-1} body weight day^{-1}.

189PBDE intakes for average and high dust intake scenarios: average 20 mg d^{-1}, high 50 mg d^{-1}

190(Jones-Otazo et al., 2005) and diet intakes determined from the 24 h duplicate diet

191concentrations were added together for comparison with the European Food Safety

192Authority's (EFSA) chronic human daily dietary intake estimations to determine the margins

193of exposure (MOEs). As PBDE exposure during infancy is considered to present a greater risk

194to health than that for adults, estimated average and high exposure scenarios for infants

195aged 1.5 to 4.5 years old were developed as well. Daily average (50 mg d^{-1}) and high (200 mg

196d^{-1}) dust intake estimations (Jones-Otazo et al., 2005) per kg body weight were extrapolated

197from individual adult intake values determined for the study. These were added to average

198and high dietary PBDE intake estimations from the UK total diet study (TDS) (2012) data for

199infants aged 1.5 to 4.5 years old. Risk assessment for infants from PBDE in breast milks

200collected for the study has been previously reported (Bramwell et al., 2014).

201**2.7   Data Analysis**

202Associations between PBDE concentrations and intakes and potential predictors were
203explored with scatter plots, box plots and correlations using IBM SPSS Statistics for
204Windows, Version 22.0. Armonk, NY: IBM Corp, Minitab 17 and Excel (Microsoft Office
2052013). The distribution of PBDEs in the different matrices was assessed using Shapiro–Wilk
206statistic. As the majority of distributions were not normal, non-parametric Spearman's
207ranking correlation coefficients were determined. The criteria of $\alpha = 0.05$ for statistical
208significance was used. A one sample t test was used to compare PBDE intake of omnivorous
209participants as determined by duplicate diet collection and similar data collected by Harrad
210et al. (2004) to investigate any temporal trend in dietary exposure. Statistical analyses were
211mostly descriptive and correlations do not have sufficient sample numbers to be robust.
212Details of further statistical analyses of room survey data are presented in the
213Supplementary Information. Where measurements were below limits of detection (LOD)
214values of LOD*0.5 have been assumed (median bound). $\sum BDEs_{3-7}$ was calculated as the sum
215of all BDE congeners measured except for BDE-209.

216

217**2.8   Human health risk characterisation**

218Potential health risks were calculated from the sum of dust and dietary intake of PBDEs
219using the margin of exposure (MOE) approach as applied by the European Food Safety
220Authority (EFSA) for dietary exposure health risk assessment. The MOE is the ratio of the
221dose at which a small but measureable adverse effect has been reported versus the level of
222exposure of the population under current consideration. The EFSA Panel on Contaminants
223in the food chain (EFSA, 2011) identified effects on neurodevelopment as the critical
224endpoint using $BMDL_{10}$ for neurobehavioural effects in mice induced during a relevant
225period for brain development. Chronic human intakes, associated with body burdens at the
226$BMDL_{10}$ for BDEs-47, -99, -153 and -209, were estimated to be 172, 4.2, 9.6 and 1,700,000
227ng kg^{-1} bw day^{-1} respectively. For PBDEs, EFSA consider that an MOE ratio above 2.5
228indicates that a health concern is unlikely, with risk decreasing as the MOE increases (EFSA,
2292011). It should be noted that although human intakes of concern are presented as daily
230doses these represent chronic intake and as such would be better represented as weekly or
231monthly intakes as daily intakes can be exceeded on occasion without concern as long as
232other days have lower exposures.

233

234 3   Results and Discussion

235 Our cohort consisted of 10 male-female cohabiting couples living in northeast England in
236 2011/12. All participants completed full sample and data set collection. Participants were
237 recruited from as wide a pool of socio-economic class, occupation, diet and location as
238 possible, however, the small number of participants and the focus on breastfeeding
239 mothers means that results are not representative of all UK residents' exposures. The
240 benefit of the small cohort was that detailed information could be collected for each
241 individual allowing the investigation to include almost all contributing factors in PBDE
242 exposure known at the time. Further details of occupations, diets, parity, breastfeeding and
243 other lifestyle and anthropometric factors are presented in Supplementary Information.
244 Previously published serum, breastmilk, and duplicate diet concentrations (Bramwell et al.,
245 2014; Bramwell et al., 2016b) have been further examined in this investigation, along with
246 new matched dust concentrations, diet and dust intake estimations and exposure and food
247 frequency questionnaire, seven day food and activity diary and room survey information in
248 order to provide as complete a picture of participants' PBDE exposures as possible.

249 **3.1   Dust PBDE concentrations**

250 Dust samples were collected from 40 micro-environments frequently used by the study
251 participants. Main living areas (n=10), bedrooms (n=12) and home offices (n=2) were
252 sampled. Workplaces were sampled if access was granted by employers (n=8). None of the
253 domestic samples were from open plan homes. Four of the workplace samples were from
254 open plan indoor spaces. Vehicles were sampled if participants regularly spent more than
255 five hours each week in them (n=8). We measured PBDEs in dust from all of the
256 microenvironments sampled. Individual concentrations for all PBDEs in each dust sample
257 are presented in Supplementary Information Tables SI 1-4 and summaries of the dust
258 concentrations in different rooms are presented in Table 1. Median dust $\sum BDEs_{3-7}$
259 concentrations were highest in vehicles (179 ng g^{-1}) followed by living rooms, bedrooms
260 then workplaces (137, 102 and 84 ng g^{-1} respectively). Median BDE-209 concentrations in
261 dust were also highest in vehicles (19,000 ng g^{-1}) then bedrooms, living rooms and
262 workplaces (3,530, 2,960, and 2,300 ng g^{-1} respectively).   The highest concentration of

263∑BDEs$_{3-7}$ was measured in a bedroom (7,320 ng g^{-1} dust), the highest BDE-183 in the rear of

264a work van (367 ng g^{-1}) and the highest BDE-209 in a car (137,000 ng g^{-1}). Summaries of dust

265PBDE concentrations in the different microenvironments are compared with previous UK

266and international data in Table 2. Measurements in this study were in keeping with

267previously published UK data (Harrad et al., 2008a; Harrad et al., 2008b; Pless-Mulloli et al.,

2682006; Sjödin et al., 2008) and in agreement with the theory that BDE-209 usage was greater

269in the UK (Fromme et al., 2016; Harrad, 2015). Results were directly comparable to studies

270by Harrad et al. (2008a; 2008b) as we used the same sampling protocol, sampling

271equipment and laboratory techniques.

272We compared room survey information such as counts and age of soft furnishings and

273electronics and room cleaning frequencies with the concentrations of PBDEs in each room.

274Details from individual room surveys are provided in Supplementary Information Table SI5.

275We did not find that simple counts of soft furnishings or electronics were good predictors of

276high or low PBDE loading. The clearest association between room contents and PBDE

277concentrations in dust were for BDE-209 if the room contained a carpet or rugs over 20

278years of age (see Supplementary Information Figure 2)   . Counts of large PUF items over 20

279years old or office chairs from the USA (adhering to Californian state fire retardancy

280regulations TB117) correlated significantly with concentrations of Penta mix BDEs only, BDE-

28147 (r=0.37, p=0.036), -99 (r=0.35, p=0.047) and ∑BDE$_{3-7}$ (r=0.37, p=0.039). Higher dusting

282frequency demonstrated the greatest correlation with lower dust PBDE concentrations, with

283BDEs-47, -99, -153, -154 and -209 all with correlation significant at the 0.01 level and BDE-

284100 with correlation significant at the 0.05 level. Table SI 6 in the Supplementary

285Information contains further correlation data. Discussion of apparent differences between

286repeat sampling weeks' dust data is provided as Supplementary Information.

287We found that concentrations of ∑Penta product BDEs in the bedroom were significantly

288correlated with those in all other environments measured; living rooms (r=0.43, p=0.05),

289workplaces (r=0.71, p=0.05) and vehicles (r=0.90, p=0.02). Concentrations of ∑Penta product

290BDEs in living room dusts correlated strongly with those in workplaces (r=0.90, p=0.01) but

291not vehicles (r=0.30, p=0.60). A larger data set may have revealed alternative findings,

292particularly for workplaces and vehicles. We suggest that dust particles may briefly adhere

293to and then be shaken from skin, hair, clothing and footwear causing distribution among key

294environments used by participants. Further correlation data is provided in Supplementary

295Information Table SI13.

296**3.2   Intake of PBDEs via dust**

297The ranges of average (20 mg dust ingested d^{-1}) and high (50 mg dust ingested d^{-1}) PBDE

298intakes via dust for our study participants was 13.8-1,010 and 35-2,520 pg kg^{-1} bw day^{-1} for

299∑BDEs$_{3-7}$, with 281 to 15,900 and 702 to 39,600 pg kg^{-1} bw day^{-1} for BDE-209 via dust. Our

300∑BDEs$_{3-7}$ estimates were similar to previous UK and German ∑BDEs$_{3-7}$ intake estimates

301(Fromme et al., 2009; Harrad et al., 2008a) and an order of magnitude lower than those in

302the USA (Harrad et al., 2008b). In contrast, our BDE-209 intakes from dust were similar to

303those of the USA (Harrad et al., 2008b) and an order of magnitude higher than Belgian and

304German estimates (Fromme et al., 2009; Roosens et al., 2009) (see Supplementary

305Information Table 6). The wide range of intakes reflected the diverse PBDE loadings

306measured in microenvironment dusts. For this cohort, the influence of specific items in

307specific microenvironments could be reasonably speculated on a case by case basis.

308However, although we expected our participant with occupational PUF and furnishing fabric

309exposure to have a raised PBDE body burden, their fastidious cleaning habits appear to have

310reduced their exposure.

311The greatest proportion of the estimated dust intake for ∑BDEs$_{3-7}$, BDE-183 and BDE-209

312took place in the bedroom (means 43%, 38% and 33% respectively) due to the greater

313amount of time spent in bedrooms. Workplaces and living rooms were the second most

314important microenvironments for ∑BDEs$_{3-7}$ exposure (mean 19%, 13%) and BDE-183 (20%,

31521%). Vehicles were the second most important microenvironment for BDE-209 intake

316(20%). The relative proportions of PBDE intakes in different microenvironments for

317individual participants is illustrated in Figure 1. Our finding that the greater proportion of

318exposure to all congeners occurs in the bedroom is in keeping with our finding of an

319association between bedroom dust and serum concentrations of the PBDE congeners found

320in the commercial Penta-BDE products (BDE-47, -99, -100, -153) (r=0.42, p=0.04), an

321association that has also been reported elsewhere (Ali et al., 2014; Coakley et al., 2013;

322Watkins et al., 2012). Relationships between PBDE in dust and body burdens

323 We compared PBDE concentrations in dust in the different indoor environments with their
324 matched PBDE body burdens. Significant associations were noted between Penta-mix BDEs
325 in bedroom dust and serum ($r=0.45$, $p=0.04$). BDE-153 in bedroom dust was significantly
326 associated with BDEs-47 ($r=0.45$, $p=0.03$), -99 ($r=0.45$, $p=0.03$), -209 ($r=0.41$, $p=0.05$) and
327 $\sum BDEs_{3-7}$ ($r=0.45$, $p=0.03$) in serum. BDE-153 in serum was associated but not significantly
328 with BDEs-153 (0.39, 0.06) and $\sum BDEs_{3-7}$ (0.39, 0.06) in bedroom dust. BDE-47 was
329 associated but not significantly in living room dust and breast milk (0.77, 0.07). BDE-209 was
330 significantly correlated in serum and workplace dusts (0.72, 0.02) however this was strongly
331 influenced by one data point. Also correlated but not significantly in workplace dusts were
332 BDEs-47 (0.57, 0.07) and -99 (0.53, 0.09). Table SI 7 in Supplementary Information provides
333 further dust and body burden correlation data. No significant correlations were found
334 between vehicle dust and serum despite vehicles having the highest PBDE concentrations in
335 their dust, possibly due to participants spending less time in their cars than in other
336 environments measured. The associations between bedroom dust and serum might be
337 expected due to participants spending the greatest proportion of their day in this room,
338 similarly for associations with workplace dust and serum.

339

340 **3.3   Dietary intake of PBDEs**

341 We estimated participants' PBDE intake from diet using three different methods, (i) a 24
342 hour duplicate diet sample collected the day before taking serum and milk samples, (ii) a
343 seven day food diary completed the seven days prior to serum and milk sampling and (iii) a
344 food frequency questionnaire (FFQ) to represent longer term eating habits. Concentrations
345 of PBDEs in the 24 hour duplicate diet samples summarised in Table 1. $BDEs_{3-7}$ were
346 measurable in all of the duplicate diet samples and BDE-209 in 79% of them. 24 hour
347 duplicate diet PBDE concentrations were converted to daily dietary intake estimates which
348 ranged from 82 – 1,320 pg kg^{-1} bw for $\sum BDEs_{3-7}$ and <0.8- 1,860 pg kg^{-1} bw for BDE-
349 209 made up a median of 73% of the total PBDE exposure from diet. Estimates of
350 individuals' PBDE intake via diet are provided in Supplementary Information Table SI 11. The
351 mean intake estimates of BDEs-47, -99, -100, -153 and -154 for the omnivores in this study
352 were significantly lower than those measured by Harrad et al. (2004) for duplicate diet
353 samples collected in the West Midlands of the UK in 2002 ($p=0.01$). The 2002 lower bound

13

mean intakes were within the maximum intakes estimated by this study for BDEs -47, -100, -153 and -154 and upper bound intakes for BDEs -47, -100, and -154. These findings indicate a reduction in dietary exposure during the 10 years between the two studies, with the greatest reductions being for BDE-99 then BDE-153.

Meat, fish and dairy portion consumption estimates compared well between the FFQ and seven day food diaries. Meat portions consumed per week ranged from none to 14 or 15 (FFQ and diary respectively), with median 6.3 or 8 portions. Fish and seafood portions consumed per week ranged from none to 3.5 (maximum for both FFQ and diary), with median 1.8 or 2 portions. Dairy portions consumed per week ranged from none to 25 or 18 (FFQ and diary respectively), with median 8.0 or 8.5 portions. A summary of selected information from the FFQ, diary and 24h duplicate diet is presented in Table 3.

3.4 Relationships between PBDE in diet, serum and breastmilk

We compared PBDE body burdens with concentrations in the duplicate diet finding a significant association for $\sum BDEs_{3-7}$ in both (r=0.41, p=0.05). Serum samples were collected from fasted participants in order for the serum sample to represent the participants' background PBDE body burden without influence from recently consumed food. Breastmilk samples were not necessarily collected in a fasted state. The complex relationship between historic PBDE deposits in adipose tissue, recent diet, serum and breastmilk is beyond the scope of this paper. We found limited correlation between congeners in serum and breastmilk (see Supplementary Information Table SI 8), possibly the result of transfer of PBDEs from serum to milk varying between different congeners. Mean serum/milk ratios generally increased with molecular size and hydrophobicity, e.g. 1.3, 3.1 and 6.0 for BDEs-47, -99 and -209. This pattern was in keeping with findings of a 2012 review of PBDE in matched serum and breastmilk samples (Mannetje et al., 2012). BDE-153 in the body appears to follow a different pattern with a serum/milk ratio of 0.4, i.e. more in milk than serum.

382We found that the number of meat portions consumed in the week prior to sampling had
383significant positive correlations with BDEs-99 (r=0.46, p=0.01) -153 (r=0.44, p=0.03) and
384$\sum$BDEs$_{3-7}$ (r=0.43, p=0.04) in serum. Further correlation data between dietary information is
385provided in Supplementary Information Table SI9. The UK FSA 2006 TDS found meat
386products (followed by fish) to contribute most to the PBDE intake of the general UK
387population (EFSA, 2011; FSA, 2006). For participants in this study, meat portions consumed
388exceeded fish portions. Our earlier review of associations between PBDE body burden, dust
389and diet (Bramwell et al., 2016a) also found eating meat to be the most frequently reported
390association (eating dairy and fish were next). Similarly, a nationwide study in the USA found
391vegetarians to have 23% lower, and heavy red meat consumers to have 18% higher total
392PBDEs in serum than omnivores (Fraser et al., 2009).

393

394**3.5   Anthropometric and questionnaire covariates of PBDE body burden**

395As well as participants' height, weight and body fat mass measurements, information on
396travel habits, hand to mouth behaviours, parity, numbers of household members, hobbies
397and occupations was also collected to look for indicators of higher serum and breast milk
398PBDE concentrations. These associations are presented in Supplementary Information Table
399SI10. We found serum BDE-153 concentrations to be significantly associated with sex (r= -
4000.60, p=0.01), percentage of body fat mass (r=-0.49, p=0.02), parity in women (r=-0.57,
401p=0.05) and working with electronics (r=0.59, p=0.01). Males generally had higher BDE-153
402in serum than females, in keeping with the findings of a recent Swedish study of 170 adults
403(Bjermo et al., 2017) and a nationwide study in the USA that found males generally had
404higher BDE$_{3-7}$ body burdens (Fraser et al., 2009). We hypothesise there may be two factors
405influencing the higher serum concentrations of males in this study, (i) men generally had
406lower BMI values; seven of the females had recently been pregnant which would increase
407their BMI and (ii) 9 of the 10 female participants in the study had undergone some
408depuration effect during pregnancy and breast feeding which their male partners had not. In
409a study of the breastmilk of 83 women at three and 12 months postpartum, BDE-153
410showed a significant increase over time (Daniels et al., 2010) suggesting that BDE-153
411present in adipose fat compartments from historic exposures may have been mobilised
412during the nursing period. Storage of BDE-153 in fat compartments in the body has been

413suggested as the reason for dilution in the serum of people with higher BMI (Cequier et al.,
4142015; Fraser et al., 2009). Why these findings for BDE-153 are not consistent with findings
415for other congeners is not clear but it may be linked to its longer human half-life (Geyer et
416al., 2004).

417

4183.6 Was diet or dust the major source of PBDE exposure for this cohort?

419Diet was the major source of $\sum BDEs_{3-7}$ for this cohort making up a median of 85% of the total
420intake when using duplicate diet data with the average dust ingestion estimate of 20 mg d^{-1}.
421This was a somewhat lower proportion than comparable previous studies estimates of 95%
422(UK), 96% (Belgium) and 97%, (Germany) (Abdallah and Harrad, 2014; Fromme et al., 2009;
423Roosens et al., 2009) due to our higher median $\sum BDEs_{3-7}$ dust concentration and the notably
424higher concentration of $\sum BDEs_{3-7}$ in the German duplicate diets (see Table SI 6). We did not
425include estimates of intake of PBDEs from indoor air in our totals. Previous studies have
426found PBDE intake from air to constitute <1% of total PBDE intake (Fromme et al., 2009) and
427a maximum of 2% (Abdallah and Harrad, 2014).

428Considering only a cohort's average intake hides the substantial variation between
429individuals and their exposure sources - something this study has been able to demonstrate
430clearly (see Figure 2 and Supplementary Information Table SI 6). An individual's total PBDE
431intake is a combination of dust concentrations in different environments, time spent in
432them and dietary habits. For example, the proportion of $\sum BDEs_{3-7}$ BDE intake provided by
433dust for an average dust intake rate had a median 4% but ranged between 0.7% (8M) and
43432% (5F). Both these participants lived rurally, the former on a smallholding, the other on a
435farm. 8M spent the most time outdoors (almost 9 hours each day), had a low Penta-BDE
436loading in their bedroom dust and, despite a generally home-grown and organic diet, a
437duplicate diet intake in the 3rd quartile. 5F's relatively high dust intake (32% using average
438dust intake and 54% using high dust intake rates) was due to having the room (bedroom)
439with the highest $\sum BDEs_{3-7}$ concentrations measured in the study. Although 5F consumed a
440vegetarian diet their dietary $\sum BDEs_{3-7}$ intake was in the top quartile.

441Dust was the greatest source of BDE-209 for our entire cohort, with median intakes making
442up 75% and 88% of the total BDE-209 intake for average and high dust intake rates

443respectively, lower than previous UK estimates of 94% and 99% (Abdallah and Harrad, 2014;

444Harrad, 2010) possibly due to declining use of Deca-BDE product and differences between

445cohorts in the different studies. Individual participants' proportion of total BDE-209 intake

446provided by dust for average dust intake rate ranged from 14% (8M) to 100% (1Fii and

4471Mii). Participant 10M had a significantly greater BDE-209 concentration than their partner

448possibly a reflection of the relatively high amount of time spent in their vehicle (23% of their

449time) and BDE-209 concentration in their car (30,338 ng/g).

450We found the range of individuals' intakes of $\sum BDEs_{3-7}$ from dust to be five times greater

451than their intakes from diet. The highest total intake (using average dust intake scenario)

452was 16 times greater than the lowest reported intake. Our data agrees with previous

453hypotheses that the wide range in PBDE concentrations in room dusts (compared with the

454range seen in diets) may be the reason some individuals have significantly higher internal

455dose (Harrad et al., 2008b; Petreas et al., 2003; Thomas et al., 2006; Wu et al., 2007). Dust

456generation, dust ingestion rates, and cleaning frequencies (both microenvironments and

457hand washing) may also be influential.

458Our study corroborates previous studies findings that average PBDE intakes in the UK are broadly

459similar to those in mainland Europe, where meat is the major source of Penta-BDEs for the average

460person but dust is the major source of BDE-209 (Bramwell et al., 2016a; Harrad et al., 2008b). For

461infants, the average contribution to total intakes from diet were >90% for $\sum BDEs_{3-7}$ and 69% for BDE-

462209. At the high dust ingestion rate this decreased to 35-50% for $\sum BDEs_{3-7}$ and 88% for BDE-209.

463These figures indicate similar proportional intake for infants from diet to our adults, although with

464considerably higher amounts ingested per kg body weight (see Table 3).

465

466**3.7   Study Limitations**

467This study involved a relatively small cohort of 20 individuals (10 UK couples). The study philosophy

468concentrated more on the details and habits of the volunteers in order to understand their

469individual exposures. The volume of usage of PBDE mixtures such as PentaBDE, the timelines of

470product introduction and restriction, either voluntary or regulation enforced, and the type of usage,

471are all variables in general population exposure. For example, a far greater volume of the PentaBDE

472mixture was used in the USA and Canada compared to Europe and this is reflected in the relatively

473higher concentrations of related congeners measured in serum, and in house dust levels from North

474America. Also, where we found diet to be the most important exposure pathway for Penta mix BDEs, 475studies such as (Lorber, 2008) have shown that dust is a major pathway for PentaBDE in North 476American populations. When personal details and habits are considered, the exposure assessment 477is even more unique. Thus, the finding of this study are not intended to be representative of the UK 478as a whole, or even less, other regions of the world.

479

480**3.8   Risk characterisation**

481The most relevant congener from a health risk perspective is BDE-99 but there is no 482agreement on a safe intake. The US-EPA suggests a reference dose 100 ng/kg bw/day (US-483EPA, 2006) whereas the more recent EFSA suggested health reference value is 4.2 ng/kg 484bw/day with an MOE of 2.5 (EFSA, 2011). We investigated potential health risk from our 485estimated PBDE intakes by comparing them with both these reference values (see Table 4 486and Table SI12). The combined uncertainties from household types, sampling and 487measurement is likely be quite high and should be borne in mind. No health concerns are 488expected from the PBDE intakes estimated in this study for adults as all had MOEs over 2.5 489(EFSA, 2011). The lowest adult MOEs were 2.8 and 3.7 for BDE-99 using a high dust intake 490rate for household 5 with the high BDE_{3-7} measurements in their bedroom. Accordingly, 491estimated infant daily exposures to BDE-99 for the same home have MOEs below those 492recommended by EFSA for chronic exposure. Using average diet intake data from the 2012 493UK TDS with dust exposure data from this study with average dust intake rates we found the 494lowest MOE estimation to be 2.3 which is similar to the EFSA recommended MOE of 2.5 495deemed to indicate a potential health risk. Using high dust intake rates with dust data for 496this study and 97.5[th] percentile (P97.5) dietary intake estimates from the 2012 UK TDS this 497MOE dropped to 0.7 and two additional homes indicated high infant intake MOEs between 4982.5 and 3. All other adult and infant MOEs using EFSA reference values and all MOEs using 499US EPA values were comfortably above the recommended MOE. Follow-up measurement of 500the PBDE body burdens for infants of parents participating in this study could help describe 501associations with raised intake estimations.

502

503   4 Conclusions

504 This detailed study is the first anywhere to document concentrations of PBDEs, including
505 BDE-209, in samples of indoor dust and diet with matched human serum and breast milk
506 concentrations. Our findings confirmed that both diet and dust make a contribution to PBDE
507 body burdens and provide new evidence of a wide range in their relative contributions
508 between individuals. Diet appeared to be the primary source of intake of BDE_{3-7} congeners
509 for the majority of this cohort, and meat consumption demonstrated the strongest
510 significant positive association between diet type and serum $BDEs_{3-7}$ concentrations.   Dust
511 was the cohort's primary source of BDE-209. Rooms containing a carpet or rugs over 20
512 years old had higher BDE-209 concentrations in their dust. Rooms that were dusted more
513 frequently had less BDE-209, as well as less Penta mix PBDE congeners. Rooms containing
514 sofas or armchairs over 20 years old had higher concentrations of commercial Penta mix
515 PBDE congeners. BDE-209 concentrations in room dusts did not widely correlate with BDE-
516 209 body burdens, possibly due to the congener's relatively large molecular size and low
517 bioaccessibility. Correlations between BDE_{3-7} congeners in serum and indoor dust were
518 strongest in bedrooms in keeping with the greater proportion of time spent there. Being
519 male and having a lower body fat mass were indicators of higher serum BDE-153 for this
520 cohort. BDE-99 was the congener demonstrating the lowest MOE (and therefore the
521 greatest health risk) and although we found a reduction in dietary exposure to this and
522 other Penta-mix PBDEs since 2002, reducing dietary exposure would still have the greatest
523 effect in reducing body burdens.

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530

531 **Conflicts of interest:** None

532

533**References**

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