Impact of dietary guidelines on lifetime exposure to chemical contaminants: Divergent conclusions for two bioaccumulative substances

Manon Pruvost-Couvreur, Bruno Le Bizec, Irène Margaritis, Jean-Luc J.L. Volatier, Camille Béchaux, Gilles Rivière

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5 Manon Pruvost-Couvreur[a,b], Bruno Le Bizec[a], Irène Margaritis[b], Jean-Luc Volatier[b], Camille Béchaux[b]

6 and Gilles Rivière[b]

7

8 [a]Laboratoire d'Etude des Résidus et Contaminants dans les Aliments (LABERCA), INRAE, Oniris,

9 Nantes F-44307, France

10 [b]Risk Assessment Department - French Agency for Food, Environmental and Occupational Health and

11 Safety, 14 Rue Pierre et Marie Curie, F-94700 Maisons-Alfort, France

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13 Corresponding author:

14 Gilles RIVIERE

15 Gilles.riviere@anses.fr

16 Tel : ++ 33 (0)1 49 77 27 94

Abbreviations: ANSES (French agency for food, environmental and occupational health & safety), FBDG (Food Based Dietary Guideline), FNHP (French Nutrition Health Program), HBGV (Health Based Guidance Value), INCA2 (name of the French individual and national study on food consumption 2006-2007), iTDS (French infant Total Diet Study), Nutri-Baby SFAE 2005 (name of the study on food behaviours and consumption in French children between 0 and 35 months of age), PBTK (Physiologically Based Toxicokinetic), PCBs (polychlorinated biphenyls), PI (Prediction Interval), TDS2 (French second Total Diet Study), TDSs (Total Diet Studies)

Abstract

Food based dietary guidelines (FBDGs) are developed to promote appropriate nutrients intake. However, FBDGs may trigger higher exposure to some food chemical contaminants while recommending the consumption of specific food groups that are more contaminated than others. In some cases, the balance between benefits and risks is difficult to achieve.

In the present article, we describe the long-term impact of some FBDGs on the exposure to food contaminants. Two examples of bioaccumulative substances were studied: cadmium and PCBs. Lifetime dietary exposure trajectories were simulated for two populations: the first representing the general French population, the second generated using virtual individuals following national FBDGs during their entire life. Exposure trajectories were converted into lifetime cadmium and PCB internal concentrations by using physiologically based toxicokinetic models. Finally, trajectories were compared with reference values to assess the health risk related to cadmium and PCBs, for both simulated populations.

This work highlights that FBDGs may have a major impact on PCB dietary exposures and lead to significantly higher PCB plasma concentrations than those observed in the general population. On the contrary, cadmium exposure is only slightly impacted when FBDGs are followed. This underscores the relevance of taking into account lifetime exposures when establishing FBDGs.

Keywords

1. Introduction

Consumption of certain food groups may limit or increase the risk of chronic diseases for consumers, such as obesity, cardiovascular diseases, type 2 diabetes or cancers (Schulze et al. 2018; WHO/FAO 2003). So, healthy and balanced diet is crucial to non-communicable diseases prevention.

Food based dietary guidelines (FBDGs) "are intended to establish a basis for public food and nutrition, health and agricultural policies and nutrition education programmes to foster healthy eating habits and lifestyles. They provide advice on foods, food groups and dietary patterns to provide the required nutrients to the general public to promote overall health and prevent chronic diseases." (FAO 2020).

In France, the FNHP (French Nutrition Health Program), a government plan implemented in 2001, aims to improve the health of the population through better food composition and consumptions and physical activity practices (Hercberg et al. 2008). The FNHP is mentioned in the Public Health Code since 2010 and has various missions of prevention and dissemination of recommendations on dietary practices and physical activity (Public Health Code 2010).

Although the FNPH provides FBDGs intended to cover weekly nutritional needs of the population, these recommendations may induce consequences on population exposure to chemical contaminants. In 2016, the French agency for food, environmental and occupational health & safety (ANSES) highlighted the difficulty to derive FBDGs covering nutritional needs while exposing to doses of contaminants below safe levels, in particular for acrylamide, inorganic arsenic and lead (ANSES 2016a). Maximum levels of contaminants in food are set by EU regulation 1881/2006 for a large set of chemical contaminants and their main food contributors to dietary exposure, however, this regulation is based on actual food intake in Europe and not FBDGs (Commission of the European communities 2006).

59   In the present article, we illustrate differences of lifetime exposures to contaminants between a

60   general population and a sub-population following the FBDGs provided by the FNHP. The aim was to

61   evaluate the long-term impact of FBDGs on exposures but also on body burden of chemicals,

62   especially in the case of substances known to accumulate in the human body. To this end, exposures

63   of a general population were compared with those of a population of individuals following the FBDGs

64   of the FNPH during their entire life.

65   The method was applied to the examples of two chemical substances: cadmium, which is a

66   ubiquitous heavy metal and polychlorinated biphenyls (PCBs), persistent organic pollutants including

67   209 congeners.

68   For non-smoking individuals, food is the main source of exposure to cadmium and PCBs (EFSA 2005,

69   2009). In France, bread and dried bread products, as well as potatoes and potato products are the

70   foods contributing the most to cadmium dietary exposure, for children and adults. Fish and dairy

71   products are the foods contributing the most to PCB dietary exposure (ANSES 2011).

72   To model the bioaccumulation of cadmium and PCBs, we simulated lifetime body burdens of the

73   general population and individuals following the FBDGs during their entire life, using physiologically

74   based toxicokinetic (PBTK) models.

75   Simulated exposures and body burdens were then compared to reference values in order to assess

76   the health risk related to modelled lifetime trajectories.

77

78   2. Material and methods

79   2.1.   Consumption and exposure data

80   In this work, consumption data are those from the cross-sectional individual dietary survey in

81   children under 3 years conducted by the Syndicat Français des Aliments de l'Enfance (SFAE) et de la

82   Nutrition Clinique (Fantino and Gourmet 2008) and from the second individual and national dietary

83   survey INCA2 for the rest of the population (AFSSA 2009). The SFAE survey recorded the

84   consumption of 705 non-breast-fed children in France in 2005 during three consecutive days. The

85   INCA2 survey recorded the consumption of 1455 children over the age of 3 and 2624 adults in 2006-

86   2007 in France during one week.

87   Cadmium and PCB exposures associated with intakes recorded in the SFAE and INCA2 surveys were

88   estimated in the French infant Total Diet Study (iTDS) for children under the age of 3 and the French

89   second Total Diet Study (TDS2) for individuals between 3 and 79 years old, respectively (ANSES 2011,

90   2016b). As part of these total diet studies (TDSs), concentrations of more than 400 substances were

91   measured in samples of commonly eaten foods, cooked as consumed. Next, the mean dietary

92   exposures for the duration of the survey were assessed for each individual of the SFAE and INCA2

93   surveys.

94   In the TDS2, only 52% of the consumption of fish of the French population was covered by sampling

95   even though fish and seafood are the largest contributors to PCB dietary exposure. Therefore, an

96   additional exposure scenario was performed in the TDS2 to take into account the consumption of not

97   sampled fishes, by imputing the contamination of sampled fishes to not sampled ones based on their

98   lipid content and their metabolism (Sirot et al. 2012b).

99

100   ## 2.2.   Food based dietary guidelines

101   Before the age of 3, the main FBDG is to exclusively breastfeed until the age of 6 months. Then

102   breastfeeding may be prolonged in addition to the gradual diversification of the diet (ANSES 2019;

103   INPES 2015; WHO 2017). Otherwise, until 6 months of age, the diet should be exclusively composed

104   of infant formula specific to children under the age of 6 months. Then, the diet should be

105   progressively diversified and supplemented with infant formula dedicated to children over the age of

106   7 months. In any case, cow milk must not be introduced into the diet before at least the age of 1

107   year. In the present study, since we do not have information on the consumption of breast milk or on

108   concentrations of cadmium and PCBs in breast milk, FBDGs covering infant formula were considered.

109   From the beginning of the diversification of the diet, quantifiable FBDGs cover consumption of milk,

110   dairy products, meat, fish and eggs, according to age:

111   -   7-8 months old: at least 500 mL of infant formula per day and 10 g of meat, fish or egg per

112   day,

113   -   9-12 months old: at least 500 mL of infant formula per day and 20 g of meat, fish or egg per

114   day,

115   -   13-36 months old: less than 800 mL of milk or dairy products per day and 30 g of meat, fish

116   or egg per day (INPES 2015).

117   For children over the age of 3, the FBDGs proposed by the French agency for food safety (AFSSA)

118   were:

119   -   5 portions of fruits and vegetables per day,

120   -   Cereal products at each meal,

121   -   3 or 4 portions of dairy meal products to have an adequate daily calcium intake,

122   -   1 or 2 portions of meat, egg or fish per day, with size of portions evolving with age,

123   -   2 portions of fish per week (INPES 2015).

124   For adults, the quantitative studied FBDGs were:

125   -   At least 5 portions of fruits and vegetables per day,

126   -   A least 2 portions of legumes per week,

127   -   Wholegrain and unrefined cereal products every day,

128   -   2 portions of dairy products per day,

129   -   2 portions of fish and seafood per week, including one oily fish,

130   -   Maximum 500 g of red meat per week,

131   -   Maximum 150 g of processed meat per week (HCPH 2017).

132   As there are many FBDGs for children and adults, people following all guidelines are scarce. Since the

133   aim of this work was to estimate the long-term impact of FBDGs on exposure, exposure trajectories

134   were simulated for individuals following the guidelines for foods that appear to be the most

135   significant contributors to dietary exposures. To this end, food groups recorded in the SFAE and the

136   INCA2 surveys, and being subject to at least one FBDG, were identified. Then, contributions of these

137   food groups to exposure to the chemical of interest were assessed. Consequently, selected FBDGs

138   were not the same according to the studied chemical.

139

140   ## 2.3.   Simulation of lifetime exposure trajectories

141   First, a general virtual population was simulated. To this end, exposures estimated in the TDSs were

142   grouped by age. Age groups were defined to correspond to specific dietary habits and social

143   behaviours. Then, a statistical distribution was fitted to exposures for each age group, using the

144   function *fitdist* of the *fitdistrplus* package (Delignette-Muller et al. 2019) in R version 3.6.1.

145   The trajectory of a virtual individual was computed by randomly drawing a weekly exposure in the

146   distribution of the corresponding age group, for every week of life, from birth to the age of 80. The

147   process was iterated to simulate a population of 10 000 individuals.

148   A sub-population of individuals following the FBDGs during their entire life was similarly simulated.

149   Individuals following the FBDGs selected for the studied chemical were identified in the TDSs.

150   Distributions were fitted to exposures of these individuals, by age group. Then, lifetime exposure

151   trajectories were simulated by randomly drawing exposures in the corresponding distribution, for

152   every week of life.

153   This method does not simulate realistic lifetime individual profiles. In fact, since the follow-up of

154   FBDGs, like food consumption behaviours in general, is correlated with certain sociodemographic

155 and economic characteristics, it may change over time. However, the method proposed here allows

156 the assessment of the mean impact of following the FBDGs in a life-long framework, *i.e.* in the

157 context of a theoretical scenario that assumes a lifetime follow-up of the FBDGs.

158

2.4.   Simulation of lifetime body burden trajectories

160 In order to estimate the impact of FBDGs on the accumulation of chemicals in the body, body burden

161 trajectories were simulated from dietary exposure trajectories. To this end, previously developed

162 physiologically based toxicokinetic (PBTK) models were used. The PBTK model for cadmium was that

163 from the study of Kjellström and Nordberg (1978) and included several modifications described by

164 Pruvost-Couvreur et al. (2020a). This model allowed simulating trajectories of cadmium urinary

165 concentrations, adjusted to creatinine, from cadmium exposure trajectories. The PBTK model used

166 for PCBs was described by Pruvost-Couvreur et al. (2020b) and allowed the computation of

167 trajectories of PCB plasma concentrations, adjusted to lipid weight, from PCB dietary exposure

168 trajectories. Both models accounted for evolution of physiological parameters with age.

169

3. Results and discussion

3.1.   Selection of FBDGs

172 For children under the age of 5 months, the exclusive consumption of infant formula adapted to age

173 was considered. In the SFAE survey, too few children between the ages of 5 and 12 months, amongst

174 the already low headcount, had dietary habits following FBDGs to be able to fit a statistical

175 distribution to exposures of individuals following FBDGs. For children between 1 and 3 years old,

176 FBDGs covering dairy products and meat, fish and eggs were considered.

177 In the INCA2 survey, food groups covered by at least one quantitative FBDG were cereal products,

178 legumes, dairy products, alcohol, fish, seafood, meat, fruits and vegetables. Amongst these food

179 groups, those contributing the most to cadmium dietary exposure were cereal products, fruits and

180 vegetables, plus dairy products for children and fish and seafood for adults. The food groups

181 contributing the most to PCB exposure were fish and seafood, dairy products and meat (Figure 1,

182 ANSES 2011).

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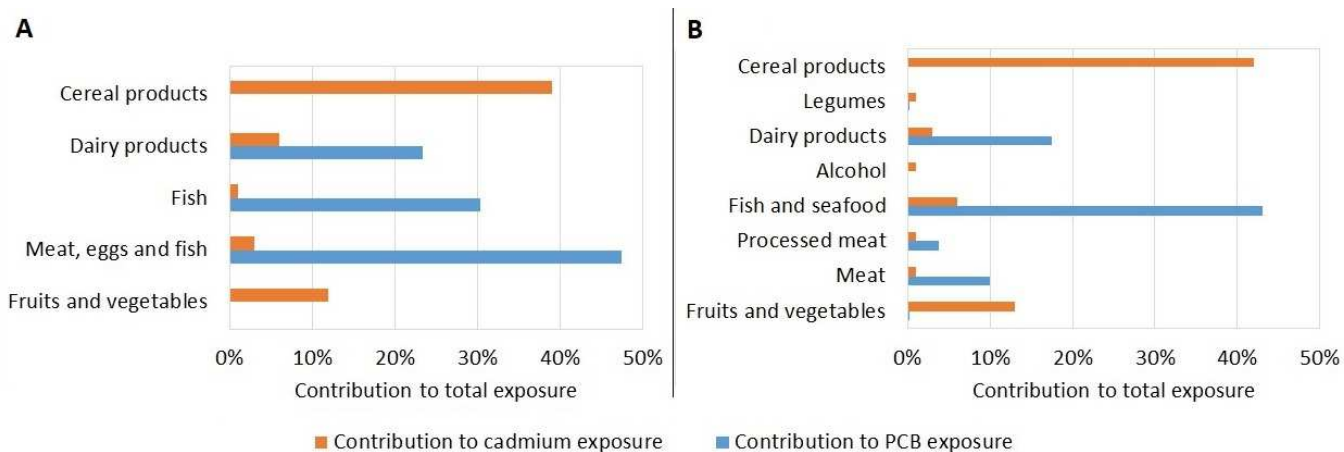
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185 *Figure 1: Contribution of food groups covered by a FBDG to cadmium and PCB exposures for children (A) and adults (B)*

186

187 Individuals following FBDGs covering the most contributing food groups were scarce. For example,

188 96% of adults consumed cereal products every day but only 5% consumed wholegrain cereal

189 products every day. Furthermore, 25% of adults consumed at least 5 portions of fruits and vegetables

190 per day, but only 2% consumed at least 5 portions of fruits and vegetables and wholegrain cereal

191 products every day. Similarly, only 2% of children of the TDS2 population followed FBDGs covering

192 cereals products, fruits and vegetables. Considering FBDGs covering dairy products, meat, eggs and

193 fish, only 1% of children and 5% of adults followed all of them (Figure 2). It was therefore necessary

194 to select FBDGs to have a sufficient number of individuals following the FBDGs in each age group, in

195 order to be able to fit a distribution to dietary exposures.

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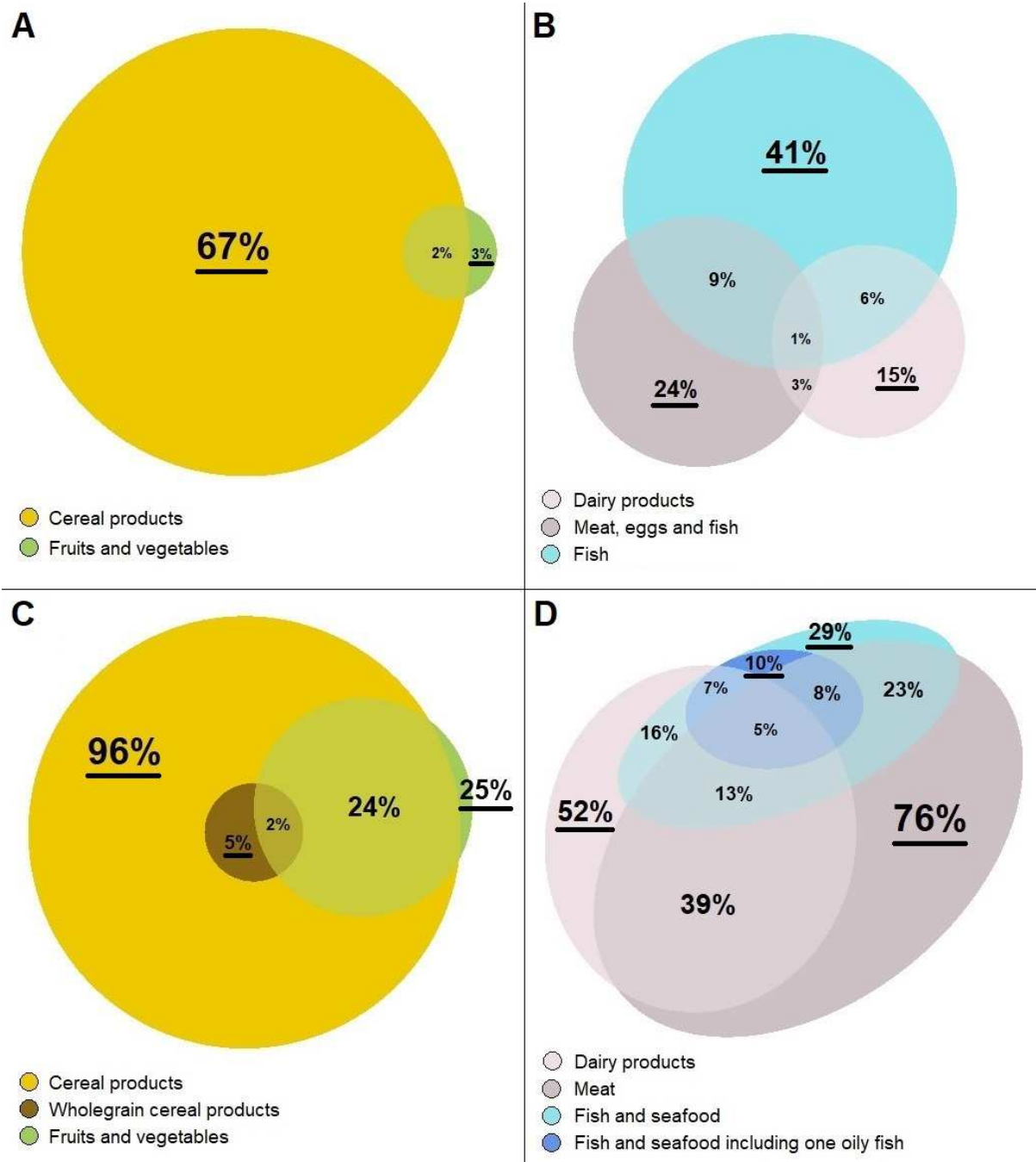
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Figure 2: Percentage of children (A, B) and adults (C, D) following FBDGs covering food groups contributing to cadmium (A, C) and PCB (B, D) exposures in the TDS2. Underline values correspond to the percentages of individuals following at least one FBDG. Other values correspond to percentages of individuals following a combination of FBDGs.

FBDGs selected to simulate dietary exposure trajectories to cadmium and PCBs for the sub-population following FBDGs are presented in Table 1. For cadmium, selected FBDGs were followed by

204   67% of children and 24% of adults in the INCA2 survey population. For PCBs, 9% of children and 13%

205   of adults followed FBDGs.

206

207   *Table 1: FBDGs selected to simulate lifetime exposure trajectories to cadmium and PCBs*

|	Cadmium	PCBs
Infants (1-4 months)	• Exclusive consumption of infant formula adapted to age	• Exclusive consumption of infant formula adapted to age
Infants (1-3 years)	• Less than 800 mL of milk and dairy products per day • 30 g of meat, fish or egg per day	• Less than 800 mL of milk and dairy products per day • 30 g of meat, fish or egg per day
Children	• Cereal products at each meal	• 2 portions of fish per week • 1 or 2 portions of meat, eggs or fish per day, with size of portions evolving with age
Adults	• At least 5 portions of fruits and vegetables per day • Cereal products every day (but not necessarily wholegrain or unrefined)	• 2 portions of fish and seafood per week (but not necessarily including one oily fish) • 2 portions of dairy products per day • Maximum 500 grams of red meat per week

208

3.2.   Exposure trajectories

210   Above the age of 10, dietary exposures to cadmium and PCBs were significantly lower in the general

211   population than those in individuals following the selected FBDGs (Figure 3). During the first months

of life, cadmium and PCB dietary exposures were significantly lower for children consuming

exclusively infant formula than those for children having a diversified diet. Differences of exposure

distributions between both populations were more pronounced for PCB exposures than for cadmium

exposures, for which differences of exposure were not biologically relevant because there were

small. This may be due to the fact that PCBs are mostly present in fatty foods whereas cadmium is a

ubiquitous chemical. Consequently, the impact of FBDGs on exposures appears more pronounced in

the case of PCBs than in the case of cadmium. For example, fish, seafood, dairy products and meat

contribute to more than 70% to PCB exposure in adults whereas fruits, vegetables and cereal

products contribute to 55% to cadmium exposure. Moreover, we can observe that, in particular for

individuals above the age of 10, PCB exposure distribution were shifted to the right. Thus, exposures

were higher for individuals following the FBDGs, on average but although for highest exposures.

However, because exposures were obtained from fitted distributions, the level of confidence in the

extreme values, simulated from the distribution tail, is low.
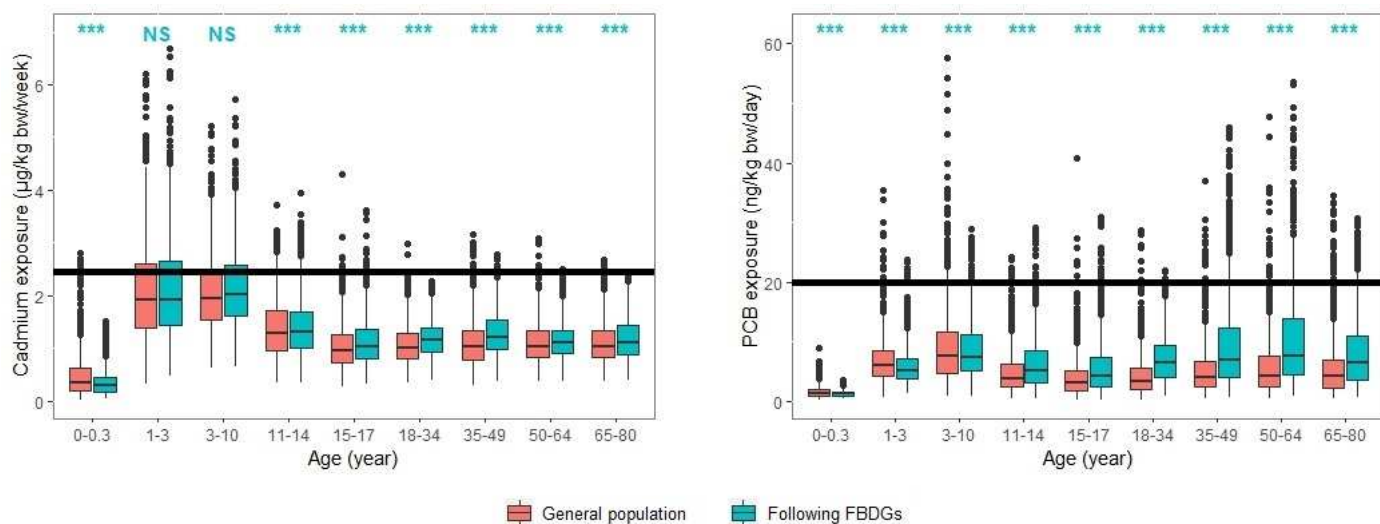
*Figure 3: Distributions of cadmium and PCB exposures fitted in data from the TDS2, according to age group and following of
the selected FBDGs. Dots represent outlier exposures (i.e. exposures higher than the third quartile plus 1.5 times the
interquartile range) and indications above boxplots illustrate the statistical Kolmogorov-Smirnov test significance (NS: Not
Significant, ***: p-value<0.001). Horizontal black lines represent HBGVs.*

231

Comparing lifetime exposure trajectories of both studied populations, the mean PCB exposure

through life appeared on average 1.5 times higher for individuals following FBDGs than for

individuals of the general population. For cadmium, differences were not as pronounced as for PCBs:

average lifelong exposures were 1.2 µg Cd/kg bw/week in the general population and

1.3 µg Cd/kg bw/week for individuals following FBDGs (Table 2).

However, not all FBDGs have been taken into account because of the small number of individuals

following all FBDGs. For example, for the simulation of PCB exposure trajectories, the FBDGs covering

butter consumption were not considered because they were not quantifiable, whereas butter

contributes to 11.7% of the PCB exposure in children over the age of 3 and to 11.1% of the PCB

exposure in adults. Since the FNHP recommends to limit the use of fats and to give preference to fats

of vegetable origin, following this FBDG would lead to decrease the butter consumption. Because

concentrations of PCBs in vegetable oils and margarine are on average 10 times lower than those

measured in butter (ANSES 2011), decreasing butter consumption would means decreasing PCB

dietary exposure. On the contrary, the FNHP recommends to consume one portion of oily fish per

week for a satisfactory intake of omega 3 (ANSES 2016a). Because of the high lipophilicity of PCBs,

they are more concentrated in oily fish than in other fish. Therefore, strict compliance with fish

consumption guidelines would lead to higher PCB dietary exposures.

The main FBDGs for infants until the beginning of the seventh month is exclusive breastfeeding. For

cadmium, impact of breastfeeding on infants' exposures was assumed negligible because of the low

levels of cadmium in breast milk (ATSDR 2012; EFSA 2009; Lehmann et al. 2018). On the contrary, it

has already been demonstrated that breastfeeding exposes infants to much higher levels of PCBs

that formula feeding (Lehmann et al. 2018). However, PCB plasma concentrations were shown to

decrease after cessation of breastfeeding and to converge to body burden of formula-fed children in

adulthood (Pruvost-Couvreur et al. 2020b). Thus, a risk related to PCB exposures via breastfeeding

256 cannot be excluded, particularly because it occurs during a critical period for child development.

257 Consequently, the transitory nature of high PCB exposures via breast milk, as well as the

258 uncertainties associated with critical values for young children, have to be studied further in order to

259 quantify the long-term impact on health of PCB exposures related to the following of breastfeeding

260 guidelines.

261 In order to assess health risk related to dietary exposures, lifetime trajectories were compared with

262 health based guidance values (HBGVs). The HBGV for PCBs was 20 ng PCB/kg bw/day as selected by

263 several health agencies (AFSSA 2007; ATSDR 2000; RIVM 2001; US EPA 1994). The HBGV for cadmium

264 was the value of 2.45 µg Cd/kg bw/week set by ANSES (2017) and close to the value of

265 2.5 µg Cd/kg bw/week set by EFSA (2009).

266 On average, the general population exceeded the HBGV for PCBs during 113 weeks through life

267 whereas individuals following FBDGs covering fish, meat and dairy products exceeded the HBGV

268 during 310 weeks. In simulations, the mean magnitude of exceedance of the HBGV through life was

269 8.9 ng/kg bw/day. For individuals following FBDGs the mean magnitude of exceedance of the HBGV

270 through life was 10.3 ng/kg bw/ (Table 2).

271 For cadmium, durations of exceedances of the selected HBGV were similar for both simulated

272 populations: on average 3.7 years through life for the general population and 3.9 years for individuals

273 following FBDGs. Magnitudes of exceedance of the HBGV were similar for both populations: the

274 mean magnitude through life was 0.7 µg/kg bw/week and the maximum magnitude was on average

275 5.8 µg/kg bw/week (Table 2).

276 However, it should be noted that the proposed method for simulating lifetime exposure trajectories

277 does not cover all the variability that would be observed in a population following the FBDGs

278 throughout its lifetime, just as the variability of the general population is not covered. Indeed,

279 Pruvost-Couvreur et al. (2020a) showed that taking into account individual profiles allows a greater

280 variability of exposure in the simulated population. In fact, considering individual profiles makes

281 possible to isolate characteristics that influence exposure over the life course, leading to more

282 extreme lifetime exposures than those observed in this study. However, the low number of

283 individuals following FBDGs in the INCA2 survey did not allow us to examine scenarios considering

284 complex individual profiles while taking into account the correlation between following FBDGs and

285 socioeconomic characteristics.

286 Conversely, a part of the simulated variability is overestimated. Indeed, at the individual level,

287 consumption habits related to food tastes and household habits are not considered, even though

288 they smooth exposures over the long term. However, methods that reduce intra-individual variance

289 used regularly in dietary risk assessment, as those presented in Goedhart et al. (2012) and Mancini et

290 al. (2015), do not allow the consideration of changes in food consumption behaviours over time and

291 have therefore not been used here.

292 Consequently, the variability at the population level is underestimated but the individual total

293 variance is overestimated. It should therefore be kept in mind, that the results presented here are

294 average cases and do not represent the total variability of a general French population.

295

3.3. Body burden trajectories and risk assessment

297 Body burdens were expressed as the concentration of PCBs in plasma, adjusted to lipid weight, and

298 for cadmium by the concentration of cadmium excreted in urine, adjusted to creatinine.

299 For cadmium and PCBs, body burdens increased through life because of bioaccumulation (Figure 4).
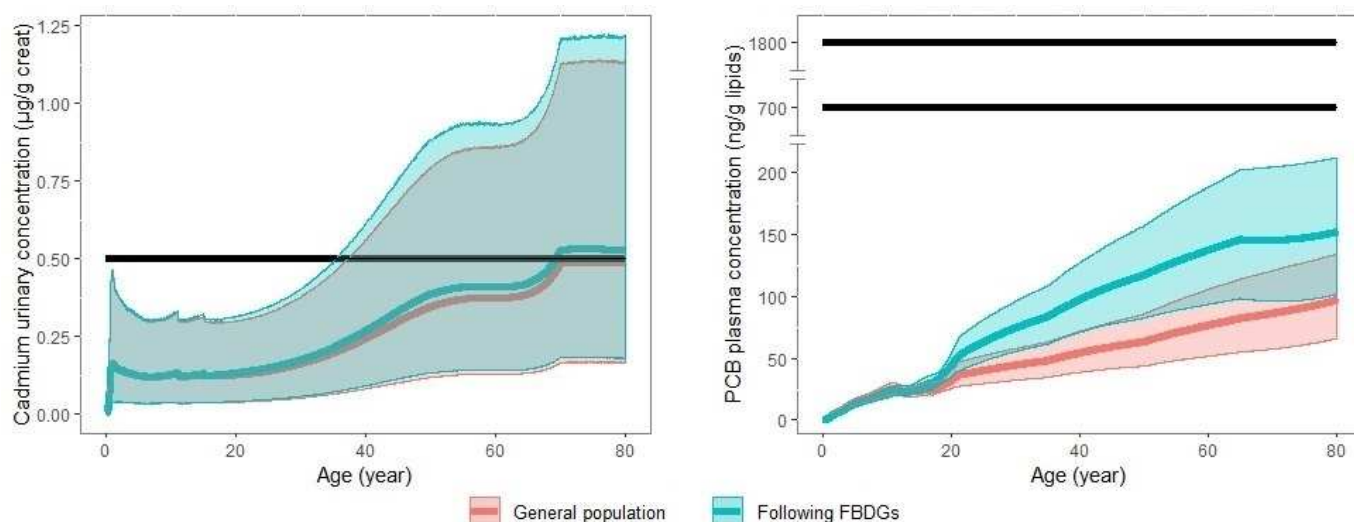
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Figure 4: Mean cadmium and PCB body burden trajectories and 95% prediction intervals, according to following of selected

302 *FBDGs. Horizontal black lines represent critical concentrations.*

303

304 Cadmium body burden trajectories of the general population and individuals following FBDGs were

305 similar. The concentration of cadmium in urine was on average 0.2 µg/g creatinine at the age of 40

306 and 0.5 µg/g creatinine at the age of 80 for the general population. For individuals following FBDGs,

307 cadmium body burdens were 0.3 and 0.5 µg/g creatinine at 40 and 80, respectively (Table 2).

308 PCB plasma concentrations were higher for individuals following FBDGs than for the general

309 population (PCB plasma concentration ratios between both populations were around 1.8 at 40 years

310 old and 1.6 at 80 years old, Table 2).

311

312 *Table 2: Description of dietary exposure and body burden trajectories for cadmium and PCBs. Comparison with HBGVs and*

313 *critical concentrations according to following of FBDGs. Given values are means in the considered population and 95%*

314 *prediction intervals (NR: Not Relevant).*

	Cadmium		PCBs	
Population	General	Following FBDGs	General	Following FBDGs
Mean exposure	1.2 µg/kg	1.3 µg/kg	5.7 ng/kg	8.8 ng/kg

	bw/week [1.2; 1.3]	bw/week [1.3; 1.4]	bw/day [5.5; 5.8]	bw/day [8.5; 9.0]
through life				
Duration of exceedance of the HBGV	3.7 years [3.3; 4.2]	3.9 years [3.5; 4.4]	2.2 years [1.8; 2.6]	5.8 years [5.3; 6.5]
Mean magnitude of exceedance of the HBGV	0.7 µg/kg/week [0.6; 0.8]	0.7 µg/kg/week [0.6; 0.8]	8.9 ng/kg/day [7.0; 10.9]	10.3 ng/kg/day [9.0; 11.7]
Maximum magnitude of exceedance of the HBGV	5.8 µg/kg/week [3.1; 12.8]	5.8 µg/kg/week [3.0; 12.5]	59.3 ng/kg/day [34.3; 103.4]	77.1 ng/kg/day [55.6; 96.2]
Body burden at 40	0.2 µg/g creat [0.08; 0.6]	0.3 µg/g creat [0.09; 0.6]	54.3 ng/g lip [38.6; 71.7]	96.9 ng/g lip [70.4; 126.5]
Body burden at 80	0.5 µg/g creat [0.2; 1.1]	0.5 µg/g creat [0.2; 1.2]	97.0 ng/g lip [65.9; 133.8]	147.9 ng/g lip [99.8; 205.5]
Percentage of the population exceeding the critical concentration over the life course	40.8% [39.9; 41.7]	47.9% [46.9; 48.8]	0%	0%
Age of first exceedance for people exceeding the critical concentration	50.1 years [0.6; 70.8]	50.5 years [0.6; 70.5]	NR	NR

315

316   To assess the health risk related to lifetime body burdens, simulated trajectories were compared

317   with critical concentrations. For cadmium, the value of 0.5 µg Cd/g creatinine in urine, set by ANSES

318   (2017) based on skeletal effects and by ATSDR (2012) based on renal effects, was selected. For PCBs,

319   ANSES derived two critical values: 700 ng/g lipids for children under the age of 3, young girls and

320   women of childbearing age, and 1 800 ng/g lipids for boys over the age of 3, adult men and women

321   above the age of 45 (AFSSA 2010).

322   Differences in terms of cadmium body burden between the general population and individuals

323   following FBDGs were low. In both populations, more than 40% of individuals had cadmium

324   concentrations in urine higher than the critical concentration of 0.5 µg/g creatinine. The mean age, at

325   the first exceedance for individuals exceeding the critical concentration, was around 50 years old for

326   both populations (Table 2). These simulations may be validated by comparison with cadmium urinary

327   concentrations measured in the French population. The ENNS study recorded in 2006 a geometric

328   mean of 0.27 µg/g creatinine and a 95th percentile of 0.79 µg/g creatinine in 913 non-smokers

329   between 18 and 74 years of age (Fréry et al. 2011). In comparison, the geometric means of body

330   burdens simulated between 18 and 74 years old were 0.2 µg/g creatinine and 0.3 µg/g creatinine for

331   the general population and individuals following FBDGs, respectively. The 95th percentiles were 0.7

332   and 0.8 µg/g creatinine.

333   No individual in the simulated population had PCB body burdens exceeding the critical

334   concentrations of 700 and 1 800 ng/g plasma lipids (Table 3). However, because exposure

335   trajectories were simulated from food contamination data measured in 2006-2007, the evolution of

336   contamination was not considered. Even if it was shown that cadmium food concentrations did not

337   change much in past years (EFSA 2009; Pruvost-Couvreur et al. 2020a), PCB dietary exposures varied

338   through last decades because of regulations (IARC 2016). This evolution was shown to have lifetime

339   impact on PCB plasma concentrations (Pruvost-Couvreur et al. 2020b). Thus, trajectories simulated in

340   this work do not reflect actual body burdens of the French adult population. However, they allow the

341   quantification of the impact of FBDGs on lifetime body burden with present food contamination. This

342   modelling highlights that, with the actual food contaminations, lifetime PCB plasma concentrations

343   remain far below the reference values of 700 and 1 800 ng/g lipids. However, it must be noted that,

344   when considering a scenario of exclusive breastfeeding during the first six months of life, as

345   recommended by the World Health Organization (WHO 2017), PCB body burdens would be higher in

346   early childhood than that was simulated in this work, and may exceed the critical concentration

347   during a short but critical period for child development (Pruvost-Couvreur et al. 2020b).

348   This work highlights the difficulty of deriving FBDGs that cover nutritional requirements while limiting

349   the exposure to contaminants. In fact, considering only nutritional requirements, a first theoretical

350   scenario had been computed by ANSES in order to study the possibility of covering all nutritional

351   requirements with foods currently available (ANSES 2016a). The results of this scenario showed that

352   to cover nutritional requirements, oily fish consumption should be from 5 to 12 times higher than the

353   average actual consumption in the population measured in the INCA2 survey and the consumption of

354   wholegrain cereal products should be much higher than that actually consumed in the population

355   (about 315 times higher than the average measured in the INCA2 survey). However, considering the

356   limits imposed by French dietary habits, some constraints had to be relaxed in the optimisation

357   model. In addition, due to the contamination of certain foods as fish (especially with methylmercury

358   and PCBs), other constraints were relaxed in order to limit the consumption of highly contaminated

359   foods. These new constraints led to decrease the consumption of oily fish, which is rich in long-chain

360   omega-3 fatty acids and therefore helps to reduce the incidence of cardiovascular diseases. Similarly,

361   the quantity of wholegrain cereal products has been reduced in favour of refined products, despite

362   the fact that the latter are less rich in fibre.

363   In the case of PCBs, these results are supported by a benefit/risk analysis (Sirot et al. 2012a) and

364   show that until there is a decrease in food contamination, a balance between nutritional intake and

365   food contamination is necessary.

366

367   ## 4. Conclusions

368   Lifetime PCB body burdens were higher for individuals following FBDGs covering fish, meat and dairy

369   products than those for the general population but in all cases they remain below critical values.

370　For cadmium, lifetime exposures and body burdens were similar for both populations. Our

371　simulations showed that following or not the FBDGs covering cereal products, fruits and vegetables,

372　exceedances of critical internal concentrations were similar.

373　If recommendations are established to minimise the exposure to contaminants while optimising

374　nutrients intakes, they induce PCB exposures and body burdens higher than those observed in the

375　general population: there is a 1.8 factor at the age of 40 between PCB plasma concentrations of the

376　general population and of individuals following the FBDGs during their entire life. Furthermore, even

377　if FBDGs do not induce higher cadmium exposures than those measured in the general population,

378　they lead to body burdens exceeding the critical value for a large part of the population.

379　For both PCBs and cadmium, the foods on which action should be taken to reduce exposure are also

380　those that contribute to the benefits of the diet proposed by FBDGs. Vegetables, fruits and

381　wholegrain cereal products food groups are on average major contributors to cadmium exposure but

382　reduce the risk of cardiovascular diseases, cancers, and type 2 diabetes. Similarly, fish and

383　particularly oily fish are one average major contributors to PCB exposure but reduce the risk of

384　cardiovascular diseases. Even if environmental contaminations are decreasing and are expecting to

385　decrease further in the coming years, efforts should be continued to limit the contamination of

386　certain food groups. In addition, it is necessary to consider the French eating habits when developing

387　FBDGs, in order to propose guidelines that are acceptable by the population. This constraint also

388　limits the actions that can be implemented to reduce exposure to food contaminants.

389　Even though the simulation method can be improved to better estimate the inter- and intra-

390　individual variabilities, and consequently the extreme trajectories, these results highlight the

391　relevance to study the long-term impact of specific dietary patterns on lifetime exposures and body

392　burdens when establishing FBDGs. In addition, a potential improvement would be to be able to

393　consider more precise food groups, making it possible to refine the assessment of exposures to food

394　contaminants, and thus to adjust the scenarios for optimising FBDGs.

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477

Figure and table captions

478

479 Figure 1: Contribution of food groups covered by a FBDG to cadmium and PCB exposures for children

480 (A) and adults (B)

481 Figure 2: Percentage of children (A, B) and adults (C, D) following FBDGs covering food groups

482 contributing to cadmium (A, C) and PCB (B, D) exposures in the TDS2. Underline values correspond to

483 the percentages of individuals following at least one FBDG. Other values correspond to percentages

484 of individuals following a combination of FBDGs.

485 Table 1: FBDGs selected to simulate lifetime exposure trajectories to cadmium and PCBs

486 Figure 3: Distributions of cadmium and PCB exposures fitted in data from the TDS2, according to age

487 group and following of the selected FBDGs. Dots represent outlier exposures (i.e. exposures higher

488 than the third quartile plus 1.5 times the interquartile range) and indications above boxplots

489 illustrate the statistical Kolmogorov-Smirnov test significance (NS: Not Significant, ***: p-

490 value<0.001). Horizontal black lines represent HBGVs.

491 Figure 4: Mean cadmium and PCB body burden trajectories and 95% prediction intervals, according

492 to following of selected FBDGs. Horizontal black lines represent critical concentrations.

493 Table 2: Description of dietary exposure and body burden trajectories for cadmium and PCBs.

494 Comparison with HBGVs and critical concentrations according to following of the FBDGs. Given

495 values are means in the considered population and 95% prediction intervals (NR: Not Relevant).

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