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1 Personalized fish intake recommendations: the 2 effect of background exposure on optimization

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9 programming: background exposure

10 Abstract

11 National dietary guidelines are directed at the general population. However, these guidelines may be
12 perceived as unrealistic by a substantial part of the population, as they differ considerably from
13 individual consumption patterns and preferences. Personalized dietary recommendations will probably
14 improve adherence and it has been shown that these recommendations can be derived by mathematical
15 optimization methods. However, to better account for risks and benefits of specific foods, the
16 background exposure to nutrients and contaminants needs to be considered as well. This background
17 exposure may come from other foods and supplements, and also from environmental sources like the
18 air and the sun. The objective of this study was therefore to analyse the effect of including individual
19 variation in background exposure when modelling personalized dietary recommendations for fish. We
20 used a quadratic programming model to generate recommended fish intake accounting for personal
21 preference by deviating as little as possible from observed individual intake. Model constraints ensure
22 that the modelled intake meets recommendations for eicosapentaenoic acid (EPA), docosahexaenoic
23 acid (DHA), and vitamin D without violating tolerable exposure to methyl mercury, dioxins, and
24 polychlorinated biphenyls (dl-PCBs). Several background exposures were analysed for 3,016 Danish
25 adults, whose food intakes and body weights were reported in a national dietary survey. We found that
26 the lower nutrient constraints were critical for the largest part of the study population, and that a total of
27 55% should be advised to increase their fish intake. The modelled fish intake recommendations were
28 particularly sensitive to the vitamin D background exposure.

29 **Introduction**

30 Dietary guidelines are developed to inform the population about healthy food consumption. They are
31 based on evidence that is obtained for a representative selection of population and directed at the
32 population as a whole. However, it can be argued that personalized dietary recommendations should be
33 available because of the variation within the population. Personalized recommendations may be
34 perceived as more relevant and have stronger motivational effects because these can account for an
35 individual's preferences, requirements, needs, beliefs, etc. ⁽¹⁾.

36 Previous diet optimization studies have explored personalized guidelines by modelling personalized
37 intake recommendations that deviate as little as possible from observed intake levels, while fulfilling
38 several health-related criteria on nutrient and contaminant recommendations, energy intake and/or
39 intake weight ⁽²⁻⁴⁾. The arguments for minimizing the deviation from individual intake were that such
40 recommendations will be more relevant, realistic, and achievable for consumers, and therefore a higher
41 compliance with the recommendation could be expected.

42 An example of a national dietary guideline is the recommendation for fish intake in Denmark, which
43 states that the Danes should eat 350 g of fish per week, of which 200 g should be fatty fish ⁽⁵⁾. This
44 guideline is directed at the healthy population over 3 years of age. As a step towards developing
45 personalized guidelines, we previously modelled individual fish intake recommendations for eight
46 species of fish for 3,016 Danes, using mathematical optimization methods and found that 74% of the
47 study population should be advised to increase their fish consumption ⁽²⁾. The modelled intakes fulfilled
48 constraints on eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), vitamin D, methyl mercury,
49 dioxins, and dioxin-like polychlorinated biphenyls (dl-PCBs), as these nutrients and contaminants are
50 the main contributors of beneficial and adverse health effects from fish consumption ⁽⁶⁾.

51 Most nutrients and contaminants present in a specific food (such as fish) can be provided by
52 background exposure as well, which can impact the critical intake levels of the food product
53 considered. When optimizing the intake of one specific food, the background exposure to nutrients and
54 contaminants that can be found in the food product in question needs to be considered. While previous
55 studies ^(2, 7) estimated average background exposure values for the whole population, background
56 exposures will also vary between individuals and may therefore have a different impact for different
57 consumers. The objective of this study was to analyse the effect of including individual variation in

58 background exposure when modelling personalized dietary recommendations for fish. It is primarily a
59 methodological study, in which fish consumption is used to demonstrate the potential of the method.

60 **Methods**

61 **Data**

62 **Observed intakes and body weights**

63 Observed individual food intake (7-day estimated records) along with self-reported body weight from
64 the Danish national survey of diet and physical activity (DANSDA) (unpublished data, April 2011–
65 August/September 2013) were used. Individuals aged 18-75 y (1,552 women and 1,464 men; total of
66 3,016 individuals) defined our study population. In total, 433 foods were reported and 17 were defined
67 as fish in this study. Raw, smoked, canned, and marinated fish were included. The fish consumed
68 corresponded to 11 species of fish (see **Table 1**), denoting the elements of the optimization
69 variable ($d=11$). The observed fish intake was not normally distributed, according to the Lilliefors test
70 at significance level 5%. Species with fat content up to 5% were classified as lean fish (six species) and
71 species with fat content higher than 5% were classified as fatty fish (five species) ⁽⁶⁾. See the observed
72 intake amounts of lean and fatty fish in **Figure 1a**. Fish roe and fish liver were not included. The
73 average daily intake was converted to average weekly intake by multiplying the average daily intake by
74 seven. As eel is considered critically endangered, marketing and consumption of European eel is
75 debated, and therefore it was excluded from this study. Individual body weights are required in the
76 model since the limit values for the contaminants are body-weight dependent. There were 47 missing
77 recorded values (for 16 men and 31 women) for body weight in DANSDA. For these individuals, the
78 gender-specific average body weight of an individual in the study population was used: 69.7 kg for
79 women and 84.4 kg for men.

80 **Concentrations**

81 Nutrient concentration data (EPA, DHA and vitamin D) were from the Danish food composition
82 database ⁽⁸⁾ and contaminant concentration data (mercury and dioxins + dl-PCBs) were from two
83 different chemical contaminant reports ^(9, 10). The weighted averages of the nutrient and contaminant
84 concentrations for the 11 species were calculated with weights equal to the reported intake amounts of
85 the categories raw, smoked, canned, and marinated. The weighted averages of the two contaminant

86 reports were calculated with the number of samples per report serving as weights. To get
 87 concentrations for methyl mercury, we used the same conservative approach as used by EFSA ⁽¹¹⁾:
 88 100% of mercury in fish was considered as methyl mercury, and methyl mercury comprised 80% of
 89 total mercury in seafood other than fish. For three lean fish species (European flounder, garfish, and
 90 saithe), data on one or more nutrient or contaminant were missing. European flounder is in the same
 91 family as plaice and therefore the data on plaice was used when a value was missing (methyl mercury).
 92 Saithe is in the same family as cod, and data on cod was used accordingly (EPA + DHA and
 93 dioxins + dl-PCBs). Garfish is not in the same family as any of the other species included in this study.
 94 For garfish, the average value of the lean species was used when a value was missing (methyl
 95 mercury). The concentrations used in this study are presented in **Table 2**.

96 **Limit values**

97 The recommended daily intake for EPA + DHA ⁽¹²⁾ and vitamin D ⁽¹³⁾, and the tolerable weekly intake
 98 per body weight for methyl mercury ⁽¹¹⁾ and dioxins + dl-PCBs ⁽¹⁴⁾ were used as limit values (**Table 3**).
 99 These recommendations are for total **intake and exposure**, and therefore background **intake and**
 100 **exposure** had to be subtracted from them in the model. Daily values were converted to weekly values
 101 by multiplying daily recommendations by seven, and per-body-weight values were converted to
 102 individual values by multiplication with individual body weight. For vitamin D, there is an upper level
 103 of 100 µg/d ⁽¹⁵⁾, but it was neglected because the contaminant constraints were limiting the fish intake
 104 amount long before this value could be reached.

105 **Model overview**

106 The quadratic programming model ⁽²⁾ is expressed as:

$$\underset{\mathbf{x}}{\text{minimize}} \quad \|\mathbf{x} - \mathbf{x}_{\text{obs}}\|_2 \quad (\text{a})$$

$$\text{subject to} \quad \mathbf{B}\mathbf{x} \geq \mathbf{b} \quad (\text{b})$$

$$\mathbf{R}\mathbf{x} \leq \mathbf{r} \quad (\text{c})$$

$$\mathbf{x} \geq \mathbf{0} \quad (\text{d})$$

107 where the vector \mathbf{x} ($d \times 1$) is the optimization variable representing weekly intake amounts of d different
 108 fish species, and the vector \mathbf{x}_{obs} ($d \times 1$) is a constant vector describing the corresponding observed intake

109 amounts of an individual. The optimization variable denotes 11 species of fish reported in the intake
 110 data ($d=11$). The objective function (a) of the model is the L_2 -norm of $\mathbf{x} - \mathbf{x}_{\text{obs}}$:

$$\|\mathbf{x} - \mathbf{x}_{\text{obs}}\|_2 = \sqrt{|x_1 - x_{\text{obs},1}|^2 + |x_2 - x_{\text{obs},2}|^2 + \dots + |x_n - x_{\text{obs},d}|^2}$$

111 The objective function is minimized, hence the sum of the square of the deviations between the
 112 individual observed intake \mathbf{x}_{obs} (from individual intake data) and the optimized (by the model) intake \mathbf{x}
 113 is minimized. Personal objective functions are thereby defined by the personal intake amounts
 114 $x_{\text{obs},1}, x_{\text{obs},2}, \dots, x_{\text{obs},d}$. The objective function can be rewritten to a quadratic function, since \mathbf{x} is real-
 115 valued:

$$(x_1 - x_{\text{obs},1})^2 + (x_2 - x_{\text{obs},2})^2 + \dots + (x_n - x_{\text{obs},d})^2$$

116 The model constraints ensure that the optimized intake meets weekly lower limits on the nutrients
 117 EPA + DHA and vitamin D (b) without violating weekly upper limits on the contaminants methyl
 118 mercury and dioxins + dl-PCBs (c), and the constraints make sure that no negative intake occurs (d).
 119 The vector \mathbf{b} ($m \times 1$) describes the weekly lower limits for the nutrient intake amounts due to fish intake
 120 ($m=2$), and \mathbf{r} ($k \times 1$) describes the weekly upper limits for the contaminant intake amounts ($k=2$). The
 121 matrix \mathbf{B} ($m \times d$) describes the mean nutrient concentrations for the different fish species, and \mathbf{R} ($k \times d$)
 122 describes the mean contaminant concentrations. The model allows an individual's non-reported fish
 123 species in her/his output intake. As it may be unlikely that people start choosing fish species they did
 124 not eat before, the model can be modified to only allow reported species by employing equality
 125 constraints in (d) for the non-reported species of the individual. Different background exposure
 126 scenarios correspond to different limit values (vector \mathbf{b} and \mathbf{r}) in the constraints. All vectors \mathbf{x} that
 127 satisfy the constraints make up the feasible region of the problem. If there is no combination of fish
 128 species that can meet the constraints, no feasible solution is obtained and the model cannot generate a
 129 recommendation.

130 **Background exposure**

131 **Other foods**

132 The background intake of nutrients and exposure to contaminants due to foods other than fish were
 133 potentially supplied by the 416 of the 433 reported foods in the intake data that were not fish (Danish

134 national survey of diet and physical (DANSDA 2011–13, unpublished data). **The food intake is not**
135 **normally distributed, according to the Lilliefors test ($\alpha = 5\%$).** Individually reported whole diets,
136 excluding fish intake, were multiplied with concentrations of the nutrients and contaminants of the
137 different foods. Hence, the total intake of the different nutrients and contaminants was obtained for
138 each individual in the study population (**Table 4**). EPA + DHA could be supplied by 27 of the reported
139 foods; mainly seafood (shrimp, mussels, fish roe, fish liver, etc.), and a smaller fraction by chicken and
140 a few additional animal products. The background intake of EPA + DHA was 14% and 12% of the total
141 average intake for women and men, respectively. For vitamin D, the relative importance of sources
142 other than fish was higher and the respective numbers were 61% and 63%. Background intake of
143 vitamin D was potentially supplied by 116 of the reported foods, and the major sources were animal
144 products including dairy products. For methyl mercury, 11 seafoods were the source of background
145 exposure. These seafoods contributed to 9% and 6% of the total average dietary exposure for women
146 and men, respectively. For dioxins + dl-PCBs, 64% and 65% of the total average dietary exposure was
147 due to background exposure for women and men, respectively. The background exposure to
148 dioxins + dl-PBCs was potentially supplied by 153 foods and the major sources were animal products
149 including dairy products, as for vitamin D.

150 **Supplements**

151 Data on individual vitamin D intake from vitamin D supplements and multi-minerals from DANSDA
152 were used (Table 4). In the study population, 62% of the women and 49% of the men had recorded
153 intake of supplements containing vitamin D. No data on EPA + DHA supplement intake were available
154 and therefore only vitamin D supplement intake was included in this study.

155 **Sun and airborne contaminants**

156 Vitamin D can be provided by UVB radiation from the sun that gets synthesized in the skin. In
157 Denmark (latitude 55°N to 58°N), there is a significant seasonal variation in how much UVB radiation
158 that reaches the surface of the earth; the highest level is in summer, and the lowest in winter^(16, 17). **We**
159 **calculated (see Appendix) three different scenarios for sun exposure to cover the seasonal variation;**
160 **Winter, Mid-season, and Summer.** Food consumption is the major source of dioxins, contributing to
161 more than 90% of the total human exposure⁽¹⁸⁾. **We calculated (see Appendix) two different scenarios**
162 **for airborne dioxin exposure; baseline (default) and low dioxin (LD).** For methyl mercury, fish and
163 seafood consumption is considered the major source of exposure^(11, 19), and the average exposure due

164 to air is $< 0.04 \mu\text{g/d}$ ⁽¹⁹⁾. Since our assumptions for methyl mercury concentration in food were
165 conservative, we assumed food as the only source.

166 **Software**

167 The models were implemented using Matlab (R2015b, version 8.6). The package CVX, for specifying
168 and solving convex programs ⁽²⁰⁾, was used for the optimization.

169 **Background exposure scenarios**

170 To analyse the impact of background exposure, 24 background exposure scenarios were created. First,
171 six scenarios for the sun and airborne contaminant exposure were defined, combining the Winter, Mid-
172 season, and Summer sun exposure scenario with the baseline and LD airborne dioxin scenarios (see
173 **Table 5a**). These six scenarios were run with individual intake of foods other than fish and individual
174 supplement intake, individual intake of foods other than fish without supplements (by assigning all
175 individuals zero supplement intake), gender-specific average values for intake of foods other than fish
176 and gender-specific average supplement intake, and gender-specific average values for intake of foods
177 other than fish without supplements. Hence, in total, 24 background exposure scenarios were created
178 and each scenario was given a short name (**Table 5b**). The Mid-season scenario with individual intake
179 of foods other than fish and individual supplement intake (Mid-season Ind) is the baseline background
180 exposure scenario of our study.

181 **Results**

182 **Mid-season and individual values**

183 Out of the 3,016 individuals in the study population, there were 24 individuals not obtaining a feasible
184 solution, i.e., no personalized recommendation could be generated **with the Mid-season sun exposure**
185 **scenario with and without supplement intake (Mid-season Ind and Mid-Season Ind No Sup)** (see
186 **Table 6**). Out of these, 22 had a background exposure to dioxins + dl-PCBs that was higher than the
187 threshold (14 pg TEQ/kg BW/wk). The other two had a background exposure to dioxins + dl-PCBs just
188 below the threshold, but there was a conflict with the nutrient constraints, so that no fish intake could
189 fulfil all constraints. **The observed intake and the modelled recommendations with the Mid-season Ind**
190 **scenario, which is our baseline scenario, are grouped into lean and fatty fish, for the purpose of**

191 visualization (see **Figure 1**). The average modelled fish intake recommendations (also grouped into
192 lean and fatty fish) with the 24 different background exposure scenarios can be seen in
193 **Supplemental Table 1**. The suggested changes in fish intake (delta intake), modelled
194 recommendations minus observed intakes, can be visualized with empirical cumulative distribution
195 functions. For these functions, the value on the y-axis at any specified value of the delta fish intake is
196 the fraction of individuals in the study population that should be suggested to make a change less than
197 or equal to the specified value. **Figure 2** shows this for the Mid-season Ind scenario (2 a, c, and d) and
198 for the Mid-season Ind No Sup scenario (d). Our results suggest that 43% of the 2,992 individuals with
199 feasible solutions (99% of the study population) should be advised to maintain their current fish
200 consumption pattern, that 55% should be recommended to increase their total fish intake up to
201 184 g/wk (24% with more than 100 g/wk), and that only 2.0% should be recommended to decrease
202 their fish intake (see Figure 2 a). With the Mid-season sun exposure scenario, the difference in the
203 results generated with and without supplements is small, and so is the difference with individual and
204 average data (see Supplemental Table 1). Different species dominate the recommended intakes, which
205 depends on whether the EPA + DHA or the vitamin D constraint is the critical lower constraint. For
206 example, saithe dominate the lean fish species and trout dominate the fatty fish species when the
207 vitamin D constraint is critical, whereas garfish and herring dominate when the EPA + DHA constraint
208 is critical (see Figures 2 c and d). When the model was modified to only allow reported fish intake in
209 the modelled recommendations, 536 individuals had no feasible solutions and different species
210 dominated the modelled intakes: tuna, plaice and cod dominate the lean fish species, and mackerel and
211 salmon dominate the fatty fish species (see **Figure 3**).

212 **Winter and individual values**

213 The recommended intake modelled with the Winter sun exposure scenario with and without
214 supplement intake (Winter Ind and Winter Ind No Sup) shows the impact of vitamin D supplements
215 (see Figure 4). When the supplement intake is excluded, 960 women and 715 men should be
216 recommended to increase their fish intake a lot more than with the scenario including the observed
217 supplement intake. With the Winter scenario, one additional woman had no feasible solution as
218 compared with the Mid-season scenario. Her reported body weight was low (41 kg) and a conflict
219 between the vitamin D constraint and the dioxins + dl-PCBs constraint (which is body-weight
220 dependent) occurred with this scenario that has no sun exposure contributing to vitamin D intake. With
221 the Winter scenario, the same fish species as for the Mid-season scenario dominate, depending on the

222 critical lower constraint. However, a larger fraction of the study population has the vitamin D
223 constraint as the critical lower constraint (see **Figure 5**). When **the Winter Ind scenario** is analysed
224 under the condition that only reported fish intake is allowed in the modelled recommendations, 791
225 individuals had no feasible solutions and tuna dominate the lean fish species, and herring and salmon
226 dominate the fatty fish species (see **Figure 6**).

227 **Winter and average values**

228 **The Winter scenarios with average values for intake of other foods and supplements** show how average
229 values can give misleading results (see **Figure 7**). The modelled recommendations differ greatly
230 compared with when individual values are used (**Winter Av and Winter Av No Sup**) (Figure 4). With
231 average values, all individuals had a feasible solution due to the fact that the 25 individuals with high
232 background exposure to dioxins + dl-PCBs get a lower value that is compatible with the other
233 constraints, and the individuals not consuming supplements (592 women and 749 men) get a great
234 addition to their background intake of vitamin D when the average values for supplements are used.

235 **Summer and average values**

236 The vitamin D intake due to sun exposure in the Summer scenario (15 µg/d) is higher than the
237 recommended vitamin D intake (10 µg/d). Hence, the vitamin D constraint is already fulfilled, and the
238 EPA + DHA constraint is the lower critical constraint for all individuals. **The Summer scenario is hard**
239 **to distinguish from the Mid-season scenario in a figure**, and hence not shown.

240 **Low dioxin**

241 With the **low dioxin airborne exposure scenarios** (LD), two more individuals (one woman and one
242 man) had feasible solutions compared with when the baseline value for dioxins + dl-PCBS is used. The
243 majority of the study population should be recommended the same intake with the low dioxin exposure
244 as with the baseline value, since the number of individuals with high reported fish intake are fewer than
245 those with lower reported intake (see Figure 1).

246 **Non-fish consumers**

247 In the study population, 12% of the individuals reported no fish intake. With **the Winter sun exposure**
248 **scenario with individual values** (**Winter Ind and Winter Ind No Sup**), the modelled intake
249 recommendations located on an imaginary line (see Figure 4) correspond to recommendations for

250 individuals with no fish intake. The ratio between lean and fatty fish is 1 to 2.3 for these
251 recommendations, and the line is orthogonal to the individual critical lower vitamin D constraints. With
252 the Summer sun exposure scenario (**Sun Ind and Sun Ind No Sup**), the EPA + DHA constraint is the
253 critical lower constraint for all individuals, and with this scenario, the ratio between lean and fatty fish
254 species is 1 to 3.3 for non-fish consumers.

255 Discussion

256 To our knowledge, this is the first intake optimization study exploring the effect of individual
257 background exposure to nutrients and contaminants due to the consumption of other foods and
258 supplements, as well as sun and airborne contaminant exposure. We showed that individual differences
259 in background exposure can be included in the analysis and that these differences provide additional
260 insights and affect the personalized recommendations. The majority of the 3,016 Danes in our study
261 population had reported a fish intake that was lower than her/his individual model constraints allowed,
262 and hence the lower nutrient constraints (EPA + DHA and vitamin D) were critical for the largest part
263 of the study population. The modelled recommendations were specifically sensitive to the vitamin D
264 background exposure. Comparing the **Mid-season scenario (the baseline scenario) with the Winter
265 scenario**, that differ with 7.25 µg/d vitamin D background intake, the individuals not taking vitamin D
266 supplements should be recommended a much higher fish intake in winter. A few individuals with high
267 background intake of dioxins + dl-PCBs were affected by a lower dioxin airborne exposure than the
268 baseline value, but the largest part of the study population was not. The exposure to EPA + DHA and
269 methyl mercury is mainly due to fish consumption, and therefore the background exposure to these
270 compounds had little effect. **However, as mentioned, EPA + DHA supplements may have been taken,
271 which we unfortunately had no data on. Such input would have been very important for the individuals
272 and scenarios where the EPA + DHA constraint dominated, since a higher background intake will
273 lower the constraint resulting in lower fish intake recommendations.**

274 According to our criteria on fish intake (the model constraints on EPA + DHA, vitamin D, methyl
275 mercury and dioxins + dl-PCBs), following the recommendation for fish intake in the official Danish
276 dietary guideline (350 g fish/wk of which 200 g should be fatty fish) is, as expected, healthy and not
277 harmful. However, the official guideline demands larger changes in consumption than necessary, which
278 may lead to a lack of compliance. **This is concluded using our baseline scenario for background
279 exposure (Mid-season Ind).** This was also concluded in our previous study on individual fish intake

280 recommendations ⁽²⁾. In the present study, we show that fewer individuals need to be recommended to
281 increase their fish intake when individual background exposures are used: 55% of the study population
282 compared with 74% as concluded in our previous study using the same average background exposures
283 for all individuals.

284 **When only reported fish species are allowed in the modelled recommendation, larger intake amounts of**
285 **fish should be suggested compared with when all species are allowed. Since the reported intake was a**
286 **7-day estimated record, and other species of fish may well have been consumed by an individual during**
287 **another week, we concluded that the results from the model only allowing reported species in this study**
288 **are less relevant.** However, if the observed intake data were, for example, individual yearly average
289 values, the modified model only allowing individual reported fish species may be appropriate for
290 generating the personalized recommendations, since the intake data would reflect which species an
291 individual consumes. If data on which fish species an individual could consider consuming and which
292 species she/he do not wish to consume was available, the results could be further personalized by only
293 allowing the species she/he wants in the personalized recommendation.

294 A future application of our model could be to create software that individuals could use and generate
295 personalized recommendations themselves. The user would be asked by the software to insert how
296 much she/he currently consumes of some food items, and to select which additional food items she/he
297 would consider for consumption. By application of our model, the software could then generate a
298 personalized recommendation that accounts for the individual's inserted preferences. If the individual
299 would set too few foods she/he is willing to consume to obtain a feasible solution, the software would
300 have to ask the individual to select additional foods.

301 In our previous study ⁽²⁾, all individuals obtained a feasible solution, i.e., a personalized
302 recommendation could be made. With the inclusion of individual background exposures, 24 individuals
303 (0.8% of the study population) had unfeasible solutions due to a too high background exposure to
304 dioxins + dl-PCBs with **the Mid-season scenario. It is important to stress that there are other ways to**
305 **modify diets to fulfil the requirements on the EPA, DHA, and vitamin D without exceeding the limit**
306 **value for methyl mercury and dioxin + dl-PCBs than to only modify fish intake. As mentioned, vitamin**
307 **D and dioxin + dl-PCBs, for example, can be provided by several animal products including dairy. So,**
308 **the 24 individuals without feasible solutions should typically be suggested to eat less of these foods. In**
309 **this paper, fish was the only food in focus, foods other than fish were defined as background exposure,**
310 **and substitution with other foods was not considered, but the optimization approach can be extended to**

311 include foods other than fish in the optimization variable; even whole diets can be optimized^(3, 4, 21). By
312 expanding the optimization to several foods and ultimately whole diets, the substitution issue is
313 resolved. This may require inclusion of several additional constraints on nutrients and contaminants on
314 top of those mentioned in this fish intake optimization study.

315 When using average values for the background exposures in this study, all individuals had feasible
316 solutions with all scenarios. This suggests that individuals at risk of exceeding the upper levels for the
317 contaminants may not be detected when average background exposures are used. Some individuals
318 would be recommended a fish intake that would result in too high of an exposure to contaminants
319 (dioxins + dl-PCBs in this case) when using average background exposures. In general, when the
320 variation in background exposure from a food compound is large, average values may be misleading.
321 This is also the case when a nutrient (or contaminant) constraint is critical and hard to reach for several
322 individuals due to relatively low (or high) background exposure to the compound. This was shown for
323 the vitamin D background exposure by comparing individual background exposure from foods and
324 supplements with average values. With the Winter scenario and average values, the model resulted in
325 much lower recommended intakes than appropriate, especially for individuals not taking supplements.

326 In previous fish intake optimization studies, it has been concluded that when a substantial amount of
327 vitamin D is required to come from fish, there is a conflict between vitamin D and contaminants^(2, 7). In
328 these studies, all individuals were assigned the same average background exposures. In the present
329 study, we concluded that there is a conflict only for 25 individuals when sun exposure and supplements
330 are excluded, which is the extreme case, and 24 individuals when including sun exposure and
331 supplements. Hence, this study shows that the conflict between vitamin D and contaminants is not as
332 critical as concluded before. When a high level of vitamin D is required to come from fish, the
333 recommended fish intake should be high, but still within the feasible region for the majority of the
334 study population. It is however clear that vitamin D exposure from the sun greatly affects the modelled
335 intake. From this, it could be argued that all individuals in Denmark should eat supplements to reach
336 the vitamin D recommendation, whereby only the EPA + DHA constraint would be relevant for the fish
337 consumption. This would result in lower and hence more achievable fish intake recommendations.
338 Obviously, if we would have been able to include the intake of fish oil supplements as well, fish intake
339 recommendations based on EPA + DHA requirements would have reduced even more.

340 This approach can be used to estimate personalized intake recommendations for other foods and/or
341 other populations. When considering using average values for background exposure, we suggest

342 starting by performing a rough scenario analysis with different average values to investigate the
343 sensitivity of the results on the background exposure, and to obtain an indication of how many
344 individuals can be at risk of exceeding the tolerable intake levels for the contaminants. After this, a
345 conscious decision on whether or not to include individual background exposure data can be made.
346 This applies to all background exposures, but especially to supplements because the nutrient
347 concentration(s) in supplements are usually high (and often cover the recommended intake(s) alone),
348 and individuals either take or not take supplements. If individual supplement intake data are used, the
349 modelled recommendations may be grouped into two clusters of individuals, with and without reported
350 supplement intake, which is important to stress when communicating the modelled recommendations.

351 **Lastly, this method builds upon the assumption that personalized dietary recommendations deviating as**
352 **little as possible from current consumption have a higher compliance than national guidelines, which**
353 **has not been confirmed. How individuals respond to personalized recommendations is an area that**
354 **requires additional research.**

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362 **Conflict of Interest**

363 None

364 **Authorship**

365 The authors contributions are as follows: M.P. and M.J.N. formulated the research question; M.P. and
366 M.J.N. designed the study; S.F. provided essential material; M.P. carried out the study, M.P. analysed
367 the data; M.P. and M.J.N. drafted the manuscript and all authors approved the final version.

368 **References**

- 369 1. Brug J, Campbell M, van Assema P (1999) The application and impact of computer-generated
370 personalized nutrition education: A review of the literature. *Patient Educ Couns* **36**:145–156
- 371 2. Persson M, Fagt S, Pires SM, et al (2018) Use of Mathematical Optimization Models to Derive
372 Healthy and Safe Fish Intake. *J Nutr* **148**:275–284
- 373 3. Maillot M, Vieux F, Amiot MJ, et al (2010) Individual diet modeling translates nutrient
374 recommendations into realistic and individual-specific food choices. *Am J Clin Nutr* **91**:421–430
- 375 4. Maillot M, Vieux F, Ferguson E, et al (2009) To Meet Nutrient Recommendations, Most French
376 Adults Need to Expand Their Habitual Food Repertoire. *J Nutr* **139**:1721–1727
- 377 5. Tetens I, Andersen LB, Astrup A, et al (2013) Evidensgrundlaget for danske råd om kost og
378 fysisk aktivitet.
- 379 6. Norwegian Scientific Committee for Food Safety (VKM) (2014) Benefit-risk assessment of fish
380 and fish products in the Norwegian diet – an update. Scientific Opinion of the Scientific Steering
381 Committee.
- 382 7. Sirot V, Leblanc J-C, Margaritis I (2012) A risk –benefit analysis approach to seafood intake to
383 determine optimal consumption. *Br J Nutr* **107**:1812–1822
- 384 8. National Food Institute at Technical University of Denmark (DTU) (2017) Frida version 2 |
385 udgave 2017-06-06.
- 386 9. National Food Institute at Technical University of Denmark (DTU) (2011) Chemical
387 contaminants 2004-2011.
- 388 10. National Food Institute at Technical University of Denmark (DTU) (2013) Chemical
389 contaminants 2012-2013.
- 390 11. EFSA (2012) Scientific Opinion on the risk for public health related to the presence of mercury
391 and methylmercury in food. *EFSA J* **10**:2985 [241 pp.]
- 392 12. EFSA (2010) Scientific Opinion on Dietary Reference Values for fats, including saturated fatty
393 acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol.
394 *EFSA J* **8**:1461 [107 pp.]

- 395 13. Nordic Council of Ministers (2014) Nordic Nutrition Recommendations 2012 Integrating
396 nutrition and physical activity.
- 397 14. EU Scientific Committee on Food (2001) Fact Sheet on dioxin in feed and food.
- 398 15. EFSA (2012) Scientific Opinion on the Tolerable Upper Intake Level of vitamin D. EFSA J
399 **10**:2813 [45 pp.]
- 400 16. Andersen R, Brot C, Jakobsen J, et al (2013) Seasonal changes in vitamin D status among
401 Danish adolescent girls and elderly women: the influence of sun exposure and vitamin D intake.
402 Eur J Clin Nutr **673**:270–274
- 403 17. Hansen L, Tjønneland A, Køster B, et al (2016) Sun Exposure Guidelines and Serum Vitamin D
404 Status in Denmark: The StatusD Study. Nutrients. doi: 10.3390/nu8050266
- 405 18. European Commission (2000) Dioxin contamination of feeding stuffs and their contribution to
406 the contamination of food of animal origin.
- 407 19. Hong Y-S, Kim Y-M, Lee K-E (2012) Methylmercury exposure and health effects. J Prev Med
408 Public Health **45**:353–63
- 409 20. Grant M, Boyd S (2013) CVX: Matlab software for disciplined convex programming, version
410 2.0 beta.
- 411 21. Barre T, Vieux F, Perignon M, et al (2016) Reaching Nutritional Adequacy Does Not
412 Necessarily Increase Exposure to Food Contaminants: Evidence from a Whole-Diet Modeling
413 Approach. J Nutr **146**:2149–2157
- 414 22. Cashman KD, Hill TR, Lucey AJ, et al (2008) Estimation of the dietary requirement for vitamin
415 D in healthy adults. Am J Clin Nutr **88**:1535–42

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417

Table 1. Observed fish intake. Reported fish intake data from DANSDA. Study population: 3,016 individuals aged 18-75 y.

| | Women, n = 1,552 | | | | | Men, n = 1,464 | | | | |
|----------------------------------------------|------------------|---------------|-------------|-----------------|--------------|----------------|---------------|-------------|-----------------|--------------|
| | n _r | Mean, g/wk | SD, g/wk | Median, g/wk | IQR, g/wk | n _r | Mean, g/wk | SD, g/wk | Median, g/wk | IQR, g/wk |
| Total fish intake | 1,397 | 188 | 186 | 144 | 228 | 1,272 | 235 | 252 | 165 | 311 |
| Lean fish (\leq 5% fat) | 1,108 | 80 | 107 | 36 | 120 | 1,039 | 102 | 150 | 45 | 159 |
| Cod (raw) | 591 | 25 | 56 | 0.0 | 22 | 545 | 30 | 69 | 0.0 | 26 |
| European plaice (raw) | 408 | 25 | 66 | 0.0 | 9.7 | 387 | 34 | 101 | 0.0 | 9.7 |
| Tuna (canned) | 753 | 21 | 49 | 0.0 | 15 | 698 | 25 | 64 | 0.0 | 19 |
| European flounder (raw) | 233 | 7.6 | 24 | 0.0 | 0.0 | 242 | 11 | 30 | 0.0 | 0.0 |
| Garfish (raw) | 13 | 0.93 | 11 | 0.0 | 0.0 | 7 | 1.4 | 27 | 0.0 | 0.0 |
| Saithe (raw) | 20 | 0.41 | 7.2 | 0.0 | 0.0 | 19 | 0.45 | 5.3 | 0.0 | 0.0 |
| Fatty fish ($>$ 5% fat) | 1,231 | 108 | 138 | 58 | 161 | 1,089 | 134 | 191 | 50 | 197 |

| | | | | | | | | | | |
|------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|------|------|
| Salmon (raw, smo) | 924 | 41 | 68 | 8.6 | 54 | 728 | 42 | 77 | 0.0 | 45 |
| Herring (mar, raw, smo) | 860 | 31 | 63 | 1.4 | 38 | 783 | 49 | 103 | 0.72 | 54 |
| Mackerel (can, smo, raw) | 947 | 23 | 40 | 9.2 | 33 | 832 | 31 | 57 | 9.2 | 37 |
| Trout (raw) | 355 | 11 | 24 | 0.0 | 0.0 | 270 | 11 | 29 | 0.0 | 0.0 |
| Greenland halibut (raw, smo) | 487 | 1.4 | 5.7 | 0.0 | 1.5 | 374 | 1.8 | 12 | 0.0 | 0.63 |

DANSDA, Danish national survey of diet and physical activity; n_r, number of individuals with reported intake, wk, week; IQR, interquartile range; smo, smoked; mar, marinated

Table 2. Nutrient and contaminant concentrations for fish ⁽⁸⁻¹⁰⁾.

| | EPA + DHA, mg/g | Vitamin D, µg/g | Methyl mercury, µg/g | Dioxins + dl-PCBs, pg TEQ/g |
|---------------------------------|----------------------------|----------------------------|---------------------------------|----------------------------------------|
| Lean fish (≤ 5% fat) | | | | |
| Cod (raw) | 2.2 | 0.010 | 0.045 | 0.13 |
| European plaice (raw) | 6.0 | 0.011 | 0.035 | 0.31 |
| Tuna (canned) | 2.0 | 0.027 | 0.151 | 0.05 |
| European flounder (raw) | 4.2 | 0.0080 | 0.035† | 0.65 |
| Garfish (raw) | 7.8 | 0.052 | 0.056‡ | 0.81 |
| Saithe (raw) | 2.2§ | 0.079 | 0.014 | 0.13§ |
| Fatty fish (> 5% fat) | | | | |
| Salmon (raw, smo) | 16 | 0.079 | 0.011 | 0.81 |
| Herring (mar, raw, smo) | 18 | 0.095 | 0.037 | 1.2 |
| Mackerel (can, smo, raw) | 26 | 0.044 | 0.28 | 1.0 |
| Trout, rainbow (raw) | 14 | 0.16 | 0.023 | 0.38 |
| Greenland halibut (smo, raw) | 8.0 | 0.048 | 0.057 | 0.56 |

EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; dl-PCBs, dioxin-like polychlorinated biphenyls; TEQ, toxic equivalency; smo, smoked; mar, marinated

† Plaice data

‡ Average value of lean fish species data

§ Cod data

Table 3. Recommendations for nutrients and contaminants.

| | Value | Reference |
|------------------------------------|--------------|------------------|
| Recommended daily intake | | |
| EPA + DHA, mg/d | 250 | (12) |
| Vitamin D, µg/d | 10 | (13) |
| Tolerable weekly intake | | |
| Methyl mercury, µg/kg BW/wk | 1.3 | (11) |
| Dioxins + dl-PCBs, pg TEQ/kg BW/wk | 14 | (14) |

EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; d, day; BW, body weight; wk, week; dl-PCBs, dioxin-like polychlorinated biphenyls

Table 4. Nutrient and contaminant exposure. Reported whole diet data and supplement intake data from DANSDA multiplied with concentration data for nutrients and contaminants ⁽⁸⁻¹⁰⁾. Study population: 3,016 individuals aged 18-75 y.

| | Women, n = 1,552 | | | | Men, n = 1,464 | | | |
|--------------------------------------------|-------------------------|-----------|---------------|------------|-----------------------|-----------|---------------|------------|
| | Mean | SD | Median | IQR | Mean | SD | Median | IQR |
| Exposure from all foods | | | | | | | | |
| EPA + DHA, mg/wk | 2.8 | 3.2 | 1.8 | 3.5 | 3.4 | 4.1 | 1.9 | 4.3 |
| Vitamin D, µg/wk | 28 | 20 | 23 | 19 | 35 | 24 | 29 | 23 |
| Methyl mercury, µg/wk | 11 | 13 | 8.2 | 13 | 15 | 18 | 8.9 | 17 |
| Dioxins + dl-PCBs, pg TEQ/wk | 326 | 306 | 265 | 220 | 428 | 303 | 346 | 275 |
| Exposure from foods other than fish | | | | | | | | |
| EPA + DHA, mg/wk | 0.38 | 0.92 | 0.23 | 0.34 | 0.41 | 0.84 | 0.25 | 0.41 |
| Vitamin D, µg/wk | 17 | 14 | 15 | 9.0 | 22 | 16 | 19 | 12 |
| Methyl mercury, µg/wk | 0.96 | 2.1 | 0.095 | 1.0 | 0.90 | 2.1 | 0.054 | 0.78 |
| Dioxins + dl-PCBs, pg TEQ/wk | 210 | 251 | 178 | 98 | 277 | 198 | 246 | 135 |
| Exposure from supplements | | | | | | | | |

| | | | | | | | | |
|------------------------------------|----|----|----|----|----|----|-----|----|
| Vitamin D, $\mu\text{g}/\text{wk}$ | 65 | 96 | 33 | 93 | 39 | 66 | 0.0 | 70 |
|------------------------------------|----|----|----|----|----|----|-----|----|

DANSDA, Danish national survey of diet and physical activity; SD, standard deviation; IQR, interquartile range; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; wk, week; dl-PCBs, dioxin-like polychlorinated biphenyls; TEQ, toxic equivalency

Table 5a. Background exposure scenarios.

| | Winter | Mid-season | Summer | Winter LD | Mid-season LD | Summer LD |
|-------------------------------------------------|---------------|-------------------|---------------|------------------|----------------------|------------------|
| Sun: Vitamin D, µg/d | 0 | 7.25 | 14.5 | 0 | 7.25 | 14.5 |
| Airborne: Dioxins + dl-PCB, pg TEQ/wk | 42 | 42 | 42 | 20 | 20 | 20 |

LD, low dioxin; d, day; dl-PCBs, dioxin-like polychlorinated biphenyls; TEQ, toxic equivalency; wk, week

Table 5b. Background exposure scenarios.

| | Winter | Mid-Season | Summer | Winter LD | Mid-season LD | Summer LD |
|------------------------------------------------------------------------------|----------------------|--------------------------|----------------------|----------------------------|-----------------------------|-------------------------|
| Individual intake other foods Individual intake supplements | Winter Ind | Mid-season Ind† | Summer Ind | Winter LD Ind | Mid-Season LD Ind | Summer LD Ind |
| Individual intake other foods No supplements | Winter Ind No Sup | Mid-season Ind No Sup | Summer Ind No Sup | Winter LD Ind No Sup | Mid-Season LD Ind No Sup | Summer LD Ind No Sup |
| Average intake other foods Average intake supplements | Winter Av | Mid-season Av | Summer Av | Winter LD Av | Mid-Season LD Av | Summer LD Av |
| Average intake other foods No supplements | Winter Av No Sup | Mid-season Av No Sup | Summer Av No Sup | Winter LD Av No Sup | Mid-Season LD Av No Sup | Summer LD Av No Sup |

LD, low dioxin

† Baseline scenario

Table 6. Number of individuals out of 3,016 with no feasible solution for the different background exposure scenarios.

| | Winter | Mid-season | Summer | Winter LD | Mid-season LD | Summer LD |
|----------------------------------------------------------|---------------|-------------------|---------------|------------------|----------------------|------------------|
| Women/men | | | | | | |
| Individual intake other foods | 15/10 | 14/10 | 14/10 | 13/9 | 13/9 | 13/9 |
| Individual intake supplements | 384/407† | 251/285† | | | | |
| Individual intake other foods No supplements | 15/10 | 14/10 | 14/10 | 14/9 | 13/9 | 13/9 |
| Average intake other foods Average intake supplements | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |
| Average intake other foods No supplements | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 | 0/0 |

LD, low dioxin

† Only individual reported species allowed in modelled recommendations

420 **Figure legends**

421 **Figure 1.** Observed intake of lean and fatty fish for 3,016 individuals (1,552 women and 1,464 men)
422 (a) and modelled recommended fish intake for 2,992 of the individuals with the **Mid-season Ind**
423 **scenario (the baseline scenario) (b).**

424 **Figure 2.** Empirical cumulative distribution functions for delta fish intake (modelled recommendation
425 minus observed intake) for 2,992 individuals with **the Mid-season Ind scenario (a, c, d), the Mid-**
426 **season Ind No Sup scenario (b), the Mid-season Ind scenario, lean fish species (c), and the Mid-season**
427 **Ind scenario, fatty fish species (d).**

428 **Figure 3.** Empirical cumulative distribution functions for delta fish intake (modelled recommendation
429 minus observed intake) for 2,480 individuals with **the Mid-season Ind scenario, lean fish species (a),**
430 **and the Mid-season Ind scenario, fatty fish species (b)** when only individual reported fish species are
431 allowed in the modelled intake.

432 **Figure 4.** Modelled recommended fish intake for 2,991 individuals with the **Winter Ind scenario (a),**
433 **and the Winter Ind No Sup scenario (b).**

434 **Figure 5.** Empirical cumulative distribution functions for delta fish intake (modelled recommendation
435 minus observed intake) for 2,991 individuals with the **Winter Ind scenario (a), the Winter Ind No Sup**
436 **scenario (b), the Winter Ind scenario, lean fish species (c), and the Winter Ind scenario, fatty fish**
437 **species (d).**

438 **Figure 6.** Empirical cumulative distribution functions for delta fish intake (modelled recommendation
439 minus observed intake) for 2,225 individuals with **the Winter Ind scenario, lean fish species (a), and the**
440 **Winter Ind scenario, fatty fish species (b)** when only individual reported fish species are allowed in the
441 modelled intake.

442 **Figure 7.** Modelled recommended fish intake for 3,016 individuals with the **Winter Av scenario (a)**
443 **and the Winter Av No Sup scenario (b).**

444 Appendix

445 Sun exposure

446 To estimate a value for vitamin D intake due to sun exposure, we assumed a linear relationship between
 447 vitamin D status and intake. For Danish adults ($n = 2,625$) not taking vitamin D supplements, the
 448 median serum 25-hydroxyvitamin D [25(OH)D] concentrations (from blood samples) were in a study
 449 on vitamin D status in Denmark measured to 68.4 nmol/L and 40.0 nmol/L in the autumn and spring,
 450 respectively ⁽¹⁷⁾. We used data from an Irish study to define the linear relation between this vitamin D
 451 status and intake. In the Irish study ⁽²²⁾, conditional distributions of serum 25(OH)D concentration (in
 452 late winter) at specific values of vitamin D intake (from foods and supplements) were modelled for
 453 healthy adults ($n=215$) living in Ireland and Northern Ireland (latitudes 51°N and 55°N) and the mean
 454 log-transformed 25(OH)D concentration was defined as a linear function of vitamin D intake. The
 455 slope of the relation between total vitamin D intake and 25(OH)D concentration was 1.96 in the study
 456 population, and for the lowest vitamin D intake (0.01 µg) the 50th percentile 25(OH)D concentration
 457 was 34.5 nmol/L. For this study, we used this slope value of 1.96 and the value 34.5 nmol/L as vertical
 458 intercept to define our linear equation:

$$c = 1.96 \times i + 34.5$$

459 where i = vitamin D intake (µg/d) and c = mean 25(OH)D concentration (nmol/L). This assumption
 460 was considered appropriate for our study. The median intake 17.3 µg/d and 2.81 µg/d in the autumn
 461 and spring, respectively, were obtained by converting the median concentrations ⁽¹⁷⁾ with the linear
 462 equation. We assumed that the difference between the autumn and spring intake, 14.5 µg/d, is only due
 463 to sun exposure and not a change in food intake, and it was interpreted as the exposure to vitamin D
 464 due to UVB radiation in summer. We defined a summer scenario with this value and we also defined a
 465 winter scenario with an intake of 0 µg vitamin D/d due to sun exposure. A mid-season scenario with
 466 the average of the summer and the winter value, 7.25 µg/d, defined the baseline value. Daily values
 467 were multiplied with 7 days to obtain weekly values.

468 Airborne dioxin

469 To estimate a value of the exposure to airborne dioxin, we defined the relations:

$$\textit{Total mean exposure} = \textit{Mean airborne exposure} + \textit{Mean exposure from food}$$

$$\text{Mean exposure from food} = x\% \times \text{Total mean exposure}$$

470 From these relations, we derived a formula for calculating the mean airborne exposure to dioxin

$$\text{Mean airborn expsoure} = \text{Mean exposure from food} \times \left(\frac{100}{x} - 1 \right)$$

471 where $x = \%$ of total exposure from food, $0 < x \leq 100$. We calculated the mean airborne exposure for

472 the study population, using the population mean (376 pg TEQ/wk). As the baseline value, a

473 conservative assumption, $x = 90\%$, was used. An alternative low dioxin (LD) value corresponded to

474 $x = 95\%$.