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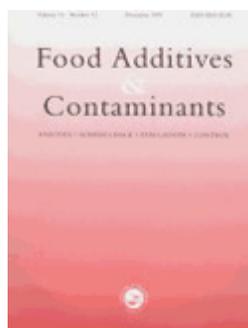
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Modelling the intake of polychlorinated dibenzo-p-dioxins and dibenzofurans: impact of energy under-reporting and number of reporting days in dietary surveys

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3 **Modelling the intake of polychlorinated dibenzo-*p*-dioxins and dibenzofurans:**
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6 **impact of energy under-reporting and number of reporting days in dietary**
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8 **surveys**
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Abstract

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12 5 A probabilistic long-term intake estimation of dioxins was carried out using food consumption
13 data obtained from the National FINDIET 2007 Survey. The study population consisted of 606
14 participants who were first interviewed with a 48-h recall and then filled in a 3-day food record
15 twice. The concentrations of dioxins were obtained from previously published studies. The intake
16 was estimated using a semi-parametric Monte Carlo simulation. The analyses were done
17 separately for the whole study population and for the population excluding energy under-reporters.
18 To diminish the impact of intra-individual variation and nuisance effects, adjustment with software
19 (C-SIDE[®]) was also done after Monte Carlo simulation. It was found that when C-SIDE[®] was
20 used, the 95th percentile of intake and its confidence limit was higher with 2 reporting days than
21 with a higher number of days. However, with a crude intake estimation (no adjustment), the
22 confidence intervals of the 95th percentile were also smaller with a higher number of days, but the
23 95th percentiles were higher with a higher number of reporting days. When under-reporters were
24 excluded the intakes increased, but the impact of energy under-reporting was smaller with 8
25 reporting days than with 2 days and smaller using C-SIDE[®] than with a crude estimation. To
26 conclude, adjustment for intra-individual variation and taking energy underreporting into account
27 are essential for intake estimation of dioxins with food consumption data of limited number of
28 reporting days.
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Introduction

Food of animal origin is the main source of dietary intake to polychlorinated dibenzo-*p*-dioxins and dibenzofurans (dioxins) (Liem et al. 2000). In Finland among foodstuffs the highest concentrations of dioxins are found in fish, especially Baltic Sea fatty fish (Wiborg et al. 2008) (Fig. 1). The effects of dioxins on human health have been studied vigorously during past decades. Based on animal studies and epidemiological human studies adverse health effects include cancer, immunotoxicity, developmental toxicity, and reproductive toxicity (WHO 2000). Public concern about the effects of dioxins on human health have lead to several risk assessments of these compounds, among others one carried out by the European Union Scientific Committee on Food (SCF 2001). Furthermore, not only public concern was the cause of performing risk assessments of dioxins, but also scientific and political concern. Fish on the other hand, is an important source of polyunsaturated marine n-3 fatty acids, vitamin D, vitamin B₁₂, and selenium (The National FINDIET 2007 Survey). For benefit/risk assessment of fish consumption, a precise estimation of intake of dioxins is essential. For dioxins – as for most of the contaminants – the chronic intake is the most important issue in the risk assessment. Therefore, the usual (long term) intake of dioxins was estimated.

In order to be valid, the intake estimation of contaminants should be based on demographically representative food consumption data (Kroes et al. 2002). However, such data are usually not collected primarily for the purpose of intake assessment of contaminants, but for nutritional epidemiology purposes or for dietary monitoring purposes. Nutrients usually have several sources of intake and their variation in concentration is relatively small. In addition, average intake, either for the population or at an individual level, is in most cases a sufficient level of information for nutrients. For contaminants the opposite is true: sources of individual contaminants are usually few and in food there is a great variance in contaminant concentration. In

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3 addition, for risk assessment purposes, the average intake is not sufficient, but the higher end of
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5 the intake distribution should be estimated, including parameters like the 95th percentile. The task
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7 is very challenging, as the dietary data usually cover only one or two reporting days. Furthermore,
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9 if only few reporting days are available, the intra-individual variation in food consumption is
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11 usually overestimated. However, software has been developed to take into account the intra-
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13 5 individual variation (removes the extra intra-individual variation caused by measurement error)
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15 and nuisance effects (e.g. day of the week, interviewer) in nutritional surveys (Dodd et al. 2006)
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17 and these could also be used for other substances than nutrients. The impact of the number of
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19 reporting days on contaminant intake has not, to our knowledge, been investigated earlier.
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25 10 Energy under-reporting is a situation where energy intake calculated from food
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27 consumption is not sufficient to cover the energy expenditure (Maurer et al. 2006). It is due either
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29 to misreporting of the diet or by restriction of the energy intake during the reporting period (e.g.
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31 food record). It is a serious problem in nutritional epidemiology that does not affect only the
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33 energy intake estimates, but all nutrients and foods (Hirvonen et al. 1997, Stallone et al. 1997,
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35 Cook et al. 2000). The impact of energy under-reporting on contaminant intake has not, to our
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37 15 knowledge, been investigated previously.
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42 In this study, we assessed the impact of energy under-reporting and the number of
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44 reporting days in dietary surveys on the dioxin intake. In addition, we examined the impact of
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46 software that aims at decreasing the impact of intra-individual variation and nuisance effects (e.g.
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48 20 day of the week, interviewer).
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52 **Materials and methods**

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55 Data on food consumption were obtained from the National FINDIET 2007 Survey, carried out as
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57 part of the FINRISK 2007 Study which monitors cardiovascular risk factors (Fig. 2), (The
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59 National FINDIET 2007 Survey). A random sample of 9, 958 persons aged 25-74 years in five
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3 areas, stratified by sex, area, and 10-year age groups, was taken from the population register. The
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5 study areas were: (1) Helsinki area; (2) the city of Turku and some rural municipalities in South-
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7 Western Finland; and the provinces of (3) North Karelia, (4) North Savo and (5) Oulu. The
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9 participation rate was 63%, i.e. 6,259 subjects. Of these, 2,069 persons were invited to participate
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12 in the FINDIET Study.
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15 Participants were interviewed using the 48-h dietary recall between January and
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17 March. The 48-h recall data consisted of all days except Fridays. A subsample of the participants
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19 filled in a 3-day food record twice: the first starting the day after the 48-h recall in January-March
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21 and the second in June-December (Fig. 2). The National Food Composition Database FINELI®
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23 (www.finel.fi) was used to calculate the food consumption. The content of dioxins of foods has
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25 been determined in national food monitoring surveys during 2002 and 2005 (Isosaari et al. 2006;
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27 Wiborg et al. 2008). The dioxin content in foods in these publications were expressed as PCDD
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29 equivalents.
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34 The long-term intake of dioxins was estimated by multiplying the food consumption
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36 (g/day) by respective dioxin content (pg/g) for all reporting days. The multiplication was done
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38 using bootstrapping (semiparametric Monte Carlo simulation), where food consumption data were
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40 treated as constant (Iman & Conover 1982). Bootstrapping was used in the intake estimation of both
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42 crude (C-SIDE not used) and adjusted (C-SIDE used) results. Therefore, bootstrapping was done
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44 for concentration data only. Bootstrapping was done only on 400 rounds because it was a time-
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46 demanding procedure. We used bootstrapping because concentration data has single foods with a
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48 small number of values. In this case, estimation of theoretical distribution could be unreliable for a
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50 single food concentration. Medians produced from 400 point estimates and confidence intervals of
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52 parameters were calculated directly from the bootstrapped data when no adjustment was used
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54 (crude results) and from the usual intake distributions when adjustment (C-SIDE) was used.
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3 The impact of energy under-reporting on intake of dioxins was investigated by
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6 estimating the intakes both with under-reporters and without under-reporters. Energy under-
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9 reporters were excluded using $1.00 \times \text{BMR}$ (basal metabolic rate) as a cut-off point (Goldberg et al.
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11 1991).

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13 5 The impact of intra-individual variation and nuisance effects on intake of dioxins
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15 was assessed by comparing the results adjusted for intra-individual variation and nuisance effects
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17 with non-adjusted results. This adjustment was done after probabilistic (bootstrapping) intake
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19 estimation. The adjustment was done using the method of Nusser and co-workers (Nusser et
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21 al.1996). This method gives the long-run average of daily intakes (usual daily intake) by taking
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24 10 into account day-to-day correlation and nuisance effects (such as day-of-week and interview
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26 sequence). It also allows exceptions from normality through grafted polynomial transformations
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28 and recognizes the measurement error associated with one-day dietary intakes. The estimations
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30 were done using the SAS based C-SIDE[®] program. All the analyses were done separately for men
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32 and for women, because men and women have different food consumption patterns (The National
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34 FINDIET Study 2007).
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41 Results

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43 The most important sources of intake of dioxins for both males and females were fish, especially
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45 Baltic herring and salmon (Table 1). The total daily intake of dioxins for men was 0.71 pg WHO-
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48 20 TEQ/kg bw and 0.47 pg WHO-TEQ/kg bw for women. The contribution of fish to the total intake
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50 was 94% and 91% for men and women, respectively.
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53 Of all participants, 36% of men and 39% of women were identified as energy under-
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56 reporters. The mean (standard deviation) energy intake in all males was 9000 kJ (2210 kJ) and in
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58 all females 7050 kJ (1610 kJ). Among under-reporters the mean energy intake was 6970 kJ (1110
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60 25 kJ) in males and 5630 kJ (899 kJ) in females. The Spearman correlations between intake of

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3 dioxins and energy were in all males 0.15 and in females 0.02. Among under-reporting males the
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5 correlation was -0.04 and in females 0.02.
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8 When no adjustments for intra-individual variation or nuisance effects were done
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10 (crude results), in males confidence limits of the 95th percentile of intake of dioxins were higher
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12 5 for three reporting days than for two reporting days, but tended to diminish with higher number of
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14 reporting days (Table 2). For females, the 95th percentile of intake and their confidence limits
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16 tended to increase with increasing reporting days. The impact of excluding energy under-reporters
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18 among males was largest with three reporting days on intake of dioxins, but decreased with
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20 increasing number of reporting days for crude results. In females, the impact of under-reporters
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22 was negligible, but increased during the second record period. For median intakes the impact of
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24 10 number of days or energy under-reporting was small.
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29 When the adjustment for intra-individual variation and nuisance effects was done,
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31 the 95th percentile of intake and its confidence limit was higher with 2 reporting days than with a
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33 higher number of days and both 95th percentiles and their confidence limits diminished
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35 15 monotonically in men with an increasing number of reporting days for both males. In women,
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37 however, the impact of number of reporting days was smaller (Table 2). The impact of excluding
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39 energy under-reporters diminished with increasing reporting days. In addition, for males the
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41 median intakes and their confidence limits diminished with increasing reporting days. In females,
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43 both energy under-reporting and number of reporting days had negligible impact on median
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45 20 intakes.
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53 **Discussion**

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55 In the present study, we found that the high number of reporting days had a great effect on the
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57 dioxin intake estimates, especially by narrowing the confidence intervals after adjustment for
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59 25 intra-individual variation and nuisance effects by software. In addition, adjusting for nuisance
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3 effects and decreasing the intra-individual variation by the use of software, the impact of the
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5 number of reporting days on the confidence intervals of the intake estimates was bigger. In
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7 addition, by taking into account the nuisance effects and intra-individual variation, the impact of
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9 energy under-reporting was reduced. In addition, the intake of dioxin was smaller when the
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12 5 adjustment for intra-individual variance and nuisance effects was done than the non-adjusted
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14 intakes.
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17 It is clear that two consecutive reporting days is not enough to estimate the intake of
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19 dioxins or any other contaminant – especially if the higher end of the intake is of interest.
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21 However, it is not clear how many days are enough to estimate contaminant intake. There
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24 10 probably is a trade-off between the costs of additional days and accuracy of estimates.
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26 Furthermore, the sufficient accuracy in turn depends on the margin of exposure of the
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28 contaminant, i.e. if exposure is likely to be near the tolerable intake level, then the accuracy should
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30 be higher than with a compound with higher margin of exposure. The number of reporting days
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32 depends also on the food consumption pattern, since sources of contaminants vary greatly
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35 15 culturally. If too few days are used, the intake of dioxins is overestimated and the risk for
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37 excessive intake is also overestimated, especially when adjustment for intra-individual variation
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39 and nuisance effects are made. The number of reporting days is also a question of participant
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41 compliance: participation could drop dramatically if the work load of the participants is increased.
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43 For example, in this study, 88% of the participants returned the first food record, but only 65%
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46 20 also returned the second food record (The National Findiet 2007 Survey, 2008).
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51 In addition to number of reporting days, it is also important that all days are not
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53 consecutive, since a low number of only consecutive days could result artificially to low intra-
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55 individual variation in food consumption and contaminant intake. This phenomenon was also seen
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58 in this study: only two consecutive days gave smaller confidence intervals than higher number of
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60 25 non-consecutive days. For nutrients two non-consecutive days are estimated to be sufficient for

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3 monitoring purposes (Hoffmann et al 2002). However, when the number of consecutive days is
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5 high enough (e.g. one week), the intra-individual variation is probably captured.
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8 The fact that non-adjusted intakes were much higher than adjusted intakes when
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10 reporting days were increased is surprising and should be studied further. However, the confidence
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12 5 limits diminished monotonically in adjusted intakes, whereas in non-adjusted intakes the standard
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14 error did not change. This is an expected result, since the software is able make use of the
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16 increased amount of measurements per individual. This and adds assurance that the programme
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18 functions properly. When these quite divergent results are taken together, it could be concluded
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20 that the software is useful in decreasing the intra-individual variation, but it is clear that the
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22 software cannot correct for insufficient number of reporting days.
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27 Adjusting for intra-individual variation and nuisance effects by using software seems
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29 to be an efficient way to diminish the confidence limits of the 95th percentiles and to decrease the
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31 impact of energy under-reporting. We did not, however, validate our results against a golden
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33 standard method (e.g. adipose tissue concentration of dioxins). Therefore, it is difficult to say
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35 15 whether a decrease in the intra-individual variation is in accordance with the reality. Therefore,
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37 more research – both theoretical and practical – is needed to find out the role of intra-individual
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39 variation and energy under-reporting on contaminant intake estimation.
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43 Energy under-reporting does not seem to be of great concern in the estimation of
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45 dioxin intake, especially if the number of reporting days is sufficient and if methods to adjust for
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47 20 intra-individual variation and nuisance effects are used. This is not surprising, since in a Finnish
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49 study it was found that foods that are considered healthy are under-reported less or are even over-
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51 reported (Hirvonen et al. 1997). Fish in Finland is considered to be healthy and therefore it is
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53 probably not under-reported to a great extent. On the other hand, in an American study fish was
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55 not under-reported to a lesser extent than other foods (Krebs-Smith et al. 2000). In fact, in this
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57 25 study the qualitative differences in under-reporting were in all rather small. The differences in the
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3 Finnish and the American study could be partly related to cultural factors and partly to the fact that
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5 in the Finnish study the method to measure food consumption was a 48-h recall and a 3-day food
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7 record whereas in the American study a food frequency questionnaire was used. The fact that
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9 under-reporting affected women less than men (at least in terms of absolute intake), even though
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11 women are in general more prone to under-report (Maurer et al.2006), is surprising. Perhaps this
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13 5 women are in general more prone to under-report (Maurer et al.2006), is surprising. Perhaps this
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15 has to do with higher health consciousness of women – they are more aware than men that fish is
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17 considered healthy and therefore, probably under-reported fish less or even overreport fish
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19 consumption.
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23 However, it should be kept in mind that using $1.0 \times \text{BMR}$ as a cut-off point for under-
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25 10 reporting is a rather low limit and therefore excludes only the extreme energy under-reporters.
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27 Using a higher cut-off level, however, would not be justifiable, since due to high inter-individual
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29 variation in the basal metabolic rate (Shetty 2005), part of the population has a very low basal
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31 metabolic rate and excluding them is not correct. As a consequence, the data still probably contain
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33 some bias caused by energy under-reporting.
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37 15 The present study shows that the sources of intra-individual differences (e.g.
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39 temporal variation) should be taken into account when food consumption studies that are used for
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41 intake estimation of contaminants are planned. This underlines the co-operation between those
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43 estimating contaminant intake and those who plan and carry out dietary surveys. In fact, precise
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45 calculations are needed to estimate the number of reporting days for the contaminants or other
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47 non-nutrient substances to be estimated prior to a dietary survey. The risk can only be estimated
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49 20 when the high intake levels can be compared to reference levels, e.g. tolerable daily intake.
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53 Could some other food consumption method be used to estimate contaminant intake
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55 in order to avoid the problems with 24/48-h recalls or food records? A food frequency
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57 questionnaire would be an appealing alternative because of its convenience both for the
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59 investigator and for the participant. However, for each group of contaminants a separate food
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3 frequency questionnaire should be planned and validated separately. This is seldom feasible, since
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5 this process is time consuming and costly. In addition, food frequency questionnaires are not
6
7 suitable for estimating absolute intakes, but are to group people into low and high intake groups
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9 (Willett 1998). The other problem with food frequency questionnaires is often energy over-
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11 reporting rather than under-reporting. However, these problems can partly be overcome by asking
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13 5 a small part of the participants (who fill also food frequency questionnaire) to fill in also dietary
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15 records. Dietary records could then be used to calibrate e.g. portion sizes and energy intake.
16
17 Another alternative to dietary recalls or food records would be dietary history. The problem with
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19 the low number of reporting days would be avoided, since dietary history aims at forming an
20
21 overall view of the participant's diet. However, dietary history has probably also the problem of
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23 10 energy under-reporting, since dietary history is usually started with a 24-h recall. In addition,
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25 dietary history is very time consuming both for study personnel and participants and therefore also
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27 costly.
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34 Our results are not directly generalizable to other populations or to other
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36 15 contaminants or other substances, since energy under-reporting patterns and sources of
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38 contaminants vary between populations and population groups (e.g. children). However, with a
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40 high number of reporting days the intake estimates of any contaminant in any population are
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42 probably more accurate than with a low number. In addition, estimating contaminant intake also –
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44 but not solely – excluding under-reporters is useful and gives a rough estimate of the impact of
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46 under-reporting on results.
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51 In conclusion, intra-individual variation and nuisance effects may have a large
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53 impact on contaminant intake estimates. In addition, by estimating the intake both with under-
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55 reporters and without under-reporters the impact of energy under-reporting could be assessed.
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57 Furthermore, one 48-h recall is not sufficient to estimate the intake of a contaminant. However,
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3 with software that adjusts for intra-individual variation and nuisance effects, the effect of intra-
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5 individual variation and energy under-reporting could be decreased.
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11 12 13 **5 Acknowledgement** 14

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Legends to figures

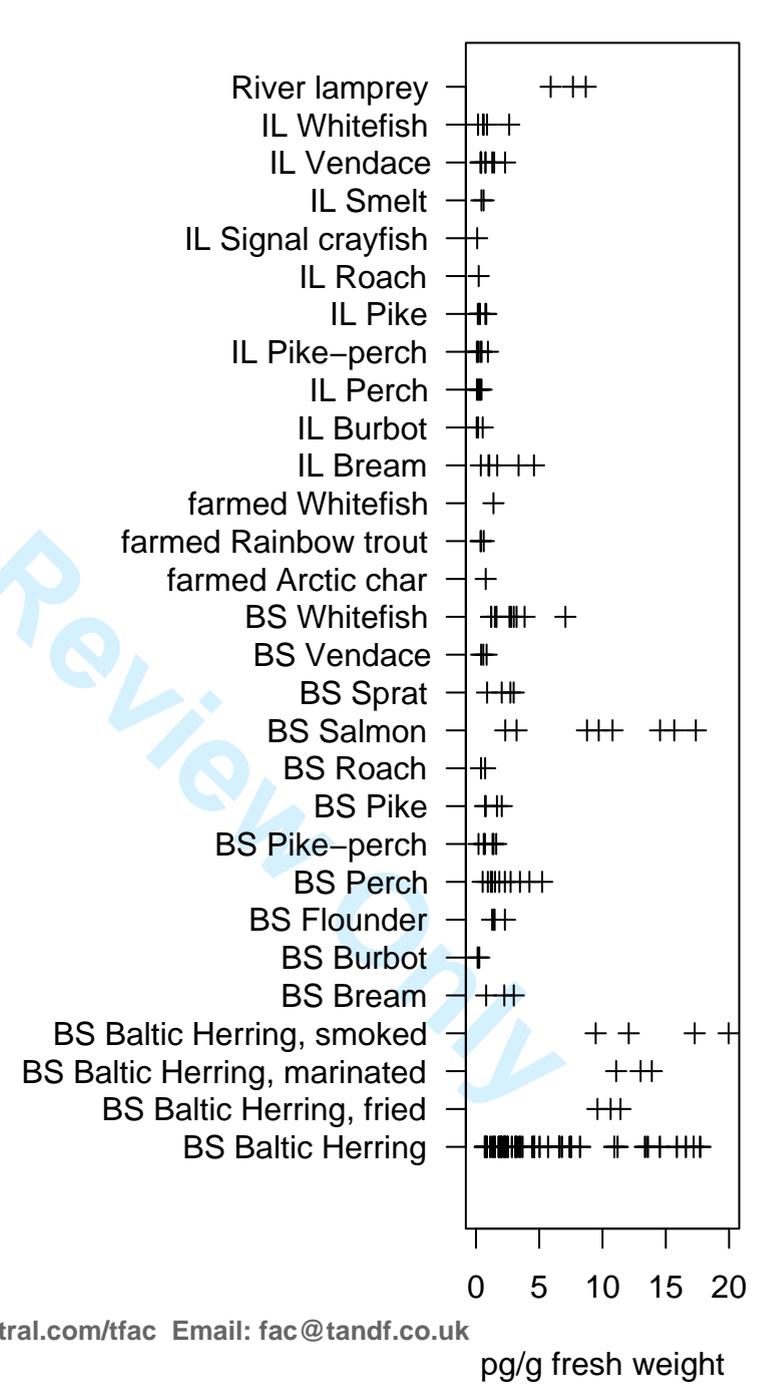
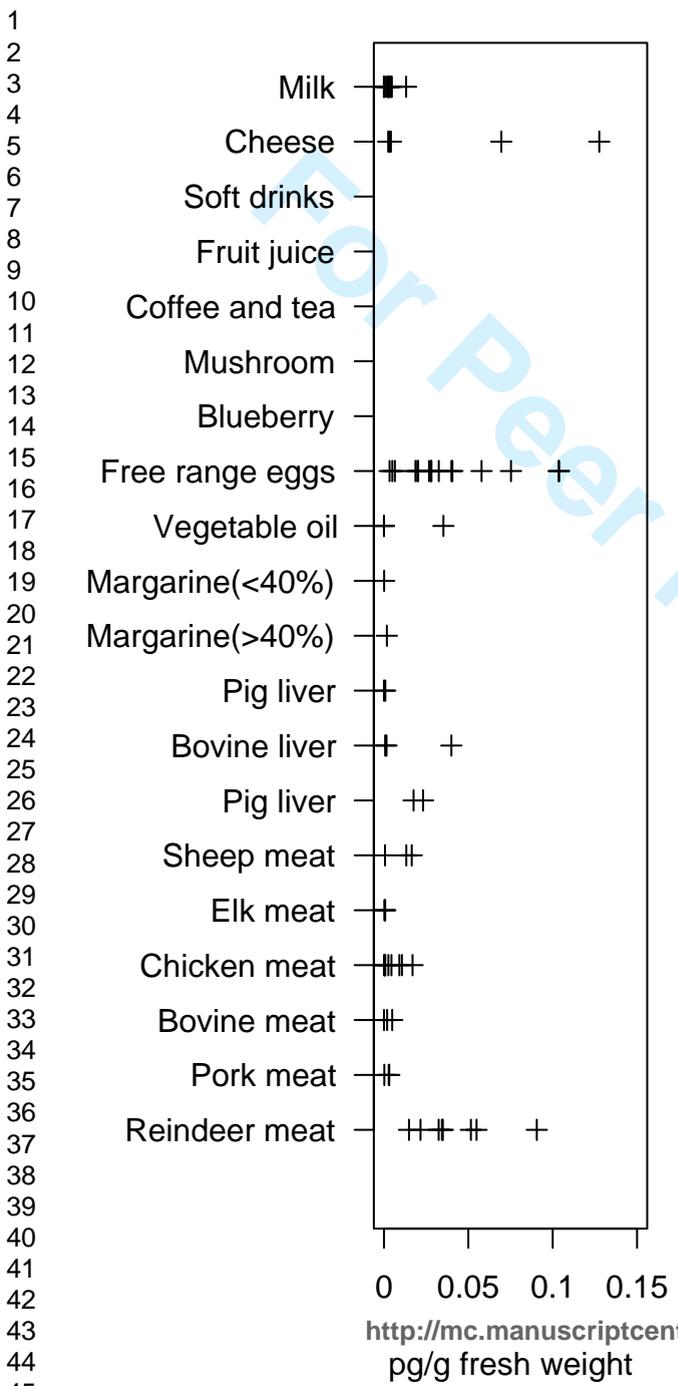
Figure 1. Concentration of dibenzo-*p*-dioxins and dibenzofurans (WHO-TEQ) in foodstuffs. BS= Baltic sea, IL=inland water.

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Figure 2. Flow chart of the study. In all intake estimations bootstrapping (probabilistic method) was used.

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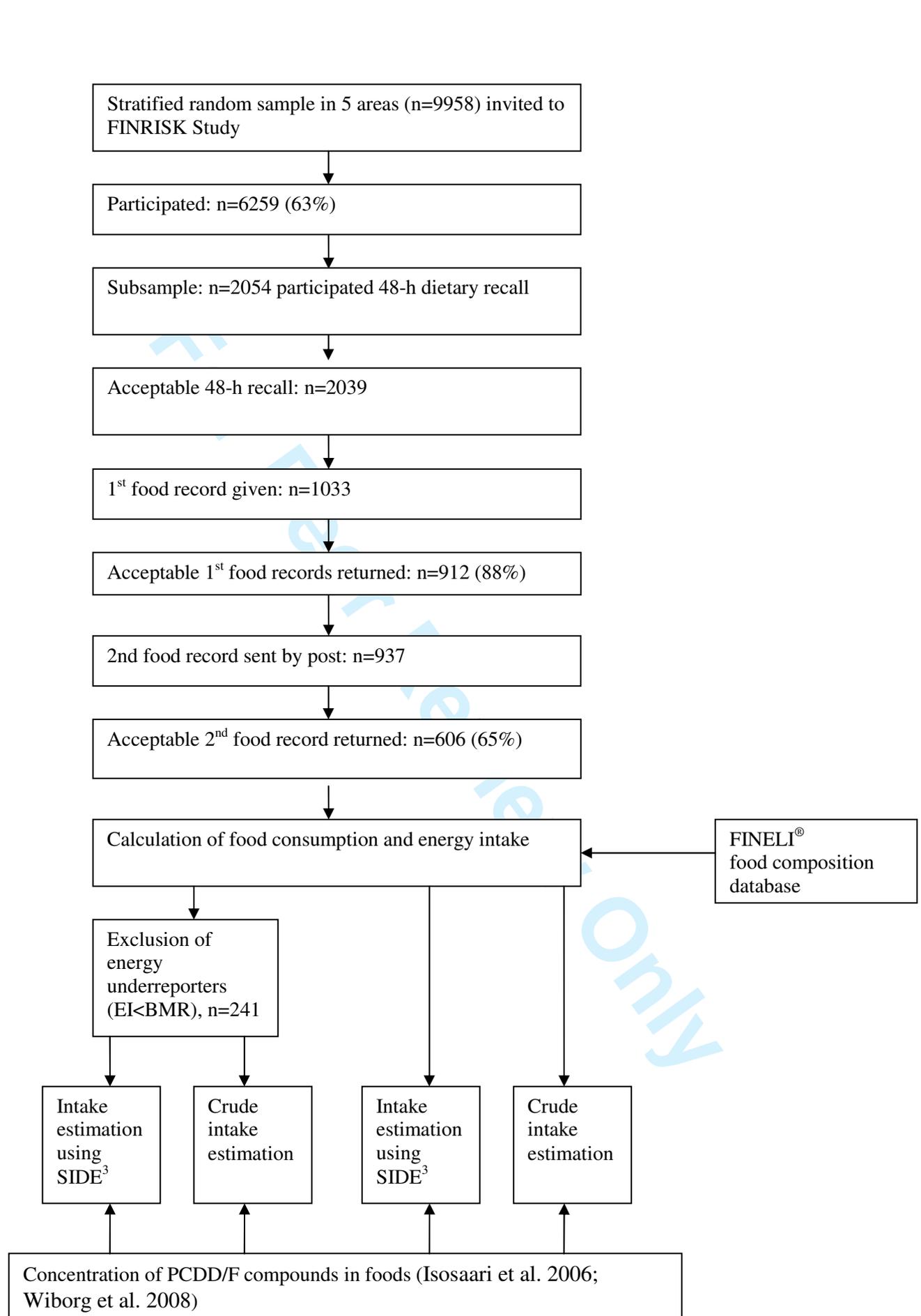


Table 1. Sources of PCDD/F compounds (intake of WHO-TEQ) by sex.

	Men		Women	
	pg/kg bw/day	%	pg/kg bw/day	%
Baltic Herring	0.2491	35.12	0.1444	30.61
Salmon	0.1893	26.69	0.1178	24.97
Farmed Rainbow trout	0.0468	6.60	0.0530	11.24
Unknown smoked fish, high fat	0.0382	5.38	0.0425	9.02
Whitefish	0.0366	5.15	0.0135	2.85
Bream	0.0312	4.40	0.0076	1.61
Vendace	0.0291	4.10	0.0165	3.49
Unknown fish	0.0198	2.79	0.0144	3.05
Cheese	0.0126	1.78	0.0139	2.94
Perch	0.0118	1.67	0.0097	2.05
Eggs	0.0111	1.56	0.0110	2.33
Pike	0.0088	1.23	0.0023	0.49
Milk	0.0073	1.03	0.0076	1.61
Flounder	0.0051	0.71	0.0056	1.18
Chicken	0.0047	0.66	0.0048	1.02
Saithe	0.0021	0.30	0.0022	0.47
Game	0.0016	0.23	0.0010	0.22
Pork	0.0016	0.22	0.0011	0.24
Berries	0.0011	0.16	0.0016	0.33
Other	0.0016	0.22	0.0013	0.28
Total	0.71	100	0.47	100

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Table 2. Intake of PCDD/F compounds (WHO-TEQ as pg/kg bw/day) in crude and adjusted estimations by sex, number of reporting days, and under-reporting,

		days	All (n=606)		Under-reporters excluded (n=365)	
			Median (CI)	95% (CI)	Median (CI)	95% (CI)
Men	Crude estimation	2	0.05 (0.05-0.06)	2.06 (1.65-2.62)	0.06 (0.05-0.06)	2.25 (1.65-3.09)
		3	0.07 (0.07-0.08)	2.78 (2.04-3.84)	0.09 (0.08-0.10)	3.88 (2.64-5.71)
		4	0.09 (0.08-0.10)	2.55 (1.93-3.58)	0.13 (0.11-0.14)	3.44 (2.39-4.95)
		5	0.11 (0.10-0.12)	2.58 (2.03-3.34)	0.16 (0.14-0.18)	3.35 (2.50-4.41)
		6	0.15 (0.13-0.17)	2.79 (2.16-3.46)	0.23 (0.20-0.27)	3.37 (2.41-4.33)
		7	0.21 (0.19-0.23)	2.96 (2.39-3.69)	0.29 (0.26-0.32)	3.33 (2.61-4.46)
		8	0.24 (0.21-0.26)	2.97 (2.48-3.78)	0.33 (0.27-0.36)	3.27 (2.60-4.28)
	Adjusted estimation	2	0.30 (0.21-0.45)	1.90 (1.34-2.54)	0.30 (0.21-0.46)	2.47 (1.58-4.25)
		3	0.31 (0.24-0.39)	1.13 (0.83-1.49)	0.33 (0.26-0.45)	1.54 (1.00-2.47)
		4	0.30 (0.25-0.37)	1.07 (0.83-1.34)	0.31 (0.24-0.42)	1.37 (0.88-1.99)
		5	0.30 (0.23-0.37)	1.04 (0.81-1.28)	0.31 (0.25-0.39)	1.19 (0.90-1.51)
		6	0.29 (0.23-0.37)	0.92 (0.73-1.12)	0.31 (0.25-0.41)	1.05 (0.80-1.28)
		7	0.28 (0.23-0.36)	0.87 (0.69-1.09)	0.30 (0.23-0.41)	1.03 (0.79-1.26)
		8	0.28 (0.23-0.34)	0.86 (0.69-1.05)	0.29 (0.23-0.40)	0.99 (0.79-1.21)
Women	Crude estimation	2	0.05 (0.05-0.05)	1.27 (1.08-1.47)	0.06 (0.05-0.07)	1.38 (1.08-1.76)
		3	0.07 (0.06-0.08)	1.44 (1.20-1.78)	0.08 (0.07-0.09)	1.56 (1.28-1.90)
		4	0.09 (0.08-0.10)	1.74 (1.42-2.07)	0.10 (0.09-0.11)	1.81 (1.37-2.25)
		5	0.11 (0.10-0.12)	1.78 (1.50-2.11)	0.13 (0.12-0.14)	1.74 (1.47-2.26)
		6	0.13 (0.12-0.14)	1.95 (1.62-2.46)	0.14 (0.13-0.16)	1.70 (1.32-2.22)
		7	0.14 (0.13-0.15)	1.96 (1.56-2.37)	0.15 (0.13-0.16)	1.66 (1.34-2.22)
		8	0.16 (0.16-0.18)	2.09 (1.72-2.60)	0.17 (0.16-0.18)	1.88 (1.37-2.55)
		Adjusted estimation	2	0.23 (0.20-0.27)	1.03 (0.65-1.82)	0.30 (0.23-0.39)
	3		0.24 (0.21-0.29)	0.81 (0.61-1.12)	0.32 (0.27-0.38)	0.94 (0.64-1.42)
	4		0.28 (0.24-0.36)	0.83 (0.64-1.07)	0.35 (0.29-0.43)	0.97 (0.68-1.33)
	5		0.27 (0.23-0.32)	0.82 (0.66-1.06)	0.33 (0.28-0.40)	0.92 (0.72-1.20)
	6		0.29 (0.25-0.33)	0.80 (0.66-1.02)	0.35 (0.29-0.42)	0.94 (0.73-1.21)
	7		0.30 (0.26-0.35)	0.82 (0.68-1.04)	0.37 (0.31-0.44)	0.98 (0.76-1.27)
	8	0.30 (0.26-0.35)	0.80 (0.65-1.04)	0.38 (0.32-0.45)	0.99 (0.77-1.28)	