Project no: 022936
Project acronym: Beneris
Project title: Benefit-risk assessment for food: an iterative value-of-information approach

Instrument: STP-Specific Targeted Project

Deliverable 26:

Evaluation of patterns

Due date of deliverable:	**1 Dec, 2007**
Actual submission date:	**15 Nov, 2009**
Dissemination level:	**PU**
Start date of project:	**April, 1st 2006**
Duration:	**3,5 years**

Organisation name of the lead contractor for this deliverable: **THL**

Evaluation of patterns
(D26)

This deliverable consists of a manuscript that will be submitted to a peer reviewed scientific journal. The manuscript is nearly finished (please see below). The study described in the manuscript utilizes probabilistic (Monte-Carlo) simulation as applied to input data from the national FINDIET 2007 Study (606 participants).

Modelling the intake of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/Fs) : impact of energy underreporting and number of reporting days in dietary surveys

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Keywords: PCDD/F compounds, energy underreporting, intake assessment, dietary surveys

Abstract

A probabilistic intake exposure was carried out using food consumption data obtained from the national FINDIET 2007 Study. The study population consisted of 606 participants who were first interviewed with 48-h recall and then filled in twice a 3-day food record. The intake was estimated using semiparametric Monte Carlo simulation. The analyses were done separately for the whole study population and for population excluding energy underreporters. To diminish the impact of intra individual variation and nuisance effects, adjustment with a software (C-SIDE®) was also done. It was found out that when the C-SIDE® was used, the 95th percentile of intake and its confidence limit was higher with 2 reporting days than with higher number of days. However, with crude intake estimation, the confidence intervals of the 95th percentile were also smaller with higher number of days, but the 95th percentiles were higher with higher number of reporting days. When underreporters were excluded, the intakes increased, but the impact of energy underreporting was smaller with 8 reporting days than 2 days and smaller using C-SIDE® than with crude estimation.

Introduction

Food of animal origin is the main source of polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCDD/F or dioxins) (Liem et al, 2000). In Finland among foodstuffs the highest concentrations of PCDD/Fs are found in fish, especially Baltic Sea fatty fish (Wiborg et al. 2008) (Fig. 1). Effects of PCDD/Fs 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 concerns on effects of PCDD/Fs on human health have lead several risk assessments of these compounds, among others one made by the European Union Scientific Committee on Food (SCF, 2001). On the other hand, fish is an important source of polyunsaturated marine n-3 fatty acids, vitamin D, vitamin B_{12}, and selenium (The National FINDIET 2007 Survey). For benefit/risk assessment of fish, a precise estimation of dioxin intake is essential. For dioxins – as for the most of the contaminants – the chronic exposure is the most important issue in the risk assessment. Therefore, the usual (long term) intake of dioxins should be estimated.

In order to be valid, the intake estimation of contaminants needs to have a demographically representative food consumption data (Kroes et al. 2002). However, such a data is usually not collected primarily for the purpose of intake assessment of contaminants, but for nutritional epidemiology purposes or for dietary surveys. Nutrients usually have several sources and their variation of concentration is relatively small. In addition, average intake, either in population or individual level, is in most cases sufficient level of information for nutrients. For contaminants the opposite is true: sources of individual contaminants are usually few and in food they have great variance of contaminant concentration. In addition, for risk assessment purposes, the average intake is not sufficient, but the higher end of the intake distribution should be estimated, including parameters like 95^{th} percentile. The task is very challenging, as the dietary data usually covers only one or two reporting days and is often not representative for day of the weeks or for season. However, softwares are developed to take account the intraindividual variation in nutritional surveys (Dodd et al. 2006) and these could also be used for other substances. The impact of number of reporting days on contaminant intake has not, to our knowledge, been investigated earlier.

Energy underreporting is a situation where energy intake calculated from food consumption is not sufficient to cover the energy expenditure (Maurer et al. 2006). It is due either to misreporting of the diet or by restriction of the energy intake during the reporting period of the food consumption (e.g. food record). It is a serious problem in nutritional epidemiology that does not affect only the energy intake estimates, but all nutrients and foods (Hirvonen et al. 1997, Stallone et al. 1997, Cook et al. 2000). The impact of energy underreporting on contaminant intake has not, to our knowledge, been investigated previously.

In this study, we wanted to assess the impact of energy underreporting and number of reporting days in dietary survey on the dioxin intake. In addition, we wanted to find out the suitability of software that aims at decreasing the impact of intraindividual variation and nuisance effects.

Methods

Data on food consumption was obtained from the FINDIET 2007 Survey, carried out as part of the FINRISK 2007 Study which monitors cardiovascular risk factors (Fig. 2.), (The National FINDIET 2007 Survey). A random sample of 9, 958 persons aged 25-74 years in five areas, stratified by sex, area, and 10-year age groups, was taken from the population register. The study areas were: (1) Helsinki area; (2) the city of Turku and some rural municipalities in the south-western Finland; and the provinces of (3) North Carelia, (4) North Savo and (5) Oulu. The participation rate was 63%, i.e. 6259 subjects. Of these, 2,069 persons were invited to participate the FINDIET Study.

The participants were interviewed using the 48-h dietary recall between January and March. The 48-h recall data consisted of all days except Fridays. A subsample of participants filled in 3-day food record twice: the first starting the day after the 48-h recall in January-March and the second in June-December (Fig. 2.). The National Food Composition Database FINELI® (www.fineli.fi) was used to calculate the food consumption. The PCDD/F content of foods has been determined in national food monitoring surveys during 2002 and 2005 (Isosaari et al. 2006; Wiborg et al. 2008).

The PCDD/F intake was estimated using bootstrapping, where food consumption data was treated as constant (Iman & Conover 1982, Harri: onko OK?)) . Therefore, bootstrapping was done for concentration data only. Bootstrapping was done only 400 rounds because it was time-demanding procedure. We used bootstrapping because concentration data has single foods with small number of values. In this case estimation of theoretical distribution could be unreliable for single food concentration. Confidence intervals of parameters were calculated directly from bootstrapped data when no adjustment was used and from usual intake distributions when adjustment was used.

The impact of energy underreporting on intake of PCDD/Fs was investigated by estimating the intakes both with underreporters and without under,reporters. Energy under reporters were excluded using 1.00*BMR (basal metabolic rate) as a cut-off point (Goldberg et al. 1991).

The impact of intra individual variation and nuisance effects on intake of PCDD/Fs was assessed by comparing the results adjusted for intra individual variation and nuisance effects with non-adjusted results. The adjustment was done using the method of Nusser and co-workers (Nusser et al.1996). This method gives the long-run average of daily intakes (usual daily intake) by taking into account day-to-day –correlation and nuisance effects (such as day-of-week and interview sequence). It also allows exceptions from normality through grafted polynomial transformations and recognizes the measurement error associated with one-day dietary intakes. The estimations were done using the SAS based C-SIDE® program.

Results

The most important sources of PCDD/F compounds were both for males and females fish, especially Baltic herring and salmon (Table 1). The total daily intake of PCDD/Fs for men was 0.71 pg WHO-TEQ/kg bw and 0.47 pg WHO-TEQ/kg bw for women. The contribution of fish to the total intake was 94% and 91% for men and women, respectively.

Of all participants, 36 % of men and 39% of women were identified as energy underreporters. The mean (stardard deviation) of energy intake in all males was 9000 kJ (2210 kJ) and in all females 7050 kJ (1610 kJ). Among undereporters the mean energy intake was 6970 kJ (1110 kJ) in males and 5630 kJ (899 kJ) in females. The Spearman correlations between PCDD/F and energy intake were in all males 0.15 and in females 0.02. Among underreporting males the correlation was -0.04 and in females 0.02.

When no adjustment for intra-individual variation or nuisance effects were done, the 95th percentile of PCDD/F intake and their confidence limits (CL) for males was at highest with three reporting days, but both 95th percentiles and their confidence limits diminished with increasing reporting days (Fig. 3, Table 2.). For females the 95th percentile of intake and their confidence limits increased with increasing reporting days. The impact of excluding energy under reporters among males was largest with three reporting days, but decreased with increasing number of reporting days. In females, the impact of under reporters was small, but increased during second record period. For median intakes the impact of number of days or energy underreporting was small.

When the adjustment for intra-individual variation and nuisance effects was done, the 95th percentile of intake and its confidence limit was higher with 2 reporting days than with higher number of days and both 95th percentiles and their confidence limits diminished monotonously with increasing number of reporting days for both males and for females (Figure 3, Table 2). The impact of energy underreporting diminished with increasing reporting days. In addition, for males the median intakes and their confidence limits diminished with increasing reporting days. In females, both energy underreporting, and number of reporting days had only a small impact on median intakes.

Discussion

In the present study, we found that the number of reporting days had great impact on the dioxin intake estimates and, especially their confidence intervals. In addition, adjusting for nuisance effects and decreasing the intra individual variation by a software strengthened the association between the number of reporting days and the confidence intervals of the intake estimates. In addition, by taking into account the nuisance effects and intra individual variation, the impact of energy underreporting was smaller.

It is clear that two consecutive reporting days is not enough to estimate the intake of dioxins or any other contaminant – especially if higher end of the intake is of interest. However, it is not clear how many days is enough to estimate contaminant intake. This probably is a trade off between costs of additional days and accuracy of estimates. The sufficient accuracy in turn depends on the margin of exposure of the contaminant, i.e. if exposure is likely to be near the tolerable intake level, then the accuracy should be higher than with compound with higher margin of exposure. The number of reporting days depends also on the food consumption pattern, since sources of contaminants vary culturally greatly. If too few days are used, the intake of dioxins is overestimated and the risk for excessive intake is also overestimated. The number of reporting days is also a question of participant compliance: participation could drop dramatically if the work load of participant is increased. For example in this study, 88% of the participants returned the first food record, but only 65% returned also the second food record (The National Findiet 2007 Survey, 2008).

The fact that non-adjusted intakes were much higher than adjusted intakes when reporting days were increased is surprising and should be studied further. However, the standard error diminished monotonously in adjusted intakes, whereas in non-adjusted intakes standard error did not change. This is an expected result and adds assurance that the program functions properly. Taken these quite divergent results together, it could be concluded that a software is useful in decreasing the intra individual variation, but the software cannot correct for insufficient number of reporting days.

Adjusting for intra individual variation and nuisance effects by a software seems to be an efficient way to diminish confidence limits of 95th percentiles and to decrease the impact of energy underreporting. We did not, however, validate our results against a golden standard method (e.g. doubly-labelled water). Therefore, it is difficult to say whether decrease of the intra individual variation is in accordance with the reality. Therefore, more research – both theoretical and practical – is needed to find out the role of intra individual variation and energy underreporting on contaminant intake estimation.

Energy underreporting does not seem be to be a great concern estimation of dioxin intake, especially if the number of reporting days is sufficient and if methods to adjust for intra individual variation and nuisance effects are used. This is not surprising, since in a Finnish study it was found out that foods that are considered healthy are underreported less or are even over reported (Hirvonen et al. 1997). Fish in Finland is considered to be healthy and therefore it is probably not underreported in a great extent. On the other hand, in an American study fish was not underreported in a lesser extent than other foods (Krebs-Smith et al. 2000). In fact, in this study the qualitative differences in underreporting were in all rather small. The differences in the Finnish and American study could be partly related to cultural factors and partly to the fact that in Finnish study the method to measure food consumption were 48-h recall and 3-day food records whereas in the American study a food frequency questionnaire was used. The fact that underreporting affected less women than men, even though women are in general more prone to underreport (Maurer et al.2006), is surprising. Perhaps this has to do with higher health consciousness of women – they are more aware than men that fish is considered healthy and therefore, probably, underreported fish less.

However, it should be kept in mind that using 1.0*BMR as a cut-off point for underreporting is a rather low limit and therefore excludes only the extreme energy under reporters. Using higher cut-off level, however, would not be justifiable, since due to high inter individual variation in basal metabolic rate (Shetty 2005), part of the population has very low basal metabolic rate and excluding them is not correct. As a consequence, the data still probably contains some bias caused by energy underreporting.

. The present study shows that the sources of intra-individual differences (e.g. temporal variation) should be taken into account already when food consumption studies are planned that are used for intake estimation of contaminants. This underlines the co-operation between those estimating contaminant intake and those who plan and carry out dietary surveys. In fact, precise calculations are needed to estimate the number of reporting days for the contaminants or other non-nutrient substances to be estimated prior to dietary survey. The risk can only be estimated when the high intake levels can be compared to reference levels, e.g. tolerable daily intake.

Could some other food consumption method be used to estimate contaminant intake in order to avoid the problems with 24/48-recall or food records? Food frequency questionnaire would be an appealing alternative because of its convenience both for investigator and for the participant. However, for each group of contaminants a separate food frequency questionnaire should be planned and validated separately. This is seldom feasible, since this process is time consuming and costly. In addition, food frequency questionnaires are not suitable to estimate absolute intakes, but to group persons to low and high intake groups (Willett 1998). The other problem with food frequency questionnaires is energy overreporting rather than underreporting. Another alternative for dietary recalls or food records would be dietary history. The problem with low number of reporting days would be avoided, since dietary history aims at forming an overall view of the participant's diet. However, dietary history has probably also the the problem of energyunderreporting, since dietary history is usually started with a 24-h recall.. In addition, dietary history is very time consuming both for study personnel and participants and therefore also costly.

Our results are not directly generalizable to other populations or to other contaminants or other substances, since energy underreporting patterns and sources of contaminants vary between populations and population groups (e.g. children). However, with high number of reporting days the intake estimates of any contaminant in any population are probably more accurate than with low number. In addition, estimating contaminant intake also – but not solely – excluding under- reporters is useful and gives a rough estimate the impact of underreporting on results.

In conclusion, intra individual variation and nuisance effects may have large impact on contaminant intake estimates. In addition, by estimating the intake both with under reporters and without under reporters the impact of energy underreporting could be assessed. Furthermore, one 48-h recall is not sufficient to estimate the intake of contaminant. However, with a software that adjust for intra individual variation and nuisance effects, the effect of intra individual variation and energy underreporting could be decreased.

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Legends to figures

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

Figure 2. Flow chart of the study.

Figure 3. Medians (lower values) and 95^{th} point estimates (upper values) of intake of dibenzo-*p*-dioxins and dibenzofurans (WHO-TEq) by number of reporting days,by sex, and by energy underreporting. Crude intakes are shown in the left panel and adjusted intakes in the right panel.