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Gauthier Eppe, Claude Saegerman

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**Risk assessment of Belgian adults for furan contamination through the food chain**

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Methods/Techniques:	Risk assessment, GC, Extraction, Exposure assessment
Additives/Contaminants:	Process contaminants
Food Types:	Animal products – meat, Bakery products, Canned foods, Cereals
Abstract:	Risk assessment is an interdisciplinary process used to quantify the risk linked to a hazard. In the present paper, it is applied to quantify the risk linked to furan ingestion through the food chain for the Belgian adult population. Two approaches, deterministic and probabilistic, are carried out in parallel. The deterministic method relies on a case-study, whereas the probabilistic approach involves statistical distributions of contamination and consumption data to calculate a statistical distribution of the daily intake. First, the deterministic method revealed a low Estimated Daily Intake (EDI) for the average population (380 ng * (kgb.w.*day) <sup>-1</sup> ) and a huge contribution of coffee consumption to the EDI (55%). Increasing or decreasing by one cup the daily coffee consumption can affect the EDI by about 22%. Afterwards, the probabilistic approach showed that the average population has a low EDI (494 ng * (kgb.w.*day) <sup>-1</sup> ), and that high contamination levels were only registered in a small proportion of the population. Finally, a comparison to the RfDchronic-oral showed that less than 10% of the Belgian population presents an EDI above the reference dose proposed by the US-EPA; the majority of the population presents an

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	EDI 20% below the reference dose. The Margin of Exposure (MoE) approach revealed that the level of risk related to furan intake through ingestion is low, with a MoE above 10,000 for more than 10 % of the population and no result below 100.

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3 1 **Risk assessment of Belgian adults for furan contamination through the food**  
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12 5 Gauthier Eppe<sup>4</sup> and Claude Saegerman<sup>1</sup>  
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## 26 Abstract

27 Risk assessment is an interdisciplinary process used to quantify the risk linked to a hazard. In  
28 the present paper, it is applied to quantify the risk linked to furan ingestion through the food  
29 chain for the Belgian adult population. Two approaches, deterministic and probabilistic, were  
30 carried out in parallel. The deterministic method relied on a case-study, whereas the  
31 probabilistic approach involved statistical distributions of contamination and consumption  
32 data to calculate a statistical distribution of the daily intake. First, the deterministic method  
33 revealed a low Estimated Daily Intake (EDI) for the average population ( $380 \text{ ng} \cdot$   
34  $(\text{kg}_{\text{b.w.}} \cdot \text{day})^{-1}$ ) and a huge contribution of coffee consumption to the EDI (55%). Increasing or  
35 decreasing by one cup the daily coffee consumption can affect the EDI by about 22%.  
36 Afterwards, the probabilistic approach showed that the average population has a low EDI  
37 ( $494 \text{ ng} \cdot (\text{kg}_{\text{b.w.}} \cdot \text{day})^{-1}$ ), and that high contamination levels were only registered in a small  
38 proportion of the population. Finally, a comparison to the  $\text{RfD}_{\text{chronic-oral}}$  showed that less than  
39 10% of the Belgian population had an EDI above the reference dose proposed by the US-  
40 EPA; the majority of the population had an EDI 20% below the reference dose. The Margin  
41 of Exposure (MoE) approach indicated that the level of risk related to furan intake through  
42 ingestion is low, with a MoE above 10,000 for more than 10 % of the population and no result  
43 below 100.

44  
45 **Keywords:** Furan, Adult, Risk assessment, Food Chain, Belgium

## 46 Introduction

47 Risk assessment is: *'The estimation of the nature and probability of adverse health effects*  
48 *related to a hazard, e.g., microbiology, chemistry, fire, riots, etc. (US-EPA risk assessment<sup>1</sup>;*

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57 <sup>1</sup> <http://epa.gov/riskassessment/index.htm>

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3 49 Renwick et al., 2004; Feinberg et al., 2006). In the present paper, the risk related to furan  
4  
5 50 ingestion throughout the food chain is discussed for the Belgian adult population.  
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7  
8 51 Furan is a low molecular mass toxicant mainly found in food undergoing heat  
9  
10 52 treatment such as canned, jarred or roasted food (Hasnip et al., 2006; Crews et al., 2007;  
11  
12 53 Roberts et al., 2008; Fromberg et al., 2009; Kim et al., 2009). Maga first reported its  
13  
14 54 occurrence in food in the late 70s (Maga, 1979), but its toxicity was only studied since the 90s  
15  
16 55 (Kedderis et al., 1993; Chen et al., 1995; Peterson et al., 2006; Bakhiya et al. 2010).  
17  
18 56 Consecutively, the American National Toxicology Program (NTP) published a report on its  
19  
20 57 toxicity (NTP, 1993), the American National Academy of Science (NAS) classified it as a  
21  
22 58 narcotic (NAS, 2000), and the International Agency for Research on Cancer (IARC) involved  
23  
24 59 it as possibly carcinogenic to humans (group 2B). Nevertheless, furan has only gained interest  
25  
26 60 since 2004, when the United State Food and Drug Administration published a report about its  
27  
28 61 wide occurrence in food (US-FDA, 2004). Since then, national and international food control  
29  
30 62 authorities started gathering information on furan levels, toxicity and risk for the population  
31  
32 63 (Hepner et al., 2007; Stadler, 2007).  
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36 64 Several contamination assessments have been carried out to date, which led to the  
37  
38 65 implementation of food control plans in some countries (Reinhard et al., 2004; Kim et al.,  
39  
40 66 2009; Liu and Tsai, 2010). The main contamination assessment was recently achieved for the  
41  
42 67 European population by the European Food and Safety Authorities (EFSA, 2009). It was  
43  
44 68 based on a set of contamination data collected from European control plans, and on several  
45  
46 69 independent contamination studies. EFSA combined these contamination data with the results  
47  
48 70 of consumption surveys from several Europeans countries to estimate the furan daily intake.  
49  
50 71 Nevertheless, the risk linked to furan firstly depends on food consumption habits, and  
51  
52 72 secondly on food contamination levels (Feinberg et al., 2006). As consumption habits are  
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54 73 related to subpopulations and locations, the present paper describes a risk assessment  
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2  
3 74 targeting the Belgian adult population. The Estimated Daily Intake (EDI) was calculated  
4  
5 75 using the deterministic and probabilistic methodologies. Afterwards, the risk was estimated  
6  
7 76 both by comparing it to a toxicological reference dose (classical way) and also by calculating  
8  
9 77 the Margin of Exposure (MoE).

## 11 12 13 78 **Materials and methods**

### 14 15 16 79 *Contamination data*

17  
18 80 The contamination dataset only included products sold in Belgium, which were analysed by a  
19  
20 81 previously described methodology (Scholl et al., 2009). This assessment was performed using  
21  
22 82 496 items sampled in the whole country (Scholl et al., 2011). Samples were taken all along  
23  
24 83 the food chain, in several food markets. The sampling plan included weighting factors, such  
25  
26 84 as food consumption and already reported contamination levels, to focus on the main food  
27  
28 85 groups. This methodology was also applied to avoid the bias resulting from a similar product  
29  
30 86 sold in several countries, but for which the preparation and/or composition can be different  
31  
32 87 (Wegener and Lopez-Sanchez, 2010).

33  
34  
35  
36 88 The assessment relied on a sole methodology to avoid the bias resulting from applying  
37  
38 89 several approaches with different detection capabilities ( $CC_{\beta}$ ) (in a first approach equivalent  
39  
40 90 to the limit of quantification (LOQ)), repeatability, precisions, and expanded uncertainties  
41  
42 91 (Scholl et al., 2009). The procedure used is a solid phase micro-extraction (SPME) coupled to  
43  
44 92 a gas chromatography separation followed by a mass spectrometry detection using the  
45  
46 93 isotopic dilution technique for quantification. The analytical approach is very sensitive and  
47  
48 94 provides a response rate of up to 78.2% above the LOQ.

### 49 50 51 52 53 95 *Consumption data*

54  
55 96 The Belgian Institute of Public Health provided consumption data. In 2004, De Vriese and co-  
56  
57 97 workers carried out a consumption assessment of the Belgian population (De Vriese et al.,  
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1  
2  
3 98 2005). This assessment involved 3,200 people of at least 15 years old from the whole country.  
4  
5 99 The protocol was a recall performed on two non-consecutive days combined to a self-  
6  
7 100 administrated questionnaire on food consumption frequency and a final face-to-face  
8  
9 101 interview. This assessment focused not only on consumption habits, but also on socio-  
10  
11 102 economic data of each participant, providing relevant information to study some  
12  
13 103 subpopulations.  
14  
15

#### 17 104 ***Methodology of risk assessment***

##### 18 105 *Hazard Identification*

19  
20  
21 106 Furan is a toxic present in the food chain. In 1993, the NTP published a first report on furan  
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23 107 toxicity and carcinogenicity based on *in vivo* studies on rat. This report was used in 1995 by  
24  
25 108 the International Agency for Research on Cancer (IARC) to classify it in the group 2B, which  
26  
27 109 means 'possibly carcinogenic to humans'. Five years later, the NAS also classified it as a  
28  
29 110 narcotic. Several independent toxicological studies highlighting the carcinogenic effect of its  
30  
31 111 metabolites have been performed since the 90s, (Kedderis et al., 1993; Chen et al., 1995;  
32  
33 112 Peterson et al., 2000; Peterson et al., 2005; Peterson et al., 2006; Bakhiya et al. 2010;  
34  
35 113 Hamberger et al., 2010). More recent studies revealed that furan toxicity was linked to its  
36  
37 114 major primary metabolite, the *cis*-2-butene-1,4-dial, able to induce tumours through a  
38  
39 115 genotoxic effect on liver cells (Chen et al., 1995; Peterson et al., 2000; Peterson et al., 2005;  
40  
41 116 Peterson et al., 2006). This metabolite results from the first hepatic transformation of furan by  
42  
43 117 cytochrome P-450. To date, toxicity for humans has only been extrapolated from *in vitro* and  
44  
45 118 animals studies.  
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##### 50 119 *Hazard characterisation*

51  
52 120 Hazard characterisation corresponds to a dose-response assessment. It is a toxicological step  
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54 121 describing the mechanism of action including dynamic and kinetic aspects. The main intake  
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3 122 pathway of furan into the body is the food chain. The low polarity of furan allows it to easily  
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5 123 cross biological membranes. Studies on rats revealed that about 80 % of furan is eliminated  
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7 124 within 24 hours: 40 % by respiration, 22 % in faeces and 20 % in urine (Burka et al., 1991).  
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9 125 The remaining 18% are rapidly metabolised by hepatic enzymes of the cytochrome P-450 into  
10  
11 126 more than 10 metabolites (Bakhiya et al., 2010). Its major primary metabolite, the *cis*-2-  
12  
13 127 butene-1,4-dial resulting from furan oxidation, is known to induce hepatocellular tumour and  
14  
15 128 mononuclear cell leukaemia in rats. Furan is also known to induce cholangiocarcinomas in rat  
16  
17 129 liver through an oxidative stress mechanism (Hickling et al., 2010a,b)

20  
21 130 In the late 80s, the US-EPA proposed a Reference Dose for Chronic Oral Exposure  
22  
23 131 (RfD) based on NTP studies (US-EPA Integrated Risk Information System<sup>2</sup>). This dose was  
24  
25 132 calculated according to a 13 week-study involving rat gavages aiming at inducing hepatic  
26  
27 133 lesions. The Lowest Observed Adverse Effect Level (LOAEL) was then estimated to be 4  
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29 134 mg\*(kg<sub>body weight</sub> and day)<sup>-1</sup> for rats. The No Observed Adverse Effect Level (NOAEL) was  
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31 135 fixed at 2 mg \* (kg<sub>b.w.</sub>\*day)<sup>-1</sup>. The application of several precaution factors allowed the US-  
32  
33 136 EPA to recommend a RfD<sub>chronic-oral</sub> of 1 µg \* (kg<sub>b.w.</sub>\*day)<sup>-1</sup> for humans.

34  
35  
36 137 In addition, based on the NTP and on the Moser and co-workers studies (Moser et al.,  
37  
38 138 2009), a benchmark dose for 10% extra risk (BMD<sub>10</sub>) of hepatocellular adenomas and  
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40 139 carcinoma was established. Subsequently, a 95% lower confidence limit for this benchmark  
41  
42 140 dose (BMDL<sub>10</sub>) for the same Mode of Action (MoA) was reported to be 0.96 mg \*  
43  
44 141 (kg<sub>b.w.</sub>\*day)<sup>-1</sup> (Benford et al., 2010; Carthew et al., 2010; Williams et al, 2011).

#### 47 48 142 *Exposure Assessment*

49  
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51 143 The exposure assessment aims at estimating the daily intake of a toxic (EDI). When available,  
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53 144 the EDI may be combined to the daily out-take to estimate the mean absorption.

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56  
57 <sup>2</sup> <http://www.epa.gov/iris/subst/0056.htm>

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3 145 Furan daily intake throughout the food chain is calculated by applying three equations,  
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5 146 namely Equation 1, Equation 2 and Equation 3. The first equation means the global EDI  
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7 147 equals the sum of individual EDIs (EDI of each food group). The second equation explains  
8  
9 148 that a food group EDI results from multiplying the specific food group relative consumption  
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11 149 by the food group contamination. The third equation shows that the relative daily  
12  
13 150 consumption corresponds to the ratio between the daily consumption and the 'population'  
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15 151 weight.

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18 152 Equation 1: Calculation of global EDI

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21 153 
$$EDI_{Global} = \sum_{FoodGroup} EDI_{FoodGroup}$$

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23  
24 154 Equation 2: calculation of EDI

25  
26 155 
$$EDI_{FoodGroup} = [Furan]_{FoodGroup} \times (relativeDailyConsumption)_{FoodGroup}$$

27  
28  
29 156 Equation 3: Estimation of the relative daily consumption

30  
31 157 
$$relativeDailyConsumption = \frac{DailyConsumption}{Weight}$$

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35 158 Two approaches were applied to calculate the EDI: deterministic and probabilistic;  
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37 159 both methods are described in the following sections.

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39  
40 160 *1.1.1.1. Deterministic approach*

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42  
43 161 In the deterministic approach, the EDI was calculated for several categories of the population  
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45 162 according to selected cases, e.g. mean or worst case. As furan contamination is directly  
46  
47 163 related to food origin and preparation (Crews and Castle, 2007; Wegener and López-Sánchez,  
48  
49 164 2010), only the results of the previously mentioned Belgian contamination assessment were  
50  
51 165 used (Scholl et al., 2011). Three different approaches are recommended by the WHO to deal  
52  
53 166 with contamination data below the quantification limits (WHO, 2003). These approaches are  
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55 167 named Lower Bound (LB), Middle Bound (MB) and Upper Bound (UB), where results below  
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3 168 the limit of quantification (LOQ) are respectively replaced by 0, half-LOQ and LOQ itself. In  
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5 169 the present study, as the proportion of non-quantifiable results was very low (< 12 %), these  
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7 170 approaches were expected to provide quite similar results. Consumption depends on the  
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9 171 population studied; therefore, only data from the 'First Belgian consumption survey' (De  
10  
11 172 Vriese et al., 2005) were used. Several categories of population were studied for each food  
12  
13 173 group such as the average consumption, the 2.5<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, and 97.5<sup>th</sup> consumption  
14  
15 174 percentiles. These categories of population are assessable by two ways depending on how  
16  
17 175 unconsumed items are dealt with. On one hand, the statistical analysis is performed by  
18  
19 176 considering only the subpopulation consuming the food group; statistical results of  
20  
21 177 consumption are therefore not representative of the whole population. On the other hand, the  
22  
23 178 whole population is included, and the no-consumption of a food item is characterised by a  
24  
25 179 null-consumption value. The first approach is usually applied in cases of acute toxicity as is  
26  
27 180 more related to a punctual dose, which is the most appropriate for a worst case-study. The  
28  
29 181 second approach is generally applied in case of chronic toxicity as it considers the possibility  
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31 182 of not consuming a food item. As furan is known to have a chronic toxicity, only the second  
32  
33 183 procedure was applied in the present paper.

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35  
36  
37  
38 184 The real weight of each participant to the food consumption survey was used to  
39  
40 185 estimate the EDI more accurately as it was available.

#### 41 42 43 44 186 *Probabilistic approach*

45  
46 187 In this approach, raw (consumption and contamination) data are converted into a function of  
47  
48 188 occurrence (Table I) and computed using the @Risk software (version 5.5; Palisade  
49  
50 189 Corporation, New York, USA). Afterwards, functions are combined through Eq.1, Eq.2 and  
51  
52 190 Eq.3 by using a Monte-Carlo simulation with 500,000 iterations to obtain a function of furan  
53  
54 191 EDI.

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3 192 Functions of contamination occurrence are computed in two steps. The function of  
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5 193 each food group is first determined by only including contamination data >LOQ (this function  
6  
7 194 is truncated such as no result <LOQ can be drawn). Thereafter, a function dealing with the  
8  
9 195 probability to have a data <LOQ is added to the occurrence function determined in the first  
10  
11 196 step. The nature of the second function depends on the approach used to deal with data  
12  
13 197 <LOQ. In the probabilistic method, the three approaches described in the deterministic section  
14  
15 198 (LB, MB and UB) were also applied. A fourth approach named Uniform and involving a  
16  
17 199 random distribution of data <LOQ, was used as well, because it appears more representative  
18  
19 200 of the reality. Practically, in the first three approaches, a discrete function corresponding to,  
20  
21 201 respectively, 0, LOQ/2 and LOQ was used, while a uniform distribution between 0 and LOQ  
22  
23 202 was applied in the fourth approach. Four bimodal functions corresponding to the four  
24  
25 203 approaches were calculated for each food group.

26  
27  
28  
29 204 The functions of consumption occurrence were also computed in two steps based on  
30  
31 205 raw data of the Belgian consumption survey. First of all, a function was computed for each  
32  
33 206 food group by including only the consuming subpopulation (functions are also truncated to  
34  
35 207 avoid a  $\leq 0$  consumption draw). Secondly, the subpopulation not consuming the food item  
36  
37 208 was calculated. A discrete function set to 0 was then proportionally added to the function  
38  
39 209 calculated in the first step. Therefore, the resulting function of consumption occurrence  
40  
41 210 resulting is bimodal like the contamination function.

42  
43  
44  
45 211 In this approach, the real population weight was also used and represented by a  
46  
47 212 statistical distribution of the population weight reported in the consumption survey.

#### 48 49 50 213 *Risk characterisation*

51  
52  
53 214 Two risk characterisation approaches are presented in this paper: a classical way and a new  
54  
55 215 method. In the first one, conclusions have been drawn from comparing the EDIs of several  
56  
57 216 proportions of the population to toxicological reference doses. However, as carcinogenic  
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3 217 effects have no threshold values, a new methodology called Margin of Exposure (MoE) was  
4  
5 218 recently developed (ILSI, 2009). In the MoE approach, a level of concern for the risk linked  
6  
7 219 to a Mode of Action (MoA) is calculated (Eq.4).  
8

9  
10 220 Equation 4: MoE calculation for a carcinogenic MoA

$$MoE = \frac{BMDL_{10}}{EDI}$$

11  
12  
13  
14  
15 221 Where  $BMDL_{10}$  is the 95% lower confidence limit for this benchmark dose for 10% extra risk  
16  
17 222 of hepatocellular adenomas and carcinoma and EDI is the estimated daily intake.

18  
19  
20 223 The risk may be considered as negligible if the MoE is  $>10,000$ . On the other hand, a  
21  
22 224 MoE  $<100$  is of major concern. Finally, discussions are needed, according to the involved  
23  
24 225 MoA, for a MoE included in a range between 10,000 and 100 (ILSI, 2009).  
25  
26

## 27 226 **Results**

### 28 29 30 227 *Deterministic approach*

31  
32  
33 228 Results of the deterministic risk assessments are summarised in Table II and Figure 1. The  
34  
35 229 three approaches used to deal with values  $<LOQs$  gave quite similar results, as shown in  
36  
37 230 Table II. There is a  $<2 \text{ ng} * (\text{kg}_{b.w.} * \text{day})^{-1}$  difference between LB and UB for the average  
38  
39 231 population; it is a consequence of the high proportion of results  $> LOQs$  ( $>78\%$ ) in the  
40  
41 232 contamination assessment. In Figure 1, only the MB approach was illustrated for a question of  
42  
43 233 readability.  
44

45  
46 234 Average and median population EDIs are close (respectively 380 and 330  $\text{ng} * (\text{kg}_{b.w.} * \text{day})^{-1}$ ).  
47  
48 235 Therefore, the distribution of the 3,200 individual EDIs across the population  
49  
50 236 tends to normality, as illustrated in Figure 2A. The figure also shows that the majority of the  
51  
52 237 population has a low EDI with a mode at  $225 \text{ ng} * (\text{kg}_{b.w.} * \text{day})^{-1}$  for 9.5% of the studied  
53  
54 238 population. In this approach, the minimal and maximal EDIs were 0.7 and 3,843  $\text{ng} * (\text{kg}_{b.w.} * \text{day})^{-1}$ ,  
55  
56 239 respectively.  
57  
58  
59  
60

1  
2  
3 240 Only 2.7% of the population presented an EDI above the  $RfD_{\text{chronic-oral}}$ . The majority of  
4  
5 241 the population has an EDI equivalent to 22% of the  $RfD_{\text{chronic-oral}}$ , and the average population  
6  
7 242 EDI is equivalent to 38% of the  $RfD_{\text{chronic-oral}}$ .  
8

9  
10 243 Figure 2A also displays the MoE calculation while the proportion of the population at  
11  
12 244 a given MoE is presented in Figure 2C. About 10% of the population presents a MoE >10,000  
13  
14 245 and a MoE >1,500 is observed for >90% of the population. The minimal calculated MoE was  
15  
16 246 404 for 0.02% of the population and no MoE was <100. Finally, the MoE dispersion mode is  
17  
18 247 4,266 for 9.5% of the population. The main contributors to the EDI are shown in Figure 1.  
19  
20 248 Coffee contributes by 55% to the average EDI, and the other main groups are: soups, prepared  
21  
22 249 meat, pasta and rice and potatoes with an overall contribution of 26% to the EDI (ranging  
23  
24 250 individually from 4 to 9%).  
25  
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### 28 251 *Coffee consumption scenario*

29  
30 252 Coffee was shown to be the major contributor (55%) to the average EDI. This average EDI  
31  
32 253 was achieved after a daily consumption of three cups. The influence of reducing or increasing  
33  
34 254 by one cup the daily consumption was tested in the proposed scenario, as shown in Figure 3.  
35  
36 255 These variations induced a 21% increase ( $460 \text{ ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ) and a 23% decrease ( $294 \text{ ng}$   
37  
38 256  $* (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ) of the average EDI ( $380 \text{ ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ), corresponding to a 12%  
39  
40 257 reduction (or 8% increase) of the contribution to the EDI when simulating both scenarios.  
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### 45 258 *Probabilistic approach*

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47 259 Results of the probabilistic risk assessment are summarized in Table III and Figure 2B. Figure  
48  
49 260 2B displays the distribution of EDIs across the population. A uniform distribution for the  
50  
51 261 results <LOQ and a statistical distribution of the body weights were used to estimate the  
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53 262 EDIs.  
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3 263 Differences between the contamination approaches are shown in Table III. A  
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5 264 difference of  $6 \text{ ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$  (from 488 to 494) was highlighted for the average  
6  
7 265 population. Consequently, it was decided to show only the results of the uniform distribution  
8  
9 266 approach in the figures. The median EDI represents 43% ( $212 \text{ ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ) of the  
10  
11 267 average EDI and is not a normal distribution as confirmed by Figure 2B. The EDI of the  
12  
13 268 majority of the population is low ( $23 \text{ ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ), corresponding to 5% of the average  
14  
15 269 EDI.

16  
17  
18 270 An EDI below the  $\text{RfD}_{\text{chronic-oral}}$  was reported for 91.9% of the population. The average  
19  
20 271 EDI and the EDI of the majority of the population represented, about 49% and 0.2% of the  
21  
22 272  $\text{RfD}_{\text{chronic-oral}}$ , respectively.

23  
24  
25 273 MoEs related to specific EDIs are displayed in Figure 2B, while the proportion of the  
26  
27 274 population relative to a MoE are shown in Figure 2D. A MoE above 10,000 was reported for  
28  
29 275 30% of the population. Seventeen percent of the population presented a MoE of 38,400  
30  
31 276 (distribution mode) and 90% of the population had a MoE above 1,164. Calculated MoE  
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33 277 decreased until 0.1 for a maximum estimated EDI of  $9.2 \text{ mg} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$  (<0.0002% of  
34  
35 278 the population), while only 0.03% of the population displayed a MoE <380.

## 36 37 38 39 279 **Discussion**

### 40 41 42 280 *Consumption data*

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44  
45 281 As previously mentioned, it was decided to use Belgian datasets with the objective to avoid  
46  
47 282 bias linked to consumption habits observed in other countries. Several consumption surveys  
48  
49 283 have been carried out to date in Belgium, but only the Belgian study achieved in 2004  
50  
51 284 included the whole adult population. This survey was representative of the Belgian population  
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53 285 as it included 3,200 people (out of a 10,400,000-global population registered in 2004), from  
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55 286 the whole country, and homogeneously distributed according to gender, age, education level,  
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3 287 working field, etc. Nevertheless, data are out-dated as the survey was performed 7 years ago.  
4  
5 288 However, consumption habits have probably not evolved a lot since the end of the survey.  
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7 289 Thus, one can assume that differences between current and reported consumption habits are  
8  
9 290 minor. The ideal situation would have been to work on a freshly updated survey involving a  
10  
11 291 constant review of data, but such a tool is not yet available.

### 12 13 14 15 292 *Contamination data*

16  
17 293 The contamination dataset was provided by a survey focusing on local products in order to  
18  
19 294 avoid any bias linked to different preparations and compositions of the same product sold in  
20  
21 295 other countries. In addition, the study relied on a highly sensitive analytical methodology  
22  
23 296 specifically designed to reach low quantification limits. There are two beneficial  
24  
25 297 consequences. Firstly, a high proportion of data >LOQ (up to 78%), characterised by small  
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27 298 differences between LB and UB, were observed. Secondly, inter-laboratory analytical biases  
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29 299 resulting from applying different methodologies (different LOQs, expanded uncertainties,  
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31 300 etc.) were eliminated.

32  
33  
34  
35 301 The representativeness of this study comes from its design. It was constructed to avoid  
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37 302 a geographical or branding side effect. The dataset is not out-dated as it was compiled only  
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39 303 two years ago. But as already mentioned for the consumption study, regular updates are  
40  
41 304 needed to avoid biases related to a modified production and/or distribution scheme. An on-  
42  
43 305 going survey based on a constant re-evaluation through a food control plan would be suitable.

### 44 45 46 47 306 *Deterministic vs. probabilistic approach*

48  
49 307 Deterministic and probabilistic approaches should not be seen as different but rather as  
50  
51 308 complementary methods.

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53  
54 309 The comparison of average EDIs only displayed few differences. However, comparing  
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56 310 EDI distributions and medians or modes displayed important differences, especially for the  
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3 311 low daily intake. Furthermore, the EDI distribution is narrower and the EDI increases faster in  
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5 312 the probabilistic approach compared to the deterministic approach. This is a consequence of a  
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7 313 difference of contamination data management. In the deterministic approach, only the average  
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9 314 contamination value of each food group was taken into account, whereas in the probabilistic  
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11 315 approach, a distribution of values (including 0 and very high levels) was used. Therefore,  
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13 316 average EDIs and extreme values are biased, in the deterministic and in the probabilistic  
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15 317 approaches respectively.

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17  
18 318 MoE distributions are very different, but led to similar conclusions. The majority of  
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20 319 the population presented a high MoE and a >10,000 MoE was reported for a meaningful  
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22 320 percentage of people. Differences were however observed for extreme values: the minimal  
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24 321 MoE was 404 in the deterministic approach, while it decreased to 0.1 in the probabilistic  
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26 322 method. Such a low MoE value results from very high consumption and contamination  
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28 323 values, only encountered in a statistical distribution. Therefore, such a combination is very  
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30 324 unlikely and should be ignored.

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34 325 The same differences were observed in the  $RfD_{\text{chronic-oral}}$  approach: the EDI of the  
35  
36 326 majority of the population corresponded to <50 % of the  $RfD_{\text{chronic-oral}}$  and few percents had an  
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38 327  $EDI > RfD_{\text{chronic-oral}}$ . The probabilistic methodology tended to display a higher risk than the  
39  
40 328 deterministic approach. As already observed for the MoE, it finds its explanation in the  
41  
42 329 unlikely extreme EDI values and biased average values in the probabilistic and in the  
43  
44 330 deterministic approaches respectively. Consequently, most results tended to display a low risk  
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46 331 level for furan intake. The real situation should fit between both approaches.

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50 332 ***Coffee consumption scenario***

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53 333 Coffee consumption was shown to be a critical parameter regarding its impact on furan daily  
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55 334 intake. Several straightforward or basic recommendations such as a reduction of the daily  
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3 335 consumption, a thorough mixing of coffee before drinking or even a coffee percolation allows  
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5 336 reducing the exposure (Kuballa et al., 2007).  
6  
7

### 8 337 **Conclusion**

9  
10 338 The present study showed that the majority of the population presents a low daily intake; only  
11  
12 339 extreme consumers are really at risk. The major contamination is due to coffee consumption  
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14 340 (one of the most contaminated items) and changing consumption habits can strongly impact  
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16 341 the EDI.  
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18  
19 342 One must be cautious regarding the conclusions drawn from the risk characterisation.  
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21 343 If it is commonly accepted that a MoE >10,000 corresponds to a low risk level, and that a  
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23 344 MoE <100 means a high risk, there is no consensus for the results included between 10,000  
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25 345 and 100. In the present survey, 10 to 30% of the population are exposed to a low risk level.  
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27 346 Nevertheless, the risk level is not defined for the remaining 70 to 90%. The majority of the  
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29 347 population displays a high MoE and therefore a low risk for the selected MoA (hepatocellular  
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31 348 adenomas and carcinomas). Similar conclusions drawn when using the classical way  
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33 349 (comparison between EDI and the RfD<sub>chronic-oral</sub>).  
34

35  
36 350 Finally, the present study only focused on the adult Belgian population, and a question  
37  
38 351 remains pending about furan exposure of subpopulations at risk, like babies and children.  
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40 352 Carrying out a risk assessment targeting these subpopulations would be relevant but remains a  
41  
42 353 great challenge, as few data are available on their consumption habits.  
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55 358 this study.  
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479 **Table and figure caption**

480

481 **Table I.**

482 List of the distributions used for the probabilistic risk assessment (only distributions for  
483 samples >LOQ and for 'consuming' people are presented) according to the @Risk software  
484 notations.

485 **Table II.**

486 Deterministic EDI ( $\text{ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ) for several contamination approaches.

487

488 **Table III.**

489 Probabilistic EDI ( $\text{ng} * (\text{kg}_{\text{b.w.}} * \text{day})^{-1}$ ) for several contamination approaches.

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491

492 **Figure 1.**

493 Title: Deterministic EDI for the average population, including the contribution of the most  
494 relevant food groups.

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496

497

497 **Figure 2.**

498 Title: (A): Distribution of the EDI across the population in the *deterministic* approach, and  
499 evolution of the MoE according to the EDI; (B): Same as A but for the *probabilistic*  
500 approach; (C): Distribution of the MoE across the population in the *deterministic* approach;  
501 (D): Same as C for the *probabilistic* approach.

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504

504 **Figure 3.**

505 Title: Influence of decreasing or increasing the daily coffee consumption by one cup on the  
506 EDI of the average population, including the contribution of the most relevant food groups.

507

Table I. List of the distributions used for the probabilistic risk assessment (only distributions for samples >LOQ and for 'consuming' people are presented) according to the @Risk software notations.

Food group	@Risk Contamination distribution	@Risk Consumption distribution
Vegetables	RiskBetaGeneral(0.21931;0.22834;0.8;30.68)	RiskPearson5(7.9716;1688.8;RiskShift(-75.196))
Fruits	RiskPearson5(0.87353;1.1588;RiskShift(0.13385))	RiskPearson5(6.8822;1997.4;RiskShift(-120.74))
Milk and Milky beverages	RiskLognorm(3.3751;2.9041;RiskShift(-0.5535))	RiskLoglogistic(-54.643;288.93;5.0313)
Dessert cream	RiskNormal(7.358;7.209)	RiskLoglogistic(-16.106;148.06;3.764)
Pasta, Rice, Other Grain	RiskExtvalue(22.516;27.748)	RiskLognorm(203.84;132.09;RiskShift(-27.127))
Breakfast Cereals	RiskLognorm(33.178;32.292;RiskShift(-1.3011))	RiskPearson5(8.3866;564.71;RiskShift(-23.071))
Biscuits	RiskNormal(25.721;19.913)	RiskInvgauss(49.638;67.916;RiskShift(-4.3678))
Raw Meat	RiskBetaGeneral(0.27138;0.35639;0.32;66.93)	RiskInvgauss(101.66;226;RiskShift(-11.664))
Processed meat	RiskInvgauss(4.0861;0.7775;RiskShift(0.17294))	RiskInvgauss(67.906;106.439;RiskShift(-4.1765))
Fish	RiskExpon(23.148;RiskShift(-0.79903))	RiskBetaGeneral(1.4836;5.9922;1.6382;526.32)
Chocolate, Candy Bars, Paste, etc.	RiskUniform(-0.33556;8.9656)	RiskPearson5(3.793;147.04;RiskShift(-11.33))
Confectioner and Non-Chocolate	RiskBetaGeneral(0.18312;0.21331;0.72;8.79)	RiskInvgauss(37.276;33.348;RiskShift(-2.6119))
Cakes	RiskPearson5(1.2746;5.7504;RiskShift(1.4743))	RiskInvgauss(48.025;79.124;RiskShift(-3.4931))
Fruit And Vegetable Juices	RiskLoglogistic(-0.6429;2.0314;5.2505)	RiskLoglogistic(-72.436;278.71;3.2801)
Soft drinks	RiskTriang(-0.018347;0.95;1.6178)	RiskInvgauss(635.46;1093.9;RiskShift(-57.616))
Coffee	RiskBetaGeneral(0.4086;0.47225;1.13;106.23)	RiskPearson5(4.9426;2648.5;RiskShift(-191.14))
Tea	RiskBetaGeneral(0.29271;0.27597;0.37;2.87)	RiskLognorm(338.95;321.83;RiskShift(39.603))
Herbal Tea	RiskBetaGeneral(0.18842;0.20477;0.22;3.68)	RiskPearson5(4.2366;1363.5;RiskShift(-80.915))
Wine	RiskLoglogistic(0.19764;0.30883;2.0584)	RiskLognorm(287.29;189.16;RiskShift(-26.305))
Beer, Cider	RiskInvgauss(3.9075;19.794;RiskShift(-1.2641))	RiskPearson5(3.0816;1457;RiskShift(-129.34))
Tomato Sauces	RiskLogistic(11.2955;2.9182)	RiskInvgauss(73.018;30.148;RiskShift(-0.36396))
Soups	RiskInvgauss(25.542;10.767;RiskShift(-0.5567))	RiskExtvalue(241.22;109.2)
Miscellaneous	RiskPearson5(5.8123;82.114;RiskShift(-7.3599))	RiskLoglogistic(2.7612;71.036;2.4976)
Soya Products	RiskExtvalue(1.3338;1.1449)	RiskInvgauss(135.6;45.027;RiskShift(-4.31))



Table II. Deterministic EDI ( $\text{ng} \cdot (\text{kg}_{\text{b.w.}} \cdot \text{day})^{-1}$ ) for several contamination approaches.

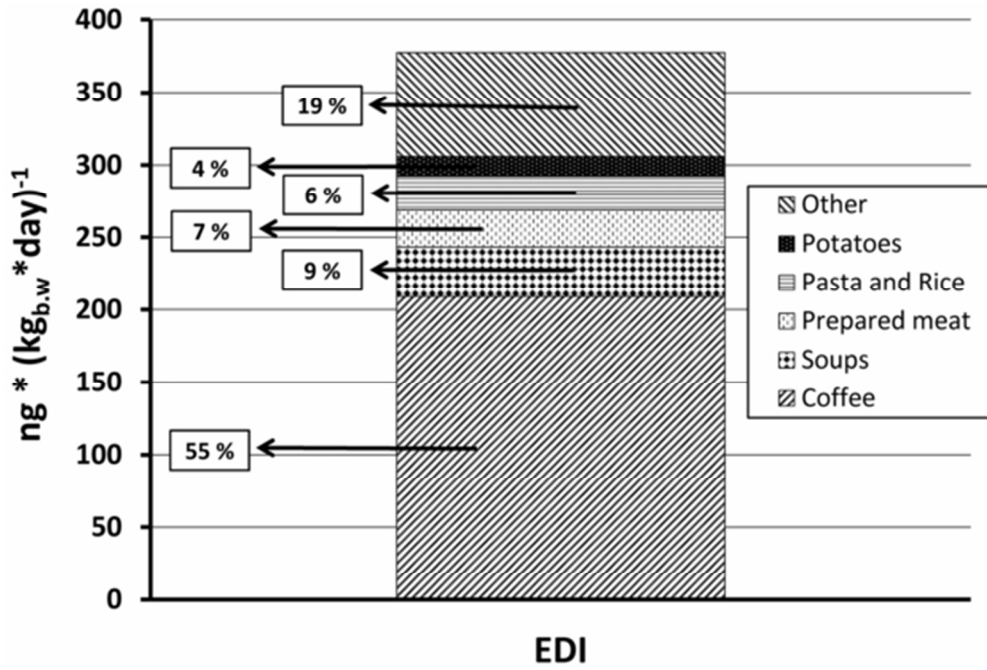
	<b>Lower Bound</b>	<b>Middle Bound</b>	<b>Upper Bound</b>
<b>First Quartile</b>	191	192	193
<b>Median</b>	329	330	331
<b>Mean</b>	379	380	381
<b>Third Quartile</b>	500	501	501

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Table III. Probabilistic EDI ( $\text{ng} \cdot (\text{kg}_{\text{b.w.}} \cdot \text{day})^{-1}$ ) for several contamination approaches.

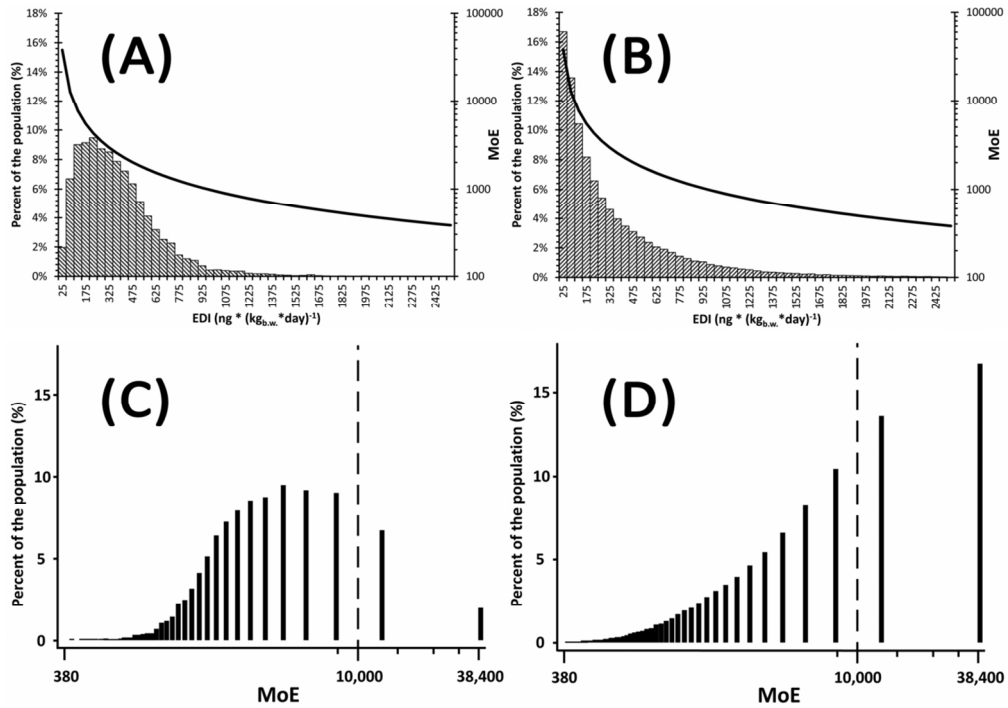
	Lower Bound	Middle Bound	Upper Bound	Uniform
<b>Mode</b>	25	23	27	23
<b>First Quartile</b>	80	80	82	81
<b>Median</b>	211	212	213	212
<b>Mean</b>	494	494	488	494
<b>Third Quartile</b>	492	493	493	493
<b>Proportion of results &gt; RfD<sub>ora</sub> (%)</b>	8.1	8.1	8.1	8.1

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53x35mm (300 x 300 DPI)

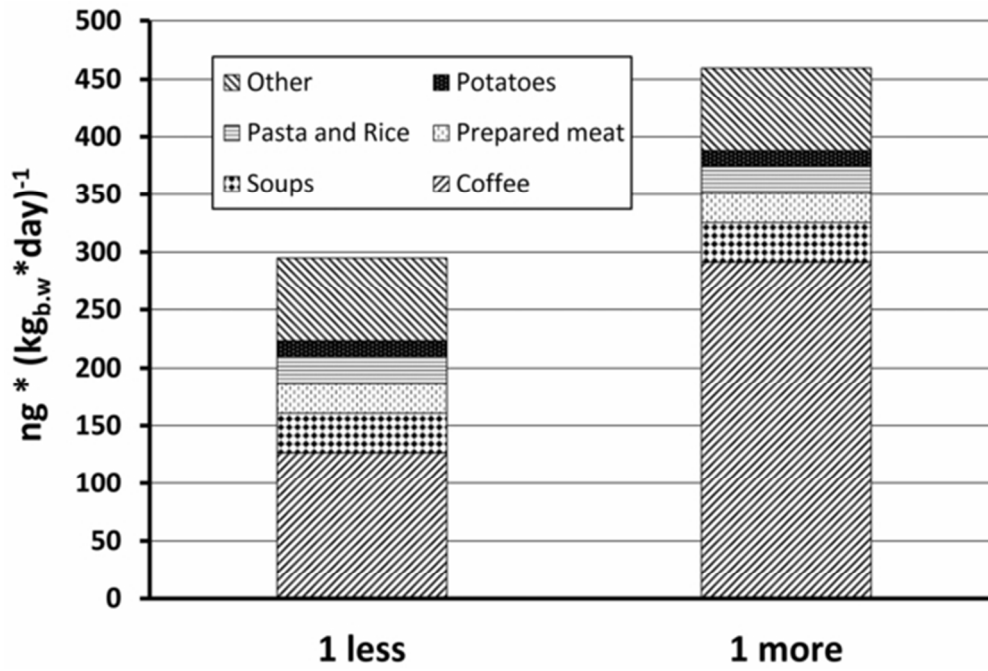
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