



## Life cycle human health impacts of 875 pesticides

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1 **Life cycle human health impacts of 875 pesticides**

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3

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11 **Abstract**

12 *Purpose* Residues in field crops grown and harvested for human consumption are the  
13 main contributor to overall human exposure toward agricultural pesticides for the general  
14 population. However, exposure from crop residues is currently not considered in life cycle  
15 assessment practice. We therefore present a consistent framework for characterizing human  
16 toxicological impacts associated with pesticides applied to agricultural crops in the frame of  
17 life cycle impact assessment based on state-of-the-art data and methods.

18 *Methods* We combine a dynamic multicrop plant uptake model designed for evaluating  
19 human exposure to residues for a wide range of pesticide-crop combinations with latest  
20 findings of pesticide dissipation kinetics in crops and post-harvest food processing. Outcome  
21 is a set of intake fractions and characterization factors for 875 organic pesticides and 6 major  
22 food crops along with specific confidence intervals for each factor.

23 *Results and Discussion* Intake fractions aggregating exposure via crop residues and  
24 exposure via fractions lost to air and soil for pesticides applied to agricultural crops vary  
25 between  $10^{-8}$  and  $10^{-1}$  kg intake per kg applied as a function of pesticide and crop. Intake  
26 fractions are typically highest for lettuce and tomato and lowest for potato due to differences  
27 in application times before crop harvest and soil as additional barrier for uptake into potato  
28 tubers. Uncertainty in intake fractions is mainly associated with dissipation dynamics in  
29 crops, where results demonstrate that using pesticide- and crop-specific data is crucial.  
30 Combined with the uncertainty in effect modeling, characterization factors per pesticide and  
31 crop show squared geometric mean standard deviations ranging from 38 to 15560 over a  
32 variability range across pesticide-crop combinations of 10 orders of magnitude.

33 *Conclusions* Our framework is operational for use in current life cycle impact assessment  
34 models, is made available for USEtox, and closes an important gap in the assessment of  
35 human exposure to pesticides. For ready use in life cycle assessment studies, we present  
36 pesticide-crop combination-specific characterization factors normalized to pesticide mass

37 applied and provide default data for application times and loss due to post-harvest food  
38 processing. When using our data, we emphasize the need to consult current pesticide  
39 regulation, since each pesticide is registered for use on certain crops only, which varies  
40 between countries.

41

42 **Keywords:** dynamiCROP plant uptake model; human toxicity characterization factors;  
43 pesticides; life cycle impact assessment (LCIA); food crop consumption; intake fractions

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## 44 **1 Introduction**

45 Food is an important source of human exposure to toxic chemicals which includes  
46 residues of pesticides, perfluorinated chemicals, metals, phthalates, and persistent organic  
47 pollutants including dioxins and polychlorinated biphenyls. Common sources of residues in  
48 food along food product life cycles are agricultural production and harvesting, food  
49 packaging, storage, industrial and domestic food processing, and finally serving (Dickson-  
50 Spillmann et al. 2009, Freeman 2011, Lippmann 2009, Muncke 2009, Tittlemier et al. 2007).  
51 In this context, pesticides are a special chemical class of interest, because they are  
52 intentionally applied to agricultural field crops, they have by design toxic properties, and the  
53 general public in various countries is concerned about chronic effects from low-level  
54 exposure (European Commission 2006, McKinlay et al. 2008, Pretty 2005, Slovic 2010). For  
55 pesticides, food crop consumption is the predominant pathway for human exposure (Caldas &  
56 Jardim 2012, Fantke et al. 2011a, Lu et al. 2008). Therefore, assessing pesticide residues in  
57 food crops is a key component in current pesticide authorization in Europe (European  
58 Commission 2009) and elsewhere and needs to be considered for assessing the environmental  
59 performance of food products over their life cycle.

60 Life cycle assessment (LCA) is a tool that is frequently applied to evaluate the  
61 environmental performance of agricultural production systems as well as various food  
62 products including crops (Andersson 2000, Perrin et al. 2014, Roy et al. 2009, Schau & Fet  
63 2008). However, although health impacts from environmental emissions associated with the  
64 use of pesticides in food crop production are considered in some agrifood-related LCA  
65 studies, human exposure to pesticide residues in the treated food crops is still mostly  
66 disregarded (Fantke et al. 2011b, Juraske & Sanjuán 2011). This is mainly due to the fact that  
67 current tools for estimating pesticide residues in food crops show considerable uncertainties –  
68 mostly associated with dissipation kinetics in crops (Fantke et al. 2012a, Juraske et al. 2008).  
69 Furthermore, these tools are not implemented in current life cycle impact assessment (LCIA)

70 models and methods for assessing human health impacts from exposure to potentially toxic  
71 chemicals including pesticides. To address this gap, we propose to (a) develop an operational  
72 framework for consistently incorporating health impacts from exposure to residues in food  
73 crops associated with field applications of agricultural pesticides into LCIA. We further aim  
74 at reducing uncertainty of pesticide-related characterization factors by integrating the latest  
75 findings from Fantke and Juraske (2013) and Fantke et al. (2014) in estimating dissipation  
76 kinetics in crops to (b) calculate harvest fractions, intake fractions and characterization factors  
77 for 875 pesticides and to (c) estimate the resulting specific uncertainty for each of these  
78 factors.

79

## 80 **2 Methods**

81 The general framework applied in LCIA for characterizing human toxicological impacts  
82 associated with chemical emissions combines factors representing environmental fate, human  
83 exposure, and health endpoint-specific dose-response into characterization factors (European  
84 Commission 2010, Udo de Haes et al. 2002). At midpoint level, human toxicological  
85 characterization factors relate numbers of health incidences to emitted chemical mass. At  
86 endpoint level, characterization factors contain an additional term accounting for the (damage  
87 or health endpoint-specific) severity and are expressed in terms of disability-adjusted life  
88 years (DALY) per emitted chemical mass. Environmental fate and human exposure can be  
89 aggregated into the human intake fraction that directly relates the chemical mass taken in by  
90 an exposed (or the entire global) human population to the chemical mass emitted (Bennett et  
91 al. 2002). This general framework for assessing human toxicity impacts in LCIA under  
92 assumed steady-state conditions was originally designed to be applied for environmental  
93 emissions, i.e. related characterization factors are normalized to a unit mass continuously  
94 released into a specific environmental compartment, such as air, water, or soil (Rosenbaum et  
95 al. 2008). However, pesticides are not emitted continuously, but are rather applied as pulses to

96 agricultural crops that are harvested within days to weeks after the (latest) application.  
97 Steady-state might, hence, often not be reached, especially when pesticides are applied shortly  
98 before crop harvest (Fantke et al. 2013, Rein et al. 2011). In addition, the fraction of the  
99 applied pesticide mass that is intercepted by the crop surface and that ends up as residues in  
100 crop harvest along with the fractions that are lost during and after the application and that  
101 reach target field and off-target soil, air and water including surface and groundwater are not  
102 typically reported or available for LCA practitioners (Perrin et al. 2014). Instead, in most  
103 cases the applied pesticide mass or mass per area is available, from which fractions reaching  
104 the treated crop and fractions reaching the environment as emissions then need to be  
105 estimated (Rosenbaum et al. 2015). Consequently, the current framework applied for human  
106 toxicity assessment of chemicals in LCIA needs to be extended and modified as detailed in  
107 the following to reflect the mass distribution dynamics between pesticide application and food  
108 crop harvest.

109

## 110 2.1 Modeling framework for pesticide exposure

111 *Characterization factors:* Our starting point is the multicrop model for characterizing  
112 health impacts from pesticide residues in food crops, dynamiCROP, that describes the mass  
113 evolution of pesticides in different crop-environment systems based on solving a set of  
114 coupled differential equations. This model is fully described in Fantke et al. (2011a) and  
115 Fantke et al. (2011b) and is designed for evaluating human toxicological impacts associated  
116 with pesticide residues in wheat, paddy rice, apple, tomato, potato and lettuce, representing  
117 the most relevant crop archetypes with respect to human vegetal food consumption.

118 Following this approach, human toxicity characterization factors,  $CF_{x,t,e}$  [incidences  $\text{kg}_{\text{applied}}^{-1}$   
119 at midpoint level,  $\text{DALY kg}_{\text{applied}}^{-1}$  at endpoint level], for pesticides applied to crop  $x$  harvested  
120 at time  $t$  [days after application] associated with health endpoints  $e$  are calculated from

121 toxicity effect factors for aggregated cancer and non-cancer health effects,  $EF_e$   
 122 [incidences  $\text{kg}_{\text{intake}}^{-1}$  at midpoint level,  $\text{DALY kg}_{\text{intake}}^{-1}$  at endpoint level] and  
 123 human intake fractions,  $iF_{x,t}$  [ $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ ], as  
 124  $CF_{x,t,e} = EF_e \times iF_{x,t}$  (1)

125 *Effect factors:* Effect factors are derived as

$$126 \quad EF_e = \begin{cases} DRF_e & \Rightarrow \text{midpoint level} \\ DRF_e \times SF_e & \Rightarrow \text{endpoint level} \end{cases} \quad (2)$$

127 with  $DRF_e$  [incidences  $\text{kg}_{\text{intake}}^{-1}$ ] as dose-response slope factor and  $SF_e$  [ $\text{DALY incidence}^{-1}$ ] as  
 128 damage or severity factor. Dose-response slope factors relate risks of humans to potentially  
 129 develop a health effect from pesticide exposure to the quantity inhaled or ingested and are  
 130 mainly taken from Rosenbaum et al. (2008). In case of missing data,  $DRF_e$  are extrapolated  
 131 from chronic lifetime doses affecting 50% of exposed humans or – if chronic data are not  
 132 available as for most non-cancer effects – from no-observed effect levels of exposed animal  
 133 species assuming linear dose-response relationships (Huijbregts et al. 2005, Kramer et al.  
 134 1996). The difference in the units of the effect factors (Eq. 2) and consequently of the  
 135 characterization factors is related to the fact that at midpoint level, the effect factor is solely  
 136 derived from (and therefore equal to) the dose-response slope factor, whereas at endpoint  
 137 level, a severity factor is included accounting for differences in effect severity. Severity  
 138 factors of 11.5 and 2.7  $\text{DALY incidence}^{-1}$  are applied for cancer and non-cancer effects,  
 139 respectively (Huijbregts et al. 2005), to be used for comparative purposes rather than for  
 140 estimating absolute damages. Disability-adjusted life years are undiscounted and without age-  
 141 weighting.

142 *Human intake fractions:* To account for both the pesticide mass fraction reaching the crop  
 143 as residues and the fractions lost as emissions to air and soil during and after application,  
 144 human intake fractions relate the mass that is ultimately taken in by humans via all exposure

145 pathways to the mass of applied pesticide. Hence, the total intake fraction per mass applied  
 146 combines the specific intake fractions for exposure to crop residues from the applied mass  
 147 reaching the treated crop with intake fractions for different exposure pathways  $p$  including  
 148 inhalation and ingestion of drinking water and different food items from the applied mass  
 149 reaching air and soil:

$$150 \quad iF_{x,t} = iF_{x,t}^{\text{residues}} + fr_x^{\text{air}} \times \sum_p iF_p^{\text{air}} + fr_x^{\text{soil}} \times \sum_p iF_p^{\text{soil}} \quad (3)$$

151 where  $iF_{x,t}^{\text{residues}}$  [ $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ ] is the intake fraction associated with exposure to residues in  
 152 the treated crop at harvest time based on a mechanistic plant uptake model accounting for  
 153 partitioning, transport and dissipation kinetics (see Section 2.2),  $iF_p^{\text{air}}$  [ $\text{kg}_{\text{intake}} \text{kg}_{\text{emitted to air}}^{-1}$ ] is  
 154 the exposure pathway-specific intake fraction related to the fraction lost to air via e.g. wind  
 155 drift,  $fr_x^{\text{air}}$  [ $\text{kg}_{\text{emitted to air}} \text{kg}_{\text{applied}}^{-1}$ ], and  $iF_p^{\text{soil}}$  [ $\text{kg}_{\text{intake}} \text{kg}_{\text{emitted to soil}}^{-1}$ ] is the exposure pathway-  
 156 specific intake fraction related to the fraction lost to soil via e.g. deposition,  $fr_x^{\text{soil}}$   
 157 [ $\text{kg}_{\text{emitted to soil}} \text{kg}_{\text{applied}}^{-1}$ ]. Intake fractions referring to mass emitted to air (beyond treated field  
 158 boundaries) and to soil (considering run-off and leaching to freshwater and disregarding direct  
 159 crop uptake as already considered in the intake fractions related to crop residues) are  
 160 calculated with USEtox (Rosenbaum et al. 2008) assuming continuous emissions and steady-  
 161 state conditions. Related fractions lost (emitted) to air during and after pesticide application  
 162 are assumed to be pesticide-generic, but crop-specific for a typical foliar application and  
 163 range from 5% for lettuce, 14.8% for potato, and 16.5% for wheat and paddy rice to 23.7%  
 164 for tomato and 35.4% for apple (Ganzelmeier et al. 1995, Rautmann et al. 2001, van de Zande  
 165 et al. 2007). We thereby acknowledge that different application techniques, such as aerial or  
 166 soil application would yield different fractions lost to air. Fractions lost to soil range from 2.3  
 167 to 81% assuming foliar application and are a function of pesticide properties (e.g. molecular  
 168 weight influencing deposition velocities), application time (where we distinguish per crop

169 between averages for herbicides and other pesticides), and crop characteristics (e.g. growth  
 170 stage and interception area influencing intercepted pesticide mass).

171

## 172 2.2 Exposure to residues in crops

173 Intake fractions for crop residues are calculated from harvest fractions representing the  
 174 residual mass fraction of applied pesticide found in crop harvest,  $hF_{x,t}$  [ $\text{kg}_{\text{in harvest}} \text{kg}_{\text{applied}}^{-1}$ ], and  
 175 a food processing factor,  $PF_x$  [ $\text{kg}_{\text{intake}} \text{kg}_{\text{in harvest}}^{-1}$ ], accounting for post-harvest reduction of crop  
 176 residues due to subsequent food processing steps:

$$177 \quad iF_{x,t}^{\text{residues}} = PF_x \times hF_{x,t} \quad (4)$$

178 Since data are only available for a limited number of pesticide-crop combinations, pesticide-  
 179 generic food processing factors are applied as proxies, i.e.  $0.59 \text{ kg}_{\text{intake}} \text{kg}_{\text{in harvest}}^{-1}$  for washing  
 180 with tap water,  $0.31 \text{ kg}_{\text{intake}} \text{kg}_{\text{in harvest}}^{-1}$  for parboiling or cooking, and  $0.33 \text{ kg}_{\text{intake}} \text{kg}_{\text{in harvest}}^{-1}$  for  
 181 bread making (Kaushik et al. 2009, Keikotlhaile et al. 2010, Liang et al. 2014).

182 Harvest fractions are defined as the ratio of residual pesticide mass in all harvested crop  
 183 components  $c$ ,  $m_{x,c,t}^{\text{residues}}$  [ $\text{kg}_{\text{in harvested crop component}}$ ], and the sum of applied pesticide mass,  $m_x^{\text{applied}}$   
 184 [ $\text{kg}_{\text{applied}}$ ], and background mass,  $m_x^{\text{background}}$  [ $\text{kg}_{\text{in crop-environment system}}$ ]:

$$185 \quad hF_{x,t} = \frac{\sum_c m_{x,c,t}^{\text{residues}}}{m_x^{\text{applied}} + m_x^{\text{background}}} \approx \frac{\sum_c m_{x,c,t}^{\text{residues}}}{m_x^{\text{applied}}} \quad (5)$$

186 Both the pesticide mass applied directly to the treated crop and the soil residues from  
 187 deposition or from earlier applications (background mass) that are taken up into the crop via  
 188 the root system need to be considered according to Eq. 5. However, following the FAO  
 189 recommendations for good agricultural practices for pesticide application (FAO 2003) as best  
 190 estimate in LCIA, we assume that the background pesticide input via root uptake from  
 191 previous applications and/or cross-field wind drift and subsequent deposition onto soil are

192 negligible, i.e. we assume  $m_x^{\text{background}} \approx 0$  kg. We justify this assumption with the fact that even  
 193 when applied in relatively quick succession to the same crop, previous studies have  
 194 demonstrated that typically only the latest direct application is dominating overall residues in  
 195 crop harvest (Juraske et al. 2011, Rein et al. 2011). Hence, harvest fractions and all  
 196 subsequent metrics, i.e. intake fractions and characterization factors, are normalized to the  
 197 (latest) pesticide mass applied to the respective crop,  $m_x^{\text{applied}}$ .

198 To obtain harvest fractions, we have solved the dynamics of a mass balance system of  
 199 environmental compartments including air, soil and paddy water (the latter only for paddy  
 200 rice) and crop components including root, stem, leaves, leaf surface, fruit and fruit surface  
 201 (the latter two for all crops but lettuce and potato), which are all coupled by inter-  
 202 compartment transfers (Fantke et al. 2011a, Rein et al. 2011). Crop residues and resulting  
 203 harvest fractions were found to be highly dependent on degradation in crops and time to  
 204 harvest (Fantke et al. 2012b). From comparing modeled crop residues with measured data, we  
 205 found that predicted residual masses over time were in good agreement with measured  
 206 residues with  $R^2$  between 0.81 and 0.99 (Fantke et al. 2011a, Fantke et al. 2011b, Itoiz et al.  
 207 2012, Juraske et al. 2012). Since most input parameters that are required for solving the  
 208 underlying mass balance system are typically not available to LCA practitioners and to be  
 209 compatible with the format of assessment models and intake fractions applied in LCIA for  
 210 human toxicity assessment, the dynamicCROP model was linearized and a parametric  
 211 regression model was developed for each of the six crops still accounting for the main  
 212 influences on the dynamics between pesticide application and crop harvest (Fantke et al.  
 213 2012b, Fantke et al. 2013). Each model combines the contributions of different crop and  
 214 environmental components  $c \in \{\text{crop interior, crop surface, soil}\}$  at harvest time to the overall  
 215 residual pesticide mass found in crop harvest:

$$216 \quad \text{hF}_{x,t} = \sum_c \text{hF}_{x,c,t} = \sum_c 10^{(\alpha_{x,c}^* + \beta_{x,c} \times k_{x,c} \times t_x)} \quad (6)$$

217 where  $\alpha_{x,c}^*$  and  $\beta_{x,c}$  denote dimensionless coefficients,  $k_{x,c}$  [ $\text{kg}_{\text{reaching component}} \text{day}^{-1}$  per  
 218  $\text{kg}_{\text{in component}}$ ], represent removal rate coefficients and  $t_x$  [day] is the time between pesticide  
 219 application and crop harvest. Crop- and crop/environmental component-specific coefficients  
 220  $\alpha_{x,c}^*$  and  $\beta_{x,c}$  are detailed in the Supporting Information (SI), Section S-1, and are adapted  
 221 from Fantke et al. (2012b). Removal rate coefficients for the soil component  
 222  $k_{x,c \in \{\text{soil}\}} = 1/\text{FF}_{\text{soil}}$  are derived from the inverse of pesticide residence times in soil  
 223 corresponding to the fate factors for continental agricultural soil,  $\text{FF}_{\text{soil}}$  [ $\text{kg}_{\text{in soil}}$  per  
 224  $\text{kg}_{\text{emitted to soil}} \text{day}^{-1}$ ], in the USEtox matrix of fate factors (Rosenbaum et al. 2008). Removal  
 225 rate coefficients for crop interior and crop surface are generally obtained as  
 226  $k_{x,c \in \{\text{crop}; \text{crop-surface}\}} = \ln(2)/\text{HL}_{x,c}^{\text{dissipation}}$  from overall removal (dissipation) half-lives  $\text{HL}_{x,c}^{\text{dissipation}}$   
 227 [day] estimated by Fantke et al. (2014) by fitting dissipation kinetics for 1485 distinct  
 228 pesticide-crop combinations reported in Fantke and Juraske (2013). For tomato, apple and  
 229 lettuce, additional terms contribute to  $k_{x,c \in \{\text{crop}; \text{crop-surface}\}}$  accounting for the influence of  
 230 substance properties (see SI, Section S-1). Finally, crop-specific harvest times are taken from  
 231 Fantke et al. (2011b), Table S1, separately averaged for herbicides typically applied before or  
 232 during early crop stages and other pesticides, such as fungicides and insecticides, applied  
 233 during all crop stages including shortly before harvest and during post-harvest storage. With  
 234 these assumptions, we yield best estimates for crop residues and typically do not exceed  
 235 regulatory maximum residue limits (MRL) as demonstrated by Juraske et al. (2011), Juraske  
 236 et al. (2012), Itoiz et al. (2012), and Fantke et al. (2011a).

237

### 238 2.3 Uncertainty analysis

239 Uncertainty of harvest fractions, intake fractions and characterization factors (model  
 240 output) is expressed as 95% confidence interval ranges. Confidence intervals around model

241 output  $y$  are derived from a combination of uncertainty related to model input variables (input  
 242 parameter uncertainty) and uncertainty related to modeling of harvest fractions (regression  
 243 model uncertainty). Input parameter and model uncertainty are expressed as squared  
 244 geometric standard deviations  $\text{GSD}_{x_i}^2 := \exp(2 \times \sigma_{x_i})$  with  $\sigma_{x_i} > 0$  the standard deviation of  
 245 the natural logarithm of input variable or regression model  $x$  and the probability  
 246  $\{x_i / \text{GSD}_{x_i}^2 < x_i < \text{GSD}_{x_i}^2 \times x_i\} = 0.95$  representing the 95% confidence interval around  $x$ :

$$247 \quad \text{GSD}_y^2 = \exp\left(2 \times \sqrt{\sum_i \text{var}(\ln(x_i))}\right) = \exp\left(\sqrt{\sum_i (\ln(\text{GSD}_{x_i}^2))^2}\right) \quad (7)$$

248 In Eq. 7, we use the fact that the variance of each input variable is related to the  
 249 corresponding  $\text{GSD}_{x_i}^2$  by  $\text{var}(\ln(x_i)) = (\ln(\text{GSD}_{x_i}^2))^2$ . The choice of 2 in the exponent of the  
 250 geometric standard deviations reflects the rounded critical value from the Student's  $t$ -  
 251 distribution. All input variables are mutually independent – see Fantke et al. (2012b) for  
 252 details. With that, relative sensitivities  $S_{x_i}$  are unity, i.e.  $S_{x_i} = 1$ , for all input variables and  
 253 regression models (Slob 1994) and the uncertainty of model output exclusively depends on  
 254 the variances of input variables and regression models. Considered in this analysis are  
 255 pesticide-specific uncertainty factors for regression models and data for dissipation half-lives  
 256 in crops (Fantke et al. 2014) representing the most uncertain variable in determining pesticide  
 257 mass in crop harvest (Fantke et al. 2012b, Juraske et al. 2008), degradation half-lives in soil as  
 258 proxy for soil residence times taken from the Pesticide Properties Database (Footprint 2014)  
 259 or U.S. EPISuite (US-EPA 2012), crop-specific residue regression models for different  
 260 harvest fraction ranges (Fantke et al. 2012b), post-harvest food processing (Keikotlhaile et al.  
 261 2010, Liang et al. 2014), fractions of applied pesticides lost to air and soil (DEFRA 2006),  
 262 cancer and non-cancer dose-response information and severity factors (Huijbregts et al. 2005).  
 263  $\text{GSD}_{x_i}^2$  for all considered input variables and regression models are summarized in the SI,  
 264 Section S-2. Since the harvest fraction regression model for each crop  $c$  in Eq. 6 involves an

265 exponent of the complex form  $hF_{x,c,t} = 10^{(\alpha_{x,c}^* + \beta_{x,c} \times k_{x,c} \times t_x)}$ , Eq. 7 was first applied within its  
266 domain of application to determine the 95% confidence interval of  
267  $\log(hF_{x,c,t}) = \alpha_{x,c}^* + \beta_{x,c} \times k_{x,c} \times t_x$ . The two-sided limits forming the confidence interval are  
268 then calculated as  $hF_{x,t} = \sum_c 10^{\log(hF_{x,c,t})}$ , yielding separate upper and lower 95% confidence  
269 interval limits at the level of harvest fractions, intake fractions and characterization factors.

270

### 271 3 Results

#### 272 3.1 Intake fractions from pesticides applied to food crops

273 The variability of intake fractions for 875 pesticides applied to six crops is shown in  
274 <Figure 1, contrasting the contributions of the fractions of applied pesticide reaching the  
275 agricultural food crops as residues and of the fractions reaching air and soil as emissions  
276 during and after application, of which the latter two are summed over all contributing  
277 exposure pathways. Intake fractions aggregated over crop residues and fractions lost to air and  
278 soil vary between 4 (tomato) and 6 (wheat, paddy rice, lettuce) orders of magnitude across  
279 pesticides applied to the same crop, demonstrating the importance of substance properties on  
280 crop residue dynamics. Aggregated intake fractions for the same pesticide applied to different  
281 crops vary between a factor 2.6 for herbicide florasulam and more than 5 orders of magnitude  
282 for 1-naphthol, a metabolite of insecticide carbaryl, demonstrating that the influences of crop  
283 characteristics and pesticide application times on crop residue dynamics are as important as  
284 the influence of substance properties. Individual intake fractions are provided for each of the  
285 875 pesticides and six crops in the SI, Section S-3.

286

287 <Figure 1>

288

289 Highest aggregated intake fractions are found in lettuce and tomato with median values  
290 across pesticides of 0.035 and 0.013  $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ , respectively, which is mostly due to very  
291 short averaged application times before harvest for insecticides and fungicides. In contrast,  
292 lowest aggregated intake fractions are found in potato with a median of  $6 \times 10^{-6}$   
293  $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ . The highest intake fractions for individual pesticide-crop combinations are  
294 found for fungicides cyproconazole and fuberidazole on lettuce yielding each 0.27  
295  $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ . Exposure from intake of crop residues is the main contributor to aggregated  
296 intake fractions for 88 to 97% of all pesticides in wheat, paddy rice, tomato, apple, and  
297 lettuce. For these crops, exposure from fractions lost to air and soil is the main contributor to  
298 aggregated intake fractions for only 1.3 to 7% of all pesticides (<Figure 1, grey vs. white  
299 boxes). Potato is an exception, where exposure from fractions lost to air and soil is generally  
300 exceeding exposure from residues in treated crop and where the fraction lost to soil is the  
301 main contributor to aggregated intake fractions for 60% of the pesticides. For 35% of  
302 pesticides, the main contribution is from fractions lost to air and only 5% of all pesticides  
303 show main contribution from crop residues in potato.

304 The largest variability is shown for intake fractions associated with crop residues, which  
305 is mainly due to differences in application times between crops and between herbicides and  
306 other pesticides applied to the same crop. As an example, intake fractions associated with  
307 pesticides applied to apple trees show a variability of 6 orders of magnitude due to the large  
308 difference in average application times of 150 days (herbicides) and 14 days (non-herbicides)  
309 before crop harvest. Lower intake fraction ranges for all crops are associated with herbicides  
310 that are on average applied much longer before harvest than other pesticides, thereby allowing  
311 removal processes to limit crop residues at harvest time. In contrast, fungicides and  
312 insecticides are typically applied at later crop stages (sometimes even quickly before harvest)  
313 and therefore cover the upper range of crop residue-related intake fractions. Aggregated

314 intake fractions for the individual pesticides and crops per kg applied are given in the SI,  
315 Section S-3, along with their 95% confidence intervals.

316

### 317 3.2 Human toxicological characterization factors for pesticides

318 Combining human intake fractions per mass of pesticide applied to different crops with  
319 toxicological effect information yields characterization factors shown in <Figure 2. Whereas  
320 intake fractions could be derived for all 875 pesticides, cancer and non-cancer effect data are  
321 only available for a subset of 177 pesticides (20%) and 395 pesticides (45%), respectively.  
322 Hence, characterization factors are provided in the SI for a total of 465 pesticides associated  
323 with each of the six considered crops representing 53% of all pesticides included in this study.

324

325 <Figure 2>

326

327 Characterization factors for cancer-related effects typically show a lower variability than  
328 factors for non-cancer effects, which is linked to the fewer dose-response data available for  
329 cancer; hence, we provide carcinogenicity-related characterization factors only for a limited  
330 number of pesticides. In contrast, characterization factors for cancer effects seem to be more  
331 evenly distributed over the variability range than factors for non-cancer effects, most visible  
332 for lettuce and least visible for tomato (white boxes in <Figure 2). This effect is linked to the  
333 influence of the variability of crop residue-related intake fractions (dominating overall human  
334 intake for all crops but potato) shown in <Figure 1, where 50% of the data around the mean  
335 value for lettuce spread over more than 2 orders of magnitude, while 50% of data around the  
336 mean for tomato only differ by a factor 4.5. In line with this, the variability of characterization  
337 factors combining cancer and non-cancer effects (grey boxes in <Figure 2) is influenced by  
338 the crop-specific variability of all contributing intake fractions (related to crop residues, air  
339 and soil fractions) and the variability of effect factors weighted by the number of contributing

340 data points (less for cancer, more for non-cancer effects). The highest variability of  
341 characterization factors is seen for lettuce with more than 9 orders of magnitude between  
342 lowest and highest factors of  $4.4 \times 10^{-9}$  DALY kg<sub>applied</sub><sup>-1</sup> for ethanol and  $9.3$  DALY kg<sub>applied</sub><sup>-1</sup>  
343 (attributable to the population-based cumulative risk of 3.4 non-cancer incidences kg<sub>applied</sub><sup>-1</sup>) for  
344 phenylmercuric acetate, respectively. Tomato shows the lowest variability in characterization  
345 factors of about 7 orders of magnitude ranging from  $5.3 \times 10^{-8}$  DALY kg<sub>applied</sub><sup>-1</sup> for florasulam  
346 and  $1.5$  DALY kg<sub>applied</sub><sup>-1</sup> (attributable to  $1.6 \times 10^{-3}$  cancer incidences and 3.9 non-cancer  
347 incidences kg<sub>applied</sub><sup>-1</sup>) for 2,4/2,6-toluene diisocyanate. Median values of characterization  
348 factors in aboveground crops across pesticides vary by less than a factor of 2 in descending  
349 order as lettuce > tomato > apple > paddy rice > wheat, whereas the median value for potato  
350 is 5 orders of magnitude lower. Characterization factors at midpoint level (cancer and non-  
351 cancer incidences kg<sub>applied</sub><sup>-1</sup>) and endpoint level (DALY kg<sub>applied</sub><sup>-1</sup> given separately for cancer and  
352 non-cancer effects as well as aggregated over both) are given for all pesticide-crop  
353 combinations in the SI, Section S-3, including their 95% confidence intervals.

354 In Fig, we demonstrate along a realistic example how we arrived at characterization  
355 factors given in <Figure 2 and given per pesticide in SI (Section S-3), and how to apply  
356 human intake fractions and characterization factors in the context of LCA. We used as  
357 example pesticides tebuconazole and pyraclostrobin, both currently authorized e.g. in the  
358 European Union (European Commission 2011), and registered e.g. in Germany for use  
359 against leaf rust (*Puccinia recondita*) on wheat (BVL 2015).

360

361 <Figure 3>

362

### 363 3.3 Uncertainty in characterization modeling of pesticides

364 Uncertainty expressed as 95% confidence interval (CI) ranges is shown in Figure 4 for  
365 harvest fractions of 5250 pesticide-crop combinations. Confidence intervals are generally  
366 smallest for potato (median ratio of 97.5%-ile and 2.5%-ile CI limits of a factor 20), followed  
367 by tomato and apple (median 95% CI limit ratios of a factor 120 and 140, respectively), and  
368 are largest for lettuce and wheat (median 95% CI limit ratios of a factor 570 and 2680,  
369 respectively). The high end uncertainty for wheat is partly attributable to the long assumed  
370 time between application and crop harvest for herbicides (see SI, Section S-1). The much  
371 lower harvest fraction uncertainty ranges for pesticides applied to potato compared with  
372 applications to other crops is related to lacking uncertainty data for residence times in soil  
373 and, hence, does not indicate higher quality of regression models for potato.

374 Accuracy is in general higher in the range of high intake fractions and for the upper 97.5<sup>th</sup>  
375 percentile, whereas uncertainty grows with decreasing intake fractions as well as for the 2.5<sup>th</sup>  
376 percentile lower uncertainty limit. Accounting for improved estimates of half-lives in crops  
377 from Fantke et al. (2014) compared to earlier correlations from e.g. Juraske et al. (2008) has  
378 led to substantial changes and improvement in the accuracy of estimated harvest fractions (see  
379 SI, Figure S1). The range of pesticide half-lives in crops is now much narrower than the  
380 earlier estimates leading to a significant reduction in the variability between harvest fractions.

381  
382 <Figure 4>

383

384 In all crops except potato, half-lives in/on crops along with time between pesticide  
385 application and crop harvest are the main contributor to crop residue dynamics. In case of  
386 potato the overall residence time in soil is the most influential factor that accounts for the  
387 various removal processes in the heterogeneous soil layer, before pesticides can enter the  
388 tuber via root uptake mechanisms (Juraske et al. 2011). Applying relatively large uncertainty

389 to the crop-specific residues regression models compared with a relatively low generic  
390 uncertainty to soil degradation as proxy for overall soil residence time (most important for  
391 potato) yields generally lower uncertainty ranges of harvest fractions for potato than for all  
392 other crops. Harvest fractions for all pesticide-crop combinations are given in the SI, Section  
393 S-3, along with their 95% confidence intervals.

394

395 Despite uncertainty related to harvest fractions, uncertainty in subsequent human intake  
396 fractions (not shown) is scaled for each crop by the uncertainty associated with food  
397 processing factors, which were applied for each crop assuming a specific food processing step  
398 (see SI, Section S-1), but which were available as specific factors only for very few of the  
399 considered pesticides. Uncertainty from food processing, however, contributes on average  
400 only with 5.8% to intake fraction uncertainty across crops.

401 The highest share of characterization factor uncertainty with an average contribution of  
402 70% is attributable to dose-response information, especially for extrapolated non-cancer  
403 effects. This is inherently limited by the availability of toxicity data for both risk assessment  
404 and LCA. Effective doses causing an effect in 50% of the exposed population have therefore  
405 mainly been extrapolated from toxicological studies with animals for which the specific  
406 health endpoints are mostly unknown, but derived from no-observed effect levels (NOEL).  
407 Using NOEL as starting point for estimating no-effect exposures leads to higher uncertainties  
408 (e.g. Landis & Chapman 2011) due to the large uncertainty around dose-response  
409 information. Since this type of effect information has been used in USEtox, we relied on the  
410 same data to ensure comparability across impact pathways and chemicals.

411

412 <Figure 5>

413

414 Figure 5 shows human health endpoint characterization factors for 465 pesticides with  
415 available effect information applied to 6 crops along with pesticide-specific uncertainty  
416 ranges that vary up to 9 orders of magnitude across pesticides applied to the same crop.  
417 Regarding the level of uncertainty and since uncertainty in the upper range of characterization  
418 factors is lower, Figure 5 is especially useful to provide an upper limit on the human health  
419 characterization factors and to identify with a food crop-related LCA study which pesticide(s)  
420 may provide a significant contribution compared to other life cycle impacts on human health  
421 associated with e.g. respiratory effects from exposure to fine particulate matter.

422

## 423 **4 Discussion**

### 424 4.1 Influences on intake fraction variability

425 Our results show that pesticide properties and crop characteristics are both strongly  
426 contributing to the variability of crop residues, fractions lost to air and soil, and subsequent  
427 human intake fractions of pesticides applied to agricultural food crops. We acknowledge that  
428 site characteristics, such as local soil and climate conditions during crop growth, and scenario  
429 characteristics, such as food processing and human consumption pattern might additionally  
430 contribute to the variability of our results, although to a lesser extent. The importance of crop  
431 characteristics, such as water content, growth, and leaf area index evolution, for crop residue  
432 dynamics is well in line with other studies demonstrating the strong influence of the choice of  
433 crop data on chemical distribution kinetics in crops (Trapp 2015) and on plant uptake  
434 dynamics from soil (Sun et al. 2014). Most importantly, the influence of all factors  
435 contributing to the variability of intake fractions from exposure to crop residues – the  
436 predominant component in the aggregated intake fractions from pesticide application to all  
437 considered crops except potato – is mostly associated with uncertainty of pesticide dissipation  
438 half-lives in crops. Uncertainty is additionally growing with increasing time between  
439 application and harvest. Accordingly, uncertainties around intake fraction values are also

440 increasing with longer time to harvest allowing different uncertain model input variables to  
441 develop a significant influence on model output. However, with increasing time to harvest,  
442 intake fractions are typically lower, which makes the larger uncertainty less relevant than the  
443 (comparatively) lower uncertainty in the main range of interest, i.e. intake fractions  $\geq 10^{-5}$   
444  $\text{kg}_{\text{intake}} \text{kg}_{\text{applied}}^{-1}$ . This effect is shown in Figure 4 for harvest fractions as main driver of the  
445 magnitude of intake fractions. Uncertainty around fractions lost to air and soil along with  
446 associated intake fractions for emissions to air and soil are likely being underestimated in our  
447 study, since generic values for fractions lost and generic uncertainty for intake fractions have  
448 been used lacking more detailed data. This will not influence the general trends of our results,  
449 since these indirect contributions are low for most crops. Incorporating more realistic  
450 uncertainty values would nevertheless increase the variability of aggregated intake fractions  
451 for potato (with increasing time to harvest), where fractions lost to air and soil are dominating  
452 aggregated intake fractions for most pesticides (see <Figure 1).

453 Overall, we reduced intake fraction variability between 1 and 9 orders of magnitude for  
454 pesticides applied to potato and apple, respectively, compared with estimates reported by  
455 Fantke et al. (2011b) for 121 pesticides (accounting for only 14% of the number of pesticides  
456 included in the present study). This reduction of variability in intake fractions is mainly  
457 attributable to improved dissipation data in crops. Overall, the uncertainty around intake  
458 fractions that is mainly driven by uncertainty in crop residues (Figure 4), is generally limited  
459 compared to uncertainty of characterization factors (Figure 5) that is strongly increased and  
460 dominated by uncertainty of (mainly non-cancer) dose-response information.

461

## 462 4.2 Accounting for realistic pesticide application

463 According to current national and international pesticide legislation we acknowledge that  
464 not all pesticides are allowed for use on all crops. In fact, there are many pesticides that are  
465 registered in some countries but banned for use in agriculture in other countries. Atrazine for

466 example is a herbicide with endocrine disrupting properties (Hayes et al. 2011) that is one of  
467 the most widely used agricultural pesticides registered for use in the U.S. primarily on maize  
468 and sugarcane (US-EPA 2006), whereas its authorization in EU member states is withdrawn  
469 since 2004 (European Commission 2004). Given the heterogeneity in pesticide regulation  
470 between countries, we emphasize the need to verify the authorization status of all pesticides  
471 when applying our data. This is especially relevant when using our results for purposes of  
472 pesticide substitution and similar comparative assessments, where comparing two pesticides  
473 of which only one is registered for use on a specific crop could be misleading, if the  
474 unregistered pesticide shows lower intake fractions or characterization factors. Furthermore,  
475 we acknowledge that application times (days before crop harvest) are pesticide-crop  
476 combination-specific as a function of distribution dynamics in each crop-specific  
477 environment. In this study, we used application times before harvest that are averaged  
478 separately for herbicides and other pesticides to represent “typical” application times as best  
479 estimates for LCA that can also be applied to pesticides currently not included in our  
480 assessment. However, the uncertainty related to pesticide-specific application times before  
481 harvest for each crop (and country) is not included in our study and varies strongly between  
482 pesticides.

483

#### 484 4.3 Data limitations and applicability in LCA studies

485 Our study shows several limitations. Experimental data for the most sensitive input  
486 variable, that is dissipation half-lives in crops, are only available for 311 out of 875 pesticides  
487 (35%). To account for the related uncertainty, we considered the higher uncertainty of the  
488 regression model to estimate crop dissipation to all pesticides, where experimental data were  
489 missing. The new correlations on half-lives have however substantially improved the  
490 accuracy of estimating related crop residues. Residence times in soil are the output of a  
491 generic system of mass balance equations accounting for the environmental fate of pesticides

492 solved under the assumption of steady-state conditions with continuous emission input  
493 (Rosenbaum et al. 2008). Soil residence times are thereby influenced by a wide range of  
494 environmental characteristics including crop-related aspects and pesticide properties, of which  
495 degradation in soil plays an important role (Dubus et al. 2003). Lacking uncertainty data for  
496 soil residence times we applied uncertainty associated with soil degradation as proxy. We  
497 thereby acknowledge that we might underestimate the overall uncertainty specifically for  
498 potato, where soil residence time is driving the magnitude of crop residues and subsequent  
499 human intake. Whenever possible, soil degradation data are based on measurements  
500 aggregated in Footprint (2014) and only complemented by estimated data from the US-EPA  
501 (2012) when no experimental data were available. Differences in soil degradation data sources  
502 lead to differences in associated uncertainty, which were not considered in our study. We  
503 thereby acknowledge that data estimated from pesticide physicochemical properties may  
504 exceed measured field soil degradation half-lives by up to more than two orders of magnitude  
505 as can be seen when comparing e.g. tralomethrin or 8-quinolinol. These differences are  
506 becoming relevant in regulatory contexts, but are not as important in pure comparative  
507 assessments like LCA, where we are not bound to absolute thresholds for e.g. persistence in  
508 soil. Another limitation in our study is the use of generic fractions lost to air during and after  
509 pesticide application and associated uncertainty estimates. Further research is required to  
510 estimate these fractions more accurately in the context of LCA (Rosenbaum et al. 2015).  
511 However, for the majority of pesticide-crop combinations, this will not substantially influence  
512 related intake, since fractions lost to air are mostly not dominating intake fractions. Finally,  
513 we apply pesticide-specific data and averaged uncertainty factors for human health dose-  
514 response slope factors that are extrapolated from distinct exposed animal populations,  
515 exposure durations and routes and that are aggregated over a wide range of health endpoints  
516 (particularly for non-cancer effects). The difficulty to extrapolate effect factors from such  
517 inherently heterogeneous data leads to a significant contribution of dose-response information

518 to overall uncertainty in characterization factors, which has already been acknowledged in  
519 previous studies (Huijbregts et al. 2005, Rosenbaum et al. 2008). While the quality of data  
520 underlying human toxicological effect factors needs to be improved accordingly, the  
521 variability of characterization factors across all pesticide-crop combinations spanning more  
522 than 9 orders of magnitude shows that relative to variability, overall uncertainty is not higher  
523 for toxicity-related impacts than for other impact categories.

524 Despite abovementioned limitations, our study contributes to significantly advancing the  
525 assessment of human health-related impacts from exposure to pesticides in LCA by including  
526 the predominant exposure pathway (i.e. intake of crop residues) and by improving the quality  
527 of the most uncertain input data for estimating pesticides in crop harvest (i.e. dissipation data  
528 in crops; see SI, Figure S1). Since our characterization factors are based on mass applied,  
529 LCA practitioners can and need to directly combine our results with pesticide application data  
530 as demonstrated in Fig. Whenever such data are not at hand, recommended application  
531 dosages as provided in The Pesticide Manual (Tomlin 2012) or on pesticide product labels  
532 can be applied as proxy.

533

## 534 **5 Conclusions**

535 We provide an operational framework for including human toxicity-related effects from  
536 exposure to pesticides via consumption of treated food crops into LCIA and provide for the  
537 first time uncertainty ranges around harvest fractions, intake fractions and characterization  
538 factors that are specific for each pesticide and crop. Results demonstrate that impacts of  
539 pesticides in terms of human toxicity are largely underestimated when ignoring exposure to  
540 residues in harvested and subsequently consumed crop components. For ready use in LCA  
541 studies, we present pesticide-crop combination-specific characterization factors normalized to  
542 pesticide mass applied and provide default data for application times and loss due to post-  
543 harvest food processing. Uncertainty needs to be considered when comparing results between

544 different pesticides or with other chemicals to properly interpret ranking and maximum  
545 contributions, as it has been shown that pesticides with lower median characterization factors  
546 can be as important as pesticides with higher median characterization factors when  
547 considering the pesticide-specific uncertainty ranges. Improving dissipation half-lives in crops  
548 derived from experimental data has been essential in limiting uncertainties on harvest  
549 fractions. Further studies are required to better estimate fractions lost to air and soil during  
550 and after pesticide application and to reduce the inherent uncertainty in non-cancer toxicity  
551 effect information. When using our data, we emphasize the need to consult current pesticide  
552 regulation to allow for realistic scenarios where each pesticide is registered for use on certain  
553 crops only, which varies between countries.

554

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559

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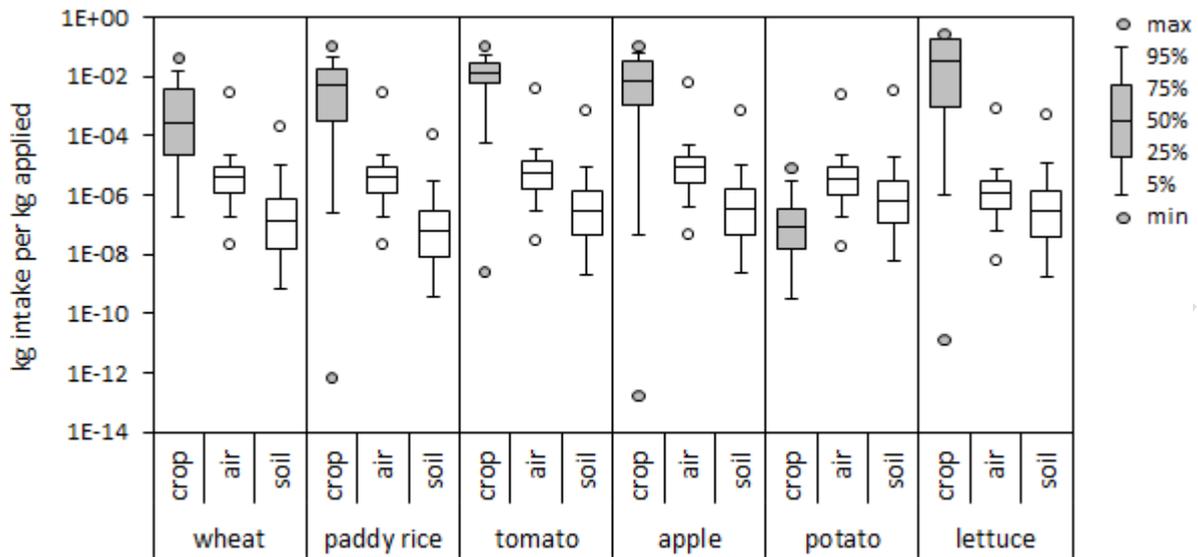
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714 **Figures**

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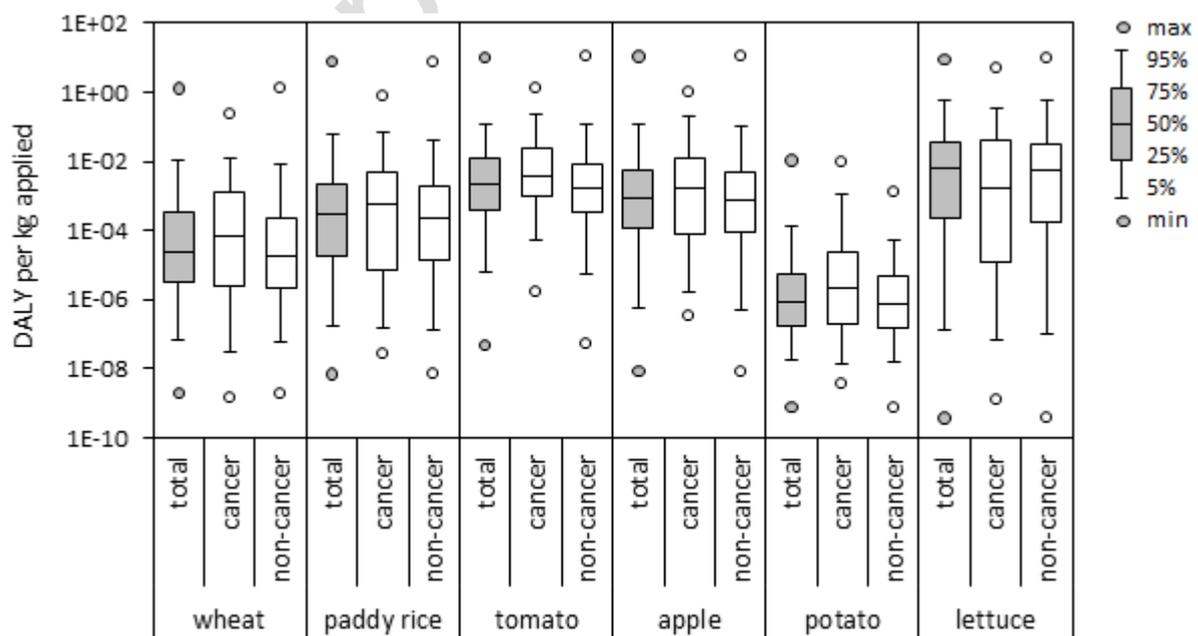
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717 Figure 1 Variability of human intake fractions expressed as kg intake per kg applied pesticide  
 718 grouped for each crop according to fractions reaching the crop as residues (grey boxes) and  
 719 fractions reaching air and soil as emissions during and after application (white boxes).

720 Minimum values below  $10^{-14}$  are not displayed.

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724 Figure 2 Variability of human toxicity endpoint characterization factors expressed as  
 725 disability-adjusted life years (DALY) per kg applied pesticide grouped for each crop into total  
 726 aggregated effects (grey boxes), and cancer and non-cancer effects (white boxes).

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<b>(a) human intake = mass applied per functional unit × total intake fraction</b>	
human intake (tebuconazole) =	$0.25 \text{ kg}_{\text{Applied}}/\text{ha} \times 7.1 \times 10^{-4} \text{ kg}_{\text{Intake}}/\text{kg}_{\text{Applied}} = 1.8 \times 10^{-4} \text{ kg}_{\text{Intake}}/\text{ha}$
human intake (pyraclostrobin) =	$0.125 \text{ kg}_{\text{Applied}}/\text{ha} \times 2.0 \times 10^{-5} \text{ kg}_{\text{Intake}}/\text{kg}_{\text{Applied}} = 2.2 \times 10^{-6} \text{ kg}_{\text{Intake}}/\text{ha}$
<b>(b) characterization factor* = total ingestion intake fraction × non-cancer dose-response for ingestion × non-cancer severity factor</b>	
CF (tebuconazole) =	$7.1 \times 10^{-4} \text{ kg}_{\text{Ingested}}/\text{kg}_{\text{Applied}} \times 0.015 \text{ incidences}_{\text{non-cancer}}/\text{kg}_{\text{Ingested}} \times 2.7 \text{ DALY}/\text{incidence}_{\text{non-cancer}} = 2.9 \times 10^{-5} \text{ DALY}/\text{kg}_{\text{Applied}}$
CF (pyraclostrobin) =	$2.0 \times 10^{-5} \text{ kg}_{\text{Ingested}}/\text{kg}_{\text{Applied}} \times 0.042 \text{ incidences}_{\text{non-cancer}}/\text{kg}_{\text{Ingested}} \times 2.7 \text{ DALY}/\text{incidence}_{\text{non-cancer}} = 2.2 \times 10^{-6} \text{ DALY}/\text{kg}_{\text{Applied}}$
<b>(c) health impact = mass applied per functional unit × characterization factor</b>	
health impact (tebuconazole) =	$0.25 \text{ kg}_{\text{Applied}}/\text{ha} \times 2.9 \times 10^{-5} \text{ DALY}/\text{kg}_{\text{Applied}} = 7.3 \times 10^{-6} \text{ DALY}/\text{ha}$
health impact (pyraclostrobin) =	$0.125 \text{ kg}_{\text{Applied}}/\text{ha} \times 2.2 \times 10^{-6} \text{ DALY}/\text{kg}_{\text{Applied}} = 2.8 \times 10^{-7} \text{ DALY}/\text{ha}$

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\*In this example, we calculated the characterization factors exclusively from ingestion intake fractions (inhalation intake fractions contribute to overall intake fraction only with 0.02% for tebuconazole and 0.32% for pyraclostrobin) and non-cancer dose-response (cancer effect data were not available). Whenever inhalation intake fractions and/or cancer effects become relevant, they need to be included in the characterization factor calculations.

Figure 3 Calculation steps for deriving human intake per treated hectare (a), endpoint

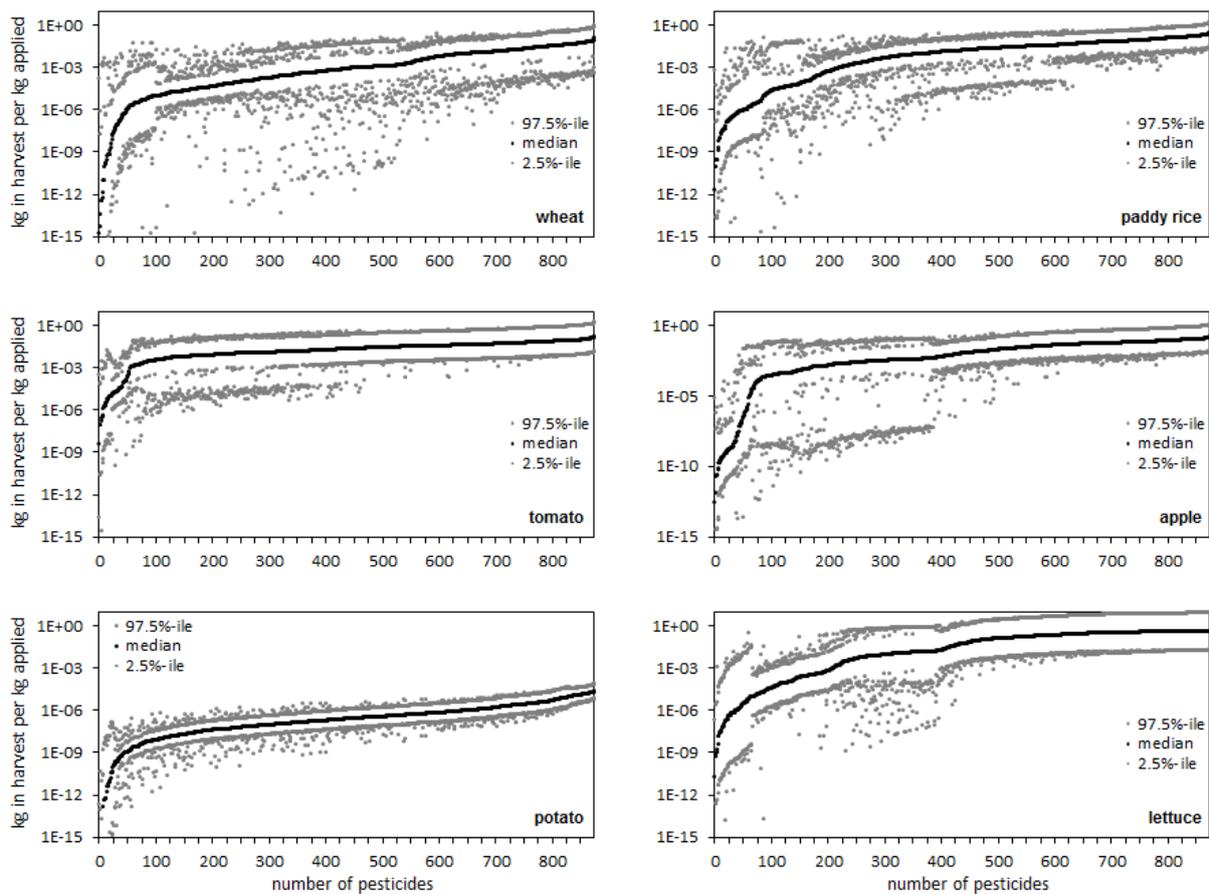
characterization factors (b), and health impacts per treated hectare (c) for two example

fungicides applied to wheat. Tebuconazole is typically applied as 250 g/l emulsion at 1 l/ha

(Bayer 2014) and pyraclostrobin is typically applied as 250 g/l emulsion at 0.5 l/ha (BASF

2012). Intake fractions, dose-response factors and characterization factors are given in SI

(Section S-3).

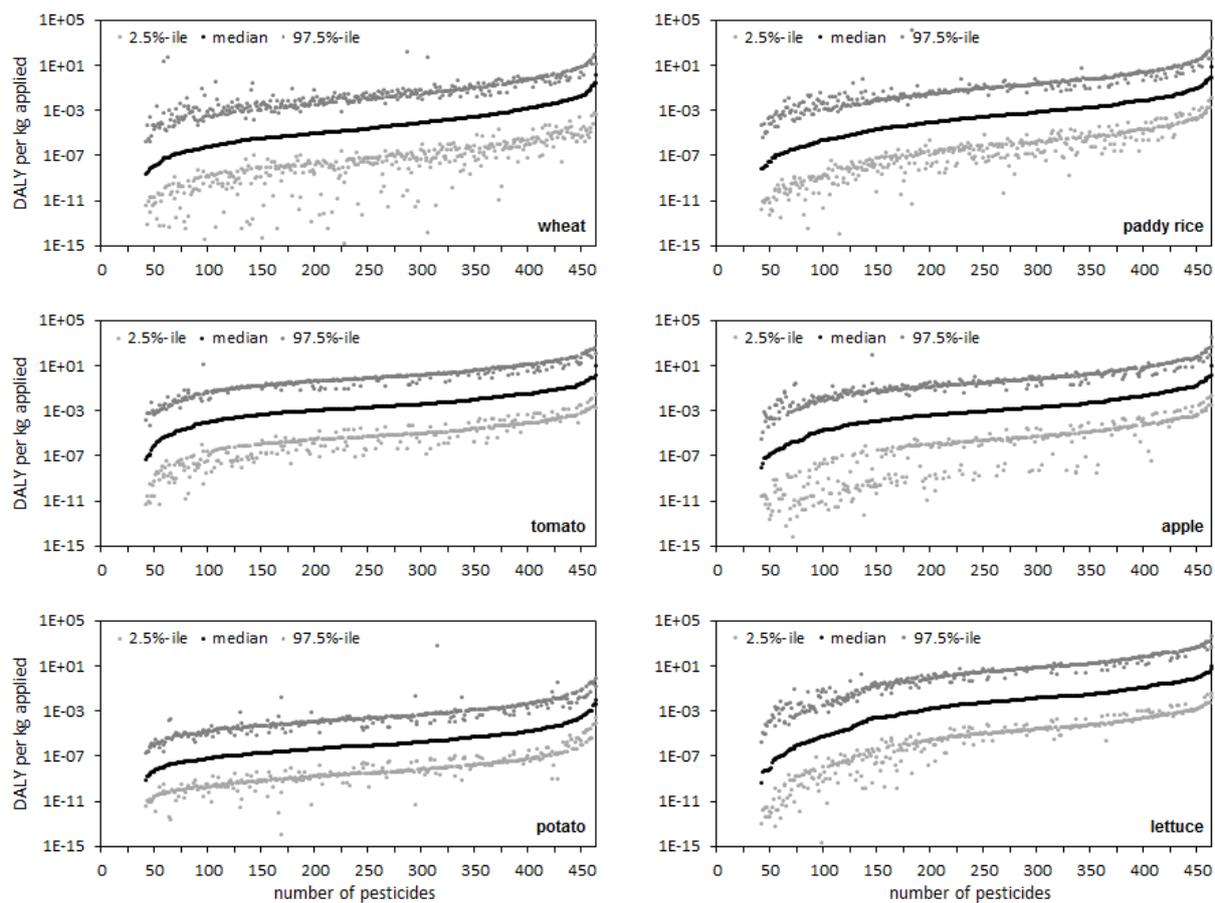


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745 Figure 4 Uncertainty of harvest fractions for 875 pesticides and 6 crops expressed as 95%  
 746 confidence interval ranges of pesticide mass in crop harvest per kg applied pesticide.

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750 Figure 5 Uncertainty of human toxicological characterization factors at endpoint level for the  
 751 reduced set of 465 pesticides with available toxicity effect information and 6 crops expressed  
 752 as 95% confidence interval ranges of disability-adjusted life years (DALY) per kg applied  
 753 pesticide.