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Review

Quick Roadmap for Exposure Assessment of Contaminants in Food

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Abstract: The presence of chemical contaminants in food is often unavoidable and associated with many adverse health effects. Exposure assessment is the essential element of an overall risk assessment process. While the specific purpose of the exposure assessment process can vary, the main goal is to provide a foundation for health-protective decisions. In recent years, there have been significant advances in exposure assessment methodologies and procedures, subsequently contributing to an increased complexity of the process. This paper aims to provide a generalized, simplified, and practical road map for exposure assessment, pointing to the pros and cons of different methods and challenges that occur while performing this type of study.

Keywords: exposure assessment; roadmap; pros and cons; data sources; approaches

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1. Introduction

An exposure assessment is defined as the qualitative and/or quantitative evaluation of the likely intake of biological, chemical, or physical agents via food, as well as exposure from other relevant sources [1], and it is the essential element of an overall risk assessment process. Risk assessment involves a four-step process encompassing: (i) hazard identification, (ii) hazard characterization, (iii) exposure assessment, and (iv) risk characterization [2]. This process serves as a foundation for informed decision-making within the risk-based management process. Performing a risk assessment results in a characterization of the relationships between exposure(s) to an agent and the likelihood that adverse health effects will occur in members of exposed populations [3]. While the information for the initial two steps is gathered by many toxicological, clinical, epidemiological, and surveillance studies and can be obtained from the scientific literature, from the food industry and government agencies, an exposure assessment is considered as a practical tool consisting of data collection and calculation steps, which, if performed incorrectly can lead to the misinterpretation of the risk.

Exposure assessments are mainly performed for different chemical hazards present in human diets, with similar methods being appropriate for contaminants, pesticide residues, veterinary drug residues, nutrients, food additives, processing aids, and other chemicals in foods [4]. Dietary exposure can be assessed for a chemical before it has been approved for use in food (pre-regulation stage), after it has been approved and has potentially been in the food supply for years (post-regulation stage), or when present naturally in foods or as a result of contamination [5]. There is a general distinction between chemicals intentionally introduced to the food and nonintentional present chemicals (contaminants), which results in some methodological differences. For intentionally added chemicals, there is much greater potential for control on conditions of use and consequently their presence in food. They are intensively assessed in the pre-regulation stage with exposure estimates intended to be highly protected for the consumer's health (conservative) [5].

The presence of hazardous chemical contaminants or undesirable substances in food is often unavoidable as these substances may occur ubiquitously or are of natural origin;

therefore, human exposure to such substances is certain and associated with adverse health effects [6]. The assessment of exposure (risk) to chemical contaminants holds particular significance due to the lack of control over the presence and potential for causing severe consequences and long-term effects. Exposure assessment for these chemicals is usually aimed at estimating true exposure, using a valid and trustworthy methodology. Some of the intentionally added chemicals, such as pesticides and veterinary drugs, can also be considered as contaminants due to their widespread illegal use or misuse, which commonly lead to exceeding the safe tolerance levels [7–9]. In parallel, from a food safety point of view, the presence of different contaminants intentionally added (whilst not needed) strives towards food fraud and/or food defense, resulting in intentional food crime [10].

Over the past two decades, numerous methods and approaches for assessing the exposure of food chemicals have been developed. Corresponding tools and databases have also emerged, offering a spectrum of options, from quick worst-case estimations to more sophisticated methods designed to evaluate actual exposure [5,11]. However, in certain cases, some of the tools, databases, and software are not available to independent researchers (not related to specific institutions or governmental bodies) or can only provide summary results for external users. Some of the methods, particularly the ones developed by the European Food Safety Authority (EFSA), are open-access tools developed to estimate dietary exposure to food-borne chemical hazards and intended for use by EFSA experts, industry applicants of regulatory product dossiers, researchers, or any stakeholder with an interest in estimating dietary exposure [12]. Nevertheless, most of these methods are based on European food consumption data and are not fully applicable to countries outside of the European region.

While detailed publications on the methods and principles for the risk assessment of chemicals in food have been published [5,13,14], this paper aims to provide a generalized, simplified, and practical road map for a researcher deciding to estimate the exposure of food contaminants, pointing to pros and cons of different methods and challenges that occur while performing this type of study.

2. Road Map to Exposure Assessment

In general, dietary exposure assessments combine two types of data—food consumption data and data on the concentration of chemicals in food making. These subsets of data are central aspects in the assessment of exposure as the accuracy of any exposure assessment will ultimately depend on their quality. The general equation [5] for any type of dietary exposure can be expressed as follows:

$$\text{Dietary exposure} = \Sigma\,(\text{Concentration of chemical in food} \times \text{Food consumption})/\text{Body weight (kg)} \quad (1)$$

The resulting dietary exposure estimate is then compared with the relevant toxicological reference value for the food chemical of concern in the risk characterization step, the fourth and final step of the risk assessment [15]. The roadmap to exposure assessment is depicted in Figure 1 and examples of databases, software, and tools used for dietary exposure assessment are presented in Table 1.

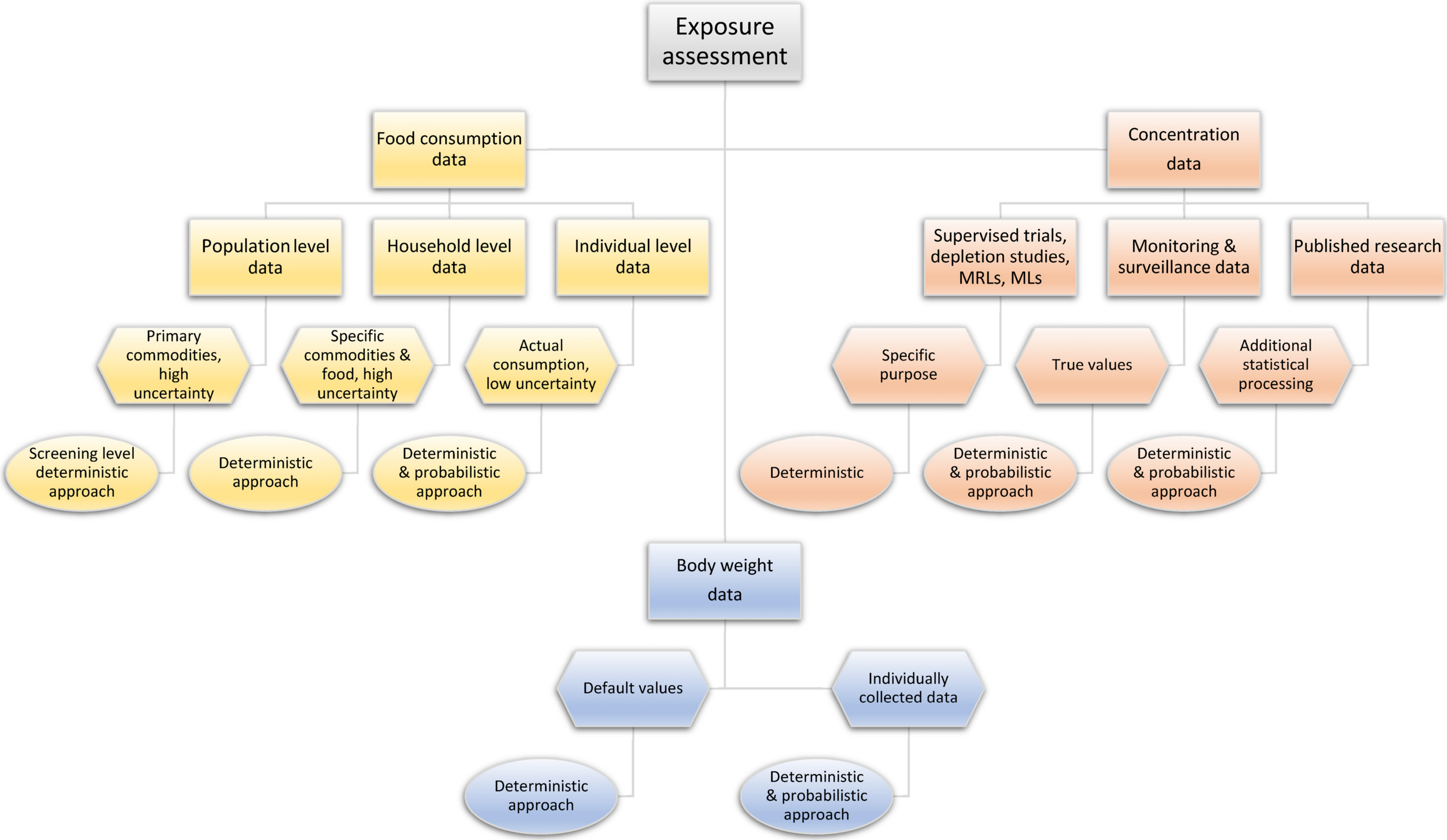

Figure 1. Quick roadmap to exposure assessment.

Table 1. Examples of databases, software, and tools used for dietary exposure assessment.

Database	Type/Use	Location	Open Access
(FAO) Food balance sheets 2010–2021	Population-based food consumption data	https://www.fao.org/faostat/en/#data/FBS (accessed on 23 February 2024)	Yes
(EFSA) Comprehensive Food Consumption Database	Individual-level food consumption data	https://www.efsa.europa.eu/en/microstrategy/food-consumption-survey (accessed on 23 February 2024)	For summary statistics only
(EU) Pesticide residue(s) and maximum residue levels	Maximum residue limits data	https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/start/screen/mrls/searchpr (accessed on 23 February 2024)	Yes
(WHO) GEMS database	Concentrations of chemicals in food	https://extranet.who.int/gemsfood/?DisplayFormat=1 (accessed on 23 February 2024)	Yes
Software			
Minitab (21.1.0)	Statistical software/general use/Monte Carlo simulation	https://www.minitab.com/en-us/ (accessed on 23 February 2024)	Commercial
@risk (8.0)	Standalone software/Monte Carlo simulation	https://lumivero.com/software-features/monte-carlo-simulation/ (accessed on 23 February 2024)	Commercial
R (4.3.3)	Software environment	https://www.r-project.org/ (accessed on 23 February 2024)	Yes
Tool			
(EFSA) PRIMo (3.1)	Pesticide residue chronic/acute intake model	https://www.efsa.europa.eu/en/applications/pesticides/tools (accessed on 23 February 2024)	Yes
(EFSA) FAIM (2.1)	Chronic exposure to food additives model	https://www.efsa.europa.eu/en/applications/food-improvement-agents/tools (accessed on 23 February 2024)	Registration needed
(RIVM and EFSA) MRCA (10.0.9.)	Various models	https://mcra.rivm.nl/mcra (accessed on 23 February 2024)	Registration needed

3. Food Consumption Data

As one of the main parameters in exposure assessments, food consumption data reflect what either individuals or groups consume in terms of solid foods, beverages, including drinking water, and supplements [11]. Food consumption data can be collected at population, household, and individual levels.

3.1. Population-Level Data

Population-based methods provide data on the annual amount of food available to the whole population for consumption as raw commodities and for some food groups as semi-processed or fully processed foods [15]. An example of population-based consumption data is Food Balance Sheets (FBSs) (Table 1). FBSs represent data derived from the Food and Agriculture Organization (FAO)'s statistical database currently containing data on national food accounts, supply/utilization accounts, food disappearance data, or food consumption level estimates from over 240 countries [16]. Data in FBSs include primary commodities such as wheat, rice, fruit, vegetables, and some processed commodities such as vegetable oils and butter, presented as amounts for the entire population or per capita per year. However, a drawback of these data is their failure to accurately reflect the actual consumption of specific foods. Since these databases predominantly rely on raw commodities, conducting exposure assessment calculations necessitates the inclusion of processing factors. Exposure assessments carried out with this type of consumption data are associated with a high level of uncertainty and are typically employed as preliminary screening assessments for average population exposure, utilizing a basic deterministic approach.

3.2. Household-Level Data

Food consumption data at the household level are obtained through a variety of household consumption survey methods (household income and expenditure surveys, income surveys, budget surveys, etc.). As these surveys are usually performed by national agencies, variations occur both across countries and over time as statistical offices alter survey designs [17]. Variations include the method of data capture, the level of the respondent's status (individual versus household), the reference period for which consumption is reported, and the degree of commodity detail [17], making international comparison difficult. While these kinds of food consumption data are of higher quality than FBS data, there are still several limitations, particularly the difficulty of estimating the intrahousehold allocation of foods and therefore of quantifying the actual food intake of individual household members and the lack of information on the variability of consumption over time, making it difficult to estimate the distribution of usual consumption [18]. Like FBS data, household-level consumption data are associated with uncertainty and are more suitable for use with a deterministic approach.

3.3. Individual-Level Data

Individual-level data will generally provide the most precise estimates of food consumption as they more closely reflect actual consumption and provide a distribution of consumption data over various well-defined groups of individuals [14].

The most common methods used to collect consumption data are through food records (food diary), 24-hour dietary recall (24hR), and the Food Frequency Questionnaire (FFQ). These surveys are essential for understanding the dietary habits, nutritional intake, and health patterns of the population. Depending on the method, data collection is performed by self-reporting or by face-to-face and phone interviews with the help of a trained interviewer. In recent years, a variety of internet-based (self-administered) methods, mostly based on 24hRs and FFQs, have been created and used [19,20]. This kind of food consumption data is generally of the highest quality and can be used to create any exposure scenario with both deterministic (as point estimate values can be easily calculated from distributional data) and probabilistic approaches. Consumption data obtained by different collection methods may be combined or used in conjunction to improve accuracy, facilitate the validity of the dietary data, and to ease modeling different consumption and exposure scenarios [5,21–24].

Food record is a weighed record method where taught subjects record all foods and beverages immediately before eating and weigh and describe any leftovers [25]. Next to the information on the amount and type of food consumed, information on the source of food and preparation practices is collected. Usually, 3–4 days of intake (up to 7 days) are recorded as participant burden generally causes a decline in the quality of information recorded if more days are included [26]. This method provides detailed intake with no recall bias but is expensive and time-consuming and requires a literate and motivated population [19,26]. Previous reports have described reactivity as an issue with record keeping, which is changing usual dietary patterns for ease of recording or due to a social desirability to report foods perceived as "healthy" [26]. As information is collected on consecutive days, they cannot be considered as independent days and, in general, allow only an assessment of acute exposure, but statistical techniques can be used to estimate usual food intake [14,25,27].

The 24hHR method is a retrospective method that refers to the current diet and is the most used. In the interview, the subject is asked by a trained interviewer to recall and describe the kinds and amounts of all foods and beverages consumed during the immediate past, mostly a 24- or 48-hour period [14]. Twenty-four hours provide an accurate mean intake, but it also presents a limitation as it represents only a single day, which could lead to an extensive misclassification of individual intakes [28]. The recall has the potential to capture a wide variety of foods [26]. It is often structured with specific probes to help the respondent to remember all foods consumed throughout the day, and sometimes, at the end of the interview, there is a checklist of foods or snacks that might have been easily forgotten [25]. Utilizing a single day of consumption for the 24hR method is generally deemed acceptable for estimating acute exposure. However, incorporating non-consecutive days into the assessment allows for the consideration of day-to-day variations, enhancing the suitability of the collected data for evaluating chronic exposure [25].

The FFQ is a retrospective method that consists of a questionnaire containing a list of foods, for which subjects are asked to estimate the habitual frequency of consumption over a relatively long period (e.g., 6 months or 1 year) [19,25]. FFQs are designed to capture habitual food intake, especially for foods that vary greatly from day to day. FFQs may be qualitative, semi-quantitative, or quantitative. While comprehensive FFQs are designed to estimate a large number of nutrients, generally including between 50 and 150 food items, brief FFQs may focus on one or several specific chemicals [14]. It has also been shown that increasing the number of items can lead to overestimation of intake [29]. The use of FFQ could lead to errors in intake calculation as the FFQ is designed to capture usual intake and to obtain the relative distribution of intake across tested population groups [19,28]. While it is suitable for assessing long-term intake, FFQs can be subject to certain personal biases, such as overestimation of the frequency of consumption of infrequently consumed foods and underestimation of the frequency of consumption of foods that the respondent perceives as unhealthy [5,30].

3.4. General Considerations for Food Consumption Data Collection and Use

Some general concerns must be considered when collecting consumption data, mainly on an individual-level basis. The assessment of portion size stands out as one major source of error in measuring food consumption within dietary epidemiological surveys [31]. Weighing before and after eating is of course the most accurate method for measuring food intake, but this approach is not applicable for retrospective methods. For retrospective methods, several measurement aids can be used while estimating food intake, which can help to capture accurate diet intake. Such aids, frequently referred to as portion size measurement aids, including photographs, food models, household measures, rulers, reference objects, portion size suggestions, etc., have been used separately or in combination in dietary data collection [20,32–35]. Nevertheless, it is unavoidable that inaccuracies in portion size assessment will persist [25]. Foods can be consumed in their original form or as ingredients in composite (mixed) dishes. In such instances, standardized food preparation recipes become essential to break down the components into the main ingredients of interest for exposure assessment. The proportion of each ingredient (as a conversion factor) from the recipe is applied to the total amount of the mixed food consumed, which is then added to the total consumption of that ingredient from all sources for each person in the survey [5]. The demographic profile of the sample population used for the collection of food intake data should as closely as possible be in line with the national statistics for the general population, while also considering different demographic characteristics of the population. In national-based studies, a sample is selected from sampling frames consisting of a list of sampling units (in most cases, a population register) [25]. In cases when such a register is not available for public access, a convenient sampling method such as "quota sampling method" is a method fit for this purpose. This is a commonly used method in consumer research, where the choice of units for inclusion in the sample is aimed at representing certain structural aspects of the population [25]. In some cases, convenience sampling is also used as it provides ease of access to interviewees, such as in the form of an online survey [36]. Sample size is another crucial issue when collecting food consumption data. There are several strategies for determining the sample size, including using a census for small populations, imitating a sample size of similar studies, using published tables, and applying formulas to calculate a sample size [37]. Sex and age stratification should also be considered when collecting food consumption data and, later, for the exposure assessment process [25]. Additionally, it is advisable to distribute the collection of food intake data across all four seasons to capture the inter-seasonal variability in consumption patterns.

In addition, body weight is another demographic parameter collected during these types of surveys. It enables an understating of the sample and the potential dietary concern, such as body mass index, classifying the respondents into different categories such as underweight, healthy weight, or overweight [38]. When such data is not available, national medical and statistical bodies can be sources of this information, and in most cases, this information can be easily obtained. In rare cases, the default body weight of 70 kg for the whole population, estimated by the EFSA, or of 60 kg (55 kg for the Asian population) estimated by the World Health Organization (WHO) can be used [5].

Many countries conduct national dietary surveys to collect food consumption data at the individual level. International organizations, such as the WHO and the FAO, often encourage and support countries in conducting these surveys to ensure a comprehensive understanding of global dietary patterns and nutritional trends. The Comprehensive Food Consumption Database (Table 1) is a source of information on food consumption across the European Union. The use of food consumption data from the Comprehensive Database at the individual level is restricted to the EFSA, but summary statistics are made available to the public on the EFSA website [39]. However, the use of summary statistics from the Comprehensive Database is intended to produce conservative estimates of exposure and is more suitable for use with a deterministic approach.

4. Concentration Data

Various types and origins of concentration data can be chosen based on the specific objectives of the dietary exposure assessment. Many of the intentionally added chemicals (food additives, nutrients, novel foods) are extensively assessed in the pre-regulation or post-regulation stage with data on concentrations of the chemicals in food generally available from or estimated by the manufacturer and food processors or from supervised trials and depletion studies (in case of pesticides and veterinary drugs) [5]. On the other hand, the dietary intake of contaminants (organic pollutants, natural toxins and plant toxicants, metals and metalloids, reaction products from thermal food processing or food contact materials) requires analytical information on their distribution in foods. In pre-regulation assessments, proposed maximum levels (MLs) or maximum residue limits (MRLs) are commonly used for intentionally added chemicals [5]. This approach is also used for contaminants for evaluation and revaluation of MLs as those values have an impact on the future exposure of the population to the chemical over time [5,13]. Otherwise, this approach is not often used as these values do not accurately mirror the real levels present in foods.

For an exposure assessment of contaminants, concentration data obtained from the analysis of foods (monitoring and surveillance data), if available, are the best choice. In the raw form (results for each sample presented), these kinds of data are of the highest value and can be used by both deterministic and probabilistic approaches.

Before collecting these kinds of concentration data, some important considerations must be taken into account. All foods that are vehicles for certain contaminants must be considered for sampling. Food can be sampled from any point of the production chain but is preferable to be sampled as close to the point of consumption as possible, as the concentration of the chemicals in the consumed food is one of the central aspects in the assessment of exposure [11]. Concentration data should be obtained using methods fit for purpose and validated in line with appropriate standards. As a result of the technical advances in the field of analytics, there are a variety of methods that can be used for contaminant detection, most of which are based on UV−visible spectroscopy and other colorimetric techniques, immunoassays and lateral flow assays, chromatography, surface-enhanced Raman spectroscopy, and electrochemical field-effect transistors [40]. Nonetheless, not all of the current methods can produce data that are fit for purpose for exposure assessment. Analytical methods are generally classified as screening and official (confirming) methods [41]. While screening methods are typically considered less reliable in providing accurate information, in some cases, they can be used for exposure assessment. For example, ELISA, a screening method for determining aflatoxins in food, can generate fit-for-purpose data for the exposure assessment [15]. Ultimately, the choice of method will depend on the contaminant of interest and the availability of the best possible data. Sampling is another important consideration. There are two different sampling strategies: targeted and representative. Targeted data are collected for enforcement purposes in response to specific problems and should be used with caution in dietary exposure assessments [13], while representative sampling aims to obtain a representative picture of chemical levels present in food without a priori knowledge of what levels can be found [14].

In some cases, data for contaminants in food from the national and regional monitoring and surveillance programs are available in publicly available databases in both raw forms and summarized reports. Global Environment Monitoring System (GEMS)/Food Contamination database (Table 1) provides access to over 8 million analytical results of many contaminants in raw and some processed foods. Nevertheless, they are grouped per global region and are suitable for international- and global-level assessments.

Additional sources of concentration data are from published research papers. They can be useful tools when trying to assess exposure to certain contaminants in a particular country and can generally be used in a deterministic approach as they are in most cases presented as mean, standard deviation of mean, and minimum and maximum values. Nonetheless, in many cases, especially as part of independent scientific research, these papers have drawbacks in terms of the number of analyzed products and samples, geographical and seasonal distribution of samples, and the use of analytical methods. Combining and using data from several studies to obtain a representative sample is an additional challenge.

5. Approaches and General Considerations to Exposure Assessment

5.1. Types of Exposure Assessments

Regardless of type and approach, exposure assessments should cover the general population, and, if possible, critical groups that are vulnerable or are expected to have exposures that are significantly different from those of the general population, such as infants, children, pregnant women, or the elderly [13]. Considering the length of intake, dietary exposure assessments can be performed for acute and chronic exposure. Acute exposure is estimated for a period of up to 24 h, while chronic (long-term) exposure covers the average daily exposure over several years or an entire lifetime [42]. When the presence of a chemical substance in food can pose acute toxicity risks from the consumption of a single meal or through a single day's consumption, acute exposure is estimated [15]. In most cases, this type of assessment is performed by food safety agencies for pesticide and veterinary drug residues. While most of the contaminants can also pose the risk of acute poisoning, an acute exposure assessment for them is, in general, performed less often because, firstly, for some, there is no established acute reference dose [5]; and secondly, in today's food safety culture, they rarely occur in doses high enough to cause acute adverse effects. Assessment of chronic exposure is perhaps of greater importance for food contaminants, as prolonged exposure to small amounts can cause a variety of serious and life-threatening conditions. Among others, toxic effects of chronic exposure to contaminants in food include damage to various organ systems, DNA damage, teratogenicity, carcinogenicity, reproductive and developmental problems, damage to the immune system, and interference with hormones.

Exposure assessments can be conducted for a specific chemical(s) originating from either a singular food product or multiple food products. Aggregate exposure takes into consideration additional non-dietary sources of contaminants, while cumulative exposure assesses the combined exposure from multiple chemicals targeting the same endpoint organs. Cumulative exposure to multiple chemicals poses a complex challenge to researchers as there is a myriad of anthropogenic and natural chemicals involved, and the amount of data needed to describe the toxicological profiles and exposure patterns is extensive [43]. And while a certain level of progress was achieved in recent years for some chemicals such as pesticides [44,45], there are still countless chemical mixtures that have to be evaluated.

An example of these mixtures include micro/nanoplastics, emergent pollutants that have become a significant environmental concern, especially when combined with other contaminants [46]. These anthropogenic contaminants are ubiquitous materials and humans are estimated to ingest tens of thousands to millions of these particles annually [47], while potential toxic consequences from exposure to them arise from microplastics/nanoplastics themselves, not only from diffused monomers and additives, but also from sorbed contaminants [48,49].

Depending on the type and sources of the data, an exposure assessment can be performed for screening purposes or to evaluate true exposure.

5.2. Deterministic or Probabilistic Exposure Assessment

The approach to any exposure assessment can be deterministic or probabilistic. Deterministic approach is most commonly used and there are many studies utilizing this approach [50–52]. On the other hand, while initially less used, probabilistic techniques gained attention in recent years [23,53–55].

The deterministic approach uses single values, or point estimates, as inputs, resulting in the output as a point value for exposure. It produces a point estimate of exposure that falls somewhere within the full distribution of possible exposures. While it is typically used in screening-level assessments, depending on the input values, this approach can provide assessors with meaningful estimates of central tendency or high-end exposures within a defined population [56]. A deterministic approach does not reflect the full range of possible outcomes but is a good tool for creating the worst case, best case, high consumer, and average exposure scenario of dietary exposure. While several combinations of data can be applied, a high consumer scenario is usually calculated with higher percentiles (90th, 95th) of food consumption data, while worst case scenarios use high values of concentration data or ML and MRL values [5]. For average exposure scenarios, arithmetic mean is commonly used, especially for chronic exposure assessments. Alternatives are median, mode, and in some cases, geometric mean values [5]. On the other hand, the probabilistic approach uses distributions of data from which multiple points are selected as inputs to the exposure equation throughout multiple simulations, and as a result, the output of a probabilistic assessment is a distribution of potential exposure values, thus providing a more comprehensive characterization of variability in exposure or risk estimates and uncertainty [56]. Monte Carlo simulation is the most common tool to estimate exposure with a probability approach. In Monte Carlo simulation, the process involves repeatedly sampling the probability distributions of one or more parameters. Each time this is conducted, the exposure estimate is calculated, resulting in a distribution of potential values for exposure. There is a variety of Monte Carlo simulations available for commercial use (Table 1), being part of standalone software or part of statistical software packages (Minitab (21.1.0), @RISK (8.0), Oracle Crystal Ball (11.1.3.0.0.), XLSTAT (5.2.1413.0). Over the past decade, R—an open-access language and environment for statistical computing [57]—has been one of the most popular programming languages for conducting Monte Carlo simulations; with both built-in functions and many user-created packages, it allows researchers to design and implement very simple to very comprehensive simulation studies [23,58,59].

Next to these two basic approaches, a refined deterministic approach is used, in which single-point concentration values are combined with the distribution of individual food consumption values, or vice versa [5]. Observed individual means is another model commonly used as a cross between deterministic and probabilistic approaches [45,60]. It is just a simple multiplication of consumption amounts with mean concentrations of relevant foods, resulting in a distribution of average exposures per person [60].

5.3. General Considerations to Exposure Assessment

When raw commodities are analyzed, processing factors can be integrated to enhance the accuracy of dietary exposure assessments and align the results more closely with actual exposures. The processing of raw commodities could either elevate or diminish chemical concentrations or modify the characteristics of chemicals within foods, and typically, processing studies are tailored to the food, active substance, or process under investigation [13,61]. There is ample research and countless review papers on the effects of food processing on specific contaminants [61–65] Commodity contaminant combination can have only one processing factor (e.g., peeling of mandarins and pesticide residues [61]) or can have several of them accounting for the whole food production process (e.g., cleaning, sorting, milling, and heat treatment for maize products [22]). In the deterministic approach, these values are set as point estimates, while in the probabilistic approach, they can be set both as point estimate values and as distribution values. One of the three-point distributions can be assigned to represent variations in processing factors [54].

It is common practice to use concentration data from published studies in the literature. The pooled mean procedure is an acceptable method for integrating data from multiple studies to derive a more representative dataset [66]. As the literature usually presents data as point estimate values, to further enhance the exposure assessment, distribution values can be assumed and applied to the datasets [66]. Estimating the probability distribution fitting of the data (such as triangular distribution using minimum and maximum concentration values) compared to using the mean concentration of the sample enables creation of different scenarios in further calculating the exposure assessment [22,67]. This choice also influences the estimation, depending on the number of values below threshold of the analytic methods employed (level of detection and/or level of quantification). Still, this approach can lead to a certain level of uncertainty in the result of the assessment.

All (raw) analytical data represent a mixture of positive values and values below a limit of detection (LOD) and a limit of quantification of an analytical method. Neglecting non-detect values, i.e., values below the LOD, may result in several consequences [68]. There are several methods for dealing with non-detect values: deletion, substitution, maximum likelihood estimation, log-probit regression, and non-parametric methods [68]. Deletion will lead to overestimation of exposure. In the substitution method, non-detect values are replaced with LOD/2, or 0 and LOD values, which will create lower, middle, and upper bounds of the exposure. The substitution method is used in both deterministic and probabilistic approaches. In the deterministic approach, the use of the substitution method requires simple data handling and calculation steps. In a probabilistic approach, this method can be implemented with the use of the logical function "IF" [54,69]. This logical function is also applicable for handling negative values in datasets related to food intake, specifically addressing cases where individuals have not reported the consumption of specific items. Other methods of dealing with non-detect data are more suitable for the probabilistic approach and can be implemented by different statistical software but are more complex and demand more experienced users.

Finally, regardless of type, approach, and source of data, uncertainty reports should be included in all exposure assessments. Uncertainty is a general term referring to all types of limitations in available knowledge that affect the range and probability of possible answers to an assessment question [70]. Assessors must identify sources of uncertainties and their overall effect on the exposure calculations.

6. Conclusions

This paper was intended to give an overview of the current roadmaps to exposure assessment while not jeopardizing any previously published studies and/or publications. The main purpose of this paper is to simplify the exposure assessment process and guarantee that the resulting estimates are as robust and useful as possible. It clearly outlines the types of data needed (food consumption data, concentration data, and body weight data), and a combination of approaches in processing the data (deterministic or deterministic and probabilistic). It finally provides some considerations related to exposure assessment in terms of processing values from different sources and calculating uncertainty levels. The limitation of the paper is that not all sensitive points in the roadmap have been considered.

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Abbreviations

European Food Safety Authority (EFSA); Food Balance Sheets (FBSs); Food and Agriculture Organization (FAO); 24 h dietary recall (24 hR); Food Frequency Questionnaire (FFQ); World Health Organization (WHO); proposed maximum levels (MLs); maximum residue limits (MRLs); Global Environment Monitoring System (GEMS); limit of detection (LOD).

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