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Risk Assessment of Food Contaminants: A Systematic Review of Toxicological Parameters, Analytical Models, and Reference Values

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ABSTRACT

Food safety is now a major public health issue due to the wide range of chemical contaminants present along the food chain, including heavy metals, pesticides, mycotoxins, emerging pollutants, and process-related contaminants. This systematic review strictly followed the PRISMA 2020 methodology, relying on three major databases (ScienceDirect, PubMed, Scopus) and applying explicit inclusion and exclusion criteria. Out of 560 references identified, 31 articles were retained after full screening and analysis. The findings reveal a predominance of deterministic approaches: Estimated Daily Intake (EDI) or Average Daily Intake (ADI) were applied in 70.96% of studies, Hazard Quotient (HQ) in 61.29%, and Cancer Risk (CR/ILCR) in 45.16%. Probabilistic approaches also appeared significant, with Monte Carlo Simulation (MCS) used in 48.38% of cases and Margins of Exposure (MoE/MoET) in 32.25%. Advanced methods such as PBPK and QSAR models remain marginal, reported in only 3.22% and 9.67% of publications, respectively. From a toxicological perspective, several studies highlighted concerning risks, such as margins of exposure below 10,000 for aflatoxins or Hazard Quotients above 1 for lead and cadmium in children. Notably, only 6.45% of studies addressed risk assessment related to plastic migrants, underscoring a major gap in the literature. This review demonstrates substantial heterogeneity in the models applied and stresses the need for international harmonisation of toxicological reference values to improve comparability of results across regions and contaminant families. Probabilistic and integrative approaches are presented as a necessary pathway to enhance the robustness and relevance of food risk assessment.

Keywords: Chemical contaminants; Health risk assessment; Deterministic methods; Probabilistic methods; Food safety

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1. Introduction

Food safety has become a major global public health concern (Hashemi et al., 2023; Thorsen et al., 2025). In a context marked by population growth, rapid urbanisation, and intensified trade, managing risks associated with food consumption has become a priority for governments, regulatory bodies, and the scientific community (Thorsen et al., 2025). Food quality and safety directly determine population well-being, as exposure to certain chemical contaminants is associated with chronic, metabolic, or carcinogenic diseases, the health and socio-economic impacts of which are considerable (Li, 2025; Sinha et al., 2025).

The diversity of chemical contaminants along the food chain illustrates the complexity of exposure sources. Heavy metals such as lead, cadmium, and arsenic originate from environmental contamination and the use of certain agricultural inputs (Angon et al., 2024; Kaur et al., 2025). Mycotoxins, produced by mould growth, occur in a wide range of foodstuffs, particularly cereals. Pesticide residues constitute another group of contaminants frequently reported in fruits, vegetables, and processed products (Hisashi Kato-Noguchi, 2023; Beyuo et al., 2024). Beyond these "classical" substances, emerging pollutants such as micro/nanoplastics, phthalates, and certain industrial additives, as well as process-related contaminants formed during cooking or processing such as acrylamide and polycyclic aromatic hydrocarbons have been increasingly documented (Alizadeh et al., 2025; Zimmermann et al., 2025). This diversity highlights the need for assessment approaches that consider multiple exposure pathways and a wide range of toxicological effects.

Faced with this complexity, the scientific literature reveals considerable heterogeneity in the methodological approaches used to assess health risks associated with these contaminants (Rigaud et al., 2024).

Deterministic methods, such as Estimated Daily Intake (EDI), Hazard Quotient (HQ), and Carcinogenic Risk (CR), are frequently applied due to their simplicity and operational value (Doménech & Martorell, 2024). However, they tend to standardise exposure and overlook inter-individual variability. To address this, probabilistic approaches particularly Monte Carlo Simulation are increasingly adopted to better account for uncertainty and parameter variability (Wang & Yu, 2024; Zuo et al., 2025). Alongside these classical models, advanced approaches such as physiologically based pharmacokinetic (PBPK) models, quantitative structure–activity relationships (QSAR), and hybrid methods combining toxicological and environmental data illustrate the shift towards more realistic and integrative risk assessment (Huang et al., 2024; Mi et al., 2025).

Against this backdrop, there is a need for a systematic synthesis of available data to identify the most widely used mathematical and quantitative models, describe their principles, and highlight their strengths and limitations. The aim of this review is therefore to provide an integrated analysis of methodological approaches applied to health risk assessment of chemical contaminants in food, in order to identify general trends and contribute to the harmonisation of scientific and regulatory practices.

2. Methods

2.1. Study Design

This study adopts a systematic review approach with the objective of identifying, analysing, and synthesising existing research on health risk assessment related to chemical contaminants in food. It specifically aims to identify the mathematical models and quantitative approaches used to characterise such risks, regardless of the origin of the contaminants (residues, additives, packaging migration, or processing-derived compounds). Through this synthesis, the study seeks to provide an overview of the methods applied in the food sector to assess human exposure, toxicity, and overall risk. A literature search was conducted in accordance with the PRISMA methodology (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), as defined by Page et al. (2021). This methodology is designed to ensure transparency, rigour, and reproducibility of systematic reviews. It guides each stage of the process, from the formulation of the research question to study selection, data extraction, and synthesis of findings. By following these guidelines, this review ensures a robust methodological framework that minimises bias and provides a reliable critical analysis of the publications retained. To identify relevant studies, a documentary search was carried out in three major scientific databases: Scopus, PubMed, and ScienceDirect. Among these sources, ScienceDirect was found to contain the most relevant and specific publications related to the issue of health risk assessment of chemical contaminants in food.

2.2. Literature Search Process

A preliminary literature search was conducted using logical operators “AND” and “OR” as well as wildcard characters, through two distinct search equations designed to maximise both relevance and specificity of the results. The first equation was oriented towards identifying studies on the modelling of chemical migration and dietary exposure, using the following keywords: “chemical migration*” OR “contaminant transfer*” OR “exposure estimation*” AND “food*” OR “dietary intake*” AND “risk assessment*” OR “hazard characterization*” AND “mathematical model*” OR “exposure model*” OR “deterministic modeling*”. The second equation targeted more broadly studies related to health risk assessment of chemical contaminants in food, using the following terms: “food contaminants*” OR “chemical residues*” OR “food additives*” OR “processing contaminants*” AND “health risk assessment*” OR “toxicological evaluation*” AND “modeling*” OR “mathematical model*” OR “risk characterization*” OR “PBPK*” OR “QSAR*”. These equations were successively applied across the selected databases to identify studies relevant to the objectives of the review. The bibliographic searches were performed exclusively in English, with no time restriction applied at this stage, in order to ensure access to the widest and most comprehensive body of international scientific literature. This linguistic restriction to English publications was adopted to ensure methodological consistency and to avoid potential misinterpretation or translation bias that could arise from multilingual sources, while still capturing the vast majority of peer-reviewed and high-impact studies available in the field. In total, 495 articles were identified in ScienceDirect, 54 in PubMed, and 11 in Scopus after combining the results from both search equations. The entire literature search was carried out on 23 June 2025.

2.3. Study Selection

A total of 560 references was collected from the three databases and imported into EndNote X9 (Build 12062) for bibliographic management and organisation. Search results were exported in RIS format in each case before being centralised in EndNote. To identify potential duplicates, the automatic “Find Duplicates” function was applied, based on matching bibliographic elements such as article title, authors, year of publication, and DOI. To reinforce the reliability of this step, an additional manual verification was performed. This process allowed the identification and removal of 9 duplicates, thereby reducing the dataset to 551 unique references. These references were subsequently exported in XML format and imported into the SysRev platform (Sysrev © 2025, Insilica LLC) for the pre-screening phase based on title and abstract analysis. The criteria for inclusion and exclusion of publications in this review are summarised in Table 1. Each article was deemed eligible if it met the predefined inclusion conditions and complied with the publication period requirement. Following this screening process, 94 articles were retained and subjected to full-text review for in-depth analysis. At the eligibility assessment stage, only original works of an experimental, observational, or analytical nature were considered for the extraction of quantitative data relevant to this study. The selection procedure was rigorously focused on publications providing a direct response to the central research question of the review: What mathematical models and quantitative approaches are used in the scientific literature for health risk assessment related to chemical contaminants in foodstuffs? The comprehensive examination of the preselected publications resulted in a final selection of 31 articles, which were judged to comply with the defined methodological and thematic criteria. These studies formed the dataset retained for the conduct of the systematic review, as illustrated in Fig 1.

Table 1: Inclusion and Exclusion Criteria in SysRev

Inclusion	Exclusion
Studies addressing chemical contaminants present in food	Studies not addressing food
Presence of a risk assessment (partial or complete), based on a quantitative approach or a mathematical model (e.g., MOE, HQ, BMD, PBPK, QSAR, Monte Carlo, etc.)	Complete absence of a quantitative approach or any modelling related to risk assessment
Studies contributing to the understanding, modelling, or application of methods for health risk assessment of chemical contaminants	Studies focusing on regulatory, economic, or social aspects without any health risk assessment
Publications published from 2015 onwards were considered	Publications prior to 2015

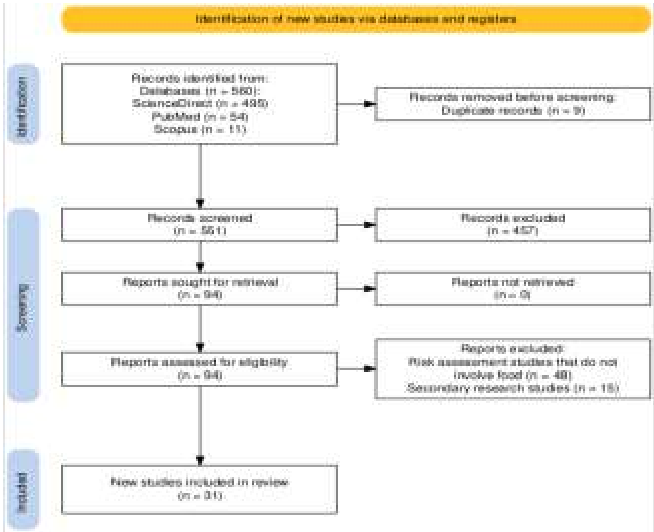

Fig 1: PRISMA flow diagram showing the study selection process.

3. Results and Discussion

3.1. Characteristics and types of contaminants investigated

The studies included in this systematic review highlight a wide diversity of chemical contaminants present in foodstuffs and drinking water, originating both from natural sources such as metals and mycotoxins, and from anthropogenic sources such as pesticides, additives, polycyclic aromatic hydrocarbons, and emerging pollutants. This variability reflects not only the specificity of the matrices investigated ranging from cereals, fruits, vegetables, oils, animal products, and processed foods to drinking water. In but also the diversity of exposure pathways. In this context, Suppplementary Table 2 below summarises the main analytical and contextual characteristics of the 31 studies included in the review. It provides a structured overview of the information extracted from each publication, including authors, countries or regions of study, types of contaminants investigated, food matrices concerned, probable sources of contamination, and analytical methods employed.

3.1.1. Geographical distribution of the included studies (n = 31)

The analysis shows a highly heterogeneous distribution: China accounts for 9 publications (29%), Iran 5 (16.1%), Turkey 3 (9.7%), and Ireland 2 (6.5%). Twelve other countries are represented by only one study each (3.2% per country): South Africa, Bangladesh, Brazil, Spain, Greece, Italy, Nigeria, Pakistan, Poland, Portugal, Sweden, and Taiwan (Fig 2). This pattern highlights the leading role of a few scientific hubs and the persistent under-documentation of large regions that are nonetheless exposed.

China's predominance is explained by a broad thematic scope, strong analytical capacity, and systematic use of probabilistic approaches. The studies cover process-related contaminants (e.g., acrylamide in Liu et al., 2025) as well as industrial and environmental pollutants: phthalates in oils (Tang et al., 2022), metals and bioaccumulation in tea (Zhang et al., 2021), multiple mycotoxins in cereals and derived products (Yang et al., 2020; Wang et al., 2018), and exposure/transport modelling integrating the environment (atmospheric mercury, Wai et al., 2017; water quality dynamics, Zhao et al., 2022; multiple residues in berries, Yang et al., 2017). Taken together, this forms a coherent corpus where LC/GC–MS/MS and ICP–MS are combined with Monte Carlo simulations to quantify exposure and characterise risk. Iran, the second-largest contributor, mainly highlights exposures linked to agronomic practices and local pressures: pesticides and metals in key food crops such as dates (Taghizadeh et al., 2021) and cucurbits (Taghizadeh et al., 2024), metals in orchard fruits (Rezaei et al., 2019), nitrates in drinking water (Moeini & Azhdarpoor, 2021), and PAHs in infant food (Badibostan et al., 2019). These studies consistently combine field measurements with probabilistic risk assessment (HQ/HI/CR, MoE) and point to recurrent determinants of risk: wastewater irrigation, industrial proximity, and the use of pesticides and fertilisers. Turkey investigates matrices directly linked to consumption habits, illustrating both process-related contaminants and trophic transfers: acrylamide in fried products and snacks (Basaran et al., 2024), metals in fish (Şirin et al., 2024), and lead in eggs (Kılıç Altun et al., 2024). These findings show that compliance with regulatory limits does not always suffice to control cumulative risk, particularly when multiple exposure pathways coexist. Ireland contributes two methodologically strong studies focusing on emerging pollutants and the soil plant consumer chain: modelling of absorption and exposure to micro/nanoplastics in crops (Yuan et al., 2024) and hydrological dynamics and agricultural pesticides (O'Driscoll et al., 2024). These approaches, based on simulation and sensitivity analysis, strengthen the integration of environmental links into food risk assessment. Countries represented by a single study address targeted but critical issues. In South Africa, the assessment of advanced water treatment technologies highlights the balance between technological performance and exposure reduction (Manyepa et al., 2024). In Bangladesh and Pakistan, concerning levels of contaminants in staple foods reveal insufficient control systems (Shuvo et al., 2025; Khatoon et al., 2024). In Nigeria, metal contamination in fish exceeds health benchmarks and particularly affects children (Ishola et al., 2023). In Taiwan, the presence of benzophenone UV filters in fish demonstrates the footprint of emerging pollutants and the need for targeted analytical tools (Huang et al., 2022).

In Europe, several studies illustrate strong methodological rigour and analytical granularity: lead from ammunition in game birds in Spain (Sevillano-Caño et al., 2021); pesticide cocktails in apples in Greece, showing cumulative neurotoxic risk despite frequent compliance with MRLs (Tzatzarakis et al., 2020); post-harvest processing factors reducing residues in fruits and vegetables in Poland (Jankowska et al., 2019); multiple myco &[2]toxins in children's cereals in Portugal with MoE/MoET sometimes concerning for AFB1 (Assunção et al., 2015); arsenic in vegetables grown on historically contaminated glassworks soils in Sweden, with carcinogenic risk above tolerable thresholds despite HQ < 1 (Uddh-Söderberg et al., 2015); and 3-MCPD/glycidyl esters in refined oils in Italy (Lanno et al., 2024). Finally, in Brazil, the study on greywater reuse (Etchepare & van der Hoek, 2015) broadens the scope to the domestic water micropollutant potabilisation continuum, illustrating the importance of multiple barriers in risk management.

Taken together, these findings show that scientific documentation is concentrated in countries with strong analytical capacity and high academic output, while other regions, though exposed, remain understudied. The global interpretation is threefold: first, dominant risks are still driven by metals, mycotoxins, and certain pesticides, with recurring signals for process contaminants and emerging pollutants; second, the cumulative nature of exposures argues for integrated assessment frameworks (probabilistic modelling, multi-pathway scenarios, cumulative indices) as mobilised in the cited studies; third, geographical and methodological heterogeneity justifies an international effort towards harmonisation of monitoring protocols and risk assessment, along with capacity building in regions where risk burden is high but scientific production limited.

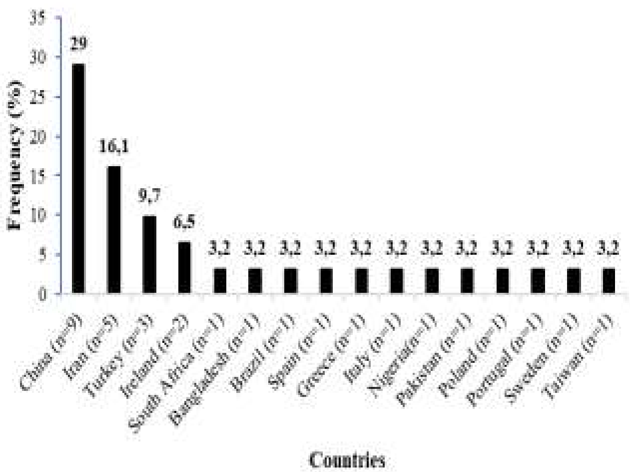

Fig 2: Geographical distribution of the included studies (n = 31).

3.1.2. Types of food matrices

The analysis of the 31 included studies shows a predominance of plant-based products, with 15 articles representing 48.4% of the total. These works focus on cereals and derived products (Yang et al., 2020; Assunção et al., 2015), fruits (Rezaei et al., 2019; Taghizadeh et al., 2021), vegetables (Taghizadeh et al., 2024), tea leaves (Zhang et al., 2021), oils (Tang et al., 2022), as well as infant formulas and baby foods (Badibostan et al., 2019). Animal products represent 7 studies (22.6%), including fish (Şirin et al., 2024; Ishola et al., 2023; Huang et al., 2022), poultry (Shuvo et al., 2025), eggs (Kılıç Altun et al., 2024), and game meat (Sevillano-Caño et al., 2021). Drinking water and treatment systems account for 5 studies (16.1%), addressing nitrates in supply networks (Moeini & Azhdarpoor, 2021), recycling/desalination and the removal of emerging contaminants (Manyepa et al., 2024), as well as agricultural surface waters exposed to pesticides (O'Driscoll et al., 2024). Industrially processed products total 3 studies (9.7%), including chips and breakfast cereals (Basaran & Sadighara, 2024), refined oils (Lanno et al., 2024), and bakery/fried products rich in acrylamide (Liu et al., 2025). Finally, 1 study (3.2%) concerns an atypical matrix, namely the reuse of greywater (Etchepare & van der Hoek, 2015) (Fig 3).

The overrepresentation of plant matrices is explained by their central role in diet and by multiple exposure pathways, already highlighted by Wang et al. (2018) and Yang et al. (2017), who emphasised the vulnerability of crops to pre-harvest contamination (agricultural practices, fertilisers, pesticides) and post-harvest contamination (storage, climate). Animal products constitute critical vectors due to bioaccumulation and potentially biomagnification phenomena; exceedances observed in Nigerian tilapias (Ishola et al., 2023) and lead levels in hunted bird meat (Sevillano-Caño et al., 2021) illustrate the contribution of the trophic chain to health risk. Water emerges as a strategic matrix, as it conditions food quality throughout the environment–food continuum: Moeini & Azhdarpoor's (2021) work on nitrates highlights the importance of diffuse sources, while Manyepa et al. (2024) show that, despite abatements below 95% for some emerging pollutants, advanced technologies still face spatio-temporal variability of loads and chemical diversity; O'Driscoll et al., (2024) findings on pesticides in agricultural water bodies further confirm this vector role. Processed products raise a distinct issue: process contaminants (acrylamide, 3-MCPD/glycidyl esters) do not originate from external inputs but emerge during cooking or refining, as shown by Lanno et al. (2024) and Liu et al. (2025), requiring technological mitigation strategies rather than simple control of inputs. Finally, atypical matrices expand the perspective of food safety to domestic water cycles: Etchepare & van der Hoek (2015) document the presence of hundreds of micropollutants (phthalates, parabens, UV filters, solvents), underscoring that reuse requires multiple barriers and risk assessment adapted to mixtures. Overall, the observed distribution calls for an integrated risk assessment approach that articulates matrix heterogeneity, regional specificities, and the emergence of new contaminant families. It also justifies the use of cumulative frameworks (HQ/HI/CR, MoE/MoET, Monte Carlo) and harmonised monitoring policies to reflect the real exposures of consumers.

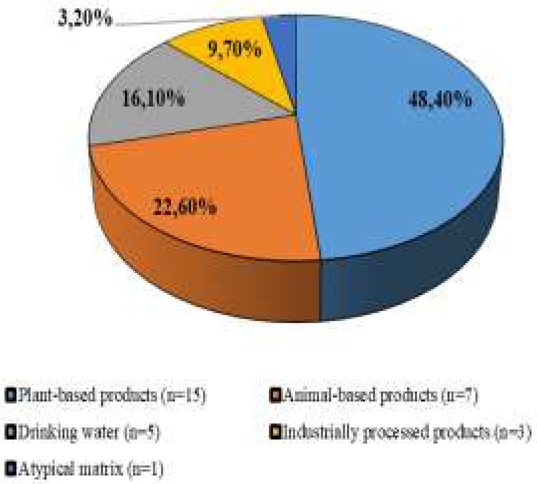

Fig 3: Types of food matrices investigated (n = 31)

3.1.3. Types of contaminants addressed in the risk assessments

Of the 31 included studies, metals and metalloids represent the most frequent category, with 11 articles (35.5%). Pesticides follow with 6 articles (19.4%), emerging pollutants (micro/nanoplastics, benzophenone-type UV filters, domestic micropollutants, phthalates) with 5 articles (16.1%), process contaminants (acrylamide, 3-MCPD and glycidyl esters) and mycotoxins with 3 articles each (9.7%), nitrates/water quality indicator parameters with 2 articles (6.5%), and finally, polycyclic aromatic hydrocarbons (PAHs) with 1 article (3.2%) (Fig 4).

The predominance of metals is explained by their environmental ubiquity, persistence, and both acute and chronic toxic potential. Studies on fish and other animal-derived products highlight significant transfer and bioaccumulation, as shown by Şirin et al. (2024) in Turkey and Ishola et al. (2023) in Nigeria, where Pb and Cd levels exceeded health benchmarks for consumers, particularly children. In plant matrices, arsenic, lead, cadmium, and nickel are regularly detected, whether in tea leaves (Zhang et al., 2021) or fruits (Rezaei et al., 2019), with non-negligible risks under continuous exposure; moreover, the Swedish study by Uddh-Söderberg et al. (2015) illustrates that carcinogenic risk linked to arsenic can persist even when HQ < 1. Pesticides form the second thematic block, driven by contexts of intensive agricultural use and the issue of cumulative risk. Multi-residue cocktails were observed in Greek apples (Tzatzarakis et al., 2020) and Chinese berries (Yang et al., 2017), while specific supply chains (dates, cucurbits) in Iran revealed profiles combining pesticide residues and other contaminants (Taghizadeh et al., 2021; 2024). Post-harvest approaches show that part of these residues can be mitigated through technological processing, without however eliminating the question of combined effects (Jankowska et al., 2019). The emerging pollutants documented here encompass families that are both ubiquitous and poorly regulated: micro/nanoplastics in soil–plant systems (Yuan et al., 2024), benzophenone UV filters in fish (Huang et al., 2022), phthalates in edible oils (Tang et al., 2022), and domestic micropollutants in greywater (Etchepare & van der Hoek, 2015). South African results show that advanced treatment chains can achieve >95% removal for several compounds, while still facing chemical diversity and variability in loads (Manyepa et al., 2024). Process contaminants represent a distinct issue: they do not enter food via inputs but emerge from processing conditions (temperature, duration, formulation). Acrylamide levels reported in chips and fried products (Basaran & Sadighara, 2024; Liu et al., 2025) and 3-MCPD/glycidyl esters in refined oils (Lanno et al., 2024) emphasise that technological mitigation (optimising recipes, thermal conditions, refining processes) is the priority pathway for action. Mycotoxins remain a cornerstone of food toxicology: Deoxynivalenol (DON), Ochratoxin A (OTA), and especially Aflatoxin B1 (AFB1) retain a significant health burden in cereals and derived products (Yang et al., 2020; Assunção et al., 2015) and in dried fruits/nuts (Wang et al., 2018), with MoE/MoET values sometimes falling into areas of concern. Nitrates and water quality parameters confirm the role of water as a vector of exposure: nitrate loads in urban networks (Moeini & Azhdarpoor, 2021) and biogeochemical dynamics in surface waters (Zhao et al., 2022) condition the safety of downstream food systems. Finally, PAHs identified in infant foods (Badibostan et al., 2019) show that matrices with high population sensitivity can be exposed to genotoxic contaminants, even at low levels. Taken together, these results confirm the hierarchy of concerns (metals, pesticides, and mycotoxins foremost) while underscoring the emergence of new families linked to materials, processes, and usage patterns. They justify the use of cumulative and probabilistic assessments (HQ/HI/CR, MoE/MoET, Monte Carlo simulations) to reflect real exposures and guide risk management.

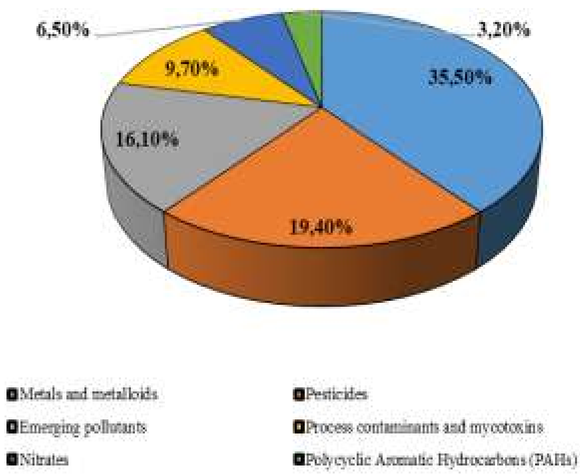

Fig 4: Types of Contaminants Investigated (n = 31).

3.2. Risk Assessment

The studies included in this review employed a wide diversity of toxicological parameters and risk assessment models. These choices varied according to the nature of the contaminants investigated (heavy metals, pesticides, mycotoxins, polycyclic aromatic hydrocarbons, plastics, etc.), the food or environmental matrices considered, as well as the objectives of the authors (assessment of carcinogenic, non-carcinogenic, or cumulative risk).

In this context, Suppplementary Table 3 below summarises the main methodological and analytical characteristics of the 31 included studies. It provides, in a structured manner, the information extracted from each publication, including: the authors and year, the toxicological parameters applied (RfD, NOAEL, BMDL, TDI, etc.), the mathematical models employed (HQ, HI, ILCR, MoE, Monte Carlo Simulation, QSAR, PBPK, etc.), a brief description of the approaches used, the reference values adopted (EFSA, US EPA, JECFA, WHO), the general conclusions of the authors regarding risk perception, as well as the limitations or uncertainties identified in each study.

3.2.1. Diversity of Toxicological Parameters Used

The analysis of the 31 included studies shows substantial diversity in the toxicological parameters employed. The most frequently reported are the Reference Dose (RfD), the Tolerable Daily Intake (TDI) or the Provisional Tolerable Daily Intake (PTDI), as well as values derived from the benchmark dose approach such as the Benchmark Dose Lower Confidence Limit (BMDL). Some studies also use thresholds such as the No Observed Adverse Effect Level (NOAEL) or the Lowest Observed Adverse Effect Level (LOAEL) to establish safety margins. For carcinogenic risk assessment, the Cancer Slope Factor (CSF) and BMDL10 or BMDL01 values are often applied, particularly for arsenic, heavy metals, and polycyclic aromatic hydrocarbons. Finally, several studies refer to Provisional Tolerable Weekly Intakes (PTWI) or Provisional Tolerable Monthly Intakes (PTMI), especially for lead, cadmium, and certain mycotoxins.

These findings reveal significant heterogeneity in the toxicological references adopted, linked to the diversity of contaminants investigated and the regulatory bodies consulted. For example, Shuvo et al. (2025) and Ishola et al. (2023) mainly used RfD and TDI values issued by the United States Environmental Protection Agency (US EPA) and the Food and Agriculture Organization/World Health Organization (FAO/WHO) for heavy metals, while Şirin et al. (2024) and Khatoon et al. (2024) combined these with CSF values to calculate carcinogenic risks. In contrast, Liu et al. (2024) and Assunção et al. (2015) favoured BMDL10 and PTDI values from the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for mycotoxins, underlining the relevance of these parameters in the context of genotoxic contaminants.

Some studies stand out for their use of alternative thresholds. For instance, Basaran & Sadighara (2024) and Liu et al. (2025) employed NOAEL and BMDL10 values for acrylamide, reflecting EFSA practices, while Badibostan et al. (2019) used Toxic Equivalency Factors (TEFs) for polycyclic aromatic hydrocarbons, converting measured levels into benzo[a]pyrene equivalents. Other, more recent approaches appear in specific contexts, such as the use of Thresholds of Toxicological Concern (TTC) for emerging contaminants by Etchepare & van der Hoek (2015), or the application of reference values for micro- and nanoplastic particles in Yuan et al. (2024), although these remain largely hypothetical.

This diversity reflects both the researchers' adaptation to the contaminants studied and a lack of harmonisation in the reference values applied. It highlights the need to align EFSA, US EPA, JECFA, and WHO frameworks to ensure greater comparability of results across studies, while underlining the persistent uncertainties, particularly for emerging contaminants (microplastics, secondary mycotoxins, plastic additives).

3.2.2. Deterministic Methods of Risk Assessment

The review of the 31 included studies shows that deterministic approaches largely dominate the risk assessment methods used. As summarised in Table 4 below, the Estimated Daily Intake (EDI) or the Average Daily Intake (ADI) are employed in 70.96% of studies, thus representing the most common basis for estimating daily population exposure. Hazard Quotient indicators (HQ, THQ, TTHQ) appear in 61.29% of the works, while the Hazard Index (HI) is applied in 38.70% of cases to aggregate risks associated with multiple substances. Carcinogenic risk parameters, such as Cancer Risk (CR), Incremental Lifetime Cancer Risk (ILCR), or Target Cancer Risk (TCR), are reported in 45.16% of publications. Finally, Margins of Exposure (MoE/MoET) are mentioned in nearly one-third of studies (32.25%), mainly for genotoxic contaminants such as mycotoxins and acrylamide.

These methods are widely recognised by international agencies due to their simplicity and operational value. For example, studies such as Shuvo et al. (2025) and Ishola et al. (2023) combined EDI, HQ, and HI to assess risks from heavy metals, highlighting concerning non-carcinogenic risks in children. Similarly, Rezaei et al. (2019) showed that HQ and CR calculated for Iranian fruits remained below US EPA thresholds, indicating no significant risk. In the case of genotoxic contaminants, Liu et al. (2024) and Assunção et al. (2015) prioritised the use of margins of exposure (MoE and MoET), which revealed insufficient margins for aflatoxins, thereby indicating a potential risk. Likewise, Basaran & Sadighara (2024) and Liu et al. (2025) applied BMDL10 and HQ values for acrylamide, confirming the relevance of these parameters in evaluating this concerning contaminant.

However, these approaches have intrinsic limitations: they rely on fixed assumptions (body weight, average food consumption) and do not account for interindividual variability or uncertainties associated with experimental data. Several authors have highlighted this restrictive nature: Badibostan et al. (2019) note, for polycyclic aromatic hydrocarbons, that reliance on BMDL and TEF values may underestimate certain risks, while Yang et al. (2017) indicate that strict application of HQ for pesticide residues may overestimate acute exposure in some scenarios.

In summary, the quantitative results confirm the predominance of deterministic methods in risk assessment, but the discussion highlights their limitations, thereby justifying the increasingly frequent use of probabilistic approaches and advanced models.

Table 4 : Proportion of Risk Assessment Methods Used in the 31 Included Studies

Method / Model Used	Count (n)	Percentage (%)
EDI / ADI (Estimated/Average Daily Intake)	22	70.96%
HQ / THQ / TTHQ (Hazard Quotient / Target HQ / Total HQ)	19	61.29%
HI (Hazard Index)	12	38.70%
CR / ILCR / TCR (Cancer Risk / Incremental Lifetime Cancer Risk / Target Cancer Risk)	14	45.16%
MoE / MoET (Margin of Exposure / Total MoE)	10	32.25%
BMD / BMDL (Benchmark Dose / Benchmark Dose Lower Limit)	8	25.80%
Monte Carlo Simulation (MCS)	15	48.38%
QSAR / Read-across	3	9.67%
PBPK (Physiologically-Based Pharmacokinetic models)	1	3.22%
Other specific models (OPBT, Igeo, APCS/MLR, WQEM, PI, MoS)	6	19.35%

n = 110

3.2.3. Probabilistic methods and advanced approaches

The review of the 31 included studies shows that nearly half (48.38%) employed probabilistic methods, mainly through Monte Carlo Simulation (MCS), used to quantify variability and uncertainty related to exposures. Margins of Exposure (MoE) and Total MoE (MoET) appear in 32.25% of the works, mainly for genotoxic contaminants such as mycotoxins and acrylamide. Benchmark Dose approaches (BMD/BMDL), which allow derivation of thresholds from dose–response curves, are found in 25.80% of the studies. More marginally, advanced tools such as QSAR (Quantitative Structure Activity Relationship) models (9.67%) or PBPK (Physiologically-Based Pharmacokinetic) models (3.22%) are used to predict the toxicological behaviour of specific contaminants. Finally, around 19.35% of studies employed hybrid or specific approaches, such as geochemical indices (Igeo), multivariate regressions (APCS/MLR), or dynamic water quality models (WQEM) (Table 5).

These methods go beyond classical deterministic approaches by integrating exposure variability and toxicological uncertainties. For instance, Taghizadeh et al. (2021, 2024) and Assunção et al. (2015) demonstrated, through Monte Carlo simulations, that the resulting risk distributions are more representative than point estimates, particularly for pesticides and mycotoxins. Similarly, Badibostan et al. (2019) used margins of exposure for polycyclic aromatic hydrocarbons, showing that despite measured concentrations sometimes close to regulatory thresholds, the MoE values remained well above the critical value of 10,000 defined by EFSA.

Some studies applied innovative approaches. For example, Etchepare & van der Hoek (2015) used TTCs (Thresholds of Toxicological Concern) and QSAR tools to evaluate emerging contaminants in drinking water, while Zhao et al. (2022) employed a hybrid dynamic model (H-WQEM) to describe the evolution of water quality and its link with public health. In turn, Yuan et al. (2024) introduced hypothetical reference values for micro- and nanoplastic particles, illustrating current challenges in regulating these substances.

These findings highlight the growing interest in probabilistic and advanced methods, which better reflect real exposures and improve the accuracy of risk assessments. However, their application remains limited by the lack of robust toxicological data, model complexity, and the need for specialised expertise. In practice, complementarity between deterministic and probabilistic approaches appears essential to producing reliable and operational risk assessments.

Table 5 : Proportion of probabilistic methods and advanced approaches used in the 31 included studies.

Method / Approach	Count (n)	Percentage (%)
Monte Carlo Simulation (MCS)	15	48.38%
MoE / MoET (Margin of Exposure / Total MoE)	10	32.25%
BMD / BMDL (Benchmark Dose / Benchmark Dose Lower Limit)	8	25.80%
QSAR / Read-across	3	9.67%
PBPK (Physiologically-Based Pharmacokinetic models)	1	3.22%
Other advanced models (OPBT, Igeo, APCS/MLR, WQEM, PI, MoS)	6	19.35%

n = 43

3.2.4. Reference values and regulatory thresholds used

The included studies refer to a wide range of reference values established by major international agencies. The most frequently used originate from the European Food Safety Authority (EFSA), the United States Environmental Protection Agency (US EPA), the Joint FAO/WHO Expert Committee on Food Additives (JECFA), and the World Health Organization (WHO). These references notably include

Acceptable/Tolerable/Provisional Tolerable Daily Intakes (ADI, TDI, PTDI), Provisional Tolerable Weekly or Monthly Intakes (PTWI, PTMI), as well as values derived from benchmark dose approaches (BMDL10, BMDL01). For carcinogenic substances, several studies relied on Cancer Slope Factors (CSF) and the risk thresholds set by the US EPA (10^{-6} to 10^{-4}). Finally, some studies applied European Union Maximum Residue Limits (MRLs) or Chinese and Iranian standards to compare measured concentrations in food commodities.

This diversity of references reflects the coexistence of several regulatory frameworks, resulting in divergences in risk interpretation. For instance, Shuvo et al. (2025) and Ishola et al. (2023) relied on RfD and TDI values from the US EPA and JECFA for heavy metals, while Şirin et al. (2024) and Khatoon et al. (2024) integrated CSFs to quantify carcinogenic risks. For mycotoxins, Liu et al. (2024) and Assunção et al. (2015) preferred BMDL and PTDI values established by EFSA, emphasising their relevance for genotoxic contaminants. In the case of polycyclic aromatic hydrocarbons, Badibostan et al. (2019) referred to European Union thresholds, while for pesticides, Yang et al. (2017) and Tzatzarakis et al. (2020) used European and Chinese MRLs.

This heterogeneity illustrates how the choice of reference value can influence the final outcome of the assessment. It also reflects the absence of a harmonised framework enabling direct comparison of risks across regions or contaminant types. Authors such as Etchepare & van der Hoek (2015) also highlight the need for alternative thresholds, such as TTCs (Thresholds of Toxicological Concern), to regulate emerging substances still lacking robust toxicological values. In the same vein, Yuan et al. (2024) illustrate the difficulties encountered in defining applicable reference values for micro- and nanoplastics, which remain outside the scope of traditional regulatory frameworks.

Ultimately, while the use of reference values established by EFSA, US EPA, JECFA, and WHO remains common practice, the observed discrepancies highlight the need for international harmonisation in order to ensure comparability and consistency in food risk assessment.

3.2.5. Risk assessment of migrants from plastic food packaging

The analysis of the 31 articles included in this review highlights a clear lack of studies focusing on the health risk assessment of contaminants migrating from plastic packaging into food. Indeed, only two publications, representing 6.45% of the total, specifically addressed this topic.

Tang et al. (2022) focused their study on phthalates, particularly DBP, DEHP, and DMP, three commonly used plasticisers. Their approach relied on toxicological reference parameters (RfD DBP = 100 µg/kg/day; DEHP = 20 µg/kg/day; CSF DEHP = 1.4×10^{-5}) and combined the calculation of Estimated Daily Intake (EDI), Non-Cancer Risk (NCR), and Cancer Risk (CR). Probabilistic evaluation through Monte Carlo Simulation revealed that while NCR remained below 1, the carcinogenic risk associated with DEHP nevertheless exceeded the 10^{-6} threshold in more than 50% of cases, highlighting a non-negligible health concern.

Yuan et al. (2024), on the other hand, investigated micro and nanoplastics (MNPs), emerging contaminants for which toxicological reference values (RfD, TDI, NOAEL) are not yet available. Their methodology was based on a Human Health Exposure Assessment (HHEA) approach integrating a Monte Carlo Simulation (100,000 iterations) and a sensitivity analysis. Estimated dietary exposure ranged from 10^2 to 10^3 particles/kg body weight/day, with higher levels in vegetables than in fruits and cereals, pointing to a potential risk that remains difficult to characterise in the absence of normative benchmarks.

Overall, these studies confirm both the scarcity of dedicated research (6.45% of the corpus) and the relevance of the approaches employed (probabilistic exposure models, comparison with reference values, or exploratory assessments in the absence of toxicological data). They underscore the need to strengthen future research on risk assessment, particularly for emerging contaminants such as micro- and nanoplastics, and in the context of multiple migrations and combined effects of substances from plastic packaging.

3.2.6. Convergences and divergences in the study conclusions

The conclusions reported by the authors reveal both points of convergence and notable divergences. In most cases, the studies conclude that non-carcinogenic risks are low, particularly when Hazard Quotient (HQ) and Hazard Index (HI) values are below 1. Similarly, Margin of Exposure (MoE) values exceeding the critical threshold of 10 000 were often interpreted as an indication of negligible risk. However, several studies highlight concerning situations: HQ values greater than 1 for vulnerable groups (children), Incremental Lifetime Cancer Risk (ILCR) exceeding 10^{-4} for carcinogenic contaminants such as arsenic or polycyclic aromatic hydrocarbons, or insufficient margins of exposure for aflatoxins and acrylamide. Finally, some studies point out that even when values fall below regulatory thresholds, chronic exposure or cumulative effects may still justify health concerns.

These convergences and divergences reflect the complexity of food risk assessment. For example, Rezaei et al. (2019) and Moeini & Azhdarpoor

(2021) conclude that there is no significant risk for heavy metals and nitrates, whereas Ishola et al. (2023) and Shuvo et al. (2025) report concerning levels of lead and cadmium, particularly for children. In the case of mycotoxins, Assunção et al. (2015) and Liu et al. (2024) emphasise that exposure margins for aflatoxins are insufficient, in contrast to the more reassuring conclusions of Wang et al. (2018) for ochratoxin A and zearalenone. Polycyclic aromatic hydrocarbons have also yielded contrasting results: Badibostan et al. (2019) estimate that risks remain tolerable in infant formulas, whereas Sevillano-Caño et al. (2021) identify a high hazard associated with the consumption of game meat heavily contaminated with lead.

These divergences can be explained by several factors: differences in targeted contaminants, geographical and contextual variations, populations studied (adults vs children), and the reference values adopted. They underscore the importance of contextualising each conclusion and avoiding the generalisation of results from one study to other food matrices or regions. They also highlight the need to integrate cumulative and multi-exposure effects still too rarely considered in order to better reflect the reality of food-related risks.

3.2.7. Cross-cutting limitations and uncertainties

The review of the included studies highlights a recurring set of limitations and uncertainties. Several works report restricted sample sizes or limited geographical scope, which can reduce the representativeness of the results. Most assessments rely on simplified assumptions, such as average body weight or standard food consumption, without always distinguishing vulnerable sub-populations such as children or pregnant women. In many cases, concentrations below detection limits are replaced with arbitrary values (e.g., LOD/2), which introduces additional uncertainty. Finally, few studies consider the combined effects of multiple contaminants, with most models restricted to additive approaches.

These methodological limitations partly explain the divergences observed between studies. For instance, Rezaei et al. (2019) and Moeini & Azhdarpoor (2021) acknowledge that their risk estimates for heavy metals and nitrates were based on simplified consumption assumptions, without accounting for seasonal variations or local dietary habits. Similarly, Badibostan et al. (2019) and Sevillano-Caño et al. (2021) emphasise that the limited size of their samples (infant formulas and game meat) constrains the scope of their conclusions. Uncertainty related to the treatment of censored data is also reported by Taghizadeh et al. (2021) and Wang et al. (2018), who recognise that substituting non-detected values may lead to over- or underestimation of risk.

Another critical issue is the frequent absence of multi-exposure and synergistic assessments. Current approaches generally assume additive effects of contaminants (via HI or TTHQ), whereas certain interactions may amplify or mitigate toxic effects. This gap is highlighted in the studies of Etchepare & van der Hoek (2015) and Yuan et al. (2024), who stress the need for more integrative models for emerging contaminants such as micropollutants or plastic particles.

In summary, the limitations and uncertainties observed in these studies call for greater caution in the interpretation of results and reinforce the need to develop more robust methodologies, including more representative samples, realistic consumption scenarios, and improved consideration of combined effects.

4. Recommendations and Perspectives

This systematic review emphasises the necessity of reinforcing methodological harmonisation and analytical coherence in the field of food health risk assessment. The synthesis of the 31 studies analysed reveals persistent disparities in toxicological reference values and modelling approaches, underscoring the need for a unified global framework to ensure the comparability and reliability of results. Future research should prioritise the harmonisation of reference values issued by major international agencies such as EFSA, US EPA, WHO, and JECFA, while promoting the integration of probabilistic and mechanistic approaches, including Monte Carlo simulations, PBPK and QSAR models. Such methods allow a more realistic consideration of variability and uncertainty in exposure, thereby improving the robustness of risk characterisation.

In addition, efforts must focus on improving the representativeness and quality of primary data through expanded sampling, transparent uncertainty analysis, and harmonised data reporting protocols. Particular attention should be given to emerging contaminants such as micro- and nanoplastics, plastic additives, and process-related compounds whose toxicological characterisation remains limited. Incorporating cumulative and multi-exposure models will be essential to reflect real-world exposure scenarios and interactions between contaminants.

Finally, international cooperation and capacity building, especially in low- and middle-income countries, are key to reducing geographical disparities in food safety research. Developing regional analytical infrastructures, training programmes, and open-access databases will contribute to more equitable and evidence-based decision-making. Overall, advancing food risk assessment requires the convergence of methodological rigour, probabilistic modelling, and cross-sectoral collaboration to produce harmonised, reliable, and policy-relevant outcomes that can better inform global public health strategies.

5. Conclusion

This systematic review highlights the diversity and heterogeneity of approaches used to assess health risks associated with chemical contaminants in food. While deterministic methods remain predominant due to their simplicity and operational value, probabilistic approaches, such as Monte Carlo simulation, and advanced methods, including PBPK and QSAR models, are progressively emerging as indispensable tools to better capture variability and uncertainty in exposures. The findings also underline concerning risks for certain vulnerable populations, particularly children, in relation to exposure to contaminants such as heavy metals, mycotoxins, or acrylamide. However, the absence of international harmonisation of reference values and methodological protocols still limits the comparability of studies and the formulation of universal recommendations. Ultimately, the adoption of probabilistic and integrative methods, coupled with harmonisation of regulatory frameworks, constitutes an essential step towards strengthening the reliability and relevance of food risk assessments at the global scale.

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CRediT authorship contribution statement

Séfou-Dine Alabi Badarou: Writing-review & editing, Writing-original draft, Visualization, Formal analysis, Conceptualization, Data curation. **Camel Lagnika**: Project administration, Methodology, Validation. **Achille Todègnon Gantongbé**: Conceptualization, Writing-original draft. **Abdou Madjid Amoussa**: Conceptualization, Writing-original draft. **Latifou Lagnika**: Supervision, Writing-original draft.

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