Exposure to Dietary Glycidyl and 3-MCPD Fatty Acid Esters and Associated Burden of Cancer in Selected Asian and European Countries: A Review and Data Synthesis

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ABSTRACT: This study evaluated the health implications and oncological impact of consuming glycidyl esters (GE) and 3-monochloro-1,2-propanediol esters (3-MCPDE) in selected Asian and European populations. Data on dietary GE and 3-MCPDE were compiled from 10 studies conducted in China, Taiwan, Poland, and Spain, identified through a systematic search in PubMed and ScienceDirect databases from 2012 to 2022. Studies on food supplements and analytical methods were excluded from the analysis. Health metrics for these nations, spanning 2015 to 2019, were sourced from the Institute of Health Metrics and Evaluation, among others. A Monte Carlo Simulation was employed for data analysis. The results showed that "grains and grain products" was the most consumed food category (260.45-395.35 g/day), whereas "food for infants and children" was the least consumed (0.01-0.09 g/day). Additionally, "fats from animal or plant origin" had the highest contamination levels. While 3-MCPDE exposures remained within safe limits, median GE exposure correlated with an incidence of colon cancer ranging from 3.66×10^{-8} to 0.744%, lung cancer from 0.00256 to 0.287%, and breast cancer from 0.0262 to 2.42% within the study areas. This translated to a total cancer burden of 6.69 to 1020 Disability-Adjusted Life Years (DALYs) per 100 000 individuals. The population in China recorded the highest DALY rate (1,020), followed by Spain (30.2), Poland (19.7), and Taiwan (6.69). Projections suggest an uptick in GE-related cancer cases and associated burdens in the coming decades attributed to demographic shifts, ageing populations, and dietary changes. The study underscores the urgency of mitigating GE and 3-MCPDE food contamination, bolstering public health awareness, and establishing safety guidelines.

KEYWORDS: 3-MCPD ester, glycidyl ester, dietary exposure, human cancer risk, burden of disease

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Introduction

Cancer remains a formidable challenge in public health, significantly influencing global mortality rates and life expectancy. In 2019, it was a leading cause of death before the age of 70 in over half of the countries worldwide,[1] and by 2020, it was responsible for nearly 10 million deaths.[2] Without strategic interventions at the national level, cancer is poised to continue as a primary cause of premature mortality throughout this century.[3] The World Health Organization (WHO) has identified breast, lung, and colorectal cancers as the most common, with their incidence stemming from an interplay between genetic factors and external agents, such as chemical carcinogens.[2]

Among these external agents, glycidyl esters (GEs) and 3-monochloro-1,2-propanediol fatty acid esters (3-MCPDEs) have been implicated in developing these prevalent cancers.[4] These contaminants are byproducts of the high-temperature deodorization process in edible oil refining, leading to their presence in foods produced with refined oils.[5-7] They are also produced during the thermal treatment of oil-containing foods.[6,8,9] GE and 3-MCPDE are metabolized upon consumption into glycidol and free 3-MCPD, respectively.[10] The International Agency for Research on Cancer (IARC) has categorized free 3-MCPD as a "possible human carcinogen" (category 2B) based on limited data on its carcinogenicity potential.[4] However, it has been associated with other health risks, including nephrotoxicity and reproductive issues.[11-13] These findings led the European Food Safety Authority (EFSA) to recommend a tolerable daily intake (TDI) of 2 µg/kg bw per day for 3-MCPD/3-MCPDE, singly or in combination.[14] Similarly, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) set a maximum combined intake for these compounds at 4 µg/kg bw per day.[15] Glycidol, however, is known for its carcinogenicity in animal models, resulting in its classification as a "probable human carcinogen" (group 2A)[16] and the adoption of the "as low as reasonably achievable" principle for its intake.[4,17]

The margin of exposure (MoE) approach is used to evaluate the carcinogenic risk from dietary GE exposure, with MoEs below 25 000 indicating potential health concerns.[4,6,17] However, this method does not account for the overall contribution of GE to the cancer burden within populations. The burden of disease (BoD) is a comprehensive measure that

Table 1. Studied foods in eligible articles from which data were extracted.

STUDIED FOOD	NO. OF FOOD TYPES	COUNTRY	REFERENCE
Vegetable oil	11	China	Li et al[24]
Infant formula	1	China	Cui et al[7]
Vegetable oil	8	China	Fan et al[25]
Mixed	16	China	Chung et al[26]
Mixed	5	China	Zhang et al[27]
Mixed	3	China	Jiang et al[8]
Vegetable oil	20	Taiwan	Chen et al[28]
Mixed	19	Spain	González et al[9]
Carbohydrate-rich food	60	Poland	Sadowska-Rociek et al[29]
Chocolate	58	Poland	Sadowska-Rociek[30]

captures the impact of a disease on a population, incorporating aspects of morbidity, mortality, and disability. It is quantified in Disability-Adjusted Life Years (DALYs), and 1 DALY represents the loss of 1 year of total health, summing Years of Life Lost due to premature death (YLLs) and Years Lived with Disability (YLDs).[18-20] This metric is pivotal in assessing the health impact of various cancers and understanding the influence of risk factors on the overall disease burden. The IARC's Cancer Surveillance Section has reported over 19 million cancer cases globally, with Asia and Europe accounting for a major portion of these cases.[21] The specific contribution of dietary exposure to GE and 3-MCPDE to the disease burden of these cancers is not well-defined. Consequently, this study aimed to estimate the DALYs attributable to the 3 most prevalent cancers, breast, lung, and colorectal, stemming from dietary exposure to GE and 3-MCPDE in selected countries across Asia and Europe. Thus, this study will provide a clearer picture of the impact of these contaminants on public health.

Methods

Data for exposure estimation

Exposures were quantified based on GE and 3-MCPDE concentrations, mass of contaminated food ingested, and consumer body weight. Concentration data were obtained via a systematic review following PRISMA and Cochrane guidelines.[22,23] Searches were conducted in PubMed and ScienceDirect from January 2012 to December 2022 independently by 2 reviewers (DSY and IWO) using keywords: "3-MCPD," "3-MCPD esters," "glycidol," and "glycidyl esters." The review included the title and abstract screening, followed by a full-text review. Selection criteria were: (1) publication in English with full-text availability, (2) original research from Asia and Europe, and (3) quantitative data on GE and/or 3-MCPDE in commonly consumed foods. Studies on food supplements and analytical methods were excluded. Fifteen articles from 3 Asian and 5 European countries met the criteria. Finally, ten articles from China, Taiwan, Poland, and Spain were selected for the study based on the following inclusion criteria: countries with multiple articles and/or articles covering diverse food types (Table 1). The 2 reviewers extracted information like the author, year of publication, type of food studied, and the concentrations of the contaminants and captured them in Microsoft Excel 2010 software. Afterwards, all the concentration units were converted to mg/kg. The review protocol is summarized in Figure 1.

Daily consumption data for the 4 countries was sourced from WHO's GEMS/Food cluster diets.[31] Although the latest consumption data was dated 2013, it was assumed that cultural influences kept dietary habits consistent, so food consumption patterns were considered stable throughout the study period.[32] Selected food categories matched those identified as contaminated with GE and 3-MCPDE in the studies. In Asian countries, these included fats from animal or plant origin; grains and grain products; meat and meat products; fish and other seafoods; herbs, spices, condiments and sauces; milk and dairy products; fruits and vegetable juices and other non-alcoholic beverages; food for infants and children; and other (snacks and mixed diet). In Europe, categories included fats from animal or plant origin; grains and grain products; food for infants and children; herbs, spices, condiments and sauces; sugar and confectionary, cocoa and cola solid products; starch roots and tubers; and pulses, nuts and oilseeds, categories.

Finally, the WHO standard average body weight of 60 kg was used to calculate exposure levels.[33]

Breast, lung, and colorectal cancer data

Data on the prevalence, mortality, YLLs, and YLDs of breast, lung, and colorectal cancers in China, Taiwan, Poland, and

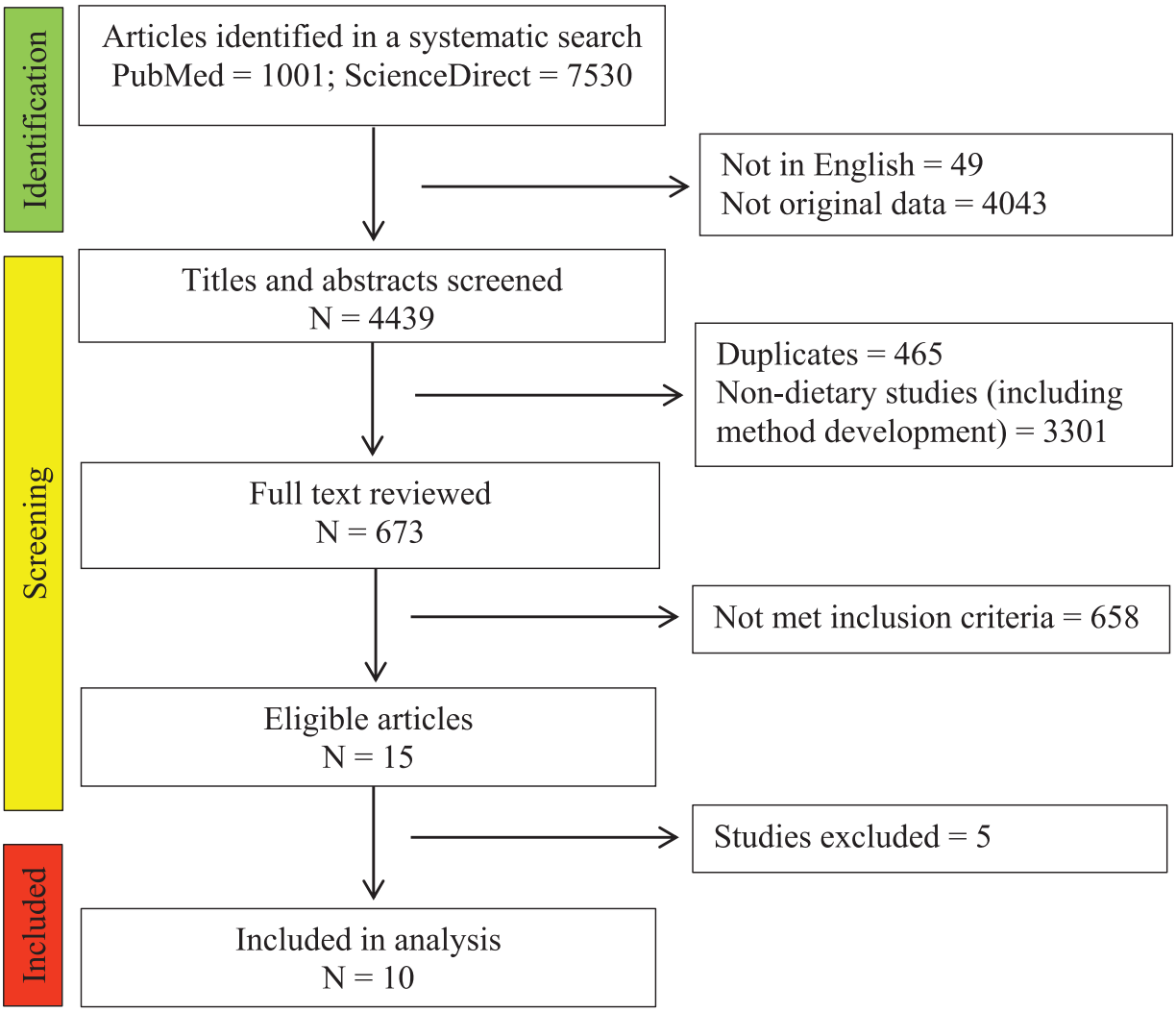

Figure 1. Flow chart of systematic review of literature.

Spain (2015-2019) were obtained from the Global Burden of Disease (GBD) Compare database.[34] Lung and colorectal cancer data included both genders across ages (5-19, 20-54, and 55-89 years), while breast cancer data were exclusive to females, as less than 1% of cases occur in males.[35]

Exposure and cancer risk assessment

The daily exposures to dietary GE in the countries under study were estimated using equation (1).[19,36]

$$E_{EST} = \frac{C \times M_F}{Bw} \quad (1)$$

where E_{EST} = estimated daily exposure, C = concentration distribution of GE or 3-MCPDE, M_F = daily food mass consumed, and Bw = body weight (60 kg).

Due to limited data on the carcinogenicity of 3-MCPDE, cancer risk estimation was not performed. However, glycidol, a GE metabolite, is considered a potential carcinogen.[16] As a result, the California EPA's Office of Environmental Health Hazard Assessment (OEHHA) assigned it a cancer slope factor (CSF) of 1.3 mg/kg bw per day.[37] CSF values vary by cancer type and are determined as outlined in other studies.[20,38] Scaled CSF (CSF_{sp}) for the 3 cancers were derived using mortality (equation (2a)) and prevalence data (equation (2b)):

$$CSF_{sp} = CSF \frac{Mort_{sp}}{Mort_{tot}} = CSF_{LL} \quad (2a)$$

$$CSF_{sp} = CSF \frac{Prev_{sp}}{Prev_{tot}} = CSF_{LD} \quad (2b)$$

where $Mort_{sp}$ and $Prev_{sp}$ represent the mortality and prevalence of specific cancer, while $Mort_{tot}$ and $Prev_{tot}$ represent the total mortality and prevalence for the study period.

Cancer risk from chronic GE exposure was calculated by determining the risk of YLL (R_{LL}) and YLD (R_{LD}) for each cancer type using equations (3a) and (3b):

$$R_{LL} = CSF_{LL} \times E_{EST} \quad (3a)$$

$$R_{LD} = CSF_{LD} \times E_{EST} \quad (3b)$$

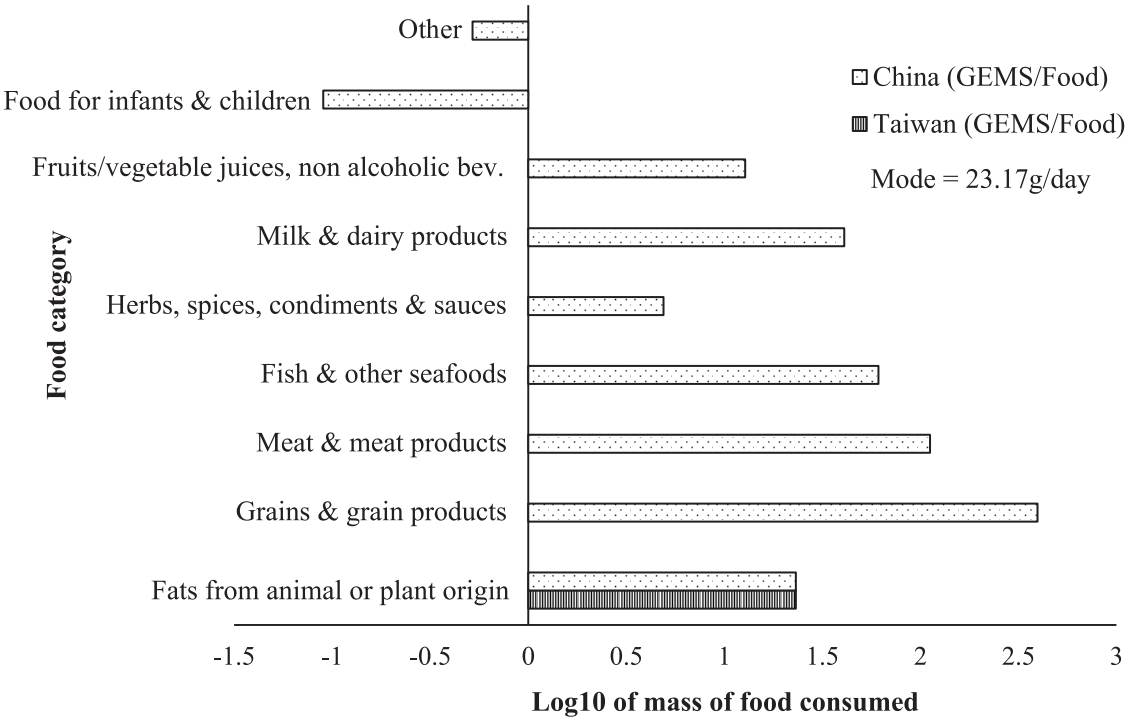

Figure 2. Mass of food consumed in the 2 Asian countries (expressed in Log10).

Burden of disease (BoD)

The BoD, expressed as DALYs, was computed as described by Quartey et al.[19] The primary components for BoD calculation are YLL and YLD. Equations (4a) and (4b) integrated total YLL and mortality data to derive YLL per fatal case (YLL_{pp}) and total YLD and prevalence data to obtain YLD per case (YLD_{pp}):

$$YLL_{pp} = \frac{YLL_{sp}}{Mort_{sp}} \quad (4a)$$

$$YLD_{pp} = \frac{YLD_{sp}}{Prev_{sp}} \quad (4b)$$

For the 5-year (2015-2019) period, the GE-induced specific cancer prevalence (5-YRC) resulting in YLL (5-YRC_{LL}) and YLD (5-YRC_{LD}) were estimated according to equations (5a) and (5b):

$$5 - YRC_{LL} = \frac{N_{pop}}{LE_{pop}} \times R_{LL} \quad (5a)$$

$$5 - YRC_{LD} = \frac{N_{pop}}{LE_{pop}} \times R_{LD} \quad (5b)$$

where N_{pop} and LE_{pop} are the specific 2019 national populations[39,40] and national age-related life expectancies,[41] respectively.

Subsequently, GE-induced YLL and YLD distributions for each cancer type were calculated using equations (6a) and (6b), and specific DALY rates per 100 000 population were estimated by summing individual YLL_{sp} and YLD_{sp} (equation (7)):

$$YLL_{sp} = 5 - YRC_{LL} \times YLL_{pp} \quad (6a)$$

$$YLD_{sp} = 5 - YRC_{LD} \times YDL_{pp} \quad (6b)$$

$$DALY_{sp} = YLL_{sp} + YDL_{sp} \quad (7)$$

Data analysis by probabilistic approach

Monte Carlo simulations were used to quantify uncertainties and harmonize estimates, as recommended by Maertens et al.[42] The Palisade @Risk software facilitated distribution fitting and simulation over 10^5 iterations. The mode and median were analyzed to mitigate outlier bias.[43]

Results and Discussion

The mass of food consumed

Figure 2 shows the masses of food categories (expressed in Log10) consumed between 2012 and 2019 in the selected Asian countries. The average daily intake per person ranged from 0.09 g (log10 = −1.05) to 395.35 g (log10 = 2.60). "Grains and grain products" was the most consumed, followed by "meat and meat products" at 111.92 g/day (log10 = 2.05). The least consumed category was "food for infants and children." In comparison, China's consumption data in 2022 indicated a decrease in average daily grain consumption to 328.25 g/person, while "vegetables and mushrooms" surpassed "meat and meat products" as the second most consumed category, averaging 313.28 g/person.[44] Taiwan's dietary survey, limited to vegetable oils ("fats from animal or plant origin"), showed an average consumption of

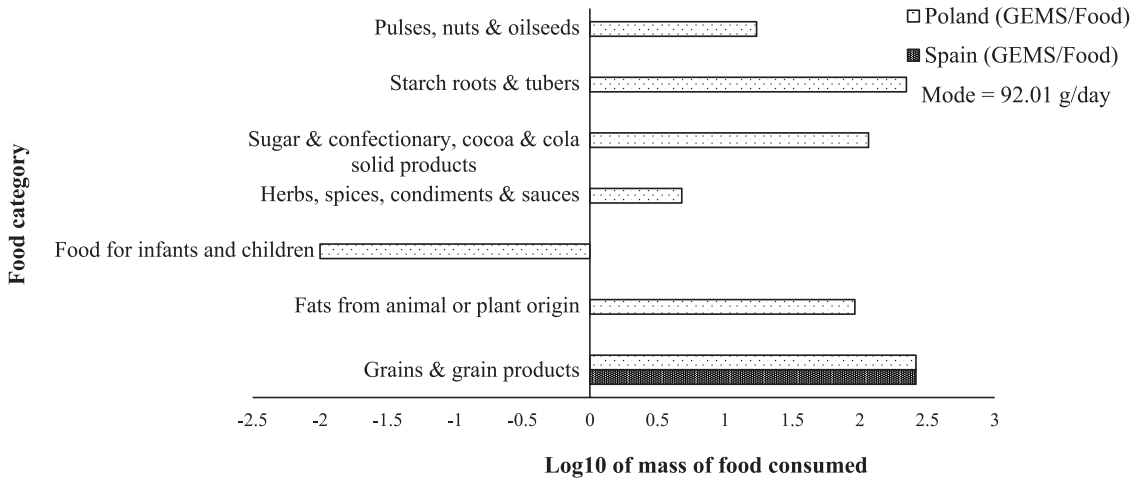

Figure 3. Mass of food consumed in 2 European countries (expressed in Log10).

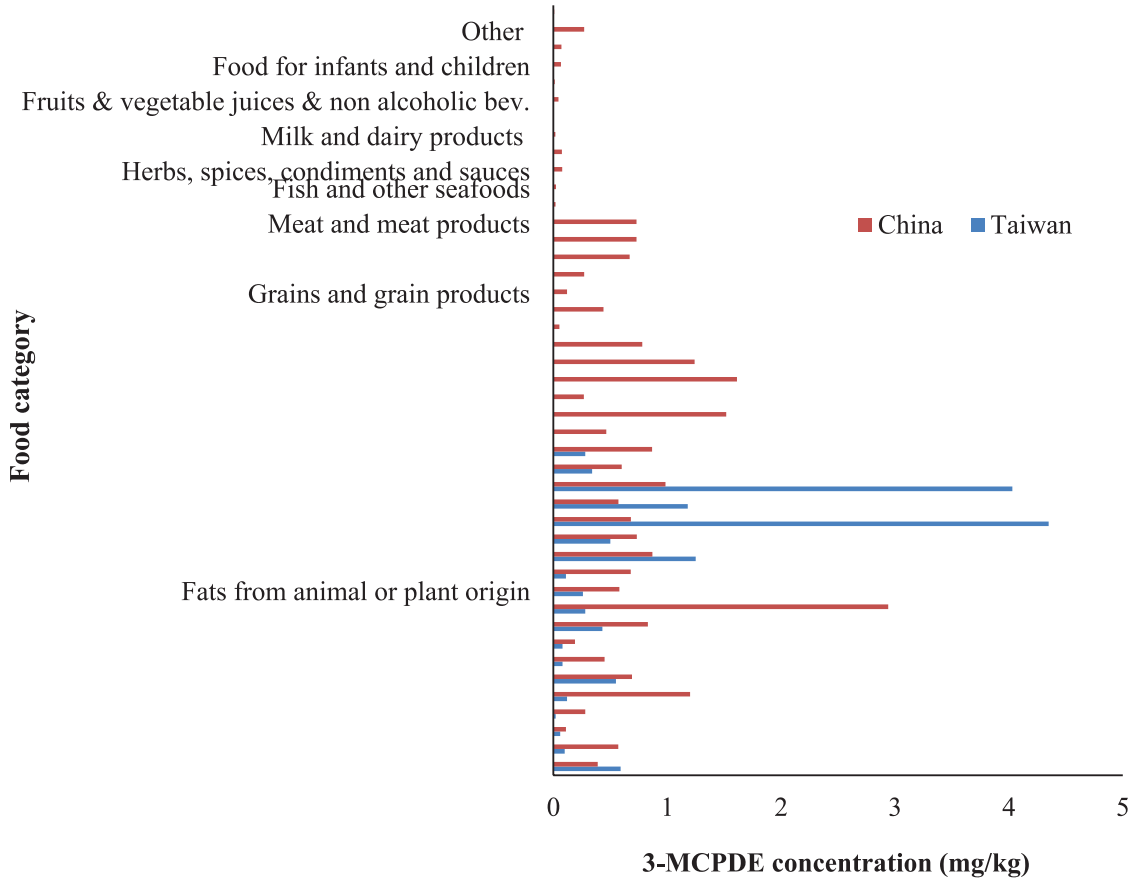

Figure 4. 3-MCPDE concentration in food categories from the 2 Asian countries.

23.17 g/day (log10 = 1.36), aligning both Taiwan and China within the G09 food cluster of the WHO's GEMS/Food Clusters Diets.[31]

The masses of food categories consumed by the selected European countries are shown in Figure 3. "Grains and grain products" was the highest consumed food category in Spain and Poland at 260.45 g/day (log10 = 2.42), while "food for infants and children" was the least consumed at 0.01 g/day (log10 = −2). Both countries were categorized within the G08 cluster due to similar dietary patterns.[31]

GE and 3-MCPDE concentrations in foods

The GE and 3-MCPDE concentrations in the studied foods are shown in Figures 4 through 7. In Asian countries, 3-MCPDE concentrations varied from 7.28×10^{-3} mg/kg (other: snacks and mixed diet) to 4.35 mg/kg (fats from animal or plant origin) (Figure 4). European studies showed a range from 6.7×10^{-4} mg/kg (grains and grain products) to 2.27 mg/kg ("fats from animal or plant origin") (Figure 5). Similarly, the GE concentrations of studied foods in Asia

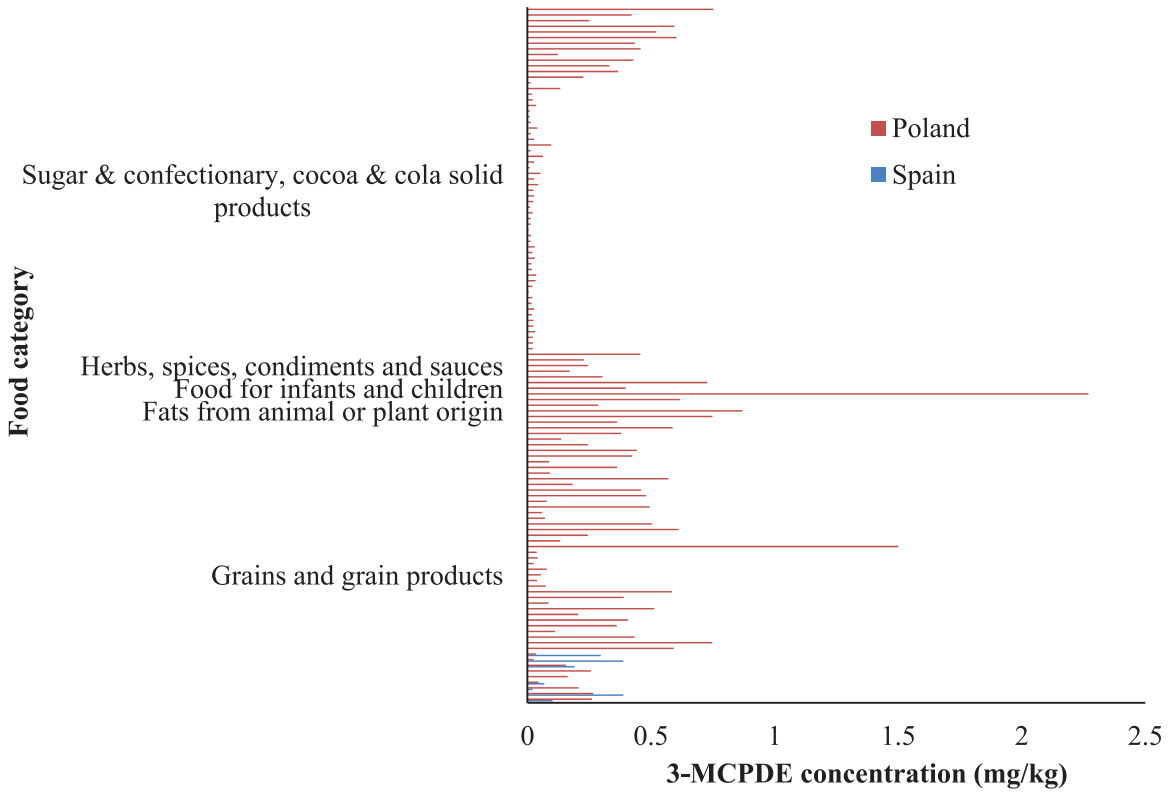

Figure 5. 3-MCPDE concentration in food categories from the 2 European countries.

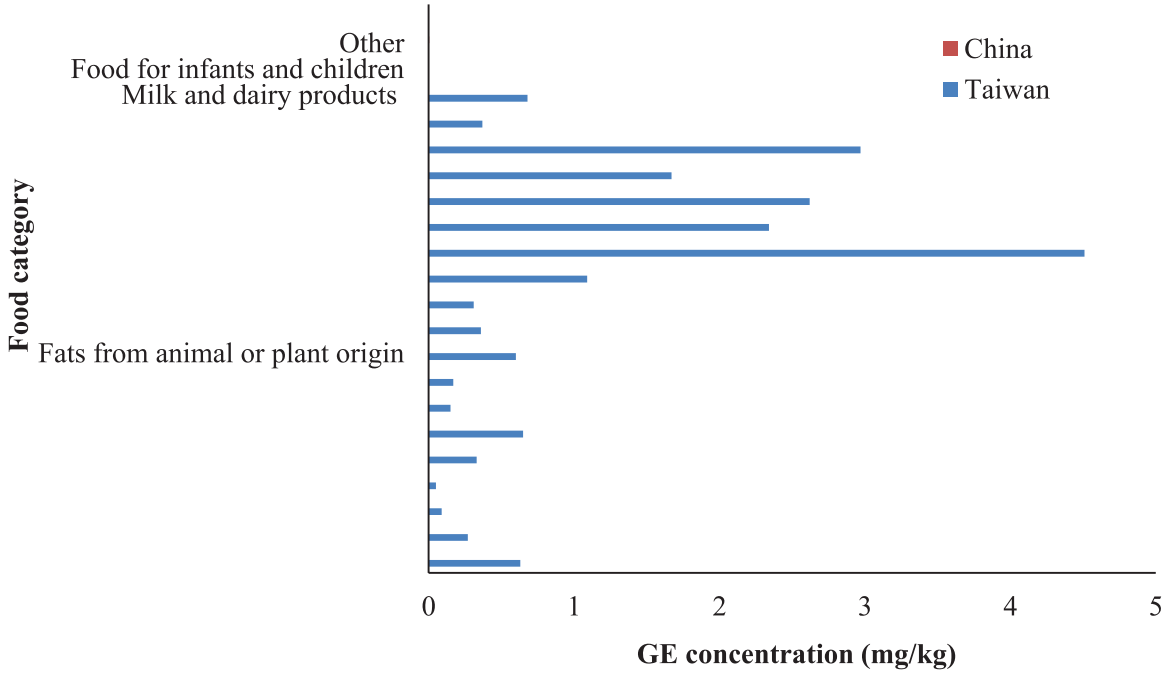

Figure 6. GE concentration in food categories from the 2 Asian countries.

ranged from 1.05×10^{-3} mg/kg (milk and dairy products) to 4.51 mg/kg (fats from animal or plant origin) (Figure 6), and that of Europe ranged from 1.0×10^{-3} mg/kg (grains and grain products) to 0.737 (fats from animal or plant origin) (Figure 7). Notably, "fats from animal or plant origin" consistently exhibited the highest contamination levels, corroborating previous findings of significant GE and 3-MCPDE presence in refined fats and oils, particularly palm oil derivatives.[45-47] The formation of these toxicants predominantly occurs during the deodorization phase of oil refining.[48] Reports have indicated varying levels of GE (0.33-6.29 mg/kg) and 3-MCPDE (2.49-6.61 mg/kg) in refined palm oils across different regions, including the United States,[45] Brazil,[47] and Russia.[46] These findings are consistent with the

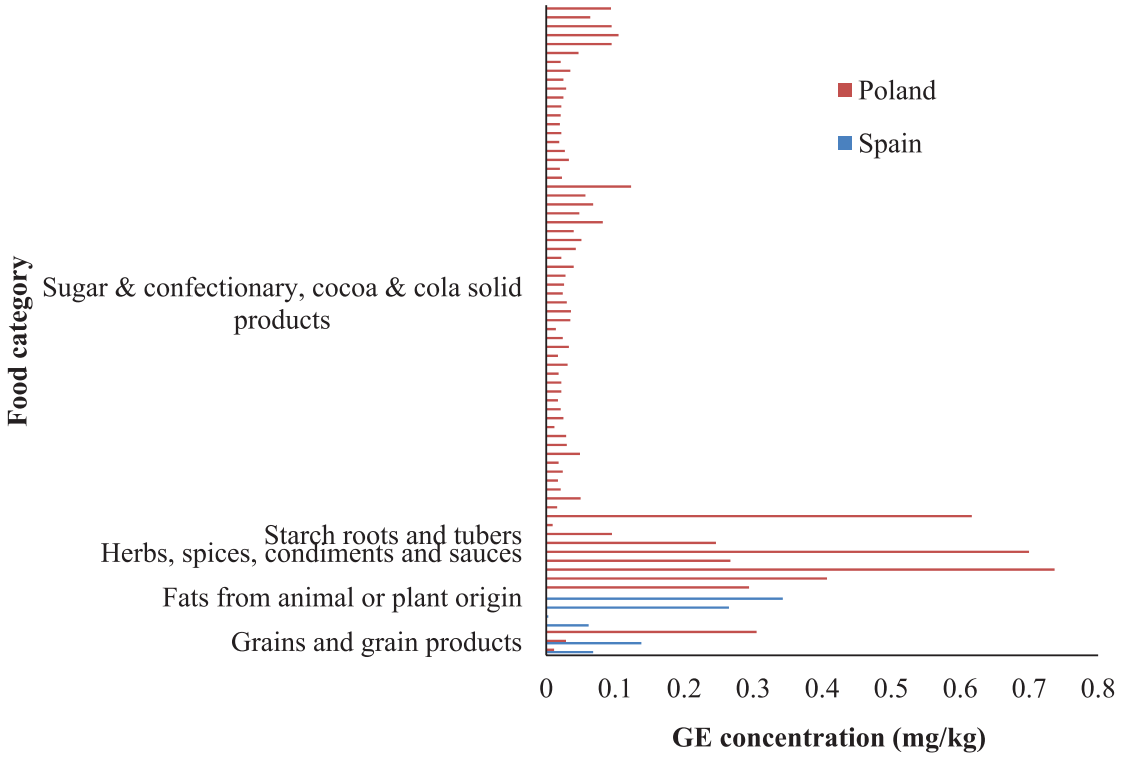

Figure 7. GE concentration in food categories from the 2 European countries.

Table 2. Statistical distribution of dietary GE and 3-MCPDE occurrence and estimated exposures in Asian and European countries.

MEASURE	HAZARD	CHINA-TAIWAN		POLAND-SPAIN	
		MODE	MEDIAN	MODE	MEDIAN
Level (mg/kg)	3-MCPDE	1.87×10^{-2}	4.30×10^{-1}	1.30×110^{-2}	9.10×110^{-2}
	GE	2.30×10^{-3}	3.60×10^{-1}	2.10×110^{-2}	3.00×110^{-2}
Exposure (μg/kg bw/day)	3-MCPDE	1.89×10^{-4}	1.64×10^{-1}	3.03×110^{-2}	2.20×10^{-1}
	GE	7.25×10^{-4}	9.20×110^{-2}	3.06×110^{-2}	7.22×110^{-2}

contamination levels observed in this study. Unrefined oils generally contained negligible amounts of these contaminants, with exceptions like sesame oil, which may contain up to 0.22 mg/kg of GE and 0.45 mg/kg of 3-MCPDE.[47] Notably, GE and 3-MCPDE in other food categories can be attributed to using contaminated oils in production,[5,49] thermal processing,[26] and enzymatic pathways in non-thermally treated foods.[50]

GE and 3-MCPDE exposure

The distributions of the dietary occurrence and exposure estimates for GE and 3-MCPDE are presented in Table 2. The China-Taiwan region exhibited a slightly higher modal dietary concentration of 3-MCPDE (1.87×110^{-2} mg/kg) than the Poland-Spain region (1.30×110^{-2} mg/kg). Conversely, the exposure level of 3-MCPDE was more significant in the Poland-Spain region (3.03×110^{-2} μg/kg bw per day) than in the China-Taiwan region (1.89×10^{-4} μg/kg bw per day). The most frequently occurring (modal) dietary GE occurrence and exposure levels followed a similar pattern of regional disparity, with the Poland-Spain region having higher estimates than the China-Taiwan region. These differences are influenced by the quantity of food consumed and the concentration of toxicants within those foods. The study also observed a trend of higher dietary 3-MCPDE concentrations than GE, aligning with other dietary studies.[51,52] The synthesis of 3-MCPDE is contingent upon chlorine ions; higher chloride ion levels in food lead to increased 3-MCPDE concentrations.[53] Furthermore, at elevated temperatures (280-290°C), GEs are reported to degrade shortly after formation.[54] The exposure levels to 3-MCPDE were significantly below the PMTDI set by JECFA at 4 μg/kg bw per day[15] and the TDI by EFSA at 2 μg/kg bw per day.[14] This observation indicates a negligible risk of 3-MCPD toxicity. However, any level of GE is a health concern due to the absence of a safe threshold.[4]

GE risk characterization

The risk of life lost (R_{LL}) and risk of life with disability (R_{LD}) due to breast, lung, and colorectal cancers across all age groups in China, Taiwan, Poland, and Spain are detailed in Tables 3 and 4. A consistent trend was observed, with R_{LL} and R_{LD} estimates increasing from younger to older populations within these regions. Notably, the modal R_{LL} and R_{LD} for the 3 cancers were below the significance threshold ($<1010^{-6}$) for all age groups, suggesting a low incidence of cancer-related mortality and morbidity from dietary GE exposure. In contrast, median R_{LL} and R_{LD} values for adults (20-89 years) were above the significance threshold ($>10^{-6}$). However, for the younger demographic (3-19 years), median R_{LL} values indicated a marginal risk (~1010^{-6}), except in China, where significant risks for lung (male: 2.48×10^{-5}; female: 1.340×1010^{-5}) and colorectal (male: 2.49×1010^{-5}; female: 1.32×1010^{-5}) cancers were recorded, and in Taiwan for males with colorectal cancer (1.12×1010^{-5}). For R_{LD}, most young age groups exhibited significant median risks for breast and colorectal cancers, except females in Spain, who displayed a marginal median risk (7.50×1010^{-6}) for colorectal cancer. The median R_{LD} for lung cancer remained marginal across all young age groups in the 4 countries.

The general trend in most dietary studies is that younger people have higher GE exposure than older groups.[6,24] Therefore, it was expected that these exposures would translate into a higher risk of GE-induced cancer deaths and disability among children than adults. However, this study found lower GE-induced cancer risks among children than adults. This could be due to underreported childhood cancer cases, as many countries lack comprehensive cancer registries.[55] Additionally, advancements in age are recognized as a significant cancer risk factor.[56] More so, improvements in childhood cancer treatments have led to better survival rates over the past 7 decades.[57]

Sex-specific disparities in cancer incidence and outcomes are increasingly evident, with males generally facing higher mortality risks than females, especially for lung and colorectal cancers.[58,59] This study corroborates previous findings, showing higher R_{LL} and R_{LD} estimates for males across all age groups for GE-related lung and colorectal cancers. Such differences may stem from biological variances between sexes, including genetic polymorphisms affecting drug metabolism,[60] hormonal influences such as estrogen's role in bile acid excretion,[61] testosterone's link to certain cancers,[62] and the potential for a more robust immune response against tumors in females due to X chromosome-linked tumor suppressor genes.[63]

Burden of disease

This study quantified and presented the overall burden of breast, lung, and colorectal cancers attributable to dietary exposure to GE in terms of DALYs. This approach assists policymakers and the public in comprehending the health risks of this toxicant, informing policy development and resource allocation for mitigating its presence in food. Tables 5 through 8 detail age- and gender-specific estimates for the 5-year cancer prevalence (5-YRC_{LD}), YLLs, YLDs, and DALYs per 100 000 population in China, Taiwan, Poland, and Spain from 2015 to 2019. The 5-YRC_{LD} prevalence of the 3 cancers increased with age, affirming the influence of ageing on cancer development.[56] However, modal 5-YRC_{LD} prevalences were low (10^{-14} to 10^{-3}), resulting in negligible modal percentages (1010^{-16} to 10^{-8}%) of GE-induced cancers in the study areas. China exhibited the highest median 5-YRC_{LD} prevalence for GE-induced breast cancer (245-581 000 cases), lung cancer (47.5-302 000 cases), and colorectal cancer (0.000342-186 000 cases) during the study period (Table 5). Males generally had higher median 5-YRC_{LD} prevalences than females, except in specific age groups in China (55-89 years) and Poland (5-19 years), where females exhibited higher lung cancer prevalences. Compared to national cancer cases, the median percentages of breast (0.0262-2.42%), lung (0.00256-0.287%), and colorectal (3.66×10^{-8} to 0.744%) cancers induced by dietary GE were low across all 4 countries.

The modal DALYs estimated for the 4 countries were very low (1010^{-13} to 1010^{-9}), except for Spain, which recorded 15.4 years of life lost per 100 000 population for the 55 to 89-year-old group, potentially due to higher modal GE exposure levels in the Poland-Spain area. Conversely, median DALYs were higher, with China (1020 years of life lost per 100 000 population) recording a higher total median DALY than Taiwan (6.69 years of life lost per 100 000 population) (Tables 5 and 6) and Spain (30.2 years of life lost per 100 000 population) exceeding Poland (19.7 years of life lost per 100 000 population) (Tables 7 and 8). The relative contributions of YLLs (60.5-100%) to DALYs surpassed those of YLDs (0-39.5%) across the study areas, emphasizing mortality as a primary driver of cancer's impact on population health.[64] YLLs and YLDs increased with age, leading to an age-dependent rise in DALYs. Additionally, males experienced higher YLLs and YLDs than females, translating to a more significant cancer burden among males (0.00096 to 391 years of life lost per 100 000 population) compared to females (0.000402 to 134 years of life lost per 100 000 population).

Only 2 studies have assessed cancer risk based on in vivo doses of glycidol. One study using a multiplicative risk model estimated that lifetime exposure to glycidol could result in 200 cancer cases per 100 000 Swedish children.[65] Another study projected 0.08 to 0.52 cancer cases per year per 100 000 population and 16.8 to 41.6 cancer cases per 100 000 children in Italy based on varying exposure scenarios.[66] It is important to note that the current study focused on dietary fatty acid esters of glycidol rather than free glycidol, complicating direct comparisons with these studies. Glycidol has been implicated in

Table 3. Modal and median risk of years of life lost for breast, lung, and colorectal cancers of age groups in the study areas.

AGE GROUP (YEARS)		RISK OF YEARS OF LIFE LOST									
		CHINA					TAIWAN				
		BREAST CANCER	LUNG CANCER		COLORECTAL CANCER		BREAST CANCER	LUNG CANCER		COLORECTAL CANCER	
	GENDER	FEMALE	MALE	FEMALE	MALE	FEMALE	FEMALE	MALE	FEMALE	MALE	FEMALE
	STATISTICS										
5-19	Mode	3.77×10^{-16}	2.26×10^{-15}	1.16×10^{-15}	2.30×10^{-15}	1.21×10^{-15}	2.25×10^{-15}	5.51×10^{-15}	4.87×10^{-15}	1.65×10^{-14}	9.04×10^{-15}
	Median	4.12×1010^{-6}	2.48×1010^{-5}	1.340×1010^{-5}	2.49×1010^{-5}	1.32×1010^{-5}	1.51×1010^{-6}	3.72×1010^{-6}	3.28×1010^{-6}	1.12×1010^{-5}	6.15×1010^{-6}
20-54	Mode	4.20×10^{-13}	1.13×10^{-12}	4.84×1010^{-13}	4.61×1010^{-13}	2.26×1010^{-13}	4.35×1010^{-12}	3.97×1010^{-12}	2.66×1010^{-12}	4.36×1010^{-12}	2.38×1010^{-12}
	Median	5.22×10^{-3}	1.13×110^{-2}	5.13×10^{-3}	5.69×10^{-3}	2.49×10^{-3}	2.92×10^{-3}	2.68×10^{-3}	1.81×10^{-3}	2.98×10^{-3}	1.62×10^{-3}
55-89	Mode	9.44×1010^{-13}	7.83×1010^{-12}	3.00×1010^{-12}	2.09×1010^{-12}	1.24×1010^{-12}	7.97×1010^{-12}	3.32×10^{-11}	1.88×10^{-11}	2.52×10^{-11}	1.68×10^{-11}
	Median	1.07×110^{-2}	7.99×110^{-2}	3.26×110^{-2}	2.14×110^{-2}	1.31×110^{-2}	5.36×10^{-3}	2.22×110^{-2}	1.25×110^{-2}	1.73×110^{-2}	1.15×110^{-2}
	POLAND						SPAIN				
5-19	Mode	1.89×1010^{-16}	3.27×1010^{-16}	4.35×1010^{-16}	1.16×10^{-15}	5.17×1010^{-16}	1.91×10^{-15}	3.69×10^{-15}	2.76×10^{-15}	3.30×10^{-15}	2.27×10^{-15}
	Median	1.49×1010^{-6}	2.56×1010^{-6}	3.40×1010^{-6}	9.13×1010^{-6}	4.06×1010^{-6}	2.14×1010^{-6}	4.24×1010^{-6}	3.12×1010^{-6}	3.75×1010^{-6}	2.56×1010^{-6}
20-54	Mode	4.06×1010^{-13}	5.81×1010^{-13}	2.56×1010^{-13}	2.53×1010^{-13}	1.58×1010^{-13}	2.71×1010^{-12}	3.37×1010^{-12}	1.57×1010^{-12}	1.35×1010^{-12}	9.86×1010^{-13}
	Median	3.20×10^{-3}	4.58×10^{-3}	2.00×10^{-3}	1.97×10^{-3}	1.23×10^{-3}	3.05×10^{-3}	3.81×10^{-3}	1.78×10^{-3}	1.52×10^{-3}	1.12×10^{-3}
55-89	Mode	2.22×1010^{-12}	7.14×1010^{-12}	3.09×1010^{-12}	3.09×1010^{-12}	2.46×1010^{-12}	1.09×10^{-11}	7.92×1010^{-12}	3.38×10^{-11}	2.06×10^{-11}	1.29×10^{-11}
	Median	1.73×110^{-2}	5.49×110^{-2}	2.44×110^{-2}	2.43×110^{-2}	1.93×110^{-2}	1.24×110^{-2}	8.96×10^{-3}	3.82×110^{-2}	2.14×110^{-2}	1.46×110^{-2}

Table 4. Modal and median risk of years of life lived with disability for breast, lung, and colorectal cancers of age groups in the study areas.

AGE GROUP (YEARS)		RISK OF YEARS OF LIFE WITH DISABILITY									
		CHINA					TAIWAN				
		BREAST CANCER	LUNG CANCER		COLORECTAL CANCER		BREAST CANCER	LUNG CANCER		COLORECTAL CANCER	
	GENDER	FEMALE	MALE	FEMALE	MALE	FEMALE	FEMALE	MALE	FEMALE	MALE	FEMALE
	STATISTICS										
5-19	Mode	1.83×1010^{-13}	5.85×10^{-14}	3.55×10^{-14}	3.47×1010^{-13}	1.75×1010^{-13}	7.11×10^{-14}	9.15×10^{-15}	8.65×10^{-15}	1.57×1010^{-13}	8.51×10^{-14}
	Median	1.16×1010^{-5}	3.72×1010^{-6}	2.27×1010^{-6}	2.22×1010^{-5}	1.12×1010^{-5}	4.69×1010^{-5}	6.02×1010^{-6}	5.69×1010^{-6}	1.04×10^{-4}	5.60×1010^{-5}
20-54	Mode	1.30×10^{-10}	1.20×10^{-11}	6.34×1010^{-12}	5.64×10^{-11}	2.57×10^{-11}	6.57×10^{-11}	2.78×1010^{-12}	2.11×1010^{-12}	3.06×10^{-11}	1.76×10^{-11}
	Median	8.27×10^{-3}	7.63×10^{-4}	4.00×10^{-4}	3.60×10^{-3}	1.64×10^{-3}	4.34×110^{-2}	1.83×10^{-3}	1.40×10^{-3}	2.01×110^{-2}	1.16×110^{-2}
55-89	Mode	1.56×10^{-10}	5.65×10^{-11}	2.25×10^{-11}	1.22×10^{-10}	7.24×10^{-11}	7.46×10^{-11}	1.12×10^{-11}	7.07×1010^{-12}	8.78×10^{-11}	5.73×10^{-11}
	Median	1.00×110^{-2}	3.57×10^{-3}	1.44×10^{-3}	7.74×10^{-3}	4.63×10^{-3}	4.91×110^{-2}	7.41×10^{-3}	4.60×10^{-3}	5.77×110^{-2}	3.76×110^{-2}
	POLAND						SPAIN				
5-19	Mode	3.08×10^{-15}	2.70×1010^{-16}	3.78×1010^{-16}	2.11×10^{-15}	2.14×10^{-15}	8.41×10^{-15}	8.89×1010^{-16}	7.52×1010^{-6}	4.35×10^{-15}	3.14×10^{-15}
	Median	1.62×1010^{-5}	1.42×1010^{-6}	1.99×1010^{-6}	1.11×1010^{-5}	1.11×1010^{-5}	2.00×1010^{-5}	2.10×1010^{-6}	1.79×1010^{-6}	1.03×1010^{-5}	7.50×1010^{-6}
20-54	Mode	3.54×1010^{-12}	1.67×1010^{-13}	8.51×10^{-14}	5.92×1010^{-13}	4.41×1010^{-13}	7.30×1010^{-12}	4.15×1010^{-13}	1.95×1010^{-13}	1.35×1010^{-12}	1.10×1010^{-12}
	Median	1.86×110^{-2}	8.75×10^{-4}	4.46×10^{-4}	3.12×10^{-3}	2.32×10^{-3}	1.71×110^{-2}	9.88×10^{-4}	4.66×10^{-4}	3.20×10^{-3}	2.63×10^{-3}
55-89	Mode	9.36×1010^{-12}	1.34×1010^{-12}	6.00×1010^{-13}	3.45×1010^{-12}	2.45×1010^{-12}	1.48×10^{-11}	2.50×1010^{-12}	4.17×1010^{-13}	9.46×1010^{-12}	6.20×1010^{-12}
	Median	4.92×110^{-2}	7.01×10^{-3}	3.16×10^{-3}	1.80×10^{-1}	1.28×110^{-2}	3.51×110^{-2}	5.95×10^{-3}	9.90×10^{-4}	2.26×110^{-2}	1.47×110^{-2}

Table 5. Estimations of 5-YRC$_{LD}$s, YLLs, YLDs, and DALYs for breast, lung, and colorectal cancers among different age or sex groups in China.

AGE GROUP (YEARS)	GENDER	5-YRC$_{LD}$		YLL		YLD		DALY		% CANCER	
		MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN
		BREAST CANCER									
5-19	Female	3.66×1010^{-6}	2.45×10^{2}	5.23×1010^{-12}	6.00×110^{-2}	3.42×1010^{-12}	2.28×10^{-4}	8.65×1010^{-12}	6.02×110^{-2}	3.92×10^{-10}	2.62×110^{-2}
20-54		4.24×10^{-3}	5.81×10^{5}	3.92×1010^{-9}	4.64×10	2.42×1010^{-9}	1.62×10^{-1}	6.34×1010^{-9}	4.66×10	1.24×10^{-8}	8.27×10^{-1}
55-89		3.14×10^{-3}	2.11×10^{5}	4.35×1010^{-9}	5.00×10	2.71×1010^{-9}	1.80×10^{-1}	7.06×1010^{-9}	5.02×10	1.20×10^{-8}	8.07×10^{-1}
LUNG CANCER											
5-19	Male	1.63×10^{-7}	8.99×10	2.34×1010^{-12}	4.21×10^{-1}	2.03×1010^{-13}	1.12×10^{-4}	2.54×1010^{-12}	4.21×10^{-1}	1.40×10^{-11}	7.74×10^{-3}
	Female	7.14×1010^{-7}	4.75×10	3.30×10^{-11}	3.73×10^{-1}	8.67×1010^{-13}	5.79×1010^{-5}	3.39×10^{-11}	3.73×10^{-1}	7.64×10^{-11}	5.09×10^{-3}
20-54	Male	3.32×1010^{-5}	1.84×10^{4}	7.21×10^{-10}	1.11×10^{2}	6.14×10^{-11}	3.39×110^{-2}	7.82×10^{-10}	1.11×10^{2}	2.03×10^{-10}	1.12×10^{-1}
	Female	1.27×10^{-4}	8.43×10^{3}	4.02×1010^{-9}	4.43×10	2.16×10^{-10}	1.45×110^{-2}	4.24×1010^{-9}	4.43×10	6.00×10^{-10}	3.99×110^{-2}
55-89	Male	1.57×10^{-4}	8.61×10^{4}	2.39×1010^{-9}	3.91×10^{2}	3.22×10^{-10}	1.77×10^{-1}	2.71×1010^{-9}	3.91×10^{2}	4.52×10^{-10}	2.48×10^{-1}
	Female	4.58×10^{-4}	3.02×10^{5}	1.24×10^{-8}	1.34×10^{2}	9.19×10^{-10}	6.15×110^{-2}	1.33×10^{-8}	1.34×10^{2}	1.75×1010^{-9}	1.15×10^{-1}
COLORECTAL CANCER											
5-19	Male	9.62×1010^{-7}	5.33×10^{2}	2.35×1010^{-12}	4.06×10^{-1}	1.18×1010^{-12}	6.52×10^{-4}	3.53×1010^{-12}	4.07×10^{-1}	8.29×10^{-11}	4.59×110^{-2}
	Female	5.05×1010^{-12}	3.42×10^{-4}	1.89×10^{-11}	2.02×10^{-1}	6.08×10^{-18}	4.13×10^{-10}	1.89×10^{-11}	2.02×10^{-1}	5.40×1010^{-16}	3.66×10^{-8}
20-54	Male	1.58×10^{-4}	8.66×10^{4}	2.96×10^{-10}	5.71×10	1.61×10^{-10}	8.86×110^{-2}	4.57×10^{-10}	5.72×10	9.66×10^{-10}	5.29×10^{-1}
	Female	5.16×10^{-4}	3.45×10^{4}	2.08×1010^{-9}	2.28×10	6.19×10^{-10}	4.16×110^{-2}	2.70×1010^{-9}	2.28×10	2.44×1010^{-9}	1.63×10^{-1}
55-89	Male	3.38×10^{-4}	1.86×10^{5}	7.10×10^{-10}	1.04×10^{2}	3.69×10^{-10}	2.02×10^{-1}	1.08×1010^{-9}	1.04×10^{2}	9.74×10^{-10}	5.37×10^{-1}
	Female	1.46×10^{-3}	9.74×10^{4}	4.99×1010^{-9}	5.22×10	1.52×1010^{-9}	1.01×10^{-1}	6.51×1010^{-9}	5.23×10	5.58×1010^{-9}	3.72×10^{-1}
	Total	1.06×110^{-2}	1.61×10^{6}	3.59×10^{-8}	1.01×10^{3}	9.32×1010^{-9}	1.06	4.53×10^{-8}	1.02×10^{3}	3.79×10^{-8}	3.83

Table 6. Estimations of 5-YRC$_{LD}$s, YLLs, YLDs, and DALYs for breast, lung, and colorectal cancers among different age or sex groups in Taiwan.

AGE GROUP (YEARS)	GENDER	5-YRC$_{LD}$		YLL		YLD		DALY		% CANCER	
		MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN
		BREAST CANCER									
5-19	Female	1.68×10^{-8}	4.99	5.53×1010^{-13}	3.98×10^{-4}	1.45×10^{-14}	4.30×1010^{-6}	5.68×1010^{-13}	4.02×10^{-4}	9.08×10^{-11}	2.69×110^{-2}
20-54		1.56×1010^{-5}	4.62×10^{3}	6.32×10^{-10}	4.55×10^{-1}	1.44×10^{-11}	4.23×10^{-3}	6.46×10^{-10}	4.59×10^{-1}	2.49×1010^{-9}	7.36×10^{-1}
55-89		1.77×1010^{-5}	5.23×10^{3}	6.36×10^{-10}	4.63×10^{-1}	1.43×10^{-11}	4.21×10^{-3}	6.50×10^{-10}	4.67×10^{-1}	1.89×1010^{-9}	5.59×10^{-1}
LUNG CANCER											
5-19	Male	2.10×10^{-10}	6.70×10^{-1}	1.34×1010^{-12}	9.59×10^{-4}	2.29×1010^{-16}	7.31×1010^{-7}	1.34×1010^{-12}	9.60×10^{-4}	8.62×1010^{-13}	2.75×10^{-3}
	Female	2.05×1010^{-9}	6.05×10^{-1}	1.21×1010^{-12}	8.81×10^{-4}	2.22×10^{-15}	6.53×1010^{-7}	1.21×1010^{-12}	8.82×10^{-4}	1.10×10^{-11}	3.26×10^{-3}
20-54	Male	6.37×10^{-8}	2.03×10^{2}	5.54×10^{-10}	3.93×10^{-1}	1.15×1010^{-13}	3.68×10^{-4}	5.54×10^{-10}	3.93×10^{-1}	1.24×10^{-11}	3.96×110^{-2}
	Female	5.03×1010^{-7}	1.49×10^{2}	3.83×10^{-10}	2.79×10^{-1}	8.82×1010^{-13}	2.59×10^{-4}	3.84×10^{-10}	2.79×10^{-1}	8.01×10^{-11}	2.37×110^{-2}
55-89	Male	2.58×1010^{-7}	8.23×10^{2}	2.16×1010^{-9}	1.52	5.88×1010^{-13}	1.87×10^{-3}	2.16×1010^{-9}	1.52	2.19×10^{-11}	6.97×110^{-2}
	Female	1.66×1010^{-6}	4.89×10^{2}	1.22×1010^{-9}	8.85×10^{-1}	3.56×1010^{-12}	1.05×10^{-3}	1.22×1010^{-9}	8.86×10^{-1}	1.78×10^{-10}	5.23×110^{-2}
COLORECTAL CANCER											
5-19	Male	3.62×1010^{-9}	1.16×10	3.91×1010^{-12}	2.91×10^{-3}	4.03×10^{-15}	1.28×1010^{-5}	3.91×1010^{-12}	2.92×10^{-3}	1.49×10^{-11}	4.74×110^{-2}
	Female	1.63×1010^{-12}	4.97×10^{-4}	2.24×1010^{-12}	1.65×10^{-3}	1.79×10^{-18}	5.50×10^{-10}	2.24×1010^{-12}	1.65×10^{-3}	8.76×10^{-15}	2.68×1010^{-6}
20-54	Male	7.03×1010^{-7}	2.23×10^{3}	6.11×10^{-10}	4.54×10^{-1}	6.98×1010^{-13}	2.22×10^{-3}	6.12×10^{-10}	4.56×10^{-1}	1.37×10^{-10}	4.36×10^{-1}
	Female	4.18×1010^{-6}	1.23×10^{3}	3.48×10^{-10}	2.56×10^{-1}	4.60×1010^{-12}	1.36×10^{-3}	3.53×10^{-10}	2.57×10^{-1}	6.65×10^{-10}	1.96×10^{-1}
55-89	Male	2.05×1010^{-6}	6.52×10^{3}	1.64×1010^{-9}	1.21	2.14×1010^{-12}	6.81×10^{-3}	1.64×1010^{-9}	1.22	1.73×10^{-10}	5.53×10^{-1}
	Female	1.36×1010^{-5}	4.02×10^{3}	1.02×1010^{-9}	7.40×10^{-1}	1.43×10^{-11}	4.22×10^{-3}	1.03×1010^{-9}	7.44×10^{-1}	1.46×1010^{-9}	4.30×10^{-1}
	Total	5.63×1010^{-5}	2.55×10^{4}	9.21×1010^{-9}	6.66	5.56×10^{-11}	2.66×110^{-2}	9.27×1010^{-9}	6.69	7.23×1010^{-9}	3.18

Table 7. Estimations of 5-YRC$_{LD}$s, YLLs, YLDs, and DALYs for breast, lung, and colorectal cancers among different age or sex groups in Poland.

AGE GROUP (YEARS)	GENDER	5-YRC$_{LD}$		YLL		YLD		DALY		% CANCER	
		MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN
		BREAST CANCER									
5-19	Female	1.75×1010^{-9}	9.12	6.47×10^{-14}	5.36×10^{-4}	1.62×10^{-15}	8.47×1010^{-6}	6.63×10^{-14}	5.44×10^{-4}	9.99×1010^{-12}	5.20×110^{-2}
20-54		2.05×1010^{-6}	1.07×10^{4}	9.39×10^{-11}	7.78×10^{-1}	1.87×1010^{-12}	9.80×10^{-3}	9.58×10^{-11}	7.88×10^{-1}	4.63×10^{-10}	2.42
55-89		5.31×1010^{-6}	2.80×10^{4}	2.41×10^{-10}	1.99	4.48×1010^{-12}	2.35×110^{-2}	2.45×10^{-10}	2.01	3.68×10^{-10}	1.94
LUNG CANCER											
5-19	Male	1.57×10^{-10}	8.40×10^{-1}	1.45×1010^{-13}	1.10×10^{-3}	2.12×1010^{-16}	1.14×1010^{-6}	1.45×1010^{-13}	1.10×10^{-3}	6.99×1010^{-13}	3.75×10^{-3}
	Female	2.15×10^{-10}	1.12	1.64×1010^{-13}	1.36×10^{-3}	2.73×1010^{-16}	1.44×1010^{-6}	1.64×1010^{-13}	1.36×10^{-3}	1.22×1010^{-12}	6.40×10^{-3}
20-54	Male	9.72×10^{-8}	5.19×10^{2}	1.42×10^{-10}	1.08	2.21×1010^{-13}	1.18×10^{-3}	1.42×10^{-10}	1.08	2.24×10^{-11}	1.20×10^{-1}
	Female	4.81×10^{-8}	2.52×10^{2}	5.58×10^{-11}	4.61×10^{-1}	1.03×1010^{-13}	5.40×10^{-4}	5.59×10^{-11}	4.62×10^{-1}	1.11×10^{-11}	5.82×110^{-2}
55-89	Male	7.72×1010^{-7}	4.14×10^{3}	8.91×10^{-10}	6.74	1.98×1010^{-12}	1.06×110^{-2}	8.93×10^{-10}	6.75	5.36×10^{-11}	2.87×10^{-1}
	Female	3.41×1010^{-7}	1.80×10^{3}	3.60×10^{-10}	2.99	8.73×1010^{-13}	4.58×10^{-3}	3.61×10^{-10}	2.99	2.37×10^{-11}	1.25×10^{-1}
COLORECTAL CANCER											
5-19	Male	1.22×1010^{-9}	6.55	2.29×1010^{-13}	1.73×10^{-3}	1.53×10^{-15}	8.20×1010^{-6}	2.31×1010^{-13}	1.74×10^{-3}	5.44×1010^{-12}	2.92×110^{-2}
	Female	6.64×10^{-14}	3.46×10^{-4}	1.90×1010^{-13}	1.57×10^{-3}	8.16×10^{-20}	4.27×10^{-10}	1.90×1010^{-13}	1.57×10^{-3}	3.79×1010^{-16}	1.97×1010^{-6}
20-54	Male	3.43×1010^{-7}	1.84×10^{3}	6.37×10^{-11}	4.81×10^{-1}	3.70×1010^{-13}	1.98×10^{-3}	6.41×10^{-11}	4.83×10^{-1}	7.91×10^{-11}	4.24×10^{-1}
	Female	2.50×1010^{-7}	1.31×10^{3}	3.56×10^{-11}	2.97×10^{-1}	3.08×1010^{-13}	1.62×10^{-3}	3.59×10^{-11}	2.99×10^{-1}	5.77×10^{-11}	3.03×10^{-1}
55-89	Male	2.00×1010^{-6}	1.07×10^{4}	3.82×10^{-10}	2.86	2.37×1010^{-12}	1.27×110^{-2}	3.84×10^{-10}	2.87	1.39×10^{-10}	7.44×10^{-1}
	Female	1.38×1010^{-6}	7.27×10^{3}	2.33×10^{-10}	1.93	1.63×1010^{-12}	8.55×10^{-3}	2.35×10^{-10}	1.94	9.60×10^{-11}	5.05×10^{-1}
	Total	1.26×1010^{-5}	6.65×10^{4}	2.50×1010^{-9}	1.96×10	1.42×10^{-11}	7.51×110^{-2}	2.51×1010^{-9}	1.97×10	1.33×1010^{-9}	7.02

Table 8. Estimations of 5-YRC$_{LD}$s, YLLs, YLDs, and DALYs for breast, lung, and colorectal cancers among different age or sex groups in Spain.

AGE GROUP (YEARS)	GENDER	5-YRC$_{LD}$		YLL		YLD		DALY		% CANCER	
		MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN	MODE	MEDIAN
		BREAST CANCER									
5-19	Female	5.83×1010^{-9}	1.30×10	9.12×1010^{-13}	1.00×10^{-3}	5.52×10^{-15}	1.24×1010^{-5}	9.18×1010^{-13}	1.01×10^{-3}	1.51×10^{-11}	3.36×110^{-2}
20-54		5.00×1010^{-6}	1.11×10^{4}	7.66×10^{-10}	8.38×10^{-1}	4.38×1010^{-12}	9.79×10^{-3}	7.70×10^{-10}	8.48×10^{-1}	4.05×10^{-10}	9.02×10^{-1}
55-89		1.02×1010^{-5}	2.28×10^{4}	1.54×10	1.53×10	8.27×1010^{-12}	1.85×110^{-2}	1.54×10	1.53×10	3.37×10^{-10}	7.54×10^{-1}
LUNG CANCER											
5-19	Male	6.02×10^{-10}	1.43	1.67×1010^{-12}	1.93×10^{-3}	6.19×1010^{-16}	1.49×1010^{-6}	1.67×1010^{-12}	1.93×10^{-3}	1.08×1010^{-12}	2.56×10^{-3}
	Female	5.29×10^{-10}	1.16	1.36×1010^{-12}	1.49×10^{-3}	4.99×1010^{-16}	1.12×1010^{-6}	1.36×1010^{-12}	1.49×10^{-3}	1.35×1010^{-12}	3.00×10^{-3}
20-54	Male	2.81×1010^{-7}	6.73×10^{2}	8.94×10^{-10}	1.03	4.33×1010^{-13}	1.03×10^{-3}	8.94×10^{-10}	1.03	3.37×10^{-11}	8.09×110^{-2}
	Female	1.35×1010^{-7}	3.03×10^{2}	4.25×10^{-10}	4.64×10^{-1}	2.16×1010^{-13}	4.82×10^{-4}	4.25×10^{-10}	4.64×10^{-1}	1.10×10^{-11}	2.46×110^{-2}
55-89	Male	2.81×1010^{-7}	6.73×10^{2}	4.43×1010^{-9}	5.09	2.88×1010^{-12}	6.84×10^{-3}	4.43×1010^{-9}	5.10	4.04×10^{-11}	9.66×110^{-2}
	Female	2.88×1010^{-7}	6.42×10^{2}	2.52×1010^{-9}	2.74	6.62×1010^{-13}	1.48×10^{-3}	2.52×1010^{-9}	2.74	9.50×1010^{-12}	2.12×110^{-2}
COLORECTAL CANCER											
5-19	Male	2.95×1010^{-9}	7.01	1.66×1010^{-12}	1.91×10^{-3}	4.09×10^{-15}	9.74×1010^{-6}	1.66×1010^{-12}	1.92×10^{-3}	5.27×1010^{-12}	1.25×110^{-2}
	Female	1.08×1010^{-13}	2.47×10^{-4}	1.18×1010^{-12}	1.30×10^{-3}	1.51×10^{-19}	3.45×10^{-10}	1.18×1010^{-12}	1.30×10^{-3}	2.80×1010^{-16}	6.39×1010^{-7}
20-54	Male	9.18×1010^{-7}	2.18×10^{3}	3.68×10^{-10}	4.23×10^{-1}	9.47×1010^{-13}	2.25×10^{-3}	3.69×10^{-10}	4.25×10^{-1}	1.10×10^{-10}	2.62×10^{-1}
	Female	7.62×1010^{-7}	1.70×10^{3}	2.71×10^{-10}	2.98×10^{-1}	1.01×1010^{-12}	2.36×10^{-3}	2.72×10^{-10}	3.00×10^{-1}	6.19×10^{-11}	1.38×10^{-1}
55-89	Male	6.42×1010^{-6}	1.54×10^{4}	2.14×1010^{-9}	2.46	6.80×1010^{-12}	1.62×110^{-2}	2.15×10^{-9}	2.48	1.53×10^{-10}	3.67×10^{-1}
	Female	4.27×1010^{-6}	9.59×10^{3}	1.31×1010^{-9}	1.44	4.42×1010^{-12}	9.85×10^{-3}	1.31×1010^{-9}	1.45	1.41×10^{-10}	3.16×10^{-1}
	Total	2.86×1010^{-5}	6.51×10^{4}	15.4	3.01×10	3.00×10^{-11}	6.88×110^{-2}	1.54×10	3.02×10	1.33×1010^{-9}	3.01

multiple-site cancers,[37] and earlier studies have concentrated on the aggregated incidences of these cancers. However, trends observed in 1 study,[66] such as increasing cancer prevalences and DALYs with age, are consistent with the findings of this study. The 5-YRC prevalence significantly impacts the DALYs and varies among the study areas. This variation may stem from the cultural food processing practices unique to the ethnic groups in the study areas.[67] They could also arise from dietary habit variations, resulting in GE-exposure differences in the population.[68] Population size may also account for the variation. Earlier studies have noted that countries with larger populations tend to have higher cancer-induced mortality and morbidity than others.[62,69]

In this study, China, which had the highest population size of 1 407 745 000 in 2019, recorded the highest median prevalence and DALYs, followed by Spain (47 134 837), Poland (37 965 475), and lastly Taiwan (23 777 737).[39,40] However, it is noteworthy that the elements of exposure gathered for this study from the literature are riddled with uncertainties regarding body weight, dietary GE concentrations, and the population's dietary habits. As reported elsewhere,[68,70] there are significant differences in dietary GE concentrations based on the food producer, the cooking time, cooking technique and temperature. However, these uncertainties do not lessen the importance of an unsafe diet in cancer development. According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) in 2019, unsafe diet accounts for 5.1 to 5.9% of all cancer DALYs globally, compared to the DALY contribution of other cancer risk factors such as smoking (10.7-33.9%), alcohol use (7.4% of male cancer DALY), air pollution (4.4% male cancer DALY), and unsafe sex (8.2% of female cancer DALY).[71] These findings demonstrate that the consumption of unsafe diets significantly contributes to cancer burden and premature death globally.

In the present study, while the modal estimates generally suggest negligible cancer concern from dietary GE exposure among the population under study, the median estimates raise concerns. The median GE-induced breast, lung and colorectal cancer cases were as high as 581 000, 302 000, and 186 000, respectively, within the space of 5 years (2015-2019), causing 6.66 to 1,012 years of life lost through death, 0.0266 to 1.06 years of life lived with disability and a total loss of healthy lives of 6.69 to 1020 DALYs per 100 000 population. Even though these cancer cases form a relatively small percentage (3.66×10^{-8}-2.42%) of the total breast, lung and colorectal cancer cases in the study areas, projections suggest the prevalence and health burden of these GE-induced cancers will rise in the ensuing decades due to population growth, ageing, and dietary habits influenced by economic development.[62] Hence, there is a need for a pragmatic measure tailored to mitigating GE occurrence in diets.

Limitation

This study, while comprehensive, is subject to certain limitations. The reliance on GBD data for cancer prevalence, YLL, and YLD estimates is contingent upon the accuracy and completeness of cancer registration data within each country. Disparities in screening criteria and reporting levels among China, Taiwan, Poland, and Spain may introduce biases, potentially affecting the comparability of results. The extent of this bias is difficult to quantify and could either understate or overstate the actual cancer burden.

Furthermore, the dietary GE concentration data were derived from a limited number of articles (10) selected based on stringent inclusion criteria. While ensuring data quality, this selection process may not fully represent the entire spectrum of available literature, potentially leading to underestimation or overestimation of dietary GE and 3-MCPDE exposure.

The study also faced challenges due to the lack of age- and gender-specific body weight distributions, necessitating a standardized body weight (60 kg) as recommended by the EFSA.[43] This assumption may not accurately reflect the diverse body weight profiles across different populations, potentially skewing exposure assessments. Additionally, the lack of data on exposure duration and frequency to compute the chronic lifetime exposure compelled the authors to rely on the average daily exposure for the risk determination. Although this approach is recommended in such situations,[19,36] it might not account for the cumulative effects over a lifetime, potentially leading to underestimating the risk associated with chronic exposure.

Despite these limitations, the study's methodological rigor, characterized by a probabilistic approach and a substantial 5-year analysis period, provides valuable insights. These results contribute meaningfully to the discourse on public health implications of dietary GE exposure and underscore the necessity for careful interpretation when guiding public health decisions.

Conclusion

This study has critically evaluated the health impact of dietary GE and 3-MCPDE, presenting a nuanced picture of their influence on cancer prevalence and disease burden. Our findings indicate that while 3-MCPDE exposure remained within safe limits, GE exposure has led to a considerable number of cancer cases across China, Taiwan, Poland, and Spain. Specifically, median estimates suggest 4.99-581 000 breast cancer cases, 0.605-302 000 lung cancer cases, and 0.000247-186 000 colorectal cancer cases, with the total median DALYs ranging from 6.69 to 1,020 years of life lost per 100 000 population. These figures underscore the differential impact of GE based on gender, life stage, dietary habits, and population size.

Projections indicate an upward trend in GE-induced cancer prevalence and associated health burdens, driven by demographic shifts, ageing populations, and changing dietary patterns influenced by economic growth. In response to these challenges, it is imperative to implement strategies to reduce GE and 3-MCPDE contamination in food. Public awareness campaigns, alongside

the development of robust dietary guidelines, are essential to mitigate the risks posed by these contaminants.

Author contribution

Daniel Sitsofe Yabani: Writing – Original draft, Resources, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. Isaac Williams Ofosu: Writing – review & editing, Supervision. Gloria Mathanda Ankar-Brewoo: Writing – review & editing, Supervision, Resources. Herman Erick Lutterodt: Writing – review & editing, Supervision.

Consent to participate

Not applicable

Consent for publication

Not applicable

Data availability

Data associated with this study can be assessed from the Mendeley data repository via: https://data.mendeley.com/datasets/hwsf3z853p/1

Ethical considerations

Not applicable

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