BMC Global and Public Health

REVIEW

Open Access

Overview of foodborne hazards associated with inflammation and metabolic health

Srishti Sinha[1,2†], Laura S. Hackl[2†], Samantha L. Huey[1,2], Elisabetta Lambertini[3], Stella Nordhagen[4], Anna M. Bennett[1,2], Nidhi Shrestha[1,2], Nathaniel L. Cole[1,2], Julia L. Finkelstein[1,2] and Saurabh Mehta[1,2*]

Abstract

Access to safe and nutritious food is key to ensuring health and well-being and is critical to meeting the United Nations' Sustainable Development Goals. However, a synthesis of the associations between foodborne illness and malnutrition, such as metabolic health, remains a gap in the literature base. In this review, we summarized existing evidence on the impacts of biological and chemical hazards on nutrition-related health outcomes, specifically overweight and obesity, inflammation, metabolic disease, thyroid function, cancer development, and adverse birth outcomes, examining physiological mechanisms, epidemiological associations, and animal studies. Mechanisms between some foodborne hazards, such as *H. pylori*, and adverse pregnancy outcomes, e.g., gestational diabetes mellitus, or between nitrates and impaired thyroid function, are relatively well-studied. However, evidence on the effects of many other chemical hazards on metabolic and human health remains limited: for example, while arsenic exposure is associated with adverse birth outcomes, the limited availability of dose-response studies and other challenges limit ascertaining its causal role. Untangling these associations and physiological mechanisms is of high relevance for both high- as well as low- and middle-income countries. Emerging technologies and novel assessment techniques are needed to improve the detection and understanding of understudied and complex foodborne diseases, particularly those arising from chemical hazards. These evidence gaps are highlighted in this review, as well as the need for establishing surveillance systems for monitoring foodborne diseases and metabolic health outcomes across populations.

Keywords Foodborne disease, Metabolic health, Nutrition, Chemical hazards, Biological hazards

Background

The availability of healthy foods that are safe to consume is paramount to achieving global food and nutrition security [1]. Adequate nutrition is crucial to health and well-being; poor-quality (e.g., high-energy with low nutrient density) diets have consistently ranked among the top risk factors for morbidity and mortality worldwide [2, 3] and are often the focus of dietary recommendations, guidelines, and programming. However, improving diets, and subsequently health, requires food to be safe. Food safety, defined as "the absence—or safe, acceptable levels—of hazards in food that may harm the health of consumers" [4] is also critical to achieving the United Nations' Sustainable Development Goal 2 to "end hunger, achieve food security and improved nutrition and promote sustainable agriculture" [5]. The bidirectional relationship between exposure and impacts of foodborne diseases (FBDs) and health outcomes related to nutrient intake and absorption, inflammation, and

†Srishti Sinha and Laura S. Hackl are joint first authors in this manuscript.

*Correspondence:
Saurabh Mehta
smehta@cornell.edu
[1] Cornell Joan Klein Jacobs Center for Precision Nutrition and Health, Cornell University, 3101 Martha van Rensselaer Hall, Ithaca, NY 14853, USA
[2] Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853, USA
[3] Global Alliance for Improved Nutrition, Washington, DC 20036, USA
[4] Global Alliance for Improved Nutrition, Geneva, Switzerland

metabolic health leading to metabolism-related disorders, and chronic disease development such as cancer [6] is critical to understand but remains mostly overlooked.

FBDs refer to a range of acute and chronic adverse health outcomes caused by foodborne hazards such as pathogenic microbes and helminths, chemical compounds, and biogenic toxins ingested with food [7]. In the longer term, exposure to foodborne hazards exacerbates socioeconomic and health disparities, particularly in low- and middle-income countries (LMICs). While economic consequences can include increased healthcare costs, lost productivity, and declining local and global trade [1], the health impacts of unsafe food are striking. Together, 31 foodborne hazards—including 11 diarrheal disease agents, 10 helminths, seven invasive infectious disease agents, and three chemicals/toxins—were responsible for 600 million episodes of FBD, 420,000 deaths, and 33 million disability-adjusted life years (DALYs) in 2010 [7]. In the most recent 2021 update, the global age-standardized DALYs of enteric infections was 1020.15 per 100,000 population [8].

Many of the major health impacts of compromised food safety are known, as are the major impacts of malnutrition [9]; however, the effects of exposure to foodborne hazards—such as pathogens and chemical agents—on nutrition-relevant outcomes remain poorly understood, in both direction of causality and in their joint contribution to health outcomes [6]. While increasing evidence exists on the association between diarrheal disease and stunting, an endpoint relevant to nutrition, evidence is still scattered on other health endpoints relevant to both foodborne exposure and nutrition, such as inflammation and metabolic health like glucose or lipid metabolism and chronic disease condition like cancer. Chronic low-grade inflammation could disrupt metabolic homeostasis and favor the development of a wide range of noncommunicable diseases (NCDs) such as diabetes, cardiovascular diseases, and cancer [10]. With the rising prevalence of NCDs, it is essential to tackle the related factors across various domains including exposure to foodborne hazards such as cyanogenic glycosides, mycotoxins, or heavy metals.

In this review, we illustrate current evidence examples of physiological or epidemiological associations between acute or chronic FBDs and nutrition-relevant outcomes [6, 11]. We focus on foodborne hazards associated with inflammation and metabolic health endpoints while mentioning that the foodborne hazards associated with gastrointestinal health, nutrient absorption, and growth and development have been extensively reviewed elsewhere [12–14].

Type of hazards related to foodborne diseases and their health implications

Biological hazards

Biological hazards include certain bacteria, viruses, protozoa, fungi, and helminths that can result in disease. Among these, bacteria are one of the most prevalent biological foodborne hazards [15]. Acute gastrointestinal illness (AGI) is among the most common manifestations of FBD and presents with a variety of symptoms such as diarrhea with or without hemorrhage, constipation, nausea, vomiting, and abdominal pain, as well as immediate consequences of diarrhea such as dehydration and blood loss. This has been studied in human populations as well as experimental studies and extensively reviewed [12–14] and is discussed briefly here. Food- and waterborne AGI are most commonly caused by microbial hazards and often present with diarrheal symptoms. Inflammatory diarrhea—an AGI—can be caused by non-invasive organisms (e.g., non-invasive pathogenic *Escherichia coli (E. coli)* strains such as enterohemorrhagic *E. coli* (EHEC)) that stimulate the release of inflammatory mediators in the intestinal mucosa or by invasive organisms (e.g., enteroinvasive *E. coli* (EIEC), *Shigella* spp., and *Salmonella* spp.), via activation of cytokines and inflammatory mediators [16]. Research has suggested that elevated exposure to some enteropathogens, in the absence of diarrheal illness, may adversely impact nutrition outcomes such as growth. It is hypothesized that cryptic enteric pathogen exposure contributes to impairing gut function and altering nutrient absorption and immunity [17]. The evidence of chronic inflammation and reduced intestinal nutrient absorption due to infections and its lasting negative effects on linear growth has been extensively covered by other reviews [18]. The World Health Organization (WHO) identified norovirus, *Campylobacter*, and non-typhoidal *Salmonella* as major causes of foodborne diarrhea, with a significant burden in sub-Saharan Africa, where rotavirus, pathogenic *E. coli*, adenovirus, and *Giardia lamblia* are common pathogens in children under five [7, 14].

Foodborne pathogens are not only responsible for enteric or diarrheal symptoms but also manifestations including among others fever, pain, kidney failure, hemolytic uremic syndrome, jaundice, meningitis, ulcers, paralysis, miscarriage, and septicemia [19]. Furthermore, acute FBD can lead to severe long-term sequelae including irritable bowel syndrome, inflammatory bowel disease, reactive arthritis, Guillain-Barré Syndrome, neurological and cognitive impairment, and kidney disease, among those currently most supported by evidence as described in a 2019 scoping review [20].

Chemical hazards

Foodborne disease caused by ingested chemicals can result from naturally occurring chemicals (e.g., cyanogenic glycosides in cassava or solanine in potatoes and other *Solanaceae* plants) or end-products from microbial metabolism, i.e., biogenic chemicals (e.g., mycotoxins such as fumonisins and aflatoxins, or bacterial toxins from spores formed by *Bacillus cereus*) [21–24]. There is evidence that mycotoxins, which contaminate a wide range of staple foods across LMICs, potentially contribute to childhood stunting by mediating intestinal damage, inflammation, and the development of environmental enteric dysfunction (EED) [21, 22]. Exposure to foodborne mycotoxins such as aflatoxin, fumosin, and deoxynivalenol is suspected to impair child growth by mediating EED and intestinal damage [21]. Nitrites used in food processing have been associated with higher risks of breast, prostate, thyroid, and colorectal cancers via inhibiting iodide update and the formation of carcinogenic compounds [25, 26].

Exposure to agricultural pesticides, fertilizers, and industrial byproducts through ingested food (e.g., heavy metals like cadmium and arsenic, and polychlorinated biphenyls (PCBs)) have been associated with higher risks of colorectal, liver, and kidney cancers and cardiovascular diseases [23, 27–29]. Heavy metals can accumulate in the skeleton and adipose tissues, depleting specific nutrients in the body and resulting in deficits of the central nervous system, as well as cardiac, gastric, hematological, and cognitive function, and intrauterine growth [23, 30]. One example is cadmium, a heavy metal that is toxic to humans [31–33]. Dietary cadmium has been shown to promote colorectal cancer metastasis, liver, kidney, and cardiovascular disease [27–29]. In terms of arsenic, some evidence suggests that malnourished individuals, regardless of age, are more susceptible to the detrimental health effects—skin lesions, neuropathy, gastrointestinal symptoms, diabetes, cardiovascular disease, and cancer—of dietary arsenic exposure, and these effects can take years of chronic exposure to develop [34]. In addition, PCBs have been known to adversely affect children's neurological development and increase the risk of attention deficit disorders, autism, cerebral palsy, and mental retardation [23, 35]. Food contaminated by chemicals from PCBs and crop pesticides causes neural and kidney damage, reproductive problems, and cancer [36, 37].

There is evidence from in vitro, animal models, as well as epidemiological studies that endocrine-disrupting compounds (EDCs, also known as endocrine disruptors or hormonally active agents) can leach from everyday products such as plastic beverage bottles and food containers into food and are highly correlated with male and female infertility, obesity, diabetes, and fetal development [38]. EDCs interfere with hormone production, metabolism, and/or transport throughout the body [39]. The common EDCs are PCBs, dichlorodiphenyltrichloroethane (DDT), bisphenol A (BPA), phthalates, and dichlorodiphenyldichloroethylene (DDE).

Chemical hazards can also enter the food system via wastewater. While there are numerous processes in place, e.g., microbial digestion, to remove contaminants from wastewater [40, 41], many chemicals are unaffected by such mitigation leading to their direct consumption through drinking water or food preparation [42, 43]. The potential risk to human health increases when these chemical hazards accumulate in the food chain [42]. Agricultural use of contaminated wastewater on crops can lead to the bioaccumulation of certain contaminants, including heavy metals. If these crops are also used to feed livestock, further bioaccumulation can occur rendering the effective dose of a particular contaminant higher than it would have been at its source (the original wastewater) [42, 44].

Association between food hazards, inflammation, and metabolic health

Table 1 illustrates examples of the impacts of foodborne hazards, both biological and chemical, on inflammation and metabolic health —endpoints that are also relevant to nutrition. Below, we describe these in more detail.

Overweight and obesity

Foodborne hazards have been associated with weight gain or loss through various pathways. Strong short-term associations exist between AGI and weight loss, while long-term associations are less well defined [59]. Pathogens like *Cyclospora cayetanensis*, *Taenia saginata*, *Taenia solium*, and *Cryptosporidium*, to name a few, cause loss of appetite, nausea, diarrhea, and vomiting, which eventually leads to weight loss [60]. *Helicobacter pylori (H. pylori)* infection was also found to be associated with an increased likelihood of hyperemesis gravidarum during pregnancy, which is a severe manifestation of nausea and vomiting, weight loss, dehydration, electrolyte imbalances, and ketonuria in nearly 40 cross-sectional and case–control studies [45]. EDCs have also been hypothesized to induce weight gain, acting as "obesogens," by interfering with the endocrine system [61], via pathways such as increased oxidative stress and lowered thyroid hormone levels, due to organochlorine pesticides and PCBs, and slower metabolic rates [62]. Other hormones that are also affected by chemical toxins are estrogen, testosterone, corticosteroids, insulin, growth hormone, leptin, and catecholamines [63]. Agents with obesogenic potential (e.g., persistent organic pollutants (POPs), BPA, PCB) can act through impairing thermogenesis,

Table 1 Impact of key FBD biological and chemical hazards on inflammation and metabolic health

Key foodborne hazard	Physiological effect(s) and nutrition outcome	Putative mechanism(s) *and physiological effect/nutrition outcome*	Evidence for physiological impact
Helicobacter pylori (H. pylori)	Significant positive association between *H. pylori* infection and the following: •Gestational diabetes mellitus •Preeclampsia •Hyperemesis gravidarum •Fetal growth restriction •Low birthweight •Preeclampsia •Spontaneous abortion •Birth defects Infection with *iceA1*-positive *H. pylori*: •Overall 1.26-fold risk increase for peptic ulcer •*iceA1* presence significantly associated with peptic ulcer •*iceA2* presence: inversely associated with peptic ulcer •*iceA* presence: not associated with gastric cancer	•**Changes in glucose metabolism** → chemical changes in the gastric mucosa → proinflammatory cytokines↑ → structural alterations of insulin receptors → inhibition of insulin–insulin receptor interactions •**Oxidative damage** (free radicals) → endothelial damage → blood pressure↑ •**Vessel damage** (indirect): activation of clotting cascade or lymphocytes to produce/secrete cytokines in addition to proinflammatory cytokine pathway •**Gastric cancer:** Chronic gastric inflammation → precancerous changes of atrophic gastritis and intestinal metaplasia; ↑ risk of gastric cancer •**Hypochlorhydria** Chronic *Helicobacter pylori* infection → gastric acid secretion↓ → mucosal genetic instability → *H. pylori* adherence and gastric colonization↑ with bacteria that can convert dietary components into mutagens and induce transcription of *iceA1* gene	•Meta-analysis of 38 cross-sectional and case–control studies, *n* = 10,289 pregnant women with or without hyperemesis gravidarum and/or *H. pylori* infection. *H. pylori* infection increased the likelihood of hyperemesis gravidarum during pregnancy (OR 1.348, 95%CI 1.156–1.539) [45] •Meta-analysis of 5 cross-sectional, 17 case–control, and 9 cohort studies, *n* = 22,845 pregnant women with *H. pylori* infection reporting at least 1 adverse outcome. Significant association of *H pylori* infection with preeclampsia (OR 2.51; 95% CI 1.88–3.34), fetal growth restriction (OR 2.28; 95% CI 1.21–4.32), gestational diabetes mellitus (OR 2.03; 95% CI 1.56–2.64), and birth defect (OR 1.63; 95% CI 1.05–2.54) [46] •Meta-analysis of 10 RCTs, *n* = 10,164 individuals testing positive for gastric cancer but otherwise healthy and asymptomatic. Subsequent occurrence of gastric cancer reduced with eradication therapy (RR 0.66, 95% CI 0.46–0.95) [47] •Meta-analysis of 22 randomized trials and 2 observational studies, *n* = 48,064 individuals receiving *H. pylori* eradication and/or chemopreventive interventions. Eradication provided significant benefits (incidence rate ratio, 0.62; 95% CI 0.49 − 0.79) [48] •Meta-analysis of 32 RCTs and cohort studies, *n* = 31,106 individuals reporting gastric cancer incidence as an outcome. Eradication lowered the risk for gastric cancer (OR 0.46, 95% CI 0.39–0.55) [49]

Table 1 (continued)

Key foodborne hazard	Physiological effect(s) and nutrition outcome	Putative mechanism(s) *and physiological effect/nutrition outcome*	Evidence for physiological impact
Toxoplasma gondii (*T. gondii*)	Positive association with •Type 1 and T2DM •Chronic toxoplasmosis possible risk factor for T2DM, but no significant association with type 1 diabetes mellitus	**Autoimmune response** •Infected white blood cells: → facilitated spread in organs (e.g., pancreas); autoimmune response → autoantibody production •Improved replication in insulin-producing β-cells → activation of autoimmunity pathways + inflammation of Langerhans islets → diabetes development •Direct invasion/destruction of pancreatic β-cells → pancreatitis and diabetes •Oxidative damage → reactivation of latent parasite cysts (acute infection) •Inability of neutrophils to perform phagocytosis → response to intracellular pathogens ↓ •Opsonization activity/leukocyte cytotoxicity ↓ → susceptibility to opportunistic infections ↑	Meta-analysis of 7 case–control studies, $n = 2248$ individuals with or without diabetes (OR 1.10, 95% CI 0.13–9.57 and 2.39, 95% CI 1.20–4.75) for type 1 and T2DM, respectively [50]
Phthalates[a]	•Ø Glucose tolerance and blood glucose in pregnancy •Associations with T2DM and: (1) DEHP exposure (2) DBP, DIBP exposure (3) DINB, BBP, DEP exposure •Obesity: limited evidence (for low molecular weight phthalates •Thyroid: limited evidence •Limited number of studies, lack of coherence with diabetes	•Alteration of peroxisome proliferator-activated receptors which contribute to adipogenesis, lipid metabolism, and **metabolic homeostasis**	Systematic review of 17 case–control and cross-sectional studies, $n = 10{,}643$ across age, sex, and physiological states [51]
POPs, e.g. p,p′- DDT, p,p′-DDE, PCBs, phthalates	•p,p′-DDT and p,p′-DDE: "presumed" obesogenic in in vivo/in vitro studies •p,p′-DDT exposure and adiposity ↑ •Biological plausibility of obesogenic effects of p,p′-DDT and p,p′-DDE •Positive associations between p,p′-DDE exposure and body mass index (BMI) •Dose effect for some chemicals (PCB, p.p′-DDE, phthalates): weight gain at lower doses and weight loss at higher doses. Higher obesity susceptibility upon PCB exposure in girls	**Impaired thermogenesis:** •Underlying mechanisms sparsely studied; one in vivo study suggests brown adipose RNA responsible for regulating thermogenesis↓ •p,p′-DDT exposure → energy expenditure via thermogenesis Ø → energy imbalance → **obesity**	Meta-analysis of 7 human epidemiological studies, $n = 114$–788 per study; 19 animal in vivo studies; and 7 in vitro studies. Positive associations between exposure to p,p′-DDE and BMI *z*-score ($\beta = 0.13$ BMI *z*-score (95% CI 0.01, 0.25 [52]

Table 1 (continued)

Key foodborne hazard	Physiological effect(s) and nutrition outcome	Putative mechanism(s) *and physiological effect/nutrition outcome*	Evidence for physiological impact
Nitrite/nitrate (NO_2^-/ NO_3^-), Inorganic NO_3^-, perchlorate, thiocyanates	NO_3^- exposure and thyroid cancer/hyper-/hypothyroidism risk Positive association between NO_3^-/NO_2^- exposure and hypothyroidism Higher NO_3^- exposure and thyroid cancer risk Animal studies: high NO_2^-/NO_3^- exposure (~ 10–600 times acceptable daily intake) ⟶ antithyroid effects: ↓ thyroid hormone serum levels and histomorphological thyroid gland changes. No similar observations in humans	•Iodine (I-) uptake inhibition agents ⟶ binding to sodium (Na^+)/I^- symporter ⟶ I^- bioavailability↓, thyroidal I^- stores↓, thyroid hormone production↓ ⟶ thyroid-stimulating hormone release↓ from the pituitary gland •Chronic thyroid gland stimulation ⟶ change of follicular cells and **hypertrophy/hyperplasia induction** •Chronic exposure to high NO_3^- levels ⟶ **hypertrophy, goiter development**	Meta-analysis of 3 cohort studies comprising seven subgroups of different levels of NO_3^- ($n=4$) and NO_2^- ($n=3$) exposure (risk 1.48, 95% CI 1.09–2.02) [53]
BPA	•Positive correlation between BPA levels and obesity risk •Dose–response: 1-ng/mL BPA increase increased the obesity risk by 11%. Similar results for different types of obesity, gender, and age	Adipocyte cell differentiation↑ ⟶ excess fat accumulation ⟶ weight gain/obesity	Meta-analysis of 13 observational studies, $n=888$–4793 per study, individuals with BMI or body weight and urinary BPA concentration measured (OR 1.566, 95% CI 1.097–2.234) [54]
PCB	Association between prenatal PCB exposure and •Body weight/BMI ↑ at low (< 1 ng PCB/mg lipid) exposure; weight ↓ at high (> 4 ng PCB/mg lipid) exposure •Pubertal girls: body size ↑ •Women (20–50 years), children (3–5 years): no association •Girls (4 years): body weight ↓ at intermediate (≥ 1–≤ 4 ng PCB/mg lipid) exposure	•Agonist/antagonist of steroid hormone receptors •Induction of specific metabolic pathways	Review of 24 studies, $n=17{,}015$ individuals with information on exposure to EDCs and body size measures [55]
Arsenic	↑ Risk of •Low birth weight (< 2500 g) •Preterm delivery • Birth weight↓ •Birth size↓ GAP: Studies investigating possible paternal effects are lacking	•Inorganic As crosses the placenta ⟶ **As accumulation** in developing fetal organs/systems •**Placental accumulation** ⟶ disruption/alteration of cord blood methylation	Systematic review of 15 cohort and case–control studies, $n=1929$ pregnant women, $n=3316$ children, $n=7{,}742$ mother-infant pairs [56] Review of 16 cross-sectional and prospective studies, $n=33{,}675$ infants where arsenic exposure was measured; no meta-analysis due to methodological differences in study protocols [57]
Cadmium	Associated with •Diabetes and diabetes-related kidney disease •Cardiovascular diseases •Cancer of the vital organs like prostate, urinary bladder, breast, and liver	•Lowers glucose transport and GLUT-4 expression by downregulating PPARγ •Elevates pro-inflammatory lipids and cytokines •Produces reactive oxygen species and depletes glutathione reductase	Cross-sectional analysis of 9645 adults enrolled in the Korea National Health and Nutrition Examination Survey [58]

Ø, impaired; ↑, increased; ↓, decreased; As, arsenic; BBP, butylbenzyl phthalate, BMI, body mass index; BPA, bisphenol A; CI, confidence interval; DEHP, di(2-ethylhexyl) phthalate; DBP, dibutyl phthalate; DEP, diethyl phthalate; DIBP, diisobutyl phthalate; DINP, diisononyl phthalate; EDC, endocrine disrupting chemicals; FBD, foodborne disease; GLUT-4, glucose transporter type 2; *iceA*, epithelium antigen virulence gene in H. pylori; *iceA1* or *iceA2*, allele 1 or 2 of *iceA* gene; NO, nitric oxide; NO_2-; nitrite; NO_3-, nitrate; PCB, polychlorinated biphenyls; p,p′-DDE, dichlorodiphenyldichloroethylene; p,p′-DDT, p,p′-dichlorodiphenyltrichloroethane; POPs, persistent organic pollutants; PPARγ, proliferator-activated receptor γ; RCTs, randomized controlled trials, T2DM, type 2 diabetes mellitus

[a] Phthalates considered here include di(2-ethylhexyl) phthalate (DEHP), diisononyl phthalate (DINP), dibutyl phthalate (DBP), diisobutyl phthalate (DIBP), butyl benzyl phthalate (BBP), and diethyl phthalate (DE)

increasing adipocyte cell differentiation, or interaction with steroid hormone receptors [54, 55]. Mechanisms for POP-related obesity in humans are incompletely understood; however, evidence from in vivo and in vitro studies suggests thermogenesis impairment through a decrease in brown adipose ribonucleic acid [52]. In contrast, BPA has been suggested to cause an increased adipocyte cell differentiation leading to excess fat accumulation [55], while PCBs have been suggested to antagonize steroid hormone receptors or induce specific metabolic pathways that can either increase or decrease body weight [52, 54, 55]. The evidence on the effects of chemical hazards and body weight is variable, highlighting a need for further research.

Metabolic disease

Metabolic disease can impair physiological processing and use of nutrients, hence affecting nutrition processes and outcomes. Several foodborne hazards have been associated with metabolic disease. Chemical hazards that can affect glucose metabolism include phthalates, which can alter receptors that contribute to adipogenesis, lipid metabolism, and metabolic homeostasis, or act via induction of oxidative damage [51]. *H. pylori* is a pathogen highly prevalent in LMICs which can be spread through feces as well as contaminated water and food [64, 65]. *H. pylori* infection contributes to metabolic disease via different pathways—for example, one review found *H. pylori*-induced inflammation caused insulin resistance and the development of diabetes mellitus [66]. *H. pylori* has also been shown to cause changes in perinatal glucose metabolism and subsequently inhibit insulin-receptor interactions, leading to strong associations with gestational diabetes mellitus [46]. It can also affect the production of the hunger hormones ghrelin and leptin subsequently modulating the secretion of the growth hormone [65], which may lead to growth retardation among malnourished children or children exposed to *H. pylori* in early childhood [65, 67, 68]. In addition, epidemiological evidence suggests that *H. pylori* infection affects micronutrient status through various mechanisms, including inhibiting iron absorption by inducing the conversion of ascorbic acid (vitamin C) to dehydroascorbic acid; changing gastric pH which in turn causes malabsorption of dietary cobalamin and inactivation of ingested vitamin C, inhibiting vitamin B_{12} absorption, and lowering the mucosal concentration of α-tocopherol (vitamin E) in the colon [65].

An additional foodborne pathogen, *Toxoplasma gondii (T. gondii)*, is a protozoan parasite for which one-third of the world population is seropositive. The prevalence between communities can range between 10 and 90% [69], with contaminated meat and dairy representing the main source of infection [70, 71]. The prevalence of latent toxoplasmosis in pregnant women is estimated to be the highest in South America [72] with prevalence on the decline in certain developed countries, possibly due to changes in food habits and improved hygiene [73]. Infection with the parasite is difficult to detect as most healthy people with toxoplasmosis are asymptomatic; acute flu-like symptoms occur in only 20% of infected individuals. *T. gondii* may contribute to type 2 diabetes mellitus (T2DM) development via different pathways: it can trigger an autoimmune response eventually causing inflammation of the Langerhans islets, a pancreatic tissue, or directly invade and destroy pancreatic β cells [50, 74]. While the association between *T. gondii* and T2DM is supported by epidemiological research [75], its exact mechanisms in T2DM pathogenesis remain understudied, though recent work points toward *T. gondii's* manipulation of the host cell metabolic environment [69].

There is mounting in vitro, in vivo, and epidemiological evidence that EDCs, particularly phthalates, BPA, and acrylamides have also been identified as playing roles in diabetes development and progression [76] as well as obesity [77]. These chemicals can interfere with glucose and lipid homeostasis, including affecting the function of beta-cells in the pancreas [77]. A report from the European Union found that EDC exposures contribute substantially (20–69% depending on the EDC) to both diabetes as well as obesity in children, adults, and older women, with a probability of >€18 billion in costs per year [78]. Heavy metals like arsenic and cadmium can cause insulin resistance leading to T2DM. Arsenic and cadmium inhibit proliferator-activated receptor γ, which plays a crucial role in glucose metabolism. Cadmium also induces pro-inflammatory lipids and cytokines which are associated with chronic inflammatory diseases like obesity and T2DM. This has been extensively covered in a recent review [79].

Food additives like nitrates and nitrites, e.g., food dyes, titanium dioxide, phosphate-containing additives, artificial sweeteners, and emulsifiers, are often used to enhance the taste, texture, and shelf life of food, may also pose chemical hazards. While food additives are subjected to rigorous toxicity assessments, some studies raise concerns about their safety. For example, there are mixed associations between metabolic syndrome and non-caloric artificial sweeteners (NAS), such as sucralose, saccharine, and aspartame. As their name indicates, they are low in calories while still providing sweetness to foods. In contrast to energy-containing sugars such as sucrose, NAS passes through the digestive system without being digested and absorbed by the host, instead directly encountering the colonic microbiota [80]. Some studies have found that NAS improved

glycemic response, while other studies have found NAS caused weight gain and a higher risk of T2DM in humans [80]. In animals, NAS consumption has been associated with more adverse outcomes. For example, aspartame at doses 7–15% of the maximum recommended daily intake caused learning and memory deficits in mice, which were passed down to offspring [81]. In another study, saccharin, sucralose, and aspartame consumption by mice, dose exceeding 5 mg/kg of body weight (the acceptable daily intake limit set by the US Food and Drug Administration) caused impaired glucose tolerance, which was mediated by changes in the gut microbiome, including increases in the abundances of taxa associated with T2DM in humans [80]. This topic has been reviewed extensively elsewhere [82, 83]. A thorough review of other food additives and human health remains less explored in the literature but is beyond the scope of the current manuscript.

Thyroid function

Thyroid hormone and its optimal functioning are essential for regulating metabolism in humans. The association between thyroid hormone, body weight, and energy expenditure is well established. Excess production of thyroid hormone could induce weight loss, increased energy expenditure, reduced cholesterol levels, and increased lipolysis and gluconeogenesis. Low hormone levels could increase weight gain, reduce energy expenditure, and increase cholesterol levels [84]. A systematic review and meta-analysis found that exposure to nitrites and nitrates has been associated with inhibition of iodine uptake and resulting impaired thyroid function, which can cause hypertrophy and goiter development, in humans part of experimental and clinical studies [53]. Environmental toxins can affect women's reproductive health by increasing the risk of cancer and ovulatory dysfunction. EDCs have been shown to cause reproductive development disorders, subfertility, and polycystic ovarian syndrome in women [85]. Higher serum BPA concentrations also contribute to these factors in addition to increasing insulin resistance and hyperandrogenism.

Cancer development

The carcinogenic potential has been attributed to various foodborne hazards, mostly chemical but also biological. For example, epidemiological evidence has shown *H. pylori* infection or aflatoxicosis is associated with an increased risk of stomach cancer across several systematic reviews and meta-analyses [47–49], cadmium ingestion was shown to play a role in colorectal cancer metastasis via cell culture in vitro and in mice [29], and dietary nitrites and nitrates from processed meats have been associated with greater risks of breast, prostate, thyroid, and colorectal cancers among adults in large cohort studies [25, 26] (Table 1). The colonization of *H. pylori* in the stomach may lead to stomach cancer from chronic gastric inflammation, hypochlorhydria (decreased gastric acid secretion), and immunomodulation [47–49]. Cadmium may increase metastasis through epidermal growth factor receptor signaling [29]. Nitrites, commonly used as a food additive in processed and cured meats, combine in the human body to form carcinogenic *N*-nitroso compounds (NOCs). Circulating vitamins C and E have been shown to inhibit the metabolism of NOCs in the gut [86].

Birth outcomes

Foodborne hazards can jeopardize the health and nutritional status of pregnant women and newborns, affecting a range of development endpoints for the fetus and infant, as well as the health of the pregnant woman. Several systematic reviews have found *H. pylori* infection was associated with an increased risk of gestational diabetes [46], and mycotoxin and arsenic exposure impaired fetal growth and neurologic function [57, 87]. Arsenic can cross the placenta and accumulate in developing fetal organs, as well as in the placenta leading to disruption or alteration of cord blood methylation [56, 57]. Arsenic has also been identified as a potential risk factor for adverse birth outcomes such as neural tube defects as described in a systematic review and meta-analysis [88], which could be a result of increased fetal folate requirements due to arsenic exposure [89, 90]. However, more research is needed to ascertain the causal association between arsenic due to limited studies on dose response and methodological challenges [88]. Mercury and lead toxicity have been associated with poor fetal development and are known causes of neurodevelopment disorders in offspring. These heavy metals also lower maternal manganese and zinc levels during the prenatal period and 5 months postnatally [63].

Population considerations

High-risk populations

Foodborne pathogens are more likely to cause severe disease in individuals with weakened or immature immune systems. Immunologically vulnerable groups including infants and young children, pregnant women, the elderly, and immuno-compromised individuals may be at increased risk of contracting food-related diseases [7]. The extent to which vulnerable populations are more susceptible to short- and long-term adverse FBD-related nutritional outcomes as compared to non-vulnerable groups has not been established. Children under 5 years of age carry a large proportion (40%) of the disease burden attributable to FBD, despite representing only 9% of the global population [7]. Given their developing immune system and small body size, malnourished infants and

children are at higher risk of developing serious forms of foodborne diarrheal diseases—exacerbating malnutrition and further increasing the morbidity and mortality risk [7, 91]. Children can also exhibit behaviors that can lead to FBD, for example, by eating food contaminated with soil or animal feces [92].

Gender and occupational factors

Gender and occupation are important determinants of FBD exposure and potential drivers of adverse health outcomes. A recent assessment of traditional livestock and fish value chains in 20 LMICs identified socially constructed gender differences in exposures and occupations as major drivers of FBD in 19 of 20 reviewed studies [93]. While men are more likely to sustain injuries associated with livestock production, fishing, hunting, and slaughterhouse work, women are more exposed to foodborne pathogens during food processing, selling, and preparation [93]. These risks are particularly relevant in the context of traditional markets where vendors and food handlers are in close and frequent contact with food and food-contact surfaces that can be highly exposed to foodborne or zoonotic pathogens [94]. Differences in FBD outcomes attributable to sex or biology have been identified for several FBD-related pathogens. For example, susceptibility to *Listeria monocytogenes* infection is elevated during pregnancy [93], whereas invasive amebiasis is more common in adult males than females, though no gender differences have been reported in children [95]. A possible sex-dependent association between arsenic exposure and child growth in girls has also been identified [56]. Likewise, PCB exposure was associated with obesity in girls, whereas prenatal PCB exposure was associated with reduced birth weight among male infants [55].

Research gaps and future directions

In this review, we have examined the epidemiological, animal, and in vitro evidence on the associations between foodborne biological or chemical hazards, and nutrition-related outcomes including overweight and obesity, metabolic health, thyroid function, cancer development, and adverse birth outcomes. We have also considered gender differences in exposure to these hazards, noting the particular risks for women. Findings demonstrate that integration of food safety and nutrition programs is critical to improving population health (Fig. 1). Risks associated with unsafe foodborne hazards are substantial, and there are ongoing efforts to systematically quantify them at the global level [7]. The lack of certainty of evidence, as well as limited data attributing disease burden to specific foodborne hazards or food categories, limits the ability for an adequate response [96]. Evidence points toward a negative impact of certain hazards on nutrient absorption (e.g., helminths, *H. pylori*) and metabolic functions such as glucose and thyroid metabolism (e.g., persistent organic pollutants and other chemicals), as well as gastrointestinal ulcers (*H. pylori*). For some hazards (e.g., *H. pylori*), mechanisms are better understood, at least partially, because they have been investigated for decades, while there is limited evidence on the effects of other biological and chemical hazards on metabolic and human health due to a small number of studies and methodological differences, such as *T. gondii* and T2DM pathogenesis. For most associations between foodborne hazards and health outcomes, cytokine-induced inflammation serves as an intermediary pathway. EDCs cause mitochondrial dysfunction with an increase in reactive oxygen species, causing inflammation-induced obesity. Biological hazards such as *H. pylori* and *T. gondii* can produce inflammatory cytokines leading to insulin resistance and T2DM. Heavy metals like lead and cadmium can also produce oxidative stress and inflammation causing insulin resistance. Emerging technologies may allow for more accessible (i.e., cheaper and faster) detection and mechanistic assessment of currently understudied hazards. There is also a need to identify novel metrics or techniques for assessing more complex foodborne diseases.

Given the high complexity of foodborne hazards and metabolic health outcomes combined with a lack of consistent data, this review contextualized the available evidence on how FBD impacts physio-pathological processes. Other relevant health implications, such as the impacts of FBD on cognitive development or impaired work productivity are beyond the scope of this article. Mortality resulting from FBD was not extensively reviewed but should be acknowledged as the extreme boundary of FBD-related detrimental health impacts. This review highlights the physiological impacts of FBD; however, non-physiological effects, such as modified consumption behavior in response to FBD scares or outbreaks as well as other socioeconomic aspects were not considered. These behavior changes could have important nutrition impacts. With the growing consumer interest in organic foods, it is important to compare the foodborne hazards associated with organic produce to those of conventionally grown crops. While organic foods may contain lower levels of pesticide residues, studies have found no significant differences in contamination levels of heavy metals, mycotoxins, or bacteria [97]. We refer the reader to a recent systematic review on the impact of organic foods on chronic diseases [98]. Further, the effects of per- and polyfluoroalkyl substances (PFASs), which have pleiotropic effects on human health through endocrine functions were not covered here but can be found in the review by Gaillard et al. [99]. PFASs

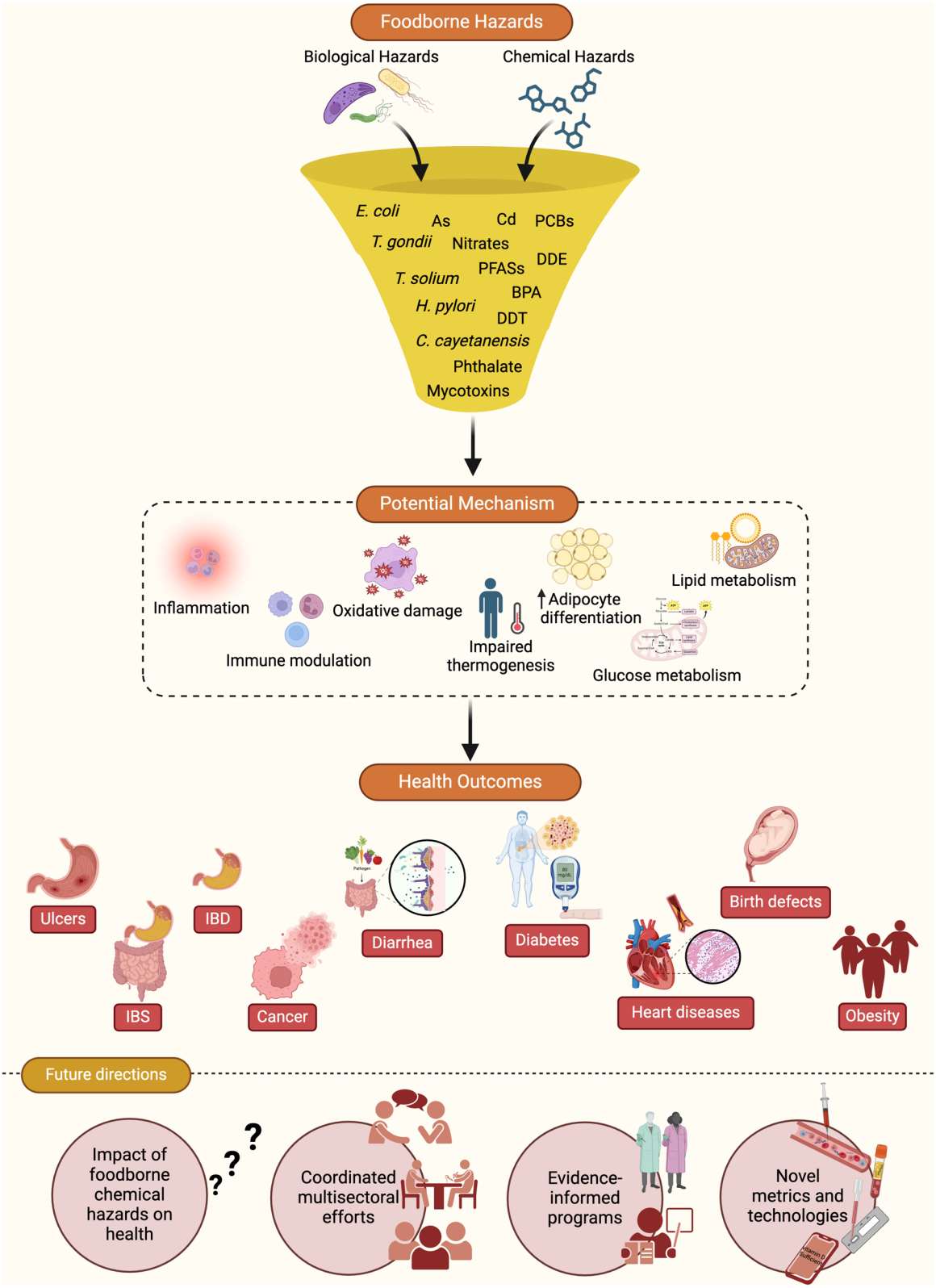

Fig. 1 Comprehensive overview of health outcomes of foodborne diseases and future directions. As, arsenic; BPA, bisphenol A; Cd, cadmium; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; PCBs, polychlorinated biphenyls; PFASs, perfluoroalkyl and polyfluoroalkyl substances. Created in BioRender

are found to disrupt thyroid function and hormone synthesis and are associated with metabolic syndrome [100].

Programs and research efforts examining the impact of FBDs on health and nutrition status, possibly including causal and enabling factors, health outcomes, or potential mitigating actions are rare but exist. For example, research efforts such as the MAL-ED study investigated the interaction between enteric disease and malnutrition in birth cohorts across eight countries [101]. Other projects have jointly measured enteric illness and nutrition endpoints to evaluate the impact of food safety, water, sanitation, and/or nutrition interventions [102]. In the USA, federal nutrition programs could be leveraged to address food safety. The special supplemental nutrition program for Women, Infants and Children (WIC) protects beneficiaries from lead exposure by providing food packages that are rich in vitamin C, calcium, and iron—these nutrients help to limit lead absorption in the body [103]. Food safety regulations in the US are designed by the Food and Drug Administration (FDA) known as the Integrated Food Safety System (IFSS). The IFSS provides vision, guiding principles, and key components of a coordinated approach to food safety. This involves continuous improvements and collaboration through multiple initiatives, programs, and projects [104]. Further, the Food and Nutrition Service (FNS) under the U.S. Department of Agriculture develops food safety education, training, and technical assistance resources to support FNS program operators [105].

Further, there are regulations and standards for the use of PCBs under the Toxic Substances Control Act which addresses the production, importation, use, and disposal [106]. However, these programs and regulations focus on public health generally. The regulation to address the nutritional impact of foodborne hazards is often overlooked. Globally, the Codex Alimentarius—a joint Food and Agriculture Organization (FAO) and WHO Food Standards Program—formulates a voluntary international standard, codes of practice, and guidelines to promote the health of the consumers and ensure fair practice in food trade [107]. This also overlooks the direct impact on the nutritional status of the population. In contrast, the U.S. Agency for International Development (USAID) Feed the Future: EatSafe program worked with traditional markets in Nigeria and Ethiopia to improve food safety by engaging and empowering consumers and vendors to demand safe, nutritious food through food safety interventions [108]. The EatSafe program is also facilitating the development and adoption of international standards for food safety in traditional markets [109, 110]. This type of program ensures appropriate implementation of regulations and ensures safe and nutritious food for population health.

Methodological differences across disciplines arise when examining the effect of agriculture interventions on nutrition status [111], and similar challenges are evident when connecting food safety, nutrition, and public health, emphasizing the need to harmonize the interpretability and actionability of current research. Longitudinal studies are required to better assess the temporal relationships and long-term impacts of FBDs on nutritional outcomes. To assess the impact at the population level, there is a need for consistent surveillance of FBDs and metabolic health outcomes. Of note, the FDA recently launched a new unified Human Foods Program. This initiative aims to enhance public health through science-based strategies to prevent foodborne illnesses, reduce diet-related chronic diseases, and ensure the safety of chemicals in food. The program focuses on three key areas: microbial food safety, chemical food safety, and nutrition, through the Nutrition Center for Excellence. While each area will operate independently with its own priorities, they share a common vision of making food a source of wellness for everyone [112]. More such transdisciplinary and intersectoral efforts are needed across the globe to fully understand the burden of FBDs, and the role of other associated risk factors including available treatments, sex, gender, and environmental stressors to inform the design of effective programs and interrupt the cycle of poor food safety, malnutrition, and health.

Abbreviations

AGI	Acute gastrointestinal illness
BBP	Butylbenzyl phthalate
BMI	Body mass index
BPA	Bisphenol A
DALYs	Disability-adjusted life years
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
DBP	Dibutyl phthalate
DEP	Diethyl phthalate
DIBP	Diisobutyl phthalate
DINP	Diisononyl phthalate
DEHP	Di(2-ethylhexyl) phthalate
E. coli	*Escherichia coli*
EDCs	Endocrine-disrupting compounds
EED	Environmental enteric dysfunction
EHEC	Enterohemorrhagic*Escherichia coli*
EIEC	Enteroinvasive*Escherichia coli*
FAO	Food and Agriculture Organization
FBDs	Foodborne diseases
FDA	Food and Drug Administration
FNS	Food and Nutrition Service
H. pylori	*Helicobacter pylori*
IFSS	Integrated Food Safety System
LMICs	Low- and middle-income countries
NAS	Non-caloric artificial sweeteners
NCDs	Noncommunicable diseases
NOCs	*N*-nitroso compounds
PCBs	Polychlorinated biphenyls
PFASs	Per- and polyfluoroalkyl substances
POP	Persistent organic pollutants
T2DM	Type 2 diabetes mellitus
T. gondii	*Toxoplasma gondii*
USAID	U.S. Agency for International Development

WIC Special supplemental nutrition program for Women, Infants and Children
WHO World Health Organization

Acknowledgements
The authors wish to thank and acknowledge Kate Ghezzi-Kopel and Anika Sharma for their assistance with searching and screening the literature, respectively, and Haley Swartz for the thorough editorial review of the draft.

Authors' contributions
SM conceptualized the review objective. SS, LH, SLH, SN, EL, AMB, NS, NC, JLF conducted literature review and drafted the initial versions of the manuscript. SS and SLH revised the manuscript to current form. LH, SN, EL, AMB, NS, NC, JLF provided critical inputs to the manuscript and reviewed the revised versions. All authors read and approved the final manuscript.

Funding
This work was made possible through support provided by Feed The Future through the U.S. Agency for International Development (USAID), under the terms of Agreement #7200AA19CA00010. The opinions expressed herein are those of the authors and do not necessarily reflect the views of USAID or the United States Government. SLH was supported by the NIH under award 5T32HD087137. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) or the National Institutes of Health.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
SM declares no conflict related to this topic. In the interest of full disclosure, SM is an unpaid board member and holds equity in VitaScan, a startup commercializing technology for point-of-care assays for nutritional status partially developed in his research laboratory at Cornell University. The remaining authors declare no competing interests.

Received: 8 October 2024 Accepted: 20 March 2025
Published online: 08 April 2025

References

1. Jaffee S, Spencer H, Laurian U, Delia G, Emilie C: The safe food imperative: accelerating progress in low-and middleincome countries. In: Agriculture and Food Series. Washington D.C.: World Bank; 2019. Accessed from: http://hdl.handle.net/10986/30568.
2. Institute for Health Metrics and Evaluation: Findings from the global burden of disease study 2017. In: Global Burden of Disease. Seattle, WA; 2017.
3. Global Burden of Disease: Global burden of disease study results. 2019. Accessed from: https://ghdx.healthdata.org/gbd-2019.
4. US Agency for International Development: Diets and food safety: U.S. government's global food security strategy activity design guidance. In: Feed the Future; 2022.
5. United Nations: Transforming our world: the 2030 agenda for sustainable development. A/RES/70/1. 2015. Accessed from: https://docs.un.org/en/A/RES/70/1.
6. S Nordhagen E Lambertini C DeWaal B McClafferty L Neufeld 2022 Integrating nutrition and food safety in food systems policy and programming. Glob Food Sec. 32 March 100993
7. Havelaar AH, Kirk MD, Torgerson PR, Gibb HJ, Hald T, Lake RJ, et al on Behalf of World Health Organization Foodborne Disease Burden Epidemiology Reference Group: World Health Organization global estimates and regional comparisons of the burden of foodborne disease in 2010. PLoS Med. 2015;12(2):e1001923. https://doi.org/10.1371/journal.pmed.1001923.
8. T Li N Qiang Y Bao Y Li S Zhao KC Chong X Deng X Zhang J Ran L Han 2024 Global burden of enteric infections related foodborne diseases, 1990–2021: findings from the Global Burden of Disease Study 2021. Science in One Health. 3 100075
9. YA Helmy H El-Adawy YM Sanad M Ghanem 2023 Editorial: food safety and public health. Front Microbiol. 14 1169139
10. Tristan Asensi M, Napoletano A, Sofi F, Dinu M. Low-grade inflammation and ultra-processed foods consumption: a review. Nutrients. 2023;15(6):1546. https://doi.org/10.3390/nu15061546.
11. Food and Agriculture Organization. Influencing food environments for healthy diets. Italy: Food and Agriculture Organization of the United Nations; 2016.
12. RE Black 1991 Would control of childhood infectious diseases reduce malnutrition?. Acta Paediatr Scand Suppl. 374 133 140
13. AE Schnee WA Petri Jr 2017 Campylobacter jejuni and associated immune mechanisms: short-term effects and long-term implications for infants in low-income countries. Curr Opin Infect Dis. 30 3 322 328
14. TBYH Oppong C Amponsem-Boateng EKD Kyere T Abdulai G Duan G Opolot 2020 Enteric pathogens associated with gastroenteritis among children under 5 years in sub-Saharan Africa: a systematic review and meta-analysis. Epidemiol Infect. 148 e64
15. Elbehiry A, Abalkhail A, Marzouk E, Elmanssury AE, Almuzaini AM, Alfheeaid H, Alshahrani MT, Huraysh N, Ibrahem M, Alzaben F, et al. An overview of the public health challenges in diagnosing and controlling human foodborne pathogens. Vaccines (Basel). 2023;11(4):725. https://doi.org/10.3390/vaccines11040725.
16. U Navaneethan R Giannella 2008 Mechanisms of infectious diarrhea. Nat Clin Pract Gastroenterol Hepatol. 5 11 637 647
17. MAL-ED Network Investigators 2017 Relationship between growth and illness, enteropathogens and dietary intakes in the first 2 years of life: findings from the MAL-ED birth cohort study. BMJ Glob Health. 2 4 e000370
18. KM Harper M Mutasa AJ Prendergast J Humphrey AR Manges 2018 Environmental enteric dysfunction pathways and child stunting: a systematic review. PLoS Negl Trop Dis. 12 1 e0006205
19. Todd E. Foodborne diseases: overview of biological hazards and foodborne diseases. Encyclopedia of Food Safety. 2014;2014:221–42. https://doi.org/10.1016/B978-0-12-378612-8.00071-8.
20. K Pogreba-Brown E Austhof A Armstrong K Schaefer L Villa Zapata DJ McClelland MB Batz M Kuecken M Riddle CK Porter 2020 Chronic gastrointestinal and joint-related sequelae associated with common foodborne illnesses: a scoping review. Foodborne Pathog Dis. 17 2 67 86
21. LE Smith RJ Stoltzfus A Prendergast 2012 Food chain mycotoxin exposure, gut health, and impaired growth: a conceptual framework. Adv Nutr. 3 4 526 531
22. Smith LE, Prendergast AJ, Turner PC, Mbuya MN, Mutasa K, Kembo G, Stoltzfus RJ: The potential role of mycotoxins as a contributor to stunting in the shine trial. Clin Infect Dis. 2015, 61 Suppl 7(Suppl 7):S733–737.
23. Rather IA, Koh WY, Paek WK, Lim J. The sources of chemical contaminants in food and their health implications. Front Pharmacol. 2017;8:830. https://doi.org/10.3389/fphar.2017.00830.
24. M Schirone P Visciano R Tofalo G Suzzi 2017 Histamine food poisoning. Handb Exp Pharmacol. 241 217 235
25. B Aschebrook-Kilfoy XO Shu YT Gao BT Ji G Yang HL Li N Rothman WH Chow W Zheng MH Ward 2013 Thyroid cancer risk and dietary nitrate and nitrite intake in the Shanghai women's health study. Int J Cancer. 132 4 897 904
26. Chazelas E, Pierre F, Druesne-Pecollo N, Esseddik Y, Szabo de Edelenyi F, Agaesse C, De Sa A, Lutchia R, Gigandet S, Srour B et al: Nitrites and nitrates from food additives and natural sources and cancer risk: results from the NutriNet-Santé cohort. Int J Epidemiol. 2022, 51(4):1106–1119.
27. Cui J, Yin S, Zhao C, Fan L, Hu H. Combining patulin with cadmium induces enhanced hepatotoxicity and nephrotoxicity in vitro and

in vivo. Toxins (Basel). 2021;13(3):221. https://doi.org/10.3390/toxins13030221.
28. J Liu Y Li D Li Y Wang S Wei 2022 The burden of coronary heart disease and stroke attributable to dietary cadmium exposure in Chinese adults, 2017 Sci Total Environ. 825 153997
29. M Sun Z Jiang P Gu B Guo J Li S Cheng Q Ba H Wang 2023 Cadmium promotes colorectal cancer metastasis through EGFR/Akt/mTOR signaling cascade and dynamics. Sci Total Environ. 899 165699
30. AA El-Kady MA Abdel-Wahhab 2018 Occurrence of trace metals in foodstuffs and their health impact. Trends Food Sci Technol. 75 36 45
31. M Gallo L Ferrara A Calogero D Montesano D Naviglio 2020 Relationships between food and diseases: what to know to ensure food safety. Food Res Int. 137 109414
32. Rai UN, Tripathi RD, Vajpayee P, Pandey N, Ali MB, Gupta DK: Cadmium accumulation and its phytotoxicity in Potamogeton pectinatus L. (Potamogetonaceae)*. Bull Environ Contamin Toxicol. 2003, 70(3):0566–0575.
33. Sanità di Toppi L, Gabbrielli R: Response to cadmium in higher plants. Environmental and Experimental Botany 1999, 41(2):105–130.
34. World Health Organization: Exposure to arsenic: a major public health concern. In: Preventing Disease Through Healthy Environments. World Health Organization; 2019. WHO Reference Number: WHO/CED/PHE/EPE/19.4.1
35. SL Schantz JJ Widholm DC Rice 2003 Effects of PCB exposure on neuropsychological function in children. Environ Health Perspect. 111 3 357 576
36. KL Bassil C Vakil M Sanborn DC Cole JS Kaur KJ Kerr 2007 Cancer health effects of pesticides: systematic review. Can Fam Physician. 53 10 1704 1711
37. CC Abnet 2007 Carcinogenic food contaminants Cancer Invest 25 3 189 196
38. Rolfo A, Nuzzo AM, De Amicis R, Moretti L, Bertoli S, Leone A. Fetal-maternal exposure to endocrine disruptors: correlation with diet intake and pregnancy outcomes. Nutrients. 2020;12(6):1744. https://doi.org/10.3390/nu12061744.
39. C Casals-Casas B Desvergne 2011 Endocrine disruptors: from endocrine to metabolic disruption. Annu Rev Physiol. 73 135 162
40. Sangamnere R, Misra T, Bherwani H, Kapley A, Kumar R. A critical review of conventional and emerging wastewater treatment technologies. Sustain Water Resources Manag. 2023;9(58). https://doi.org/10.1007/s40899-023-00829-y.
41. Center for Sustainable Systems - University of Michigan: U.S. wastewater treatment factsheet. Michigan: University of Michigan; 2024:260.
42. A Thakali JD MacRae 2020 A review of chemical and microbial contamination in food: what are the threats to a circular food system?. Environ Res. 194 110635
43. RK Mishra SS Mentha Y Misra N Dwivedi 2023 Emerging pollutants of severe environmental concern in water and wastewater: a comprehensive review on current developments and future research. Water-Energy Nexus. 6 74 95
44. E Martí J Sierra M Mari C Ortiz N Roig M Nadal M Schuhmacher JL Domingo 2018 Long-term amendment of soils with compost and pig manure: effects on soil function, production and health risk assessment. Acta Hort. 1146 199 212
45. Ng QX, Venkatanarayanan N, De Deyn MLZQ, Ho CYX, Mo Y, Yeo W-S. A meta-analysis of the association between Helicobacter pylori (H pylori) infection and hyperemesis gravidarum. Helicobacter. 2018;23(1):e12455.
46. Zhan Y, Si M, Li M, Jiang Y. The risk of Helicobacter pylori infection for adverse pregnancy outcomes: a systematic review and meta-analysis. Helicobacter. 2019;24(2):e12562. https://doi.org/10.1111/hel.12562.
47. AC Ford D Forman RH Hunt Y Yuan P Moayyedi 2014 Helicobacter pylori eradication therapy to prevent gastric cancer in healthy asymptomatic infected individuals: systematic review and meta-analysis of randomised controlled trials. BMJ. 348 g3174
48. Lee YC, Chiang TH, Chou CK, Tu YK, Liao WC, Wu MS, Graham DY: Association between helicobacter pylori eradication and gastric cancer incidence: a systematic review and meta-analysis. Gastroenterol. 2016, 150(5):1113–1124 e1115.
49. Sugano K. Effect of Helicobacter pylori eradication on the incidence of gastric cancer: a systematic review and meta-analysis. Gastric Cancer. 2019;22(3):435–45. https://doi.org/10.1007/s10120-018-0876-0.
50. Majidiani H, Dalvand S, Daryani A, Galvan-Ramirez ML, Foroutan-Rad M. Is chronic toxoplasmosis a risk factor for diabetes mellitus? A systematic review and meta-analysis of case-control studies. Braz J Infect Dis. 2016;20(6):605–9. https://doi.org/10.1016/j.bjid.2016.09.002.
51. Radke EG, Galizia A, Thayer KA, Cooper GS. Phthalate exposure and metabolic effects: a systematic review of the human epidemiological evidence. Environ Int. 2019;132:104768. https://doi.org/10.1016/j.envint.2019.04.040.
52. G Cano-Sancho AG Salmon MA Merrill La 2017 Association between exposure to p, p'-DDT and its metabolite p, p'-DDE with obesity: integrated systematic review and meta-analysis. Environ Health Perspect. 125 9 096002
53. Z Bahadoran P Mirmiran A Ghasemi A Kabir F Azizi F Hadaegh 2015 Is dietary nitrate/nitrite exposure a risk factor for development of thyroid abnormality? A systematic review and meta-analysis Nitric Oxide. 47 65 76
54. Kim KY, Lee E, Kim Y: The association between bisphenol A exposure and obesity in children—a systematic review with meta-analysis. Int J Environ Res Public Health. 2019, 16(14).
55. JL Tang-Péronard HR Andersen TK Jensen BL Heitmann 2011 Endocrine-disrupting chemicals and obesity development in humans: a review Obes Rev 12 8 622 636
56. A Rahman C Granberg LA Persson 2017 Early life arsenic exposure, infant and child growth, and morbidity: a systematic review Arch Toxicol. 91 11 3459 3467
57. MS Bloom S Surdu IA Neamtiu ES Gurzau 2014 Maternal arsenic exposure and birth outcomes: a comprehensive review of the epidemiologic literature focused on drinking water Int J Hyg Environ Health. 217 7 709 719
58. T Jin EY Park B Kim JK Oh 2024 Environmental exposure to lead and cadmium are associated with triglyceride glucose index Sci Rep. 14 1 2496
59. SA Richard RE Black RH Gilman RL Guerrant G Kang CF Lanata K Molbak ZA Rasmussen RB Sack P Valentiner-Branth 2013 Diarrhea in early childhood: short-term association with weight and long-term association with length. Am J Epidemiol. 178 7 1129 1138
60. What you need to know about foodborne illnesses [https://www.fda.gov/food/consumers/what-you-need-know-about-foodborne-illnesses]
61. R Gupta P Kumar N Fahmi B Garg S Dutta S Sachar AS Matharu KS Vimaleswaran 2020 Endocrine disruption and obesity: a current review on environmental obesogens. Curr Res Green Sustain Chem. 3 100009
62. Hyman M: Systems biology, toxins, obesity, and functional medicine. In: 13th International Symposium of The Insitute for Functional Medicine: 2007; 2007.
63. Baillie-Hamilton PF. Chemical toxins: a hypothesis to explain the global obesity epidemic. J Alternative and Complementary Med. 2004;8(2):185–92. https://doi.org/10.1089/107555302317371479.
64. NC Quaglia A Dambrosio 2018 Helicobacter pylori: a foodborne pathogen?. World J Gastroenterol. 24 31 3472 3487
65. F Franceschi T Annalisa DR Teresa D Giovanna G Ianiro S Franco G Viviana T Valentina LL Riccardo G Antonio 2014 Role of Helicobacter pylori infection on nutrition and metabolism. World J Gastroenterol. 20 36 12809 12817
66. Q Xie Y He D Zhou Y Jiang Y Deng R Li 2023 Recent research progress on the correlation between metabolic syndrome and Helicobacter pylori infection. PeerJ. 11 e15755
67. RM Mera P Correa EE Fontham JC Reina A Pradilla A Alzate LE Bravo 2006 Effects of a new Helicobacter pylori infection on height and weight in Colombian children. Ann Epidemiol. 16 5 347 351
68. JE Thomas A Dale JE Bunn M Harding WA Coward TJ Cole LT Weaver 2004 Early Helicobacter pylori colonisation: the association with growth faltering in The Gambia Arch Dis Child 89 12 1149 1154
69. Gallego-Lopez GM, Contreras Guzman E, Desa DE, Knoll LJ, Skala MC: Metabolic changes in Toxoplasma gondii-infected host cells measured by autofluorescence imaging. mBio. 2024, 15(8):e0072724.
70. Almeria S, Dubey J. Foodborne transmission of Toxoplasma gondii infection in the last decade **An overview** . Res Vet Sci. 2021;135:371–85. https://doi.org/10.1016/j.rvsc.2020.10.019.
71. Marin-Garcia PJ, Planas N, Llobat L: Toxoplasma gondii in foods: prevalence, control, and safety. Foods. 2022, 11(16).

72. A Rostami SM Riahi HR Gamble Y Fakhri M Nourollahpour Shiadeh M Danesh H Behniafar S Paktinat M Foroutan AH Mokdad 2020 Global prevalence of latent toxoplasmosis in pregnant women: a systematic review and meta-analysis. Clin Microbiol Infect. 26 6 673 683
73. F Nogareda Y Strat Le I Villena H Valk De V Goulet 2014 Incidence and prevalence of Toxoplasma gondii infection in women in France, 1980–2020: model-based estimation. Epidemiol Infect. 142 8 1661 1670
74. Q Asgari MH Motazedian A Khazanchin D Mehrabani S Naderi Shahabadi 2021 High prevalence of toxoplasma gondii infection in type I diabetic patients. J Parasitol Res. 2021 8881908
75. Soltani S, Tavakoli S, Sabaghan M, Kahvaz MS, Pashmforosh M, Foroutan M. The probable association between chronic toxoplasma gondii infection and type 1 and type 2 diabetes mellitus: a case-control study. Interdiscip Perspect Infect Dis. 2021;2021:2508780. https://doi.org/10.1155/2021/2508780.
76. M Milanovic N Milosevic N Milic MM Stojanoska E Petri JM Filipovic 2023 Food contaminants and potential risk of diabetes development: a narrative review. World J Diabetes. 14 6 705 723
77. United Nations Environment Programme and the World Health Organization: State of the science of endocrine disrupting chemicals 2012. In: Summary Report. Edited by WHO/UNEP: WHO Library; 2012: 260.
78. J Legler T Fletcher E Govarts M Porta B Blumberg JJ Heindel L Trasande 2015 Obesity, diabetes, and associated costs of exposure to endocrine-disrupting chemicals in the European Union. J Clin Endocrinol Metab. 100 4 1278 1288
79. Haidar Z, Fatema K, Shoily SS, Sajib AA. Disease-associated metabolic pathways affected by heavy metals and metalloid. Toxicol Rep. 2023;10:554–70. https://doi.org/10.1016/j.toxrep.2023.04.010.
80. J Suez T Korem D Zeevi G Zilberman-Schapira CA Thaiss O Maza D Israeli N Zmora S Gilad A Weinberger 2014 Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature. 514 7521 181 186
81. SK Jones DM McCarthy GD Stanwood C Schatschneider PG Bhide 2023 Learning and memory deficits produced by aspartame are heritable via the paternal lineage Sci Rep. 13 1 14326
82. Herzog H, Zhang L, Fontana L, Neely GG: Impact of non-sugar sweeteners on metabolism beyond sweet taste perception. Trends Endocrinol Metab. 2024.
83. E Gauthier FI Milagro S Navas-Carretero 2024 Effect of low-and non-calorie sweeteners on the gut microbiota: a review of clinical trials and cross-sectional studies. Nutrition. 117 112237
84. R Mullur YY Liu GA Brent 2014 Thyroid hormone regulation of metabolism. Physiol Rev. 94 2 355 382
85. Singh MJM: Environmental toxins and infertility: StatPearls Publishing; 2023.
86. S Kotopoulou A Zampelas E Magriplis 2022 Dietary nitrate and nitrite and human health: a narrative review by intake source Nutr Rev. 80 4 762 773
87. NNA Kyei D Boakye S Gabrysch 2020 Maternal mycotoxin exposure and adverse pregnancy outcomes: a systematic review Mycotoxin Res. 36 2 243 255
88. R Quansah FA Armah DK Essumang I Luginaah E Clarke K Marfoh SJ Cobbina E Nketiah-Amponsah PB Namujju S Obiri 2015 Association of arsenic with adverse pregnancy outcomes/infant mortality: a systematic review and meta-analysis. Environ Health Perspect. 123 5 412 421
89. M Mazumdar MOS Ibne Hasan R Hamid L Valeri L Paul J Selhub EG Rodrigues F Silva S Mia MG Mostofa 2015 Arsenic is associated with reduced effect of folic acid in myelomeningocele prevention: a case control study in Bangladesh Environ Health. 14 1 34
90. Li X, Li G, Cui S, Hou Y, Li Z, Yan Z, Huang T, Zhao T, Su H, Zhou B, et al. Arsenic disturbs neural tube closure involving AMPK/PKB-mTORC1-mediated autophagy in mice. Food Chem Toxicol. 2024;186:114538. https://doi.org/10.1016/j.fct.2024.114538.
91. Grace D, Dominguez-Salas, P., Alonso, S., Lannerstad, M., Muunda, E., Ngwili, N., Omar, A., Khan, M. and Otobo, E. The influence of livestock-derived foods on nutrition during the first 1,000 days of life. ILRI Policy Brief 25. Nairobi: International Livestock Research Institute; 2018.
92. World Health Organization: Soil-transmitted helminth infections. 2023 [https://www.who.int/news-room/fact-sheets/detail/soil-transmitted-helminth-infections].
93. Grace DRK, Kang'ethe E, Bonfoh B, Theis S. Gender roles and food safety in 20 informal livestock and fish value chains. IFPRI Discussion Paper 1489. Washington: International Food Policy Research Institute (IFPRI); 2015.
94. Roesel KaG, D.: Food safety and informal markets: animal products in sub-saharan africa: routledge.; 2014.
95. Shirley DT, Farr L, Watanabe K, Moonah S: A review of the global burden, new diagnostics, and current therapeutics for amebiasis. Open Forum Infect Dis. 2018, 5(7):ofy161.
96. MD Kirk SM Pires RE Black M Caipo JA Crump B Devleesschauwer D Dopfer A Fazil CL Fischer-Walker T Hald 2015 World health organization estimates of the global and regional disease burden of 22 foodborne bacterial, protozoal, and viral diseases, 2010: a data synthesis PLoS Med. 12 12 e1001921
97. Gomiero T. Food quality assessment in organic vs. conventional agricultural produce: findings and issues. Appl Soil Ecol. 2018;123(12):714–28.
98. Poulia KA, Bakaloudi DR, Alevizou M, Papakonstantinou E, Zampelas A, Chourdakis M. Impact of organic foods on chronic diseases and health perception: a systematic review of the evidence. Eur J Clin Nutr. 2025;79(2):90–103. https://doi.org/10.1038/s41430-024-01505-w.
99. Gaillard L, Barouki R, Blanc E, Coumoul X, Andreau K: Per- and polyfluoroalkyl substances as persistent pollutants with metabolic and endocrine-disrupting impacts. Trends Endocrinol Metab. 2024.
100. M Wu Z Zhu R Wan J Xu 2024 Exposure to per- and polyfluoroalkyl substance and metabolic syndrome: a nationally representative cross-sectional study from NHANES, 2003–2018 Environ Pollut. 346 123615
101. T Ahmed M Mahfuz MM Islam D Mondal MI Hossain AS Ahmed F Tofail SA Gaffar R Haque RL Guerrant 2014 The MAL-ED cohort study in Mirpur **Bangladesh** Clin Infect Dis. 59 Suppl 4 S280 286
102. RJ Crane KD Jones JA Berkley 2015 Environmental enteric dysfunction: an overview Food Nutr Bull. 36 1 Suppl S76 87
103. Protect against lead exposure with WIC foods [https://wicworks.fns.usda.gov/resources/protect-against-lead-exposure-wic-foods]
104. What is an IFSS? [https://www.fda.gov/federal-state-local-tribal-and-territorial-officials/integrated-food-safety-system-ifss-programs-and-initiatives/what-ifss]
105. U.S. Department of Agriculture: Food and Nutrition Service: Food Safety. 2024 [https://www.fns.usda.gov/fs/food-safety].
106. US Environmental Protection Agency: Summary of the toxic substances control act. Vol. 15 U.S.C. §2601 et seq. (1976); 1976. [https://www.epa.gov/laws-regulations/summary-toxic-substances-control-act]
107. Joint FAO/WHO Codex Alimentarius Commission: Codex alimentarius. Rome: World Health Organization : Food and Agriculture Organization of the United Nations; 2007.
108. Global Alliance for Improved Nutrition: Impact story 22: increasing food safety in traditional markets. [https://www.gainhealth.org/sites/default/files/publications/documents/22_eatsafe_0.pdf]
109. US Agency of International Development: EatSafe: evidence and action towards safe, nutritious food. EatSafe Program Brief. [https://www.gainhealth.org/sites/default/files/publications/documents/eatsafe-brief.pdf]
110. Global Alliance for Improved Nutrition: Literature review linking food safety and nutrition. A USAID EatSafe Project Report. 2020. [https://www.gainhealth.org/sites/default/files/publications/documents/eatsafe-literature-review-linking-food-safety-and-nutrition.pdf].
111. Masset E, Haddad L, Cornelius A, Isaza-Castro J: Effectiveness of agricultural interventions that aim to improve nutritional status of children: systematic review. BMJ (Clinical research ed). 2012, 344 (jan17 1):d8222-d8222.
112. Human Foods Program [https://www.fda.gov/about-fda/fda-organization/human-foods-program]

Publisher's Note