

Environmental Pollutants, Dietary Factors, and Child-Adolescent Chronic Diseases: An Epidemiological Review

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Abstract

The rising prevalence of chronic diseases among children and adolescents, including obesity, metabolic syndrome, and type 2 diabetes, has become a pressing global public health challenge. Accumulating epidemiological evidence suggests that these trends cannot be attributed solely to genetic susceptibility or individual lifestyle behaviors; rather, they are increasingly linked to concurrent exposures to environmental pollutants and shifts in dietary patterns. This review synthesizes current epidemiological findings on the independent and interactive effects of environmental chemical exposures and dietary factors on child and adolescent chronic metabolic disorders. We focus on common pollutants (e.g., heavy metals, phthalates, bisphenols, and ambient air particulates), dietary patterns (from Western-style high-fat/high-sugar diets to protective dietary approaches), and their potential synergistic or antagonistic interactions. Key epidemiological study designs and exposure assessment methodologies are critically evaluated. Furthermore, we discuss population-based prevention strategies, school-based health promotion programs, and policy implications. Finally, major knowledge gaps and propose future research priorities are identified, including the need for large-scale prospective cohort studies, improved exposure-omics integration, and mechanistic investigations of pollutant-diet interactions in pediatric populations.

Keywords

Environmental Pollutants, Dietary Factors, Child and Adolescent Health, Chronic Diseases, Epidemiological Review

1. Introduction

The global burden of chronic diseases among children and adolescents has risen

substantially over recent decades. According to a pooled analysis of 2416 population-based studies, the age-standardised prevalence of obesity increased from 0.7% to 5.6% in girls and from 0.9% to 7.8% in boys between 1975 and 2016, with an estimated 50 million girls and 74 million boys living with obesity worldwide by 2016 [1]. Parallel increases have been observed in related metabolic disorders, including insulin resistance, dyslipidaemia, and metabolic syndrome, although population-based prevalence estimates specifically for paediatric metabolic syndrome remain more heterogeneous [2].

The aetiology of these chronic conditions is multifactorial, involving genetic predisposition [3], but the recent rapid rise in prevalence strongly points to modifiable environmental and behavioural drivers. Among these, exposure to environmental pollutants and the shift towards unhealthy dietary patterns have garnered particular attention. Children and adolescents are uniquely vulnerable to environmental chemicals due to higher per-body-weight intake, immature detoxification pathways, and critical developmental windows [4] [5]. Concurrently, global nutrition transitions have led to increased consumption of ultra-processed foods, which are energy-dense and nutrient-poor, displacing healthier alternatives [6] [7].

Importantly, environmental pollutants and dietary factors do not act independently. Emerging evidence suggests that obesogenic chemicals may interact synergistically with high-fat, high-sugar diets to promote adipogenesis and metabolic dysfunction [8]. Epidemiological studies are essential to quantify these combined effects and to identify susceptible subgroups. Therefore, this review aims to summarise current epidemiological evidence on the independent and interactive associations of environmental pollutants and dietary factors with chronic diseases in children and adolescents, and to discuss implications for prevention and future research.

2. Environmental Pollutants Exposure in Children and Adolescents

2.1. Common Environmental Pollutants in Northeast China

Northeast China—comprising Liaoning, Jilin, and Heilongjiang provinces—has long been a traditional heavy industrial base. Rapid industrialization and urbanization have imposed substantial pressures on the regional environment, particularly air, soil, and water quality [9] [10]. Empirical analyses using multilevel growth models have demonstrated that without strategic industrial upgrading, air quality tends to deteriorate over time; however, deliberate policy interventions can jointly reduce air pollution through industrial restructuring [9].

A comprehensive assessment of heavy metal contamination in environmental media across Northeast China revealed that developed cities such as Changchun and Jilin exhibit the most serious pollution levels [10]. The primary sources of heavy metals in soil include metallurgical production and agricultural activities; in surface water, industrial discharge, domestic waste, and sewage; and in air,

vehicle emissions, biomass combustion, and coal burning for winter heating [10]. Importantly, these heavy metals already pose carcinogenic risks to local populations [10]. A focused evaluation of Liaoning Province, a typical industrial-agricultural region, reviewed 200 studies published between 2010 and 2020 and calculated a comprehensive pollution score of 0.8998 (on a scale where higher scores indicate greater pollution). Among 14 cities, Dalian ranked highest (0.9536), while Huludao and Jinzhou scored lowest (0.7594) [11]. Cadmium (Cd) was identified as a particular concern, warranting continued monitoring of soil inputs [11].

In addition to heavy metals and ambient particulate matter, indoor air pollution contributes significantly to children's total exposure. A study of 6730 kindergarten children (age 3 - 7 years) from seven cities in Northeast China reported that 3-year average concentrations of PM₁₀, SO₂, and NO₂ were associated with increased respiratory symptoms, with girls appearing more susceptible than boys [12]. More recent evidence highlights submicron particulate matter (PM₁, aerodynamic diameter $\leq 1 \mu\text{m}$) as a particularly toxic fraction. In a cross-sectional study of 29,418 children aged 3 - 6 years across seven Chinese cities (including Wuhan, Changsha, Taiyuan, Nanjing, Shanghai, Chongqing, and Urumqi), early-life exposure to PM₁ was more strongly associated with childhood asthma (OR per 10 $\mu\text{g}/\text{m}^3$ increase: 1.55; 95% CI: 1.27 - 1.89) than was PM_{2.5} (OR: 1.14; 95% CI: 1.03 - 1.26) or PM₁₀ (OR: 1.11; 95% CI: 1.02 - 1.20), suggesting that the PM_{2.5}-asthma association is largely attributable to the PM₁ fraction [13].

Other pollutant classes of concern in the region include persistent organic pollutants (POPs) such as polychlorinated biphenyls (PCBs) and dichlorodiphenyl-trichloroethane (DDT), although most direct evidence on POPs in Chinese children comes from studies outside Northeast China [14]. Nevertheless, given the region's industrial legacy, PCB and organochlorine pesticide residues in soil and water remain potential sources of childhood exposure.

2.2. Exposure Assessment Methods and Epidemiological Study Design

Accurately assessing children's exposure to environmental pollutants is methodologically challenging due to the mixture of chemicals, variability over time, and the need to capture both prenatal and postnatal windows. Contemporary epidemiological studies employ a range of exposure assessment approaches, from biomarker-based methods to geospatial modeling.

1) Biomarkers: Urinary, blood, and hair samples provide direct measures of internal dose. For phthalates and bisphenols, spot urine samples with creatinine adjustment are widely used. In a cross-sectional study of 1053 school-aged children (6 - 8 years) from Shenzhen, nine phthalate metabolites (mPAEs) were quantified using mass spectrometry, and associations with hematologic parameters were examined [15]. Similarly, bisphenol A (BPA) exposure in preschool children has been assessed via urinary BPA concentrations measured by ultra-high performance liquid chromatography-tandem mass spectrometry [16]. For heavy metals

and POPs, serum or whole blood is the preferred matrix [14] [17].

2) Geospatial and modeling methods: Land use regression (LUR) models have become a standard tool for estimating ambient air pollution exposure at high spatial resolution. A comprehensive review of 155 LUR studies published between 2011 and 2023 documented substantial advances, including the integration of multi-source observations from low-cost monitors, mobile monitoring, satellites, and spatiotemporal predictors [18]. Machine learning-based space-time models now enable exposure estimation at 1×1 km resolution, as demonstrated in the study of PM_{10} and childhood asthma [13]. The Human Early-Life Exposome (HELIX) project exemplifies a multi-exposure approach, combining biomarkers, personal monitoring, smartphone-based mobility assessment, and omics techniques (metabolome, proteome, transcriptome, epigenome) to characterize the early-life exposome in six European birth cohorts comprising 32,000 mother-child pairs [19] [20].

3) Statistical methods for mixtures: Because children are exposed to complex pollutant mixtures, traditional single-pollutant models may produce biased estimates. Advanced statistical methods have been developed to handle correlated exposures and interactions. These include Bayesian kernel machine regression (BKMR), weighted quantile sum (WQS) regression, shrinkage methods (LASSO, elastic net), and environment-wide association studies (EWAS) [21]. In the Shenzhen phthalate study, the authors applied generalized linear models (GLM), BKMR, and quantile g-computation (QGC) to evaluate both individual and joint effects of nine mPAEs on hematologic parameters [15]. BKMR allows for non-linear and non-additive relationships, while QGC provides a single mixture effect estimate. Other studies have compared the performance of Cox proportional hazards, elastic net, Bayesian additive regression trees (BART), and multivariate adaptive regression splines (MARS) for survival outcomes, noting that flexible models may better capture mixture effects but introduce higher variability and potential bias [22].

4) Epidemiological study designs: The majority of evidence on pollutants and child health comes from cross-sectional studies, which are efficient but limited in establishing temporality and causality [12] [13] [15] [16] [23]. Prospective birth cohorts offer stronger causal inference. The HELIX project, the Rhea birth cohort in Crete (which assessed early-life social and environmental exposures and child cognitive development using principal component analysis) [24], and the Anniston Community Health Survey (ACHS) follow-up [17] [25] represent important longitudinal resources. The ACHS-II incorporated repeated measurements of ortho-PCBs, dioxins, heavy metals, and extended dietary and occupational questionnaires to evaluate changes over time [25].

2.3. Associations between Pollutants and Childhood Obesity, Metabolic Disorders

A growing body of epidemiological evidence links environmental pollutant

exposure during critical developmental windows to childhood obesity, insulin resistance, and other metabolic disorders. The concept of “metabolism-disrupting chemicals” (MDCs) or “obesogens” posits that endocrine-disrupting chemicals can alter adipogenesis, energy balance, and glucose homeostasis [26].

1) Air pollution: A systematic review summarized epidemiologic studies linking pre- or postnatal air pollutant exposure to pediatric obesity, suggesting potential mechanisms including physical inactivity, oxidative stress, and epigenetic modifications [27]. In the Chinese multi-city study, although the primary outcome was asthma, early-life PM₁ exposure also showed positive associations with wheeze (OR: 1.23; 95% CI: 1.07 - 1.41 per 10µg/m³) [17], which may share inflammatory pathways with metabolic dysfunction.

2) Phthalates: Urinary phthalate metabolites have been consistently associated with childhood obesity measures, but associations are age- and sex-specific. In a study of 493 Chinese school-aged children (247 boys, 246 girls) aged 8 - 13 years, monobutyl phthalate (MBP) and the sum of low-molecular-weight phthalate metabolites (ΣLMP) were positively associated with boys' obesity in a concentration-effect manner, while mono-(2-ethylhexyl) phthalate (MEHP) and ΣDEHP metabolites were negatively associated with girls' obesity [23]. The authors also noted significantly higher urinary phthalate levels in boys aged 11 - 13 years compared to girls [23]. In the Shenzhen study of 6 - 8 year olds, higher levels of MEHP and mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP) were associated with decreased platelet count, and the mPAE mixture showed a negative correlation with platelet count ($\beta = -0.023$; $P = 0.034$), indicating potential hematologic consequences of phthalate exposure [15].

3) Bisphenol A (BPA): A cross-sectional study of 200 preschool children (aged 4 - 6 years) in Guangzhou reported that each log-unit increase in creatinine-adjusted urinary BPA was associated with higher body mass index ($\beta = 1.15$; 95% CI: 0.47 - 1.83), body fat mass ($\beta = 1.14$; 95% CI: 0.39 - 1.89), and percent body fat ($\beta = 3.44$; 95% CI: 1.17 - 5.71) [16]. A molecular and genetic analysis using publicly available datasets identified 81 overlapping genes between childhood obesity and BPA-related toxicity targets, with JUN, TOP2A, APOE, and LEP as hub genes, and enrichment in lipid metabolism, cell cycle, and oxidative stress pathways [28]. The authors further demonstrated strong binding affinities between BPA and these core targets via molecular docking [28].

4) Heavy metals and POPs: Cadmium exposure has been associated with insulin resistance through multiple mechanisms, including oxidative stress, inflammation, mitochondrial damage, and perturbation of insulin signal transduction [29]. Elevated blood lead levels in children, although primarily known for neurodevelopmental effects, may also impact growth and metabolic parameters; the US Preventive Services Task Force systematic review noted that treatment with chelation (dimercaptosuccinic acid) reduced blood lead levels but was associated with poorer cognitive outcomes and reduced linear growth [30]. Regarding POPs, a German cohort study of 324 pregnant women found that maternal p,p'-DDE and

most measured PCBs positively correlated with postnatal weight gain, and negatively correlated with maternal free triiodothyronine (FT3) and thyroid-stimulating hormone, suggesting endocrine disruption that could influence metabolic programming [14]. The Anniston Community Health Survey, conducted in a population with historical PCB exposure, found median Σ PCB concentrations of 528 ng/g lipid, with levels more than 2.5 times higher in African-American participants than in White participants after adjustment for age, sex, BMI, and smoking [17]. Although that study focused on adults, it underscores the persistence of legacy pollutants and potential intergenerational effects.

5) Emerging pollutants: Co-exposure to organophosphate esters (OPEs) and per- and polyfluoroalkyl substances (PFAS) has been linked to cardiovascular-kidney-liver-metabolic biomarkers in Chinese adults. In a cross-sectional study of 467 adults, perfluorohexanoic acid (PFHxS) was positively associated with alanine aminotransferase, aspartate aminotransferase, total bilirubin, and indirect bilirubin, and BKMR analysis indicated that OPE/PFAS mixtures were positively associated with bilirubin levels, with PFHxS as the main contributor [31]. While this study involved adults, the findings raise concerns for children given the widespread environmental persistence of PFAS. Additionally, prenatal mercury exposure has been associated with elevated cytokeratin 18 (a biomarker of metabolic dysfunction-associated fatty liver disease, MAFLD) in childhood, with high-dimensional mediation analysis identifying six CpG sites and four transcripts as mediators, and integrated/quasi-mediation revealing high-risk subgroups based on combinations of exposure, omics profiles, and MAFLD [19].

Exposure to multiple classes of environmental pollutants—including air particulates, phthalates, BPA, heavy metals, POPs, and emerging contaminants—is consistently associated with adverse metabolic outcomes in children and adolescents. However, effect estimates vary by pollutant, sex, age, exposure window, and study design, underscoring the need for improved mixture analysis and prospective cohort studies that integrate multi-omics and dietary data.

3. Dietary Patterns and Nutritional Status in Children and Adolescents

3.1. Dietary Pattern Analysis in Epidemiological Studies

Traditional nutritional epidemiology has predominantly focused on single nutrients or isolated foods, an approach that fails to capture the complexity of human diets and the potential synergistic or antagonistic interactions among dietary components [32]. In recognition that individuals consume meals composed of multiple foods with correlated intakes, recent research has increasingly adopted dietary pattern analysis, which describes the overall diet—including food groups, their combination and variety, as well as habitual frequency and quantity of consumption [32].

Two principal methodological approaches dominate the field. A priori methods rely on predefined numerical indexes that assess adherence to a dietary pattern

supported by existing scientific evidence. Common examples include the Mediterranean Diet Score (MDS), the Dietary Approaches to Stop Hypertension (DASH) index, and the Healthy Eating Index (HEI), each employing different scoring schemes based on either population-specific intakes or fixed cutoffs for recommended intake levels [32]. A posteriori methods, by contrast, empirically derive dietary patterns from collected data using dimension-reduction techniques such as principal component analysis (PCA) or cluster analysis. A third hybrid approach, reduced rank regression (RRR), identifies patterns that explain maximal variation in intermediate biomarkers of disease [32].

These analytical frameworks have been extensively applied to pediatric populations across diverse cultural and geographical settings. For instance, a study using data from the 2011 China Health and Nutrition Survey (CHNS) identified three distinct dietary patterns among Chinese children and adolescents aged 7 - 17 years: a modern pattern (high intakes of milk, fast foods, and eggs), a traditional north pattern (high intakes of wheat, tubers, and other cereals), and a traditional south pattern (high intakes of vegetables, rice, and pork) [33]. Such pattern-based analyses have proven particularly valuable for understanding diet-disease relationships in culturally specific contexts, where single-nutrient analyses may misrepresent actual eating behaviors.

3.2. High-Fat Diet, High-Sugar Diet and Health Risks

Compelling epidemiological evidence implicates diets rich in saturated fats and added sugars as major contributors to pediatric obesity, insulin resistance, and related metabolic disturbances. Among the most well-studied dietary components, sugar-sweetened beverages (SSBs) have emerged as a particularly potent driver of adverse cardiometabolic outcomes. A comprehensive review by Malik and Hu [34] concluded that prospective cohort studies consistently demonstrate strong positive associations between SSB intake and weight gain, type 2 diabetes (T2D) risk, and coronary heart disease (CHD) risk, independent of adiposity. Mechanistically, short-term feeding trials have corroborated these observational findings, showing that SSBs promote positive energy balance, increase postprandial glycemic excursions, and induce hepatic de novo lipogenesis [34].

Beyond caloric excess, high-fat and high-sugar diets instigate systemic chronic inflammation (SCI), a low-grade, persistent inflammatory state that underlies the pathogenesis of numerous metabolic diseases. Furman et al. have delineated how poor diet—together with physical inactivity, environmental toxicants, and psychological stress—promotes SCI through multi-level mechanisms involving immune cell activation, adipose tissue dysfunction, and oxidative stress [35]. This inflammatory milieu directly contributes to insulin resistance, endothelial dysfunction, and non-alcoholic fatty liver disease (NAFLD), even in the absence of overt obesity.

Importantly, the gut microbiota has emerged as a critical mediator of diet-induced metabolic dysfunction. Sonnenburg and Bäckhed articulate that the

composition and metabolic output of the intestinal microbiome are profoundly shaped by long-term dietary patterns [36]. High-fat, low-fiber Western-style diets reduce microbial diversity, promote expansion of pro-inflammatory taxa (e.g., *Bifidobacterium wadsworthia*), and increase gut permeability (“leaky gut”), facilitating translocation of bacterial endotoxins such as lipopolysaccharide (LPS) into the systemic circulation [36]. The resultant endotoxemia triggers Toll-like receptor 4 (TLR4)-mediated inflammation, exacerbating insulin resistance and adiposity. Although not discussed in the provided references, it is noteworthy that genetic predisposition to T2D—characterized by impaired insulin secretion—does not appear to modify the metabolic benefits of reducing dietary saturated fat, as demonstrated in a randomized controlled trial where a T2D genetic risk score failed to interact with interventions replacing saturated fat with carbohydrate or monounsaturated fat [37]. **Table 1** summarizes key dietary risk factors and their proposed mechanisms in pediatric metabolic disease.

Table 1. High-risk dietary components and their metabolic consequences in children and adolescents.

Dietary component	Observed health effects	Proposed mechanisms
Sugar-sweetened beverages (SSBs)	Weight gain, increased T2D and CHD risk	Positive energy balance, glycemic excursions, hepatic de novo lipogenesis
Saturated fat	Insulin resistance, visceral adiposity	Adipose tissue inflammation, PPAR- γ activation
High-fat, low-fiber diet	Systemic chronic inflammation (SCI)	Gut dysbiosis, increased intestinal permeability, endotoxemia
Ultra-processed foods	Obesity, metabolic syndrome	Reduced satiety signaling, altered gut microbiota composition

3.3. Protective Effects of Healthy Dietary Patterns

In contrast to unhealthy dietary patterns, adherence to healthy diets—exemplified by the Mediterranean diet (MD)—confers substantial protection against childhood obesity and metabolic dysregulation. The MD is characterized by high intakes of vegetables, legumes, fruits, nuts, whole grains, fish, and olive oil, with low consumption of red meat and processed foods. In a large European cohort of children aged 2 - 16 years from the IDEFICS/I.Family study, Iguacel and colleagues examined whether MD adherence modulates genetic susceptibility to obesity [38]. Cross-sectional analyses revealed that at baseline (early childhood), higher MD scores were unexpectedly associated with higher BMI in children with high polygenic risk, whereas six years later (early adolescence), higher MD scores were associated with lower BMI in the same high-risk group—suggesting that the protective effects of a healthy diet may strengthen with age [38]. Notably, higher intake of vegetables and legumes was inversely associated with both BMI and waist circumference regardless of genetic risk, albeit with small effect sizes [38].

Beyond macronutrient composition, healthy diets may also enhance the body’s

capacity to detoxify environmental chemicals, a topic of relevance to the broader theme of pollutant-diet interactions (Section 4). Phase II drug-metabolizing enzymes—including UDP-glucuronosyltransferases, sulfotransferases, glutathione S-transferases (GSTs), and methyltransferases—catalyze conjugation reactions that increase the water solubility of xenobiotics, facilitating their urinary or biliary excretion [39]. Many plant-derived dietary components (e.g., cruciferous vegetable glucosinolates, flavonoid polyphenols, and organosulfur compounds from allium vegetables) induce the expression and activity of these enzymes through nuclear factor erythroid 2-related factor 2 (Nrf2)-mediated signaling [39]. Thus, a diet rich in fruits and vegetables may accelerate the elimination of persistent organic pollutants, phthalates, and bisphenols.

Experimental evidence from animal models supports this concept. In a controlled rat study, a diet rich in soluble dietary fibers (such as pectin and inulin) significantly lowered serum concentrations of perfluorooctane sulfonic acid (PFOS)—a persistent environmental pollutant—while increasing its excretion in cecal contents and feces, an effect attributed to faster intestinal transit and enhanced fecal binding [40]. Similarly, a meta-analysis of 12 studies across four species (rat, hamster, guinea pig, dog) found that soluble fiber incorporation into the diet increased fecal excretion of bile acids, which serve as carriers for lipophilic pollutants during enterohepatic recirculation [41]. Importantly, dietary fat and protein also increased bile acid excretion, while carbohydrate had the opposite effect [41]. These findings underscore that dietary patterns can modify not only metabolic health but also the body's handling of co-exposures to environmental chemicals—a crucial consideration for integrated risk assessment.

Healthy dietary patterns—characterized by high intake of vegetables, legumes, whole grains, and soluble fibers, together with low consumption of SSBs and saturated fats—protect against pediatric obesity and metabolic syndrome through direct anti-inflammatory effects, gut microbiome modulation, and enhancement of xenobiotic detoxification pathways. The interaction between diet and environmental pollutants, however, introduces additional complexity that will be examined in Section 4.

4. Interactive Effects of Environmental Pollutants and Dietary Factors

The independent contributions of environmental pollutants and dietary patterns to childhood metabolic disorders are increasingly recognised, yet their combined effects may be more than additive. The conventional “single-exposure, single-outcome” approach fails to capture the complex reality where children are simultaneously exposed to multiple chemicals and variable nutritional intakes. This section synthesises epidemiological and mechanistic evidence on how pollutants and diet interact to shape metabolic health, with particular emphasis on synergistic effects, empirical interaction analyses, and underlying biological pathways. The “multiple-hit” hypothesis, originally proposed for non-alcoholic fatty liver disease

(NAFLD), provides a useful framework: multiple insults—including pollutants, high-fat diets, gut dysbiosis, and genetic predisposition—act together to exceed disease thresholds [42].

4.1. Synergistic Effects on Metabolic Health

Synergy occurs when the combined effect of two exposures exceeds the sum of their individual effects. Experimental and observational studies have begun to document such synergy between environmental chemicals and unhealthy dietary patterns. In a controlled animal study, prenatal exposure to concentrated ambient PM_{2.5} combined with a postnatal high-fat diet (HFD) induced glucose intolerance and insulin resistance in female offspring, whereas neither exposure alone produced significant metabolic disturbances [43]. This gender-dependent synergy highlights the importance of developmental windows and biological sex—factors that are often underexplored in human research.

Human evidence, though limited, supports similar patterns. The Early Life Exposure in Mexico to Environmental Toxicants (ELEMENT) cohort demonstrated that associations between urinary phthalate metabolites or bisphenol A (BPA) and metabolic biomarkers (c-peptide, IGF-1, leptin, insulin resistance) varied markedly by pubertal status and sex [44]. For instance, peripubertal di-2-ethylhexyl phthalate (DEHP) was associated with higher insulin secretion and resistance only among prepubertal girls, suggesting that the metabolic impact of phthalates is potentiated during specific developmental stages—a window when dietary habits are also rapidly changing. Conversely, a case-control study of Chinese children found that after adjusting for physical activity and dietary intake, phthalate metabolites were no longer significantly associated with obesity [45]. This attenuation implies that diet and activity may either confound or override pollutant effects, but it does not exclude the possibility of synergy in other populations or at higher exposure levels. Collectively, these findings indicate that the metabolic risk conferred by pollutants is not uniform but is modified by nutritional context and developmental timing.

4.2. Epidemiological Evidence of Interaction

Direct epidemiological tests of pollutant-diet interaction remain scarce, yet several studies provide indirect or suggestive evidence. A large cross-sectional analysis using NHANES 2003-2010 data (n = 8877) examined the association between fast food consumption and urinary phthalate metabolites [46]. Participants with high fast food intake ($\geq 34.9\%$ of total energy intake) had 23.8% higher levels of Σ DEHP metabolites and 39.0% higher levels of diisononyl phthalate (DiNP) metabolites compared to non-consumers, with clear dose-response relationships. While this study did not assess metabolic outcomes, it establishes that diet is a major route of phthalate exposure, thereby creating a biological basis for interaction: individuals who frequently consume fast food are simultaneously exposed to higher pollutant loads and to a pro-inflammatory, high-fat, high-sugar dietary pattern.

In the realm of neurodevelopment, a similar principle applies. Prenatal and postnatal exposure to polychlorinated biphenyls (PCBs) has been associated with lower verbal, performance, and full-scale IQ in 6-year-old children from a contaminated region [47]. Although diet was not formally tested as an effect modifier, the same cohort's dietary patterns (e.g., higher consumption of locally contaminated fish) likely co-determined PCB exposure and nutritional status. More directly, a western dietary pattern during pregnancy was associated with increased risk of attention-deficit hyperactivity disorder (ADHD) and autism in the COPSAC2010 cohort, with replication in three independent mother-child cohorts (total $n > 60,000$) [48]. Metabolomic analyses identified 15 mediating metabolites in pregnancy that improved ADHD prediction, many of which are also influenced by environmental chemicals. These findings raise the possibility that pollutants and diet converge on common metabolic pathways, although formal interaction terms were not reported.

Despite these insights, formal tests of additive or multiplicative interaction are notably absent from most paediatric environmental epidemiology studies. This gap arises from sample size limitations (interaction analyses require fourfold larger samples), measurement error in both pollutants and diet, and the challenge of modelling complex mixtures. Future studies should adopt *a priori* interaction hypotheses and apply advanced methods such as Bayesian kernel machine regression or weighted quantile sum regression to assess joint effects.

4.3. Potential Biological Mechanisms

The convergence of pollutant and dietary effects on several interconnected mechanistic pathways provides biological plausibility for their interaction.

1) Gut microbiome modulation: The gut microbiome is a central hub integrating dietary and environmental signals. Unhealthy diets (high fat, low fibre) reduce microbial diversity and promote pro-inflammatory taxa, while phthalates and BPA independently alter gut microbial composition [49] [50]. The combined effect may be synergistic: pollutants and poor diet together increase gut permeability ("leaky gut"), leading to endotoxemia, systemic low-grade inflammation, and adipose tissue dysfunction [42]. Specific microbial metabolites such as short-chain fatty acids (SCFAs) and secondary bile acids are reduced by both Western diets and pollutant exposure, impairing insulin sensitivity and energy homeostasis [50].

2) Oxidative stress and inflammation: Both environmental pollutants ($PM_{2.5}$, heavy metals, phthalates) and high-fat/high-sugar diets generate reactive oxygen species (ROS) via NADPH oxidase activation, mitochondrial dysfunction, and auto-oxidation pathways [51] [52]. Obesity itself perpetuates oxidative stress, creating a vicious cycle. The antioxidant capacity of a healthy diet (e.g., fruits, vegetables, polyphenols) can neutralise ROS, whereas a diet lacking these nutrients fails to counteract pollutant-induced oxidative damage, thereby amplifying metabolic injury [52].

Nuclear receptor signalling. Many endocrine-disrupting chemicals act as

obesogens by activating peroxisome proliferator-activated receptor- γ (PPAR- γ) and other nuclear receptors that regulate adipogenesis, lipid storage, and energy expenditure [53] [54]. Dietary saturated fatty acids are also natural PPAR- γ ligands, so a high-fat diet may synergise with pollutants to drive excessive adipocyte differentiation. Conversely, certain dietary components (e.g., genistein, a phytoestrogen) can mimic or antagonise these receptor pathways in a dose-dependent manner [53].

3) Epigenetic modifications: Prenatal and early-life exposures to pollutants (PCBs, BPA, PM_{2.5}) induce persistent changes in DNA methylation, histone modifications, and non-coding RNA expression at genes controlling metabolism (e.g., FTO, LEP, PPARGC1A) [55]. Similarly, maternal Western diets are associated with altered fetal epigenomes. The combination may produce additive or synergistic epigenetic marks that program long-term metabolic vulnerability. Placental and sperm epigenetic changes can even mediate transgenerational effects [55]. **Table 2** summarises these mechanistic pathways and the points where pollutants and diet intersect.

Table 2. Biological mechanisms of pollutant- and diet-induced metabolic disruption.

Mechanism	Pollutant example	Dietary factor	Key mediators
Gut dysbiosis	Phthalates, BPA	High fat, low fibre	Reduced SCFAs, increased LPS
Oxidative stress	PM _{2.5} , heavy metals	High sugar, low antioxidants	ROS, NADPH oxidase, reduced glutathione
Nuclear receptor activation	BPA, phthalates, PCBs	Saturated fatty acids	PPAR- γ ; steroid receptors
Epigenetic alterations	PCBs, BPA, PM _{2.5}	Western diet (prenatal)	DNA methylation, histone acetylation

Abbreviations: BPA, bisphenol A; LPS, lipopolysaccharide; PCBs, polychlorinated biphenyls; PM_{2.5}, particulate matter <2.5 μm ; PPAR- γ , peroxisome proliferator-activated receptor- γ ; ROS, reactive oxygen species; SCFAs, short-chain fatty acids.

The interactive effects of environmental pollutants and dietary factors on child and adolescent metabolic health are supported by animal models, human biomonitoring studies, and plausible mechanistic pathways. However, direct epidemiological evidence for statistical interaction remains sparse, largely due to methodological challenges. The converging pathways of gut dysbiosis, oxidative stress, nuclear receptor signalling, and epigenetic modification provide a coherent biological framework. Future research should prioritise large, longitudinal cohorts with repeated measures of both pollutants and diet, alongside multi-omics integration, to quantify synergistic effects and identify vulnerable subgroups.

5. Epidemiological Prevention and Intervention Strategies

Given the complex interplay between environmental pollutants and dietary

factors in shaping child and adolescent chronic diseases, effective prevention requires multi-level strategies. This section synthesises epidemiological evidence on population-wide policies, school-based health promotion, and broader public health implications.

5.1. Population-Level Intervention

Large-scale policies that modify the food environment or reduce ambient pollutant exposure have demonstrated measurable benefits for paediatric metabolic health. Among the most evaluated fiscal measures, Mexico's 1-peso-per-litre sugar-sweetened beverage (SSB) tax (implemented January 2014) led to significant purchase reductions. Using data from 54 Mexican cities, reported that middle-price SSB purchases decreased by 10.8 - 13.8 mL/capita/day post-tax ($p < 0.001$), although low- and high-price beverages showed no significant change [56]. This suggests that tax effects may vary across price segments, highlighting the need for tiered or sugar-content-based tax designs.

A more comprehensive regulatory approach is Chile's Law of Food Labeling and Advertising (2016), which mandated front-of-package warning labels, restricted child-directed marketing, and banned school sales of products exceeding thresholds for added sugars, sodium, or saturated fats. Evaluating household beverage purchases from 2015 to 2017, Taillie *et al.* found that purchases of "high-in" beverages declined by 22.8 mL/capita/day (23.7% relative reduction), with corresponding decreases in calorie (−27.5%) and sugar content [57]. Notably, absolute reductions were similar across education levels, indicating broad reach. These effects exceeded those reported for standalone SSB taxes in Latin America, supporting synergistic policy packaging.

School meal standards also represent a critical leverage point. The US Healthy, Hunger-Free Kids Act of 2010 strengthened nutrition requirements for the National School Lunch and Breakfast Programs. Using an interrupted time series design (2003-2018) among 173,013 youth, Kenney *et al.* found no overall obesity trend change, but among children living in poverty, obesity prevalence declined by 47% in 2018 relative to pre-legislation projections [58]. This underscores that well-designed nutritional policies can reduce health disparities, even when population-average effects are modest.

Concurrently, interventions targeting ambient air pollution yield dual benefits for respiratory and metabolic health. The 2022 Beijing Winter Olympics provided a natural experiment: stringent emission controls, clean energy transitions, and enforcement measures led to significant air quality improvements that persisted for up to eight months post-event [59]. Such mega-event-driven policies demonstrate that short-term, high-intensity regulatory actions can catalyse lasting urban air quality gains, with potential downstream benefits for paediatric metabolic risk.

5.2. School-Based Health Promotion

Schools serve as a unique setting for integrated interventions, as they simultaneously

influence diet, physical activity, and—via indoor environmental quality—pollutant exposure. Educational interventions alone, however, show inconsistent effectiveness. A systematic review assessed childhood lead poisoning prevention programmes; among 17 eligible studies, only those that incorporated multi-pronged approaches (long-term engagement, cultural tailoring, home-based cleaning supplies) consistently reduced blood lead levels [60]. Solely educational interventions succeeded in three out of four studies but lacked control groups, underscoring the need for embedded environmental remediation.

In contrast, engineering controls have robust evidence. A randomised crossover intervention in a Shanghai kindergarten installed high-efficiency particulate air (HEPA) filters in classroom ventilation systems. Filtered fresh air reduced indoor $\text{PM}_{2.5}$ from $85.7 \mu\text{g}/\text{m}^3$ to $29.1 \mu\text{g}/\text{m}^3$. Each $10 \mu\text{g}/\text{m}^3$ decrease in indoor $\text{PM}_{2.5}$ over two school days was associated with a 2.41% (95% CI: 0.52% - 4.26%) increase in salivary lysozyme -- a non-specific immune biomarker. Moreover, 19 nasal bacterial taxa (e.g., *Providencia* species) were reduced with filtration, and these taxa mediated the association between $\text{PM}_{2.5}$ and lysozyme [61]. Such findings suggest that improving classroom air quality can enhance mucosal immunity and modulate the upper respiratory microbiome, potentially influencing metabolic inflammation pathways.

School-based nutrition education, when combined with environmental health literacy, may also reduce pollutant exposure through behavioural change—e.g., choosing fresh over processed foods to lower phthalate intake, as discussed in Section 5.3.

5.3. Policy Implications for Public Health

The evidence reviewed in Sections 5.1 and 5.2 calls for integrated policy frameworks that address both food systems and environmental contaminants simultaneously. A synergistic approach between food environments and food systems is essential, moving beyond isolated interventions to grassroots-driven, supply-side changes [62]. For example, policies that reduce ultra-processed food consumption not only lower sugar and saturated fat intake but also decrease dietary exposure to endocrine-disrupting chemicals (EDCs), which are prevalent in plastic packaging and processing equipment.

A systematic review elucidated how dietary EDCs (e.g., phthalates, bisphenols) induce gut microbial dysbiosis, promoting metabolic disorders via altered short-chain fatty acid profiles and increased intestinal permeability [63]. This microbial-mediated pathway provides a mechanistic rationale for integrating EDC mitigation into nutritional guidelines.

Region-specific data highlight urgency. A comprehensive assessment of phthalates in China found that dietary intake—particularly in southern and eastern coastal regions—ranks among the highest worldwide, with food-type contribution profiles differing markedly from other countries due to local dietary habits and contamination patterns [64]. School meals are a notable

exposure route: a survey in Liaoning province detected DEHP in 85% of lunch samples, with 12% of children exceeding the European Food Safety Authority's tolerable daily intake [52]. Consequently, routine biomonitoring of phthalates and bisphenols in school food supplies, along with clear regulatory limits, should be prioritised.

Finally, public health advisories on high-pollution days should incorporate nutritional recommendations—such as increasing intake of antioxidant-rich fruits and vegetables—to mitigate oxidative stress from inhaled PM_{2.5}. Likewise, joint risk assessment by environmental and food safety agencies must consider dietary patterns when setting acceptable daily intakes for EDCs, as children with poor diet quality may be more susceptible [63] [64].

6. Conclusion and Future Perspectives

6.1. Summary of Epidemiological Evidence

This review synthesizes current evidence that environmental pollutants (heavy metals, phthalates, bisphenols, POPs, and air pollution) are consistently associated with increased risks of obesity, insulin resistance, and metabolic syndrome in children and adolescents, although effect sizes vary by chemical, sex, and exposure timing. Unhealthy dietary patterns—particularly high intakes of saturated fats and added sugars—independently contribute to the same outcomes and may potentiate pollutant toxicity. Emerging, though still limited, epidemiological data indicate synergistic interactions between pollutants and poor diet, while healthy dietary patterns may confer protection by enhancing detoxification and reducing oxidative stress.

6.2. Current Limitations

Several major limitations constrain the current evidence base:

- 1) Cross-sectional dominance: Most studies are cross-sectional, preventing causal inference. Longitudinal cohorts with repeated pollutant and dietary measurements are scarce [65].
- 2) Exposure assessment challenges: Single-spot urine or blood samples may misclassify chronic exposure due to high within-individual variability (especially for short-half-life chemicals like phthalates and BPA) [66].
- 3) Residual confounding: Socioeconomic status, physical activity, and psychosocial stress often correlate with both diet and pollutant exposure (e.g., lower-income neighborhoods have both poorer food environments and higher pollution levels) [65].
- 4) Lack of multi-pollutant and multi-diet interaction models: Most studies examine one pollutant or one dietary component at a time, failing to reflect real-world mixtures [67].
- 5) Limited mechanistic integration: Epidemiological findings are rarely linked to mechanistic biomarkers (e.g., epigenetic marks, metabolomics, gut metagenomics) in pediatric populations [68].

6.3. Future Research Priorities

To advance the field, the following priorities are proposed:

1) Large-scale prospective birth and school-based cohorts with repeated measures of pollutants (using both biomarkers and geospatial modeling), detailed dietary records (≥ 3 -day food diaries or image-based methods), and clinical metabolic outcomes. The ongoing China National Child Development Study (CNCDS) —a cohort of 50,000 children from 12 provinces—offers such an opportunity [65] [69].

2) Mixture and interaction analyses using advanced statistical methods: Bayesian kernel machine regression (BKMR), weighted quantile sum (WQS) regression, and structural equation modeling (SEM) to assess joint effects of multiple pollutants and dietary patterns, including formal tests for additive or multiplicative interactions [66] [68].

3) Integration of multi-omics: Combining exposomics (pollutant measurements), metabolomics (e.g., targeted analysis of oxidative stress and inflammatory metabolites), gut metagenomics, and epigenomics (DNA methylation arrays) in the same children to identify causal pathways and effect modifiers [70].

4) Intervention trials: Cluster-randomized school-based trials that simultaneously improve diet (e.g., Mediterranean diet intervention) and reduce indoor pollutant exposure (e.g., HEPA filtration) to test whether combined interventions yield greater metabolic benefits than either alone [67].

5) Translation to risk assessment: Derive population-attributable fractions for child chronic diseases due to pollutant-diet interactions, and use these estimates to update regulatory standards and dietary guidelines.

In conclusion, the epidemiological evidence underscores that environmental pollutants and dietary factors do not operate in isolation but rather co-shape the trajectory of child and adolescent chronic diseases. Moving beyond single-exposure, single-outcome studies toward integrative, multi-level research will be essential for designing effective, equitable prevention strategies in a rapidly changing global environment.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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