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Nutrition-Gut Microbiota Interactions During Adolescence: Hormonal, Metabolic, Immune, and Neuropsychological Bidirectional Pathways

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Abstract

Background: Adolescence is a critical developmental stage characterized by profound hormonal, metabolic, immunological, and neuropsychological changes. During this period, the gut microbiota undergoes maturation toward an adult-like configuration while remaining highly plastic and sensitive to environmental influences, particularly nutrition. Increasing evidence suggests that bidirectional interactions between diet, pubertal hormones, and the gut microbiota play a key role in shaping long-term health outcomes.

Objective: To synthesize current evidence on the interactions between nutrition and gut microbiota during adolescence and to analyze their implications for metabolic regulation, immune homeostasis, and neuropsychological development.

Methods: An integrative review with systematic search and qualitative synthesis (PRISMA 2020-guided reporting was conducted using peer-reviewed human studies and mechanistic reviews indexed in PubMed and PubMed Central. Articles addressing gut microbiota composition, pubertal hormonal changes, dietary factors, microbial metabolites, immune maturation, and gut-brain axis signaling during adolescence were included.

Results: Available evidence indicates that pubertal progression is associated with sex-specific remodeling of the gut microbiota. Nutritional patterns strongly influence microbial diversity and metabolic function, particularly through the production of short-chain fatty acids and modulation of bile acid metabolism. These microbial signals interact with host endocrine pathways, immune maturation, intestinal barrier integrity, and stress-related neurobiological processes. Dysbiosis during adolescence has been linked to increased susceptibility to metabolic disturbances, low-grade inflammation, and neuropsychological vulnerability.

Conclusion: Adolescence represents a window of opportunity for microbiota-targeted nutritional interventions. Promoting healthy dietary patterns during this stage may support optimal microbiota maturation and contribute to the prevention of metabolic, immune, and mental health disorders later in life.

Keywords: *Nutrition-Gut Microbiota Interactions; Adolescence; Neuropsychological Bidirectional Pathways*

Abbreviations

ADH: Antidiuretic Hormone; BMI: Body Mass Index; CRP: C-Reactive Protein; FXR: Farnesoid X Receptor; GI: Gastrointestinal; HPG: Hypothalamic-Pituitary-Gonadal (Axis); HPA: Hypothalamic-Pituitary-Adrenal (Axis); IGF-1: Insulin-Like Growth Factor 1; IgA: Immunoglobulin A; IL-6: Interleukin 6; LBP: Lipopolysaccharide-Binding Protein; LPS: Lipopolysaccharide; MEDLINE: Medical Literature

Analysis and Retrieval System Online; NOS: Newcastle-Ottawa Scale; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RoB 2: Risk of Bias Tool for Randomized Trials; ROBINS-I: Risk Of Bias In Non-randomized Studies of Interventions; SCFA: Short-Chain Fatty Acid; sCD14: Soluble Cluster of Differentiation 14; SYRCLE: Systematic Review Centre for Laboratory animal Experimentation; TGR5: Takeda G-Protein-Coupled Receptor 5; VO_2: Oxygen Consumption

Introduction

Adolescence is a critical developmental transition characterised by profound endocrine, metabolic, immune, and neuropsychological changes that interact bidirectionally with the gut microbiota. During this period, the microbiome progresses toward a more stable, adult-like configuration while remaining highly plastic and environmentally responsive, making puberty a window of heightened susceptibility- and opportunity-for microbiome-targeted prevention strategies [1-4,10,22].

Pubertal activation of the hypothalamic-pituitary-gonadal (HPG) axis coincides with shifts in insulin/IGF-1 signalling, body composition, sleep timing, psychosocial stress, diet, and physical activity. In parallel, human studies indicate that gut microbial trajectories during puberty show sex-related patterning and pubertal-stage associations, supporting a close interplay between sexual maturation and intestinal ecology [1-4,13,22].

Mechanistically, rising oestrogens, progesterone, and androgens can reshape the gut ecosystem through changes in intestinal motility and transit, epithelial barrier integrity, mucus dynamics, and mucosal immune tone [5,7,18,20]. In addition, the microbiome can influence systemic sex-steroid availability through the estrobolome, including microbial enzymatic activities such as β-glucuronidase that participate in enterohepatic oestrogen recirculation, thereby linking microbial composition and function to sex-steroid signalling [6,19,20].

Diet is the dominant modifiable environmental driver of microbiome structure and function during adolescence and may modulate pubertal timing through microbiome-metabolite pathways. Nutritional patterns influence microbial diversity and functional output, particularly during periods of rapid growth and hormonal change [9,10,14,23]. Emerging human evidence supports the concept that habitual dietary composition can shape pubertal development partly through gut microbial signatures and metabolite-mediated host signalling [1,3,9,10,14].

From a metabolic standpoint, adolescence is marked by transient, physiological insulin resistance and dynamic changes in lipid and bile acid metabolism, which can alter intestinal substrate availability and microbial niche selection [13,15,17]. Microbiota-derived short-chain fatty acids (SCFAs) provide a key mechanistic bridge between diet and host physiology, influencing metabolic inflammation, insulin sensitivity, and enteroendocrine signalling [8,16,17]. Meanwhile, bile acid-microbiota crosstalk further integrates diet, microbial ecology, and endocrine-metabolic phenotypes through FXR- and TGR5-dependent pathways [15,17].

Low-grade endotoxin exposure, often referred to as metabolic endotoxaemia, represents another relevant pathway linking diet, intestinal barrier function, and systemic inflammation. Dietary quality and gut permeability influence circulating lipopolysaccharide activity, contributing to cardiometabolic risk during adolescence and beyond [11,12,16].

Finally, the gut microbiota participates in neurodevelopmental and stress-related biology through the microbiota-gut-brain axis. Adolescence is characterised by heightened vulnerability to sleep disruption, circadian misalignment, and psychosocial stress, all of which can modify gut permeability and microbiome composition [21,24-27]. In turn, microbial metabolites and immune mediators influence stress responsivity, neuroinflammation, and emotional regulation. Recent syntheses and adolescent-focused studies associate dysbiosis with depressive symptoms and stress-related phenotypes, underscoring the relevance of lifestyle- and nutrition-based interventions

during this sensitive developmental window [24,26-28]. Figure 1 illustrates an integrative conceptual framework summarizing the bidirectional interactions between nutrition, gut microbiota, and key physiological systems during adolescence.

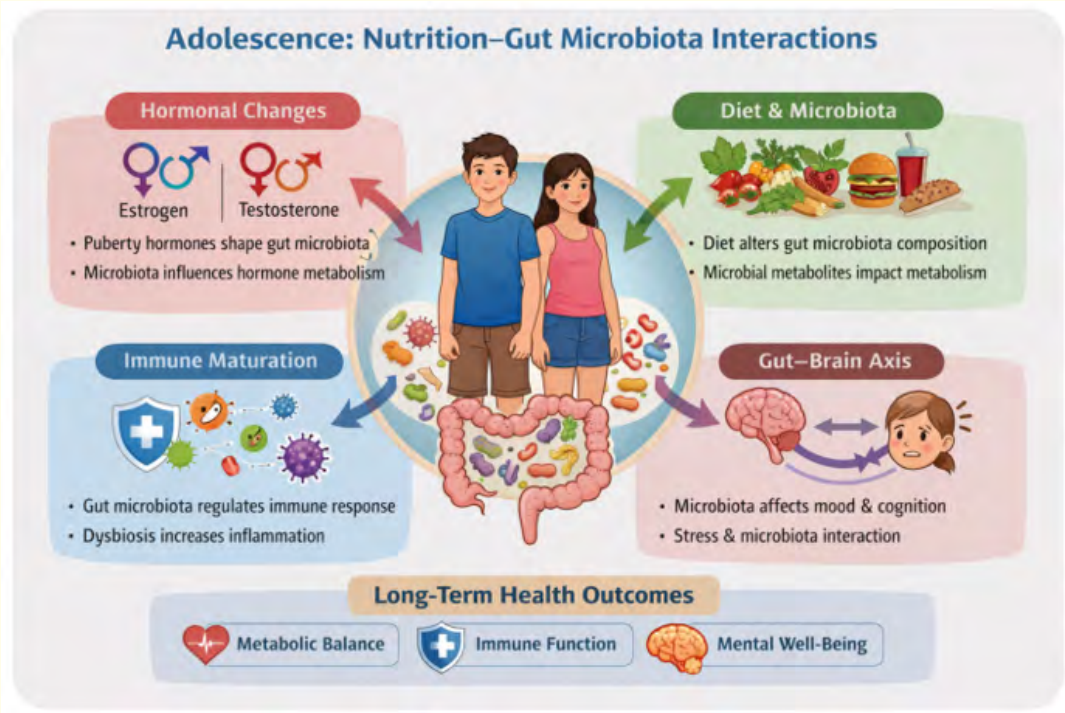

Figure 1: *Nutrition-gut microbiota interactions during adolescence.*

Source: Authors' own elaboration.

This schematic illustration summarizes the bidirectional interactions between nutrition, gut microbiota, and key physiological systems during adolescence. Pubertal hormonal changes, dietary patterns, immune maturation, and gut-brain axis signaling collectively shape gut microbiota composition and function. In turn, microbial metabolites influence metabolic regulation, immune homeostasis, stress responsiveness, and neuropsychological outcomes. Adolescence is depicted as a critical window in which nutritional and lifestyle factors can modulate the microbiota with potential long-term effects on metabolic, immune, and mental health.

Materials and Methods

Study design

This study was conducted as an integrative review with systematic search and qualitative synthesis (PRISMA 2020-guided reporting, following PRISMA 2020 guidance to ensure transparent reporting of identification, screening, and inclusion processes [29,30]. Given substantial heterogeneity across study designs (observational cohorts, cross-sectional studies, interventions, and mechanistic animal studies), microbiome profiling platforms (16S rRNA sequencing, shotgun metagenomics, metabolomics), dietary exposure definitions, and outcome measures, quantitative meta-analysis was not pursued. Instead, a structured qualitative synthesis was undertaken to integrate mechanistic and translational evidence across endocrine, metabolic, immune, and neuropsychological domains [31].

Information sources and search strategy

Electronic searches were performed in PubMed/MEDLINE, PMC, Scopus, Web of Science Core Collection, Embase, and the Cochrane Library. The search period was January 2005 to September 2025, aligned with the widespread adoption and maturation of high-throughput microbiome sequencing and analytic pipelines [32-35]. Search strategies combined controlled vocabulary (MeSH/Emtree) with free-text terms, including: adolescence, puberty, pubertal development, gut microbiota, intestinal microbiome, dysbiosis, nutrition, dietary patterns, fiber, ultra-processed foods, sex hormones, HPG axis, immune maturation, inflammation, cytokines, neurodevelopment, mental health, stress, and HPA axis. Boolean operators (AND/OR) and truncation were applied. Reference lists of key studies and authoritative reviews were hand-searched to identify additional eligible records [36,37].

Eligibility criteria

Inclusion criteria:

1. **Population:** Human adolescents (approximately 9-19 years) and/or animal models explicitly designed to study pubertal development.
2. **Exposure:** Nutritional factors (dietary patterns, nutrient exposures, or nutrition interventions) and/or gut microbiota composition or function.
3. **Outcomes:** At least one of the following domains: pubertal timing/progression; sex hormone profiles/HPG axis activity; metabolic outcomes (insulin sensitivity, adiposity, lipid/bile acid metabolism); immune maturation/inflammation; neuropsychological, behavioural, or stress-related outcomes.
4. **Study designs:** Original observational/interventional human studies, longitudinal cohorts, mechanistic animal studies, and high-quality reviews synthesising adolescent-relevant mechanistic pathways.
5. **Language:** English or Spanish.

Exclusion criteria

Studies restricted to neonates/infants or adults; case reports/editorials/conference abstracts without full text; studies lacking explicit relevance to nutrition-microbiota-pubertal biology; and reports with insufficient methodological detail or inaccessible full text.

Study selection process

The database search identified 268 records. After removing 64 duplicates, 204 records underwent title/abstract screening; 158 were excluded for irrelevance. Forty-six full-text articles were assessed and included in the final qualitative synthesis, in accordance with PRISMA 2020 flow reporting [29]. Disagreements during screening were resolved by consensus.

Data extraction

Data were extracted using a standardised template including: author/year/country; study design; population characteristics; pubertal assessment method (e.g. Tanner staging); dietary exposure assessment; microbiome platform and bioinformatics approach; endocrine/metabolic/immune/neuropsychological outcomes; key mechanistic findings; and limitations as reported by the authors.

Quality assessment and risk of bias

Methodological quality was evaluated according to study design. Observational studies were appraised using the Newcastle-Ottawa Scale [38]. Randomised trials were assessed with RoB 2 [39]. Non-randomised intervention studies were assessed using ROBINS-I [40]. Animal studies were assessed using the SYRCLE risk of bias tool [41]. Quality assessments informed interpretation and weighting of evidence, but were not used as exclusion criteria, consistent with integrative review methodology.

Data synthesis and conceptual integration

Findings were synthesised using a thematic, pathway-oriented framework across four domains:

1. Nutritional modulation of the gut microbiota during pubertal development;
2. Microbiota-hormone interactions affecting HPG/HPA signalling;
3. Immune maturation, barrier function, inflammation, and metabolic signalling;
4. Neuropsychological development, stress responsivity, circadian factors, and gut-brain axis signalling.

This framework guided the construction of schematic conceptual figures illustrating bidirectional interactions between diet, microbiota, and host systems during adolescence [8,15-17,21,29].

Ethical considerations

This study used previously published data only and did not involve direct human or animal experimentation; therefore, ethics approval and informed consent were not required.

The study selection process was conducted in accordance with the PRISMA 2020 recommendations and is summarised in figure 2.

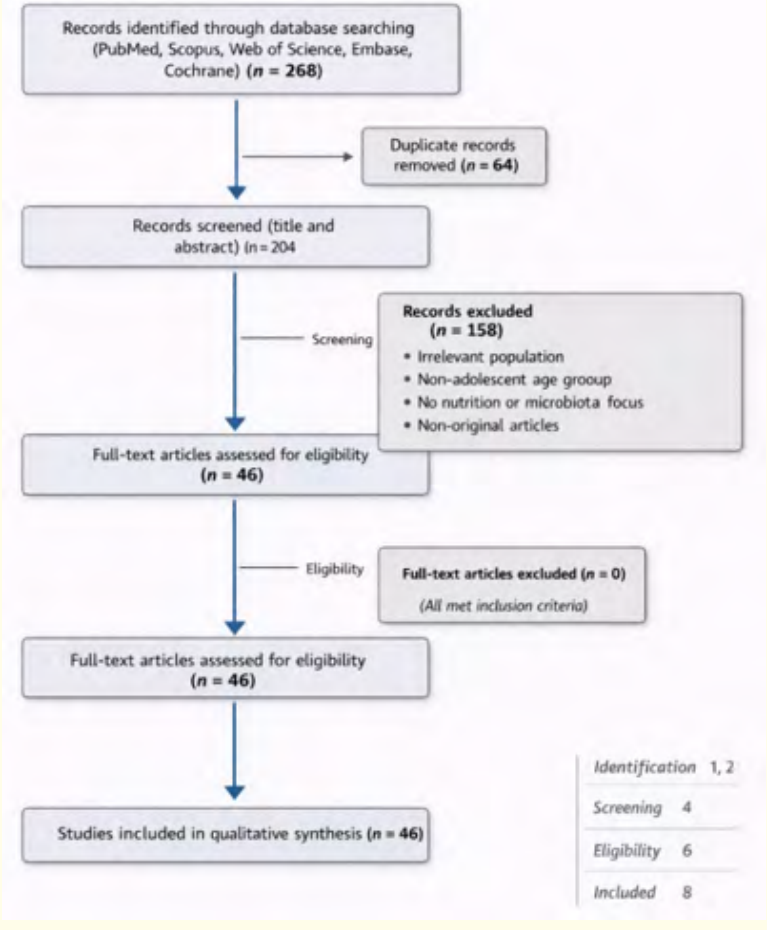

Figure 2: *PRISMA 2020 flow diagram of the literature search and study selection process.*

Source: Authors' own elaboration.

The flow diagram summarizes the literature search and selection process. A total of 268 records were identified; after removal of duplicates, titles/abstracts were screened and irrelevant reports excluded. Forty-six full-text articles met eligibility criteria and were included in the qualitative synthesis.

Results

Study selection and evidence base

Following the systematic search and selection process described in the materials and methods, 46 studies were included in the qualitative synthesis. These comprised longitudinal human cohort studies, cross-sectional observational studies, nutritional and microbiota-focused interventions, and mechanistic animal models, collectively addressing interactions between pubertal development, nutrition, gut microbiota composition, and host hormonal, metabolic, immune, and neuropsychological pathways [1-4,9,14,21,26,28]. Study selection, quality appraisal, and data synthesis were conducted in accordance with established systematic review and integrative review methodologies and validated risk-of-bias tools [29-31,38-43].

Pubertal development, sexual dimorphism, and microbiota maturation

Across multiple human studies, pubertal progression was consistently associated with age- and stage-dependent changes in gut microbiota composition, with a trajectory toward a more stable, adult-like microbial profile during mid-to-late adolescence [1-4]. Several studies reported increasing sexual dimorphism in microbial community structure, particularly after the onset of gonadarche, with distinct taxa enrichment patterns observed between males and females [1,3,4,7]. These sex-specific differences became more pronounced with advancing pubertal stage, suggesting an interaction between biological sex, pubertal maturation, and microbial ecology.

Hormonal modulation of gut microbiota composition

Evidence from human observational studies and experimental models indicated that sex hormones modulate the intestinal environment, influencing gut motility, epithelial barrier integrity, bile acid metabolism, and mucosal immune signaling [2,5,7,18]. These hormone-driven physiological changes were associated with shifts in microbial diversity and relative abundance of specific taxa during puberty. Animal studies further supported a contributory role of gonadal hormones in shaping post-pubertal microbiota configurations, with hormonal manipulation leading to reproducible alterations in microbial composition [7,18].

Microbiota-driven influences on hormonal and metabolic pathways

Several included studies highlighted the reciprocal role of the gut microbiota in modulating host hormonal and metabolic signaling. Microbial enzymatic activity related to the estrobolome was shown to influence estrogen deconjugation and enterohepatic recirculation, thereby affecting systemic sex steroid availability during adolescence [5,6,19,20]. In parallel, microbiota-derived metabolites-particularly short-chain fatty acids (SCFAs)-were consistently associated with dietary fiber intake, insulin sensitivity, energy homeostasis, and markers of low-grade inflammation during pubertal metabolic remodeling [8,11,12,16].

Immune maturation, intestinal barrier function, and inflammation

Adolescence emerged as a critical period for the consolidation of mucosal immune tolerance and immune-microbiota equilibrium. The reviewed evidence indicated that a balanced gut microbiota supports epithelial barrier integrity and immune homeostasis [10], whereas diet- or stress-associated dysbiosis was linked to increased intestinal permeability and low-grade systemic inflammation [11,12,25]. These immune alterations were particularly evident in studies examining dietary quality, obesity, or chronic psychosocial stress during adolescence [14,26,28].

Neuropsychological development and gut-brain axis interactions

Multiple studies addressed the interaction between gut microbiota and neuropsychological development during adolescence, a period marked by heightened neuroplasticity and vulnerability to stress-related disorders. Microbiota-derived metabolites, immune mediators, and neural signaling pathways were implicated in bidirectional gut-brain axis communication [21,26,27], with associations reported between microbial composition, stress reactivity, anxiety-related behaviors, and mood regulation [26,28]. Evidence from both human and animal studies supported the sensitivity of the adolescent microbiota-brain axis to dietary patterns, psychosocial stressors, and inflammatory signaling [26,28].

Summary of thematic findings

Collectively, the included studies demonstrated that adolescence represents a dynamic window of interaction between nutrition, gut microbiota, and host biological systems, characterized by reciprocal influences across hormonal, metabolic, immune, and neuropsychological domains [1-4,8-12,14,16,18,21,25-28]. These findings informed the integrative conceptual framework presented in the accompanying figures and tables. Table 1 summarizes the main metabolic, immunological, and neuropsychological changes occurring during adolescence and their bidirectional interactions with the gut microbiota, highlighting key mechanisms, biomarkers, and potential clinical intervention points identified across the included studies.

Domain	Key Change in Adolescence	Typical factors at this stage	Effect of the change on the microbiota (host → microbiota)	Bidirectional effect (host → microbiota)	Biomarkers/useful examples	Clinical implications and points of intervention
Metabolic	Pubertal Physiological Insulin Resistance	Growth spurt, ↑ IGF-1, changes in body composition	Changes in substrate availability, motility, and enteroendocrine signaling; favors maturation towards adult rootstock, but vulnerable to dysbiosis with Western diet	Dysbiosis can amplify insulin resistance via metabolic inflammation and microbial metabolites; SCFA producers (e.g.butyrate) are associated with improved homeostasis	Glucose/insulin (HOMA-IR), IGF-1; SCFA profile (acetate/propionate/butyrate)	Prevent excessive weight gain; Mediterranean/high-fibre rootstock; regular physical activity [8,11,13,16]
Metabolic	Changes in lipid metabolism and bile acids	High-fat/ultra-processed diet, irregular schedules	Modification of the bile acid pool and intestinal transit, with differential microbial selection	The microbiota transforms bile acids and modulates metabolic signalling (FXR/TGR5) and cardiometabolic risk	Serum/fecal bile acids; Lipid profile	Limit saturated and ultra-processed fats; regularity of meals [15,17]

Metabolic-endocrine	Pubertal maturation and pubertal timing	Dietary changes (animal vs. vegetable protein), adiposity	The usual diet remodels the microbiota; Recent associations suggest mediation by microbial metabolites of pubertal onset	Microbial metabolites can modulate neuroendocrine and metabolic signals from the HPG axis (association/mediation in humans)	Tanner's stage, age of menarche/spermarc, leptin; Microbial signatures and metabolomics	Early nutritional intervention (dietary quality, fiber; avoiding excess animal protein if risk of precocious puberty) [1-4,18]
Immune	Consolidation of mucosal immunity (tolerance/IgA)	Environmental exposures, diet, infections, antibiotics	Changes in IgA and inflammatory tone select communities; antibiotics reduce diversity and key functions	The microbiota "trains" immunity; Dysbiosis favors low-grade inflammation and susceptibility to allergy/autoimmunity (phenotype-dependent)	Fecal IgA, fecal calprotectin (if indicated), PCR/IL-6	Prudent use of antibiotics; Diet rich in fiber and dietary diversity [10,22]
Immune	Gut barrier function and permeability	Stress, sleep deprivation, pro-inflammatory diet	↑ Permeability promotes dysbiosis and translocation of microbial components	Dysbiosis increases systemic inflammatory signaling (e.g., LPS) and perpetuates barrier dysfunction	Zonuline (controversial), LBP/sCD14; functional GI symptoms	Stress and sleep management; reduce ultra-processed foods; probiotics only with clinical indication and evidence [11,25]
Neuropsychological	↑ Stress Reactivity (HPA Axis)	Academic/social stress, family changes, anxiety	Cortisol/catecholamines alter motility, mucus and barrier; Promote dysbiosis	The microbiota modulates the stress response (microbiota-gut-brain axis) with feedback loops	Salivary cortisol, stress scales; GI and affective symptoms	Behavioral interventions (sleep, exercise, stress reduction); Family Education [21,26]
Neuropsychological	Brain remodeling and affective vulnerability	Frontolimbic changes, social pressure, use of screens	Behavioral changes (diet, sleep, activity) impact the microbiota	Recent evidence associates dysbiosis with anxiety/depression in adolescents; Mechanisms: inflammation, neurotransmitters and metabolites	Anxiety-depressive symptoms, IL-6; Tryptophan Metabolites	Multimodal approach: habits and psychotherapy; "psychobiotics" only with specific evidence and clinical supervision [21,28]

Neuropsychological-chronobiology	Circadian Phase Delay and Sleep Deprivation	Going to bed late, school sleep debt, irregular weekends	Circadian disruption alters rhythmicity and microbial diversity	Dysbiosis is associated with worse sleep and greater neuropsychological vulnerability; Revisions 2024-2025 Summary Metabolite-Sleep Mechanisms	Actigraphy/sleep diary; "social jet lag"; Cognitive symptoms	Sleep hygiene, regularity of schedules, reduction of night screens; Diet rich in fiber/polyphenols [26,27]
Cross-Lifestyle	Western and ultra-processed dietary pattern	Added sugars, sugary drinks, low fiber	Reduces diversity and fermentative functions; alters metabolomics	↓ SCFAs production and ↑ low-grade inflammation; Cardiometabolic impact	Total fiber, dietary diversity; SCFA	Structured nutritional intervention; Food education [9,23-25,36,37]
Cross-Lifestyle	Physical activity / sedentary lifestyle	Less sport, more screen time	A sedentary lifestyle is associated with less diversity and a worse metabolic profile	Better physical fitness is associated with more favourable microbial/metabolic profiles (heterogeneous evidence)	Estimated VO_2, BMI/waist, metabolic markers	Statute of limitations; reduce sedentary lifestyle [14,16]

Table 1: *Metabolic, immunological, and neuropsychological changes during adolescence and their bidirectional relationship with the gut microbiota.*

*Source: Authors' own synthesis derived from the integrative qualitative review of the literature included in this study [1-4,8-16,18,21-27,36,44,45]***,** *integrating current evidence on adolescent nutrition-gut microbiota interactions in metabolic, immune, and neuropsychological domains.*

Discussion of Results

This integrative qualitative review synthesizes current evidence demonstrating that adolescence represents a critical developmental window in which nutrition and gut microbiota interact bidirectionally with hormonal, metabolic, immune, and neuropsychological systems. Pubertal maturation is accompanied by progressive remodeling of the gut microbiota toward an adult-like configuration, while remaining highly plastic and responsive to dietary, endocrine, and psychosocial influences [1-4,9]. An integrative conceptual framework summarizing these bidirectional interactions between nutrition, gut microbiota, and host systems during adolescence is presented in figure 3.

This figure illustrates adolescence as a critical window of developmental plasticity in which pubertal hormonal changes, diet, and lifestyle factors dynamically interact with the gut microbiota. Pubertal activation of the hypothalamic-pituitary-gonadal (HPG) and hypothalamic-

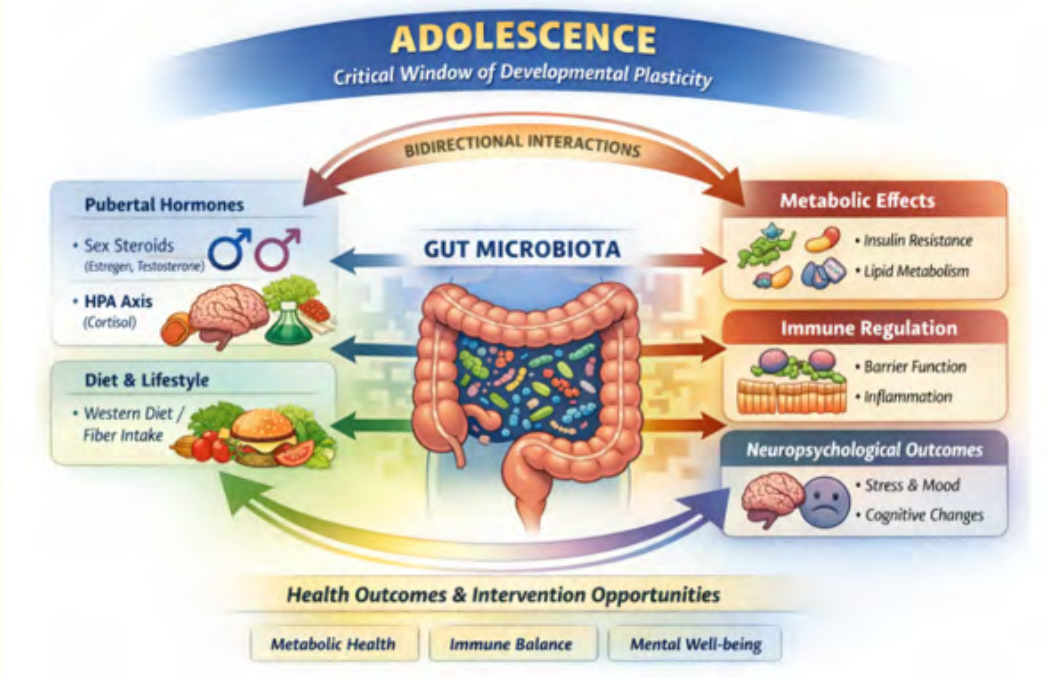

Figure 3: *Integrative conceptual model of bidirectional interactions between nutrition, gut microbiota, and host systems during adolescence.*

Source: Authors' own synthesis derived from the integrative qualitative review of the literature included in this study, following PRISMA 2020 guidance.

pituitary-adrenal (HPA) axes, together with dietary patterns and psychosocial stressors, shape gut microbiota composition and function. In turn, microbial metabolites and immune-neuroendocrine signaling pathways modulate metabolic regulation, immune homeostasis, and neuropsychological outcomes. The model highlights bidirectional feedback loops linking microbiota remodeling with metabolic health, immune balance, and mental well-being, and underscores adolescence as a window of opportunity for preventive nutritional and lifestyle interventions.

Puberty as a window for sex-specific microbiota divergence

One of the most consistent findings across the included studies is the emergence and amplification of sexual dimorphism in gut microbiota composition during puberty. Microbial community structure diverges between males and females particularly after gonadarche, paralleling rising concentrations of sex steroids [1-4]. This observation aligns with evidence indicating that pubertal endocrine activation actively contributes to microbiota restructuring rather than representing a passive, age-related process [2,5].

From a biological perspective, this divergence is plausibly mediated through hormone-driven changes in gut motility, bile acid metabolism, mucosal immunity, and epithelial barrier function, all of which shape microbial niches [5,7,15,17]. These findings highlight puberty as a developmental inflection point at which sex hormones may imprint long-lasting microbial signatures with potential implications for metabolic and immune trajectories later in life [18].

Bidirectional hormone-microbiota interactions

Beyond the influence of hormones on microbial ecology, the reviewed literature supports a reciprocal role of the gut microbiota in modulating systemic hormonal exposure. Enzymatic activities associated with the estrobolome, particularly microbial β-glucuronidases, regulate estrogen deconjugation and enterohepatic recirculation, thereby influencing circulating hormone levels during adolescence [6,19,20]. This bidirectionality reinforces the concept of a feedback loop between pubertal endocrine changes and microbial metabolism, rather than a unidirectional pathway [5,18].

Such interactions may be especially relevant in conditions characterized by altered pubertal timing, adiposity, or endocrine disruption, where microbiota-mediated modulation of hormone availability could amplify or attenuate physiological effects [9,18].

Nutritional modulation, metabolic remodeling, and inflammation

Dietary patterns emerge as a central modulator of microbiota-host interactions during adolescence. High-quality diets rich in fermentable fibers are consistently associated with increased production of short-chain fatty acids, which support insulin sensitivity, energy homeostasis, and anti-inflammatory signaling [8,16,36]. Conversely, diets high in ultra-processed foods and saturated fats are linked to dysbiosis, metabolic endotoxemia, and low-grade inflammation [11,12,23,24].

These findings are particularly relevant in the context of pubertal metabolic remodeling, a period characterized by transient physiological insulin resistance and changes in body composition [13]. The convergence of diet-induced dysbiosis and pubertal metabolic vulnerability may help explain the increased risk of obesity and metabolic disorders emerging during adolescence, especially when adverse nutritional exposures coincide with hormonal transitions [14,44,45].

Immune maturation and barrier integrity

Adolescence also represents a phase of immune consolidation, during which tolerance mechanisms and mucosal immune homeostasis are refined. The gut microbiota plays a central role in this process by shaping immune education and maintaining epithelial barrier integrity [10,16]. Evidence from the reviewed studies suggests that disruptions in microbiota composition-whether driven by diet, stress, or metabolic dysfunction-may impair barrier function and promote systemic inflammation [12,25].

This interaction between microbiota, immunity, and puberty underscores the importance of considering immune maturation as an integral component of adolescent health, rather than a background process independent of nutritional and microbial influences [10].

Neuropsychological development and the gut-brain axis

The adolescent period is marked by heightened neuroplasticity and increased vulnerability to stress-related and mood disorders. The reviewed evidence supports the involvement of the gut microbiota in gut-brain axis signaling during adolescence, mediated through microbial metabolites, immune pathways, neuroendocrine signaling, and emerging circadian mechanisms [21,26,27].

Notably, sex-dependent effects are evident in studies examining stress responsivity and mental health outcomes, suggesting that pubertal hormonal context may modulate microbiota-brain interactions [26]. These findings provide a biological framework linking nutrition, stress, microbiota composition, and neuropsychological outcomes during adolescence, including depressive and anxiety-related symptoms [21,28].

Clinical and preventive implications

From a clinical standpoint, the findings of this review emphasize adolescence as a window of opportunity for preventive strategies targeting nutrition and gut microbiota. Interventions promoting dietary quality, fiber intake, and microbiota-supportive lifestyles may exert benefits across multiple systems, including metabolic health, immune resilience, and mental well-being [9,14,36].

Importantly, the presence of sex-specific microbiota trajectories suggests that precision nutrition approaches during adolescence may need to consider biological sex and pubertal stage to optimize effectiveness [1-4,18].

Strengths and Limitations

This review benefits from a systematic search strategy, PRISMA-guided selection, and integrative synthesis across human and experimental studies [29-31]. However, limitations include heterogeneity in microbiota assessment methods, variability in pubertal staging, and the predominance of observational designs, which constrain causal inference [32-35]. Additionally, longitudinal data spanning the full pubertal transition remain limited.

Future Directions

Future research should prioritize longitudinal, puberty-stage-specific studies integrating dietary assessment, microbiome multi-omics, hormonal profiling, and neuropsychological outcomes [9,21,27]. Such approaches will be essential to disentangle causal pathways and to develop targeted interventions aimed at optimizing adolescent health across the life course.

Conclusion

The available evidence indicates that adolescence constitutes a critical developmental window in which nutrition and the gut microbiota interact dynamically with hormonal, metabolic, immune, and neuropsychological systems. Pubertal maturation is accompanied by progressive microbiota remodeling and increasing sexual dimorphism, reflecting bidirectional interactions between endocrine activation and microbial ecology.

Dietary quality emerges as a key modifiable determinant shaping microbiota composition and function during this period, with downstream effects on metabolic homeostasis, immune regulation, and gut-brain axis signaling. Disruptions in these interactions may contribute to the emergence of metabolic, inflammatory, and mental health vulnerabilities during adolescence.

Collectively, these findings underscore the potential of nutrition- and microbiota-targeted strategies during adolescence as preventive and therapeutic tools to support long-term health. Future longitudinal and mechanistic studies integrating pubertal staging, multi-omic microbiome profiling, and clinical outcomes are needed to inform precision nutrition approaches tailored to sex and developmental stage.

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