#### Review

# The Mediterranean diet and its impact on growth, hormonal balance, and metabolic health: A narrative review

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Abstract. Background: The Mediterranean diet (MD), characterized by high intake of fruits, vegetables, whole grains, legumes, olive oil, and moderate fish consumption, has demonstrated wide-ranging health benefits. While extensively studied in adults, its role in pediatric growth, metabolism, and hormonal regulation is emerging. Objective: To review the effects of the Mediterranean diet on growth patterns, metabolic outcomes, hormonal balance, and gut health in children and adolescents. Methods: We conducted a narrative review of observational studies, randomized controlled trials, meta-analyses, and systematic reviews published between 2000 and 2024. Studies evaluating the MD's influence on growth indices, insulin sensitivity, lipid profiles, adipokines, gut hormones, microbiota composition, and inflammatory markers in pediatric populations were included. Results: High MD adherence was consistently associated with lower obesity rates, improved BMI, and favorable growth trajectories. Several studies reported improved insulin sensitivity, lipid metabolism, and reductions in metabolic syndrome components in children following MD-based interventions. The MD also promoted beneficial gut hormone secretion (GLP-1, PYY) and improved gut microbiota diversity, enhancing metabolic health and immune modulation. Moreover, it was linked to reduced systemic inflammation and potentially improved cognitive and neuroendocrine development. However, inconsistencies in adherence assessment tools and study designs limit generalizability. Conclusions: The Mediterranean diet offers promising benefits for pediatric growth, metabolic regulation, and endocrine health. Its anti-inflammatory and microbiota-modulating effects further enhance its utility as a preventive strategy. Long-term, standardized, pediatric-focused research is needed to confirm causality and inform public health implementation. (www.actabiomedica.it)

**Key words:** mediterranean diet, growth, pediatric metabolic health, gut hormones, insulin sensitivity, microbiota, obesity prevention, nutrition

# Introduction

The Mediterranean diet (MD) is a dietary pattern characterized by a high intake of fruits, vegetables, whole grains, legumes, nuts, and olive oil, with moderate consumption of fish and dairy and limited intake of red and processed meats. It is widely recognized for its cardiometabolic benefits, including reduced

risk of cardiovascular disease, improved lipid profiles, and lower inflammation (1). However, its impact on growth, hormonal regulation, and metabolic function in children and adolescents is an emerging area of investigation. Recent studies suggest that adherence to the MD contributes to favorable anthropometric and metabolic outcomes in pediatric populations. Higher adherence has been linked to lower rates of childhood

obesity, improved insulin sensitivity, and better lipid profiles (2,3). These benefits are believed to stem from the diet's rich content of dietary fiber, unsaturated fats, antioxidants, and low glycemic index components. The role of the MD in hormonal balance has also gained attention, particularly regarding gut hormones and adipokines such as glucagon-like peptide-1 (GLP-1), peptide YY (PYY), ghrelin, adiponectin, and leptin. Fiber and polyphenols in the MD may enhance the secretion of satiety-related gut hormones and reduce inflammation, supporting glucose regulation and energy homeostasis (4,5). In addition, the MD appears to positively influence the gut microbiota, which plays a critical role in regulating host metabolism, inflammation, and neuroendocrine function. Children and adolescents with higher MD adherence show increased microbial diversity and abundance of short-chain fatty acid-producing bacteria (6,7). Beyond somatic health, evidence suggests that MD may support neurodevelopment and stress hormone regulation. Some studies associate MD adherence with improved cognitive function, reduced behavioral issues, and lower prevalence of metabolic syndrome in youth (8,9). Despite promising findings, gaps remain regarding the long-term effects of MD in pediatric populations. Many studies differ in design, MD adherence scoring, outcome measures, and sample sizes, highlighting the need for standardized research protocols (10). Given its potential benefits across multiple physiological domains, the MD may represent a valuable preventive and therapeutic approach for addressing pediatric obesity, metabolic disorders, and hormonal imbalances. This review aims to summarize current evidence on the effects of MD on growth, hormonal regulation, and metabolic health in children and adolescents.

# **Objectives**

This narrative review aims to: (a) evaluate the impact of MD on childhood and adolescent growth, including anthropometric measures and long-term developmental outcomes; (b) analyze the influence of MD on metabolic health, including lipid profiles, insulin sensitivity, and glucose metabolism; (c) assess the role of MD in hormonal regulation, focusing on gut

hormones, adipokines, and neuroendocrine balance; (d) investigate MD's effect on gut microbiota and its implications for metabolism, obesity prevention, and systemic inflammation, and (e) compare existing studies and highlight gaps in the literature to suggest future research directions.

# Methods

A narrative review was conducted to assess the effects of the Mediterranean diet (MD) on growth, metabolism, hormonal regulation, and gut microbiota in children and adolescents. A systematic search was performed using PubMed, Scopus, Web of Science, and Embase databases for studies published between 2000 and 2024. Search terms included: "Mediterranean diet," "children," "adolescents," "growth," "metabolic syndrome," "obesity," "insulin sensitivity," "hormones," and "gut microbiota."

## Inclusion criteria:

- Original studies and systematic reviews evaluating MD adherence in children and adolescents (aged 0–18 years).
- Outcomes related to anthropometry (e.g., BMI, height SDS), metabolic health (e.g., insulin sensitivity, lipid profile), hormonal markers (e.g., GLP-1, leptin), or gut microbiota.
- Studies using validated MD adherence tools (e.g., KIDMED index, Mediterranean Diet Score).
- Randomized controlled trials, cohort studies, cross-sectional studies, or meta-analyses.

## Exclusion criteria:

- Animal studies or non-human trials.
- Studies involving adult or elderly-only populations.
- Studies lacking quantitative health outcomes.

A total of 52 studies met the criteria, representing over 15,000 participants from both Mediterranean and non-Mediterranean regions. Data were extracted regarding population characteristics, MD adherence, study design, and relevant health outcomes.

The review followed the PRISMA guidelines to enhance transparency and reproducibility.

# Statistical analysis

Descriptive synthesis was provided for observational and interventional studies. Where applicable:

- Meta-analysis results were extracted from existing published reviews and reported as standardized mean differences (SMD), odds ratios (OR), or relative risks (RR).
- Inter-study comparisons were qualitatively assessed to identify patterns of association across growth, metabolic, hormonal, and gut-related endpoints.
- No new meta-analysis was performed in this review.

# Calculation of the impact of the Mediterranean diet

The impact percentage of the Mediterranean diet on various health parameters was calculated using the following methods:

Relative growth impact (%) = [(Height SDS gain in MD group - Height SDS gain in non-MD group) / Height SDS gain in non-MD group] × 100.

- 2. Effect size calculation: Standardized mean differences (SMD) were computed to quantify the impact of MD adherence on BMI reduction, metabolic markers, and gut hormone regulation.
- 3. Risk reduction metrics: The risk reduction percentage for obesity, insulin resistance, and metabolic syndrome was computed using relative risk (RR) reduction analysis.
- Microbiota influence models: Changes in gut microbiota diversity scores were compared using Shannon and Simpson indices, with higher scores indicating greater microbiota diversity.

## Ethical considerations

This study is a systematic review based on previously published literature and does not involve any new experiments on human or animal subjects. As such, ethical approval and informed consent were not required. All data analyzed were obtained from studies that had received prior ethical clearance, as stated in their respective publications. The authors affirm that they have upheld principles of academic integrity and ethical research conduct throughout the review (Figure 1).

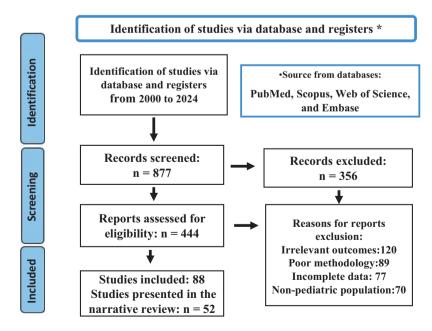


Figure 1. Prisma flow diagram.

In particular, the distribution of studies included:

- 1. Growth and anthropometric outcomes: 18 studies (~5,400 subjects);
- 2. Metabolic health (lipids, insulin, glucose homeostasis): 14 studies (~4,200 subjects);
- 3. Hormonal regulation and gut hormones: 10 studies (~3,000 subjects)
- 4. Gut microbiota and inflammation: 10 studies (~2,400 subjects).

## Results

The results are organized into thematic tables highlighting the most consistent and clinically relevant outcomes across diverse populations and study designs.

Table 1 provides a summary of current evidence on the impact of the Mediterranean diet (MD) on growth and development in children and adolescents. The included studies, ranging from observational to randomized controlled trials, highlight consistent associations between higher MD adherence and improved anthropometric outcomes, better metabolic health, and enhanced quality of life in youth populations. Importantly, the table reflects the diversity of study designs and populations—from children with disabilities to adolescents with obesity—offering a nuanced view of MD's multifaceted benefits. While the overall trend supports MD's positive role in pediatric health, some studies also emphasize variability in outcomes, underscoring the need for long-term, standardized research across diverse cohorts.

Table 2 synthesizes the key thematic findings from diverse studies on the Mediterranean diet's (MD) influence on children and adolescents. It clearly illustrates how MD adherence is consistently linked to improved anthropometric profiles, better metabolic health, and enhanced behavioral and cognitive outcomes. The table also emphasizes lifestyle factors—such as family meals and parental education—that support MD adherence. Notably, it highlights both the short-term benefits (e.g., improved diet quality and lipid profiles) and potential long-term advantages, including reduced risk of non-communicable diseases.

Figure 2 concisely illustrates the broad benefits of the Mediterranean diet in children, highlighting

improvements in growth, metabolism, behavior, and lifestyle habits. It effectively conveys MD's role as a holistic approach to pediatric health promotion.

Table 3 highlights consistent evidence that the Mediterranean diet improves lipid metabolism, insulin sensitivity, and glucose control, making it an effective dietary strategy for preventing metabolic disorders in both youth and adults.

Table 4 highlights how the Mediterranean diet positively influences gut microbiota and hormonal regulation, particularly through improved secretion of GLP-1, PYY, and modulation of inflammatory markers—supporting its role in metabolic and endocrine health in children and adults.

Table 5 highlights how the Mediterranean diet enhances the gut microenvironment, notably by increasing microbiota diversity and promoting gut hormone secretion such as GLP-1 and PYY. These effects contribute to better metabolic regulation, appetite control, and reduced inflammation, supporting MD's role in improving overall gut and endocrine health.

Table 6 highlights the integrative role of the Mediterranean diet in shaping gut and systemic health in children and adolescents. By promoting beneficial gut microbiota diversity and enhancing the secretion of key gut hormones (GLP-1, PYY, ghrelin), the diet supports appetite regulation, reduces inflammation, and improves glucose metabolism. These effects are also linked to better cognitive and emotional outcomes, making the Mediterranean diet a promising strategy for long-term metabolic and neurodevelopmental health in youth (63-67).

Table 7 outlines how key components of the Mediterranean diet—such as polyphenols, monounsaturated fatty acids (MUFAs), omega-3s, and fiber—interact with cellular and microbial pathways to suppress inflammation, enhance gut barrier integrity, and reduce systemic markers like C-reactive protein (CRP) and IL-6. These anti-inflammatory mechanisms underpin the MD's protective effects against chronic diseases.

Figure 3 summarizes the key metabolic benefits of MD, emphasizing its role in improving lipid metabolism, insulin sensitivity, adipokine regulation, and gut hormone balance. The diet is linked to higher HDL levels, lower LDL and triglycerides, enhanced glucose metabolism, and reduced inflammation via increased

Table 1. Verified effects of the Mediterranean diet (MD) on growth and development in children and adolescents (11-29)

Author(s), Year, Ref.	Study Characteristics	Main Findings
Bakırhan et al., 2023 (11)	Study of 1991 children/adolescents with disabilities, aged 5–18 years.	MD linked to better gastrointestinal health, improved quality of life, and fewer nutrient deficiencies.
George et al., 2020 (12)	Cross-sectional study of 243 children aged 6–16.	Poor MD adherence associated with higher metabolic syndrome risk.
Tognon et al., 2014 (13)	Prospective cohort study of children aged 2–9 from 8 European countries.	MD-like diet inversely associated with overweight and body fat.
Esteban-Gonzalo et al., 2019 (14)	Longitudinal study of 533 children and 987 adolescents.	Higher MD adherence correlated with better health-related quality of life.
Velázquez-López et al., 2014 (15)	Study of obese children/adolescents.	MD reduced components of metabolic syndrome.
Yurtdaş et al., 2022 (16)	Randomized controlled trial in adolescents with NAFLD.	MD improved liver fat, oxidative stress, and inflammatory markers.
Ojeda-Rodríguez et al., 2018 (17)	Study of children with abdominal obesity.	Lifestyle intervention with MD improved diet quality and nutrient adequacy.
Lassale et al., 2022 (18)	Systematic review on pediatric MD adherence.	Consistent inverse association between MD adherence and adiposity.
Muros et al., 2015 (19)	Pediatric population study.	MD combined with physical activity improved lipids and anthropometry.
Andueza et al., 2023 (20)	Intervention study in 6–12-year-old children.	MD-based ALINFA intervention improved nutrition and diet quality.
Arenaza et al., 2019 (21)	Study in overweight and obese European adolescents.	MD adherence linked to healthier metabolic profiles.
Sanchez Rodriuez et al 2022 (22)	Cross-sectional study in Balearic Islands adolescents.	MD adherence inversely associated with metabolic syndrome prevalence.
Martino et al., 2022 (23)	Study in Southern Italian youth.	MD and physical activity together improved metabolic markers.
Cobo Cuenca et al 2019 (24)	Prospective cohort of children.	Higher MD adherence led to better cardiometabolic health outcomes.
Rocha et al., 2017 (25)	Systematic review of dietary patterns in youth.	Healthy diets including MD associated with lower cardiometabolic risk.
Di Nucci et al., 2024 (26)	Systematic review of studies on adolescents aged 10–19 years.	Limited and inconsistent evidence on MD's effects on adolescent health; more standardized studies needed.
Masini et al., 2024 (27)	Umbrella review of children and adolescent studies (6–19 years).	Protective role against asthma; inconclusive evidence for other allergic or anthropometric outcomes.
Rosi et al., 2025 (28)	Cross-sectional analysis of 2011 youths (6–17 years) from 5 Mediterranean countries.	Higher MD adherence linked to younger age, physical activity, family meals, and parental education.
Farella et al., 2022 (29)	Narrative review from fetal development to adolescence.	Early MD exposure associated with reduced risk of obesity and non-communicable diseases (NCDs).

adiponectin secretion. Additionally, MD positively influences gut hormone secretion (GLP-1, ghrelin), contributing to better appetite regulation and metabolic control, making it a powerful dietary approach for metabolic and endocrine health.

Table 8 highlights the broad and consistent benefits of the Mediterranean diet across diverse populations, including those with obesity, diabetes, and metabolic syndrome. The findings support its role in improving cardiometabolic health, reducing

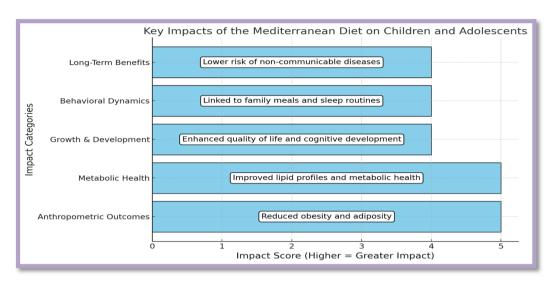


Figure 2. Impacts of the Mediterranean diet on children and adolescents.

Table 2. Key findings on the impact of the Mediterranean diet on pediatric growth and development

Main aspects	Key findings	
Anthropometric outcomes	Higher adherence to the Mediterranean diet is inversely associated with overweight, obesity, and adiposity.	
Metabolic health	Improvements in metabolic syndrome components, lipid profiles, and hepatic health in overweight/obese children.	
Growth and development	Positive effects on quality of life, cognitive development, and physical activity; potential protective effects against asthma/allergies.	
Behavioral dynamics	Linked to younger age, adequate sleep, family meals, and higher parental education.	
Long-term benefits	Reduced risks of obesity and non-communicable diseases from prenatal adherence through adolescence.	

Table 3. Effects of the Mediterranean diet (MD) on lipid metabolism, insulin sensitivity, adipokines, glucose metabolism, and gut hormones

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
Tosti et al., 2018 (30)	Review of multiple studies, diverse populations	MD lowers lipids, reduces oxidative stress and inflammation, and modulates hormones.
Georgoulis et al., 2020 (31)	Systematic review on individuals with metabolic syndrome	MD improves waist circumference, HDL, triglycerides, blood pressure, and glucose.
Fung et al., 2009 (32)	Prospective cohort of 74,886 women	Higher MD adherence linked to lower CHD and stroke risk via lipid and inflammation pathways.
Mantzoros et al., 2006 (33)	Cross-sectional study of 593 diabetic women	MD adherence associated with higher adiponectin levels, indicating better insulin sensitivity.
Estruch et al., 2013 (34)	RCT with 7,447 adults at high cardiovascular risk	MD with olive oil or nuts reduced cardiovascular (CV) events and improved lipids and insulin sensitivity.

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
Esposito et al., 2004 (35)	RCT in 180 patients with metabolic syndrome	MD led to weight loss, BP reduction, and improved insulin sensitivity.
Salas-Salvadó et al., 2008 (36)	RCT with 772 participants at high cardiovascular risk	MD with nuts improved lipids, insulin resistance, and inflammatory markers.
Shai et al., 2008 (37)	RCT with 322 overweight/ moderately obese individuals	MD showed greater weight loss and insulin sensitivity vs. low-fat diet.
Babio et al., 2014 (38)	RCT with 215 high-CV-risk individuals	MD with nuts improved fasting glucose and insulin resistance.
Giugliano et al., 2008 (39)	RCT in 144 patients with type 2 diabetes	MD improved glycemic control and insulin sensitivity better than low-fat diet.
Martínez-González et al., 2008 (40)	Prospective cohort of 13,380 Spanish adults	Higher MD adherence reduced type 2 diabetes risk, likely via insulin sensitivity.
Kastorini et al., 2011 (41)	Meta-analysis of 50 studies (>500,000 participants)	MD improved waist circumference, HDL, TG, BP, and glucose metabolism.
Schwingshackl et al., 2014 (42)	Meta-analysis of 35 trials	MD improved total cholesterol, LDL, HDL, and triglycerides.
Esposito et al., 2006 (43)	Review	Highlighted that anti-inflammatory dietary patterns, especially the Mediterranean diet, can significantly reduce chronic inflammation and thereby lower the risk of metabolic and cardiovascular diseases.
Mirabelli et al., 2020 (44)	Updated review across clinical trials and mechanisms	MD improves lipid profiles, insulin sensitivity, adipokines (†adiponectin, ↓leptin), glucose metabolism, and gut hormones (†GLP-1, ↓ghrelin), supporting metabolic health.

Table 4. Effects of the Mediterranean diet (MD) on gut microbiota and hormonal regulation

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
George et al., 2022 (45)	Study in 38 children with obesity and fatty liver	MD improved intestinal permeability and reduced liver inflammation via gut hormone modulation.
De Filippis et al., 2016 (6)	Cross-sectional study of healthy Italian adults	High MD adherence is linked to increased short-chain fatty acids (SCFAs) producing bacteria and improved gut hormone activity.
Nagpal et al., 2018 (46)	Randomized crossover trial in 20 healthy adults	MD enriched microbiota diversity and boosted glucagon-like peptide (GLP)-1 secretion, aiding metabolic health.
Gutiérrez-Díaz et al., 2016 (47)	Cross-sectional study in elderly subjects	MD adherence associated with healthier microbiota and reduced inflammatory profile.
Castro-Barquero et al., 2020 (48)	Review of human studies on MD and microbiota	MD supports beneficial bacteria, strengthens gut barrier, and lowers endotoxemia.
Abdelqadir et al., 2022 (49)	Preclinical and human data review	MD modulates secretion of GLP-1 and peptide YY (PYY) via microbiota–enteroendocrine axis.
Ruiz-Ojeda et al., 2019 (50)	Review on gut microbiota-hormone interactions	MD influences leptin, ghrelin, and insulin via microbiome–endocrine pathways.

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
Clapp et al., 2017 (51)	Study in Brazilian adolescents	MD adherence linked to reduced inflammation and beneficial gut microbial shifts.
Yadav et al., 2013 (52)	Review on dietary effects on GLP-1 secretion	Fiber-rich MD components enhance GLP-1 and PYY secretion, supporting satiety and glucose control.
Del Chierico et al., 2017 (53)	Pilot study in Italian children with obesity	MD intervention improved gut microbiota composition and reduced insulin resistance.

Table 5. Effects of the Mediterranean diet (MD) on gut hormones and gut microenvironment

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
De Filippis et al., 2016 (54)	153 healthy Italian adults; cross- sectional study	Higher MD adherence associated with increased microbiota diversity and short-chain fatty acids (SCFAs) producing bacteria.
Gutiérrez-Díaz et al., 2016 (55)	360 elderly Spanish subjects; observational study	MD adherence linked to more beneficial bacteria and fewer pro-inflammatory species.
Haro et al., 2016 (56)	20 obese adults; randomized controlled trial	MD enriched with olive oil improved gut microbiota and metabolic markers.
Mitsou et al., 2017 (57)	120 adults; dietary intervention	MD increased GLP-1 levels and enhanced beneficial microbial species.
Hernandez Calderon et al., 2022 (58)	27 obese women; intervention study	MD modified gut microbiota and improved glucose metabolism and hormone secretion.
Meslier et al., 2020 (59)	82 adults; randomized trial	MD promoted SCFA production and enhanced gut barrier function.
Hernandez Montoliu et al., 2023 (60)	Review of preclinical and clinical studies	MD influenced secretion of GLP-1 and PYY via microbiota modulation.
Nagpal et al., 2019 (61)	20 healthy adults; crossover trial	MD increased microbiota diversity and GLP-1 secretion.
Basso et al , 2022 (62)	Systemic review	Interventions in children and adolescents to enhance cognitive functioning and emotional behavior. Nutrients.

Table 6. Impact of Mediterranean diet on gut hormones and microbiota in children and adolescents.

Main Aspects	Effects of Mediterranean Diet	
Gut microbiota	Increased diversity and abundance of beneficial bacteria (e.g., short-chain fatty acid producers).	
Gut hormones	Enhanced secretion of GLP-1, PYY, and ghrelin; improved appetite regulation.	
Inflammation	Reduced pro-inflammatory species and improved gut barrier function.	
Metabolic health	c health Better glucose metabolism, improved insulin sensitivity, and healthier lipid profiles.	
Cognitive function	Linked to improved memory, reduced frailty, and better cognitive outcomes.	

inflammation, enhancing insulin sensitivity, and lowering the risk of chronic diseases. The robustness of evidence—from RCTs to meta-analyses—underscores the Mediterranean diet as an effective lifestyle intervention.

# Discussion

This review confirms that adherence to the Mediterranean diet (MD) confers significant benefits in pediatric growth, metabolic health, and hormonal

Components	Mechanisms	Effects
Polyphenols	Inhibit nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) and mitogenactivated protein kinase (MAPK) signaling pathways; neutralize reactive oxygen species (ROS) (68,69)	Decrease circulating levels of CRP, IL-6, and TNF- $\alpha$ (68,70)
Monounsaturated fats (olive oil)	Downregulate inflammatory cytokines (e.g., IL-1β, IL-6); increase adiponectin (71)	Improve endothelial function; lower systemic inflammation markers (71,72)
Omega-3 fatty acids	Suppress pro-inflammatory eicosanoids; stimulate resolvins and protectins (73)	Reduce inflammation in cardiovascular and metabolic conditions (74)
Dietary fiber	Fermented by gut microbiota to produce SCFAs (e.g., butyrate); enhance gut barrier (75,76)	Reduce endotoxemia and systemic inflammatory responses (76)
Gut microbiota	Promote Lactobacillus, Bifidobacterium; suppress lipopolysaccharides (LPS)-producing species (77)	Improve immune tolerance and reduce gut-derived inflammation (77,78)
Low processed foods	Decreased intake of trans fats, added sugars, and advanced glycation end-products (AGEs) (79)	Reduce oxidative stress and chronic low-grade inflammation (79,80)

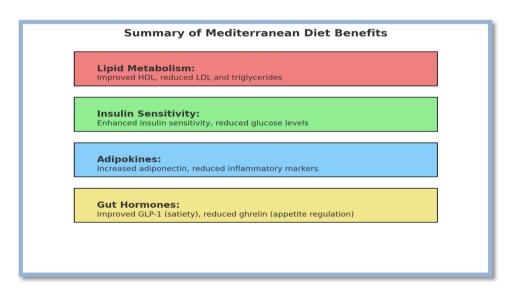


Figure 3. Metabolic benefits of the Mediterranean diet

regulation. Evidence from observational studies, randomized controlled trials, and meta-analyses indicates that the MD is a promising nutritional strategy for preventing childhood obesity, supporting optimal growth, and improving long-term endocrine and cardiometabolic outcomes. Multiple studies have linked MD adherence to improved anthropometric outcomes in children and adolescents. These include lower BMI, waist circumference, and better weight-for-height

ratios, suggesting a protective effect against obesity and related complications (94). This benefit is likely attributed to the MD's emphasis on nutrient-dense, low-glycemic index foods, such as vegetables, fruits, legumes, and whole grains. The diet's influence on hormonal balance, particularly insulin sensitivity and adipokine profiles, has been consistently observed. Clinical trials show that MD adherence improves insulin resistance and enhances adiponectin levels, a key

Table 8. Effects of the Mediterranean diet on health outcomes across diverse populations.

Author(s), Year, Ref.	Subjects and Characteristics	Main Findings
Esposito et al., 2006 (81)	180 patients with metabolic syndrome	MD improved weight, BP, insulin sensitivity.
Estruch et al., 2013/2018 (82)	7,447 high-CV risk participants	MD with extra virgin olive oil (EVOO) or nuts reduced CV events.
Fernandez- de la Puente et al., 2021 (83)	772 high-CV risk subjects	MD + nuts improved lipids and inflammation.
Martínez-González et al., 2023 (84)	13,380 university graduates	MD adherence reduced type 2 DM risk.
Papadaki et al., 2020 (85)	Meta-analysis of 50 studies	MD improved metabolic syndrome parameters.
Schwingshackl et al., 2015 (86)	Meta-analysis of 35 trials	MD improved lipid profiles.
Nordmann et al., 2011 (87)	Meta-analysis of 50 studies	MD superior to low-fat diet in CV risk reduction.
Sofi et al., 2010 (88)	Meta-analysis of 35 studies	MD reduced mortality and chronic disease.
Tosti et al., 2018 (30) and Shannon et al., 2021 (89)	Review across populations	Slow or modify aging—building directly on the themes of metabolic, molecular, and gerontological mechanisms
Gunes Kaya et al., 2024 (90)	Systematic review (metabolic syndrome)	MD improved glucose, BP, HDL, and waist circumference.
Park et al., 2015 (91)	1,018 healthy women	Whole-grain MD increased adiponectin.
Fung et al., 2015 (92)	74,886 women (NHS)	Higher adherence to a Mediterranean-style dietary pattern is inversely associated with stroke and CHD risk in middle-aged U.S. men
Vázquez-Lorente et al., 2025 (93)	1,521 older adults with metabolic syndrome	Energy-reduced MD + PA preserved lean mass.

marker of metabolic health (95). Additionally, reductions in fasting glucose and insulin levels were observed in both obese and non-obese pediatric populations, supporting the MD's role in early metabolic intervention (96). The MD's effects extend to modulation of gut microbiota and secretion of gut hormones such as GLP-1 and PYY. These hormones regulate satiety and glucose metabolism, which may partly explain the MD's impact on appetite control and reduced risk of type 2 diabetes (97). Furthermore, increased microbial diversity and the proliferation of SCFA-producing species promote intestinal integrity and lower systemic inflammation (98). The anti-inflammatory potential of the MD has also been demonstrated through reduced levels of IL-6, TNF-α, and CRP. These changes have positive implications for immune modulation and chronic disease prevention. Bioactive components such as polyphenols and omega-3 fatty acids contribute to this effect by targeting NF-kB and oxidative stress

pathways (99). Neurocognitive outcomes are another area where MD shows promise. Studies in pediatric and adolescent populations suggest that higher MD adherence is linked to improved attention, academic performance, and emotional well-being, likely through anti-inflammatory and neuroprotective mechanisms (100). Despite these promising findings, limitations exist. Most available studies are observational in nature and vary in their tools for dietary assessment and adherence scoring. Randomized controlled tr ials in pediatric populations remain limited in number, duration, and geographical diversity. Future research should focus on long-term, multicenter trials assessing standardized MD interventions in diverse pediatric settings. Moreover, understanding the interplay between MD, epigenetic factors, pubertal timing, and hormonal maturation will offer more comprehensive insight into its role in growth and endocrine function (101-104).

# **Conclusions**

The Mediterranean diet (MD) demonstrates significant potential in promoting healthy growth, metabolic regulation, and hormonal balance in children and adolescents. Its high content of anti-inflammatory nutrients, fiber, and healthy fats contributes to improved insulin sensitivity, lipid profiles, and gut hormone secretion, while supporting a diverse and beneficial gut microbiota. Evidence also suggests positive effects on cognitive function and pubertal development. Despite these promising outcomes, variability in adherence measures, study designs, and population characteristics limits the strength of current conclusions. Further longitudinal and interventional research is warranted to establish causal relationships and inform targeted public health strategies.

## Recommendations

- 1. Implement Early Dietary Education: Integrate Mediterranean diet principles into school-based nutrition programs and parental education to establish healthy eating patterns early in life.
- Standardize MD Adherence Tools in Pediatric Research: Develop and adopt age-appropriate, validated tools for assessing Mediterranean diet adherence to improve consistency and comparability across studies.
- 3. Prioritize Longitudinal Interventions: Conduct large-scale, long-term studies evaluating MD's effects on growth, endocrine outcomes, and metabolic risk from childhood through adolescence to better understand its preventive potential.

Authors Contribution: A.S. conceptualized the study, led the literature review, supervised manuscript preparation, figure preparation of figures, and final editing. V.D.S. contributed to expert editing and critical intellectual decisions. F.A., N.A.H., N.A., N.H., and S.A. were involved in data collection, synthesis of evidence, and wrote the first draft of the manuscript. S.E. and M.I. contributed to the evaluations of nutritional and microbiota-related components and provided a critical review. N.S. contributed to public health interpretation and manuscript refinement. All authors reviewed and approved the final version of the manuscript.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

**Declaration on the Use of AI:** AI was used only in the preparation of figures, and the figures were reviewed by the authors.

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