Umbrella Review

Adherence to Mediterranean Diet and Health Outcomes in Adolescents: An Umbrella Review

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Context: *Proper nutrition represents 1 of the domains of adolescents' well-being. In this context, the Mediterranean diet (MD), as a healthy, traditional, and sustainable dietary pattern, plays a crucial role in promoting adequate growth and preventing chronic noncommunicable diseases.* ***Objective:*** *The currently available evidence on the effects of adherence to the MD (AMD) in association with several physical health outcomes in adolescence is summarized in this review.* ***Data Sources:*** *Five electronic databases were searched.* ***Study Selection:*** *Systematic reviews with or without meta-analysis of observational studies and randomized clinical trials, published in English during 2013–2022, and that assessed the health impact of AMD among adolescents were eligible.* ***Data Extraction:*** *Details on study design, methods, population, assessment of dietary patterns, health outcomes, and main results were extracted.* ***Results:*** *The search yielded 59 references after removal of duplicates. Applying PICOS criteria, 4 systematic reviews and 3 meta-analyses ultimately were included in this review. The AMD was evaluated in association with overweight/obesity and adiposity in 2 studies, musculoskeletal health in another 2, inflammation in 1 study, and cardiometabolic health in 1 study. The seventh review examined all mentioned health outcomes (overweight and obesity, musculoskeletal health, inflammation, and cardiometabolic health) in relation to AMD.* ***Conclusions:*** *Overall, this umbrella review showed limited evidence and a lack of consistency about the relation between AMD and health outcomes of interest in adolescence, indicating the need for more studies to better understand it.*
Systemic Review Registration: *PROSPERO registration no. CRD42023428712.*

Key words: *Mediterranean Diet, adolescents, health outcomes.*

INTRODUCTION

Adolescence is a crucial phase of life, characterized by important physiological and psychological changes. During this period, the adoption of adequate health-related behaviors and conditions positively affects growth and health status of today's adolescents and tomorrow's adults.[1] According to the World Health Organization guidance report on Global Accelerated Action for the Health of Adolescents, proper nutrition represents 1 of the domains of adolescent well-being, without which the United Nations 2030 Sustainable Development Goals cannot be achieved.[2]

The Mediterranean diet (MD) has been widely recognized as a healthy, traditional, and sustainable dietary pattern. This model encompasses all the various eating

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habits typical of countries bordering the Mediterranean Sea, so there is no single Mediterranean pattern.[3] However, its pillars are represented by a high intake of vegetables, fruits, nuts, cereals (especially whole-grain cereals), legumes, and olive oil; a moderate-to-high intake of fish; a low-to-moderate intake of dairy products; a low intake of saturated fats, meat, and poultry; and a moderate intake of wine.[4] To date, countless studies have shown that adherence to the MD (AMD) reduces the risk of several chronic noncommunicable diseases, such as cardiovascular diseases, type 2 diabetes, certain types of cancer, and metabolic syndrome in the adult population.[5] Even during childhood, a healthy and balanced diet, such as the MD, is related to adequate growth; appropriate physical, biological, and cognitive development; and good quality of life.[6–8] However, despite the health benefits of the MD, a shift away from this dietary model has been observed in many Mediterranean countries in recent decades.[9]

In 2015, García Cabrera et al evaluated AMD among children and adolescents in Mediterranean countries. Grouping the studies by age range, their meta-analysis (MA) showed low AMD in both children (27%; 95% CI, 0.09–0.44) and adolescents (19%; 95% CI, 0.12–0.26).[10] This result was confirmed by a more recent review, which reported that adolescents living in North America, Europe, or Oceania do not follow the nutritional recommendations for fruit, vegetables, legumes, and sodium, and the principles of the MD.[11]

The potential drivers of this dietary transition are represented by globalization, westernization, and modernisation.[12] It has been hypothesized that the youth population is particularly influenced by this phenomenon. Indeed, adoption of unhealthy eating behavior, such as frequent consumption of fashionable energy-dense foods and eating out, is increasing among adolescents.[13,14]

Several noncommunicable diseases have been increasingly observed in childhood in recent decades, even those known to be associated only with adults (eg, nonalcoholic fatty liver disease [NAFLD]; hypertension).[15–18] It has been suggested that adherence to unhealthy and unsustainable dietary patterns is related to a progressive incidence of noncommunicable diseases since the first phases of life, in comparison with adherence to healthy and balanced diets, such as the MD.[19–21]

Because each age group may have different eating behaviors and health status, there is a need for solid evidence that can be used to analyze separately the health impact of dietary patterns at different phases of life. Thus, the aim of the present umbrella review (UR) was to summarize the currently available studies on the effects of AMD in association with several physical health outcomes, specifically in adolescence.

METHODS

This UR followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[22] and the Joanna Briggs Institute umbrella review methodology[23] as much as possible for our study design. The protocol was registered in the PROSPERO database (registration no.: CRD42023428712).

Eligibility criteria

The PICO (Population, Intervention, Comparison, and Outcome) strategy followed to establish eligibility criteria is presented in Table 1. According to World Health Organization definition of adolescence,[24] the age range of 10–19 years was selected as an inclusion criterion. In line with the intervention and comparison criteria, studies that estimated adherence to different dietary patterns with an a priori or an a posteriori approach (eg, principal component analysis) were included.

The following were criteria for exclusion of an article: not published as systematic review (SR) or MA in an international, peer-reviewed scientific journal; not targeted at adolescents; addressed to individuals with concomitant diseases conditions involving restrictive dietary treatment that affects AMD (eg, food allergy, celiac disease); focused on dietary patterns other than the MD as an intervention and on specific disease conditions that limit AMD as a comparison on the intake of individual nutrients, not on health-related outcomes.

Search strategy

The following electronic databases were systematically searched: MEDLINE (PubMed), Embase, Scopus, Web of Science, and Google Scholar. Search restrictions included the English language and the publication period 2013–2022. Using relevant subject headings and free text search terms, the search strategy was based on the following keywords: "Mediterranean diet," "adolescence," "systematic review," "meta-analysis" and their variants, which were used in combination with words relating to health status, including "overweight," "obesity," "diabetes mellitus," "metabolic syndrome," "hypertension," "non-alcoholic fatty liver disease," "health status," and "musculoskeletal health," or to evaluation parameters, such as "body mass index," "waist circumference," "cholesterol," "triglycerides," "blood glucose," "blood pressure," "inflammation," and their variants. The search strategies are available in Table S1.

Table 1. PICOS Criteria for Inclusion of Studies in the Umbrella Review

Parameter	Criterion	
	Inclusion	Exclusion
Population	Adolescents (10–19 y old)	Children (<10 y old), adults (>18 y old), elderly (>70 y old), adolescents affected by concomitant diseases conditions that involve restrictive dietary treatment affecting AMD (eg, food allergy, celiac disease)
Intervention	Mediterranean diet	Other type of diets, intake of individual nutrients
Comparison	Other Western/unhealthy and healthy dietary patterns	Dietary patterns for specific diseases conditions limiting AMD (eg, gluten-free diet)
Outcome	Physical health outcomes (OW/OB, diabetes mellitus, MetS, hypertension, NAFLD, musculoskeletal health, inflammation parameters, lipid and glycemic profile, anthropometric parameters [eg, BMI, WC])	Not health-related outcomes
Study design	Systematic reviews or meta-analysis of observational studies (prospective cohort studies, cross-sectional studies and case-control studies) and RCTs	Studies not published as systematic reviews and meta-analysis in peer-reviewed international scientific journals

Abbreviations: AMD, Adherence to Mediterranean diet; BMI, body mass index; MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; OW/OB, overweight/obesity; WC, waist circumference; RCT, randomized clinical trial.

Study selection

Two reviewers (A.D.N., E.C.) independently selected and screened the studies to be included in this UR. They were blinded to each other's decisions and disagreements between individual judgements were resolved by a third reviewer (M.S.). Duplicate studies were removed, and all identified articles were screened. Applying the aforementioned eligibility criteria, the article title and abstract were initially screened, followed by full-text screening. The software system used for decision recording was Covidence Systematic Review Software (Veritas Health Innovation, Melbourne, VIC, Australia; www.covidence.org).

Data extraction and quality assessment

Data extraction and quality assessment were performed independently by 2 reviewers (A.D.N., E.C.), and any disagreements were resolved by consensus.

The following data were extracted from each eligible SR and MA: first author's last name; year of publication; number and design of original studies; number and age of participants (differentiating participants from cohort studies, case–control studies, and clinical trials for each SR or MA); assessment of the dietary patterns (ie, types of dietary patterns, tools for dietary information, assessment methods); health outcomes (types of health outcomes, types of indicators); and main results. In the MAs, the pooled estimations from the random effects model with the 95% CIs, from both global and stratified analyses, were indicated, along with the percentages of heterogeneity (I^2 coefficient).

For each of the selected SRs and MAs, data were extracted only for studies based on PICO of interest. Studies with a sample of both children and adolescents were also taken into consideration in order not to exclude any findings concerning adolescents. On the other hand, reports that considered individuals aged 18–19 years as part of an adult population were excluded without analyzing the data by age subgroups. To collect these data and achieve homogeneity between the studies, the original articles included SR and MA were read to obtain missing information and modify the discrepant ones. Covidence Systematic Review Software was used for data extraction and information was recorded in a Microsoft Excel 2016 (Redmond, WA) spreadsheet.

Risk of bias and methodological quality were evaluated using the modified version of the Assessment of Multiple Systematic Reviews (AMSTAR) questionnaire, which was developed specifically to address the quality of SRs and MAs on the MD: the $AMSTAR_{MedSD}$.[25] It contains a total of 14 questions, with a maximum score of 21, divided into 4 sections: (1) a priori design; (2) literature search and duplicate effort; (3) coding of studies; and (4) analysis and interpretation. The individual $AMSTAR_{MedSD}$ items related to the different methodological aspects are described in detail by Huedo-Medina et al.[25]

RESULTS

Study selection

Figure 1 shows the detailed literature selection process. Overall, 237 references were initially identified, of which 178 were excluded after recognition of duplications. The 59

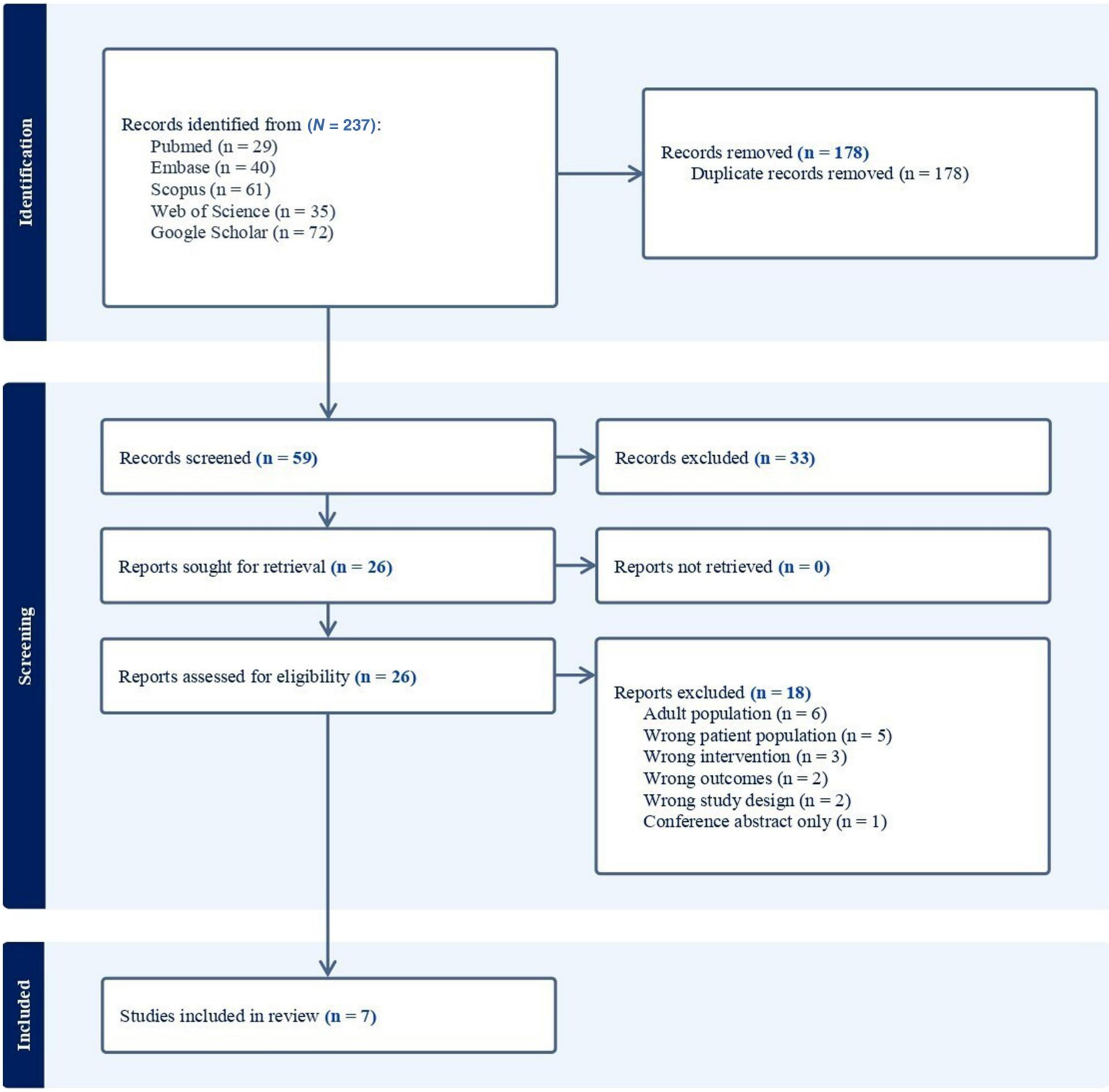

Figure 1. Flow Chart of the Literature Selection Process

potentially relevant citations were submitted to title and abstract screening, which determined the eligibility of 26 reports for full-text screening. This phase resulted in the exclusion of 19 articles for different reasons, as listed in Table S2. Ultimately, 7 studies fully met the eligibility criteria and were included in this UR: four were SRs and the other 3 were SRs that also included an MA.

Characteristics of included systematic reviews and meta-analyses

The main characteristics of the included reviews are summarized in Table 2[26–29] for SRs and Table 3[30–32] for MAs. The data reported refer only to studies based on the PICO criteria and methodology described earlier, involving a total of 810 224 children and adolescents.

Dietary patterns. Two SRs[26,29] and 1 MA[32] reported on the possible association between AMD and several outcomes of interest. In the review by Bujtor et al,[27] dietary intake was measured by dietary patterns and indices in 26 studies, 10 of them on the MD. In their SR, Teixeira et al[28] assessed healthy and/or sustainable dietary patterns and their health-related benefits. Of a total of 128 reports included in the review, 50 studied the MD, 31 of which were in line with the health outcomes of interest

Table 2. Characteristics of the Systematic Review Included in the Umbrella Review

First author, year	No. and design of original studies	Sample size and age (y)	Assessment of the dietary patterns			Health outcomes		Main results
			Type of dietary pattern	Tools for dietary information	Assessment methods	Types of health outcomes	Types of indicators	
Lassale et al (2022)[26]	8 Interventions[a] (7 with population of interest)	3938 5–17 y	MD	–	–	–	Adiposity OW/OB	6 BMI, 3 WC, 4 WHtR, 1 %BF	In 2 studies, for MD: body weight ↓; in other 2 studies: ↔; others: no comparison with a control
	1 Longitudinal	10 918 8–15 y and 15–22 y		FFQ	KIDMED[b]	A priori		BMI	MD: BMI ↓
	4 Cross-sectional and longitudinal[a] (3 on population of interest)	16 006; 2–14 y And 9856; 4–19 y		FFQ	1 KIDMED[b], 1 MDS[b], 1 Krece Plus test			3 BMI 2 WC 1 WHtR 1 TST 1 SST	In 1 longitudinal analysis, MD: BMI, markers of adiposity ↓ Others: ↔
	42 Cross-sectional[a] (37 on population of interest)	556 756 3–24 y		37 FFQ, 2 24-h dietary recall	33 KIDMED, 2 MDS, 1 Medlife index, 1 MSDPS			34 BMI, 10 WC, 1 WHtR, 1 WHR, 6 %BF	↔ No significant association in 22 studies; ↓ an inverse significant association in 18 studies
Bujtor et al (2021)[27]	8 Interventions[a] (5 on dietary patterns)	411 7–16.2 y	1 HPDP/LPDP, 1 HGIDP/LGIDP, 2 hypocaloric HGIDP/ hypocaloric LGIDP, 1 LGIDP/HND, 1 DASH/typical Iranian diet	–	–	–	Inflammation	3 CRP, 2 hs-CRP, 1 IL-2, 2 IL-6, 1 TNF-α	LGIDP: CRP, IL-6 ↓, hypocaloric HGIDP, hypocaloric LGIDP DASH: CRP ↓
	2 Longitudinal[a] (1 on dietary patterns)	843 14 and 17 y	WDP/HDP	FFQ	PCA	A posteriori		hs-CRP	WDP adherence (14 y old): hs-CRP (17 y old) ↑ HDP adherence (14 y old): hs-CRP (17 y old) ↓
	1 Cross-sectional and longitudinal	1419; 14 y And 843; 17 y	DG for Australian Children and Adolescents	FFQ	DGI-CA	A priori		hs-CRP	↔ No significant associations reported
	42 Cross-sectional[a] (13 on dietary patterns)	7019 6.5–18 y	8 MD, 1 WDP, 1 WDP/MD, 1 DG for Americans + Food Guide Pyramid[b], 1 DASH/DG for Americans + Food Guide Pyramid[b] /MD, 1 FBDG	9 FFQ, 5 24-h dietary recall, 1 dietary record	6 KIDMED[b], 3 MDS[b], 1 DASH score, 2 HEI[b], 1 DQI-A, 1 factor analysis, 1 PCA-factor analysis	11 A priori, 2 a posteriori		4 CRP, 8 hs-CRP, 3 IL-1, 2 IL-2, 3 IL-4, 1 IL-5, 5 IL-6, 1 IL-10, 1 IL-17, 1 IL-33, 1 sVCAM-1, 1 sICAM-1, 1 sE-selectin 5 TNF-α 1, TGFβ-1, 2 PAI-1, 1 IFN-γ	MD, HEI: CRP, IL-6, TNF-α ↓ (in healthy participants) MD, HEI, DASH diet: ↔ (in participants with pathologies) DQI-A: ↔ WDP: hs-CRP, IL-6 ↑ (in healthy participants)

(continued)

Table 2. Continued

First author, year	No. and design of original studies	Sample size and age (y)	Assessment of the dietary patterns				Health outcomes		Main results
			Type of dietary pattern	Tools for dietary information	Assessment methods		Types of health outcomes	Types of indicators	
Teixeira et al (2022)[28]	5 Intervention[a] (3 on health outcomes of interest)	2477 7–16 y	2 MD 1 DG for Americans + Food Guide Pyramid[b]	2 FFQ 1 24-h dietary recall	2 KIDMED, 1 HEI[b]	A priori	Adiposity OW/OB	3 BMI, 1 WHtR	After MD intervention: BMI ↓ in children with abdominal obesity After MD promotion and nutrition education intervention: No significant effects on BMI, general and abdominal obesity and no significant differences in BMI between intervention and control group, respectively
	13 Longitudinal[a] (2 on population and health outcomes of i nterest)	11 342 8–17 and 13.6–22 y	1 MD, 1 DASH	FFQ	1 KIDMED, 1 DASH score		Adiposity, OW/OB, MetS, glycemic profile, blood pressure	1 BMI, 1 WC, 1 modified ATP III criteria[50], 1 FPG, 1 SBP, 1 DBP	KIDMEDI: BMI ↓ DASH: MetS, hypertension, FPG, abdominal obesity ↓
	4 Cross-sectional and longitudinal	17 871; 2–14 y And 11 248; 4–17 y	2 MD, 1 DASH diet, 2 DG for Australian Children and Adolescents[b]	FFQ	1 KIDMED[b], 1 MDS[b], 1 DASH score, 1 DGI-CA, 1 Pd-DQI		Adiposity, OW/OB, blood pressure, musculoskeletal health, lipid profile	4 BMI, 1 WHtR, 1 TST, 1 SST, 1 SBD, 1 DBP, 1 BMD, 1 triglycerides	KIDMED: BMD ↑; BMI ↔ DASH: BMD, BMI ↔ MDS: OW/OB, % BF ↓ DGI-CA: BMI ↑; WHtR, triglycerides ↓; BP ↔ Pd-DQI: BMI ↓ (in OW participants)
	106 Cross-sectional[a] (43 on population and health outcomes of interest)	119 583 4–18.3 y	20 MD, 4 DASH, 4 DG for Americans + Food Guide Pyramid[b], 2 SEAD, 1 optimized mixed diet, 1 FBDG, 1 SBDG 2015 + Nordic Nutrition Recommendations, 1 Food Guide Pyramid + DR of AAP, 1 DR for Children by USDA's "Choose my Plate," 1 DR of AAP + DR of AMA, 1 DG for Americans 2010 + Food Guide Pyramid + DG of the Singapore HPB, 1 Brazilian DG 2006, 1 DG for Americans, 2 DG for Australian Children and Adolescents, 1 Malaysian DG for Children and Adolescents, 1 DR of Expert Committee of AAP	31 FFQ, 11 24-h dietary recall, 1 dietary record	17 KIDMED, 2 MDS, 1 Krece Plus Test, 4 DASH score[b], 5 HEI[b], 1 DGI-CA, 1 DQI-A, 2 SEAD score, 1 HuSKY, 1 SHEIA15, 2 HLD Index[b], 1 E-KINDEX, 1 BHEI-R, 1 RFS, 1 ACARFS, 1 MHEI, 1 OPLS		Adiposity, OW/OB, MetS, blood pressure, lipid profile, musculoskeletal health, inflammation, cardiometabolic risk, cardiovascular risk, cardiovascular health physical, fitness growth	28 BMI, 13 WC, 2 HC, 2 WHtR, 1 height, 3 %BF, 4 TST, 4 SST, 1 BST, 1 IST, 1 MRS[51], 1 CRS[52], 1 homocysteine, 1 insulin resistance by HOMA-IR, 1 FPG, 1 insulin, 1 total cholesterol, 3 HDL-C, 2 LDL-C, 3 triglycerides 1, n-3 fatty acid, 9 SBP, 9 DBP, 2 CRP, 1 Alpha-FIT Battery Test[d], 1 25 (OH)D	↔ No significant association with outcomes of interest in 22 studies ↓ An inverse significant association in 19 studies

(continued)

Table 2. Continued

First author, year	No. and design of original studies	Sample size and age (y)	Assessment of the dietary patterns			Health outcomes		Main results
			Type of dietary pattern	Tools for dietary information	Assessment methods	Types of health outcomes	Types of indicators	
Iaccarino Idelson et al (2017)[29]	3 Cross-sectional and longitudinal	17 251; 2–15 y And 10 67; 4–25 y	MD	2 FFQ 1 dietary history	1 KIDMED[b], 2 MDS[b] A priori	Adiposity OW/OB	3 BMI, 1 WC, 1 TST, 1 SST	In 1 study at baseline, MD: OW/OB, %BF, WC ↓; after 2 y of intervention, MD: BMI, %BF, WC ↓, ↔ no significant associations reported at baseline and after follow-up in the other studies
	55 Cross-sectional[a] (20 on population and health outcomes of interest)	25 950 3–24 y		19 FFQ, 1 dietary record	17 KIDMED, 3 MDS		20 BMI, 6 WC, 3 WHtR, 4 %BF, 1 TST, 1 SST	In 7 studies MD: BMI ↓; in 2 studies MD: WC ↓; in 1 study, MD: BMI, WC ↑; in 1 study, MD: BMI ↑ ↔ No significant associations in the other studies

[a]Reported data refer only to studies based on Population, Intervention, Comparison, and Outcome of interest.
[b]Used in different versions.
[c]Criteria used: BMI, SBP, triglycerides, and HOMA-IR.
[d]Alpha Fitness Battery Test for Children and Adolescents.

Abbreviations: –, NOT available; ↑, increase or positive association; ↓, decrease or negative or inverse association; ↔, no association; %BF, body fat percentage; 25 (OH)D, 25-hydroxyvitamin D; AAP, American Academy of Pediatrics; ACARFS, Australian Child and Adolescent Recommended Food Score; AMA, American Medical Association; BHEI-R, Brazilian Healthy Eating Index Revised; BMD, bone mineral density; BMI, body mass index; BST, biceps skinfold thickness; CRP, C-reactive protein; CRS, Cardiometabolic Risk Score; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; DG, dietary guideline; DGI-CA, Dietary Guideline Index for Children and Adolescents; DQI-A, Diet Quality Index for Adolescents; DR, dietary recommendation; E-KINDEX, Electronic Kids Dietary Index; FBDG, Flemish Food-Based Dietary Guidelines; FFQ, food frequency questionnaire; FPG, fasting plasma glucose; HC, hip circumference; HDL-C, high-density lipoprotein cholesterol; HDP, Healthy Dietary Pattern; HEI, Healthy Eating Index; HGIDP, High Glycemic Index Diet Pattern; HLD-Index, Healthy Lifestyle Diet-Index; HND, Healthy Nutritional Diet; HOMA-IR, homeostatic model assessment for insulin resistance model assessment; HPB, Health Promotion Board; HPDP, high-protein diet pattern; hs-CRP, high-sensitivity C-reactive protein; HuSKY, Healthy Nutrition Score for Kids and Youth; IFN-γ, interferon-γ; IL, interleukin; IST, ileac skinfold thickness; LDL-C, low-density lipoprotein cholesterol; LGIDP, Low Glycemic Index Diet Pattern; LPDP, low-protein diet pattern; MD, Mediterranean diet; MDS, Mediterranean Diet Score; MetS, metabolic syndrome; MHEI, Malaysian Healthy Eating Index; MRS, Metabolic Risk Score; MSDPS, Mediterranean-style dietary pattern score; OPLS, Obesity Preventive Lifestyle Score; OW/OB, overweight/obesity; PAI-1, plasminogen activator inhibitor-1; PCA, principal component analysis; Pd-DQI, Prior derived Diet Quality Index; PDL-Index, Preschoolers Diet-Lifestyle Index; PDP, prudent dietary pattern; RFS, Recommended Food Score; SBDG, Swedish Food-Based Dietary Guidelines; SBP, systolic blood pressure; sE-selectin, soluble E-selectin; SEAD, Southern European Atlantic Diet; SHEIA15, Swedish Healthy Eating Index for Adolescents 2015; sICAM-1, soluble intercellular adhesion molecule-1; SST, subscapular skinfold thickness; sVCAM-1, soluble vascular cell adhesion molecule-1; TGFβ-1, transforming growth factor-β1; TNF-α, tumor necrosis factor-α; TST, triceps skinfold thickness; WC, waist circumference; WDP, Western dietary pattern; WHR, waist to hip ratio; WHtR, waist to height ratio.

Table 3. Characteristics of the Meta-Analyses Included in the Umbrella Review

First author, year	No. and design of original studies	Sample size Age (y)	Assessment of the dietary patterns: Type of dietary patterns	Assessment of the dietary patterns: Tools for dietary information	Assessment method		Health outcome: Type of health outcomes	Health outcome: Type of indicators	Risk estimations (95% CI), I^2	Main results
Denova-Gutiérrez et al (2018)[30]	19 Longitudinal[a] (1 on population of interest)	1007 13 and 17 y	PDP WDP	FFQ	Cluster analysis	A posteriori	Bone health	BMD, BMC	–	↔ No significant association
	12 Cross-sectional[a] (3 on population of interest)	3105 13.3–20 y		2 FFQ, 1 dietary record	1 PCA-factor analysis, 2 factor analysis				PDP: 0.49 (0.38–0.63), $P < 0.001$, 4% WDP: 1.09 (0.82–1.44), $P = 0.56$, 0%	PDP: low BMD ↓
Hassani Zadeh et al (2021)[31]	6 Longitudinal[a] (1 on population of interest)	995 14 and 17 y	PDP WDP	FFQ	Factor analysis	A posteriori	NAFLD	Moderate to severe hepatic steatosis (by ultrasonography), no excessive alcohol intake, no secondary causes and concomitant diseases	–	WDP: NAFLD ↑ (no longer significant after adjusting for BMI) PDP: NAFLD ↓ (in centrally obese adolescents)
	12 Cross-sectional[a] (1 on population of interest)	1639 16.9–20.1 y	WDP		PCA-factor analysis				–	WDP: NAFLD ↑
García-Hermoso et al (2020)[32]	39 Cross-sectional[a] (12 on health outcomes of interest)	11 694 6.9–16.3 y	MD	FFQ	KIDMED	A priori	Physical fitness	9 Alpha-FIT Battery Test[b], 2 CRF, 3 muscular fitness, 1 motor agility	Studies of children/adolescents: CRF: 0.22 (0.13–0.31), 5.7%; muscular fitness: 0.11 (0.03–0.18), 95.4%; speed and agility: −0.06 (0.12–0.00), 84.2% Studies of adolescents: CRF: 0.3 (0.12–0.47), 96.5%; muscular fitness: 0.12 (0.03–0.26), 94.8%; speed and agility: −0.08 (−0.23 to 0.07), 87.1%	MD: CRF, muscular fitness ↑; speed and agility ↓

[a]Reported data refer only to studies based on population, intervention, comparison, and outcome of interest (PICO).
[b]Used in different versions.
Abbreviations: –, NOT available; ↑, increase or positive association; ↓, decrease or negative or inverse association; ↔, no association; Alpha-FIT Battery Test, Alpha Fitness Battery Test for Children and Adolescents; BMC, bone mineral content; BMD, bone mineral density; CRF, cardiorespiratory fitness; FFQ, food frequency questionnaire; MD, Mediterranean Diet; NAFLD, nonalcoholic fatty liver disease; PCA, principal component analysis; PDP, prudent dietary pattern; RRR, reduced rank regression; WDP, Western dietary pattern.

and thus were extracted. Most of the studies included in these 5 reviews evaluated AMD by an a priori method, using different tools. Among these instruments, the Mediterranean Diet Quality Index for Children and Adolescents (KIDMED) was the index most often used.[3]

The remaining 2 MAs defined different types of dietary patterns by an a posteriori method. In particular, Denova-Gutiérrez et al[30] identified the "Prudent/Healthy" and "Western/Unhealthy" dietary patterns, whereas Hassani Zadeh et al[31] selected the Western Dietary Pattern (WDP), Prudent Dietary Pattern (PDP), and the MD. The WDP was characterized by a high intake of processed foods, red meat, refined grains, and high-fat dairy. Conversely, patterns heavily loaded with whole grains, fruits, vegetables, low-fat dairy, and poultry were categorized as PDPs. The MD was distinguished from the latter and defined as a pattern consisting mainly of fish, olive oil, and high amounts of dietary fiber.[31]

Health outcomes. As mentioned, various health outcomes in association with dietary patterns were studied in the included reviews. Overall, 15 parameters of interest (adiposity, overweight and obesity, inflammation, metabolic syndrome, blood pressure, lipid profile, glycemic profile, cardiometabolic risk, cardiovascular risk, cardiovascular health, NAFLD, musculoskeletal health, physical fitness, bone health, and growth) were identified and organized into 4 macro-categories of health outcomes to facilitate the interpretation of the results: (1) overweight and obesity; (2) inflammation; (3) cardiometabolic health; and (4) musculoskeletal health. In particular, overweight and obesity were assessed in 2 SRs[26,29] and musculoskeletal health in 2 SRs with an MA.[30,32] Only the SR by Bujtor et al[27] focused on biological markers of inflammation and the MA by Hassani Zadeh et al[31] on NAFLD. The remaining review[28] aimed to evaluate, among other objectives, the benefits of healthy and sustainable dietary patterns by examining all health outcomes described so far (overweight and obesity, inflammation, cardiometabolic health, and musculoskeletal health).

Overweight and obesity. Lassale et al[26] assessed the impact of AMD on adiposity markers and obesity in children and adolescents. They concluded that there is limited evidence to prove a beneficial effect of the MD on body weight. Five intervention studies with a control group included adolescents in the sample; of these, 3 reported a statistically significant difference between the intervention and control group in terms of body mass index (BMI) and obesity.

Among the observational studies, 29 targeted adolescents and 12 also targeted children. Of these 41 studies, 24 found no statistically significant associations with general or central adiposity and 1 found a positive association. A significant inverse association was reported in 18 studies, most of which addressed only adolescents.

The SR by Iaccarino-Idelson et al[29] included 58 observational studies, of which only 3 had a cross-sectional plus prospective design. Among different objectives, the association of AMD with anthropometric variables and body composition in childhood was assessed. The latter was studied in 26 studies, including 7 with children and adolescents and 16 with adolescents only. No statically significant association with central and general adiposity was observed in 13 studies, a negative association was found in 8, and positive association in 2. The authors concluded that the relationship between AMD and weight status was not consistent and that further prospective cohort and intervention studies were needed to better elucidate the association with behavioral and health outcomes.

Finally, Teixeira et al[28] also evaluated the effects of AMD on general and central adiposity in 28 studies, 21 of which included adolescents. Of these, 2 had an interventional design and showed a statistically nonsignificant association with general obesity in 1 case and a negative association in the other. The remaining 19 studies had an observational design: In 9, no statistically significant association with general or abdominal obesity was found; in another 9, a negative correlation was found; and a positive correlation was found in only 1 study. As a whole, the authors concluded that higher adherence to healthy dietary patterns (HDPs) was associated with lower risk of abdominal obesity, but no consensus was reached on the relation with BMI.

Inflammation. In a recent review,[27] Bujtor et al investigated associations between dietary intake (by means of dietary patterns, food groups, macronutrients or micronutrients) and biological markers of low-grade inflammation in both children and adolescents. Of all the extracted studies ($n = 21$) that evaluated the effect of dietary patterns, only 20 included adolescents in the sample, and 10 of these studies focused on the MD.

The Mediterranean dietary pattern was cross-sectionally assessed in all 10 studies and was inversely associated with inflammation markers in 5 studies: positively in 2 and with no significant association reported in 5. Among the latter, Del Mar Bibiloni et al[33] also looked at the WDP in their cross-sectional study and reported a positive association with interleukin-6. Another extracted study,[34] with a longitudinal design, evaluated the effects of the WDP on inflammation markers, comparing it with an HDP. After 3 years of follow-up, the authors reported the WDP was associated with higher levels of high-sensitivity C-reactive protein, and the healthy pattern was associated with their reduction. Overall, Bujtor et al[27] concluded that adequate adherence to an HDP, such as the MD, was associated with decreased levels of pro-inflammatory biomarkers, whereas adherence to a WDP was associated with higher levels of the inflammatory profile.

Inflammation was also assessed in 2 cross-sectional studies in a SR by Teixeira et al,[28] which showed a significant negative association with an HDP, including MD, in adolescents.

Cardiometabolic health. Two reviews studied the relation between different dietary patterns and cardiometabolic outcomes. In 2021, Hassani Zadeh et al[31] published an MA with the objective of evaluating the association between diet and NAFLD in all age groups. Of the 18 reports included in the review, 2 cross-sectional studies had a sample of adolescents and reported a positive correlation with WDP and a negative correlation with PDP. An age-based subgroup analysis was not performed, and statistical analyses were conducted on all extracted studies. The authors found that the WDP was significantly associated with an increase in NAFLD risk (OR, 1.56; 95% CI, 1.27–1.92; $P \leq 0.001$), whereas a PDP (OR, 0.78; 95% CI, 0.71–0.85; $P \leq 0.001$) and the MD (OR, 0.77; 95% CI, 0.60–0.98; $P = 0.41$) were significantly associated with decreased risk of this disease. The researchers concluded that the WDP increased the risk of NAFLD by 56%, whereas a PDP and MD reduced the risk of this disease by 22% and 23%, respectively.

The other review of studies about cardiometabolic health was conducted by Teixeira et al.[28] The effects of the MD on cardiometabolic risk were assessed in 4 cross-sectional studies that included adolescents, 2 of which showed no significant association with blood pressure, 1 that showed a positive association, and the fourth reported a negative association. Considering a broader range of HDPs, the authors deduced that higher adherence to these dietary patterns was associated with lower blood pressure and metabolic risk.

Musculoskeletal health. Denova-Gutiérrez et al[30] focused on the relationship between dietary patterns and bone mineral density (BMD), bone mineral content, and fracture risk in different age groups, including 31 studies in their SR and conducting an MA on only 12 of them. A total of 4 studies were targeted at adolescents, 1 of which had a longitudinal design and reported no significant association. The remaining studies were cross-sectional and were considered for the MA. The authors reported an inverse association between a PDP and low BMD (OR, 0.49; 95% CI, 0.38–0.63; $P < 0.001$). They concluded that a PDP or HDP was inversely associated with the risk of low BMD in all age groups and a WDP or unhealthy dietary pattern was positively associated with risk of low BMD only in older adults.

In the present UR, physical fitness (PF) and growth were considered as other musculoskeletal health outcomes and were studied in 2 reviews.[28,32] García-Hermoso et al[32] analyzed the associations among AMD, physical activity, sedentary behavior, and PF among youth. Of a total of 39 included observational studies, 12 concerned PF and were thus extracted; 7 of these targeted adolescents, and the remainder also included children. The results revealed a weak to moderate positive correlation between AMD and cardiorespiratory fitness ($r = 0.22$; 95% CI, 0.13–0.31) and muscular fitness ($r = 0.11$; 95% CI, 0.03–0.18), and a weak to moderate negative correlation with speed and agility ($r = -0.06$; 95% CI, –0.12 to –0.01). After controlling for sex and age, only the association between AMD and cardiorespiratory fitness remained significant in adolescents ($r = 0.3$; 95% CI, 0.12–0.47). In conclusion, the review reported that improved dietary habits toward those of the MD could be associated with increased PF and physical activity in childhood, less sedentary behavior, and better health in general.

In the last review, Teixeira et al[28] took into consideration musculoskeletal health in relation to AMD in only 3 studies. One cohort study[35] found that among 13-year-old male adolescents, AMD was significantly associated with higher BMD when the boys reached age 17 years. The other 2 studies had a cross-sectional design and targeted children and adolescents. They reported a positive correlation with cardiorespiratory fitness in 1 case[36] and with height in the second.[37]

Quality assessment

The methodological quality assessment of the SRs and MAs according to $\text{AMSTAR}_{\text{MedSD}}$ criteria is shown in Table S3. The included studies achieved a medium quality score (mean ± SD, 13.1 ± 3.53). All reviews had an a priori design, and only 1 (14.3%) did not specify population variables in the methods. More than half of the reports (57%) reported that study selection and data extraction were duplicated; for almost all of them (85.7%), a comprehensive literature search was performed, a list of included and excluded studies made, and the search could be replicated; only 2 of them (28.6%) permitted the inclusion of grey literature. All included studies completely satisfied the criteria of the study coding domain. In the fourth and last domain (analysis and interpretation), all reports showed how the results may depend on the study quality and indicated the presence or absence of conflicts of interest. The 3 MAs included used appropriate methods to combine study findings and justified the chosen effect size index; only 2 of them assessed the likelihood of publication bias.

DISCUSSION

To our knowledge, this is the first UR to synthesize the evidence on the effect of AMD on health status in adolescence. Overall, the present review comprised 4 SRs and 3 MAs and evaluated AMD in relation to 4 macrocategories of health outcomes (overweight and obesity, inflammation, cardiometabolic health, and musculoskeletal health). The findings showed strong, limited evidence on the health benefits of AMD in adolescence.

The outcomes of overweight and obesity were examined by 3 SRs,[26,28,29] with inconclusive results. One possible explanation may be due to the observational design of most of the included studies, which does not allow for the assessment of cause-and-effect associations. Second, none of these reviews provided an MA. Third, different criteria were taken into account for the definition of obesity and the analysis of its indicators (BMI, or z score for BMI). Fourth, the associations with BMI also depend on the variables for which the analyses were adjusted. Fifth, KIDMED, as the most widely used tool for assessing AMD, may also have affected the results obtained. Indeed, this instrument evaluates the frequency of consumption of different foods and habits and does not consider quantitative food data, which influence the body weight of individuals.[3] The necessity for more intervention studies to draw definitive conclusions on the association between AMD and overweight/obesity was confirmed in a recent SR with an MA of randomized clinical trials.[38] This review aimed to evaluate the effects of MD-based interventions on anthropometric and obesity indicators among children and adolescents and showed a significant reduction in these parameters among participants compared with the control group, especially in those with excess weight.

The first evidence of the association between dietary intake and biological markers of inflammation in children and adolescents was provided by Bujtor et al.[27] Their SR indicated that adequate adherence to HDPs (eg, MD, Dietary Approaches to Stop Hypertension [DASH] diet, low glycemic index diets) was associated with decreased levels of inflammatory biomarkers, whereas a WDP elicited a pro-inflammatory response.[27] Although the MD has been defined as an anti-inflammatory model due to the properties of its components (eg, antioxidants, folate, flavonoids), the mechanisms by which the HDPs, in general, affect the inflammatory process are largely underexplored.[27] Moreover, as reported by the authors, some methodological limitations were observed in the included studies in terms of measurement of dietary intake and inflammatory biomarkers. In view of this, the results obtained should be interpreted with caution and more solid evidence would be needed.

Cardiometabolic outcomes were studied in the SR of Teixeira et al[28] and in the MA of Hassani Zadeh et al.[31] From the MA, the authors concluded that WDPs tended to increase the risk of NAFLD, whereas PDP and MD were associated with a reduced risk of this disease. These results were obtained from the entirety of the included studies, targeting all age groups and not only adolescents. Although the population was heterogeneous, a subgroup analysis based on several variables (eg, ethnic group, age, sex) was not performed, due to the small number of studies.

Hassani Zadeh et al[31] identified 3 a posteriori dietary patterns, including the PDP as distinct from the MD. Actually, according to the literature, a PDP or HDP is based on 4 principles: avoidance of excess energy intake, increased dietary fiber intake, reduced total fat intake to approximately 30% of energy intake, and increase in polyunsaturated fat consumption.[39,40] These aspects are also common to the MD, which is composed of 6 main beneficial components (vegetables, legumes, whole-grain cereal, fish, fruit, and nuts), like the PDP. Indeed, the concept of a “prudent diet” was developed by Hu et al[41–44] as a modification of the MD, which makes it possible to consider them as 2 very similar HDPs.[41] Probably for these reasons, Hassani Zadeh et al[31] obtained similar results for PDPs and the MD in their analysis. In addition, this review did not provide an MA to compare dietary patterns, due to the a posteriori methods used to derive them. Overall, more research, especially with a prospective design, is needed to fill the gaps on the existence of a true causal relationship between dietary patterns and risk of NAFLD, using both a priori and a posteriori methods in larger samples of different ethnicities.

Teixeira et al[28] reported that higher adherence to HDPs was associated with lower blood pressure and metabolic risk, whereas inconsistent results were found when analyzing only the MD. Another recent SR evaluated blood pressure in association with dietary patterns in adolescents and showed a positive association between dietary patterns characterized by the consumption of foods rich in sodium, animal fat, refined carbohydrates, and low in fiber, and increased blood pressure. On the contrary, only 1 included study observed a HDP significantly associated with reduced blood pressure. In both reviews, considering the limited number of studies that found a significant association and their limitations, the present results should be interpreted carefully and confirmed by further evidence.

Regarding musculoskeletal health, Denova-Gutiérrez et al[30] reported an inverse association between PDPs or HDPs and risk of low BMD in all age groups. This result could be extended to the MD, given its similarity to PDP, as mentioned. However, as showed by an SR and evidence map on the same topic, there is insufficient evidence to understand the relation between the MD and musculoskeletal outcomes (namely, fracture, bone density, osteoporosis, and sarcopenia) at all ages.[45]

PF is defined as the ability to perform daily activities with vigor, is associated with a low risk of developing chronic diseases and premature death, and comprises cardiorespiratory fitness, musculoskeletal fitness, motor fitness, and body composition.[46,47] For these reasons, it can be considered a musculoskeletal health outcome. The MA by García-Hermoso et al[32] evaluated this outcome in association with AMD. After an age-based subgroup analysis, a significant positive association was observed between cardiorespiratory fitness and AMD in adolescents. This finding was confirmed by another recent SR, with the objective of assessing cardiorespiratory fitness in relation to different dietary patterns, both in youth and adulthood.[48] García-Hermoso et al[32] concluded that AMD could be associated with increased PF and physical activity in childhood, less sedentary behavior, and better health in general.

The main limitation of this MA was the cross-sectional design of most of the included studies, which does not allow causal inferences to be made and is more susceptible to biases (eg, selection bias, information bias). A finding supporting the positive association between AMD and PF was recently found by Bizzozero-Peroni et al,[49] although only in an adult population.

According to the $AMSTAR_{MedSD}$ scale, the methodological quality of the included SRs and MAs showed a medium score. Two sections of the instrument did not fully comply with the quality standards. In particular, not all studies duplicated study selection and data extraction and included grey literature. Furthermore, unsatisfactory scores were obtained in the analysis and interpretation section, probably due to the inclusion of only 3 MAs.

The present study has several limitations that should be considered. First, the selected SRs applied different adolescent age cutoffs, making data extrapolation difficult. It seems necessary to standardize the age ranges to make future evidence more easily comparable. Second, several primary studies we included targeted both children and adolescents. Future evidence should analyze each age group separately because each phase of life has its own specificities that may directly interfere with health outcomes. Third, the limited number of included reviews and the high heterogeneity among them did not allow for a quantitative analysis. Fourth, a lack of high-quality research was observed in most of the selected reviews. In addition, the findings were mainly from observational studies. These aspects point out the need for further evidence to limit biases and better interpret the results.

Despite these limitations, there are some strengths to highlight. To our knowledge, this is the first UR in which the evidence on the relationship between AMD and several health outcomes in adolescence has been summarized. Another aspect is the use of the standard definition of adolescence proposed by the World Health Organization[24] as an inclusion criterion. In addition, we aimed to study not only diet-related health outcomes, known to be associated with adolescence (eg, overweight, obesity) but also those recently observed in this age group (eg, NAFLD, hypertension). Finally, we excluded studies that included adolescents with concomitant diseases conditions that involve restrictive dietary treatment and influence AMD (eg, food allergy, celiac disease).

CONCLUSION

To conclude, the current UR points out limited evidence and a lack of consistency concerning the relation between AMD and health outcomes of interest in adolescence. In view of the importance of proper nutrition for the well-being and future health of adolescents, the need for more studies is recognized. Future research specifically targeting adolescents and adopting an internationally harmonized age range and a prospective or interventional design would allow gaps to be filled and educational and behavioral interventions to be tailored to public health.

Author Contributions

A.D.N., M.S., and E.C. designed the study. A.D.N. and E.C. reviewed the articles; extracted, analyzed, and interpreted the data; assessed the quality of the studies; and wrote the manuscript. M.S. critically reviewed and edited the manuscript. All the authors approved the present version of the article.

Supplementary Material

Supplementary Material is available at *Nutrition Reviews* online.

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Conflict of Interest

None declared.

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