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The association of diet quality and lifestyle factors in children and adults with ADHD: a systematic review and meta-analysis

Corresponding author

George Papanastasiou

Institute of Informatics and Telecommunications, NCSR Demokritos, Greece

Department of Information and Communication Systems Engineering, University of the Aegean, Greece

gpapanasta@aegean.gr

Athanasios Drigas

Institute of Informatics and Telecommunications, NCSR Demokritos, Greece

Pantelis Papanastasiou

Institute of Informatics and Telecommunications, NCSR Demokritos, Greece

Abstract. Eating habits of individuals with learning and behavioral difficulties is an important and emerging area of nutrition expertise. An unhealthy diet, combined with limited physical activity, is linked with an increased risk of chronic diseases and a lower quality of life. The study aims to review in a systematic way evidence on: (a) the relationship between diet quality and ADHD; and (b) the effect of three lifestyle factors, physical activity, quality of sleep, and stress on children and adults with ADHD. In December 2020, we searched for relevant articles in PubMed and Scopus. The studies included were those that assessed diet, physical activity, sleep, and stress, of children and adults with ADHD. We identified a total of eighteen studies with an invasive and observational approach that matched our research criteria. Fourteen of these studies were included in the meta-analysis. The pooled analysis showed that a high-diet quality decreases the prevalence of ADHD in children (OR: 0.43, 95% CI: 0.28-0.70), while a poor diet quality is associated with an increased risk of ADHD in both children and adults (OR: 2.24, 95% CI: 1.49-3.65). Also, a poor lifestyle indicates a higher prevalence of ADHD in both children and adults (OR: 1.90, 95% CI: 1.43-2.61). This study is limited to its ability to extract data from some of the included studies while sampling was limited due to the absence of studies in adults with ADHD. The present study suggests that a high-quality diet with increased consumption of fruits, vegetables, and fish, may be protective against ADHD in children. On top of that, a poor-quality diet with higher consumption of sugar, sweetened drinks, and junk food, as well as a lifestyle that is characterized by reduced sleep and physical activity can be associated with increased risk of ADHD, for both children and adults. The current domain needs more experimental data to clarify the tripartite relationship between diet quality, lifestyle factors, and ADHD, and to enhance our study's findings.

Keywords: Diet quality, lifestyle factors, ADHD, attention-deficit/hyperactivity disorder

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is among the most common neurobehavioral disorders, characterized by persistent symptoms of hyperactivity and impulsivity, that commonly occurs in childhood and remain in adulthood (Wilens & Spencer, 2010). Research shows that approximately 7% of children and 2.5% of adults experience ADHD worldwide (Thomas et al., 2015; Simon et al., 2009). The etiology of ADHD continues to be discussed, whilst numerous studies predominantly focus on genetic and environmental factors (Bobb et al., 2005; Pingault et al., 2015).

However, considerable evidence proposes that ADHD is linked with many individual factors, including diet and lifestyle (Stevenson et al., 2014; Weissenberger et al., 2017; Lingineni et al., 2012; Sivertsen et al., 2015; Touchette et al., 2009; van Egmond Fröhlich et al., 2012).

The World Health Organization & United Nations Children's Fund (UNICEF) proposes that with shifting population diets, defining diet quality and how it should be assessed or monitored globally has become increasingly important (WHO & UNICEF, 2020). Assessing the quality of the diet can be vital for individuals with ADHD, as science is still

quite new and controversial behind the effect of food on behavior. Subsequently, actual food availability may vary by region, socioeconomic level, and season and therefore strategic treatment should be individualized on a case-by-case basis. Research shows that high sugar consumption, artificial food colorants, preservatives, as well as low levels of zinc, magnesium, omega-3 fatty acids, are associated with an increased risk of ADHD (Millichap & Yee, 2012; Chang et al., 2018).

Recent studies also show that there is a significant connection between ADHD, obesity, and overweight (Cortese et al., 2016). An unhealthy diet combined with limited physical activity is associated with a higher risk of chronic diseases later in life (Booth et al., 2012). Sleeping problems and less time spent in activities that stimulate cognitive function have a big impact on developing ADHD and behavior problems (Peralta et al., 2018). With that being said, ADHD is individually associated with one mode of behavior, with several variables that may be interrelated. Therefore, it is important to identify potential mechanisms, with the total number of lifestyle factors involved, that may be associated with complications of dealing with ADHD. Would there be any significant relationship among diet quality; physical activity; stress and quality of sleep, that will help us understand the impact of each variable on ADHD? The study aims to review in a systematic way evidence on: (a) the relationship between diet quality and ADHD; and (b) the effect of three lifestyle factors, physical activity, quality of sleep, and stress on children and adults with ADHD. Our study hypothesized that a high-quality diet and a healthy lifestyle would act as an inhibitory role, whereas a poor-quality diet and a poor lifestyle would raise the risk of ADHD pathogenesis.

Materials and Methods

In December 2020, we searched for relevant articles in *PubMed* and *Scopus*. Search terms included: ("ADHD" OR "diet" OR "diet quality" OR "lifestyle"). Besides, we searched reference lists of the articles identified. The authors' strategy used these terms for full text search on each database. The review was performed following PRISMA guidelines.

Studies were included in this systematic review and meta-analysis if they satisfied the following criteria: (1) they explored the effects of diet or lifestyle behaviors (physical activity, sleep, stress) on ADHD; (2) participants were children and adults with a diagnosis of ADHD. Exclusion criteria are the following: (1) studies that used micronutrient supplementation for the treatment of ADHD; (2) studies on non-human subjects; (3) studies with data that are not reliably exported; (4) systematic review studies. Authors independently exported studies to an EndNote library and then extracted data using Microsoft Excel spreadsheets. Thus, they could separate important information with pre-agreed sample export titles, main report, and key findings.

In this article, we systematically reviewed eighteen studies. Four of them, did not provide sufficient data and thus could not be included in the meta-analysis. All randomized controlled trials included had to pass a methodological quality process, using the Cochrane Collaboration tool to assess the risk of bias. Towards that goal, a series of questions ("marking questions") aimed to gather information on the potential risk of bias of each chosen study. These marking questions test the following: bias arising from the randomization process; bias due to deviations from intended interventions; bias due to missing outcome data; bias during the measurements of the outcome, and bias in the selection of the reported result. Then, studies were assessed as "low risk of bias", "high risk of bias" or "unclear risk of bias".

As a result, the authors conducted three meta-analyses from fourteen studies (eight case-controls, five cohorts, one cross-sectional) to summarize the effect of (1) high-quality diet; (2) poor-quality diet; and (3) the impact of a poor lifestyle on ADHD, for both children and adults. In addition, the effects of a healthy lifestyle on ADHD were not sufficiently assessed and could not be extracted. Fixed and random-effects model is used to calculate the pooled effects. To conclude, in the reviewed papers we found the most common diet and lifestyle factors that showed an effect on ADHD.

This evidence-based meta-analysis was carried out by the most relevant RevMan 5.4 software and forest plots were created using GraphPad Prism 9.0.0. 95% confidence intervals (CI) were used to represent the final analysis ($p \leq 0.05$). Finally, the presentation of the results and comparisons between studies of the meta-analysis were shown with a help of a forest plot. The review has been registered on the International Prospective Register of Systematic Review- PROSPERO, registration number: CRD42021231613.

Results and discussion

504 studies were detected by the database literature search, of which 263 in PubMed and 241 in Scopus (Figure 1). 120 duplicates were identified and removed. From the remaining number of studies ($n = 384$), 78 abstracts were chosen to be evaluated according to their titles. Then, 57 records were excluded after abstract screening, because they did not meet the inclusion criteria described in the Experimental Section. The remaining 21 studies were evaluated using their full text for eligibility. After this, we excluded 6 studies for the following reasons: 1 study didn't evaluate ADHD outcome; 1 study had an ongoing RCT; 1 study was a non-English article; 1 study assessed lifestyle factors that didn't match our research criteria; and 2 studies were review articles. Lastly, 3 papers were added from the references list, resulting to eighteen studies to be analyzed ($n = 18$).

The authors selected studies that had an invasive and observational design. Two studies had a randomized controlled trial design (Pelssers et al.,

2009; Ghanizadeh & Haddad, 2015), nine were case-controls (Ptacek et al., 2014; Woo et al., 2014; Yu et al., 2016; Zhou et al., 2016; Ríos-Hernández et al., 2017; Chou et al., 2018; Weissenberger et al., 2018; Wang et al., 2019; Hong et al., 2020), five were cohorts (Wiles et al., 2009; Kohlboeck et al.,

2012; Khalife et al., 2014; Wu et al., 2016; Del-Ponte et al., 2019) and two were cross-sectional (San Mauro Martin et al., 2018; Holton & Nigg, 2020). The results are exported and formatted in a data export table as seen in Table 1.

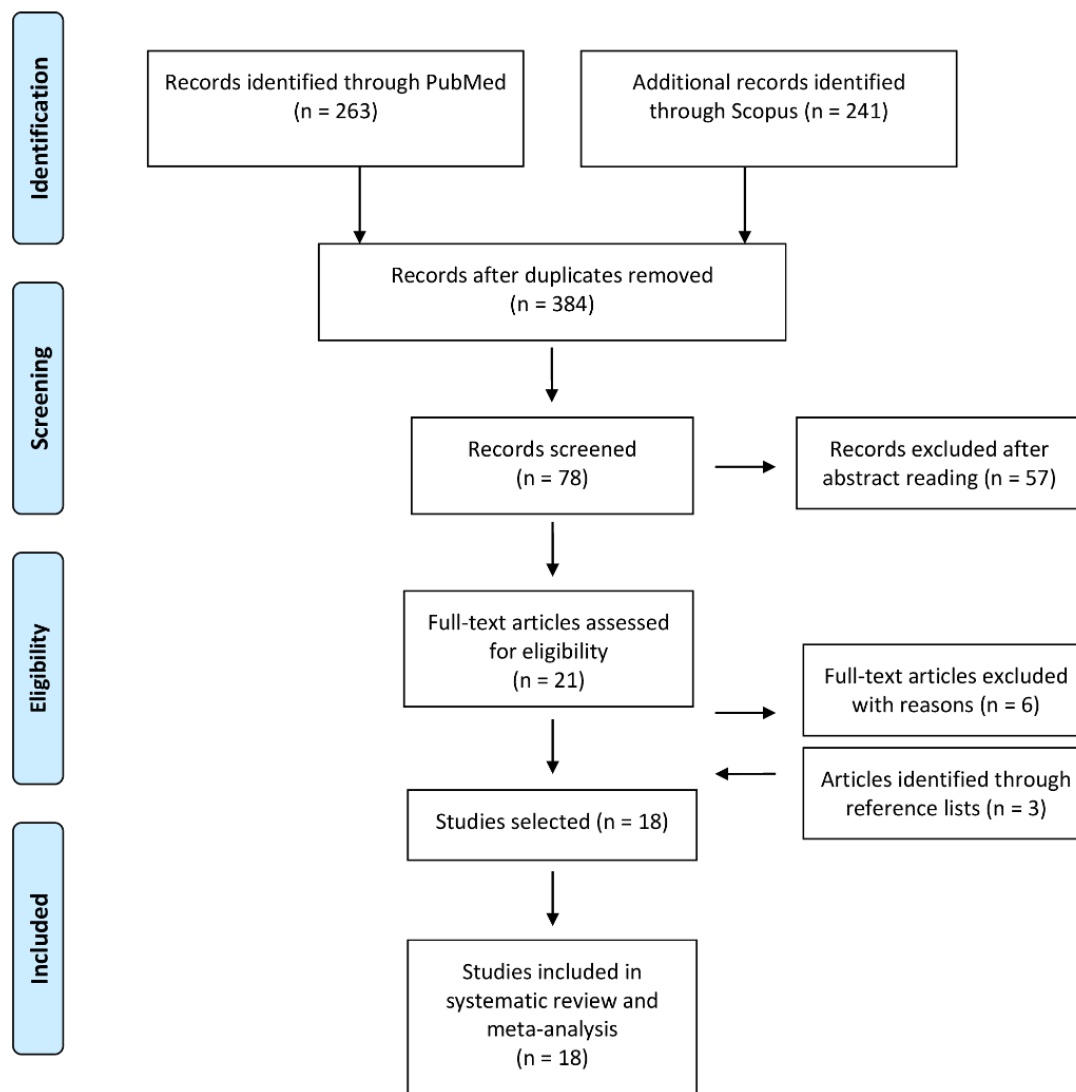


Figure 1. PRISMA flow diagram.

Table 1. Data extraction table.

Study (year)	Country /Regions	Design	Sample	ADHD Measure	Main Exposure	Key findings
Pelsser et al. (2009)	Netherlands	RCT	27 children ADHD (3 to 9 years old)	Conners and the ADHD rating scales	Food group: rice, turkey, lamb, vegetables, fruits, margarine, vegetable oil, tea, pear juice and water	In the control group, ADHD scores improved significantly by comparing baseline with the end of the trial, ACS (22.7±4.1 at baseline, 8.5±7.5 at the end), ARS number of ADHD criteria (13.8±2.3 at baseline, 4.1±4.8 at the end), ARS nine items inattention (18.7±4.8 at baseline, 6.5±5.7 at the end), ARS nine items hyperactivity/impulsivity (20.8±2.7 at baseline, 8.7±6.8 at the end), SPI ODD (6.5±1.2 at baseline, 2.9±2.7 at the end), (p<.001).
Wiles et al (2009)	United Kindom	Cohort (ALSPAC)	4000 children without ADHD aged 7 years	SDQ	Dietary intake - FFQ, PCA junk food intake- high-fat processed foods (burgers, coated poultry) and sugars (such as crisps, and chocolate	Children eating in a high junk food diet were associated with increased hyperactivity at age 7 (OR: 1.13; 95% CI: 1.01–1.15).
Kohlboeck et al. (2012)	Germany	Cohort	3361 children without ADHD 11 years old	SDQ	Food intake - (1) Dairy and dairy products (milk, cheese, yogurt), (2) Fats and oils (butter, vegetable oils, margarine), (3) Fruits and vegetables (apples, carrots, mushrooms, nuts and seeds), (4) Confectionery (chocolate, candy, chewing gum), (5) Cereals and cereal products (rice, pasta, breakfast cereals), (6) Bakery wares (bread, rolls, cakes, cookies), (7) Meat and meat products (fresh and processed meat, sausages), (8) Fish and fish products, (9) Eggs and egg products, (10) Beverages (soft and energy drinks, fruit juices/nectars, water-based flavored drinks, tea), (11) Ready-to-eat savories (snacks: crisps), FFQ, Diet quality - Optimized mixed diet (OMD)	After adjustments for (gender, study center, parental education, household income, single-parent family, BMI, physical activity, TV viewing or video/computer game use, total energy in-take) diet quality significantly associated with emotional symptoms (OR adj: 0.89, 95% CI 0.80–0.98) and hyperactivity/ inattention (OR adj: 0.92, 95% CI 0.82–1.03). "Meat and meat products" intake were associated with ADHD (OR: 1.17; 95% CI: 1.01–1.35). Weak associations were found with decreased consumption of "Fruits and vegetables" regarding hyperactivity/inattention (OR: 0.87; 95% CI: 0.72–1.02).
Khalife et al. (2014)	Finland	Cohort	8,954 children without ADHD	SWAN	BMI, physical activity, binge eating	From 8 to 16 years measurements showed significant longitudinal associations regarding inattention-hyperactivity symptoms and BMI (p < .001) inattention-hyperactivity symptoms and physical activity (p = 0.02), and physical activity and inattention symptoms

						(p =0.005). The study reports significant correlations between the onset of ADHD in the early years and physical inactivity in the following years. (OR = 1.30, 95% CI = 1.01–1.67) and reduced physical activity at 8 years and inattention at 16 years (OR = 1.53, 95% CI = 1.15–2.05)
Ptacek et al. (2014)	Czech Republic	Case-control	100 boys 6-10 years with mixed type ADHD and 100 aged-matched healthy male control subjects	Conner's scale version 3 according to DSM-IV	Eating habits—Breakfast, snack, lunch, dinner, associated lifestyles	ADHD children: Differences in eating habits such as: “the number of daily meals”; “structure of food”; “beverage intake”, between ADHD children and controls. Subjects consume significant higher portions of sweetened beverages (p<0.003) and some eat fruits vegetables once a week (p<0.003)
Woo et al. (2014)	Korea	Case-control	96 students with ADHD and 96 healthy controls, 7–12 years old	Clinical diagnosis based on DSM-IV	Dietary patterns-24h recall- PCA, Traditional Seaweed-egg, Traditional-healthy	Traditional-healthy diet showed to be protective on ADHD comparing the higher to lower consumption (T3 vs T1) (OR:0.32; 95% CI: 0.13–0.77). Snack consumption had an increased risk for ADHD (OR: 2.93; 95% CI:1.22–7.05)
Ghanizadeh & Haddad (2015)	Iran	RCT	106 children and adolescents with ADHD	K-SADS diagnostic tool based on DSM-IV	Dietary intake—FFQ, fruits, vegetables, whole grains, and dairy, sugar, soft drinks, commercially produced fruit juices, and sauces	In both groups with ADHD, (Treatment: methylphenidate plus dietary recommendations, Control: only methylphenidate), inattentiveness scores and hyperactive/impulsivity scores were reduced in comparison to baseline. Significant differences were found between the groups in both mean dietary change scores. For favorite diet: Treatment group from [(25.7±4.6) at baseline, to (28.3±4.4) at the end] and Control group: [(24.8±5.5) at baseline, to (25±5.1) at the end], (p < 0.001). For unfavorite diet: Treatment group from [(22.7±4.7) at baseline, to (16.2±5.0) at the end] and Control group [(23.2±4.5) at baseline, to (21.9±5.9) at the end], (p < 0.001).
Wu, Ohinmaa, Veugelers (2016)	New Scotland - Canada	Cohort	4875 students without ADHD 10-11 years old	Clinical diagnosis based on ICD-9 or ICD-10	Diet Quality Index- DQI-I, physical activity, sedentary behaviors— YAQ	Participants with highest diet scores, had lower number of contacts with a healthcare provider for ADHD (IRR = 0.51, 95% CI: 0.35, 0.75), compared to participants with lower diet scores. Students who reported less physical activity had an increased risk of ADHD
Yu et al. (2016)	Taiwan	Case-control	173 children with ADHD, 159 without ADHD 4-15 years old	Clinical diagnosis based on DSM-IV-TR	Dietary Habits, Consumption of Sugar Sweetened Beverages	“Sugar Sweetened Beverages” consumption showed a dose-response relationship with ADHD. After adjustments were made, children with moderate consumption 1 to 6 servings/week [1.36 (0.61–3.05)] and high consumption ≥7 servings/week of SSB's, had an increased risk of having ADHD, compared with those who did not consume SSBs (p = 0.02)
Zhou et al. (2016)	China	Case-control	ADHD (n= 296) and non-ADHD	Clinical diagnosis based on	Dietary intake—FFQ- factor analysis, Vegetable-Fruit, Fish-White meat, Gain-Bean,	After adjustments, higher consumption of “Fish-white meat” (OR, 0.44; 95% CI, 0.27–0.73; p trend = 0.006) and “Mineral-protein” (OR, 0.47; 95% CI, 0.32–0.71; p trend = 0.001) found to be

			(n= 296) aged 6–14 years old	ICD-10 and DSM-IV	Fast food- Sweet	protective on ADHD
Ríos- Hernández et al. (2017)	Spain	Case- control	60 children with ADHD and 60 controls aged 6 to 16 years	Clinical diagnosis based on DSM-IV	Dietary intake—FFQ-FA Mediterranean Diet (healthy and balanced diet)	Lower adherence to a Mediterranean diet was associated with ADHD diagnosis (OR: 7.07; 95% CI: 2.65-18.84; RR: 2.80; 95% CI: 1.54-5.25)
Chou et al. (2018)	Taiwan	Case- control	42 patients with ADHD (mean age= 8.1) and 36 healthy control children (mean age=9.8)	Clinical diagnosis ADHD-RS based on DSM-IV	Dietary patterns established a priori by FFQ, Grains, Refined grains, Meat (including seafood), Vegetable, Fruit, Dairy Oil, Nuts/seeds/legumes	Refined grains consumption was higher among ADHD children compared to controls (0.35±0.55 vs 0.10±0.23, per unit) (p= 0.026), dairy consumption lower (0.95±0.76 vs 1.27±0.79, per unit) as well as lower intake of calcium (0.59±0.25 vs 0.67±0.25, per grams) (p= 0.013) and vitamin B-2 (1.47±0.46 vs 1.64±0.44, per mg) (p= 0.024)
San Mauro Martín et al. (2018)	Spain	Cross- sectional	89 children and adolescents (41 ADHD, 48 controls)	Clinical diagnosis based on DSM-IV	Nutritional status — KIDMED, Physical activity— IPAQ, sleep quality, quality of life— SF-36	Statistically significant differences were observed between the groups on KIDMED scores, for ADHD group (6.4±2.7), for controls (7.9±2.03), (p=0.004). Sleep scores were significantly different between groups (p=0.031) and especially when analyzing sleep variables from Monday to Friday (p=0.009)
Weissenberger et al. (2018)	Czech Republic	Case- control	1012 adults aged 18–60 years	ASRS diagnostic tool	Diet, exercise routines, physical activity, meal frequency, sweets and sugar intake, sleepiness during the day, sleeping habits —ASRS	Adults with higher ADHD scores were more likely to have a poor diet, poor sleep and an overall unhealthy lifestyle with (odds ratio = 1.21). A positive correlation was found with higher ADHD symptoms and sleepiness during the day (OR= 0.46), or sleep quality (0.73). Adults with higher ADHD levels / symptoms were less likely to eat fruits and vegetables (odds ratio = 1.29) and more frequent snack on sweets (odds ratio = 1.37)
Del-Ponte et al. (2019)	Brazil	Cohort	2924 children 6 years old without ADHD	DAWBA diagnostic tool based on DSM and ICD-10	Dietary intake—FFQ, Consumption of sweets, cake, jam, sodas, SSB's, sweet cookies	At 6 years, significant differences were found between the mean sucrose intake in children with ADHD [130.81 (73.37) grams per day], and without ADHD [108.45 (68.49) grams per day] (p = 0.003). At 11 years of age, the mean intake in children with ADHD was [186.68 (183.11)] grams per day and without ADHD [147.77 (135.02)] grams per day (p < 0.001). Among ADHD cases, most consumed sucrose sources were sugar drinks (22.2%), additional sugar (18.9%), sodas (17.2%) and cookies (11.2%).
Wang et al. (2019)	Taiwan	Case- control	216 children with ADHD and 216 age-, height- and gender- matched controls	CTRS and WWPAS diagnostic tools based on DSM-IV	Dietary intake—FFQ, PCA Dietary factors: "Nutrient- Poor foods", "Vegetable- Fruit", "Flesh foods" (eat, poultry and fish)."Soy milk- Egg" (soy milk and eggs),, SEM	ADHD children had higher intake of "Nutrient-Poor foods" (fried foods, ice cream, high-fat snacks, instant noodle, sugar drinks, shaved, ice desserts, candy and chocolate). Results suggest that nutrient-poor diet can contribute to the ADHD development. Lower nutrient poor consumption may reduce risk of ADHD (OR: 0.46).

Holton & Nigg (2020)	USA	Cross-sectional	184 children with ADHD, 104 healthy controls	Clinical diagnosis based on DSM-IV pr DSM-5	Water intake, SSB consumption, use of multivitamins / supplements, reading, screen time, physical activity, sleep, Multidimensional Anxiety Scale	Children with ADHD were almost twice as likely to have less healthy behaviors (OR: 1.95; 95% CI: 1.16, 3.30), (p=0.01)
Hong et al. (2020)	USA	Case-control	55 children with ADHD, 255 healthy controls	Self-reported ADHD diagnosis	Dietary patterns—FFQ, Physical activity—CLASS, Sleep quality— CSHQ, SEM	Results show that problems with sleep were significantly explained directly by an ADHD diagnosis (p < 0.01), diet (p < 0.01) and physical activity (p < 0.01). Examining inner mediation paths, path of “Childhood ADHD -> Physical activity -> Diet -> Sleep problems” was slightly important (β= 0.007, p= 0.09). Path of “Diet -> Physical activity -> Sleep problems” path, was also significant (β= 0.04, p< 0.05)

DSM: Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; SDQ: Strengths and Difficulties Questionnaire; CTRS: Chinese Version of the Conners Teacher Rating Scale; WWPAS: Werry-Weiss-Peters Activity Scale; SWAN: Strengths and Weaknesses of ADHD symptoms and Normal Behavior; ASRS: Adult ADHD Self-Report Scale; FFQ: Food Frequency Questionnaire; KIDMED; Mediterranean Diet Quality Index; IPAQ: International Physical Activity Questionnaire; CLASS: Children’s Leisure Activities Study Survey-Parent Questionnaire; CSHQ: Children’s Sleep Habits Questionnaire; DASS: Depression Anxiety Stress Scale; DQI-I: Diet Quality Index; PCA: Principal Component Analysis; FA: Factor Analysis; SEM: Structural Equation Model; SF-36: Short Form Health Survey

Randomized Control studies

The first study was performed by Pelsser et al. (2009), evaluating 27 children aged 4 to 8 years old with DSM-IV diagnosis of ADHD. The outcome, ADHD, was assessed using the Abbreviated ten-item Conners Scale (ACS), ADHD Rating Scale (ARS), and oppositional defiant disorder was measured by Structured Psychiatric Interviews (SPI). This study aimed to investigate the effect of a restricted diet on ADHD symptoms. A list of foods was given for the experimental group consisting of rice, turkey, lamb, vegetables, fruits, margarine, vegetable oil, tea, pear juice, and water. Children in the control group were following a flexible diet. In the experimental group, ADHD scores improved significantly by comparing baseline with the end of the trial, ACS (22.7±4.1 at baseline, 8.5±7.5 at the end), ARS number of ADHD criteria (13.8±2.3 at baseline, 4.1±4.8 at the end), ARS nine items inattention (18.7±4.8 at baseline, 6.5±5.7 at the end), ARS nine items hyperactivity/impulsivity (20.8±2.7 at baseline, 8.7±6.8 at the end), SPI ODD (6.5±1.2 at baseline, 2.9±2.7 at the end), (p<.001). The controls that followed a diet of their own, freely chosen diet, showed no improvement and even had worse ADHD scores by comparing baseline with the end of the trial. Ghanizadeh and Haddad (2015), conducted a 21-day, double-blind, placebo-controlled trial at a clinic in Iran, with 106 children with a DSM-IV diagnosis of ADHD. ADHD outcome was evaluated through the ADHD checklist, containing a total of 18 items for attention, hyperactivity/impulsivity. The food intake was measured using FFQ. “Favored food” and “Unfavored” food lists were given containing dairy, homemade fruit juices, vegetables, and low-fat meat, sugar, soft drinks, commercially produced fruit juices, and sauces. The distribution of the

participants was randomized using a random number generator. Only one group received dietary recommendations (favored food, unfavored food) and both groups received methylphenidate. In both groups, inattentiveness scores and hyperactive/impulsivity scores were reduced in comparison to baseline. Significant differences were found between the groups in both mean dietary change scores. For favored diet: Treatment group from [(25.7±4.6) at baseline, to (28.3±4.4) at the end] and Control group: [(24.8±5.5) at baseline, to (25±5.1) at the end], (p < 0.001). For unfavored diet: Treatment group from [(22.7±4.7) at baseline, to (16.2±5.0) at the end] and Control group [(23.2±4.5) at baseline, to (21.9±5.9) at the end], (p < 0.001).

Risk of bias assessment

The studies performed well overall in assessing the risk of bias as shown in the following figures. (Figure 2, Figure 3). Both of the studies had a low-risk assessment for random sequence generation, allocation concealment, outcome data as well as selective reporting.

Pelsser et al. (2009), was evaluated as high risk for performance bias because participants (parents and teachers) who completed the questionnaires were not blinded, and they had to monitor children’s intake. Ghanizadeh & Haddad (2015) was graded as low-risk of bias for double-blinding.

Both of the studies were assessed as unclear for detection bias as it was insufficiently described.

Ghanizadeh & Haddad had complete information and no attrition bias, while Pelsser et al., received unclear risk as incomplete information was given. All studies received a low-risk assessment for reporting, as all predefined results were reported.

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Ghanizadeh, A., & Haddad, B. (2015)						
Pelsser, L. et al (2008)						

Key

- Low risk
- Unclear risk
- High risk

Figure 2. Individual risk of bias.

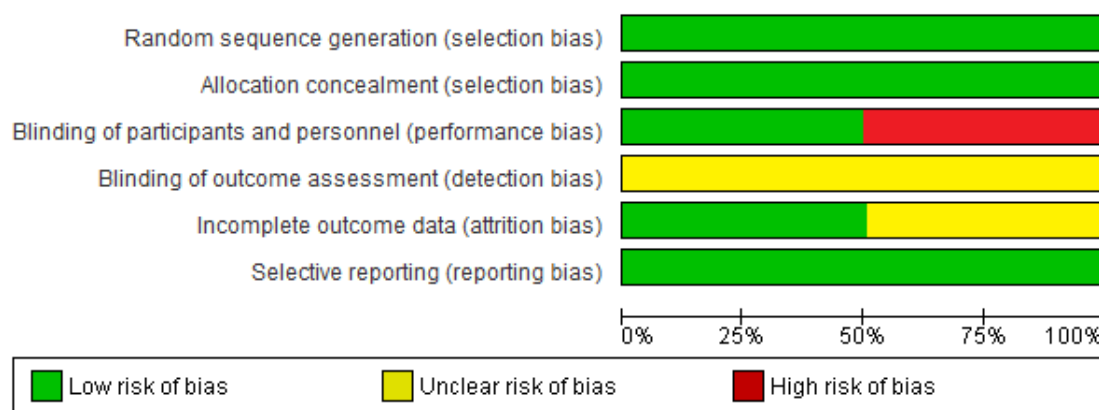


Figure 3. Risk of bias synopsis.

Case-control studies

A case-control study was carried out by Ptacek et al. (2014) in the Czech Republic, with 100 boys aged 6-10 years presenting ADHD diagnosis by DSM-IV, and 100 boys without ADHD matches by age. Eating habits and lifestyle phenomena were examined, such as breakfast, snacks, lunch, dinner, and related lifestyles. The current study indicates significant differences between groups regarding meal frequency and notes that ADHD boys tend to skip breakfast, lunch and dinner more often than controls ($p < 0.005$). Moreover, children with ADHD tend to consume significantly higher portions of sweetened beverages ($p < 0.003$), eat fruits vegetables only once a week ($p < 0.003$), and eat meals more than 5 times a day ($p < 0.001$).

Woo et al. (2014), conducted a case-control study in Korea, selecting 96 students with ADHD from Dong-A and Inje university hospitals, with a clinical diagnosis based on the DSM-IV criteria. A total of 96 controls, matched by age and gender were also selected. Dietary intake was evaluated in three consecutive 24-hour diet interviews (HR) and 32 predetermined food groups were tested on PCA. Researchers also measured omega-3 fatty acids intake by estimating overall EPA's and DHA's. PCA identified four groups: (1) "traditional"; (2) "traditional-healthy"; (3) "seaweed-egg; and (4) "snack". These groups consisted mainly of (1) spices, vegetables, tofu/soy, mushrooms; (2) kimchi, grains, bonfish, low intakes of beverages and fast food; (3) seaweeds, fats/oils, eggs; (4) high snack intake, low intake of noodles and processed meat. "Traditional" diet, linked with high total fatty acid intake. Two groups were associated with high intakes of polyunsaturated fatty acids and omega-3 fatty acids: "Seaweed-egg" and "traditional-healthy". Third tertile (higher consumption) compared to the reference, the "traditional-healthy" diet was protective and was associated with lower odds of ADHD pathogenesis (OR: 0.31; 95% CI: 0.12–0.79). On the other hand, the "snack" diet when comparing third tertile (higher consumption) to the lower tertiles (lower consumption), had an increased risk of

ADHD (OR: 2.93; 95% CI: 1.22–7.05). The rest of the diet groups were not associated with ADHD.

Yu et al. (2016), selected a total of 173 children aged 4-15 years with ADHD, as identified by board-certificated clinicians following the DSM-IV-TR criteria. 159 age-matched controls were randomly selected who visited either of the hospitals (Taipei Veterans General Hospital and Taipei City Hospital) for reasons not related to ADHD during the same study period. The outcome, ADHD, was assessed through questionnaires based on risk factors of ADHD. Current work explored the dietary habits of the participants through questionnaires. Sugar-sweetened beverages (SSB) consumption was calculated by multiplying portions of each type of SSB. Children's daily caloric intake was calculated using the Taiwan Food and Drug Administration (TFDA) Nutrients Database. It was found that ADHD subjects had a significantly higher intake of SSB (6.96 ± 9.27 , servings per week) when healthy controls had only (3.10 ± 5.08 , servings per week) ($p < 0.01$). The intake of vegetables and fruits was significantly higher in children without ADHD, compared to ADHD cases ($p < 0.01$, $p = 0.02$). ADHD children consumed more calories compared to controls (2061.1 ± 689.7 vs. 1801.6 ± 448.3 , calories per day), ($p < 0.01$, respectively). Energy intake per day was significantly different between these groups, because of SSB consumption (327.2 ± 440.0 vs. 141.4 ± 225.2 , calories per day), ($p < 0.01$, respectively). Constantly, the ADHD group had a higher intake of sugar than the control group (296.7 ± 419.5 vs. 117.3 ± 198.1 , grams per day), ($p < 0.01$, respectively). Therefore, the risk of ADHD between SSB consumption increased by 48% (OR = 1.48, 95% CI: 0.79–2.78) for children consuming 1 to 6 servings per week, with 4.66 more odds (95% CI: 2.15–10.09) for children consuming ≥ 7 servings/week. After adjusting covariates, the results remained significant (OR = 1.36, 95% CI: 0.61-3.05) for children consuming 1 to 6 servings per week and the odds ratio showed four times more chances of ADHD indication than the reference group (95% (OR: 3.76, 95% CI: 1.31–

10.80, $p = 0.02$) for children who consumed 7 or more SBB's servings/week.

Zhou et al (2016), evaluated 592 children in total, aged 6 to 14 years, that were recruited from pediatric clinics in China. Children with ADHD, were diagnosed with DSM-IV-R criteria for ADHD. The control cases were randomly selected from clinics where children were diagnosed with ADHD. Diet was assessed through Food Frequency Questionnaire (FFQ). Factor analysis created four primary diet groups: 1) "Vegetable-fruit", (2) "Fish-white meat", (3) "Grain bean", and (4) "Fast food-sweet" mainly consisted of sweets, snacks processed food. The analysis showed that there was a dose-dependent association between the risk of ADHD and the "Fish-white meat" intake. After adjustments, higher consumption of "Fish-white meat" (OR, 0.44; 95% CI, 0.27–0.73; p trend = 0.006) found to be protective on ADHD. No other associations were observed for any other dietary group.

Ríos-Hernández et al. (2017), evaluated a total of 120 children and adolescents, aged 6-16 years, that were recruited at an ADHD clinic in Spain. The control cases were either classmates of the ADHD patients or patients from other hospital services. The researchers' objective was to measure the effect of the Mediterranean diet on ADHD. The ADHD diagnosis was made by clinicians following the DSM-IV-R criteria. Nutrient intake and diet were measured using FFQ. Using the KIDMED test, the measurements could calculate scores on adherence to the Mediterranean diet. Physical activity rates were also calculated through Actigraph, Acti Sleep, on their non-dominant wrist for 7 days straight. The study findings suggest that there is a higher risk of ADHD prevalence associated with lower adherence to the Mediterranean diet (OR: 7.07; 95% CI: 2.65–18.84). Between groups, BMI rates were significantly different [(ADHD 19.6 (4.3) vs controls 18 (3.3)].

Chou et al. (2018), recruited 42 ADHD children and 36 healthy controls, that were treated in a hospital and child psychiatry in Taiwan. ADHD diagnosis was assessed using the DSM-IV-TR criteria. Dietary intake was evaluated a priori through FFQ. Eight food groups were created for research: (1) "Grains", (2) "Refined grains", (3) "Meat and seafood", (4) "Vegetables", (5) "Fruits", (6) "Dairy", (7) "Oil", and (8) "Nuts/seeds/legumes". Among the groups, children with ADHD had higher consumption of "Refined Grains" (0.35 ± 0.55 vs 0.10 ± 0.23 , per unit) ($p = 0.026$), lower dairy consumption (0.95 ± 0.76 vs 1.27 ± 0.79 , per unit) as well as lower calcium intake (0.59 ± 0.25 vs 0.67 ± 0.25 , per grams) ($p = 0.013$) and vitamin B-2 (1.47 ± 0.46 vs 1.64 ± 0.44 , per mg) ($p = 0.024$). Furthermore, dairy intake was positively correlated with calcium ($r = 0.896$, $p < 0.001$) and vitamin B-2 ($r = 0.878$, $p < 0.001$). These findings were also significantly correlated with ADHD clinical symptoms.

Weissenberger et al. (2018), conducted a case-control study with 1012 adults (507 men and 505 women) aged 18-16 years, investigating lifestyle and general ADHD symptoms in the Czech Republic. The outcome, ADHD, was assessed through the Adult Self-Report Scale of ADHD. Lifestyle factors were examined through a lifestyle questionnaire. Adults with higher ADHD scores were more likely to have a poor diet, poor sleep, and an overall unhealthy lifestyle (odds ratio = 1.21). More specifically, a positive correlation was found with higher ADHD symptoms when asked if they happen to be fatigued and sleepy during the day (OR= 0.46), or about their sleep quality (0.73). In addition, adults with higher ADHD levels/symptoms were less likely to eat fruits and vegetables (odds ratio = 1.29) and more frequent snack on sweets (odds ratio = 1.37).

A case-control study in Taiwan by Wang et al., (2017), with 216 age-, height- and gender-matched pairs of children (mean age= 9.2), evaluated and investigated the relationship between ADHD diet and nutritional biochemistry profiles. Both cases and controls were selected from schools in Taipei. The ADHD diagnoses were clinical, based on the Diagnostic and Statistical Manual, Fourth Edition (DSM-IV). Diet was assessed using FFQ. Moreover, SEM analysis was used to find the relationship and strength between food frequency, nutritional biochemistry indicators, and ADHD. Four dietary factors have been generated by PCA Dietary factors: (1) "Nutrient-Poor foods", (2) "Vegetable-Fruit", (3) "Flesh foods" (eat, poultry and fish), (4) "Soy milk-Egg" (soy milk and eggs). Compared to controls, a much higher average frequency of consumption of poor nutrient foods, characterized mainly by fried foods, ice cream, high-fat snacks, instant noodle, sweets sugar drinks, was observed in children with ADHD, while a lower average frequency of consumption of the other dietary factors was observed. In the SEM model, after adjusting for potential confounders, all factors were still significantly associated with ADHD. A nutrient-poor diet was associated with ADHD development. Likewise, lower nutrient-poor consumption may reduce the risk of ADHD (OR: 0.46).

Hong et al. (2020) conducted an online case-control study, evaluating 54 children with ADHD and 255 normally developing children, aged 9 years. The study aimed to investigate the relationship between diet, physical activity, screen time, and sleep quality with ADHD. Diet was assessed by FFQ. Physical activity scores were assessed with the CLASS questionnaire. Sleep quality was scored with CSHQ. Possible relationships among lifestyle factors were examined with SEM analysis. Only CSHQ scores, which were higher (7.06, SE= 0.22), were associated with ADHD incidence ($p = 0.001$). Current work used SEM analysis to explain sleep and ADHD and created 4 model paths: (1) "Children ADHD -> Diet -> Physical activity and screen time -> Sleep"; (2) "Children ADHD -> Diet and screen time -> Physical

activity -> Sleep”; (3) “Children ADHD -> Physical activity and [screen time] -> Diet -> Sleep”; (4) “Children ADHD -> [Physical activity] and screen time -> Diet -> Sleep” (same as model 3 but following different route). Diet was examined with 3 sub-factors: scores of fat, fiber, and vegetables. The best scores between models were achieved in Model 2, having the smallest difference in the model variance (33.834). Results show that problems with sleep were significantly explained directly by an ADHD diagnosis ($p < 0.01$), diet ($p < 0.01$) and physical activity ($p < 0.01$). Examining inner mediation paths, path of “Childhood ADHD -> Physical activity -> Diet -> Sleep problems” was slightly important ($\beta = 0.007$, $p = 0.09$). Path of “Diet -> Physical activity -> Sleep problems” path, was also significant ($\beta = 0.04$, $p < 0.05$).

Cohort and Cross-sectional studies

A British cohort was carried out by Wiles et al. [29], with data from Avon Longitudinal Study of Parents and Children (ALSPAC). The study included 4000 children and investigated the effect of diet on behavior problems. Measurements were held once at 4.5 years of age and the age of 7 years. Dietary data were collected by the FFQ, given to mothers for completion. PCA created a “Junk food” referral that was characterized by high-fat processed foods (burgers, coated poultry) and sugars (such as crisps, and chocolate). The outcome of behavior disorders was explored using the Strengths and Difficulties Questionnaire (SDQ). Children eating in a high junk food diet were associated with increased hyperactivity at age 7 (OR: 1.13; 95% CI: 1.01–1.15), even after adjustments for confounders such as (sex of the child, maternal smoking, maternal age at birth, number of siblings, socioeconomic status, birth weight, gestational age, maternal depression and anxiety (at 33 months).

In a German birth cohort Kohlboeck et al. (2012), analyzed 3361 children up to the age of 11, investigating the impact of diet specifically on symptoms of hyperactivity and inattention. The outcome of hyperactivity/inattention was assessed using SDQ. Food lists were established using FFQ on food intake: 1) Dairy and dairy products (2) Fats and, (3) Fruits and vegetables, (4) Confectionery, (5) Cereals and cereal products, (6) Bakery wares, (7) Meat and meat products, (8) Fish and fish products, (9) Eggs and egg products, (10) Beverages (11) Ready-to-eat savories. Diet quality was assessed using OM, from the FFQ scores. After adjustments for cofounders, diet quality was significantly associated with emotional symptoms (OR: 0.89, 95% CI 0.80–0.98) and hyperactivity/inattention (OR: 0.92, 95% CI 0.82–1.03). Intake of “Meat and meat products” consisted of fresh, processed meat, and sausages, was associated with ADHD (OR: 1.17; 95% CI: 1.01–1.35). Weak associations were found with decreased consumption of “Fruits and vegetables” regarding hyperactivity/inattention (OR: 0.87; 95% CI: 0.72–1.02).

Khalife et al. (2014), with data from the Northern Finland Birth Cohort, including 8954 participants, investigated whether binge eating and physical inactivity support the possible association of ADHD symptoms - obesity. The study followed participants approximately for 8 years. At 7 to 8 years, ADHD symptoms were reported by teachers. Physical activity and BMI were reported by parents. At 16 years, ADHD was measured using the SWAN tool based on DSM-IV while participants reported physical activity and binge eating. The baseline analysis, at 8 years, did not show any significant associations between ADHD and obesity or physical activity. From 8 to 16 years measurements, there were significant longitudinal associations regarding inattention-hyperactivity symptoms and BMI ($p < .001$), inattention-hyperactivity symptoms and physical activity (MET) ($p = 0.02$), and physical activity and inattention symptoms ($p = 0.005$). The study reports significant correlations between the onset of ADHD in the early years and physical inactivity in the following years. (OR = 1.30, 95% CI = 1.01–1.67) and reduced physical activity at 8 years and inattention at 16 years (OR = 1.53, 95% CI = 1.15–2.05).

Wu and Veugelers (2016), analyzed 4875 students without ADHD, at age 10 until they turn 18, in a cohort study in Nova Scotia, Canada. Nutrition information was collected from YAQ and Canadian Nutrient records. DQI-I tool was used to provide diet quality scores (higher scores equate to better diet quality). Physical activity was assessed through the CLASS tool. To assess the outcome, participants were considered to have ADHD, if they had one more diagnosis of ICD-9-CM or ICD-10-CM. Patients with poorer diet quality reported less physical activity and had an increased risk of ADHD in the following years. Normal weight children had increased odds to be diagnosed with ADHD relative to obese children. Following variable adjustments, participants with the highest diet scores, had a lower number of contacts with a healthcare provider for ADHD (IRR = 0.51, 95% CI: 0.35, 0.75), compared to participants with lower diet scores. Moreover, students who were physically active 1 to 3 times a week, had a fewer number of contacts with a healthcare provider for ADHD than children who did not engage in sports or physical activity with a coach. (IRR = 0.72, 95% CI: 0.52, 0.99).

In a Brazilian birth cohort, Del-Ponte et al. (2019), evaluated the effect of sugar consumption on ADHD. A total of 2924 children were selected at 6 years of age without ADHD. Dietary intake was measured at baseline and the end of the study (after 5 years of study) by FFQ. Consumption of sweets, cake, jam, sodas, SSB’s, sweet cookies, etc. measured to calculate sucrose intake. The instrument to evaluate ADHD was the Development and Well-Being Assessment (DAWBA) at 6 and 11 years of age, based on DSM and ICD-10 criteria. At 6 years mean sucrose intake in children with ADHD was [130.81 (73.37) grams/ day] versus children without ADHD [108.45 (68.49) grams/ day], ($p =$

0.003). At 11 years of age, mean consumption was higher in both groups, children with ADHD: 186.68 (183.11) grams/day and children without ADHD: 147.77 (135.02) grams/day, respectively ($p < 0.001$). At the age of 6 years, "artificially flavored juices" had the largest contribution (29.09 ± 32.84) (22.2%) to sucrose intake in children with ADHD. At the age of 11 years, children with ADHD presented higher consumption of sweet cookies (41.93 ± 59.19) (22.5%), artificial-flavored juices (32.69 ± 38.65) (17.5%), and additional sugar (27.12 ± 39.17) (14.5%). At age 6, ADHD prevalence among boys increased as sucrose consumption increased (from the first tertile to the third tertile) and was statistically significant (OR: 5.8, 95% CI: 3.9-7.8). Following adjustments for maternal and child characteristics, the correlation remained significant ($p = 0.02$). The prevalence in the first tertile was [T1: 1.8 (0.7-2.9)], in the second tertile [T2: 2.8 (1.5-4.2)] and the third [T3: 5.8 (3.9-7.8)]. In girls, there was no association even after adjustments ($p = 0.88$). Adjusted analyses at the age of 11 years found no correlations with the incidence of ADHD.

In Spain, a cross-sectional study held by San Mauro Martín et al. (2018), with 89 children and adolescents, of whom 41 were ADHD cases (mean age = 9.5) and 48 healthy controls (mean age = 10.4). ADHD cases were recruited only if they were diagnosed with ADHD, according to the DSM-IV, Text Revision. Adherence to the Mediterranean diet and nutritional status was assessed using the KIDMED index. Physical activity was evaluated through IPAQ. Sleep quality was measured by summing total hours of sleep per week. SF-36 was used to assess quality-of-life scores. Sleep measures showed statistically significant differences between groups ($p = 0.031$) and separately, from Monday to Friday with fewer hours of sleep for ADHD children (8.9 ± 1.4 versus 9.7 ± 1.05) ($p = 0.009$). The KIDMED scores showed statistically significant differences between groups. ADHD cases had a lower mean score (6.4 ± 2.7) while controls had (7.9 ± 2.03) ($p = 0.004$). Significant differences were found between the consumption of fish, cereals, skipping breakfast, and commercially baked foods ($p < 0.05$).

Holton and Nigg (2020), carried out a cross-sectional study with 104 children with ADHD and 184 typically developing children, aged 7-11 years, recruited from a community observational cohort. The outcome, ADHD, was assessed clinically, using DSM-IV or DSM-5. A lifestyle behavior questionnaire was used to explore habits such as

water consumption; sodas; SSB's /energy drinks; multivitamin use; reading; screen time; physical activity; sleep and hours of sleep/night. Anxiety and mood scores were evaluated. Compared to controls, children with ADHD were more likely to be male (131 out of 184) and to have oppositional behaviors or anxiety ($p < 0.001$). Besides, ADHD cases tended to consume more artificially sweetened juice, spending less time on physical activity than controls do. Sleep difficulties were more consistent in ADHD children than controls (45% vs. 9%) ($p < .0001$). When limiting the analysis to those who are not taking stimulants, results were consistent with 33% ADHD children vs. 9% controls having trouble falling asleep ($p < .0001$). Furthermore, it was found that less frequent consumption of SB's and getting more than 1 hour per day of physical activity were slightly associated with better sleep ($p < .10$).

Aggregate results of diet quality and lifestyle

In this article, we systematically reviewed eighteen studies. Four of them, did not provide sufficient data and thus could not be included in the meta-analysis. The authors conducted three meta-analyses from fourteen studies (eight case-controls, five cohorts, one cross-sectional) to summarize the effect of (1) high-quality diet; (2) poor-quality diet; and (3) the impact of a poor lifestyle on ADHD, for both children and adults. For each meta-analysis, the I-squared test showed a closeness of heterogeneity between the included studies. Therefore, the authors used a random-effects model. For the random-effects model, tau-squared (T) was calculated to describe the distribution of the true effects between the studies.

The pooled analysis showed that a high-quality diet decreases the prevalence of ADHD on children (OR: 0.43, 95% CI: 0.28-0.70) (Figure 4), while a poor-quality diet is associated with an increased risk of ADHD in both children and adults (OR: 2.24, 95% CI: 1.49-3.65) (Figure 5). Also, a poor lifestyle indicates a higher prevalence of ADHD on both children and adults (OR: 1.90, 95% CI: 1.43-2.61) (Figure 6).

Calculations for publication bias assessment could only be done with a sufficient number of studies and that is in our first and second meta-analysis (high-quality diet, poor-quality diet), where symmetry was found (Figure 7,8). Poor lifestyle meta-analysis could not be calculated for publication bias, due to the small number of included studies.

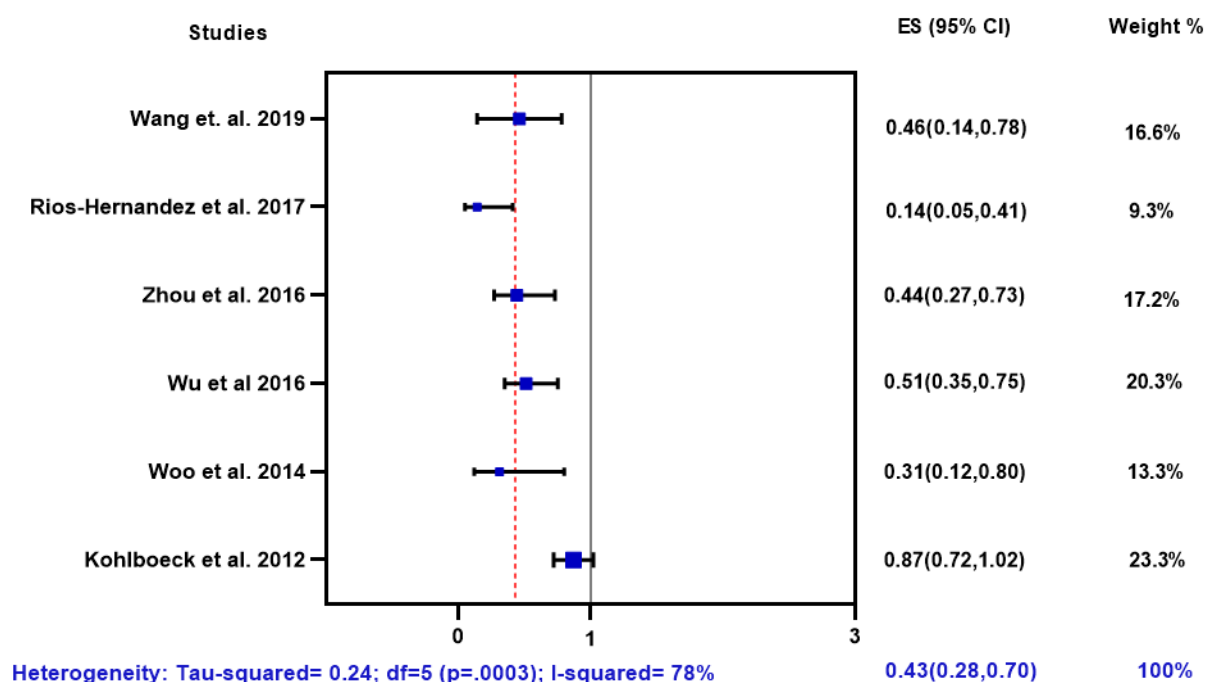


Figure 4. Effect size of high-quality diet and risk of ADHD.

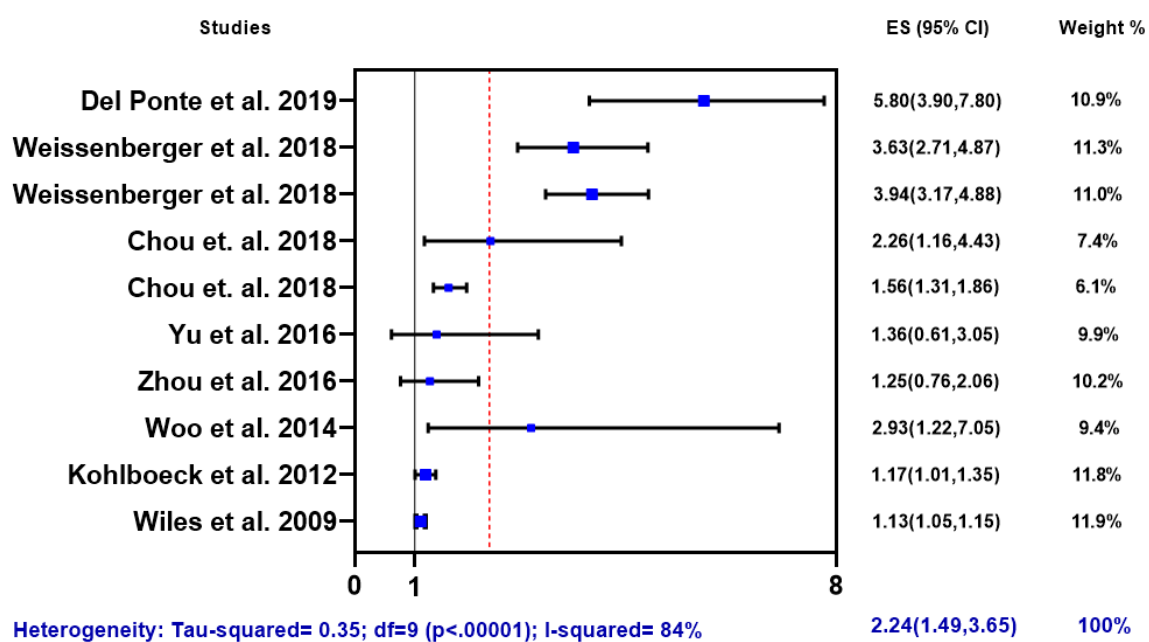


Figure 5. Effect size of poor-quality diet and risk of ADHD.

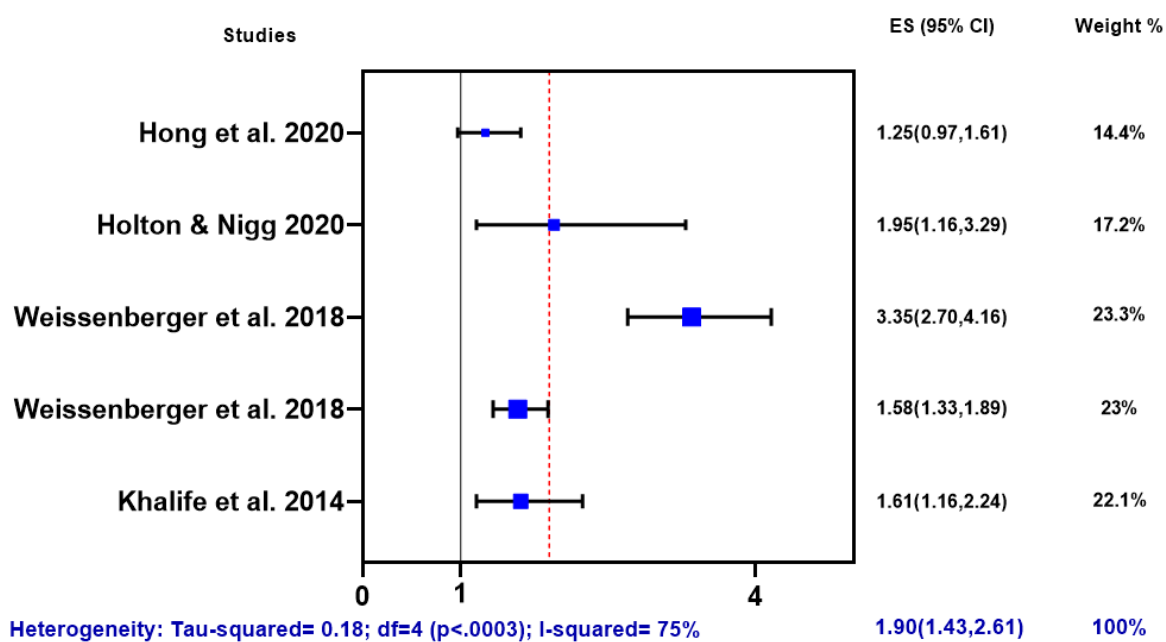


Figure 6. Effect size of poor lifestyle and risk of ADHD.

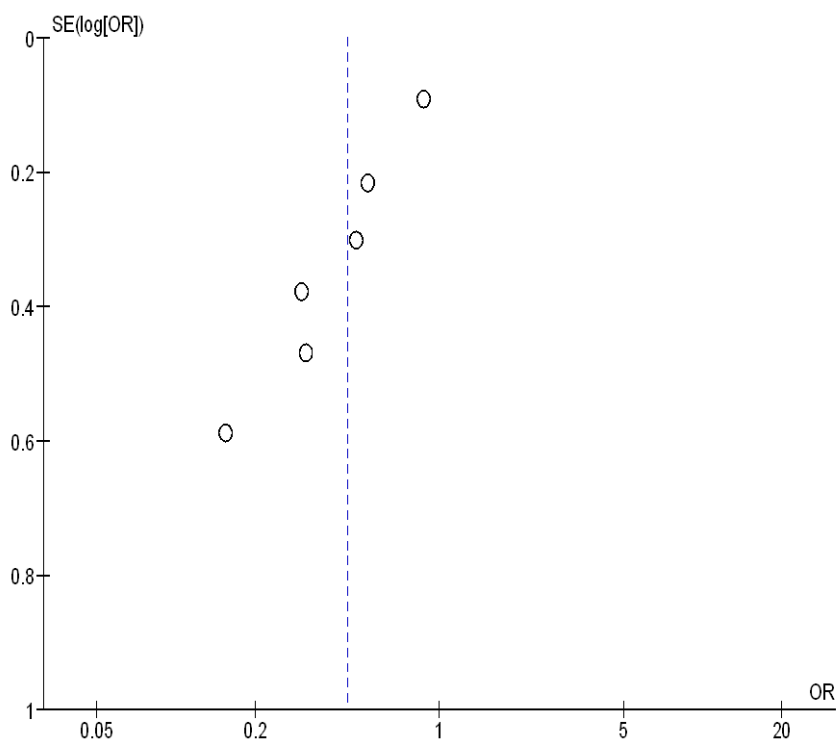


Figure 7. High-quality diet and ADHD's funnel plot.

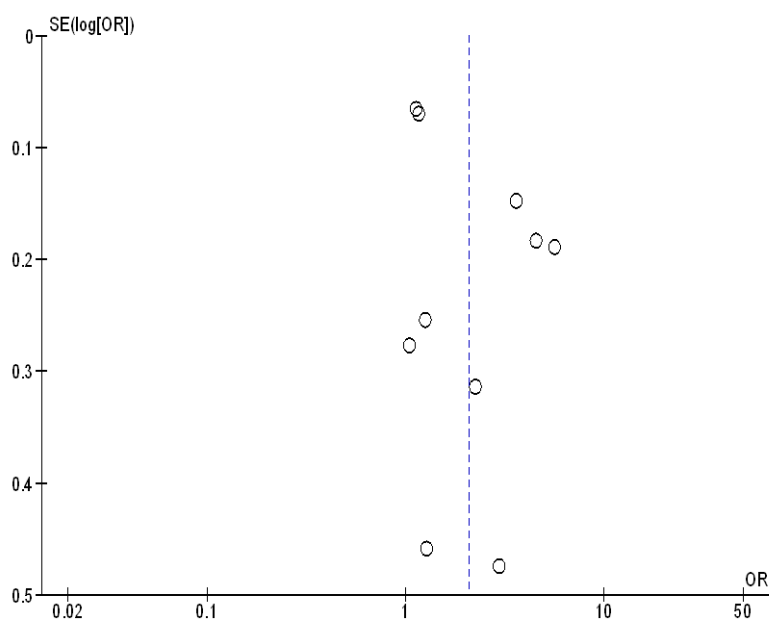


Figure 8. Poor-quality diet and ADHD's funnel plot.

Empirical research and treatment strategies have been the key to new complementary interventions as previous studies have shown an association between diet and lifestyle factors in people with ADHD. However, diet and lifestyle interventions must be carried out thoroughly for each individual, based on region, socioeconomic level, and season. Our findings indicate that diet and lifestyle factors can be associated with ADHD and may even be inversely related. In the reviewed papers we found the most common diet and lifestyle factors that showed an effect on ADHD. In terms of diet quality, consumption of fish, fruits, and vegetables can be protective on ADHD pathogenesis in children. The Mediterranean-style diet is also considered a high-quality diet which includes intake of fruits, fish, intake of fruits, fish, vegetables, and especially lower consumption of red meat and sugars. The literature explains the significance of the Mediterranean diet on cognition and ADHD in adults and children, as it is associated with improvements in cognitive function, working memory, executive function, lower impulsivity, and lower prevalence of ADHD overall (Hardman et al., 2016; Ríos-Hernández et al., 2017; San Mauro Martín et al., 2018; San Mauro Martín et al., 2019). On the other hand, a poor-quality diet, characterized by the consumption of sugars, sweetened beverages, and junk food can be associated with an increased risk of ADHD, for both children and adults. In terms of lifestyle, a poor quality of living characterized by sleeping problems and reduced physical activity can increase the risk of ADHD. The heterogeneity of the studies was high, as our meta-analysis consists of a small number of studies and consists mainly of case-control studies. More randomized controlled trials in this domain are needed to confirm our study findings.

Our systematic review found an important distinction between the number of daily meals, the structure of food and beverage intake is found between men with ADHD and healthy men (Ptacek et al., 2014). Furthermore, higher consumption of artificial sweeteners could potentially contribute to ADHD pathogenesis. Our study findings are consistent with previous studies, showing an association between sugar consumption and sugar-sweetened beverages and ADHD symptoms (Kohlboeck et al., 2013; Marmorstein, 2016). On the other hand, a meta-analysis of clinical trials conducted by Wolraich et al. (1995), found that sugar consumption does not affect ADHD core symptoms of behavior or cognitive performance. Nevertheless, a most recent meta-analysis performed by Farsad-Naeimi et al. (2020), contradicts the findings of Wolraich et al. and concludes that there is a positive relationship between total sugars from sugar-sweetened beverages and ADHD. Poor nutrition in children and adults with ADHD could be a consequence, because some kind of foods and in particular sugar, are activators of the neurotransmitter reward system (Johnson et al., 2011). According to this, studies have shown that children and adults with ADHD had significantly higher body mass ratings (BMI) and obesity rates than those without ADHD, while they also found significant associations between obesity/overweight and ADHD (Cortese et al., 2013; Cortese et al., 2016). A common paradox is that subjects with ADHD are expected to have higher energy (more physical activity rates), meaning more calories to be burned, translating into a calorie deficit. This does not seem to be true, as research findings show that childhood ADHD is connected with physical inactivity in later years and may be responsible for both obesity and behavior problems

(Khalife et al., 2014). The mechanisms that could link the diet quality and multiple lifestyle factors to the etiology of ADHD are not yet fully clarified.

Evidence of the positive impact of nutrients is explained, while there is considerable proof that fatty acids, micronutrients, and minerals play an inhibitory role in ADHD pathogenesis. Children with ADHD have been shown to consume significantly less fish than healthy peers and daily omega-3 polyunsaturated fatty acid intake is estimated to be also significantly lower (Fuentes-Albero et al., 2019). Having said that, two previous systematic reviews found significant effects with omega-3 supplementation in reducing ADHD symptoms (Chang et al., 2018; Abdullah et al., 2019). A meta-analysis of clinical trials carried out by Bloch and Qawasmi (2011), showed that higher doses of 500mg eicosapentaenoic acid (EPA) had a modest effect in the treatment of ADHD. However, Gillies et al. (2012), performed a meta-analysis to compare the efficacy of polyunsaturated fatty acids (PUFAs) with a placebo in the treatment of ADHD symptoms and concluded that most of the data showed little but no benefit with omega-3 and omega-6 supplementation. Subsequently, Sonuga-Barke et al. (2013), concluded that free fatty acid supplementation showed a small but significant effect in reducing ADHD symptoms. Moreover, the supplementation of zinc is found to be important in reducing ADHD symptoms comparing to those receiving a placebo (Akhondzadeh et al., 2004; Bilici et al., 2004).

Lifestyle variability has been extensively examined in the literature on mediating ADHD. Previous findings from randomized-controlled trials suggest that reduced sleep duration can lead to more ADHD and oppositional behavior symptoms in adolescents and children with ADHD and may also affect healthy ones (Gruber et al., 2011; Becker et al., 2019). Moreover, in 2015, a randomized-

controlled trial was conducted by Combs et al., examining the relationship between ADHD and perceived stress in adults, showing that ADHD symptoms are positively associated with stress and executive function problems. Furthermore, a meta-analysis of clinical trials performed by Cerrillo-Urbina et al. (2015), examined the impact of exercise in children with ADHD aged 6 to 18 years, indicating that physical exercise interventions have a moderate to large effect on attention, hyperactivity, impulsivity and related symptoms as stress (Cerrillo-Urbina et al., 2015). Lastly, a randomized controlled trial conducted in New Zealand examined the effect of 36 micronutrients and 3 antioxidants between stress among adults with ADHD. Adults on micronutrients reported less anxiety and stress than control group, showing a benefit of micronutrients for mental health (Rucklidge et al., 2011).

The present study notes that diet quality and lifestyle factors examined, can be inversely related, in that a better diet and lifestyle can influence one another, to reduce ADHD symptoms, while a poorer diet and lifestyle can increase the risk of ADHD (Figure 9). For example, increased physical activity could lead to a healthier diet, a healthier diet could correct sleep problems and better sleep could improve mood disorders and stress. Likewise, reduced physical activity could lead to a poorer diet, a poorer diet could worsen sleep schedule, and a bad sleep schedule can reduce performance and worsen mood disorders. The mechanisms that could help us understand the impact of diet and lifestyle behaviors on ADHD can be multidimensional, with more factors entering this relationship over and over again. The goal is to find the proper path that works for a certain individual, in order to understand the impact of every factor on ADHD.

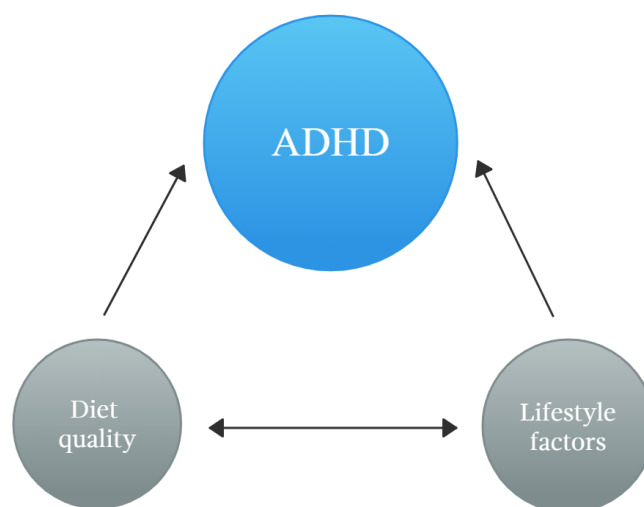


Figure 9. Inverse association between diet quality and lifestyle factors with ADHD.

Current work presents strengths and limitations. This study is limited to its ability to extract data from some of the included studies. Of the eighteen studies systematically reviewed, the authors were able to analyze fourteen of them. Sampling was limited due to the absence of studies in adults with ADHD. Furthermore, there is little evidence to assess the quality of diet or lifestyle behaviors in adult populations and that needs to be considered for future studies in the field. Another limitation is that in some studies the diet quality and lifestyle behaviors of children with ADHD may not be well characterized, because the outcome is often scored by their parents, whereas in one study the ADHD diagnosis was assessed by a single survey question (Hong et al., 2020). Last but not least, the current study is limited to two research databases.

The present study suggests possible weighted assessments of diet quality and lifestyle

Conclusion

To conclude, the present study provides some evidence about the tripartite relationship between diet quality, lifestyle factors, and ADHD, suggesting that a high-quality diet with increased consumption of fruits, vegetables, and fish, may be protective against ADHD in children. On top of that, a poor-quality diet with higher consumption of sugar, sweetened drinks, and junk food, as well as a lifestyle that is characterized by reduced sleep and physical activity can be associated with increased risk of ADHD, for both children and adults.

References

- Abdullah, M., Jowett, B., Whittaker, P. J., & Patterson, L. (2019). The effectiveness of omega-3 supplementation in reducing ADHD associated symptoms in children as measured by the Conners' rating scales: A systematic review of randomized controlled trials. *Journal of psychiatric research*, 110, 64–73. <https://doi.org/10.1016/j.jpsychires.2018.12.002>
- Akhondzadeh, S., Mohammadi, M. R., & Khademi, M. (2004). Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial [SRCTN64132371]. *BMC psychiatry*, 4, 9. <https://doi.org/10.1186/1471-244X-4-9>
- Becker, S. P., Epstein, J. N., Tamm, L., Tilford, A. A., Tischner, C. M., Isaacson, P. A., Simon, J. O., & Beebe, D. W. (2019). Shortened Sleep Duration Causes Sleepiness, Inattention, and Oppositionality in Adolescents With Attention-Deficit/Hyperactivity Disorder: Findings From a Crossover Sleep Restriction/Extension Study. *Journal of the American Academy of Child and Adolescent*
- intervention role in the management of ADHD symptoms. Therefore, it is necessary to take one step at a time and balance the idea of implementing progressive development programs on ADHD cases, that need multiple changes at the same time. Adherence to a healthy overall lifestyle can ensure the treatment of ADHD symptoms and daily life difficulties, improving an individual's well-being. It is also suggested for future studies in the field, to develop and use validated scales to assess diet, physical activity, and stress levels, in order to calculate lifestyle factors exclusively in children and adults with ADHD. Furthermore, future trials should focus more on assessing the impact of healthy lifestyle behaviors on ADHD, rather than focusing on the opposite, compared with typically developing individuals. The current domain needs more experimental data to clarify the tripartite relationship between diet quality, lifestyle factors, and ADHD. *Psychiatry*, 58(4), 433–442. <https://doi.org/10.1016/j.jaac.2018.09.439>
- Bilici, M., Yildirim, F., Kandil, S., Bekaroğlu, M., Yildirmiş, S., Değer, O., Ulgen, M., Yildiran, A., & Aksu, H. (2004). Double-blind, placebo-controlled study of zinc sulfate in the treatment of attention deficit hyperactivity disorder. *Progress in neuro-psychopharmacology & biological psychiatry*, 28(1), 181–190. <https://doi.org/10.1016/j.pnpbp.2003.09.034>
- Bloch, M. H., & Qawasmi, A. (2011). Omega-3 fatty acid supplementation for the treatment of children with attention-deficit/hyperactivity disorder symptomatology: systematic review and meta-analysis. *Journal of the American Academy of Child and Adolescent Psychiatry*, 50(10), 991–1000. <https://doi.org/10.1016/j.jaac.2011.06.008>
- Bobb, A. J., Castellanos, F. X., Addington, A. M., & Rapoport, J. L. (2005). Molecular genetic studies of ADHD: 1991 to 2004. *American journal of medical genetics. Part B, Neuropsychiatric genetics: the official publication of the International Society of Psychiatric Genetics*, 132B(1), 109–125.
- Booth, F. W., Roberts, C. K., & Laye, M. J. (2012). Lack of exercise is a major cause of chronic diseases. *Comprehensive Physiology*, 2(2), 1143–1211. <https://doi.org/10.1002/cphy.c110025>
- Cerrillo-Urbina, A. J., García-Hermoso, A., Sánchez-López, M., Pardo-Guijarro, M. J., Santos Gómez, J. L., & Martínez-Vizcaíno, V. (2015). The effects of physical exercise in children with attention deficit hyperactivity disorder: a systematic review and meta-analysis of randomized control trials. *Child: care, health and development*, 41(6), 779–788. <https://doi.org/10.1111/cch.12255>

- Chang, J. P., Su, K. P., Mondelli, V., & Pariante, C. M. (2018). Omega-3 Polyunsaturated Fatty Acids in Youths with Attention Deficit Hyperactivity Disorder: a Systematic Review and Meta-Analysis of Clinical Trials and Biological Studies. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, 43(3), 534–545. <https://doi.org/10.1038/npp.2017.160>
- Chang, J. P., Su, K. P., Mondelli, V., & Pariante, C. M. (2018). Omega-3 Polyunsaturated Fatty Acids in Youths with Attention Deficit Hyperactivity Disorder: a Systematic Review and Meta-Analysis of Clinical Trials and Biological Studies. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, 43(3), 534–545. <https://doi.org/10.1038/npp.2017.160>
- Chou, W. J., Lee, M. F., Hou, M. L., Hsiao, L. S., Lee, M. J., Chou, M. C., & Wang, L. J. (2018). Dietary and nutrient status of children with attention-deficit/ hyperactivity disorder: a case-control study. *Asia Pacific journal of clinical nutrition*, 27(6), 1325–1331. [https://doi.org/10.6133/apjcn.201811_27\(6\).0020](https://doi.org/10.6133/apjcn.201811_27(6).0020)
- Combs, M. A., Canu, W. H., Broman-Fulks, J. J., Rocheleau, C. A., & Nieman, D. C. (2015). Perceived stress and ADHD symptoms in adults. *Journal of attention disorders*, 19(5), 425–434. <https://doi.org/10.1177/1087054712459558>
- Cortese, S., Moreira-Maia, C. R., St Fleur, D., Morcillo-Peñalver, C., Rohde, L. A., & Faraone, S. V. (2016). Association Between ADHD and Obesity: A Systematic Review and Meta-Analysis. *The American journal of psychiatry*, 173(1), 34–43. <https://doi.org/10.1176/appi.ajp.2015.15020266>
- Cortese, S., Ramos Olazagasti, M. A., Klein, R. G., Castellanos, F. X., Proal, E., & Mannuzza, S. (2013). Obesity in men with childhood ADHD: a 33-year controlled, prospective, follow-up study. *Pediatrics*, 131(6), e1731–e1738. <https://doi.org/10.1542/peds.2012-0540>
- Del-Ponte, B., Anselmi, L., Assunção, M., Tovo-Rodrigues, L., Munhoz, T. N., Matijasevich, A., Rohde, L. A., & Santos, I. S. (2019). Sugar consumption and attention-deficit/hyperactivity disorder (ADHD): A birth cohort study. *Journal of affective disorders*, 243, 290–296. <https://doi.org/10.1016/j.jad.2018.09.051>
- Farsad-Naeimi, A., Asjodi, F., Omidian, M., Askari, M., Nouri, M., Pizarro, A. B., & Daneshzad, E. (2020). Sugar consumption, sugar sweetened beverages and Attention Deficit Hyperactivity Disorder: A systematic review and meta-analysis. *Complementary therapies in medicine*, 53, 102512. <https://doi.org/10.1016/j.ctim.2020.102512>
- Fuentes-Albero, M., Martínez-Martínez, M. I., & Cauli, O. (2019). Omega-3 Long-Chain Polyunsaturated Fatty Acids Intake in Children with Attention Deficit and Hyperactivity Disorder. *Brain sciences*, 9(5), 120. <https://doi.org/10.3390/brainsci9050120>
- Ghanizadeh, A., & Haddad, B. (2015). The effect of dietary education on ADHD, a randomized controlled clinical trial. *Annals of general psychiatry*, 14, 12. <https://doi.org/10.1186/s12991-015-0050-6>
- Gillies, D., Sinn, J., Lad, S. S., Leach, M. J., & Ross, M. J. (2012). Polyunsaturated fatty acids (PUFA) for attention deficit hyperactivity disorder (ADHD) in children and adolescents. *The Cochrane database of systematic reviews*, 2012(7), CD007986. <https://doi.org/10.1002/14651858.CD007986.pub2>
- Gruber, R., Wiebe, S., Montecalvo, L., Brunetti, B., Amsel, R., & Carrier, J. (2011). Impact of sleep restriction on neurobehavioral functioning of children with attention deficit hyperactivity disorder. *Sleep*, 34(3), 315–323. <https://doi.org/10.1093/sleep/34.3.315>
- Hardman, R. J., Kennedy, G., Macpherson, H., Scholey, A. B., & Pipingas, A. (2016). Adherence to a Mediterranean-Style Diet and Effects on Cognition in Adults: A Qualitative Evaluation and Systematic Review of Longitudinal and Prospective Trials. *Frontiers in nutrition*, 3, 22. <https://doi.org/10.3389/fnut.2016.00022>
- Holton, K. F., & Nigg, J. T. (2020). The Association of Lifestyle Factors and ADHD in Children. *Journal of attention disorders*, 24(11), 1511–1520. <https://doi.org/10.1177/1087054716646452>
- Hong, G., Conduit, R., Wong, J., Di Benedetto, M., & Lee, E. (2020). Diet, Physical Activity, and Screen Time to Sleep Better: Multiple Mediation Analysis of Lifestyle Factors in School-Aged Children with and without Attention Deficit Hyperactivity Disorder. *Journal of attention disorders*, 1087054720940417. Advance online publication. <https://doi.org/10.1177/1087054720940417>
- Johnson, R. J., Gold, M. S., Johnson, D. R., Ishimoto, T., Lanaspá, M. A., Zahniser, N. R., & Avena, N. M. (2011). Attention-deficit/hyperactivity disorder: is it time to reappraise the role of sugar consumption?. *Postgraduate medicine*, 123(5), 39–49. <https://doi.org/10.3810/pgm.2011.09.2458>
- Khalife, N., Kantomaa, M., Glover, V., Tammelin, T., Laitinen, J., Ebeling, H., Hurtig, T., Jarvelin, M. R., & Rodriguez, A. (2014). Childhood attention-deficit/hyperactivity disorder symptoms are risk factors for obesity and physical inactivity in adolescence. *Journal of the American Academy of*

- Child and Adolescent Psychiatry, 53(4), 425–436.
<https://doi.org/10.1016/j.jaac.2014.01.009>
- Kohlboeck, G., Heitmueller, D., Neumann, C., Tiesler, C., Heinrich, J., Heinrich-Weltzien, R., ... & Kühnisch, J. (2013). Is there a relationship between hyperactivity/inattention symptoms and poor oral health? Results from the GINIplus and LISAPlus study. *Clinical oral investigations*, 17(5), 1329–1338.
- Kohlboeck, G., Sausenthaler, S., Standl, M., Koletzko, S., Bauer, C. P., von Berg, A., Berdel, D., Krämer, U., Schaaf, B., Lehmann, I., Herbarth, O., Heinrich, J., & GINI-plus and LISA-plus Study Groups (2012). Food intake, diet quality and behavioral problems in children: results from the GINI-plus/LISA-plus studies. *Annals of nutrition & metabolism*, 60(4), 247–256.
<https://doi.org/10.1159/000337552>
- Lingineni, R. K., Biswas, S., Ahmad, N., Jackson, B. E., Bae, S., & Singh, K. P. (2012). Factors associated with attention deficit/hyperactivity disorder among US children: results from a national survey. *BMC pediatrics*, 12, 50.
<https://doi.org/10.1186/1471-2431-12-50>
- Marmorstein, N. R. (2016). Energy drink and coffee consumption and psychopathology symptoms among early adolescents: cross-sectional and longitudinal associations. *Journal of caffeine research*, 6(2), 64–72.
- Millichap, J. G., & Yee, M. M. (2012). The diet factor in attention-deficit/hyperactivity disorder. *Pediatrics*, 129(2), 330–337.
<https://doi.org/10.1542/peds.2011-2199>
- Pelsser, L. M., Frankena, K., Toorman, J., Savelkoul, H. F., Pereira, R. R., & Buitelaar, J. K. (2009). A randomised controlled trial into the effects of food on ADHD. *European child & adolescent psychiatry*, 18(1), 12–19.
<https://doi.org/10.1007/s00787-008-0695-7>
- Peralta, G. P., Forns, J., García de la Hera, M., González, L., Guxens, M., López-Vicente, M., Sunyer, J., & Garcia-Aymerich, J. (2018). Sleeping, TV, Cognitively Stimulating Activities, Physical Activity, and Attention-Deficit Hyperactivity Disorder Symptom Incidence in Children: A Prospective Study. *Journal of developmental and behavioral pediatrics* : *JDBP*, 39(3), 192–199.
<https://doi.org/10.1097/DBP.0000000000000539>
- Pingault, J. B., Viding, E., Galéra, C., Greven, C. U., Zheng, Y., Plomin, R., & Rijdsdijk, F. (2015). Genetic and Environmental Influences on the Developmental Course of Attention-Deficit/Hyperactivity Disorder Symptoms From Childhood to Adolescence. *JAMA psychiatry*, 72(7), 651–658.
<https://doi.org/10.1001/jamapsychiatry.2015.0469>
- Ptacek, R., Kuzelova, H., Stefano, G. B., Raboch, J., Sadkova, T., Goetz, M., & Kream, R. M. (2014). Disruptive patterns of eating behaviors and associated lifestyles in males with ADHD. *Medical science monitor : international medical journal of experimental and clinical research*, 20, 608–613.
<https://doi.org/10.12659/MSM.890495>
- Ríos-Hernández, A., Alda, J. A., Farran-Codina, A., Ferreira-García, E., & Izquierdo-Pulido, M. (2017). The Mediterranean Diet and ADHD in Children and Adolescents. *Pediatrics*, 139(2), e20162027.
<https://doi.org/10.1542/peds.2016-2027>
- Rucklidge, J., Johnstone, J., Harrison, R., & Boggis, A. (2011). Micronutrients reduce stress and anxiety in adults with Attention-Deficit/Hyperactivity Disorder following a 7.1 earthquake. *Psychiatry research*, 189(2), 281–287.
<https://doi.org/10.1016/j.psychres.2011.06.016>
- San Mauro Martín, I., Blumenfeld Olivares, J. A., Garicano Vilar, E., Echeverry López, M., García Bernat, M., Quevedo Santos, Y., Blanco López, M., Elortegui Pascual, P., Borregon Rivilla, E., & Rincón Barrado, M. (2018). Nutritional and environmental factors in attention-deficit hyperactivity disorder (ADHD): A cross-sectional study. *Nutritional neuroscience*, 21(9), 641–647.
<https://doi.org/10.1080/1028415X.2017.1331952>
- San Mauro Martin, I., Sanz Rojo, S., González Cosano, L., Conty de la Campa, R., Garicano Vilar, E., & Blumenfeld Olivares, J. A. (2019). Impulsiveness in children with attention-deficit/hyperactivity disorder after an 8-week intervention with the Mediterranean diet and/or omega-3 fatty acids: A randomised clinical trial. Impulsividad en el trastorno por déficit de atención e hiperactividad en niños después de una intervención de 8 semanas con dieta mediterránea y/o ácidos grasos omega-3: ensayo clínico aleatorizado. *Neurología (Barcelona, Spain)*, S0213-4853(19)30132-X. Advance online publication.
<https://doi.org/10.1016/j.nrl.2019.09.007>
- Simon, V., Czobor, P., Bálint, S., Mészáros, A., & Bitter, I. (2009). Prevalence and correlates of adult attention-deficit hyperactivity disorder: meta-analysis. *The British journal of psychiatry: the journal of mental science*, 194(3), 204–211.
<https://doi.org/10.1192/bjp.bp.107.048827>
- Sivertsen, B., Harvey, A. G., Reichborn-Kjennerud, T., Torgersen, L., Ystrom, E., & Hysing, M. (2015). Later emotional and behavioral problems associated with sleep problems in toddlers: a longitudinal study. *JAMA pediatrics*, 169(6), 575–582.
<https://doi.org/10.1001/jamapediatrics.2015.0187>
- Sonuga-Barke, E.J.S., Brandeis, D., Cortese, S., Daley, D., Ferrin, M., Holtmann, M., ... & Wong, I.A.C., Sergeant, J. & European ADHD Guidelines Group (2013). Nonpharmacological interventions for

- Attention-Deficit/ Hyperactivity Disorder: Systematic review and meta-analyses of randomised controlled trials of dietary and psychological treatments. *American Journal of Psychiatry*, 170, 275–289.
- Stevenson, J., Buitelaar, J., Cortese, S., Ferrin, M., Konofal, E., Lecendreux, M., Simonoff, E., Wong, I. C., & Sonuga-Barke, E. (2014). Research review: the role of diet in the treatment of attention-deficit/hyperactivity disorder--an appraisal of the evidence on efficacy and recommendations on the design of future studies. *Journal of child psychology and psychiatry, and allied disciplines*, 55(5), 416–427. <https://doi.org/10.1111/jcpp.12215>
- Thomas, R., Sanders, S., Doust, J., Beller, E., & Glasziou, P. (2015). Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. *Pediatrics*, 135(4), e994–e1001. <https://doi.org/10.1542/peds.2014-3482>
- Touchette, E., Côté, S. M., Petit, D., Liu, X., Boivin, M., Falissard, B., Tremblay, R. E., & Montplaisir, J. Y. (2009). Short nighttime sleep-duration and hyperactivity trajectories in early childhood. *Pediatrics*, 124(5), e985–e993. <https://doi.org/10.1542/peds.2008-2005>
- van Egmond-Fröhlich, A. W., Weghuber, D., & de Zwaan, M. (2012). Association of symptoms of attention-deficit/hyperactivity disorder with physical activity, media time, and food intake in children and adolescents. *PloS one*, 7(11), e49781. <https://doi.org/10.1371/journal.pone.0049781>
- Wang, L. J., Yu, Y. H., Fu, M. L., Yeh, W. T., Hsu, J. L., Yang, Y. H., Yang, H. T., Huang, S. Y., Wei, I. L., Chen, W. J., Chiang, B. L., & Pan, W. H. (2019). Dietary Profiles, Nutritional Biochemistry Status, and Attention-Deficit/Hyperactivity Disorder: Path Analysis for a Case-Control Study. *Journal of clinical medicine*, 8(5), 709. <https://doi.org/10.3390/jcm8050709>
- Weissenberger, S., Ptacek, R., Klicperova-Baker, M., Erman, A., Schonova, K., Raboch, J., & Goetz, M. (2017). ADHD, Lifestyles and Comorbidities: A Call for an Holistic Perspective - from Medical to Societal Intervening Factors. *Frontiers in psychology*, 8, 454. <https://doi.org/10.3389/fpsyg.2017.00454>
- Weissenberger, S., Ptacek, R., Vnukova, M., Raboch, J., Klicperova-Baker, M., Domkarova, L., & Goetz, M. (2018). ADHD and lifestyle habits in Czech adults, a national sample. *Neuropsychiatric disease and treatment*, 14, 293–299. <https://doi.org/10.2147/NDT.S148921>
- Wilens, T. E., & Spencer, T. J. (2010). Understanding attention-deficit/hyperactivity disorder from childhood to adulthood. *Postgraduate medicine*, 122(5), 97–109. <https://doi.org/10.3810/pgm.2010.09.2206>
- Wiles, N. J., Northstone, K., Emmett, P., & Lewis, G. (2009). 'Junk food' diet and childhood behavioural problems: results from the ALSPAC cohort. *European journal of clinical nutrition*, 63(4), 491–498. <https://doi.org/10.1038/sj.ejcn.1602967>
- Wolraich, M. L., Wilson, D. B., & White, J. W. (1995). The effect of sugar on behavior or cognition in children. A meta-analysis. *JAMA*, 274(20), 1617–1621. <https://doi.org/10.1001/jama.1995.03530200053037>
- Woo, H. D., Kim, D. W., Hong, Y. S., Kim, Y. M., Seo, J. H., Choe, B. M., Park, J. H., Kang, J. W., Yoo, J. H., Chueh, H. W., Lee, J. H., Kwak, M. J., & Kim, J. (2014). Dietary patterns in children with attention deficit/hyperactivity disorder (ADHD). *Nutrients*, 6(4), 1539–1553. <https://doi.org/10.3390/nu6041539>
- World Health Organization & United Nations Children's Fund (UNICEF). (2020). Landscape assessment on global monitoring of diet quality: conducted on behalf of the diet quality working group of the WHO/UNICEF technical expert advisory group on nutrition monitoring (TEAM). World Health Organization. <https://apps.who.int/iris/handle/10665/330765>. License: CC BY-NC-SA 3.0 IGO
- Wu, X., Ohinmaa, A., & Veugelers, P. J. (2016). The Influence of Health Behaviours in Childhood on Attention Deficit and Hyperactivity Disorder in Adolescence. *Nutrients*, 8(12), 788. <https://doi.org/10.3390/nu8120788>
- Yu, C. J., Du, J. C., Chiou, H. C., Feng, C. C., Chung, M. Y., Yang, W., Chen, Y. S., Chien, L. C., Hwang, B., & Chen, M. L. (2016). Sugar-Sweetened Beverage Consumption Is Adversely Associated with Childhood Attention Deficit/Hyperactivity Disorder. *International journal of environmental research and public health*, 13(7), 678. <https://doi.org/10.3390/ijerph13070678>
- Zhou, F., Wu, F., Zou, S., Chen, Y., Feng, C., & Fan, G. (2016). Dietary, Nutrient Patterns and Blood Essential Elements in Chinese Children with ADHD. *Nutrients*, 8(6), 352. <https://doi.org/10.3390/nu8060352>