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Dietary Patterns

Association Between the Maternal Mediterranean Diet and Perinatal Outcomes: A Systematic Review and Meta-Analysis

Ji-Rong Xu, Hai-Xia Wang, Jing-Feng Bian, Ming Xu, Nan Jiang, Wei Luo, Ping Zu. et. al. *Adv Nutr*. 2023 Dec 1:100159. doi: 10.1016/j.adnut.2023.100159. [Article link](#)

Significance: This study suggests that adherence to the Mediterranean diet during pregnancy may have positive impacts on perinatal outcomes.

The Mediterranean diet is a global, well-known healthy dietary pattern. This review aims to synthesize the existing evidence on the relationship between the maternal Mediterranean diet during pregnancy and perinatal outcomes, including randomized controlled trials (RCTs) and cohort studies. PubMed, Web of Science, and the Cochrane Library were searched from inception to 10 March, 2023, supplemented by manual screening. A random-effect model was used to estimate pooled sizes with 95% confidence intervals (CIs) for specific outcomes of interest. Data from 5 RCTs and 18 cohort studies with 107,355 pregnant participants were synthesized. In RCTs, it was observed that the maternal Mediterranean diet significantly reduced the incidence of gestational diabetes mellitus [odds ratio (OR), 0.56; 95% CI: 0.34, 0.93], as well as small for gestational age (0.55; 95% CI: 0.35, 0.88). In cohort studies, the highest adherence score to the maternal Mediterranean diet was inversely associated with a lower risk of various adverse pregnancy outcomes, including gestational diabetes mellitus (OR, 0.82; 95% CI: 0.67, 1.00), pregnancy-induced hypertension (0.73; 95% CI: 0.60, 0.89), pre-eclampsia (0.77; 95% CI: 0.64, 0.93), preterm delivery (0.67; 95% CI: 0.49, 0.91), low birth weight (0.70; 95% CI: 0.64, 0.78), intrauterine growth restriction (0.46; 95% CI: 0.23, 0.91), and increased gestational age at delivery (weighted mean difference, 0.11 wk; 95% CI: 0.03, 0.20). Meta-regression analyses did not identify the adjustment for confounders and geographical location as predictive factors for heterogeneity. The results suggest that adherence to the Mediterranean diet during pregnancy appears to be beneficial for perinatal outcomes. Future, larger, and higher-quality RCTs and cohort studies are warranted to confirm the present findings.

Dietary Patterns Among U.S. Children: A Cluster Analysis

Priya Fielding-Singh, Jessie X Fan. *J Acad Nutr Diet*. 2023 Dec 9:S2212-2672(23)01719-7. doi: 10.1016/j.jand.2023.12.001. [Article link](#)

Significance: A NHANES study of children 2-11 years old in the US, identified five clusters with distinct dietary patterns, showing the interrelationship of different dietary patterns with key sociodemographic variation, and the impact on Healthy Eating Index scores.

Background: Most children in the United States consume low-quality diets. Identifying children's dietary patterns and their association with sociodemographic characteristics is important for designing tailored youth dietary interventions. **Objective:** This study's objective was to use cluster analysis to investigate children's dietary patterns and these patterns' associations with sociodemographic characteristics. **Design:** Data from two cycles (2015-2016 and 2017-2018) of the National Health and Nutrition Examination Survey were evaluated to examine dietary patterns. **Participants/Setting:** Participants included 3,044 US youth aged 2 to 11 years who completed at least 1 valid 24-hour diet recall. **Main Outcome Measures:** The main outcome measures were HEI-2015 component and composite scores. **Statistical Analyses Performed:** A cluster analysis was performed on standardized scores of 11 components of the HEI-2015 to identify dietary patterns. One logistic analysis combined the two higher-HEI score clusters and the two lower-HEI score clusters to form a three-category variable of higher-, medium-, and lower-HEI score clusters. Another logistic analysis contrasted two higher- and then the two lower-HEI clusters with each other to examine sociodemographic factors contributing to cluster membership. **Results:** Five clusters were identified, each displaying a distinct dietary pattern. Older, non-Hispanic Black, and overweight children had higher odds of being in the higher-HEI clusters than the medium-HEI cluster. Being older and non-Hispanic Black were linked to higher odds of being in the lower-HEI clusters than the medium-HEI cluster. Conversely, being Mexican American and living with a college-educated reference person were associated with lower odds of being in the lower-HEI clusters compared to the medium-HEI cluster. Among the higher-HEI clusters, Mexican American and Asian American children had higher odds of being in the Pescatarian cluster. Among the lower-HEI clusters, children who were racially or ethnically minoritized had lower odds of being in the Excess Sugar cluster. **Conclusions:** Children in this study displayed different dietary patterns, with key sociodemographic variation.

Carbohydrates

Low-Carbohydrate Diet Macronutrient Quality and Weight Change

Binkai Liu, Yang Hu, Sharan K Rai, Molin Wang, Frank B Hu, Qi Sun. *JAMA Netw Open*. 2023 Dec 1;6(12):e2349552. doi: 10.1001/jamanetworkopen.2023.49552. [Article link](#)

Significance: Low carbohydrate diets that include carbohydrates from whole grains and other plant-based foods and high-quality protein and fat were associated with less weight gain.

Importance: The associations of low-carbohydrate diets (LCDs) with long-term weight management remains unclear, and the source and quality of macronutrients within LCDs are less explored. **Objectives:** To prospectively examine associations between changes in LCD indices and weight change among US adults. **Design, Setting and Participants:** This prospective cohort study included initially healthy participants at baseline from the Nurses' Health Study (NHS; 1986-2010), Nurses' Health Study II (NHSII; 1991-2015), and Health Professionals Follow-up Study (HPFS; 1986-2018). Data analysis was performed between November 2022 and April 2023. **Exposures:** Five LCD indices were examined: (1) a total LCD (TLCD) emphasizing overall lower carbohydrate intake; (2) an animal-based LCD (ALCD) that emphasized animal-sourced protein and fat; (3) a vegetable-based LCD (VLCD) that emphasized plant-sourced protein and fat; (4) a healthy LCD (HLCD) emphasizing less refined carbohydrates, more plant protein, and healthy fat; and (5) an unhealthy LCD (ULCD) emphasizing less healthful carbohydrates, more animal protein, and unhealthy fat. **Main Outcomes and Measures:** The outcome of interest was 4-year changes in self-reported body weight. **Results:** A total of 123 332 participants (mean [SD] age, 45.0 [9.7] years; 103 320 [83.8%] female) were included in this study. The median carbohydrate intake (as a percentage of energy) of the highest quintiles of TLCD score at baseline ranged from 38.3% in HPFS to 40.9% in NHSII. Mean weight gain over 4-year intervals among participants varied from 0.8 kg in the HPFS to 1.8 kg in the NHSII. After adjusting for demographics and baseline and concomitant changes of selected lifestyle factors, each 1-SD increase in TLCD score was associated with 0.06 (95% CI, 0.04-0.08) kg more weight gain over the 4-year periods. Similarly, participants gained 0.13 (95% CI, 0.11 to 0.14) kg per each 1-SD increase in ALCD score and 0.39 (95% CI, 0.37 to 0.40) kg per each 1-SD change in ULCD score. In contrast, each 1-SD increase in VLCD score was associated with 0.03 (95% CI, 0.01 to 0.04) kg less weight gain, and each 1-SD increase in HLCD score was associated with 0.36 (95% CI, 0.35 to 0.38) kg less weight gain. The associations were more pronounced among obese individuals (per 1-SD increase in HLCD score: BMI ≥ 30 , 0.88 [95% CI, 0.80, 0.97] kg less weight gain; BMI < 25 , 0.23 [95% CI, 0.20, 0.26] kg less weight gain; P for interaction $< .001$). **Conclusions and Relevance:** These findings suggest that the quality of LCDs may play a critical role in modulating long-term weight change. Only LCDs that emphasized high-quality protein, fat, and carbohydrates from whole grains and other plant-based foods were associated with less weight gain.

Protein

Lifelong Dietary Protein Restriction Accelerates Skeletal Muscle Loss and Reduces Muscle Fibre Size by Impairing Proteostasis and Mitochondrial Homeostasis

Ufuk Ersoy, Ioannis Kanakis, Moussira Alameddine, Gibran Pedraza-Vazquez, Susan E Ozanne, Mandy Jayne Peffers, Malcolm J Jackson, et. al. *Redox Biol.* 2023 Dec 2;69:102980. doi: 10.1016/j.redox.2023.102980. [Article link](#)

Significance: A study in male mice provided novel mechanistic insight of how lactational protein restriction hinders skeletal muscle growth during development. It also provided evidence that lifelong dietary protein restriction accelerated skeletal muscle loss in later life.

The early life environment significantly affects the development of age-related skeletal muscle disorders. However, the long-term effects of lactational protein restriction on skeletal muscle are still poorly defined. Our study revealed that male mice nursed by dams fed a low-protein diet during lactation exhibited skeletal muscle growth restriction. This was associated with a dysregulation in the expression levels of genes related to the ribosome, mitochondria and skeletal muscle development. We reported that lifelong protein restriction accelerated loss of type-IIa muscle fibres and reduced muscle fibre size by impairing mitochondrial homeostasis and proteostasis at 18 months of age. However, feeding a normal-protein diet following lactational protein restriction prevented accelerated fibre loss and fibre size reduction in later life. These findings provide novel insight into the mechanisms by which lactational protein restriction hinders skeletal muscle growth and includes evidence that lifelong dietary protein restriction accelerated skeletal muscle loss in later life.

Low-and No-Calorie Sweeteners

Relative Validity of Habitual Sugar and Low/No-Calorie Sweetener Consumption Assessed by Food Frequency Questionnaire, Multiple 24-h Dietary Recalls and Urinary Biomarkers: An Observational Study within the SWEET Project

Marion Ec Buso, Hendrik C Boshuizen, Novita D Naomi, Walid Maho, Marlies Diepeveen-de Bruin, Michiel GJ Balvers, Jeanne Hm de Vries, et. al. *Am J Clin Nutr.* 2023 Dec 1:S0002-9165(23)66290-2. doi: 10.1016/j.ajcnut.2023.11.019. [Article link](#)

Significance: Validation of Food Frequency Questionnaire against 24-hour recalls for the assessment of sugars and low- and no-calorie sweetened beverages were ranked from moderate to good. Self-reports and urine excretions comparisons showed moderate agreement in sugars, but underestimation of sweetener exposure using self-reports.

Background: Studies investigating associations between sweeteners and health yield inconsistent results, possibly due to subjective self-report dietary assessment methods. **Objectives:** We compared the performance of a food frequency questionnaire (FFQ), multiple 24-h dietary recalls (24hRs), and urinary biomarkers to estimate intake of sugars and low/no-calorie sweeteners (LNCSs). **Methods:** Participants (n = 848, age 54 \pm 12 y) from a 2-y observational study completed 1 semiquantitative FFQ and ≥ 3 nonconsecutive 24hRs. Both methods assessed intake of sugars (mono- and disaccharides, sucrose, fructose, free and added sugars) and sweetened foods and beverages (sugary foods, fruit juice, and sugar or LNCS-containing beverages [sugar-sweetened beverages and low/no-calorie sweetened beverages (LNCSBs)]); 24hRs also included LNCS-containing foods and tabletop sweeteners (low/no-calorie sweetened foods [LNCSFs]). Urinary excretion of sugars (fructose+sucrose) and LNCSs (acesulfame K+sucralose+steviol glucuronide+cyclamate+saccharin) were simultaneously assessed using ultrahigh-pressure liquid chromatography coupled to tandem mass spectrometry in 288 participants with 3 annual 24-h urine samples. Methods were compared using a.o. validity coefficients (correlations corrected for measurement error). **Results:** Median (interquartile range) FFQ intakes ranged from 0 (0-7) g/d for LNCSBs to 94 (73-117) g/d for mono- and disaccharides. LNCSB use was reported by 32% of participants. Median LNCSB+LNCSF intake using 24hRs was 1 (0-50) g/d and reported by 58%. Total sugar excretions were detected in 100% of samples [56 (37-85) mg/d] and LNCSs in 99% of urine samples [3 (1-10) mg/d]. Comparing FFQ against 24hRs showed VCs ranging from 0.38 (fruit juice) to 0.74 (LNCSB).

VCs for comparing FFQ with urinary excretions were 0.25 to 0.29 for sugars and 0.39 for LNCSBs; for 24hR they amounted to 0.31-0.38 for sugars, 0.37 for LNCSBs, and 0.45 for LNCSFs. **Conclusions:** The validity of the FFQ against 24hRs for the assessment of sugars and LNCSBs ranged from moderate to good. Comparing self-reports and urine excretions showed moderate agreement but highlighted an important underestimation of LNCS exposure using self-reports.

Cognitive Health

Mixed Nut Consumption Improves Brain Insulin Sensitivity: A Randomized, Single-Blinded, Controlled, Crossover Trial in Older Adults with Overweight or Obesity

Kevin Mr Nijssen, Ronald P Mensink, Jogchum Plat, Dimo Ivanov, Hubert Preissl, Peter J Joris. *Am J Clin Nutr.* 2023 Dec 20:S0002-9165(23)66340-3. doi: 10.1016/j.ajcnut.2023.12.010. [Article link](#)

Significance: Sixteen-week mixed nuts supplementation in an intervention study with older overweight and obese subjects found improved regional brain insulin action involved in modulating metabolic and cognitive processes but found no effect on peripheral insulin sensitivity.

Background: Improving brain insulin sensitivity, which can be assessed by measuring regional cerebral blood flow (CBF) responses to intranasal insulin, may prevent age-related metabolic and cognitive diseases. **Objectives:** This study aimed to investigate longer-term effects of mixed nuts on brain insulin sensitivity in older individuals with overweight/obesity. **Methods:** In a randomized, single-blinded, controlled, crossover trial, 28 healthy adults (mean \pm standard deviation: 65 \pm 3 years; body mass index: 27.9 \pm 2.3 kg/m²) received either daily 60-g mixed nuts (15 g of walnuts, pistachio, cashew, and hazelnuts) or no nuts (control) for 16 weeks, separated by an 8-week washout period. Throughout the study, participants were instructed to adhere to the Dutch food-based dietary guidelines. During follow-up, brain insulin action was assessed by quantifying acute effects of intranasal insulin on regional CBF using arterial spin labeling magnetic resonance imaging. Furthermore, effects on peripheral insulin sensitivity (oral glucose tolerance test), intrahepatic lipids, and cardiometabolic risk markers were assessed. **Results:** Body weight and composition did not change. Compared with control, mixed nut consumption improved regional brain insulin action in 5 clusters located in the left (difference in CBF responses to intranasal insulin: -4.5 \pm 4.7 mL/100 g/min; $P < 0.001$; -4.6 \pm 4.8 mL/100 g/min; $P < 0.001$; and -4.3 \pm 3.6 mL/100 g/min; $P = 0.007$) and right occipital lobes (-4.3 \pm 5.6 mL/100 g/min; and -3.9 \pm 4.9 mL/100 g/min; $P = 0.028$). A fifth cluster was part of the left frontal lobe (-5.0 \pm 4.6 mL/100 g/min; $P < 0.001$). Peripheral insulin sensitivity was not affected. Intrahepatic lipid content (-0.7%-point; 95% CI: -1.3%-point to -0.1%-point; $P = 0.027$), serum low-density lipoprotein cholesterol concentration (-0.24 mmol/L; 95% CI: -0.44 to -0.04 mmol/L; $P = 0.019$), and systolic blood pressure (-5 mm Hg; 95% CI: -8 to -1 mm Hg; $P = 0.006$) were lower after the mixed nut intervention. **Conclusions:** Longer-term mixed nut consumption affected insulin action in brain regions involved in the modulation of metabolic and cognitive processes in older adults with overweight/obesity. Intrahepatic lipid content and different cardiometabolic risk markers also improved, but peripheral insulin sensitivity was not affected.

Lipids

Graded Replacement of Carbohydrate-Rich Breakfast Products with Dairy Products: Effects on Postprandial Aminoacidemia, Glycemic Control, Bone Metabolism and Satiety

Luuk Hilken, Floor Praster, Jan van Overdam, Jean Nyakayiru, Cécile M Singh-Povel, Judith Bons, et. al. *J Nutr.* 2023 Dec 12:S0022-3166(23)72799-5. doi: 10.1016/j.tjnut.2023.12.012. [Article link](#)

Significance: An isocaloric replacement of a carbohydrate-rich breakfast with one serving of dairy has positive impacts on postprandial amino acid availability, glycemic control and bone metabolism. A second dairy replacement augments postprandial amino acid and GLP-1.

Background: Postprandial metabolic responses following dairy consumption have mostly been studied using stand-alone dairy products or milk-derived nutrients. **Objective:** Assessing the impact of ingesting dairy products as part of a common breakfast on postprandial aminoacidemia, glycemic control, markers of bone metabolism, and satiety. **Methods:** In this randomized, crossover study, 20 healthy young males and females consumed on 3 separate occasions an iso-energetic breakfast containing no dairy (NO-D), 1 dairy (ONE-D), or 2 dairy (TWO-D) products. Postprandial concentrations of amino acids, glucose, insulin, glucagon-like peptide-1 (GLP-1), calcium, parathyroid hormone (PTH), and markers of bone formation (P1NP) and resorption (CTX-I) were measured before and up to 300 min after initiating the breakfast, along with VAS-scales to assess satiety. **Results:** Plasma essential and branched-chained amino acids availability (expressed as total area under the curve (tAUC)) increased in a dose-dependent manner ($P < 0.05$ for all comparisons). Plasma glucose tAUCs were lower in ONE-D and TWO-D compared with NO-D ($P < 0.05$ for both comparisons). Plasma GLP-1 tAUC increased in a dose-dependent manner ($P < 0.05$ for all comparisons), whereas no differences were observed in plasma insulin tAUC between conditions ($P > 0.05$ for all comparisons). Serum calcium tAUCs were higher in ONE-D and TWO-D compared with NO-D ($P < 0.05$ for both comparisons), along with lower PTH tAUCs in ONE-D and TWO-D compared with NO-D ($P = 0.001$ for both comparisons). In accordance, serum CTX-I concentrations were lower in the late postprandial period in ONE-D and TWO-D compared with NO-D ($P < 0.01$ for both comparisons). No differences were observed in P1NP tAUCs between conditions ($P > 0.05$). The tAUCs for satiety were higher in TWO-D compared with NO-D and ONE-D ($P < 0.05$ for both comparisons). **Conclusions:** Iso-energetic replacement of a carbohydrate-rich breakfast component with one serving of dairy improves postprandial amino acid availability, glycemic control, and bone metabolism. Adding a second serving of dairy in lieu of carbohydrates augments postprandial amino acid and GLP-1 concentrations while further promoting satiety.

Sodium

Self-Reported Frequency of Adding Salt to Food and Risk of Incident Chronic Kidney Disease

Rui Tang, Minghao Kou, Xuan Wang, Hao Ma, Xiang Li, Yoriko Heianza, Lu Qi. *JAMA Netw Open*. 2023 Dec 1;6(12):e2349930. doi: 10.1001/jamanetworkopen.2023.49930. [Article link](#)

Significance : A large U.K. cohort study in 37-73 year olds found a positive correlation between frequency of salt addition to foods and higher risk of kidney disease, suggesting that reduction of table salt usage might reduce risks.

Importance: The self-reported frequency of adding salt to foods could reflect a person's long-term salt taste preference, and salt intake has been associated with increased risk of cardiovascular diseases (CVD). Whether self-reported adding of salt to foods is associated with increased risk of chronic kidney disease (CKD) remains unknown. **Objective:** To prospectively examine the association of self-reported frequency of adding salt to foods with incident CKD risk in a general population of adults. **Design, Setting and Participants:** This population-based cohort study evaluated UK Biobank participants aged 37 to 73 years who were free of CKD at baseline. Participants were enrolled from 2006 to 2010 and prospectively followed up for disease diagnosis. Data were analyzed from October 2022 to April 2023. **Exposure:** Self-reported frequency of adding salt to foods, categorized into never or rarely, sometimes, usually, and always. **Main Outcome and Measure:** Incident CKD cases were defined by diagnostic codes. Hazard ratios (HRs) and 95% CIs were calculated by using Cox proportional hazards models. Models were adjusted for several potential confounders including age, sex, race and ethnicity, Townsend Deprivation Index, estimated glomerular filtration rate (eGFR), body mass index, (BMI), smoking status, alcohol drinking status, regular physical activity, high cholesterol, diabetes, CVD, hypertension, infectious disease, immune disease, and nephrotoxic drugs use at baseline. **Results:** Within a cohort of 465 288 individuals (mean [SD] age 56.32 [8.08] years; 255 102 female participants [54.83%]; 210 186 male participants [45.17%]), participants with higher self-reported frequency of adding salt to foods were more likely to have a higher BMI, higher Townsend Deprivation Index score, and diminished baseline eGFR compared with those who reported a lower frequency of adding salt to foods. Participants who added salt to their foods were also more likely than those who did not add salt to their foods to be current smokers and have diabetes or CVD at baseline. During a median (IQR) follow-up of 11.8 (1.4) years, 22 031 incident events of CKD were documented. Higher self-reported frequency of adding salt to foods was significantly associated with a higher CKD risk after adjustment for covariates. Compared with those who reported never or rarely adding salt to foods, those who reported sometimes adding salt to food (adjusted HR [aHR], 1.04; 95% CI, 1.00-1.07), those who reported usually adding salt to food (aHR, 1.07; 95% CI, 1.02-1.11), and those who reported always adding salt to food (aHR, 1.11; 95% CI, 1.05-1.18) had an increased risk of CKD (P for trend < .001). In addition, eGFR, BMI, and physical activity significantly modified the associations, which were more pronounced among participants with a higher eGFR, lower BMI, or lower level of physical activity. **Conclusions and Relevance:** In this cohort study of 465 288 individuals, a higher self-reported frequency of adding salt to foods was associated with a higher risk of CKD in the general population. These findings suggest that reducing the frequency of adding salt to foods at the table might be a valuable strategy to lower CKD risk in the general population.

Gut Health

Effect of Probiotic Supplementation on Intestinal Permeability in Overweight and Obesity: A Systematic Review of Randomized Controlled Trials and Animal Studies

Zachary DiMattia, Janhavi J Damani, Emily Van Syoc, Connie J Rogers. *Adv Nutr*. 2023 Dec 8;15(1):100162. doi: 10.1016/j.advnut.2023.100162. [Article link](#)

Significance: Plasma/serum LPS was the common measure of intestinal permeability in probiotic supplementation studies. A consistent finding in both animal and clinical studies, was the reduction in intestinal permeability in formulations that included *Bifidobacterium*, *Lactobacillus* and *Akkermansia*. This suggests a need to standardize formulations.

Overweight and obesity are associated with increased intestinal permeability, characterized by loss of gut epithelial integrity, resulting in unregulated passage of lipopolysaccharide (LPS) and other inflammatory triggers into circulation, i.e., metabolic endotoxemia. In obesity, shifts in the gut microbiome negatively impact intestinal permeability. Probiotics are an intervention that can target the gut microbiome by introducing beneficial microbial species, potentially restoring gut barrier integrity. Currently, the role of probiotic supplementation in ameliorating obesity- and overweight-associated increases in gut permeability has not been reviewed. This systematic review aimed to summarize findings from both animal and clinical studies that evaluated the effect of probiotic supplementation on obesity-induced impairment in intestinal permeability (International Prospective Register of Systematic Reviews, CRD42022363538). A literature search was conducted using PubMed (Medline), Web of Science, and CAB Direct from origin until August 2023 using keywords of intestinal, permeability, overweight or obesity, and probiotic supplementation. Of 920 records, 26 eligible records were included, comprising 12 animal and 14 clinical studies. Clinical trials ranged from 3 to 26 wk and were mostly parallel-arm (n = 13) or crossover (n = 1) design. In both animal and clinical studies, plasma/serum LPS was the most common measure of intestinal permeability. Eleven of 12 animal studies reported a positive effect of probiotic supplementation in reducing intestinal permeability. However, results from clinical trials were inconsistent, with half reporting reductions in serum LPS and half reporting no differences after probiotic supplementation. *Bifidobacterium*, *Lactobacillus*, and *Akkermansia* emerged as the most common genera in probiotic formulations among the animal and clinical studies that yielded positive results, suggesting that specific bacteria may be more effective at reducing intestinal permeability and improving gut barrier function. However, better standardization of strain use, dosage, duration, and the delivery matrix is needed to fully understand the probiotic impact on intestinal permeability in individuals with overweight and obesity.

Emerging Science Areas

Emerging Area: Nutrition and Metabolism Dementia Agility

Changes in Cholesterol Homeostasis Associated with Aging and with Age-Related Conditions: Pathophysiological and Clinical Implications

Marco Bertolotti, Giulia Lancellotti, Chiara Mussi. *JGG*. Vol. 71: Issue 4, Dec. 2023. Doi: 10.36150/2499-6564-N637. [Article link](#)

Significance: This narrative review presents current knowledge on the pathophysiology and clinical implications of cholesterol on aging. Effects of cholesterol and cholesterol reduction on cognitive function are controversial, suggesting future need for personalization when assessing subject's functional status, clinical competence and skills.

The increase in life expectancy is leading to a progressive rise in the percentage of older people in the general population, and consequently in the prevalence of chronic diseases, often leading to disability. Age-related modifications in cholesterol homeostasis, the increase in plasma cholesterol levels due to aging, represents a cardio- and cerebrovascular risk factor in adjunct to age itself. Direct knowledge about the pathophysiological alterations of cholesterol metabolism is limited. Clinical-experimental evidence about cholesterol lowering treatment suggests that the benefits observed in the general population are also observed in older age groups. However, patients enrolled in clinical trials often do not represent real-life clinical scenarios, limiting the generalizability of research findings. Issues of complexity and frailty are mostly inadequately addressed in published studies and guidelines. Further, effects of cholesterol itself and cholesterol lowering on cognitive function are still controversial. This narrative review focuses on current evidence about the pathophysiology and clinical implications of the relationship between cholesterol and aging. Some suggestions will be provided, underlining the need for careful, personalized evaluation of the patient's functional status, along with clinical competence and geriatric skills.

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