

INPLASY PROTOCOL

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None declared.

Walnut intake interventions targeting biomarkers of metabolic syndrome and inflammation in middle-aged and older adults: a systematic review and meta-analysis of randomized controlled trials research protocol

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Review question / Objective: The aim of this study was to conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) in order to properly examine the evidence on the effects of walnut consumption on chosen indicators of inflammation and metabolic syndrome in mature adults.

Condition being studied: Metabolic syndrome (MetS), chronic, low-grade inflammation, and oxidative stress are all important risk factors for morbidity and death, with a higher frequency in the elderly population.

Information sources: We conducted a comprehensive search in five databases: Pubmed, EMBASE, Scopus, Cochrane, ClinicalTrials, from inception.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 June 2022 and was last updated on 13 June 2022 (registration number INPLASY202260058).

INTRODUCTION

Review question / Objective: The aim of this study was to conduct a systematic review and meta-analysis of randomized controlled trials (RCTs) in order to properly examine the evidence on the effects of walnut consumption on chosen indicators

of inflammation and metabolic syndrome in mature adults.

Rationale: Plant matrices high in antioxidant and anti-inflammatory chemicals may protect against oxidative stress and excessive inflammation, according to human and animal studies.

Tree nuts are high in monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs), as well as tocopherols, phytosterols, and polyphenols, all of which are essential bioactive phytochemicals with antioxidant qualities. Walnuts are particularly high in linoleic acid (18:2n-6), -linolenic acid (ALA) (18:3n-3), polyphenols, L-arginine, and magnesium [16], a phytochemical composition that is responsible for a variety of health benefits.

Condition being studied: Metabolic syndrome (MetS), chronic, low-grade inflammation, and oxidative stress are all important risk factors for morbidity and death, with a higher frequency in the elderly population.

METHODS

Search strategy: We used keywords like: (1) walnuts, (2) inflammatory biomarkers, (3) metabolic syndrome, (4) randomized controlled trial. The complete search strategy in Pubmed is the following: ("juglans"[MeSH Terms] OR "juglans"[All Fields] OR "walnut"[All Fields] OR "walnuts"[All Fields]) AND (("waist circumference"[MeSH Terms] OR ("waist"[All Fields] AND "circumference"[All Fields]) OR "waist circumference"[All Fields] OR "obesity, abdominal"[MeSH Terms] OR ("obesity"[All Fields] AND "abdominal"[All Fields]) OR "abdominal obesity"[All Fields] OR ("central"[All Fields] AND "obesity"[All Fields]) OR "central obesity"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obeses"[All Fields] OR "obesities"[All Fields] OR "overweight"[MeSH Terms] OR "overweight"[All Fields] OR "body mass index"[MeSH Terms] OR ("body"[All Fields] AND "mass"[All Fields] AND "index"[All Fields]) OR "body mass index"[All Fields] OR "BMI"[Title/Abstract] OR "body weight"[MeSH Terms] OR ("body"[All Fields] AND "weight"[All Fields]) OR "body weight"[All Fields] OR "kilogram"[All Fields] OR "kilogramme"[All Fields] OR "kilograms"[All Fields] OR "kg"[Title/Abstract] OR "lbs"[Title/Abstract] OR "pound"[All Fields] OR "pounds"[All Fields])

OR ("blood pressure"[MeSH Terms] OR "blood pressure determination"[MeSH Terms] OR "arterial pressure"[MeSH Terms] OR ("blood"[All Fields] AND "pressure"[All Fields]) OR "blood pressure"[All Fields] OR "arterial pressure"[MeSH Terms] OR ("arterial"[All Fields] AND "pressure"[All Fields]) OR "arterial pressure"[All Fields] OR "SBP"[Title/Abstract] OR "DBP"[Title/Abstract] OR "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR "hypertensions"[All Fields] OR "hypertensive"[All Fields] OR "hypertensives"[All Fields] OR "blood glucose"[MeSH Terms] OR "glucose"[MeSH Terms] OR "glucose"[All Fields] OR ("blood"[All Fields] AND "glucose"[All Fields]) OR "glycemia"[All Fields] OR "glycemias"[All Fields] OR "diabetes mellitus"[MeSH Terms] OR "diabete"[All Fields] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields] OR "diabetic"[All Fields] OR "diabetics"[All Fields] OR "triglycerides"[MeSH Terms] OR "triglycerid"[All Fields] OR "triglycerides"[All Fields] OR "triglyceride"[All Fields] OR "triglycerids"[All Fields] OR "cholesterol"[MeSH Terms] OR "cholesterol"[All Fields] OR "HDL"[Title/Abstract] OR "LDL"[Title/Abstract]) OR ("c reactive protein"[MeSH Terms] OR ("c reactive"[All Fields] AND "protein"[All Fields]) OR "c reactive protein"[All Fields] OR "crp"[Title/Abstract] OR "interferons"[MeSH Terms] OR "interferone"[All Fields] OR "interferones"[All Fields] OR "IFN"[Title/Abstract] OR "interleukins"[MeSH Terms] OR "interleukine"[All Fields] OR "interleukines"[All Fields] OR "IL"[Title/Abstract] OR ("e selectin"[MeSH Terms] OR "e selectin"[All Fields] "cell adhesion molecules"[MeSH Terms] OR ("cell"[All Fields] AND "adhesion"[All Fields] AND "molecules"[All Fields]) OR "cell adhesion molecules"[All Fields] OR ("intercellular"[All Fields] AND "adhesion"[All Fields] AND "molecule"[All Fields]) OR "intercellular adhesion molecule"[All Fields]) OR "CAM"[Title/Abstract] OR "ICAM"[Title/Abstract] OR ("vascular cell adhesion molecule 1"[MeSH Terms] OR

("vascular"[All Fields] AND "cell"[All Fields] AND "adhesion"[All Fields] AND "molecule 1"[All Fields]) OR "vascular cell adhesion molecule 1"[All Fields] OR ("vascular"[All Fields] AND "cell"[All Fields] AND "adhesion"[All Fields] AND "molecule"[All Fields]) OR "vascular cell adhesion molecule"[All Fields] OR "VCAM"[Title/Abstract] OR "sVCAM"[Title/Abstract] OR "tumor necrosis factor alpha"[MeSH Terms] OR "tumour necrosis factor"[All Fields] OR ("tumor"[All Fields] AND "necrosis"[All Fields] AND "factor alpha"[All Fields]) OR "tumor necrosis factor alpha"[All Fields] OR ("tumor"[All Fields] AND "necrosis"[All Fields] AND "factor"[All Fields]) OR "TNF"[Title/Abstract]) AND ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR clinical trials as topic [mesh: noexp] OR randomly [tiab] OR trial [ti]) NOT (animals [mh] NOT humans [mh])).

Participant or population: middle-aged and older adults (≥ 40 years of age or mean age ≥ 50 years).

Intervention: Walnuts consumption.

Comparator: No walnuts consumption.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Other inclusion criteria: a minimum 3 weeks intervention period, metabolic syndrome biomarkers, inflammatory biomarkers; exclusion criteria: (1) abstracts, narrative reviews, comments, opinions, methodological papers, editorials, letters, observational studies, conference abstracts, case studies, in vitro studies, non human, with a mechanistic, non-stochastic modeling or any other publications lacking primary data and/or explicit method explanations; (2) inappropriate intervention: walnuts oil, walnut extract, nut mix; (3) inappropriate comparison: compulsory comparison; (4) full text not available; (5) duplicate study or database; (6) language not known.

Information sources: We conducted a comprehensive search in five databases: Pubmed, EMBASE, Scopus, Cochrane, ClinicalTrials, from inception.

Main outcome(s): The standardized mean difference of all the biomarkers of interest: metabolic syndrome biomarkers: waist circumference, body weight, body mass index, systolic blood pressure, diastolic blood pressure, triglyceride, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting blood glucose, glycosylated hemoglobin A1c, and also on the insulin resistance index: the homeostatic model assessment for insulin resistance and insulin; (5.b) Inflammatory biomarkers: C-reactive protein, high-sensitivity C-reactive protein, interferon gamma, E-selectin, VCAM-1, ICAM-1, TNF- α , and interleukins (IL-6 and IL-1 β).

Data management: Excel was used for study screening, selection, data extraction, risk of bias assessment.

Quality assessment / Risk of bias analysis: Studies of interest were assessed regarding internal validity checking the presence of risk of bias with Risk of Bias tool 2 from Cochrane by several investigators. Disagreements were discussed, and a consensus was finally reached.

Strategy of data synthesis: The analyses were carried out using the R environment for statistical computing and graphics, as well as the package meta. Because clinical heterogeneity was anticipated to be an issue, the analyses employed random effects models with Restricted Maximum Likelihood. An x^2 -based Q-test and I² were used to assess the presence of heterogeneity amongst the included studies. To pool the findings from both designs (parallel or crossover trial), we computed the mean difference (between modifications or between final values) and the SE, as recommended by Elbourne et al. A 95 percent confidence interval and p-value was calculated for all of the pooled

results. The level of statistical significance was chosen to be 0.05.

Subgroup analysis: Subgroup analyses were employed concerning risk of bias, trial design, exposure duration, walnut quantity, health status, control group, and age, in case more than ten studies were available, if the number of selected studies was be greater or equal to 10.

Sensitivity analysis: A leave-one-out sensitivity analysis was done to test the results' robustness.

Language: No language restrictions were used.

Country(ies) involved: Romania.

Keywords: nuts; tree nuts; nut consumption; aging; age-related diseases; cardiometabolic markers; antioxidants; inflammation; lipid profile; diabetes.

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