INPLASY

Antioxidant Intake, Status, and Requirements across Vegan, Vegetarian, and Omnivorous Diets: A Preliminary Evidence Map of a Discordant Literature and the Rationale for a Systematic Review

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ADMINISTRATIVE INFORMATION

Support - This review received no specific financial or external funding.

Review Stage at time of this submission - Preliminary searches have been executed in two databases (PubMed, Semantic Scholar), and the study-selection process has been piloted by one reviewer, including a full-text round on borderline records. Data extraction has not started. Still outstanding: the full multi-database search (Scopus, Web of Science, Embase, CENTRAL, LILACS, SciELO) with PRESS peer-review; independent duplicate screening by the second reviewer; and author contact to resolve overlapping samples. No effect estimate has been computed.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202670020

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 July 2026 and was last updated on 17 July 2026.

INTRODUCTION

Review question / Objective Objective. To determine, in apparently healthy individuals, whether vegan and vegetarian diets differ from omnivorous diets, and from each other, in three separately analyzed outcome families: (i) dietary antioxidant intake (individual antioxidant nutrients and estimated dietary total antioxidant capacity [TAC]); (ii) circulating or functional antioxidant status (plasma/serum TAC, carotenoids, tocopherols, ascorbate, endogenous antioxidants such as uric acid and bilirubin, and enzymatic defenses); and (iii) oxidative-stress and oxidative-damage biomarkers. A secondary objective is to characterize the methodological and biological factors that generate the discordance in this literature — the antioxidant construct measured, confounding by endogenous antioxidants, functional vitamin B12/homocysteine status, assay heterogeneity, adiposity and age, and the quality of dietary planning — modeling endogenous antioxidants explicitly as effect modifiers rather than pooling them with dietary antioxidants.

Review question (PECO). In apparently healthy individuals (P), how do vegan and vegetarian diets (E), compared with omnivorous diets and with each other (C), differ in dietary antioxidant intake, circulating/functional antioxidant status, and oxidative-stress/oxidative-damage biomarkers (O), each analyzed separately?

A priori hypotheses. (H1) Dietary antioxidant intake is higher in well-planned plant-based diets but not in unselected, real-world plant-based eaters; (H2) between-pattern differences in plasma/serum total

antioxidant capacity are attenuated or reversed once endogenous antioxidants, particularly uric acid, are accounted for; (H3) oxidative-damage biomarkers show no consistent between-pattern difference in apparently healthy adults.

Rationale The global expansion of vegan and vegetarian eating has renewed the premise that plant-based diets necessarily supply more antioxidants than omnivorous diets and thereby lower oxidative stress. That premise conflates at least three separable constructs — dietary intake, circulating/functional status, and downstream oxidative-stress outcomes — which are not tightly coupled, because bioavailability, food-matrix effects, endogenous synthesis, and adaptive regulation intervene between diet and cell. A fourth axis, requirement, is unresolved: dietary reference values exist for individual antioxidant nutrients, but no reference intake has been defined for total antioxidant capacity, so there is no benchmark against which vegan, vegetarian, and omnivorous diets can be judged.

A preliminary, non-systematic evidence map prepared by the author (sixteen comparative studies; literature indexed through 31 May 2026) found the evidence markedly discordant: the apparent direction of the diet–antioxidant relationship depends on which construct is measured and in which population. Some studies report higher antioxidant intake and lower oxidative-stress biomarkers in plant-based groups; others report comparable status, higher antioxidant-nutrient intake among omnivores in unselected populations, lower plasma antioxidant capacity in vegetarians driven by lower endogenous uric acid, or paradoxically greater oxidative DNA damage in vegetarians. Notably, the strongest randomized evidence that a diet raises antioxidant capacity and lowers oxidative stress comes from the plant-rich but omnivore-inclusive Mediterranean pattern, implying that plant-richness and overall diet quality, rather than the exclusion of animal foods, may be the operative factor. Candidate explanations include the dissociation of intake from bioavailable status, the dominant contribution of endogenous antioxidants (uric acid, bilirubin) to assay-based plasma capacity, functional vitamin B12 deficiency with hyperhomocysteinemia, lower selenium and zinc status weakening enzymatic defenses, assay heterogeneity, and hormesis — because redox balance is a spectrum in which excess antioxidant exposure can blunt beneficial adaptation, “more” is not self-evidently better.

Existing quantitative syntheses do not resolve this. The most directly relevant compare dietary patterns on inflammatory and oxidative-stress biomarkers (e.g., Menzel et al., 2020; Ilari et al., 2025) but treat “antioxidant provision” as a single quantity: they do not disaggregate intake versus status versus outcome, do not model endogenous antioxidants as effect modifiers, and do not separate randomized from observational evidence. A registry scoping conducted during protocol drafting identified registered protocols and reviews on dietary TAC in relation to disease outcomes (e.g., stroke, diabetes, mortality, and women's health) and on dietary-pattern effects on inflammation and oxidative stress, but none evaluating the between-pattern comparison of dietary antioxidant intake, antioxidant status, and oxidative-damage outcomes as three separately analyzed families with endogenous antioxidants modeled as modifiers; the present review is therefore non-duplicative. A transparent, registered review that disaggregates these constructs would convert the qualitative discordance into quantified, certainty-graded conclusions and define the studies needed to resolve it.

Condition being studied Antioxidant provision and redox balance in relation to habitual dietary pattern in apparently healthy individuals — specifically, whether the exclusion of animal foods (vegan and vegetarian versus omnivorous diets) modifies (i) dietary antioxidant intake, (ii) circulating or functional antioxidant status, and (iii) oxidative-stress/oxidative-damage biomarkers. These are separable, loosely coupled constructs. Antioxidant intake, status, and redox balance are determinants of chronic-disease risk across the lifespan, giving the comparison public-health relevance.

METHODS

Search strategy A three-concept strategy combines dietary pattern AND antioxidant/oxidative constructs, with no outcome-design filter, to maximize sensitivity. The draft MEDLINE (Ovid) strategy below will be peer-reviewed (PRESS) and translated for each database before execution; controlled vocabulary and syntax are adapted per platform. No date, language, or publication-status limits are applied at the search stage. The final comprehensive search is scheduled for 15 July 2026.

1 exp Diet, Vegetarian/ or exp Diet, Vegan/ or exp Diet, Plant-Based/

2 (vegan* or vegetarian* or "lacto-ovo" or "lacto ovo" or "plant-based" or "plant based" or flexitarian* or pescatarian* or pesco-vegetarian*).tw,kf.

3 (omnivore* or omnivorous or "meat eater*" or "mixed diet").tw,kf.

4 or/1-3

5 exp Antioxidants/ or exp "Oxidative Stress"/
6 (antioxidant* or "total antioxidant capacity" or TAC or FRAP or ORAC or TEAC or "oxygen radical absorbance").tw,kf.
7 ("oxidative stress" or "oxidative damage" or redox or "reactive oxygen").tw,kf.
8 ("vitamin C" or ascorb* or "vitamin E" or tocopherol* or carotenoid* or "beta-carotene" or β-carotene or polyphenol* or flavonoid* or selenium or zinc).tw,kf.
9 ("uric acid" or urate or bilirubin or "superoxide dismutase" or catalase or "glutathione peroxidase" or glutathione).tw,kf.
10 (malondialdehyde or MDA or isoprostane* or "8-iso" or F2-isoprostane* or "8-OHdG" or "8-hydroxy" or "protein carbonyl*" or "comet assay" or "DNA damage" or TBARS or "advanced oxidation protein").tw,kf.
11 or/5-10
12 4 and 11.

Participant or population Inclusion: apparently healthy, free-living adolescents and adults (any sex, any geographic setting) following a defined habitual dietary pattern — vegan, vegetarian (lacto-, ovo-, or lacto-ovo-vegetarian), or, as related plant-forward comparators, pescatarian or flexitarian — compared with omnivores. Exclusion: populations defined primarily by a clinical disease in which the disease, not the diet, is the principal determinant of redox status (examined separately in a sensitivity analysis if sufficient); studies of isolated antioxidant supplementation without a dietary-pattern comparison; and pregnancy/lactation as the defining condition (handled as a subgroup rather than pooled). Mixed-population studies are included only where pattern-specific outcome data are separately extractable; otherwise they are listed and examined in a sensitivity analysis.

Intervention Because most evidence is observational, the primary "intervention" is an exposure: a habitual vegan or vegetarian dietary pattern (self-identified and/or investigator-defined by dietary assessment), sustained continuously [A1] for at least three months. Interventional evidence, random or non-random assignment to a vegan, vegetarian, or otherwise plant-based dietary pattern for at least three months, is eligible and analyzed separately from observational evidence.
[A2] Exposure ascertainment. The pattern must be ascertained by at least one of: (a) self-identification with the pattern plus a stated minimum duration; (b) a food-frequency questionnaire referring to a habitual period of at least three months; or (c) a cohort's standing diet-group classification. A dietary record of seven days or fewer, used as the sole basis for classifying the pattern, is not sufficient, because it measures intake rather than habit and cannot establish the required duration; dietary records of any length remain acceptable for quantifying intake once the pattern is established by (a)–(c).
[A1] Cyclical or intermittent plant-based patterns. Religious fasting cycles, Lent, Ramadan, and similar, are not eligible as a primary exposure, because the three-month rule exists to allow biomarker turnover and adaptive regulation to reach steady state, which an alternating fasting period of a few weeks does not achieve. Such studies are retained as contextual evidence and analysed in a pre-specified periodic-pattern sensitivity analysis, provided outcomes are measured during or at the end of the plant-based period, and the timing is reported.
Plant-richness and dietary-planning quality (well-planned versus unselected/real-world plant-based eating) are treated as pre-specified effect modifiers; plant-rich, omnivore-inclusive patterns (e.g., Mediterranean) are considered only as contextual/moderator evidence for the plant-richness hypothesis, not as a primary exposure.

Comparator The reference comparator is the omnivorous diet. A pre-specified head-to-head comparison of vegan versus vegetarian diets is conducted where data permit. Randomized and observational evidence are compared separately, and the three outcome families are synthesized separately.

Study designs to be included Studies are eligible if they meet the population, exposure, comparator, outcome, and design criteria above; document a defined dietary pattern sustained continuously for at least three months, ascertained as specified under Intervention [A1][A2]; and report at least one outcome from any of the three families with pattern-specific data that are extractable or obtainable from authors. No restriction is applied by publication date, language, or publication status (a deliberately inclusive choice to reduce bias); non-English reports are translated.
Explicitly excluded isolated single-nutrient/supplement trials without a dietary-pattern comparison; dietary patterns sustained for less than three months; patterns ascertained solely from a dietary record of seven days or fewer [A2]; cyclical or intermittent plant-based patterns as a primary exposure [A1] (retained as contextual evidence); in-vitro-only and animal studies (used only as context); studies whose only redox outcomes are measured in cell cultures exposed to participants' sera or plasma, rather than in the

participants themselves [A5]; and studies without extractable pattern-specific outcome data.

Eligibility criteria Studies are eligible if they meet the population, exposure, comparator, outcome, and design criteria above; document a defined dietary pattern sustained for at least three months; and report at least one outcome from any of the three families with pattern-specific data that are extractable or obtainable from authors. No restriction is applied by publication date, language, or publication status (a deliberately inclusive choice to reduce bias); non-English reports are translated. Explicitly excluded: isolated single-nutrient/supplement trials without a dietary-pattern comparison; dietary patterns sustained for less than three months; in-vitro-only and animal studies (used only as context); and studies without extractable pattern-specific outcome data..

Information sources MEDLINE/PubMed, Scopus, Web of Science Core Collection, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). These are complemented by regional databases (e.g., LILACS and SciELO) to reduce geographic bias, by reference-list and forward-citation screening of included studies and relevant reviews, and by contacting study authors for missing pattern-specific data. Preprints (e.g., medRxiv) are eligible but flagged as non-peer-reviewed. The accompanying Communication mapped literature indexed through 31 May 2026; the systematic review's final comprehensive search is scheduled for 15 July 2026.

Main outcome(s) Three outcome families, each synthesised separately.
(1) Dietary antioxidant intake — individual antioxidant nutrients (vitamin C, vitamin E, carotenoids/β-carotene, selenium, zinc; also vitamin A, copper, manganese) and estimated dietary total antioxidant capacity (FRAP-, ORAC-, or TEAC-based).
(2) Circulating or functional antioxidant status. [A3] This is a closed list for pooling: assay-based plasma/serum TAC; plasma carotenoids, tocopherols and ascorbate; endogenous antioxidants (uric acid, bilirubin); enzymatic defences (superoxide dismutase, catalase, glutathione peroxidase, glutathione); and selenium/zinc status reported as functional antioxidant status, including glutathione peroxidase 3 and selenoprotein P. A marker outside this list is eligible only if it directly measures a listed analyte.
Specifically not poolable: (i) gamma-glutamyl transferase, a hepatobiliary enzyme whose relation to glutathione status is inferential and bidirectional and which is confounded by adiposity, alcohol and hepatic steatosis, the very factors modelled here as modifiers; (ii) [A5] adaptive-response markers (heme-oxygenase-1, NRF2 nuclear binding, antioxidant-response-element activity), which are induced by oxidative stress and therefore carry the opposite sign to a capacity marker, circulating heme-oxygenase-1 in particular is released from cells damaged by oxidative stress and indexes burden, not defense. Studies reporting only such markers are retained narratively under the hormesis/adaptive-regulation objective stated in this protocol.
(3) Oxidative-stress/oxidative-damage biomarkers — lipid oxidation (malondialdehyde, F2-isoprostanes/8-iso-PGF2α), protein oxidation (carbonyls), and DNA oxidation/damage (8-OHdG, comet assay).
[A4] Matrix and metric (applies to families 2 and 3). Blood-derived matrices (plasma, serum, erythrocytes, whole blood, leukocytes) are poolable. Saliva, buccal cells and skin are eligible but analysed in a separate pre-specified matrix subgroup and are never pooled with blood-derived measures in the same synthesis. Urinary excretion of damage biomarkers (8-OHdG, 8-iso-PGF2α) remains poolable within family 3. Enzyme activity and concentration are poolable; gene expression, promoter methylation, and proteomic abundance are reported only narratively, because they are not on the same measurement scale as activity and the expression-to-activity relationship is not fixed in direction. Every study is coded for matrix and metric at extraction; both become levels of the pre-specified assay/measurement-method subgroup.
Effect measure: standardised mean difference (Hedges' g) with 95% confidence interval (frequentist) and 95% credible interval (Bayesian); a raw mean difference is additionally reported where a common instrument or unit is used. Outcomes are taken at the habitual assessment or at the end of the intervention.

Additional outcome(s) Functional vitamin B12 and homocysteine status and inflammatory markers (e.g., C-reactive protein) are extracted as related, interpretation-supporting outcomes and, for B12/homocysteine and endogenous antioxidants, as pre-specified effect modifiers. Adiposity/body-fat and age are recorded as potential confounders/modifiers; supplement use and indicators of selenium/zinc adequacy are recorded to support interpretation.

Data management Records are deduplicated and screened (title/abstract, then full text) independently by two reviewers using piloted forms; disagreements are resolved through

discussion or by a third reviewer; a PRISMA 2020 flow diagram documents the process. Two reviewers independently extract data into a piloted form. Values available only in figures are extracted with a calibrated digitiser (e.g., WebPlotDigitizer) and flagged as figure-derived. Software: reference manager (e.g., Zotero); screening tool (e.g., Rayyan or Covidence); frequentist synthesis in R (metafor) and Bayesian (probabilistic) synthesis in Python (PyMC/ArviZ).
[A6] Report-to-study linkage. Reports are linked to studies; they are not counted as studies. Before extraction, records are grouped by author, institution and recruitment window, and candidate overlaps are tested against recruitment dates, group sizes, age and sex distributions, and identical or near-identical summary statistics. Corresponding authors are contacted for every candidate cluster. Where overlap is evidenced (shared authorship, same institution, overlapping recruitment window, and identical or near-identical group sizes or summary values) and authors do not clarify, overlap is assumed: the most complete report per outcome family is used, and the participant sample enters each synthesis only once. The assumption is recorded and tested in a sensitivity analysis that instead treats the reports as independent. Conversely, a single report covering two independently designed samples contributes two comparisons rather than one. The PRISMA flow diagram reports the number of reports and the number of studies they represent.

Quality assessment / Risk of bias analysis Two reviewers independently appraise each study: randomised trials with Cochrane RoB 2; non-randomised intervention studies with ROBINS-I; and comparative observational studies with the Newcastle–Ottawa Scale. Each study additionally receives a measurement/assay-quality appraisal (analytical method for TAC and biomarkers; fasting state; sample handling), given that assay heterogeneity is a central source of discordance; adjustment for endogenous antioxidants (e.g., uric acid) is recorded as a signalling item. Certainty of evidence is rated with GRADE, separately for each outcome family and for randomised versus observational bodies of evidence.
[A6] Overlapping publication is recorded as a signalling item for every study: whether the report is a primary report, a secondary or duplicate report of a previously published sample, or a re-analysis of a published cohort. Studies whose comparator group is external or historical rather than concurrent are marked as high risk of bias on comparability and restricted to sensitivity analysis.

Strategy of data synthesis Continuous outcomes are synthesised as standardised mean differences (Hedges' g) using an inverse-variance random-effects meta-analysis, separately for each of the three outcome families and for randomised and observational evidence. Both frequentist and Bayesian (probabilistic) analyses are performed as appropriate. The frequentist estimator is REML or Paule–Mandel with the Hartung–Knapp–Sidik–Jonkman adjustment to the confidence interval, reporting a prediction interval; a fixed-effect estimate is reported only as a sensitivity comparison. The Bayesian analysis is a hierarchical normal–normal random-effects model with a weakly informative half-Normal prior on the between-study standard deviation τ and a weakly informative Normal prior on the pooled effect, reporting the posterior median SMD with 95% credible interval, the posterior probability of benefit, and the posterior probability of exceeding a pre-specified smallest effect size of interest, with prior-sensitivity analysis, MCMC diagnostics (R-hat, bulk/tail effective sample size, divergences), and posterior predictive checks.
Endogenous antioxidants (uric acid, bilirubin) and functional B12/homocysteine status are modelled explicitly as effect modifiers (via subgroups/meta-regression) rather than pooled with dietary antioxidants. Because redox balance is a spectrum, non-linear (hormetic) intake–response relationships are examined where dose data permit, rather than assumed monotonic. Heterogeneity is reported with τ^2 (and its confidence interval), I^2, and Cochran's Q (exact p), interpreted via the prediction interval. Missing SDs are derived from SEs/CIs/exact p-values, or imputed using established methods, with the influence assessed in a sensitivity analysis. Reporting-bias diagnostics (funnel plot, Egger's test) are used only when ≥ 10 studies contribute to a synthesis.
[A6] Because reports outnumber studies in this literature, no pooled estimate is computed until report-to-study linkage is complete. Where a report supplies medians and interquartile ranges rather than means and standard deviations, established median-to-mean conversion is applied, flagged, and its influence checked in the sensitivity analysis already specified for imputed data.

Subgroup analysis Pre-specified, hypothesis-generating subgroups, where data permit: exposure type (vegan vs vegetarian); dietary-planning quality (well-planned vs unselected/real-world); life stage (children/adolescents vs adults vs older adults); sex; supplement use; geographic region; adiposity; assay/measurement method; and study design (randomised vs observational).

Meta-regression on these moderators is conducted only when≥ 10 studies contribute to the model.
[A4] The pre-specified modifier “dietary-planning quality (well-planned versus unselected/real-world)” is operationalised, where reported, as plant-food quality: intake of whole versus refined grains, of fruit and vegetables, and of fried or ultra-processed foods. When planning quality is asserted by the study authors but not measured, it is recorded as an author interpretation rather than data. Biological matrix (blood-derived versus saliva, buccal cells or skin) and metric (activity or concentration versus expression or abundance) are added as levels of the assay/measurement-method subgroup.

Sensitivity analysis Leave-one-out (important at small numbers of studies); restriction to low-risk-of-bias studies; restriction to studies that report or adjust for endogenous antioxidants (uric acid/bilirubin), to test whether between-pattern status differences attenuate or reverse (Hypothesis H2); restriction to well-planned plant-based diets; separate analysis of randomised versus observational evidence; alternative τ^2 estimators and removal of the HKSJ adjustment; exclusion of figure-derived or imputed data; and exclusion of very small studies. Robustness across these analyses is reported.
[A1][A6] Three further sensitivity analyses: (i) periodic or cyclical plant-based patterns analysed separately from continuously sustained patterns; (ii) where overlap between reports is assumed in the absence of author confirmation, a parallel analysis treating those reports as independent, with any material disagreement reported in the Results; (iii) exclusion of studies whose comparator group is external or historical rather than concurrent.

Language restriction No language restriction is imposed; non-English reports are translated.

Country(ies) involved México.

Other relevant information Duplication assessment. INPLASY and PROSPERO, complemented by database and web searches, were/will be searched to avoid duplication. The most directly relevant existing syntheses (Menzel et al., 2020; Ilari et al., 2025) compare dietary patterns on inflammatory and oxidative-stress biomarkers but do not disaggregate dietary antioxidant intake, antioxidant status, and oxidative-damage outcomes as three separate families, do not model endogenous antioxidants as effect modifiers, and do not separate randomized from observational evidence; registered protocols on dietary total antioxidant capacity address disease-outcome associations (e.g., stroke, diabetes, mortality, women's health) rather than the between-pattern three-construct comparison. The present review is therefore non-duplicative.
Relationship to prior work and timeline. This protocol operationalizes the systematic review foreshadowed in the author's accompanying original Communication (submitted to the journal Antioxidants [MDPI]), a preliminary, non-systematic evidence map of sixteen comparative studies; literature indexed through 31 May 2026. A preliminary search of two databases was executed on 15 July 2026 and the selection process was piloted, prompting Amendment 1. The comprehensive multi-database search, independent duplicate screening, data extraction, and drafting follow. [A1–A6] The review is reported per PRISMA 2020 and conducted per PRISMA-P.

Keywords dietary antioxidants; total antioxidant capacity; oxidative stress; vegan diet; vegetarian diet; omnivorous diet; plant-based diet; uric acid; nutritional requirements; systematic.

Dissemination plans Publication in a peer-reviewed journal and presentation at a scientific conference; the dataset and analysis code will be shared in an open repository; the protocol is registered with INPLASY (registration number assigned on registration), and the final review will cite the registration.

Contributions of each author

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