*Twin Research and Human Genetics* (2026), **29**, 165–175
doi:10.1017/thg.2026.10074

CAMBRIDGE UNIVERSITY PRESS

**Article**

# Twin-Based Randomized Controlled Trials in Nutritional Research: A Scoping Review

Donya Shahamati, Jessica Nguyen and Matthew J. Landry

Department of Global Health & Biobehavioral Sciences, Joe C. Wen School of Population & Public Health, University of California, Irvine, Irvine, CA, USA

**Abstract**

Establishing causality in nutritional science is difficult. Human diets are complex, and individuals vary substantially in how they respond to dietary exposures. The nutrition literature mostly relies on observational studies, which are vulnerable to confounding and measurement error. Twin-based randomized controlled trials (RCTs), especially the co-twin control design, offer a compelling methodological solution to many of these challenges. This design enables researchers to distinguish genetic from environmental influences on health outcomes. The present scoping review was conducted to systematically map twin RCTs in nutrition science, evaluate their methodological approaches, and identify gaps and opportunities for future research. A comprehensive search across clinical trial registries and electronic databases yielded only 13 eligible studies, demonstrating that co-twin randomized dietary interventions remain rare relative to standard study designs using nontwins or twins assigned to the same arm. The interventions used in these eligible RCTs could be classified into four groups: dietary pattern interventions, nutrient- or supplement-based interventions, dietary component modification, and behavioral or multimodal interventions. This limited number of studies may be explained by recruitment challenges and concerns about generalizability. Greater international collaboration, standardized trial protocols, and integration of emerging technologies could expand the utility of twin designs in nutrition science.

**Keywords:** Twin studies; Randomized controlled trials; Co-twin control design; Dietary interventions; Nutrition research

(Received 13 April 2026 UTC; revise received 14 May 2026 UTC; accepted 19 May 2026 UTC; First Published online 24 June 2026)

Establishing causality in nutritional science is a challenge. Complexity of human diet and behaviors, substantial inter-individual variability in metabolic responses to dietary exposures, and variations in foods and food products are just a few reasons for this challenge (Vitolins & Case, 2020). Most nutrition literature relies on observational studies, but these studies are not at the top of the hierarchy of evidence. Cumulative biases, with extensive residual confounding, unclear cause-and-effect relationships, and measurement errors in dietary data, which are often self-reported and imperfectly measured, are among their key limitations (Ioannidis, 2018; Jacobs Jr., 2023). Randomized controlled trials (RCTs) are considered the gold standard for causal inference in clinical and public health research (Collins et al., 2020; Okeh & Ugwu, 2009). However, their application in nutrition is often limited due to high costs, logistical burdens, and ethical constraints. The effect sizes in nutrition RCTs are commonly modest. Therefore, they frequently require large sample sizes to achieve adequate statistical power, which complicates trial feasibility (Jadad, 1998; Reeves et al., 2005; Stolberg et al., 2004).

Combinations of bioactive compounds in human diet, influenced by cultural, behavioral, and environmental factors as part of human variations, make nutritional research even more complicated (Drewnowski & Kawachi, 2015; González, 2020). In addition, causal interpretation in nutrition is often hindered by a lack of formal training in causal inference, leading to overreliance on correlational findings from large datasets (Chiolero, 2018). Another obstacle in nutrition research is the heterogeneity in individual responses to dietary interventions. For instance, data from the POSITIVe network, a European research consortium investigating plant bioactives, demonstrated up to a 37-fold difference in metabolic responses to orange juice among participants. These differences were explained by the variation in absorption, digestion, and excretion pathways (Manach et al., 2017). Also, the findings in the PREDICT 1 study, a cohort of 1002 twins and unrelated adults in the United Kingdom, showed substantial interindividual variability in postprandial triglyceride, glucose, and insulin responses following standardized meals (Berry et al., 2020). Factors that may influence this variability include sex, age, BMI, habitual diet, microbiome composition, and genetic polymorphisms (de Roos et al., 2019; Favari et al., 2024; Head & Buckley, 2020).

Twin studies are a potential methodological tool for addressing these challenges. Monozygotic (MZ) twins are genetically identical, while dizygotic (DZ) twins share, on average, 50% of their genes. This characteristic provides the opportunity for researchers to distinguish the genetic influences from environmental exposures (Boomsma et al., 2002; Pallister et al., 2014; van Dongen et al., 2012). Utilizing international twin registries such as the CODATwins

**Corresponding author:** Matthew J Landry; Email: landrymj@hs.uci.edu

**Cite this article:** Shahamati D, Nguyen J, Landry MJ. (2026) Twin-Based Randomized Controlled Trials in Nutritional Research: A Scoping Review. *Twin Research and Human Genetics* **29**: 165–175, https://doi.org/10.1017/thg.2026.10074

© The Author(s), 2026. Published by Cambridge University Press on behalf of International Society for Twin Studies. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution and reproduction, provided the original article is properly cited.

Check for updates

Project has been a step toward conducting large-scale, diverse, and longitudinal investigations into health outcomes and their determinants in twin populations (Jelenkovic et al., 2016; Jelenkovic et al., 2017; Silventoinen et al., 2015; Silventoinen et al., 2016). Among the most valuable applications of the twin design is the co-twin control method. In this design, one twin is randomized to an intervention while the other serves as a genetically matched control. With this approach, both measured and unmeasured confounding decrease, and internal validity and statistical power increase even in small samples (Martin et al., 1982; McAdams et al., 2021; McGue et al., 2010; Plomin & Haworth, 2010).

Advantages of the twin study design in nutrition RCTs are clear, and particularly beneficial for studies on genetic or early-life environment. However, twin designs remain underutilized in nutrition research (Craig et al., 2020). Existing twin studies predominantly use observational designs or assign twin pairs to the same group rather than using discordant co-twin interventions (Sumathipala et al., 2018; Trepanowski & Ioannidis, 2018). With the shift in nutrition science toward personalization and precision, co-twin randomized trials can be an efficient design to determine whether measured outcomes are caused by the intervention itself or by biological differences (de Roos & Brennan, 2017).

This systematic review aims to evaluate randomized controlled trials using a co-twin design in nutrition science. In this review, we will synthesize methodological approaches and study characteristics of existing twin-based RCTs, with attention to their strengths, challenges, and implications for future research designs in nutrition science.

## Methods

### Study Design

This scoping review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR; Tricco et al., 2018).

### Eligibility Criteria

Studies were eligible for inclusion if they met all of the following criteria: (1) the study employed a randomized controlled trial design; (2) participants included twin pairs, with co-twins allocated to different intervention arms (i.e., a co-twin control design); (3) the intervention involved a dietary or nutritional component, including whole-diet approaches, macronutrient manipulation, or dietary supplementation; and (4) at least one health-related outcome was reported. No restrictions were placed on participant age, sex, zygosity, health status, or geographic location. Studies were excluded if: (1) they did not use an interventional design (e.g., observational, cross-sectional, or cohort studies); (2) both twins within a pair were assigned to the same treatment arm; (3) the intervention was not dietary or nutritional in nature; (4) the study was published only as a conference abstract without sufficient methodological detail; (5) full-text was unavailable; (6) the study was conducted in animals; (7) the study examined the effects of breastfeeding as the primary dietary exposure; or (8) the study focused on the effects of maternal diet on the birth outcomes of twins (i.e., the twins were the offspring rather than the participants receiving the intervention). There were no language or date restrictions applied.

### Information Sources and Search Strategy

A systematic search was conducted on July 1, 2024, across four electronic databases: PubMed (MEDLINE), CINAHL, Web of Science, and Scopus. To ensure currency of the evidence, a search update was conducted in March 2026 using the same search strategies across all four databases. Search strategies were developed using a combination of controlled vocabulary terms and free-text keywords related to two core concepts: twin study designs and dietary interventions. The PubMed strategy combined MeSH terms (Twins[Mesh]; Diet[Mesh]) with title and abstract keyword searches (twin[tiab]; diet[tiab]). Analogous strategies were applied in CINAHL using subject headings (MH Twins+; MH Diet+) and title/abstract fields, and in Web of Science and Scopus using topic and title-abstract-keyword fields respectively. Boolean operators (AND, OR) were used to combine search terms across concepts. Full search strings for all databases are provided in Supplementary File 1. Reference lists of included studies were also hand-searched to identify any additional eligible records not captured by the database searches.

### Study Selection

All records retrieved from the database searches were imported into Covidence (Veritas Health Innovation, Melbourne, Australia), a web-based systematic review management platform, where duplicate records were automatically identified and removed. Study selection proceeded in two stages. In the first stage, two reviewers independently screened all titles and abstracts against the eligibility criteria. In the second stage, full texts of potentially eligible records were retrieved and independently assessed by the same two reviewers. Disagreements at either stage were resolved through discussion and consensus between the reviewers. Reasons for exclusion at the full-text stage were recorded. The study selection process is summarised in a PRISMA-ScR flow diagram (Figure 1).

### Data Extraction

Data were extracted from all included studies by two reviewers independently using a prespecified data extraction form developed a priori. The following data items were extracted from each included study: study number; study name; year of publication; study purpose; diets or dietary exposures compared; intervention description; intervention duration; setting (e.g., free-living, clinical, metabolic ward); study design; outcome measures; number of twin pairs enrolled; zygosity (MZ, DZ, or both); recruitment source; health status of participants; age group (child, 0–18 years; adult; or older adult); participant age; study location; sex ratio (male: female); race and ethnicities; exclusion criteria; outcomes reported; study limitations; considerations specific to the use of a twin design; future research directions noted by the authors; and any additional notes. Any discrepancies in extracted data were resolved by discussion between the two reviewers. A formal quality assessment or risk of bias appraisal of included studies was not performed, consistent with the scoping review methodology, which aims to map the breadth of available evidence rather than appraise its quality (Munn et al., 2018).

### Data Synthesis

Given the heterogeneity of study designs, intervention types, participant populations, and outcome measures across included studies, a narrative synthesis approach was adopted. Findings were

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

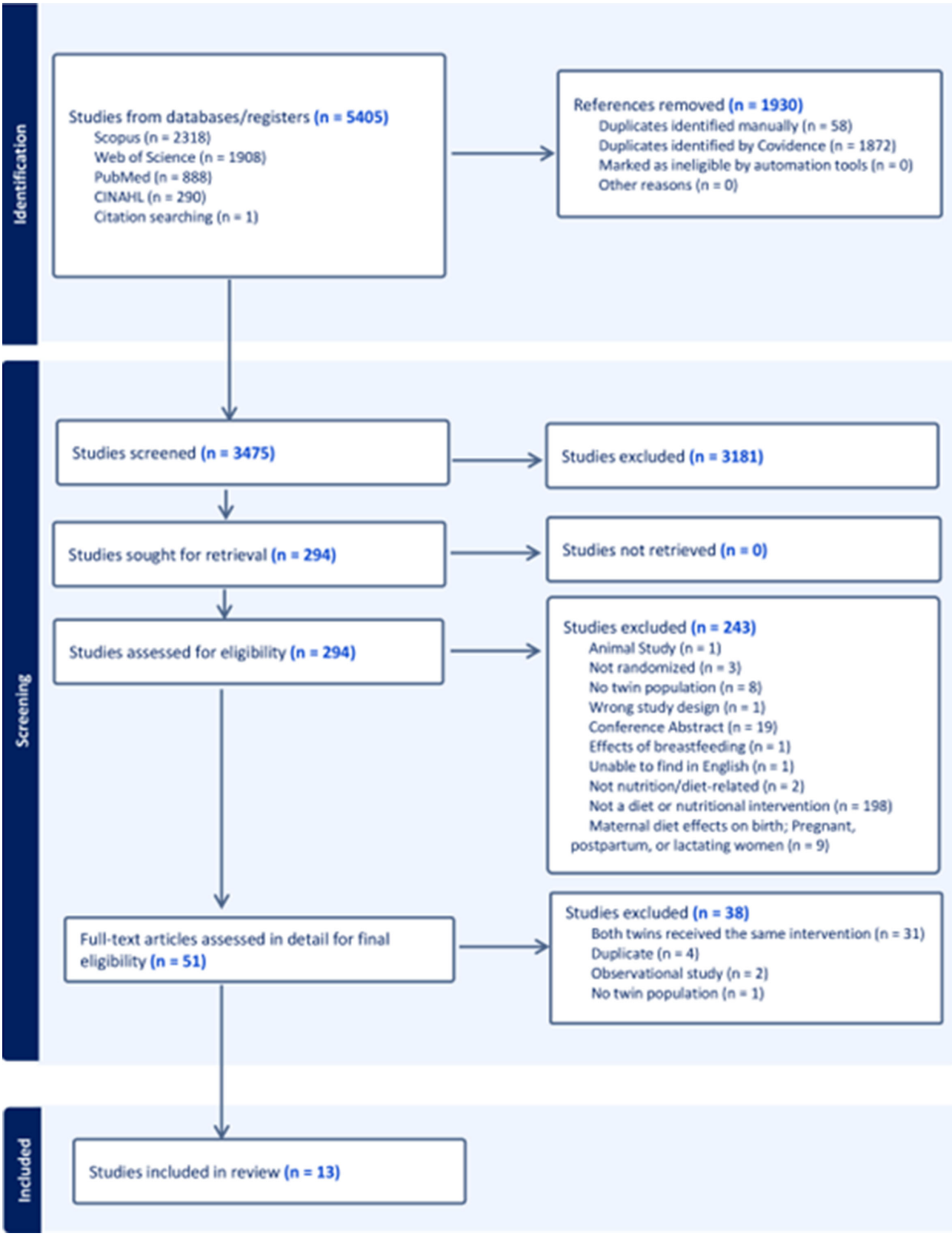



**Figure 1.** PRISMA diagram to illustrate the literature search process and the resulting number of reviewed articles.

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

summarized descriptively and organized thematically according to intervention type (e.g., whole-diet interventions, macronutrient manipulation, dietary supplementation, behavioral interventions) and primary outcome domain (e.g., cardiometabolic health, bone mineral density, sensory perception, epigenetic aging, cognition). Study characteristics were tabulated to facilitate comparison across studies. No quantitative pooling or meta-analysis was conducted.

## Results

A total of 5405 records were identified and imported for screening. Following the removal of duplicates, 3475 studies were screened by title and abstract. After excluding clearly irrelevant studies, 294 full-text articles were assessed for eligibility. The majority of full-text exclusions were due to the intervention not being diet- or nutrition-related, being conference abstracts, or not involving twin participants. After full-text screening, an additional 38 studies were excluded for reasons such as identical interventions administered to both twins, observational design, or ineligible population (Figure 1).

A total of 13 studies met the inclusion criteria for this scoping review, published between 1987 and 2025. These studies were conducted across various geographic locations, primarily the United States and Australia, with two based in Europe. The interventions varied in duration, from two study visits to longer periods lasting up to three years. In terms of the type of intervention, we can categorize them in four groups, including dietary pattern interventions, nutrient/supplement-based interventions, dietary component modification interventions, and behavioral or multimodal interventions. A detailed overview of the included studies, covering study design, intervention details, population demographics, and outcome measures, is presented in Table 1.

### *Participant Characteristics and Recruitment*

Participants' characteristics and recruitment strategies varied across the studies. Twin pairs were primarily recruited from national twin registries, such as Twins Research Australia (TRA), the TwinsUK Registry, and the Stanford Twin Registry (STR), as well as through local advertisements, community outreach, university records, and school-based initiatives. Healthy populations were targeted, and most studies had explicit exclusion criteria to screen out individuals with chronic conditions or factors that could interfere with adherence to the intervention or protocol (e.g., recent antibiotic use, pregnancy, severe allergies, or metabolic diseases).

Participants ranged in age from as young as 5 years to over 60. Some studies focused on specific life stages such as premenarcheal girls (Cameron et al., 2004) or older adults with low protein intake (Ní Lochlainn et al., 2024). In most included studies, both sexes were recruited, except for two, which focused exclusively on female participants due to sex-specific research aims (Cameron et al., 2004; Nowson et al., 1997) and one study that included only male participants (Faith et al., 2006). Reporting of sex ratios and racial/ethnic backgrounds varied across studies. Zygosity composition also differed: seven studies enrolled only MZ twins, while six included both MZ and DZ pairs. Sample sizes ranged from 3 to 70 twin pairs.

### *Interventions*

The 13 included trials used four broad types of dietary interventions. Dietary pattern interventions, defined as assignment to distinct overall dietary patterns (e.g., vegan vs. omnivorous diets; Carter et al., 2025; Dwaraka et al., 2024; Landry et al., 2023; Zeitlin et al., 2025); nutrient- or supplement-based interventions, involving the addition of specific nutrients or bioactive compounds (e.g., calcium or botanical extracts; Cameron et al., 2004; Johnston et al., 1992; Nowson et al., 1997, Perrinjaquet-Moccetti et al., 2008); dietary component modification, in which a single dietary component such as fat or sodium intake was systematically altered while maintaining overall dietary structure (Costanzo et al., 2019; Costanzo et al., 2018, Luft et al. 1987); and behavioral or multimodal interventions, combining dietary components with behavioral strategies or additional modalities such as exercise (Faith et al., 2006, Ní Lochlainn et al., 2024).

The most recent studies in this review were dietary pattern interventions that used randomized controlled trials to compare vegan and omnivorous dietary patterns over 8 weeks. In the initial phase, participants typically started with structured meal delivery and then self-prepared meals. This approach supports dietary adherence while also reflecting how these diets might realistically be adopted in everyday life (Carter et al., 2025; Dwaraka et al., 2024; Landry et al., 2023; Zeitlin et al., 2025). Dietary intake was assessed using repeated 24-hour dietary recalls to evaluate adherence to assigned dietary patterns (Landry et al., 2023; Zeitlin et al., 2025). Outcomes in the primary analyses were primarily related to cardiometabolic risk factors (Landry et al., 2023) and a subpaper provided detailed information about dietary quality (Zeitlin et al., 2025). Multiple subanalyses from this trial extended the primary findings; for example, one integrated detailed biological profiling, including metabolomic, cytokine, and gut microbiome analyses, to examine potential mechanistic pathways linking dietary patterns to metabolic regulation (Carter et al., 2025), while the other focused on DNA methylation-based epigenetic aging markers to evaluate changes in biological age following the dietary intervention (Dwaraka et al., 2024).

Nutrient- and supplement-based interventions were another major methodological category. These interventions typically used placebo-controlled or dose-comparison designs. Calcium supplementation trials used placebo-controlled co-twin designs over extended durations ranging from 6 months to 3 years in the pediatric population. These studies showed greater gains in bone mineral density in supplemented twin compared with the placebo-treated co-twin (Cameron et al., 2004; Johnston et al., 1992; Nowson et al., 1997). Perrinjaquet-Moccetti et al. (2008) evaluated the effects of two doses of olive leaf extract in MZ twins with borderline hypertension using a dose-comparison design.

Another group of studies used dietary component modification methods, such as controlled low-fat versus high-fat diets. These studies were designed to maintain weight stability while assessing molecular and sensory adaptations, including taste perception and gene expression responses. Based on the results, dietary fat modification influenced gene expression and taste sensitivity independent of genetic background (Costanzo et al., 2019; Costanzo et al., 2018). Another example is the sodium restriction protocol implemented by Luft et al. (1987), in which dietary sodium intake was reduced and subsequently reintroduced to examine blood pressure responses within twin pairs. The co-twin design showed that differences in blood pressure response to salt were likely due to genetic differences, not just environmental factors.

Behavioral and multimodal interventions represented a smaller but distinct category of twin-based trials. One of these interventions used reward systems to modify dietary behaviors, to

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press



**Table 1.** Summary of twin studies utilizing a co-twin randomized controlled trial design

| Author, year | Purpose | Diets compared | Intervention | Intervention duration | Setting | Study design | Measurements |
|---|---|---|---|---|---|---|---|
| Cameron et al. (2004) | To test the hypothesis that calcium supplementation enhances bone accrual in premenarcheal females. | Calcium supplementation vs. placebo | 1200 mg calcium carbonate (Caltrate) supplementation vs. placebo | 24 months | Australian Twin Registry, Australia | Randomized, single-blind, placebo-controlled trial | Areal bone mineral density, total body bone mineral content, height, weight, dietary calcium intake, physical activity |
| Carter et al. (2025) | To evaluate the effects of vegan versus omnivorous diets on the microbiome, metabolome, and immune system in MZ twins. | Healthy vegan vs. healthy omnivorous diet | MZ twins randomized so that one twin consumed a vegan diet and the co-twin consumed an omnivorous diet; meals provided during first 4 weeks and self-prepared during last 4 weeks. | 8 weeks | Stanford Twin Registry with clinic visits and free-living participants | Randomized controlled twin dietary intervention | Metagenomics, metabolomics, immune profiling, blood and stool biomarkers, dietary recalls |
| Costanzo et al. (2018) | To determine whether an 8-week low-fat or high-fat diet alters fatty acid taste thresholds and to assess the genetic contribution. | Low-fat (<20% fat) vs. High-fat (>35% fat) | Diet modification with either LF or HF diet maintaining weight stability. | 8 weeks | Laboratory setting (Deakin University) | Co-twin randomized controlled trial | Fatty acid taste threshold, fat ranking ability, liking, intensity ratings, anthropometry (weight, height, waist/hip), 24-h food recall |
| Costanzo et al. (2019) | To assess the associations between diet-mediated changes in fatty acid taste (FAT) receptor expression and FAT perception in humans. | Low-fat diet (<20% energy from fat) vs. High-fat diet (>35% energy from fat) | Assignment to low-fat or high-fat diet for 8 weeks with regular dietary counseling. | 8 weeks | Laboratory setting (Burwood, Victoria, Australia); free-living participants with dietary monitoring. | Co-twin randomized controlled trial (RCT) | FAT receptor gene expression, FAT perception threshold (three-alternate forced choice methodology), 24-hr dietary recalls |
| Dwaraka et al. (2024) | To assess how a healthy vegan diet vs. a healthy omnivorous diet affects DNA methylation markers of aging in twins. | Healthy vegan diet vs. healthy omnivorous diet | MZ twins randomized to healthy vegan or omnivorous diet for 8 weeks; meals provided first 4 weeks, self-prepared last 4 weeks. | 8 weeks | Single-center trial at Stanford university, US | Randomized, parallel, single-site, clinical trial | DNA methylation measures, epigenome-wide methylation, telomere length, methylation surrogates, global health surveys |
| Faith et al. (2006) | To test the use and effectiveness of the co-twin control design for behavioral economic theories of child nutrition. | Reinforced fruit and vegetable intake vs. non-reinforced intake | Contingent vs. noncontingent reinforcement based on food intake. | 2 visits | Laboratory (St. Luke's-Roosevelt Hospital) | Co-twin control design | Height, weight, BMI, fruit and vegetable intake, total energy intake, fat intake |
| Johnston et al. (1992) | To assess whether calcium supplementation in childhood increases bone mineral density and potentially reduces the risk of future fractures. | Calcium supplementation vs. placebo | 1000 mg/day calcium citrate malate. | 3 years | Home and clinical visits | Randomized, double-blind, placebo-controlled twin study | Bone mineral density (radius, spine, hip), urinary calcium/creatinine ratio, serum osteocalcin, tartrate-resistant acid phosphatase, calcium-44 enrichment |
| Landry et al. (2023) | To compare the effects of a healthy vegan diet vs. a healthy omnivorous diet on cardiometabolic measures during an 8-week intervention. | Healthy vegan diet vs healthy omnivorous diet | MZ twins randomized to healthy vegan or omnivorous diet for 8 weeks; meals provided first 4 weeks, self-prepared last 4 weeks. | 8 weeks | Single-center trial at Stanford university, US | Randomized, parallel, single-site, clinical trial | Low-density lipoprotein cholesterol (LDL-C), body weight, Fasting triglycerides, High-density lipoprotein cholesterol (HDL-C), Fasting glucose, Fasting insulin, Serum trimethylamine N-oxide, Plasma vitamin B12 level |
| Luft et al. (1987) | To examine the genetic influence on blood pressure, sodium homeostasis, and the response to dietary sodium. | Normal vs. sodium-restricted | Sodium restriction with dietary counseling; 3-phase intervention including salt reintroduction for one twin. | 12 weeks | Home & clinic | Randomized twin intervention study with controlled dietary manipulation | Blood pressure, sodium excretion, sympathetic activity, urine/plasma electrolyte and creatinine, anthropometrics |

(*Continued*)

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

**Table 1.** (*Continued*)

| Author, year | Purpose | Diets compared | Intervention | Intervention duration | Setting | Study design | Measurements |
|---|---|---|---|---|---|---|---|
| Ní Lochlainn et al. (2024) | To examine the effects of prebiotics and protein on physical function and cognition in older twins. | Prebiotic + protein vs. placebo + protein | Daily sachet of branched-chain amino acids, plus either prebiotic or placebo (maltodextrin); resistance exercises included. | 12 weeks | Remote/At home | Double-blinded placebo-controlled RCT | Chair rise time, grip strength, gait speed, stool microbiota, 3-day food diary, cognitive tests, self-reported compliance |
| Nowson et al. (1997) | To assess the effect of calcium supplementation on bone mineral density (BMD) in adolescent females. | Calcium supplement vs. placebo | 1000 mg/day calcium tablet (Sandocal 1000) vs. placebo | Up to 18 months (data at 6, 12, and 18 months) | Clinical research center (Australia) | Double-blind, placebo-controlled randomized twin study | DXA at spine, hip, total body; 4-day food record; physical activity questionnaire; anthropometrics; compliance via tablet count |
| Perrinjaquet-Moccetti et al. (2008) | To evaluate antihypertensive and cholesterol-lowering effects of olive leaf extract (EFLA®943) in borderline hypertensive MZ twins | 500 mg/day vs. 1000 mg/day EFLA®943 vs. lifestyle advice | Olive leaf extract tablets or lifestyle advice (control). | 8 weeks | Not specified | Controlled, parallel-group, co-twin study | Blood pressure, heart rate, body weight, glucose, lipids (total cholesterol, LDL), adverse events |
| Zeitlin et al. (2025) | To evaluate changes in diet quality, nutrient intake, and food group consumption among identical twins assigned to vegan vs. omnivorous diets. | Healthy vegan diet vs. healthy omnivorous diet | MZ twins randomized to healthy vegan or omnivorous diet for 8 weeks; meals provided first 4 weeks, self-prepared last 4 weeks. | 8 weeks | Single-center trial at Stanford university, US | Randomized, parallel, single-site, clinical trial | Healthy Eating Index–2015 (HEI-2015), nutrient intake, food group intake, dietary recalls, demographic characteristics, anthropometrics |

| Author, year | Twin pairs | Zygosity | Recruitment | Health status | Age | Location | Sex ratio (M:F) | Race/ethnicities |
|---|---|---|---|---|---|---|---|---|
| Cameron et al. (2004) | 51 pairs of premenarcheal female twins | 27 MZ and 24 DZ | The Australian Twin Registry | Healthy, premenarcheal females | 8–17 years | Australia | 0 : 102 | Not specified |
| Carter et al. (2025) | 21 twin pairs | MZ | Stanford Twin Registry | Healthy | Mean 39.6 years | United States | 8 : 34 | White: 32 (72.7)<br>Native Hawaiian/Pacific Islander: 1 (2.3)<br>Asian: 5 (11.4)<br>Black/AA: 2 (4.5)<br>Multiracial: 4 (9.1) |
| Costanzo et al. (2018) | 44 twin pairs | 34 MZ, 10 DZ | Twins Research Australia registry and advertisements | Healthy | Mean age 43.7 ± 15.4 years | Melbourne, Australia | 21 : 67 | Not specified |
| Costanzo et al. (2019) | 13 twin pairs | 10 MZ, 3 DZ | Twins Research Australia (TRA) | Healthy adults (no major illnesses, no dairy allergies, not pregnant or lactating) | 18–68 years | Melbourne, Australia | 2 : 16 | Not specified |
| Dwaraka et al. (2024) | 21 twin pairs | MZ | Stanford Twin Registry, other registries, Netflix recruitment | Healthy adults; BMI <40; LDL-C <190 mg/dL; no serious chronic disease | ≥18 years | USA (Stanford and other recruitment locations) | 5 : 16 | Not specified, Primarily White |
| Faith et al. (2006) | 3 twin pairs | MZ | Unclear, but subjects recruited from a local community | Healthy | 5 years | Not specified | 6 : 0 | Caucasian |
| Johnston et al. (1992) | 70 pairs enrolled, 45 completed | MZ | Twin registry and local schools (Indiana) | Healthy children | 6–14 years | Indiana, USA | 54 : 84 | White |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Landry et al. (2023) | 22 pairs of twins | MZ | Stanford Twin Registry and other outreach | Healthy | ≥18 years | United States | 10 : 34 | Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Multiracial |
| Luft et al. (1987) | 55 twin pairs | 37 MZ, 18 DZ | Twin registry, university records, advertisements | Normotensive (healthy) | 14–27 years | Indiana, USA | 34 : 21 | White |
| Ní Lochlainn et al. (2024) | 36 twin pairs | MZ and DZ | TwinsUK cohort | Older adults with low protein intake | ≥60 years | UK (remote) | 28 : 54 | Not specified |
| Nowson et al. (1997) | 42 twin pairs | 22 MZ, 20 DZ | NHMRC Twin Registry | Healthy adolescent girls, normotensive, no chronic disease | Mean age 14 years | Australia | 0 : 42 | Not specified |
| Perrinjaquet-Moccetti et al. (2008) | 20 twin pairs | MZ | Not specified | Borderline hypertensive | 18–60 years | Switzerland | 12 : 28 | Not specified |
| Zeitlin et al. (2025) | 22 pairs enrolled; 21 pairs included in final analysis | MZ | Stanford Twin Registry | Healthy | Mean ≈ 40 years | United States | 10 : 34 | Mostly non-Hispanic White (72.7%) |

Note: Key characteristics of included studies, including intervention details, study design, participant characteristics, and outcome measurements.
MZ, monozygotic; DZ, dizygotic; RCT, randomized controlled trial; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; DXA, dual-energy X-ray absorptiometry; HEI-2015, Healthy Eating Index–2015.

increase fruit and vegetable intake. This approach increased fruit and vegetable intake by 2.0 servings/day (Faith et al., 2006). Multimodal interventions combined dietary supplementation with an additional lifestyle component, resistance exercise. This intervention was implemented using remotely monitored or home-based protocols. In this study with twins sharing lifestyle conditions, the effect of prebiotic supplementation was isolated, resulting in improvements in cognitive function and gut microbiota composition (Ní Lochlainn et al., 2024).

## Discussion

Following a comprehensive search of clinical trial registries and multiple databases, only 13 studies met our inclusion criteria, suggesting that co-twin randomized dietary interventions are rare, especially when compared with standard studies using nontwins or twins assigned to the same group. Twins can be incorporated into clinical trials using three different approaches. They may be randomized to the same treatment group, independently assigned without consideration of their twin pair, or intentionally allocated to different groups, as in the co-twin control design. Each approach offers unique methodological advantages and limitations. Randomizing both twins to the same group can help them follow the study protocol better and minimize variability in treatment delivery, but it limits direct comparison within pairs (Segal, 2017). Independent randomization treats each twin as an individual. This approach increases generalizability but potentially neglects shared genetic and environmental factors that are unique characteristics in the twin population (van Dongen et al., 2012). The co-twin control design, in contrast, enhances internal validity, effectively controls for many confounding variables, and allows more precise causal inference (Polderman et al., 2015). However, this design also faces challenges, such as limited generalizability, potential carryover effects between twins, and ethical concerns about deliberately assigning different treatments within closely bonded pairs (Tan et al., 2015).

Zygosity and whether the sample includes MZ-only or mixed MZ/DZ twin pairs is another important factor in co-twin designs, because each design may offer different inferential value. MZ twins, who share nearly all of their segregating genetic variation, provide the strongest control for genetic confounding among twin designs. Therefore, MZ-only samples can provide a unique opportunity to reduce genetic confounding and more clearly estimate the effect of dietary interventions by minimizing the influence of inherited biological differences (Boomsma et al., 2002; McAdams et al., 2021; van Dongen et al., 2012). However, MZ-only trials may be more difficult to recruit and may have limited generalizability because they represent a narrower subgroup of the population. In contrast, mixed MZ/DZ samples may improve feasibility, increase sample size, and better represent the broader twin population. However, because DZ twins share only about 50% of their segregating genes on average, mixed samples provide less complete genetic control than MZ-only designs and may require stratified or sensitivity analyses by zygosity when sample size allows (Boomsma et al., 2002; Polderman et al., 2015; van Dongen et al., 2012). The choice between MZ-only and mixed MZ/DZ designs should be aligned with the study objective.

Because of the shared genetic and environmental factors among twins, when they are utilized in nutritional RCTs, many

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

confounding factors are controlled by nature. In addition, comparing co-twins can reduce between-person variability and strengthen internal validity (McAdams et al., 2021; McGue et al., 2010). Several studies in this review had relatively small sample sizes, but they were able to detect meaningful intervention-related differences. For example, Landry et al. (2023) compared healthy vegan and omnivorous diets in 22 identical twin pairs. They reported a greater reduction in LDL-C in the vegan group compared with the omnivorous group after 8 weeks (−13.9 mg/dL). In comparison, the NEW Soul trial, as a conventional nontwin RCT with a similar exposure and outcome, randomized 159 African-American adults with overweight or obesity to a vegan or low-fat omnivorous diet. They found no significant between-group differences in weight or lipid outcomes, including LDL-C, at 12 months (−2.56 mg/dL in the vegan group vs. −0.79 mg/dL in the omnivorous group; Turner-McGrievy et al., 2023). It should be considered that these two studies differed in population, intervention design, and outcome measurements, and this is just an indirect comparison.

The current evidence does not prove that co-twin RCTs produce larger effect sizes with smaller sample sizes compared with nontwin studies. There are examples that show almost the same power using these two designs. Nowson et al. (1997) reported that calcium supplementation in 42 female twin pairs produced a 1.62% greater increase in spine BMD at 18 months compared with placebo. In a conventional RCT, Lloyd et al. (1993) randomized 94 adolescent girls and found greater increases in lumbar spine BMD in the calcium group compared with placebo (18.7% vs. 15.8%). Even with twin designs, intervention effects may still be small or inconsistent, as shown in some included studies (Ní Lochlainn et al., 2024). Twin studies do not guarantee larger effects, but they may help detect intervention-related effects with less confounding variability.

Across the 13 included studies, the co-twin RCT design appeared to offer methodological advantages in three main contexts. First, for outcomes with strong biological or genetic influences, this design helped reduce genetic and shared environmental variability. Therefore, intervention-related differences could be interpreted with greater internal control. Examples include lipid response, blood pressure response, bone mineral density, taste perception, gene expression, and epigenetic markers (Costanzo et al., 2019; Costanzo et al., 2018; Dwaraka et al., 2024; Johnston et al., 1992; Landry et al., 2023; Nowson et al., 1997). Second, when studies use more controlled or structured interventions, the co-twin design adds another layer of control. The calcium supplementation trials are examples of this pattern. These studies used placebo-controlled co-twin designs, standardized calcium doses, objective measurements of bone outcome, and relatively long follow-up periods to examine bone mineral density in children and adolescents (Cameron et al., 2004; Johnston et al., 1992; Nowson et al., 1997). More recently, the vegan versus omnivorous diet trial provided meals during the first 4 weeks before participants transitioned to self-prepared meals, allowed dietary exposure to be more controlled during the early phase of the intervention (Landry et al., 2023). Third, co-twin designs may also be especially useful for mechanistic or exploratory outcomes. In these studies, the goal is not only to test whether a dietary intervention changes a clinical outcome, but also to understand the biological pathways that may explain the effect. For example, Carter et al. (2025) examined microbiome, metabolomic, and immune markers in twins assigned to vegan or omnivorous diets, while Dwaraka et al. (2024) examined DNA methylation and epigenetic aging markers from the same intervention. Because these outcomes may be influenced by inherited biological differences, the co-twin design can help reduce genetic variability and make it easier to interpret whether observed biological changes are related to the dietary intervention. Co-twin RCTs may be particularly useful for smaller mechanistic nutrition trials, while large nontwin pragmatic trials may be more appropriate when the main goal is population-level generalizability.

Despite the discussed advantages, twin studies face several methodological challenges. The potential for behavioral contamination between cohabitating twins (when twins influence each other's behaviors, such as sharing diet habit) is a concern to internal validity, especially in behavioral or dietary interventions (Sumathipala et al., 2018). Ethical concerns and participant preferences may complicate recruitment, adherence, and acceptability in co-twin RCTs. For example, some twins may be less willing to enroll or may find it more difficult to adhere to the protocol when co-twins are assigned to different interventions, although allocation itself should remain determined by the randomized study design (Craig et al., 2020). Small sample sizes and recruitment challenges may also reduce statistical power and generalizability (Collins et al., 2020; Sumathipala et al., 2018). Twin populations represent only a small subset of the general population — approximately 2.4% of all live births (J. A. Martin et al., 2015), and this makes the identification of eligible twin pairs challenging. Twin registries are valuable resources for efficiently locating and enrolling twins for research. However, not all countries have well-developed twin registries. Without access to these established resources, researchers often rely on less systematic recruitment methods such as public advertising or referrals, which may lead to slower enrollment, selection bias, and less representative samples. Consequently, these recruitment difficulties can hinder the feasibility of adequately powered twin RCTs and limit the ability to conduct large-scale, multicenter studies. International collaborations that leverage existing twin registries across countries could help overcome some of these barriers by expanding the available twin participant pool and enhancing study generalizability. Integration of twin registries into omics technologies (e.g., nutrigenomics and metabolomics) can help researchers better understand cause-and-effect relationships and create more personalized diet recommendations (Boomsma et al., 2002; de Roos & Brennan, 2017; van Dongen et al., 2012).

Twin-based RCT designs can be compared with the other causal inference approaches used in nutrition research. Mendelian randomization can support causal inference by using genetic variants related to an exposure, which may reduce confounding and reverse causation. However, unlike co-twin RCTs, it does not directly test the effect of assigning participants to a specific dietary intervention, such as a supplement or dietary pattern, under trial conditions (Davey Smith & Ebrahim, 2003; Davies et al., 2018). Other within-family designs, including sibling or family-based comparisons, can reduce confounding from shared family background, but they generally provide less complete genetic control than co-twin designs (Brumpton et al., 2020; McGue et al., 2010). Crossover trials also reduce between-person variability because each participant serves as their own control. However, they may be limited by carryover effects, washout requirements, and the need for short-term or reversible interventions (Lim & In, 2021).

Future directions should include consistent and standardized methods for conducting twin trials, find ways to reduce contamination bias, and compare twin RCTs with traditional trials involving nontwin individuals to statistically optimize power and

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

feasibility in nutritional studies (Ioannidis, 2018; Trepanowski & Ioannidis, 2018). Incorporating modern technologies, such as omics analyses, microbiome profiling and digital dietary tracking tools, into co-twin studies can help researchers better understand the many interacting factors that influence how dietary exposures affect health outcomes (McAdams et al., 2021).

This review was conducted as a descriptive scoping review without a meta-analysis and did not include a quantitative synthesis of study outcomes. Our primary focus was on the methodological aspects of the included studies, such as design, sample characteristics, and use of twin models, rather than on evaluating the efficacy of the interventions or synthesizing their results. A major strength of this review is its focused evaluation of co-twin randomized controlled trials, a relatively underutilized design in nutrition research. By emphasizing methodological features, this review provided an overview of how twin designs have been implemented to strengthen causal inference in nutrition science.

## Conclusion

This scoping review highlights the unique value and methodological advantages of using twin designs, particularly co-twin control RCTs, in nutritional intervention research. Few studies with this design were identified in the nutrition literature. Co-twin control designs strengthen causal inference and allow for more precise effect estimates by controlling for genetic and shared environmental confounding. Twin studies also present unique challenges, including limited sample sizes, recruitment barriers, and ethical concerns. As nutrition science moves toward precision and personalized approaches, co-twin randomized trials may play an important role in clarifying complex diet–health relationships and interpretability of dietary intervention studies.

**Supplementary material.** To view supplementary material for this article, please visit https://doi.org/10.1017/thg.2026.10074.

**Data availability statement.** All data generated or analyzed during this study are included in this published article and its supplementary materials.

**Financial support.** Partial funding for publishing this article open access was provided by the University of California Libraries under a transformative open access agreement with the publisher.

**Competing interests.** None.

**Ethical standards.** This scoping review was exempt from Institutional Review Board (IRB) review, as it involved the synthesis of previously published, publicly available data and did not include the collection of primary data from human participants.

## References

**Berry, S. E., Valdes, A. M., Drew, D. A., Asnicar, F., Mazidi, M., Wolf, J., Capdevila, J., Hadjigeorgiou, G., Davies, R., Al Khatib, H., Bonnett, C., Ganesh, S., Bakker, E., Hart, D., Mangino, M., Merino, J., Linenberg, I., Wyatt, P., Ordovas, J. M., … Spector, T. D.** (2020). *Human postprandial responses to food and potential for precision nutrition*. *Nature Medicine*, *26*, 964–973. https://doi.org/10.1038/s41591-020-0934-0

**Boomsma, D., Busjahn, A., & Peltonen, L.** (2002). Classical twin studies and beyond. *Nature Reviews Genetics*, *3*, 872–882. https://doi.org/10.1038/nrg932

**Brumpton, B., Sanderson, E., Heilbron, K., Hartwig, F. P., Harrison, S., Vie, G. Å., Cho, Y., Howe, L. D., Hughes, A., Boomsma, D. I., Havdahl, A., Hopper, J., Neale, M. C., Nivard, M. G., Pedersen, N. L., Reynolds, C. A., Tucker-Drob, E. M., Grotzinger, A. D., Howe, L. J., … Davies, N. M.** (2020). Avoiding dynastic, assortative mating, and population stratification biases in Mendelian randomization through within-family analyses. *Nature Communications*, *11*, Article 3519. https://doi.org/10.1038/s41467-020-17117-4

**Cameron, M. A., Paton, L. M., Nowson, C. A., Margerison, C., Frame, M., & Wark, J. D.** (2004). The effect of calcium supplementation on bone density in premenarcheal females: A co-twin approach. *Journal of Clinical Endocrinology & Metabolism*, *89,* 4916–4922. https://doi.org/10.1210/jc.2003-031723

**Carter, M. M., Zeng, X., Ward, C. P., Landry, M. J., Perelman, D., Hennings, T., Meng, X., Weakley, A. M., Cabrera, A. V., Robinson, J. L., Nguyen, T., Higginbottom, S., Maecker, H. T., Sonnenburg, E. D., Fischbach, M. A., Gardner, C. D., & Sonnenburg, J. L.** (2025). *A gut pathobiont regulates circulating glycine and host metabolism in a twin study comparing vegan and omnivorous diets*. *medRxiv* [Preprint]. https://doi.org/10.1101/2025.01.08.25320192

**Chiolero, A.** (2018). Data are not enough—hurray for causality! *American Journal of Public Health*, *108,* 622–622. https://doi.org/10.2105/AJPH.2018.304338

**Collins, R., Bowman, L., Landray, M., & Peto, R.** (2020). The magic of randomization versus the myth of real-world evidence. *New England Journal of Medicine*, *382,* 674–678. https://doi.org/10.1056/NEJMsb1901642

**Costanzo, A., Liu, D., Nowson, C., Duesing, K., Archer, N., Bowe, S., & Keast, R.** (2019). A low-fat diet up-regulates expression of fatty acid taste receptor gene FFAR4 in fungiform papillae in humans: A co-twin randomised controlled trial. *British Journal of Nutrition*, *122,* 1212–1220. https://doi.org/10.1017/S0007114519001973

**Costanzo, A., Nowson, C., Orellana, L., Bolhuis, D., Duesing, K., & Keast, R.** (2018). Effect of dietary fat intake and genetics on fat taste sensitivity: A co-twin randomized controlled trial. *The American Journal of Clinical Nutrition*, *107*, 683–694. https://doi.org/10.1093/ajcn/nqy054

**Craig, J. M., Calais-Ferreira, L., Umstad, M. P., & Buchwald, D.** (2020). The value of twins for health and medical research: A third of a century of progress. *Twin Research and Human Genetics*, *23,* 8–15. https://doi.org/10.1017/thg.2020.4

**Davey Smith, G., & Ebrahim, S.** (2003). 'Mendelian randomization': Can genetic epidemiology contribute to understanding environmental determinants of disease? *International Journal of Epidemiology*, *32*, 1–22. https://doi.org/10.1093/ije/dyg070

**Davies, N. M., Holmes, M. V., & Davey Smith, G.** (2018). Reading Mendelian randomisation studies: A guide, glossary, and checklist for clinicians. *BMJ*, *362*, Article k601. https://doi.org/10.1136/bmj.k601

**de Roos, B., Aura, A. M., Bronze, M., Cassidy, A., Conesa, M. T. G., Gibney, E. R., Greyling, A., Kaput, J., Kerem, Z., Knežević, N., Kroon, P., Landberg, R., Manach, C., Milenkovic, D., Rodriguez-Mateos, A., Tomás-Barberán, F. A., van de Wiele, T., & Morand, C.** (2019). Targeting the delivery of dietary plant bioactives to those who would benefit most: From science to practical applications. *European Journal of Nutrition*, *58*, 65–73. https://doi.org/10.1007/s00394-019-02051-5

**de Roos, B., & Brennan, L.** (2017). Personalised interventions—a precision approach for the next generation of dietary intervention studies. *Nutrients*, *9*, 847. https://doi.org/10.3390/nu9080847

**Drewnowski, A., & Kawachi, I.** (2015). Diets and health: How food decisions are shaped by biology, economics, geography, and social interactions. *Big Data*, *3*, 193–197. https://doi.org/10.1089/big.2015.29001.adr

**Dwaraka, V. B., Aronica, L., Carreras-Gallo, N., Robinson, J. L., Hennings, T., Carter, M. M., Corley, M. J., Lin, A., Turner, L., Smith, R., Mendez, T. L., Went, H., Ebel, E. R., Sonnenburg, E. D., Sonnenburg, J. L., & Gardner, C. D.** (2024). Unveiling the epigenetic impact of vegan vs. omnivorous diets on aging: insights from the Twins Nutrition Study (TwiNS). *BMC Medicine*, *22*, 301. https://doi.org/10.1186/s12916-024-03490-5

**Faith, M. S., Rose, E., Matz, P. E., Pietrobelli, A., & Epstein, L. H.** (2006). Co-twin control designs for testing behavioral economic theories of child nutrition: Methodological note. *International Journal of Obesity*, *30*, 1501–1505. https://doi.org/10.1038/sj.ijo.0803303

**Favari, C., de Alvarenga, J. F. R., Sánchez-Martínez, L., Tosi, N., Mignogna, C., Cremonini, E., Manach, C., Bresciani, L., Del Rio, D., & Mena, P.** (2024). Factors driving the inter-individual variability in the metabolism and bioavailability of (poly)phenolic metabolites: A systematic review of human studies. *Redox Biology*, *71*, 103095. https://doi.org/10.1016/j.redox.2024.103095

**González, S.** (2020). Dietary bioactive compounds and human health and disease. *Nutrients*, *12*, 348. https://doi.org/10.3390/nu12020348

**Head, R. J., & Buckley, J. D.** (2020). Human variation in response to food and nutrients. *Nutrition Reviews*, *78*, 49–52. https://doi.org/10.1093/nutrit/nuaa067

**Ioannidis, J. P.** (2018). The challenge of reforming nutritional epidemiologic research. *JAMA*, *320*, 969–970.

**Jacobs Jr., D. R.** (2023). Challenges in research in nutritional epidemiology. In *Nutritional health: strategies for disease prevention* (pp. 21–31). Springer International Publishing.

**Jadad, A. R.** (1998). Randomised controlled trials: A user's guide. *Health Technology Assessment*, *2*, 214. https://doi.org/10.3310/hta2130

**Jelenkovic, A., Sund, R., Hur, Y.-M., Yokoyama, Y., Hjelmborg, J. v. B., Möller, S., Honda, C., Magnusson, P. K. E., Pedersen, N. L., Ooki, S., Aaltonen, S., Stazi, M. A., Fagnani, C., D'Ippolito, C., Freitas, D. L., Maia, J. A., Ji, F., Ning, F., Pang, Z., … Silventoinen, K.** (2016). Genetic and environmental influences on height from infancy to early adulthood: An individual-based pooled analysis of 45 twin cohorts. *Scientific Reports*, *6*, 28496. https://doi.org/10.1038/srep28496

**Jelenkovic, A., Yokoyama, Y., Sund, R., Pietiläinen, K. H., Hur, Y.-M., Willemsen, G., Bartels, M., Aaltonen, S., Ji, F., Ning, F., Pang, Z., Rebato, E., Busjahn, A., Kandler, C., Saudino, K. J., Jang, K. L., Cozen, W., Hwang, A. E., Swan, G. E., … Silventoinen, K.** (2017). Association between birthweight and later body mass index: An individual-based pooled analysis of 27 twin cohorts participating in the CODATwins project. *International Journal of Epidemiology*, *46*, 1488–1498. https://doi.org/10.1093/ije/dyx114

**Johnston Jr, C. C., Miller, J. Z., Slemenda, C. W., Reister, T. K., Hui, S., Christian, J. C., & Peacock, M.** (1992). Calcium supplementation and increases in bone mineral density in children. *New England Journal of Medicine*, *327*, 82–87. https://doi.org/10.1056/NEJM199207093270204

**Landry, M. J., Ward, C. P., Cunanan, K. M., Durand, L. R., Perelman, D., Robinson, J. L., Hennings, T., Koh, L., Dant, C., Zeitlin, A., Ebel, E. R., Sonnenburg, E. D., Sonnenburg, J. L., & Gardner, C. D.** (2023). Cardiometabolic effects of omnivorous vs vegan diets in identical twins: A randomized clinical trial. *JAMA Network Open*, *6*, e2344457. https://doi.org/10.1001/jamanetworkopen.2023.44457

**Lim, C. Y., & In, J.** (2021). Considerations for crossover design in clinical study. *Korean Journal of Anesthesiology*, *74*, 293–299. https://doi.org/10.4097/kja.21165

**Lloyd, T., Andon, M. B., Rollings, N., Martel, J. K., Landis, J. R., Demers, L. M., Eggli, D. F., Kieselhorst, K., & Kulin, H. E.** (1993). Calcium supplementation and bone mineral density in adolescent girls. *JAMA*, *270*, 841–844.

**Luft, F. C., Miller, J. Z., Weinberger, M. H., Grim, C. E., Daugherty, S. A., & Christian, J. C.** (1987). Influence of genetic variance on sodium sensitivity of blood pressure. *Klinische Wochenschrift*, *65*, 101–109. https://doi.org/10.1007/BF017273349

**Manach, C., Milenkovic, D., Van de Wiele, T., Rodriguez-Mateos, A., de Roos, B., Garcia-Conesa, M. T., Landberg, R., Gibney, E. R., Heinonen, M., Tomás-Barberán, F., & Morand, C.** (2017). Addressing the inter-individual variation in response to consumption of plant food bioactives: towards a better understanding of their role in healthy aging and cardiometabolic risk reduction. *Molecular Nutrition & Food Research*, *61*, 1600557. doi: 10.1002/mnfr.201600557

**Martin, J. A., Hamilton, B. E., Osterman, M. J., Driscoll, A. K., & Drake, P.** (2015). Births: Final data for 2015. *National Vital Statistics Reports*, *66*, 1–70. https://www.cdc.gov/nchs/data/nvsr/nvsr66/nvsr66_01.pdf

**Martin, N. G., Carr, A. B., Oakeshott, J. G., & Clark, P.** (1982). Co-twin control studies: Vitamin C and the common cold. *Progress in Clinical and Biological Research*, *103*, 365–373.

**McAdams, T. A., Rijsdijk, F. V., Zavos, H. M., & Pingault, J. B.** (2021). Twins and causal inference: Leveraging nature's experiment. *Cold Spring Harbor Perspectives in Medicine, 11*, a039552. https://doi.org/10.1101/cshperspect.a039552

**McGue, M., Osler, M., & Christensen, K.** (2010). Causal inference and observational research: the utility of twins. *Perspectives on Psychological Science*, *5*, 546–556. https://doi.org/10.1177/1745691610383511

**Munn, Z., Peters, M. D. J., Stern, C., Tufanaru, C., McArthur, A., & Aromataris, E.** (2018). Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Medical Research Methodology*, *18*, 143. https://doi.org/10.1186/s12874-018-0611-x

**Ni Lochlainn, M., Bowyer, R. C., Moll, J. M., García, M. P., Wadge, S., Baleanu, A. F., Nessa, A., Sheedy, A., Akdag, G., Hart, D., Raffaele, G., Seed, P. T., Murphy, C., Harridge, S. D. R., Welch AA, Greig, C., Whelan, K., & Steves, C. J.** (2024). Effect of gut microbiome modulation on muscle function and cognition: the PROMOTe randomised controlled trial. *Nature Communications*, *15*, 1859. https://doi.org/10.1038/s41467-024-46116-4

**Nowson, C. A., Green, R. M., Hopper, J. L., Sherwin, A. J., Young, D., Kaymakci, B., Guest, C. S., Smid, M., Larkins, R. G., & Wark, J. D.** (1997). A co-twin study of the effect of calcium supplementation on bone density during adolescence. *Osteoporosis International*, *7*, 219–225. https://doi.org/10.1007/BF01622292

**Okeh, U. M., & Ugwu, A. C.** (2009). Randomized controlled trials: The most powerful tool in modern clinical research. *East African Journal of Public Health*, *6*, 120–124.

**Pallister, T., Spector, T. D., & Menni, C.** (2014). Twin studies advance the understanding of gene–environment interplay in human nutrigenomics. *Nutrition Research Reviews*, *27*, 242–251. https://doi.org/10.1017/S0954422414000152

**Perrinjaquet-Moccetti, T., Busjahn, A., Schmidlin, C., Schmidt, A., Bradl, B., & Aydogan, C.** (2008). Food supplementation with an olive (*Olea europaea* L.) leaf extract reduces blood pressure in borderline hypertensive monozygotic twins. *Phytotherapy Research*, *22*, 1239–1242. https://doi.org/10.1002/ptr.2455

**Plomin, R., & Haworth, C. M.** (2010). Genetics and intervention research. *Perspectives on Psychological Science*, *5*, 557–563. https://doi.org/10.1177/1745691610383494

**Polderman, T. J., Benyamin, B., De Leeuw, C. A., Sullivan, P. F., Van Bochoven, A., Visscher, P. M., & Posthuma, D.** (2015). Meta-analysis of the heritability of human traits based on fifty years of twin studies. *Nature Genetics*, *47*, 702–709. https://doi.org/10.1038/ng.3285

**Reeves, B. C., Van Binsbergen, J., & Van Weel, C.** (2005). Systematic reviews incorporating evidence from nonrandomized study designs: Reasons for caution when estimating health effects. *European Journal of Clinical Nutrition*, *59*, 155–161. https://doi.org/10.1038/sj.ejcn.1602186

**Segal, N. L.** (2017). Twins reared together and apart: The science behind the fascination. *Proceedings of the American Philosophical Society*, *161*, 1–17.

**Silventoinen, K., Jelenkovic, A., Sund, R., Honda, C., Aaltonen, S., Yokoyama, Y., Magnusson, P. K. E., Pedersen, N. L., Ooki, S., Ji, F., Ning, F., Pang, Z., Rebato, E., Busjahn, A., Kandler, C., Saudino, K. J., Jang, K. L., Cozen, W., Hwang, A. E., … Kaprio, J.** (2015). The CODATwins Project: The cohort description of collaborative project of development of anthropometrical measures in twins to study macro-environmental variation in genetic and environmental effects on anthropometric traits. *Twin Research and Human Genetics*, *18*, 348–360. https://doi.org/10.1017/thg.2015.29

**Silventoinen, K., Jelenkovic, A., Sund, R., Hur, Y.-M., Yokoyama, Y., Honda, C., Magnusson, P. K. E., Pedersen, N. L., Ooki, S., Aaltonen, S., Ji, F., Ning, F., Pang, Z., Rebato, E., Busjahn, A., Kandler, C., Saudino, K. J., Jang, K. L., Cozen, W., … Kaprio, J.** (2016). Genetic and environmental effects on body mass index from infancy to the onset of adulthood: An individual-based pooled analysis of 45 twin cohorts participating in the Collaborative Project of Development of Anthropometrical Measures in Twins (CODATwins) study. *The American Journal of Clinical Nutrition*, *104*, 371–379. https://doi.org/10.3945/ajcn.116.130252

**Stolberg, H. O., Norman, G., & Trop, I.** (2004). Randomized controlled trials. *American Journal of Roentgenology*, *183*, 1539–1544. https://doi.org/10.2214/ajr.183.6.01831539

**Sumathipala, A., Yelland, L., Green, D., Shepherd, T., Jayaweera, K., Ferreira, P., & Craig, J. M.** (2018). Twins as participants in randomized controlled trials: A review of published literature. *Twin Research and Human Genetics*, *21*, 51–56. https://doi.org/10.1017/thg.2017.74

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press

**Tan, Q., Christiansen, L., von Bornemann Hjelmborg, J., & Christensen, K.** (2015). Twin methodology in epigenetic studies. *Journal of Experimental Biology*, *218*, 134–139. https://doi.org/10.1242/jeb.107151

**Trepanowski, J. F., & Ioannidis, J. P.** (2018). Perspective: limiting dependence on nonrandomized studies and improving randomized trials in human nutrition research: Why and how. *Advances in Nutrition*, *9*, 367–377. https://doi.org/10.1093/advances/nmy014

**Tricco, A. C., Lillie, E., Zarin, W., O'Brien, K. K., Colquhoun, H., Levac, D., Moher, D., Peters, M. D. J., Horsley, T., Weeks, L., Hempel, S., Akl, E. A., Chang, C., McGowan, J., Stewart, L., Hartling, L., Aldcroft, A., Wilson, M. G., Garritty, C., Lewin, S., Godfrey, C. M., Macdonald, M. T., Langlois, E. V., Soares-Weiser, K., Moriarty, J., Clifford, T., Tunçalp, Ö., & Straus, S. E.** (2018). PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Annals of Internal Medicine*, *169*, 467–473. https://doi.org/10.7326/M18-0850

**Turner-McGrievy, G. M., Wilcox, S., Frongillo, E. A., Murphy, E. A., Hutto, B., Wilson, M., Davey, M., Bernhart, J. A., Okpara, N., Bailey, S., & Hu, E.** (2023). Effect of a plant-based vs omnivorous soul food diet on weight and lipid levels among African American adults: A randomized clinical trial. *JAMA Network Open*, *6*, Article e2250626. https://doi.org/10.1001/jamanetworkopen.2022.50626

**van Dongen, J., Slagboom, P. E., Draisma, H. H., Martin, N. G., & Boomsma, D. I.** (2012). The continuing value of twin studies in the omics era. *Nature Reviews Genetics*, *13*, 640–653. https://doi.org/10.1038/nrg3243

**Vitolins, M. Z., & Case, T. L.** (2020). What makes nutrition research so difficult to conduct and interpret? *Diabetes Spectrum, 33*, 113–117. https://doi.org/10.2337/ds19-0077

**Zeitlin, A. B., Ward, C. P., Cooper, A. O. M., Landry, M. J., Krenek, A. M., Durand, L. R., Cunanan, K. M., Robinson, J. L., Dant, C. C., & Gardner, C. D.** (2025). Diet quality and comparison of plant-based versus omnivore diets in identical twins: A secondary analysis of the Twins Nutrition Study (TwiNS). *Current Developments in Nutrition*, *9,* 107549. https://doi.org/10.1016/j.cdnut.2025.107549

https://doi.org/10.1017/thg.2026.10074 Published online by Cambridge University Press