Placenta and Reproductive Medicine

REVIEW ARTICLE

The impact of diet on male semen quality and fertility: A comprehensive review

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ABSTRACT

Male factor infertility contributes to approximately 50% of all infertility cases, and global semen quality has declined substantially over recent decades, with modifiable lifestyle factors, particularly diet, implicated as key drivers. This comprehensive review synthesizes evidence from observational studies and randomized controlled trials examining associations between dietary components and male reproductive outcomes, with emphasis on underlying biological mechanisms. Despite growing interest in this field, well-designed randomized controlled trials examining clinically meaningful fertility outcomes remain scarce, and most available evidence derives from observational studies with inherent methodological limitations. Current evidence suggests that healthy dietary patterns, particularly the Mediterranean diet, are associated with superior semen parameters through mechanisms including reduced oxidative stress, improved hormonal profiles, and epigenetic modulation. Specific foods (nuts, fish, fruits, vegetables) and nutrients (omega-3 fatty acids, selenium, zinc, coenzyme Q10, antioxidants) demonstrate beneficial effects on sperm concentration, motility, morphology, and DNA integrity. However, while improvements in conventional semen parameters are well-documented, evidence for enhanced pregnancy and live birth rates remains limited, with meta-analyses showing inconsistent associations between dietary factors and assisted reproductive technology (ART) outcomes. Whether improvements in sperm parameters translate to clinically meaningful increases in live birth rates remains an open question requiring further investigation. Conversely, Western dietary patterns, ultra-processed foods, and specific dietary components (processed meats, trans fatty acids, phytoestrogens at high doses) are associated with poorer semen quality through pro-inflammatory pathways, endocrine disruption, and direct genotoxicity. Notably, pesticide residues in conventionally grown produce may attenuate the benefits of fruit and vegetable consumption *via* oxidative stress and androgen receptor antagonism. Weight management through dietary intervention significantly improves sperm parameters, with emerging evidence suggesting glucagon-like peptide-1 (GLP-1) receptor agonists may offer additional benefits for obese men. This review identifies critical knowledge gaps—including the paucity of trials with live birth as primary outcome, heterogeneity in study designs, and limited evidence for personalized nutrition approaches—and provides evidence-based dietary recommendations for men planning paternity.

Keywords: male infertility, semen quality, diet, oxidative stress, deoxyribonucleic acid fragmentation, endocrine disruption

INTRODUCTION

Infertility, defined as the failure to achieve pregnancy after 12 months of regular unprotected intercourse, affects approximately 15% of couples worldwide, with male factors contributing to 40%-50% of cases.[1] Of

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Received: 25 March 2026; Revised: 10 May 2026; Accepted: 10 June 2026
https://doi.org/10.54844/prm.2026.1231

particular concern, multiple meta-analyses have documented a significant global decline in semen quality over the past five decades. Levine and colleagues reported a 50%-60% decrease in sperm concentration and total sperm count among men from industrialized countries between 1973 and 2011,[2] with subsequent analyses confirming this downward trajectory continuing into the twenty-first century.[3] More recently, Priskorn and colleagues extended this paradigm by demonstrating that semen quality may serve as a biomarker of overall male health, with men possessing high-quality semen living on average more than two years longer than those with severely impaired parameters.[4] This observation underscores the importance of understanding determinants of semen quality beyond fertility outcomes alone.

The multifactorial etiology of declining male reproductive health implicates environmental pollutants, occupational exposures, and modifiable lifestyle factors. Among these, diet has emerged as a particularly important and potentially reversible determinant of spermatogenic function. Spermatozoa are uniquely susceptible to nutritional influences due to their high polyunsaturated fatty acid (PUFA) membrane content, limited cytoplasmic antioxidant defenses, and dependence on adequate substrate supply for DNA synthesis and methylation.[5] The short development window of sperm (approximately 74 days) creates opportunities for dietary interventions to produce measurable improvements within relatively brief periods.

Over the past five years, research has shifted from focusing on individual nutrients to broader dietary patterns, microbiome interactions, and clinical fertility outcomes. Contemporary investigations increasingly emphasize whole dietary patterns, the role of the gut and seminal microbiomes, epigenetic modifications, and—critically—clinical fertility outcomes such as live birth rates.[6] This evolution reflects recognition that fertility is a multifactorial outcome unlikely to be dramatically altered by single nutrients in isolation, and that semen parameters, while informative, are imperfect surrogates for reproductive success.

This comprehensive review synthesizes current evidence from observational studies and randomized controlled trials examining the relationship between dietary factors and male reproductive health, with particular emphasis on the biological mechanisms linking specific dietary components to spermatogenesis, sperm function, and fertility outcomes. Where possible, we prioritize evidence from recent systematic reviews and meta-analyses, and we explicitly address the methodological challenges that complicate interpretation of this literature (Figure 1).

BIOLOGICAL MECHANISMS LINKING DIET TO MALE REPRODUCTIVE FUNCTION

Oxidative stress and antioxidant defense systems

Oxidative stress represents a central mechanism through which diet influences male fertility. Spermatozoa are uniquely vulnerable to oxidative damage due to three inherent characteristics: their plasma membrane contains exceptionally high concentrations of PUFAs (particularly docosahexaenoic acid, [DHA]), which are susceptible to lipid peroxidation; their limited cytoplasm contains minimal antioxidant enzymes; and their abundant mitochondria generate substantial reactive oxygen species (ROS) as byproducts of energy metabolism.[7] Aitken and colleagues have demonstrated that human spermatozoa possess a unique nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) oxidase system that generates ROS as part of normal sperm function, but when dysregulated, this system becomes a major source of oxidative injury.[7]

The antioxidant defense system in seminal plasma comprises both enzymatic components (superoxide dismutase, catalase, glutathione peroxidase) and non-enzymatic scavengers (vitamins C and E, glutathione, urate, and dietary polyphenols). Tremellen has estimated that oxidative stress accounts for 30%-80% of male infertility cases, with reactive oxygen species causing peroxidative damage to sperm membranes, DNA fragmentation, and impaired motility.[8] A Cochrane systematic review by de Ligny and colleagues, encompassing 61 randomized trials with 6264 subfertile men, found that antioxidant supplementation improved live birth rates (odds ratio [OR] = 1.79, 95% confidence interval [CI]: 1.17-2.75, based on 7 studies) and clinical pregnancy rates (OR = 2.97, 95% CI: 2.13-4.15, based on 17 studies).[9] However, the authors noted significant heterogeneity and called for larger, well-designed trials. Notably, the quality of evidence was rated as low to very low for most outcomes, primarily due to risk of bias, imprecision, and inconsistency across studie.[9]

The molecular basis for antioxidant protection involves multiple pathways. Vitamin E (α-tocopherol) incorporates into cell membranes and terminates lipid peroxidation chain reactions by donating hydrogen atoms to peroxyl radicals.[10] In seminal plasma, the physiological concentration of vitamin C ranges from 40-50 μmol/L; daily intake exceeding 200 mg may reduce absorption rates from 80% to below 50%, indicating a threshold effect for antioxidant supplementation.[11] Vitamin C regenerates oxidized vitamin E and directly neutralizes superoxide and hydroxyl radicals in aqueous environments.[11] Selenium, as a component of gluta-

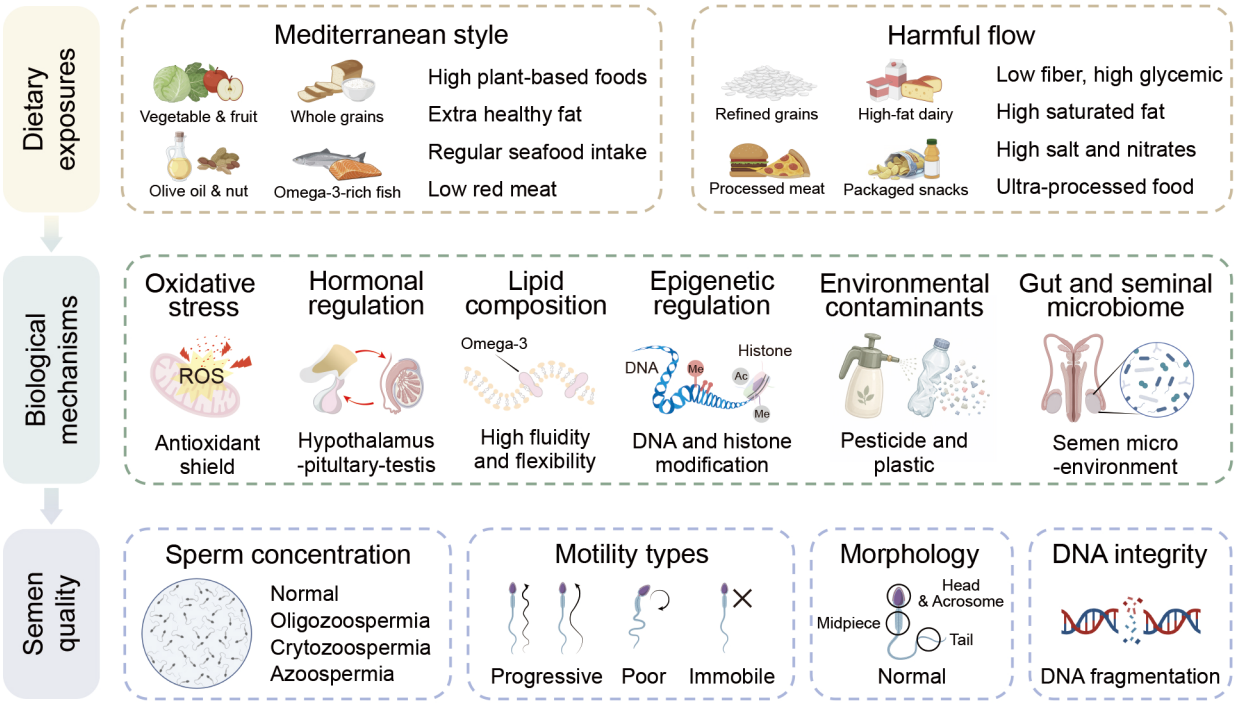

Figure 1. Dietary exposures and semen-quality outcomes: biological pathways and functional effects. Schematic overview of beneficial and harmful dietary exposures and their relationships with key biological mechanisms, including oxidative stress, hormonal regulation, membrane lipid composition, epigenetic regulation, environmental contaminants, and gut and seminal microbiome, ultimately influencing semen-quality outcomes such as sperm concentration, total sperm count, motility, progressive motility, morphology, and DNA integrity. ROS, reactive oxygen species; DNA, deoxyribonucleic acid.

thione peroxidase (GPx) and thioredoxin reductase, catalyzes the reduction of hydrogen peroxide and organic hydroperoxides.[12] A U-shaped dose-response relationship for selenium has been well-established: daily intake below 40 μg is associated with inadequate GPx activity, while intake exceeding 200 μg (several times the recommended dietary allowance of 60 μg) may impair sperm mitochondrial function through the formation of seleno-sulfide bonds.[12] Zinc stabilizes sperm chromatin and inhibits NADPH oxidase, reducing superoxide generation.[13]

Lipid metabolism and membrane fluidity

The fatty acid composition of sperm membranes is critical for fertility. Lenzi and colleagues demonstrated that DHA constitutes up to 20% of total fatty acids in mature sperm membranes, compared with only 4% in immature germ cells, indicating that DHA accumulation is an essential feature of spermiogenesis.[14] DHA content correlates positively with sperm motility (r = 0.43, $P < 0.01$) and normal morphology (r = 0.38, $P < 0.05$) in normozoospermic men.[15]

The testis possesses a unique capacity for PUFA metabolism. Sertoli cells express Δ5- and Δ6-desaturases at levels comparable to liver, enabling conversion of dietary linoleic acid (18: 2n-6) and α-linolenic acid (18: 3n-3) into longer-chain PUFAs including arachidonic acid (20 : 4, n-6), eicosapentaenoic acid (EPA, 20 : 5, n-3), and DHA (22 : 6, n-3).[16] Retterstøl and colleagues demonstrated that isolated human testicular cells preferentially convert omega-3 precursors into DHA over converting omega-6 precursors into docosapentaenoic acid (22 : 5, n-6), explaining the high DHA content of sperm despite typically higher dietary omega-6 intake.[17]

Recent advances have elucidated additional mechanistic pathways. Yang and colleagues demonstrated that omega-3 PUFAs regulate peroxisome proliferator-activated receptor (PPAR) expression in testicular cells, with PPARγ playing a particularly important role in supporting cellular energy metabolism during sperm capacitation.[18] DHA also appears essential for acrosome formation through its role in vesicle fusion during spermatogenesis, mediated by acyl-CoA synthetase 6 (ACSL6) which facilitates DHA incorporation into germ cells.[19]

Hormonal regulation via the hypothalamic-pituitary-gonadal axis

Dietary factors influence male fertility through modulation of the hypothalamic-pituitary-gonadal (HPG) axis. Testosterone synthesis in Leydig cells requires cholesterol as substrate, with steroidogenic

acute regulatory protein (StAR) mediating cholesterol transport into mitochondria—a rate-limiting step regulated by luteinizing hormone.[20] Dietary cholesterol and fatty acids directly influence substrate availability, while specific nutrients modulate enzyme activities.

Volek and colleagues demonstrated that low-fat diets (20% of energy from fat) decrease serum testosterone by 10%-15% compared with higher-fat diets (40% of energy from fat), suggesting that adequate dietary fat is necessary for optimal testosterone synthesis.[21] Conversely, obesity-induced hyperestrogenemia results from increased aromatase activity in adipose tissue, which converts testosterone to estradiol, suppressing gonadotropin secretion *via* negative feedback.[22]

Leptin, secreted by adipocytes in proportion to fat mass, directly inhibits Leydig cell steroidogenesis by reducing StAR expression and cholesterol side-chain cleavage enzyme (CYP11A1) activity.[23] Isidori and colleagues demonstrated that leptin concentrations are inversely correlated with testosterone levels independent of body mass index (BMI), suggesting direct gonadal effects.[24]

Epigenetic regulation

Emerging evidence indicates that paternal diet influences sperm epigenetics, with potential transgenerational effects. Sperm DNA methylation patterns are established during spermatogenesis and are susceptible to nutritional modulation. Lambrot and colleagues demonstrated that low dietary folate in male mice alters sperm DNA methylation at imprinted genes, with offspring showing increased congenital malformations and decreased pregnancy rates.[25]

MicroRNAs (miRNAs) in sperm represent another epigenetic mechanism. Salas-Huetos and colleagues identified that sperm from asthenozoospermic men show differential expression of multiple miRNAs compared with normozoospermic controls, and that nut consumption significantly altered expression of hsa-miR-34b-3p, which targets genes involved in cell motility.[26] This provides direct evidence that dietary interventions can modify the sperm epigenome.

Beyond miRNAs, sperm carry tRNA-derived fragments (tRFs) and ribosomal RNA-derived small RNAs (rsRNAs) that are crucial for early embryonic development. A comprehensive review by Xu and colleagues synthesized evidence that paternal diet-induced epigenetic alterations can influence offspring metabolic health through both DNA methylation-dependent and-independent mechanisms, including histone modifications and non-coding RNAs.[27] Sharma and colleagues demonstrated that in a mouse model of high-fat diet-induced obesity, the profile of sperm tRFs was altered, and injection of these tRFs into normal fertilized oocytes recapitulated the metabolic disorder phenotype in offspring.[28] This suggests that paternal diet not only affects fertilization but may also influence offspring health through non-DNA methylation pathways (*i.e.*, RNA-mediated intergenerational inheritance), representing a frontier in reproductive medicine. However, translation of these findings to humans remains limited, and the clinical significance of diet-induced epigenetic changes in human sperm awaits further investigation.[27]

DIETARY PATTERNS

The mediterranean diet

The Mediterranean diet, characterized by high consumption of vegetables, fruits, legumes, whole grains, nuts, olive oil, and moderate fish and poultry intake with limited red meat and processed foods, has been most extensively studied in relation to male fertility. Two recent meta-analyses have quantified these benefits.

Agarwal and colleagues conducted a comprehensive systematic review and meta-analysis of 11 eligible articles comprising 2558 individuals, demonstrating significant positive associations between Mediterranean diet adherence and multiple semen parameters.[29] Meta-analysis of 8 observational studies (n = 1835 individuals) revealed that higher Mediterranean diet adherence was significantly associated with increased sperm count (mean difference: 24.37 million spermatozoa; 95% CI: 1.30-47.44; I^2 = 89%), total motility (8.81%; 95% CI: 2.26-15.37; I^2 = 88%), progressive motility (7.49%; 95% CI: 1.47-13.50; I^2 = 86%), and normal morphology (1.02%; 95% CI: 0.21-1.82; I^2 = 77%).[29] The substantial heterogeneity (I^2 = 77%-89%) reflects differences in study populations, dietary assessment methods, and Mediterranean diet scoring systems. Subgroup analysis revealed that studies adjusting for physical activity, energy intake, and socioeconomic status (n = 5) showed smaller effect sizes for sperm concentrationt (β = 18.7 million/mL) compared to unadjusted studies (β = 32.4 million/mL), suggesting that residual confounding may overestimate true associations, particularly given that health-conscious men are more likely to both adopt healthy diets and engage in other fertility-promoting behaviors.

A systematic review of dietary patterns and male fertility similarly concluded that while healthy dietary patterns are consistently associated with improved sperm parameters, and the evidence for clinical outcomes such as pregnancy and live birth remains limited and inconsistent.[6] This distinction is critical: improvements in sperm concentration or motility do not automatically translate to higher live birth rates, and studies examining clinically meaningful endpoints are urgently needed.

A cross-sectional study by Palani and colleagues of 274 Kurdish men attending fertility clinics demonstrated that higher adherence to the alternative Mediterranean diet (aMED) was positively correlated with sperm concentration (B = 1.32, P = 0.001), total sperm count (B = 1.12, P = 0.001), and total motility (B = 0.71, P = 0.001).[30] Participants in the highest adherence tertile had significantly better sperm parameters (concentration: 57.53 ± 36.16 million/mL; total motility: 73.4% ± 25.9%) compared to those in the lowest tertile (11.92 ± 22.29 million/mL; 36.7% ± 33.8%, respectively).

Randomized controlled trials have now provided causal evidence supporting these observational findings. Caruso and colleagues conducted a 6-month randomized trial comparing Mediterranean diet to a low-fat diet in 160 healthy young Italian men.[31] The Mediterranean diet group demonstrated significantly greater increases in sperm concentration (mean difference: 1.93 million/mL) and total sperm count (mean difference: 8.02 million) compared to controls. Similarly, Montano and colleagues randomized 263 healthy young men living in polluted Italian areas to a 4-month Mediterranean diet and physical activity intervention versus standard dietary guidelines.[32] The intervention group showed significant improvements in sperm concentration, total and progressive motility, and normal morphology, while these parameters declined in controls. Importantly, the intervention group also showed increased semen total antioxidant capacity, directly linking dietary change to reduced oxidative stress.

Ultra-processed foods and Western dietary patterns

The Western dietary pattern, characterized by high intakes of red and processed meats, refined grains, high-fat dairy, and ultra-processed foods, has been consistently associated with poorer semen quality. Eslamian and colleagues conducted a case-control study of 107 asthenozoospermic men and 235 normozoospermic controls, finding that adherence to a Western dietary pattern was positively associated with asthenozoospermia risk (OR = 2.86; 95% CI: 1.83-2.97) after adjusting for potential confounders.[33] The Western pattern, identified through factor analysis, included high intakes of organ meats, red and processed meats, sugar, soft drinks, confectionery, refined grains, potatoes, fast foods, high-fat dairy products, hydrogenated fats, and mayonnaise.

A landmark randomized controlled crossover trial by Preston and colleagues compared 3-week periods of ultra-processed versus unprocessed diets in healthy young men, with both diets matched for caloric and macronutrient content.[34] Despite equivalent caloric intake, the ultra-processed diet resulted in significantly greater weight gain (1.3-1.4 kg) and fat mass accumulation (approximately 1 kg), increased cholesterol ratio (Low-density lipoprotein [LDL] : high-density lipoprotein [HDL]), and—critically—decreased serum follicle-stimulating hormone (FSH) levels and a trend toward reduced total sperm motility. However, a methodological limitation merits consideration: although the two phases were matched for macronutrients and calories, they could not be matched for micronutrients (zinc, selenium, folate) and phytochemical content—intake of these essential nutrients was significantly lower during the ultra-processed phase. Therefore, the observed decline in sperm parameters may partly reflect micronutrient deficiency rather than direct toxicity from ultra-processed foods or plasticizers. Within a substitution effect framework, future research should focus on the net effect of replacing Western dietary patterns with Mediterranean-style diets, rather than evaluating the harm of isolated dietary patterns.

Mechanistically, the ultra-processed diet was associated with differential accumulation of environmental pollutants, including a trend toward increased serum levels of the phthalate metabolite mono-carboxy-isononyl phthalate (cxMINP).[34] Phthalates, which migrate from plastic packaging into foods, have documented endocrine-disrupting effects and may represent an underappreciated mechanism linking ultra-processed food consumption to impaired reproductive health. Buckley and colleagues previously demonstrated that ultra-processed food consumption is associated with higher urinary phthalate metabolite concentrations in the United States (US) National Health and Nutrition Examination Survey.[35] A recent systematic review and meta-analysis by Coppeta and colleagues confirmed that micro-pollutants, including phthalates, are consistently associated with reduced sperm concentration (SMD = -0.48) and testosterone levels across 31 human studies.[36]

SPECIFIC FOODS AND NUTRIENTS

Nuts: mechanistic insights from randomized trials

Nuts represent the food group with the most robust evidence from randomized controlled trials for improving semen quality. Two landmark trials have established the efficacy of nut consumption and elucidated underlying mechanisms.

Robbins and colleagues randomized 117 healthy young men consuming Western-style diets to receive 75 g of whole-shelled walnuts daily or continue their usual diet without tree nuts for 12 weeks.[37] The walnut-supplemented group demonstrated significant improvements in sperm vitality, motility, and morphology compared to controls. Serum fatty acid analysis revealed increased

omega-6 and omega-3 (particularly alpha-linolenic acid [ALA]) concentrations, with ALA increasing from 0.61% to 0.79% of total fatty acids ($P < 0.001$). Importantly, sperm ALA levels were inversely correlated with sex chromosome nullisomy (r -0.41, $P = 0.002$), suggesting that incorporation of plant-derived omega-3 into sperm membranes may protect against chromosomal abnormalities during meiosis.

Salas-Huetos and colleagues extended these findings in a 14-week randomized trial of 119 healthy men receiving 60 g of mixed nuts (30 g walnuts, 15 g almonds, 15 g hazelnuts) daily versus continued Western diet without nuts.[26,38] The nut group showed significant improvements in total sperm count (median increase: 4.45 million; $P = 0.002$), vitality ($P = 0.003$), total motility ($P = 0.006$), progressive motility ($P = 0.036$), and normal morphology ($P = 0.008$). The clinical significance of a 4.45 million increase in total sperm count should be interpreted in context of the world health organization (WHO) fifth edition reference limit (39 million). For men with baseline sperm counts near normal (as in this study population), this absolute increase theoretically improves pregnancy probability by approximately 5%-8%. However, for oligozoospermic men (*e.g.*, < 15 million/mL), the same absolute increase would represent a relative improvement exceeding 30%, suggesting that nut interventions may offer greater benefit-cost ratios in this subpopulation—a hypothesis warranting dedicated randomized controlled trials (RCTs). Critically, this study explored potential mechanisms at multiple molecular levels:

DNA Fragmentation: Nut consumption significantly reduced sperm DNA fragmentation (SDF) measured by the terminal deoxynucleotidyl transferase dUTP nick end labeling TUNEL assay ($P < 0.001$), with SDF decreasing from 15.2% to 11.9% in the nut group while remaining unchanged in controls.[26] SDF was inversely correlated with vitality (ρ = -0.225, $P = 0.027$) and total sperm count (ρ = -0.317, $P = 0.002$), indicating that reduced DNA damage mediated improvements in conventional semen parameters.

Epigenetic Regulation: The nut group showed decreased expression of hsa-miR-34b-3p ($P = 0.036$), a microRNA implicated in cell motility regulation. Target genes of this miRNA include cyclin-dependent kinase 6 (CDK6), mitogen-activated protein kinase kinase 1 (MAP2K1), and p21 (RAC1) activated kinase 1 (PAK1)—all involved in cell motility pathways.[26] This represents the first demonstration that dietary intervention alters sperm miRNA expression in humans.

Lipid Peroxidation: Although ROS levels did not differ significantly between groups, negative correlations between total motility and ROS (ρ = -0.261, $P = 0.010$) and between total sperm count and ROS (ρ = -0.281, $P = 0.005$) support the role of oxidative stress in sperm function.

Fruits, vegetables, and pesticide residues

While fruits and vegetables are universally recommended for health, their relationship with semen quality is complicated by pesticide contamination. Chiu and colleagues developed a novel approach using United States Department of Agriculture Pesticide Data Program surveillance data to classify fruits and vegetables as high versus low-to-moderate pesticide residue foods.[39] In 155 men from the Environment and Reproductive Health Study providing 338 semen samples, total fruit and vegetable intake was unrelated to semen quality. However, high-pesticide-residue fruit and vegetable consumption was inversely associated with total sperm count, percentage of morphologically normal sperm, and ejaculate volume. Men in the highest intake quartile ($\geqslant$ 1.5 servings/d) had 49% lower total sperm count (95% CI: 31%-63%) and 32% lower normal morphology (95% CI: 7%-58%) compared to men in the lowest quartile (< 0.5 servings/d). Conversely, low-to-moderate pesticide residue fruit and vegetable intake was positively associated with normal sperm morphology, with men in the highest quartile showing 7.8% normal forms versus 5.7% in the lowest quartile (P-trend = 0.04).

From an epidemiological perspective, the exposure assessment method developed by Chiu and colleagues—a pesticide residue exposure score based on food frequency questionnaires (FFQ) linked to United States department of agriculture (USDA) surveillance data—represents an innovative tool for large-scale studies, although it cannot replace biomonitoring. This approach has measurement error limitations: it does not account for individual washing and cooking practices, assumes uniform residue sources across individuals, and cannot distinguish specific pesticides. Nevertheless, its consistency with biomonitoring studies (*e.g.*, Meeker and colleagues showing inverse associations between urinary organophosphate metabolites and sperm parameters) satisfies the Bradford Hill criterion of consistency, strengthening causal evidence for pesticide residues as modulators of male fertility.

The biological plausibility of pesticide effects is supported by mechanistic studies. Organophosphate pesticides, commonly used in conventional agriculture, inhibit acetylcholinesterase but also induce oxidative stress and DNA damage. Meeker and colleagues demonstrated that urinary concentrations of organophosphate metabolites (dialkyl phosphates) are inversely associated with sperm concentration and motility in men from the

general population.[40] Chlorpyrifos and its metabolite 3, 5, 6-trichloro-2-pyridinol (TCPY) have been shown to decrease testosterone production in Leydig cells by inhibiting StAR protein expression and cholesterol transport.[41]

A study by Juhler and colleagues of 256 Danish farmers found that men who consumed conventional fruits and vegetables had significantly lower proportions of morphologically normal spermatozoa than men who consumed organic diets (defined as ⩾ 50% of fruits and vegetables being organic).[42] This field study complements the Chiu findings by demonstrating that real-world choices between conventional and organic produce may influence semen quality.

Phytoestrogens and soy: dose-dependent effects

The relationship between soy consumption and male fertility remains contentious, with studies yielding conflicting results possibly due to differences in baseline exposure levels, population characteristics, and outcomes measured.

Evidence for adverse effects

A Chinese case-control study by Xia and colleagues of 608 infertile men and 469 fertile controls found that urinary concentrations of the isoflavones daidzein and genistein were positively associated with idiopathic male infertility risk and inversely associated with sperm concentration, total count, and motility.[43] Men in the highest quintile of daidzein exposure had 2.5-fold increased infertility odds (95% CI: 1.4-4.5) compared to the lowest quintile. The geometric mean urinary daidzein concentration in this Chinese population was 72.2 μg/g creatinine—substantially higher than levels typically observed in Western populations, reflecting the high soy content of traditional Asian diets.

Chavarro and colleagues studied 99 male partners of subfertile couples in the United States and found that soy food intake was inversely associated with sperm concentration (*P*-trend = 0.02).[44] Men in the highest intake category (⩾ 0.3 servings/d) had 41 million/mL lower sperm concentration than men who did not consume soy foods. Isoflavone intake showed similar inverse associations, though not statistically significant for individual compounds.

Evidence for null or protective effects

A large United Kingdom (UK) case-referent study by Povey and colleagues of 1907 men attending infertility clinics reported that higher daidzein intake was associated with reduced risk of low motile sperm concentration (OR = 0.58; 95% CI: 0.42-0.82) , suggesting a protective effect.[45] Genistein intake showed similar protective associations (OR = 0.60; 95% CI: 0.43-0.83) . These divergent findings may reflect the substantially lower exposure levels in the UK population (median daidzein intake approximately 3.7 μg/d) compared to China, suggesting a non-linear dose-response relationship with potential beneficial effects at low doses and adverse effects at high doses.

Mínguez-Alarcó*n* and colleagues examined 184 men from couples undergoing infertility treatment and found no association between soy food intake and fertilization rates, embryo quality, implantation, clinical pregnancy, or live birth after *in vitro* fertilization (IVF).[46] Adjusted live birth rates per initiated cycle were 0.36, 0.42, 0.36, and 0.37 across increasing quartiles of soy intake (*P*-trend = 0.87). This suggests that even if soy affects conventional semen parameters, these effects may not translate to clinically meaningful differences in assisted reproductive technology (ART) outcomes.

Mechanistic basis

The estrogenic activity of isoflavones results from their structural similarity to 17β-estradiol, enabling binding to estrogen receptors (ERα and ERβ). Kuiper and colleagues demonstrated that genistein has higher affinity for ERβ than ERα, with relative binding affinities of 87 and 4, respectively, compared to estradiol (100).[47] ERβ is the predominant estrogen receptor in testes and sperm, suggesting that isoflavones could directly influence spermatogenesis through ERβ-mediated pathways. However, studies in ERβ knockout mice show complex phenotypes, with both enhanced and impaired spermatogenesis reported depending on developmental stage and genetic background.[48] Additionally, the fermentation state of soy products may alter their biological effects. Isoflavones in fermented soy products (*e.g.*, miso, tempeh) are predominantly present as aglycones, which have higher absorption rates than the glycoside forms found in non-fermented products.[49,50] Furthermore, traditional soy foods such as tofu contain calcium, magnesium, and arginine that may partially counteract any negative effects of isoflavones, highlighting the importance of considering the complete food matrix rather than focusing solely on single components.

Omega-3 fatty acids: membrane composition and function

Multiple studies have examined omega-3 fatty acid supplementation with generally consistent results supporting benefits for sperm quality. Safarinejad conducted a double-blind, placebo-controlled randomized trial of 238 men with idiopathic oligoasthenoteratozoospermia receiving 1.84 g/d of omega-3 fatty acids (EPA + DHA) or placebo for 32 weeks.[51] The treatment group showed significant improvements in

sperm concentration (from 15.2 × 10^6 to 28.4 × 10^6/mL; $P < 0.01$), total sperm count (from 38.2 × 10^6 to 61.3 × 10^6; $P < 0.01$), motility (from 24.7% to 35.9%; $P < 0.01$), and normal morphology (from 12.3% to 18.7%; $P < 0.01$). Importantly, sperm DHA content increased from 6.7% to 11.3% of total fatty acids ($P < 0.001$), and this increase correlated with improved sperm parameters.

Martínez-Soto and colleagues conducted a randomized trial of 42 infertile men receiving 1.5 g/d DHA or placebo for 10 weeks.[52] The DHA group showed increased seminal plasma DHA levels, reduced sperm DNA fragmentation (from 26.7% to 21.3%; $P < 0.05$), and increased total antioxidant capacity (from 7.2 to 9.4 μmol/L; $P < 0.05$). No changes in conventional semen parameters were observed, possibly due to the shorter intervention period compared to Safarinejad's trial (10 weeks *vs.* 32 weeks).

Notably, DHA and EPA play distinct roles in sperm biology: DHA is primarily incorporated as a structural component of sperm membranes, constituting up to 20% of total fatty acids and directly influencing membrane fluidity and fusion capacity; EPA, by contrast, exerts anti-inflammatory effects through conversion to resolvins and protectins.[18] In Safarinejad's trial, while the supplement contained both EPA and DHA, subsequent analysis revealed that the increase in DHA content (from 6.7% to 11.3%) correlated far more strongly with improvements in sperm parameters than did changes in EPA levels.

The discrepancy between studies showing effects on DNA fragmentation but not conventional parameters (Martínez-Soto) versus those showing effects on all parameters (Safarinejad) likely reflects the duration of intervention relative to the spermatogenic cycle. Spermatogenesis takes approximately 74 days, so interventions shorter than this may affect only epididymal sperm maturation (influencing DNA integrity) without affecting testicular sperm production. Longer interventions covering complete spermatogenic cycles can influence both processes.

Dairy products: fat content and hormonal load

The relationship between dairy consumption and male fertility exhibits fat-content dependency. Afeiche and colleagues studied 189 men and found that low-fat dairy intake was positively associated with sperm motility (β = 1.4, 95% CI: 0.3-2.5) , whereas full-fat dairy intake was inversely associated with sperm motility (β = -1.2, 95% CI: -2.3--0.1) .[53] Mechanistically, low-fat dairy products may support spermatogenesis through provision of high-quality protein and vitamin D. In contrast, full-fat dairy products contain exogenous estrogens (primarily estrone sulfate from pregnant cows) and lipid-soluble environmental contaminants that may counteract their nutritional benefits. Based on current evidence, men planning paternity should prioritize low-fat or skimmed dairy products.

WEIGHT MANAGEMENT AND METABOLIC HEALTH

Obesity and reproductive dysfunction: mechanisms

Obesity represents a major modifiable risk factor for male infertility, with multiple interconnected mechanisms. A comprehensive review by Pereira and colleagues synthesized the pathophysiological pathways linking obesity to impaired male reproductive function, emphasizing that the relationship is multifactorial and extends beyond simple hormonal disruption.[54]

Hormonal disruption

Adipose tissue expresses aromatase (CYP19A1), which converts testosterone to estradiol. A systematic review and meta-analysis has found strong evidence of a negative relationship between increased BMI and total testosterone, sex hormone-binding globulin (SHBG), and free testosterone in men.[55] The resulting hyperestrogenemia suppresses gonadotropin secretion *via* negative feedback on the hypothalamus and pituitary, further reducing testicular testosterone production.

Leptin resistance

Leptin, secreted by adipocytes in proportion to fat mass, normally stimulates gonadotropin-releasing hormone (GnRH) secretion. However, obesity-induced leptin resistance reduces GnRH pulsatility, contributing to hypogonadotropic hypogonadism. *In vitro* studies demonstrate that leptin directly inhibits human chorionic gonadotropin (hCG) -stimulated testosterone secretion from rat Leydig cells, with maximal inhibition of 57% at 10 μg/L leptin.[23]

Inflammatory mediators

Adipose tissue secretes pro-inflammatory cytokines including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and IL-1β, which induce systemic inflammation and directly impair spermatogenesis. TNF-α inhibits StAR expression and steroidogenesis in Leydig cells, while IL-6 disrupts Sertoli cell tight junctions, compromising the blood-testis barrier.[56]

Oxidative stress

Obese men have elevated seminal ROS and reduced total antioxidant capacity. Tunc and colleagues demonstrated that seminal ROS levels correlate positively with BMI ($r = 0.34$, $P < 0.01$) and inversely with sperm

motility (r = -0.41, P < 0.001).[57]

Dietary weight loss interventions

Two recent randomized controlled trials have demonstrated that weight loss through dietary intervention significantly improves semen quality. Andersen and colleagues conducted a randomized controlled trial examining the effects of weight loss and subsequent weight maintenance on semen parameters in 56 men with obesity (mean BMI 37 kg/m^2).[58] Following an 8-week low-calorie diet (800 kcal/d), participants lost an average of 16.5 kg (95% CI: 15.2-17.8), resulting in 1.49-fold increased sperm concentration (95% CI: 1.18-1.88) and 1.41-fold increased total sperm count (95% CI: 1.07-1.87). The proportion of men with oligozoospermia decreased from 17% to 13%. These improvements were maintained at 52 weeks among men who sustained weight loss through exercise, liraglutide treatment, or combination therapy, with men maintaining ≥ 11.7 kg weight loss showing 1.71-fold increased sperm concentration (95% CI: 1.15-2.55) and 1.97-fold increased total sperm count (95% CI: 1.22-3.18) compared to baseline. The 52-week follow-up data from Andersen and colleagues provide critical insights: men who maintained ≥ 11.7 kg weight loss showed a 71% increase in sperm concentration from baseline, whereas those who regained > 50% of lost weight showed only a 22% increase at 52 weeks, with serum testosterone having returned to near-baseline levels. This dose-response relationship and temporal sequence (weight regain preceding sperm parameter deterioration) further strengthen causal evidence linking weight loss to fertility improvement and underscores the clinical importance of weight maintenance.

Sharma and colleagues extended these findings by comparing high-intensity (800 kcal/d formula diet for 16 weeks) versus low-intensity (single brief dietary advice) interventions in men with obesity and either normal sperm count (n = 24) or oligozoospermia (n = 43).[59] Both interventions improved sperm motility parameters. Among men with normal count, total motility increased from 48% to 60% with high-intensity diet and from 52% to 61% with brief advice; progressive motility showed similar improvements. Among oligozoospermic men, total motility increased from 35% to 52% with high-intensity diet (P < 0.05) and from 43% to 50% with brief advice (P = 0.0587). Notably, the high-intensity intervention produced (DNA fragmentation index [DFI] decreasing from 5.9% to 4.1%, P < 0.001) and significant increases in serum testosterone (from 12.6 to 14.8 nmol/L, P < 0.0001) and SHBG (from 21 to 27 nmol/L, P < 0.001). The degree of weight loss correlated with improvements in DFI (r = -0.56, P = 0.005), suggesting dose-response relationships.

Improvements in testicular function following weight loss occur through two distinct mechanisms: (1) pre-testicular mechanisms: restoration of hypothalamic-pituitary-gonadal axis function, increasing gonadotropin pulsatility and elevating serum testosterone; and (2) intratesticular mechanisms: reduction of adipose tissue deposition within the testis, decreased macrophage infiltration, lower reactive oxygen species levels, and improved Sertoli cell tight junction function.[59] The reduction in sperm DNA fragmentation observed in the high-intensity intervention group (5.9%-4.1%) is primarily attributable to alleviation of intratesticular oxidative stress, whereas the increase in serum testosterone reflects improvement in the pre-testicular pathway.

ANTIOXIDANT SUPPLEMENTATION: CLINICAL TRIAL EVIDENCE

The role of antioxidant supplementation in male infertility has been addressed by multiple randomized trials with variable results. A recent randomized, quadruple-blind, placebo-controlled trial by Drakopoulos and colleagues evaluated the antioxidant combination Spermotrend® (containing fructose, Pygeum africanum, L-arginine, L-carnitine, vitamin C, zinc, vitamin E, vitamin B6, folic acid, and vitamin B12) in 80 infertile men with at least one abnormal semen parameter.[60]

After three months of treatment, within-group analyses showed significant improvements in the antioxidant group: rapid progressive motility increased by 1.0% (95% CI: 0-2.0, P = 0.04), progressive motility increased by 3.0% (95% CI: 0-15.1, P = 0.02), and DFI decreased by 3.2% (95% CI: -5.8--0.5, P = 0.02). However, when comparing changes between the antioxidant and placebo groups, no statistically significant differences were observed for any parameter, including progressive motility, concentration, normal morphology, DFI, or 8-hydroxy-2'-deoxyguanosine (8-OH-dG) formation.[60] This highlights the critical importance of between-group comparisons in randomized trials and suggests that placebo effects and regression to the mean may account for some of the improvements seen in uncontrolled studies.

The discrepancy with earlier meta-analyses reporting larger effects may reflect differences in study populations (unselected infertile men versus those with documented oxidative stress), intervention duration (3 months may be insufficient for complete spermatogenic cycle coverage), and the specific antioxidant combination used.

DISCUSSION: INTEGRATING EVIDENCE AND CLINICAL IMPLICATIONS

Mechanisms: a unified framework

The accumulated evidence supports multiple interconnected mechanisms through which diet influences

spermatogenesis. Oxidative stress represents a central pathway, with spermatozoa uniquely vulnerable due to their high PUFA membrane content, limited antioxidant defenses, and abundant mitochondrial ROS production. The consistent reduction in sperm DNA fragmentation observed with nut supplementation,[26] weight loss,[59] and omega-3 fatty acids [52] provides direct evidence for oxidative damage mitigation.

Hormonal regulation constitutes a second major pathway. Weight loss consistently increases serum testosterone and SHBG,[54,58,59] likely through reduced adipose tissue aromatase activity and improved HPG axis function. The effects of specific dietary components on reproductive hormones are more variable—Mediterranean diet interventions show inconsistent effects on testosterone while improving semen parameters, suggesting that hormonal changes are not the sole mediators of dietary benefits.

Membrane lipid composition represents a third mechanism. The preferential incorporation of DHA into sperm membranes during spermiogenesis explains the particular importance of omega-3 fatty acids for sperm motility and morphology.[14] The inverse correlation between sperm ALA levels and aneuploidy observed in the walnut trial suggests that membrane fatty acid composition may influence chromosomal segregation during meiosis.[37]

Epigenetic mechanisms, including altered miRNA expression and potentially DNA methylation changes, represent an emerging frontier.[26] The finding that nut consumption alters sperm miR-34b-3p expression—a miRNA targeting motility-related genes—provides proof-of-concept that dietary interventions can modify the sperm epigenome within a single spermatogenic cycle. However, as Xu and colleagues caution, the clinical relevance of these epigenetic changes for offspring health remains to be established, and the field awaits prospective cohort studies linking paternal diet to child health outcomes.[27]

Environmental contaminants in foods constitute a fourth mechanism that may counteract the benefits of otherwise healthy dietary patterns. Pesticide residues in conventionally grown produce and phthalates migrating from plastic packaging into ultra-processed foods have documented endocrine-disrupting effects that may directly impair spermatogenesis.[34,35,39]

A fifth mechanism, increasingly recognized, involves the gut and seminal microbiomes. Emerging evidence suggests that diet modulates the composition of the gut microbiome, which in turn influences systemic inflammation and may affect spermatogenesis through immune-mediated pathways.[61] The seminal microbiome itself may also be diet-responsive, with preliminary data linking specific microbial taxa to sperm quality parameters.[62] This represents a fertile area for future investigation.

Explaining inconsistent findings

Several factors explain the heterogeneity observed across studies examining diet-fertility relationships.

Population differences

Studies of soy and phytoestrogens demonstrate that results may differ substantially between populations with different baseline exposures. Chinese populations with high habitual soy intake show inverse associations with semen quality,[43] while Western populations with low intake show null or protective associations.[45,46] This suggests non-linear dose-response relationships, with potential beneficial effects at low doses (antioxidant, estrogen receptor modulation) and adverse effects at high doses (estrogenic excess, endocrine disruption).

Outcome selection

Studies examining conventional semen parameters often report positive associations with dietary factors, while those examining clinical fertility outcomes (pregnancy, live birth) frequently find null results.[29] This disconnect may reflect the multifactorial nature of fertility, where improvements in male factors are insufficient to overcome female factors or other barriers to conception. Additionally, semen parameters are imperfect predictors of fertility, with substantial overlap between fertile and infertile men. Tully and colleagues, in a systematic scoping review, emphasized that only 8 of 37 eligible studies reported clinical outcomes, and none were adequately powered to detect differences in live birth rates.[6] This evidence gap must be addressed before definitive dietary recommendations can be made.

Study design

Cross-sectional studies are susceptible to reverse causation—men diagnosed with infertility may modify their diet, creating spurious associations. Prospective cohort studies and randomized controlled trials provide stronger evidence but are more resource-intensive. The increasing number of RCTs examining dietary interventions represents an important advance, enabling causal inference. However, as Tully and colleagues note, the single randomized controlled trial (RCT) examining clinical outcomes was underpowered for live birth, and most observational studies lacked adequate adjustment for confounders such as female partner factors.[6]

Intervention duration

Studies shorter than the 74-day spermatogenic cycle may

detect effects on epididymal sperm maturation (*e.g.*, DNA fragmentation) but not on testicular sperm production,[52] while longer interventions affect both processes.[51,58] This explains discrepancies between studies examining similar interventions with different durations.

Dietary assessment methods

Food frequency questionnaires, 24-hour recalls, and diet records have different strengths and limitations. food frequency questionnaires (FFQs) capture habitual intake but are subject to recall bias; diet records provide detailed intake data but may alter eating behavior. The resulting measurement error typically biases associations toward the null, potentially underestimating true effects.

Publication bias and p-hacking

It must be acknowledged that the existing literature may be affected by publication bias, with positive results more likely to be reported than negative findings. Furthermore, with the proliferation of high-throughput omics data, the risk of p-hacking has increased—without pre-specified primary outcomes and adequate correction for multiple comparisons, chance positive associations may emerge. Future systematic reviews should prioritize studies that were pre-registered in public platforms (*e.g.*, ClinicalTrials. gov, and the International Prospective Register of Systematic Reviews [PROSPERO]) to enhance evidence reliability.

Clinical recommendations

Based on current evidence, and acknowledging the limitations outlined above, the following dietary recommendations for men planning paternity are supported. It must be emphasized that these recommendations are derived primarily from studies examining semen parameters rather than live birth rates, and that individual responses may vary.[6]

Adopt a healthy overall dietary pattern resembling the Mediterranean diet, characterized by high intakes of vegetables, fruits, legumes, whole grains, nuts, fish, and poultry, with limited red and processed meats, refined grains, and sweets.[29–32]

Include nuts daily (approximately 60 g of mixed walnuts, almonds, and hazelnuts) based on consistent evidence from randomized trials demonstrating improved sperm vitality, motility, morphology, and reduced DNA fragmentation.[26,37]

Ensure adequate omega-3 fatty acid intake through consumption of fatty fish (salmon, mackerel, sardines) 2-3 times weekly or fish oil supplementation (1-2 g/d EPA + DHA).[51]

Choose fruits and vegetables with attention to pesticide residues, prioritizing low-pesticide options or organic produce for items known to carry high residues, and thoroughly washing all produce.[39,42]

Prioritize low-fat or skimmed dairy products over full-fat dairy to minimize exogenous estrogen and environmental contaminant exposure while maintaining adequate protein and vitamin D intake.[53]

Limit or eliminate ultra-processed foods, sugar-sweetened beverages, and processed meats, which are consistently associated with poorer semen quality and contain endocrine-disrupting contaminant.[33,34]

Maintain healthy body weight through dietary modification, with even modest weight loss improving sperm parameters in overweight and obese men.[58,59]

Consider targeted antioxidant supplementation under medical supervision, particularly for men with documented infertility or elevated oxidative stress markers, while recognizing that evidence for unselected populations remains limited and that routine supplementation is not recommended by current guidelines.[9,60]

Limit alcohol to moderate consumption and avoid recreational drugs, which have well-documented adverse effects on spermatogenesis through multiple mechanisms including direct genotoxicity, oxidative stress, and hormonal disruption.

Crucially, men should be counseled that dietary modifications should be maintained for at least 3-4 months (one complete spermatogenic cycle) before expecting improvements, and that the magnitude of benefit is likely modest for men with normal baseline parameters but may be clinically meaningful for those with existing impairments.[6]

CONCLUSIONS

The past decade has witnessed substantial progress in understanding the relationship between diet and male reproductive health. Evidence from observational studies and randomized controlled trials consistently demonstrates that healthy dietary patterns rich in antioxidants, omega-3 fatty acids, and fiber, while low in saturated fats, trans fats, refined carbohydrates, and ultra-processed foods, are associated with superior semen quality. The Mediterranean diet, supported by recent meta-analyses demonstrating significant benefits across multiple sperm parameters,[29] represents the most extensively studied and evidence-based dietary pattern for male fertility.

The mechanisms linking diet to spermatogenesis are

multifactorial and interconnected, involving oxidative stress modulation, hormonal regulation, membrane lipid composition, epigenetic modifications, and differential exposure to environmental contaminants. Understanding these pathways enables rational dietary recommendations and identifies targets for future intervention.

However, the translation of improved semen quality to enhanced pregnancy and live birth rates remains to be definitively established. As Tully and colleagues concluded in their systematic scoping review, "Specific dietary recommendations for improving male fertility are precluded by the lack of reporting on clinical pregnancy outcomes, heterogeneity of the available literature and the paucity of RCTs to determine causation or to rule out reverse causation".[6] The disconnect between improved semen parameters and ART outcomes observed in multiple studies highlights the complexity of fertility and the need for adequately powered randomized controlled trials with clinical fertility outcomes as primary endpoints.[29,30] Such trials should prioritize live birth as the primary outcome, employ rigorous blinding and allocation concealment, and include diverse populations to enhance generalizability.

For men planning paternity, adopting a healthy dietary pattern represents a safe, low-cost strategy to optimize reproductive health while conferring numerous other health benefits. The observation that semen quality may serve as a biomarker for overall health and longevity provides additional motivation for dietary optimization, irrespective of fertility goals.[4] As the evidence base continues to evolve, personalized nutrition approaches based on individual genetic and metabolic profiles, gut microbiome composition, and oxidative stress status may further enhance the efficacy of dietary interventions for male infertility. The integration of nutrigenomics and microbiomics into fertility research represents the next frontier, promising a future of truly personalized reproductive medicine.[27]

DECLARATIONS

Acknowledgement
None.

Author contributions
Ma BX, Zhu JJ, Huang B: Conceptualization. Zhu JJ, Huang B: Writing—Review and Editing, Supervision. Ma BX: Writing—Original Draft, Visualization. Huang B: Project administration. All authors approved the final version of the manuscript.

Source of funding
None.

Ethical approval
Not applicable.

Informed consent
Not applicable.

Conflict of interests
The authors declare no competing interests.

Use of large language models, AI and machine learning tools
No artificial intelligence (AI) tools or large language models (LLMs) were used in the design, conduct, analysis, or writing of this study.

Data availability statement
Data will be shared upon reasonable request to the corresponding author.

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