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Dietary factors and diabetic retinopathy: An umbrella review of systematic reviews and meta-analyses

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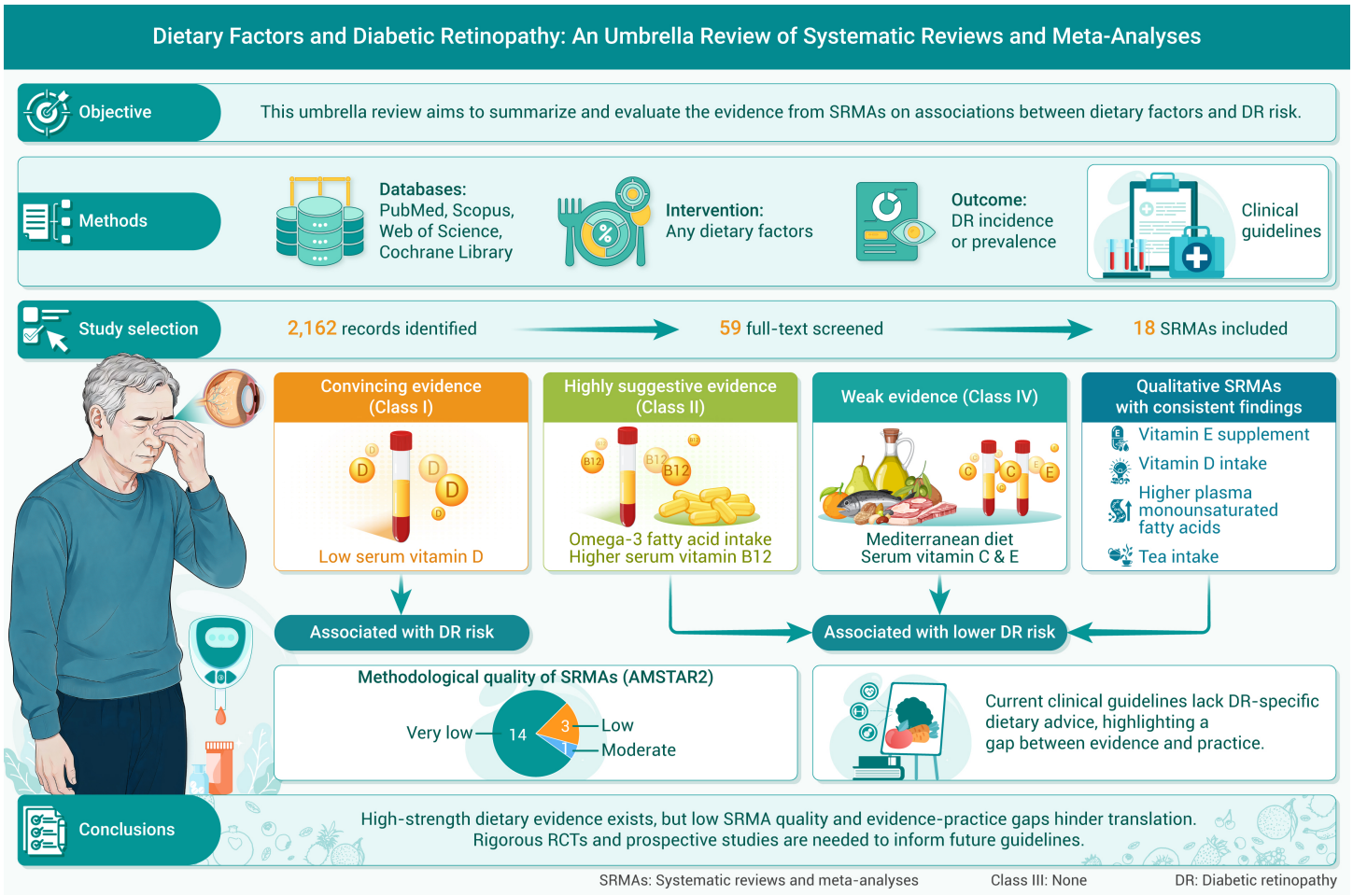
GRAPHICAL ABSTRACT



PUBLIC SUMMARY

- Low vitamin D levels were convincingly linked to a higher risk of diabetic retinopathy (DR).
- Omega-3 fatty acid intake and higher serum vitamin B12 showed highly suggestive evidence for lowering DR risk.
- Mediterranean diet, vitamins C and E consistently linked to lower DR risk, but weak evidence.
- Most systematic reviews had very low methodological quality, so findings should be interpreted cautiously.
- Current clinical guidelines lack DR-specific dietary advice, highlighting a gap between evidence and practice.

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Dietary factors and diabetic retinopathy: An umbrella review of systematic reviews and meta-analyses

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Diabetic retinopathy (DR) is a leading cause of vision impairment globally. Numerous systematic reviews and meta-analyses (SRMAs) have investigated specific dietary components, but a comprehensive synthesis is lacking. This umbrella review aims to summarize and evaluate the evidence from SRMAs on associations between dietary factors and DR risk. PubMed, Scopus, Web of Science, and the Cochrane Library were searched from inception to May 1, 2026. SRMAs of observational studies or randomized controlled trials examining any dietary factors and DR incidence or prevalence in individuals with diabetes were included. Of 2162 articles screened, 18 were included. The most consistent finding was the protective association between Mediterranean diet and DR. Low serum vitamin D demonstrated convincing evidence for DR risk, while highly suggestive evidence was identified for omega-3 fatty acid intake and serum vitamin B12. Multiple qualitative systematic reviews consistently concluded that higher serum vitamin C and E, vitamin D intake, plasma monounsaturated fatty acids, and tea intake were associated with lower DR risk. Although conclusions on other dietary factors were inconsistent, most studies showed protective effects of fish, fruits, vegetables, and dietary fiber. However, most included SRMAs were rated as very low methodological quality, indicating that even statistically robust associations should be interpreted cautiously and that rigorous prospective studies and targeted interventions are still needed.

INTRODUCTION

Diabetic retinopathy (DR) stands as one of the most frequent and severe microvascular complications of diabetes mellitus, posing a significant threat to global vision health.[1] It is a leading cause of preventable blindness among the working-age population worldwide, contributing substantially to individual disability and social healthcare burdens.[2-3] Current epidemiological data indicate that over 100 million individuals were affected by DR globally in the early 2020s, and projections suggest that the prevalence may continue to rise, potentially affecting over 160 million people by 2045.[3] Among people with diabetes, the estimated global prevalence of any form of DR is approximately 22%, underscoring its widespread impact.[2]

While stringent glycemic, blood pressure, and lipid control form the cornerstone of DR management, their efficacy in preventing progression, especially in advanced stages, is not absolute. This underscores the critical need to identify additional modifiable risk factors. Diet is a fundamental, modifiable lifestyle component that influences systemic inflammation, oxidative stress, endothelial function, and metabolic health, all of which implicated in DR pathogenesis. Consequently, the role of specific dietary components in DR has garnered significant research interest. Several systematic reviews and meta-analyses (SRMAs) have explored associations between specific dietary factors and DR risk.[4-6] Beyond nutritional strategies, systemic metabolic interventions like fibrate therapy have demonstrated protective effects against DR progression through non-glycemic mechanisms.[7] Furthermore, contemporary evidence from network meta-analyses positions anti-VEGF therapy as a highly effective treatment for vision-threatening DR, providing a benchmark against which preventive nutritional strategies can be compared.[8] The interplay between systemic metabolic disease and broader ocular health is also evident, as diabetes significantly elevates the risk of comorbid conditions such as dry eye disease, compounding the overall eye-health burden in this population.[9] However, the evidence remains fragmented and sometimes inconsistent, with individual syntheses often focusing on a single exposure, leading to a compartmentalized understanding of the association between diet and DR.

A comprehensive, high-level synthesis that systematically aggregates and critically evaluates all available evidence on the main dietary factors, including dietary patterns, foods, macronutrients, micronutrients, and beverages for DR risk is currently lacking. An umbrella review methodology is particularly well-suited to address this evidence gap and provide a comprehensive perspective. This approach has emerged as an effective methodological tool for assessing the strength, consistency, and credibility of evidence across a broad spectrum of relevant exposures.[10] It helps distinguish robust, well-supported associations from those based on weak or inconsistent data, identifies methodological limitations within the collective evidence base, and effectively maps the current knowledge landscape to guide future research priorities.

Therefore, the purpose of this study is to synthesize and evaluate the available evidence regarding the associations between general dietary factors and the risk of incident DR. Specifically, it aims to: 1) determine which dietary factors are consistently associated with a modified risk of DR; 2) assess the epidemiological credibility and robustness of these associations; 3) identify key gaps and inconsistencies in the existing literature, and 4) compare the synthesized evidence with current dietary recommendations from major clinical guidelines on diabetes and DR. It is anticipated that the findings from this review will provide a comprehensive evidence base to inform clinical nutritional counseling for DR management and to delineate clear directions for future primary research and interventions aimed at preventing DR.

MATERIALS AND METHODS

We conducted this umbrella review according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[11] Our protocol has been registered in PROSPERO (CRD42024528225).

Eligibility criteria

Studies were selected based on the following PICOS criteria:

Population (P): Adult (≥ 18 years) patients with diabetes.

Intervention/Exposure (I): Any defined dietary pattern (e.g., Mediterranean, vegetarian, low-carbohydrate), foods (e.g., fruits, vegetables, fish, meat), or nutrients (e.g., fatty acids, vitamins, minerals). Dietary factors were catego-

rized into three types: (1) dietary intake or food consumption (assessed by Food Frequency Questionnaire (FFQ), 24-hour recall, etc.), (2) supplement use (e.g., vitamin D or omega-3 capsules), and (3) circulating biomarker levels (e.g., serum 25(OH)D, plasma vitamin C). These categories were analyzed and reported separately.

Comparator (C): Lower intake, non-adherence, or a different dietary pattern.

Outcome (O): Incidence or prevalence of DR, diagnosed via standardized methods. Studies reporting only composite outcomes (e.g., any diabetic complication) without separate DR data will be excluded.

Study Design (S): Systematic reviews with or without meta-analyses of observational studies or randomized controlled trials (RCTs). Narrative reviews, scoping reviews, protocol papers, editorials, conference abstracts, and primary studies were excluded.

Search strategy

We searched PubMed, Scopus, Web of Science, and the Cochrane Library (from inception to 1 May 2026) to identify SRMAs. The search strategy combined terms related to a. diabetic retinopathy, b. diet/nutrition, and c. systematic reviews/meta-analyses (see Tables S1-S4 for full strategies). Reference lists of included articles were screened manually.

Study selection and data extraction

Two independent reviewers screened the titles and abstracts of identified records, followed by the full-text assessment of potentially eligible articles. Discrepancies were resolved through discussion or by a third reviewer. Data from the included SRMAs were independently extracted by two reviewers using a standardized, pilot-tested form. The following information were collected: first author, publication year, number and design of primary studies, total sample size, definitions of exposure and outcome, method of synthesis (narrative or quantitative), pooled effect estimates (e.g., odds ratio, hazard ratio) with corresponding 95% confidence intervals (*CIs*) and p-values, measures of heterogeneity (I^2), assessment of publication bias.

Assessment of methodological quality

The methodological quality of each included SRMA was independently assessed by two reviewers using the Assessment of multiple systematic reviews (AMSTAR) 2 tool (available at https://amstar.ca/Amstar-2.php), which is a recent update of AMSTAR.[12] Disagreements were resolved by consensus.

Data synthesis and analysis

Synthesis of evidence from qualitative systematic reviews. When synthesizing evidence from qualitative systematic reviews, a pre-specified hierarchy was applied to resolve inconsistencies in conclusions regarding the same dietary factor (e.g., a specific dietary pattern or nutrient) and its association with DR. Priority was first given to the review whose conclusions were based on studies of a higher design hierarchy: randomized controlled trials (RCTs) > cohort > case-control studies > cross-sectional studies. If the design level was equal, precedence was then given, in sequential order, to the review with the larger total sample size, the higher methodological quality rating (e.g., AMSTAR-2), and the most recent publication date.

Synthesis of evidence from meta-analyses. For each included meta-analysis, summary effect sizes and their 95%*CI* were recalculated using fixed or random effects models, as appropriate.[13] We also estimated the 95% prediction interval (*PI*), which accounts for the between-study heterogeneity and evaluates the uncertainty for the effect that would be expected in a new study addressing that same association.[14] If individual meta-analysis provided stratified results (e.g., by study design or population), these are also reported. Heterogeneity was assessed with the I^2 statistic, with < 50% being considered low, values exceeding 50% or 75% are considered to represent large or very large heterogeneity, respectively.[15] Additionally, we also tested the presence of small-study effect bias, which is deemed to be present in case of both pooled estimates larger than the individual largest study, and publication bias (Egger's regression asymmetry test $p < 0.10$).[16] We then applied the excess significance test, which evaluated whether the observed number of studies with statistically significant results differed from the expected number of positive studies.[17] When multiple meta-analyses addressed the same dietary exposure-outcome association, we selected the most representative association pair for primary reporting in the text based on a pre-specified hierarchy: the most recent publication year, the largest total sample size, and the highest AMSTAR-2 quality.

Credibility of meta-analyses was assessed according to stringent criteria established on previously published umbrella reviews.[18-19] In brief, associations that presented nominally significant summary effect sizes ($p < 0.05$) were ranked as convincing, highly suggestive, suggestive, and weak evidence based on number of events, strength of the association, and the presence of several biases (see Table 1 for full criteria).

Management of overlapping and redundant reviews

A major methodological challenge in umbrella reviews is the inclusion of multiple systematic reviews that synthesize overlapping sets of primary studies for the same exposure-outcome association. To prevent double-counting and to base our synthesis on the most reliable and current evidence, we applied the following sequential algorithm to to the qualitative synthesis of evidence when multiple systematic reviews addressed identical research questions (e.g., "Vitamin C and DR risk"):

I. Grouping: Identical research questions were grouped based on exposure and outcome.

II. Overlap assessment: For each group, the degree of overlap in their included primary studies were quantified by calculating the Corrected Covered Area (CCA). A citation matrix were constructed, and the CCA were classified as slight (0–5%), moderate (6–10%), high (11–15%), or very high (> 15%).

III. Selection for synthesis: If the CCA is slight or moderate, all systematic review were retained for a comprehensive narrative discussion. If the CCA is high or very high, only one definitive systematic review was selected for primary presentation in our qualitative synthesis. The selection followed this hierarchy: (a) highest methodological quality (AMSTAR-2 rating), (b) most recent publication, (c) comprehensiveness: if quality and recency were equivalent, the systematic review with the larger number of included primary studies or total sample size will be chosen.

Contextual comparison with clinical practice guidelines

To situate the findings of this study within the current clinical landscape, a descriptive appraisal of major international diabetes and DR guidelines was performed. The purpose was not to include guidelines as evidence units for synthesis but to identify and tabulate the explicit dietary and nutritional advice given for DR management. Guidelines from the American Diabetes Association (ADA, 2026), the International Council of Ophthalmology (ICO, 2017), the American Academy of Ophthalmology (AAO, 2024), the National Institute for Health and Care Excellence (NICE, 2024/2025), the European Society of Cardiology (ESC, 2023) and the Group of Ophthalmological Society of Chinese Medical Association (2022) and the Chinese Diabetes Society (2024) were reviewed.[20-27] Only statements directly pertaining to dietary pattern, dietary intake, or nutritional management for DR prevention/progression were extracted.

RESULTS

Study selection

Figure 1 shows the detailed literature selection. Briefly, 2162 articles were initially identified. After removing 106 duplicates, 2056 titles and abstracts were screened. Following the full-text assessment of 59 articles, a total of 18 SRMAs were included in this umbrella review: 7 were systematic reviews and another 11 were systematic reviews which also included a meta-analysis. [4-6 28-42]

Characteristics of included systematic reviews

The 18 included SRMAs were published between 2010 and 2026. Their key characteristics are summarized in Table 2. In total, they synthesized evidence from over 2 to 54 primary studies involving more than 2052 to 256727 participants with diabetes. SRMAs assessed the effects of dietary factors. Dietary factors were classified into dietary patterns, nutrients, and dietary intake of food and beverage.

Table 1. Credibility assessment criteria and grading

Grading of evidence	criteria
Class I (Convincing evidence)	• Statistical significance of $p<1*10^{-6}$, more than 1,000 cases included (or more than 20000 participants for continuous outcomes); • The largest component study reporting a significant result ($p < 0.05$); • A 95% prediction interval that excluded the null; • Absence of large heterogeneity ($I^2 < 50\%$); • No evidence of small study effect ($p > 0.10$) and excess significance bias ($p > 0.10$).
Class II (Highly suggestive evidence)	• Significance of $p < 1*10^{-6}$, more than 1,000 cases included (or more than 20,000 participants for continuous outcomes); • The largest component study reporting a significant result ($p < 0.05$).
Class III (Suggestive evidence)	• Significance of $p < 0.001$, more than 1,000 cases included (or more than 20000 participants for continuous outcomes).
Class IV (Weak evidence)	• Associations with a statistical significance of $P < 0.05$.
NS (Not significant)	• Associations with $P > 0.05$.

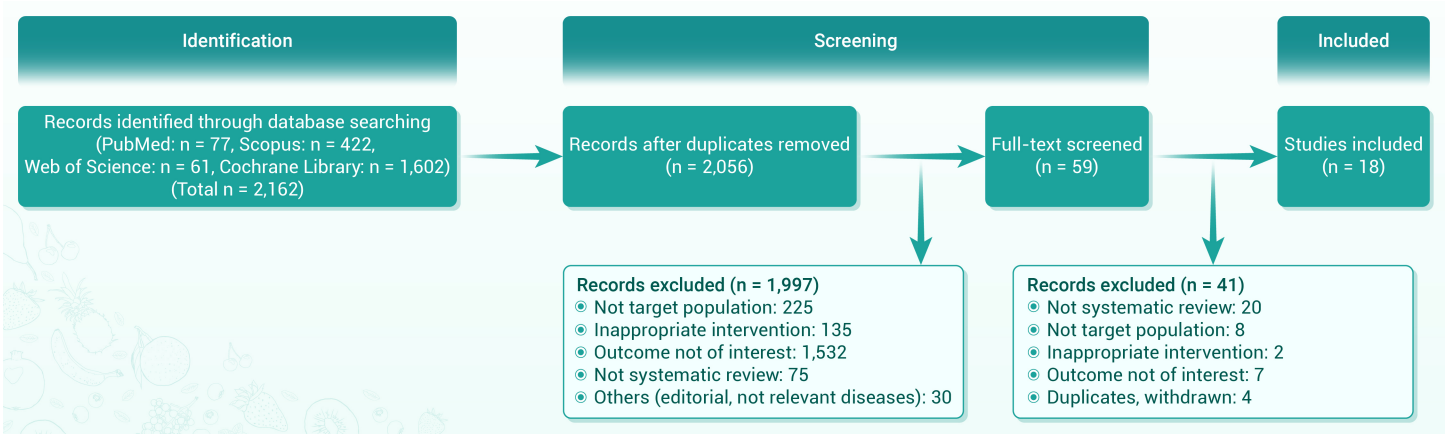

Figure 1. PRISMA flow diagram of the study selection process.

Methodological quality of included reviews

The majority of SRMAs scored very low (n = 14/18) on AMSTAR2, and one scored moderate and three as low (see Table 2). The main reasons for the very low scoring was that most studies failed to report the funding sources that the review included (AMSTAR2 question 10; 0/18 studies satisfied this criteria) and failed to provide a list of excluded studies and justify the exclusions (AMSTAR2 question 7; 3/18 studies satisfied this criteria). The quality assessment scoring for all articles is presented in Supplementary Table S5.

Assessment of evidence strength, heterogeneity and biases

Among meta-analyses recalculated, two associations reached convincing evidence (Class I): lower serum vitamin D levels were associated with an increased risk of DR in both mixed and type 2 diabetic patients. Higher serum vitamin B12 levels and higher omega-3 fatty acid intake were were supported by highly suggestive evidence (Class II). The remaining associations were supported by weak evidence (Class IV), including higher serum vitamins C and E and higher adherence to the Mediterranean diet (MD), all linked to reduced DR risk.

Regarding statistical characteristics of the meta-analyses, eighteen associations presented a statistically significant effect at $P < 0.05$, and six at $P < 10^{-6}$. Only three associations had a 95%*PI* that excluded the null value. Eleven associations showed high heterogeneous ($I^2 > 75\%$). Small-study effects and excess significance bias were each detected in four associations (see Table 3 for full details).

Synthesis of evidence from meta-analyses

Evidence from meta-analyses is summarized in Table 3 and illustrated in Figure 2. The MD showed a consistent protective association across study designs, pooled estimates from RCTs (OR = 0.64; 95%CI: 0.47-0.89) and prospective cohort studies (HR = 0.69; 95% CI: 0.49-0.96) indicated reduced DR incidence, while cross-sectional/case-control studies also reported inverse associations (OR = 0.32; 95%CI: 0.12-0.81). The overall evidence was graded as weak (Class IV).[30,38] Six studies investigated the association between serum vitamin D levels and DR risk,[5-6,28-29,31,35] the most recent study in type 2 diabetes patients reported a significantly increased DR risk (OR/HR = 1.84; 95%CI: 1.68-2.01), constituting convincing evidence (Class I). Lower vitamin D levels were also associated with sight-threatening DR (OR = 1.78; 95%CI: 1.48-2.16), classified as highly suggestive (Class II). Omega-3 fatty acid intake (≥ 500 mg/day) was associated with a 29% reduction in DR risk (HR = 0.71; 95%CI: 0.64-0.79), with consistent effects in cohort studies and RCTs, rated as highly suggestive (Class II).[32] Serum vitamin B12 levels were significantly lower in DR patients (WMD = −60.55; 95%CI: −104.1 to −16.99), also constituting highly suggestive evidence (Class II), though subgroup analyses by ethnicity were not significant. Data from 15 studies on serum vitamin B12, all of which were cross-sectional or case-control studies, exclusively in patients with type 2 diabetes, indicated significantly lower levels in DR patients compared to controls (weighted mean difference [WMD] = −60.55; 95%*CI*: -104.1 to -16.99), also constituting highly suggestive evidence (Class II), though subgroup analyses by ethnicity were not significant.[33]

Synthesis of evidence from qualitative systematic reviews

Given the heterogeneity in research questions and methodological approaches, several included systematic reviews conducted a narrative synthesis without quantitative meta-analysis.[4,30,34,36-37,40-42] The dietary factors involved are shown in Figure 3. Overall, the narrative conclusions from these qualitative reviews generally aligned with and reinforced the direction of associations reported in quantitative meta-analyses. The key findings from these reviews are summarized in supplementary Table S6, offering a complementary descriptive overview of the broader evidence landscape.

Dietary patterns. Wu and colleagues, in a systematic review that included one cohort study and one RCT, reported that adherence to MD was associated with a reduced risk of DR in patients with both type 1 and type 2

Table 2. Characteristics of included systematic reviews and meta-analyses

Author, year [Ref]	Type of SRMA	Search date	Type of included studies	Total N	Total sample size (N)	Country/region	Amstar-2	COI	Country of corresponding author
Luo, 2017	MA	2016.9	Cohort/cc/cs	8	13,435	Lebanon/China/India/Spain/Turkey/US	Very low	No	China
Yu, 2026	MA	2024.12	Cohort/cc/cs	20	22,408	Asia/Europe/North America/Middle East	Very low	No	China
Chen, 2025	MA	NR	RCT/cohort	14	139,879	USA/UK/Spain/China/France/Italy/ Australia	Very low	No	China
Zooravar, 2025	SRMA	2025.2	Cohort/cc/cs	6	112,067	Iran/UK/Spain/China	Low	No	Iran
Dow, 2018	SR	2017.10	RCT/cohort/cc/cs	27	46,173	Spain/India/Italy/Japan/UK/China/US/ Australia/Korea/Scotland	Very low	No	France
Yuan, 2019	MA	2018.9	Cohort/cc/cs	18	21,679	USA/Lebanon/India/China/Spain/Turkey/ Australia/Korea	Very low	No	China
Tabatabaei, 2019	SR	2018.1	RCT/cc/cs	21	256,727	NR	Very low	No	Iran
Wong, 2017	SR	2017.1	RCT/cohort/cc/cs	31	31,880	NR	Very low	No	Singapore
Xiong, 2022	SRMA	2020.12	Cohort/cc/cs	34	NR	Asia/Caucasians/Africa	Very low	No	China
Yang, 2023	MA	2022.4.10	cc/cs	15	2,052	East Asian/South Asian/Caucasian/ Mixed population	Very low	No	China
Yusufu, 2019	MA	2019.6	RCT	2	4,804	Spain	Very low	No	China
Benson, 2010	SR	2008.5	Cohort/cs	15	4,094	NR	Very low	No	UK
Petrea, 2025	SRMA	2024.10	RCT/cohort/cc/cs	20	22,408	Europe/Asia/America/French Guinea/Oceania and Northern Europe	Low	No	Romania
Wu, 2023	SR	2023.2.20	RCT/cohort	2	25,801	Europe/Asia	Very low	No	China
Shah, 2022	SR	2022.5	RCT/cohort/cc/cs	54	87,206	NR	Very low	No	Singapore
Milluzzo, 2022	SR	2021.11	RCT/observational studies	41	19,648	China/Turkey/Australia/NewZealand/Finland/India/Lebnon/Qatar/USA/Saudi Arabia/Japan/Italy/Spain/Denmark/Iran/ Germany/Poland/Greece	Very low	No	Italy
Trott, 2022	MA	2022.4	cc/cs	12	9,057	Turkey/UK/Spain/Bahrain/India/Iran/China/USA/South Korea/	Moderate	No	UK
Lan, 2026	MA	2026.2	Cohort/cc/cs	16	19,987	Asia (China, South Korea, India, and Saudi Arabia), Europe (Italy), and North America (United States).	Low	No	China

Abbreviation: Ref, reference; SR, systematic review; MA, meta-analysis; cc, case control study; cs, cross-sectional study; RCT, randomized controlled trial; COI, conflict of interest; MD, mediterranean diet; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; NR, not reported.

diabetes.[34] In a separate systematic review by Shah et al., which synthesized three studies on caloric intake, a high total caloric intake was linked to an increased risk of DR progression in two of the studies, while the third found no significant association.[36]

Micronutrients. In the systematic review by Shah and colleagues, six studies examined carotenoid intake, half of which reported a significant association with DR, while the remaining studies did not.[36] A separate review by Tabatabaei et al. focused on serum vitamin C levels in type 2 diabetes, including ten studies; all consistently showed that individuals with DR had lower vitamin C levels compared to those without DR.[40] However, evidence regarding the association between dietary vitamin C intake and DR remained inconsistent. In the review by Shah et al., one cohort study indicated a protective effect of higher vitamin C intake on DR incidence, whereas three cross-sectional studies found no significant association, either before or after adjustment for potential confounders.[36]

Six studies in the systematic review by Tabatabaei and colleagues focused on vitamin E level, and all of these case control studies that found a significant lower serum level in subjects with DR than others.[40] In contrast, the association between dietary vitamin E intake and DR remains uncertain, as summarized in the review by Shah et al.[36] Their synthesis noted that two cross-sectional studies observed a protective effect of vitamin E intake on DR after adjusting for confounders. However, a separate cross-sectional study published in 1998 reported that increased vitamin E intake was associated with greater DR severity among patients not using insulin. The remaining three studies did not report any significant association between vitamin E and DR.

Two systematic reviews examined the association between serum selenium and DR in type 1 and type 2 diabetes respectively. Both of them included only one studies, and observed lower serum level of selenium in diabetic patients without DR than control group.[37,40] Shah et al. found that dietary selenium intake was associated with a protective effect against DR.[36] With respect to zinc, the systematic review by Tabatabaei and colleagues included four studies on serum zinc levels; three of these reported significantly lower levels in patients with DR than in those without DR. The remaining study found no significant difference in serum zinc levels between patients with proliferative and non-proliferative DR.[40]

In a systematic review by Milluzzo et al. that included ten studies investigating the influence of vitamin D or its metabolites on the onset or progression of DR.[37] Although inconsistent results are available, in nine of these studies, an inverse association between the serum level of vitamin D and the risk of DR was detected. Only a recent observational study performed on Chinese type 2 diabetic patients, found no association between the level of vitamin D and DR. Moreover, shah et al. reported that dietary vitamin D intake was not significantly associated with DR risk in their synthesis of the evidence.[36]

Table 3. Summary of meta-analyses results: dietary patterns and nutrients and risk of diabetic retinopathy.

Author, year [ref]	Dietary pattern (Comparison)	Subgroup analysis	Population (number of studies)	Pooled effect size (95% *CI*)	P-value	95%*PI*	Publication bias	Excess significant effect	I^2 (%)	Grade
Dietary patterns										
Zooravar, 2025	Adherence to the MD [a]	Cohort	T2DM(3)	HR = 0.69 (0.49-0.96)	0.033	0.02-23.37	Yes	No	51	IV
Zooravar, 2025	Adherence to the MD [a]	cs/cc	T1DM(1)/T2DM(2)	OR = 0.32(0.12-0.81)	0.017	0-38801.21	No	No	94	IV
Yusufu, 2019	Dieary control intervention [b]	NA	T2DM(2)	OR = 0.64(0.47-0.89)	0.007	NA	NA	No	0	IV
Nutrients										
micronutrients										
Yang, 2023	Serum Vitamin B12 [c]	NA	T2DM(15)	WMD = -60.55(-104.1, -16.99)	0.006	-238.77, 117.68	No	No	88	IV
Yang, 2023	Serum Vitamin B12 [c]	East Asian	T2DM(8)	WMD = -78.65(-99.36, -57.94)	9.85e-14	-134.12, -23.18	No	No	58	II
Yang, 2023	Serum Vitamin B12 [c]	South Asian	T2DM(2)	WMD = -255.11(-591.18, 80.97）	0.137	NA	NA	No	95	NS
Yang, 2023	Serum Vitamin B12 [c]	Mixed	T2DM(2)	WMD = -18.03(-55.33, 19.28)	0.344	NA	NA	No	49	NS
Yang, 2023	Serum Vitamin B12 [c]	Caucasian	T2DM(3)	WMD = 7.56(-87.52, 102.64)	0.876	-1174.31, 1189.44	No	Yes	88	NS
Luo, 2017	vitamin D deficiency [d]	NA	T2DM(8)	OR = 2.02(1.17-3.50)	0.012	0.29-14.08	No	No	97	IV
Yu, 2026	Vitamin D deficiency [d]	NA	T2DM(20)	OR = 1.29(1.15-1.44)	7.76e-06	0.98-1.69	Yes	Yes	55	IV
Trott, 2022	Vitamin D deficiency [e]	NA	T2DM(6)/NR(5)	OR = 1.36(1.10-1.68)	0.004	0.68-2.73	No	No	70	IV
Trott, 2022	Vitamin D deficiency [e]	NA	T2DM(6)	OR = 1.35(0.96-1.90)	0.084	0.42-4.34	No	No	82	NS
Xiong, 2022	Serum Vitamin D [c]	NA	T2DM(13)/mixed(3)/ T1DM(1)/NIDDM(1)	WMD = -3.06 (-5.15, -0.96)	NR	NA	No	No	77	IV
Petrea, 2025	Serum Vitamin D [c]	NA	NR(9)	OR = 1.08(0.91-1.27)	0.380	0.59-1.94	No	Yes	89	NS
Trott, 2022	Serum Vitamin D [c]	NSTDR	T2DM(3)/NR(3)	OR = 1.05(0.91-1.21)	0.480	0.67-1.72	No	No	30	NS
Trott, 2022	Serum Vitamin D [c]	NSTDR, T2DM	T2DM(3)	OR = 0.99(0.74-1.33)	0.954	0.04-23.81	No	No	61	NS
Trott, 2022	Serum Vitamin D [c]	STDR	T2DM(3)/NR(2)	OR = 1.78(1.48-2.16)	1.75e-09	0.88-3.67	No	No	39	II
Trott, 2022	Serum Vitamin D [c]	STDR, T2DM	T2DM(3)	OR = 1.83(1.24-2.68)	0.002	0.02-136.17	No	No	67	IV
Lan, 2026	Serum Vitamin D [f]	NA	T2DM(12)/T1DM(3)/ mixed(1)	OR/HR = 1.87(1.72-2.02)	1.18e-51	1.57-2.24	No	No	5	I
Lan, 2026	Serum Vitamin D [f]	T2DM	T2DM(12)	OR/HR = 1.84(1.68-2.01)	6.69e-41	1.48-2.30	No	No	20	I
macronutrients										
Chen, 2025	Omega-3 fatty acid intake [g]	NA	Mixed(8)	HR = 0.71(0.64-0.79)	1.39e-10	0.62-0.81	Yes	Yes	0	II
Chen, 2025	Omega-3 fatty acid intake [g]	Cohort	Mixed(5)	HR = 0.71(0.62-0.81)	2.01e-07	0.34-1.19	Yes	No	0	II
Chen, 2025	Omega-3 fatty acid intak [g]	RCT	Mixed(3)	HR = 0.71(0.59-0.85)	0.0002	0.04-10.24	No	No	0	II
Xiong, 2022	Serum Vitamin C [c]	NA	T2DM(7)/DM(2)/NIDDM(5)	WMD = -11.01(-19.35, -2.67)	NR	NA	No	NA	98	IV
Xiong, 2022	Serum Vitamin A [c]	NA	T2DM(2)/mixed(1)/T1DM(1) / NIDDM(1)	WMD = 0.02(-0.14, 0.19)	NR	NA	No	NA	95	NS
Xiong, 2022	Serum Vitamin E [c]	NA	T2DM(3)/mixed(2)/T1DM(1) /NIDDM(1)	WMD = -3.03(-4.24, -1.82)	NR	NA	No	NA	85	IV

Abbreviation: Ref, reference; CI, confidence Interval; PI, predicted interval; NA, not applicable; NR, not reported; HR, hazard ratio; OR, odds ratio; WMD, weighted mean difference; MD, mediterranean diet; STDR, sight threatening diabetic retinopathy; NSTDR, non-sight threatening diabetic retinopathy; cs, cross-sectional study; cc, case control study; RCT, randomized controlled trial; NS, not significant; DM, diabetes mellitus; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; NIDDM, non-insulin dependent diabetes mellitus; [a] high vs. low or no adherence; [b] MD supplemented with extra virgin olive oil vs. MD supplemented with mixed nuts vs. low-fat control diet; [c] DR vs. no-DR; [d] serum 25(OH)D levels < 20 ng/mL (DR vs no-DR); [e] serum 25[OH]D levels < 20 ng/mL (present vs. absent); [f] low vs. high; [g] 500 mg/day vs. placebo, standard care, or no supplementation.

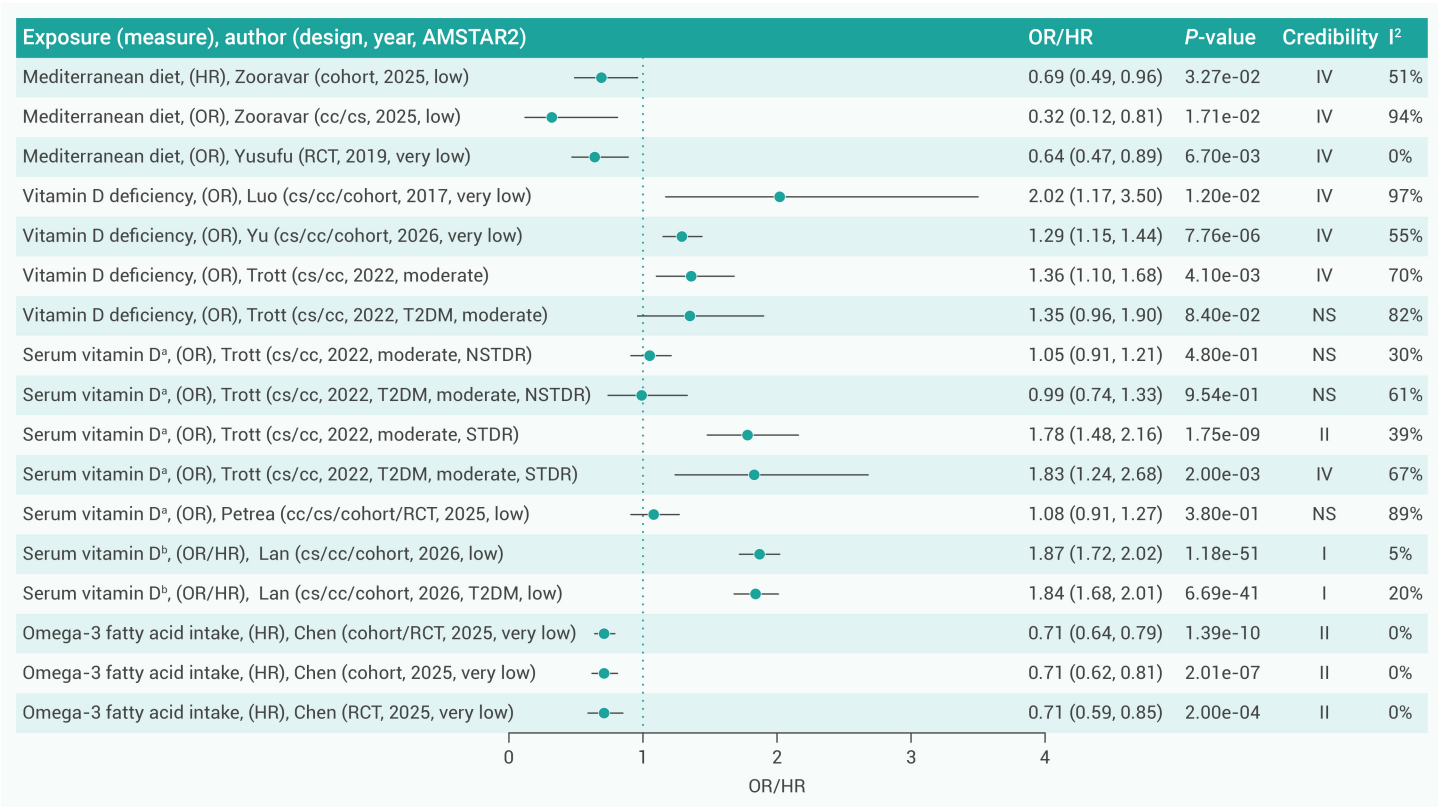

Figure 2. Forest plot of pooled hazard ratios (HRs) and odds ratios (ORs) from meta-analyses evaluating dietary factors and diabetic retinopathy risk. RCT, randomized controlled trial; cs, cross-sectional study; cc, case control study; T2DM, type 2 diabetes mellitus; STDR, sight threatening diabetic retinopathy; NSTDR, non-sight threatening diabetic retinopathy; AMSTAR2 rating (classified as high/moderate/low/very low); [a] DR vs. no-DR; [b] low vs. high.

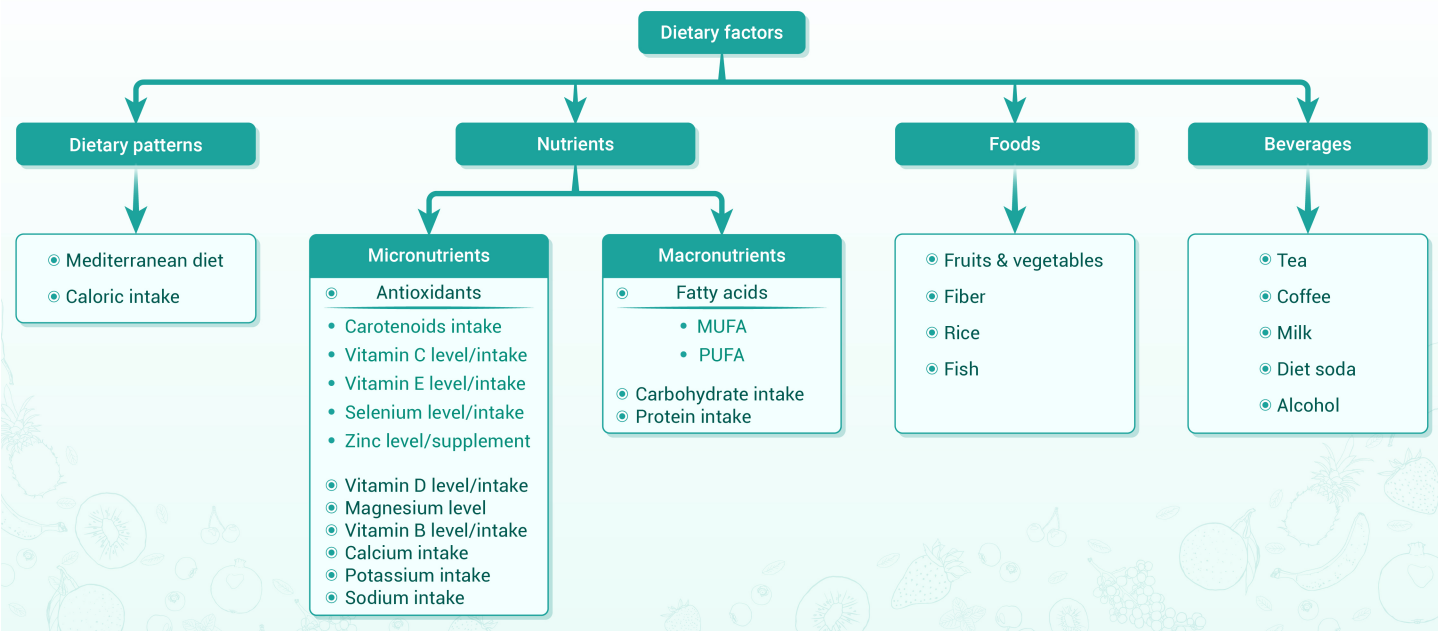

Figure 3. An overview of dietary factors included in the systematic reviews. MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acids.

Evidence regarding vitamin B and DR in type 2 diabetes remains inconclusive. Milluzzo and colleagues summarized observational studies on serum vitamin B levels, noting inconsistent findings.[37] One study involving 300 patients reported significantly lower plasma vitamin B12 levels in those with DR compared to those without. Instead, no association was observed for vitamin B1, B2, or B6. An exception was a prospective study of 978 Japanese individuals with type 2 diabetes, which found that a higher dietary intake of vitamin B6 (assessed by food frequency questionnaire) was associated with a lower risk of DR.[36]

The consideration of the serum magnesium was not very frequent in the included reviews.[4,40] Nonetheless, one systematic review by Tabatabaei et al. concluded that magnesium levels were lowest in patients with DR.[40] Another review by Benson and colleagues, which included four studies, reported inconsistent findings regarding the association between serum magnesium and DR and did not specify the direction of association in individual studies; it only noted that one cohort study demonstrated an inverse relationship between serum magnesium levels and DR progression.[4]

Macronutrients. Evidence on fatty acids and DR is mixed. Regarding

monounsaturated fatty acids (MUFA), a systematic review that included two studies reported a significant inverse association between plasma MUFA levels and DR risk. Notably, one of the included case-control studies conducted in a Chinese population identified oleic acid (a primary MUFA) as the strongest predictor of DR among patients with type 2 diabetes.[30]

For polyunsaturated fatty acids (PUFA), the association with DR remains uncertain.[36] One cross-sectional and one cohort study suggested that higher daily PUFA consumption was associated with a reduced likelihood of DR and sight-threatening DR, respectively. In contrast, another cohort study involving 1,412 participants reported an increased risk of DR progression with higher PUFA intake, although this analysis was not adjusted for potential confounders. The remaining three studies found no significant association between PUFA intake and DR. Finally, concerning total fat intake, a separate systematic review that synthesized two studies concluded that it was not associated with the odds of DR.[41]

Evidence regarding carbohydrate and protein intake in relation to DR remains inconclusive. In the systematic review by Shah and colleagues, seven studies examined carbohydrate intake. One cross-sectional study reported a positive association between the intake of complex carbohydrates and the presence of DR, whereas two other studies demonstrated an inverse association between carbohydrate intake and DR progression.[36] For dietary protein, the same review included six studies. Four of these found no significant association with DR. Among the remaining studies, one prospective study suggested that a higher protein intake was associated with a lower risk of DR progression, while one cross-sectional study indicated a positive association between protein intake and DR prevalence.[36]

Foods. Shah et al. synthesized seven studies on fruits, vegetables, and dietary fiber, noting inconsistent findings.[36] A protective association between higher consumption of these foods and DR risk was reported in four studies. In contrast, two cohort studies and one case-control study found no significant association. Specifically for dietary fiber, one study indicated a protective effect against DR, while another reported no association.[41] Concerning fish consumption, two studies suggested that frequent fish intake by individuals with diabetes was associated with a reduced risk of developing DR. One prospective study further specified that consuming two or more weekly servings of oily fish was linked to a lower incidence of DR. However, other studies included in the synthesis observed no significant association between fish or fish oil intake and DR risk.[36]

Beverages. Regarding green tea, a systematic review by Shah et al., which included two studies, reported a protective relationship between green tea intake and DR prevalence.[36] For milk, two separate systematic reviews found no significant association between DR and the consumption of either whole or low-fat milk.[36,41] The evidence for alcohol intake and DR is inconsistent. Shah and colleagues synthesized 13 studies on this topic, and the results were inconsistent.[36] Five studies (four cross-sectional and one cohort) suggested that alcohol consumption, typically defined as occasional or light-to-moderate drinking was associated with a reduced incidence of DR. In contrast, four studies identified alcohol consumption as a significant risk factor for DR development, with one of these specifically linking heavy intake to increased risk. The remaining four studies found no significant association between alcohol consumption and DR.

Assessment of overlap and reporting biases

In the qualitative synthesis, the overlapping among the included systematic reviews of dietary factors was shown in Table 4. The CCA ranged from 0% to 100%, indicating considerable overlap of primary studies among the included systematic reviews for most dietary factors. Very high overlap (CCA > 15%) was observed for MD adherence, caloric intake, vitamin D and E intake/supplementation, protein intake, sodium intake, MUFA/PUFA intake, oleic acid, vitamin C level/intake, carotenoids intake, fiber intake, tea, carbohydrates intake, fish intake, coffee, milk, and alcohol intake. High overlap (CCA: 11-15%) was noted for the combined intake of fruits, vegetables, and dietary fiber.

For the quantitative synthesis, no overlap-based selection was applied, as each meta-analysis was treated as an independent evidence unit and re-analyzed separately.

Dietary/nutrition-related recommendations in DR-related guidelines

The dietary and nutritional recommendations pertaining to DR, as extracted from contemporary clinical practice guidelines, are summarized in Supplementary Table S7. A consistent theme across all guidelines is the absence of DR-specific, nutrient-level or diet-based prescriptions. These guidelines uniformly frame DR risk reduction around the imperative to achieve and maintain optimal glycemic, blood pressure, and lipid control. These targets are acknowledged to be reached primarily through Medical Nutrition Therapy (MNT) and lifestyle modification, yet the guidelines delegate the specifics of MNT to broader diabetes management chapters or to specialist referral. The most detailed MNT framework is provided by the Chinese Diabetes Society (2024) guidelines, which specify macronutrient distributions, salt, and fiber intake, but these are intended for overall diabetes care, not as a distinct intervention for DR. No guideline explicitly recommends dietary patterns like the Mediterranean diet or specific micronutrient supplementation (e.g., vitamin D, omega-3) for the purpose of preventing or treating DR.

DISSCUSION

Principal findings

This umbrella review provides a comprehensive synthesis of the available evidence, encompassing both quantitative meta-analyses and qualitative systematic reviews, on the association between dietary factors and DR. The principal and most consistent finding across both types of syntheses is the protective association between healthful dietary patterns, particularly the MD, and a reduced risk of DR. This conclusion is supported by pooled estimates from meta-analyses that predominantly draw on prospective cohort studies and RCTs, with stronger causal inference capabilities, and is a recurrent theme in narrative reviews. High adherence to the MD is associated with improved glycemic control, reduced oxidative stress, and low levels of inflammation, all of which are key mechanisms that help mitigate the progression of DR[43]. Bioactive components of the MD, such as the polyphenols in olive oil and flavonoids abundant in fruits and vegetables, contribute to these benefits, in part by enhancing nitric oxide (NO) production, thereby improving endothelial function and reducing vascular damage.[44-45]

Furthermore, our study demonstrated a significant and consistent inverse relationship between vitamin D levels and the incidence of DR. The included studies encompass diverse populations, employ varied methodological approaches, and utilize different vitamin D measurement techniques, which enhances the generalizability of the results. These observations are biologically plausible, as the multifaceted physiological roles of vitamin D intersect with several key pathways implicated in DR pathogenesis. For instance, vitamin D is known to suppress the activation of the NF-κB signaling pathway, leading to a reduction in the expression of pivotal pro-inflammatory cytokines such as TNF-α and IL-6.[46]

Regarding antioxidant parameters, evidence from meta-analyses and systematic review indicated that a higher serum levels of vitamin C and E were associated with a lower risk of DR in population with diabetes. Furthermore, supplemental intake of vitamins C and E may decrease incidence of DR. The underlying mechanisms are biologically plausible. Vitamin C acts as a direct antioxidant by scavenging reactive oxygen species (ROS, which helps preserve nitric oxide bioavailability and reduces lipid peroxidation.[47] Besides, the combined beneficial effects of vitamins C and E have been confirmed in the context of several diabetic complications.[48] Additionally, high-dose vitamin E supplementation has been shown to improve retinal blood flow, particularly in patients with the poorest baseline retinal perfusion and glycemic control, and to reduce central macular thickness.[49]

Our findings on dietary fiber and fruits/vegetables, which were less conclusive than in other cardio-metabolic conditions, warrant careful consideration. This may reflect measurement error in dietary assessment, the specific forms or subtypes of fiber/fruits relevant to retinal health, or the overwhelming confounding effect of hyperglycemia. Fruits and vegetables are rich sources of fiber and antioxidant compounds. Dietary fiber delays glucose absorption from the intestines, thus reducing the risk of hyperglycemia and oxidative stress-induced DR.[50-51]

Despite some inconsistencies in these reviews, the majority of studies suggest that fish consumption, particularly of oily fish and fish oil, confers a protective effect against DR. Fish oil is a rich source of both vitamin D and

Table 4. The overlapping among included systematic reviews

Diet pattern/food/nutrition	Number of reviews	Number of included studies	CCA statistic (%)	Degree of overlapping
Mediterranean diet	5	6	25	Very high
Caloric Intake	2	3	100	Very high
Carotenoids intake	3	6	58	Very high
Vitamin C level	2	13	23	Very high
Vitamin C intake	4	5	60	Very high
Vitamin E level	2	9	0	Slight
Vitamin E intake/supplement	5	9	19	Very high
Vitamin D intake/supplement	2	2	100	Very high
Selenium intake	3	3	0	Slight
Zinc level	2	5	0	Slight
Serum Magnesium	2	6	0	Slight
Vitamin B6 intake	2	1	1	Slight
Sodium intake	2	5	80	Very high
MUFA intake	4	8	29	Very high
PUFA intake	3	7	71	Very high
Oleic acid	2	3	67	Very high
Carbohydrates intake	3	7	57	Very high
Protein intake	2	6	83	Very high
Fruits, vegetables, and dietary fiber intake	3	9	11	High
Fiber intake	2	6	50	Very high
Fish	3	6	25	Very high
Tea	2	2	50	Very high
Coffee	2	2	50	Very high
Milk	3	2	25	Very high
Alcohol	3	16	31	Very high

Abbreviation: MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acids; CCA, corrected covered area.

long-chain omega-3 PUFAs.[52] The immunomodulatory and anti-angiogenic properties of these nutrients are proposed to underlie their protective role, not only in reducing diabetes risk but also, as our review indicates, in mitigating DR.[53] Specifically, dietary omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), exert their protective effect by being metabolized to 4-hydroxy-docosahexaenoic acid, a compound that inhibits pathological blood vessel proliferation, a hallmark of DR.[54] Experimental studies further support the beneficial role of PUFAs in DR development, attributing it to their anti-inflammatory and anti-angiogenic properties.[55] In addition, findings from the included meta-analyses underscore the significant role of MUFAs and long-chain ω-3 PUFAs in modifying the risk of vision-threatening DR.

In contrast to the nutrients and dietary patterns discussed above, sodium, calcium, potassium, and total carbohydrate intake were not consistently associated with DR risk in the synthesized evidence. However, a high total caloric intake emerged as a potential risk factor for both DR incidence and progression. This is supported by experimental and clinical data indicating that excessive caloric intake increases the metabolic burden and oxidative stress in individuals with diabetes, which may heighten the susceptibility of the retina, a tissue particularly vulnerable to oxidative damage to the development of DR.[56] In spite of a lack of significant association with DR, the careful monitoring and management of carbohydrate consumption remain a cornerstone of diabetes care due to its direct impact on postprandial glycemic control.[57]

The association between alcohol intake and DR risk remains inconclusive, as the studies synthesized in this review yielded contradictory findings. Consequently, the present analysis could not confirm a protective effect of alcohol consumption against DR. It has been proposed that moderate alcohol intake, particularly from beverages rich in polyphenols (potent antioxidant compounds), might confer benefits by inhibiting angiogenesis, attenuating inflammation, and promoting vasodilation mechanisms that collectively could enhance retinal blood flow.[58] However, given the inconsistency of the epidemiological evidence and the potential for confounding, no definitive conclusion regarding a causal protective role can be drawn.

Evidence regarding the association between common beverages, such as tea, milk, and coffee and DR remains limited, as it is derived from a small number of studies. Within this context, evidence suggests that tea consumption, particularly of green tea, may have a protective effect against DR. Tea is among the most widely consumed beverages globally, and its extracts are reported to possess antioxidant and neuroprotective properties. These bioactive compounds are thought to contribute to improved insulin sensitivity, inhibition of ocular neovascularization, and reduction of vascular permeability, which are key pathways relevant to DR pathogenesis.[59]

Strengths and limitations

The primary strength of this study is that it represents the first umbrella review to systematically consolidate and appraise the evidence on the association between a broad spectrum of dietary factors and the risk of DR.

Second, the application of rigorous, pre-specified methodological criteria for synthesizing evidence from SRMAs provides a comprehensive landscape of the highest currently available evidence. Furthermore, the use of the AMSTAR-2 tool enabled a transparent and critical appraisal of the methodological reliability of the included evidence base. Finally, by integrating findings from both quantitative meta-analyses and qualitative systematic reviews and contextualizing them against current major clinical guidelines, this work provides a more complete and clinically relevant evidence map than would be possible by focusing on either type of synthesis alone.

However, several limitations must be acknowledged. First, the overall certainty of evidence for most associations is very low, as assessed by AMSTAR-2, due to residual confounding, high heterogeneity, and methodological shortcomings of the included SRMAs. Even statistically robust associations should therefore be interpreted with caution. Second, most studies are cross-sectional, limiting causal inference. High-quality longitudinal and intervention evidence is scarce, and RCTs with DR as a pre-specified outcome are urgently needed. Third, many meta-analyses did not report effect estimates separately by study design, precluding fully stratified evidence grading. Future meta-analyses should disaggregate results by study design. Fourth, definitions and assessments of both dietary factors and DR varied widely across studies, contributing to heterogeneity. Finally, many studies did not distinguish diabetes types, given the distinct pathophysiological mechanisms, etiologies, and management approaches between diabetes types, all of which could modulate the effect of diet on DR. Future studies should report findings separately for each type.

Consistency between synthesized evidence and current clinical guidelines

The findings reveal both alignment and divergence with current clinical guidelines. Convergence lies in the primacy of metabolic control. Our synthesis verifies and reinforces the rationality of current dietary guidelines for diabetes, suggesting that adherence to these recommendations may confer metabolic benefits that are relevant to microvascular health. However, claiming direct DR-specific protection from individual dietary components would be premature.

The principal divergence is the translation of nutrient-level evidence into clinical recommendations. Our review identified dietary factors (e.g., vitamin D, omega-3) with reliable evidence for DR risk, yet these are absent from ophthalmology guidelines. This gap likely reflects: (1) discipline-specific boundaries, ophthalmology guidelines prioritize retinal treatments, delegating nutrition to endocrinology; and (2) insufficient evidence from DR-primary-endpoint RCTs, despite robust observational data. Therefore, our findings should be regarded as hypothesis-generating, providing rationale for future confirmatory research rather than immediate clinical changes.

Implications for future research

We found the current guideline landscape presents a "metabolism-centered" view of diet in DR, where diet is a means to achieve biochemical targets. Our synthesis contributes a more "nutrition-centered" map, identifying specific dietary factors associated with DR. To bridge this gap, future research should prioritize well-designed, prospective cohort studies that employ repeated, validated dietary assessments alongside standardized, longitudinal evaluation of DR. There is a compelling and urgent need for RCTs testing the efficacy of implementing MD or other protective dietary factors in preventing DR progression. Additionally, suggest future primary studies and relevant SRMAs to investigate understudied dietary factors, including specific food groups (e.g., meat, whole grains, dairy products) and other dietary patterns (e.g., Dietary Approaches to Stop Hypertension (DASH), vegetarian, and high-salt diets). Until such evidence is available, clinicians can be informed by this review that promoting the dietary components and patterns identified here is not only aligned with good general diabetes care but may also confer targeted benefits for retinal health beyond their metabolic effects. Furthermore, future studies should recognize that dietary intake, nutrient supplementation, and circulating biomarker levels are conceptually distinct exposures. Although we have reported these separately where data permitted, further research is needed to disentangle their independent effects on DR risk, as each may operate through different biological mechanisms and carry distinct implications for clinical and public health recommendations.

CONCLUSION

In conclusion, this umbrella review, which integrates evidence from both meta-analyses and systematic reviews, indicates that overall dietary factors are modifiable factors associated with DR risk. The most robust evidence, derived from quantitative synthesis, supports a protective role for the Mediterranean diet and suggests that vitamin D deficiency is associated with an increased risk. However, given that most included systematic reviews were rated as very low methodological quality by AMSTAR-2, these findings should be interpreted with appropriate caution. Evidence for other specific dietary components is less conclusive. Qualitative syntheses enrich this picture by mapping areas of active investigation and inconsistency, while also underscoring the current paucity of high-quality, consistent data for many nutrients. Promoting healthful dietary patterns represents a prudent clinical strategy, while the field awaits more definitive evidence from targeted interventions and rigorous prospective studies.

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AUTHOR CONTRIBUTIONS

Shi SY: conceptualisation, database searches, data extraction, statistical analysis, writing. Zhou QX: database searches, statistical analysis. Song TC, Zuhaer YS: data extraction. Zhang SY, Sun HY, Zhan SY: supervision. Sun F: conceptualisation, supervision. All authors contributed to and approved the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

ETHICAL STATEMENT AND PATIENT CONSENT

Not Applicable.

DATA AND CODE AVAILABILITY

No new data were created or analyzed in this study.