

Building on the AREDS2 Foundation With Emerging Evidence for B Vitamins

PURPOSE

In January 2026, Bausch + Lomb convened an expert roundtable to discuss the evolving role of B vitamin supplementation in reducing the risk of development and progression of age-related macular degeneration (AMD).



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Perspectives from Retina Specialists

As supported by the National Eye Institute (NEI), Age-Related Eye Disease Study 2 (AREDS2) nutrients remain the cornerstone of AMD nutritional supplementation.¹ Building on this foundation, evidence supporting the role of nutritional supplementation in AMD continues to grow, with increasing attention to B vitamins.² The opportunity now lies in translating this emerging science into clinical practice while keeping supplement recommendations clear, simple, and manageable for patients.

There is an emerging opportunity across eyecare contexts for simple, consistent guidance on the use of nutritional supplements. As many patients already take multiple supplements before receiving clinical direction, clinicians commonly face questions about product selection, overlapping ingredients, safety, and long-term adherence. As such, there is a need for discussions on the science of AMD nutrition that bring evidence to bear while preserving approaches that are both practical for clinicians and clear for patients.

This roundtable discussion reviewed the emerging evidence for B vitamins in reducing the risk of AMD progression, the biological rationale for their use, and how these insights may build on the established AREDS2 foundation. The discussion also examined how counseling differs by AMD stage, from early risk-reduction conversations in optometric settings to reinforcement of adherence and long-term management in retina clinics. Current recommendations are based on a combination of epidemiologic, observational, and randomized studies. Clinical trials, like those that provided evidence of the benefits of the AREDS and AREDS2 formulations, are currently ongoing.

KEY CLINICAL TAKEAWAYS

- Emerging evidence suggests B vitamins may complement established nutritional approaches for AMD progression risk reduction^{2,3}
- Observational and randomized data suggest that B vitamins may help reduce the risk of early AMD development and progression⁴⁻⁶
- In early AMD, B vitamins may present an opportunity to extend nutritional support and help reinforce retinal health^{2,3}
- Lifestyle changes, including a Mediterranean-style diet, regular physical activity, smoking cessation, avoidance of secondhand smoke, and weight management, remain an important foundation for reducing modifiable AMD risk⁷
- Simple, unified approaches to patient counseling may help improve adherence and reduce variability across eyecare settings
- Building on the substantial body of evidence supporting B vitamins, future clinical research will help better define the magnitude of benefit and their role in AMD management²

An Opportunity Earlier in the AMD Journey

AMD care spans multiple clinical settings, which can influence how nutritional supplementation is introduced, explained, and reinforced over time. Because patients with early AMD are often first identified and managed in optometric clinics, this setting presents an opportunity to address modifiable risk factors and introduce practical management strategies before patients progress to more advanced stages.

Lifestyle modification is a central aspect of AMD management, as several modifiable behaviors have been associated with AMD development and progression. Smoking is among the most consistently identified risk factors for AMD, whereas certain dietary patterns may help reduce risk. In particular, greater adherence to a Mediterranean-style diet, which is rich in vegetables, fruits, legumes, whole grains, nuts, fish, and unsaturated fats, has been associated with lower rates of both early and advanced AMD.⁷ In one prospective cohort study, patients with high adherence to a Mediterranean diet had a lower risk of developing advanced AMD compared with those with low adherence.⁸ Obesity is another major risk factor, with each 1-kg/m² increase in body mass index within the overweight and obese ranges associated with a 2% increase in the risk of developing AMD.⁷ Counseling on smoking cessation, avoidance of secondhand smoke, regular physical activity, weight management, and healthy eating is therefore an important part of a broader risk-reduction strategy.

Alongside lifestyle modifications, emerging evidence has highlighted the potential role of B vitamins in early stages of the AMD journey. The Blue Mountains Eye Study found that elevated homocysteine levels and deficiencies in folate and vitamin B12 were associated with a higher risk of incident AMD over 10 years, while vitamin B12 supplementation was associated with a 47% lower risk.⁶ In the Women's Antioxidant and Folic Acid Cardiovascular Study (WAFACS), daily supplementation with folic acid 2.5 mg, vitamin B6 50 mg, and vitamin B12 1 mg reduced the risk of total AMD by 34% and visually significant AMD by 41% over a mean follow-up of 7.3 years.⁴

Collectively, these findings suggest that B vitamin supplementation may be an effective strategy for lowering the risk of incident AMD, although additional prospective research is needed to further assess and clarify the potential benefits and how supplementation should be incorporated into practice.

In contrast to those working in optometric clinics, retina specialists are more likely to encounter patients with intermediate or advanced AMD, many of whom are already taking AREDS2-based supplements.^{7,9,10} For these patients, the conversation often moves beyond supplement initiation to reinforcing adherence, ensuring patients have a solid understanding of the factors influencing long-term risk reduction, and setting expectations around monitoring and management.

Because these patients may receive care from several different providers as their AMD progresses, the nutritional guidance they receive may vary depending on their stage of care. Greater alignment among optometrists, retina specialists, and other members of the care team can support more consistent counseling, which may strengthen patient confidence and reinforce adherence over time.



LEJLA VAJZOVIC, MD

In my practice, the majority of patients present with intermediate or advanced AMD. Many arrive already taking AREDS2 supplements. In these cases, the conversation is less about initiation and more about adherence, often reinforcing discussions they have had with other practitioners. I explain that supplementation is a long-term strategy aimed at reducing risk over time and emphasize the importance of consistency.

Why Simplicity Matters

As research evolves, it is important to be mindful that overly nuanced or stage-specific supplement strategies can be difficult for providers to explain and even harder for patients to follow.

Limited chair time adds to the challenge, as nutritional counseling often requires more than a quick recommendation. Patients need to understand why supplementation matters, when to start, what to take, and what to expect over time.

Clarity and consistency are essential for adherence. A simpler, more unified approach to supplementation may help reduce variability in counseling, support earlier intervention, and reinforce long-term use.

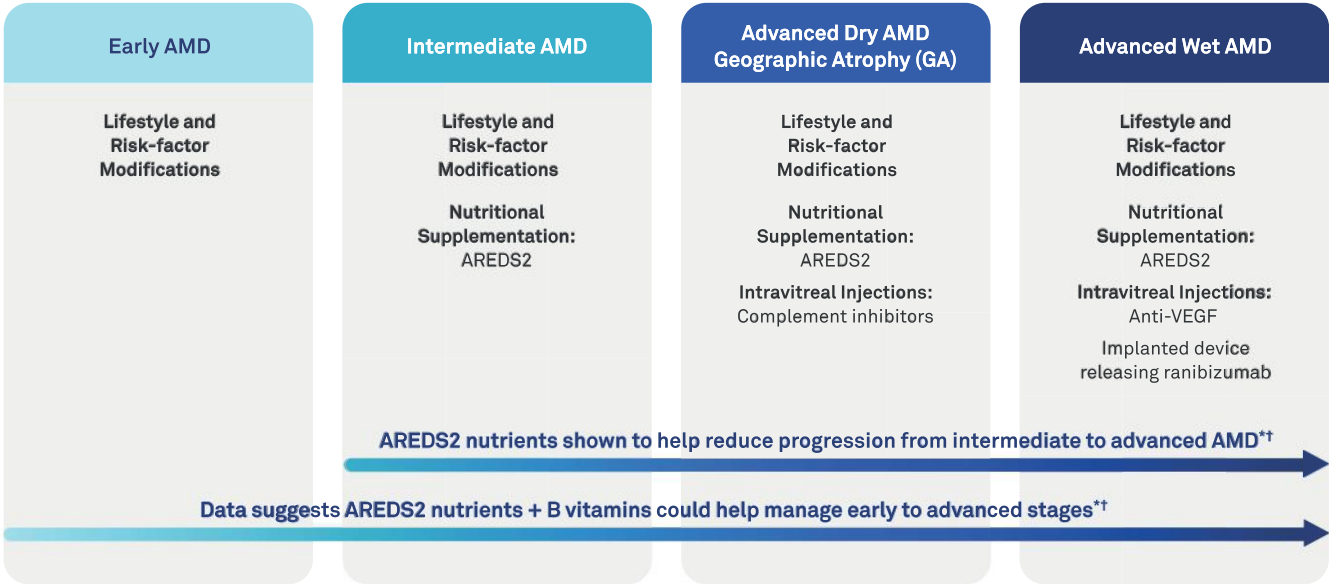


JUDY E. KIM, MD

Chair time is a substantial constraint in clinical practice, but it is important to help our patients understand their condition and gain their buy-in for long-term management. Effective nutritional counseling requires explanation, context, and expectation setting.

For new patients, I explain AREDS and AREDS2 myself, so they clearly understand why we are recommending AREDS2 supplementation for patients with intermediate AMD in both eyes or advanced AMD in one eye. They need to know that it is intended to reduce the risk of progression to advanced AMD and is not a cure. I use handouts, videos, and technician reinforcement to ensure consistency and adherence. Patients need to know that once supplementation begins, it is a long-term commitment rather than a short-term intervention.

Where Nutritional Supplements Fit Into AMD Management Across Stages^{7,10-13}



*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

[†]AREDS2 nutrients are recommended by the NEI to help reduce the risk of progression from intermediate to advanced AMD.

A Durable, Evidence-Based Foundation

AREDS and AREDS2 established nutritional supplementation as an evidence-based strategy for reducing the risk of progression from intermediate to advanced AMD, demonstrating durable safety and efficacy and shaping AMD care for patients with intermediate to advanced AMD.^{10,11,14,15} Now, emerging scientific insights related to B vitamins may allow eyecare clinicians to extend and/or complement current approaches to AMD risk reduction.²



RISHI SINGH, MD

The AREDS program represents a decades-long scientific legacy in our field. The AREDS and AREDS2 formulations demonstrated 25% and 18% reductions in the risk of progression to advanced AMD, respectively, with durable safety and efficacy maintained over 10 years. Subsequent post hoc analyses have even suggested a potential effect on GA progression toward the fovea. That body of work established nutritional intervention as a credible, evidence-based strategy in AMD management.

Parallel to that legacy, we are now seeing a growing body of literature linking B vitamins to AMD risk reduction. We know from multiple dietary studies that increased intake of vitamins B1, B5, B6, B9, and B12 is associated with reduced risk of developing and progressing to advanced AMD, including both neovascular AMD and GA. In addition, other studies have shown similar benefits of B vitamin supplementation on the development and progression of AMD.

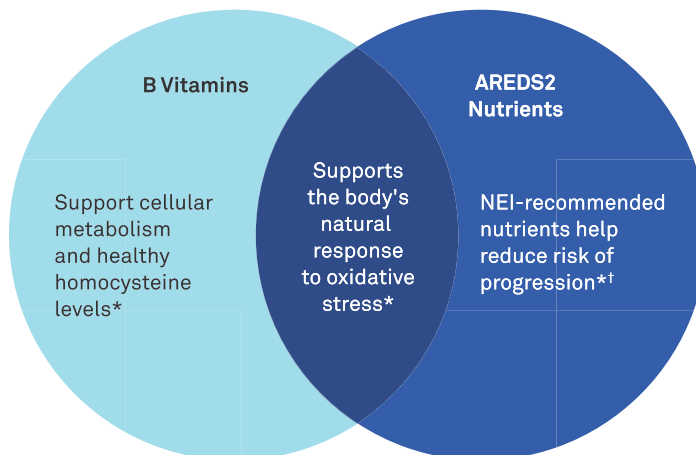
Potential Benefits of AREDS2 Nutrients and B Vitamins in AMD^{*2,4,5,10,14-16}

41%

Reduced risk of visually significant AMD

42%

Reduced risk of early AMD



25%

Risk reduction in intermediate to advanced AMD

22%

In AREDS2, lower risk of neovascular AMD

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

†In intermediate to advanced AMD patients.

Emerging Role of B Vitamins in AMD Risk Reduction

A growing body of evidence supports a potential role for B vitamins in reducing the risk of AMD development and progression.^{2,3} Lower B vitamin levels are associated with more advanced AMD, while higher intake of vitamins B1, B5, B6, B9, and B12 is associated with a reduced risk of progression.⁴⁻⁶ Observational and randomized data show that B vitamins are associated with an approximately 41% lower risk of visually significant AMD and an approximately 42% lower risk of early AMD.^{2,4,6}

AMD is increasingly viewed through a broader biological lens that includes metabolic, vascular, and inflammatory pathways. In this context, B vitamins are of interest because of their roles in homocysteine regulation, cellular metabolism, and mitochondrial function.²

Elevated homocysteine has been linked to vascular dysfunction, endothelial injury, and impaired microcirculation, all of which are relevant to retinal health. Vitamins B6, B12, and B9 (folate) support homocysteine metabolism, and reducing homocysteine levels may help support vascular and retinal health. Mitochondrial dysfunction is also increasingly recognized as a key contributor to cellular stress and retinal pigment epithelium damage in dry AMD and GA.²

As AMD is increasingly understood as a metabolic and inflammatory disease, B vitamins may play a broader role through their involvement in cellular metabolism, methylation, and gene regulation. This positions B vitamins within a broader biological framework alongside emerging mitochondrial-targeted therapies and supports their potential role in the evolving understanding of AMD pathophysiology.^{2,3,17,18}



YASHA MODI, MD

What stands out to me is the consistency of the signal. Case-control studies repeatedly show lower B vitamin levels in patients with more advanced AMD. That pattern is difficult to ignore. In addition, a large cardiovascular trial in women demonstrated a lower incidence of AMD with B vitamin supplementation. Although it was not designed primarily as an ophthalmic study, it was randomized and well conducted, which strengthens its relevance.

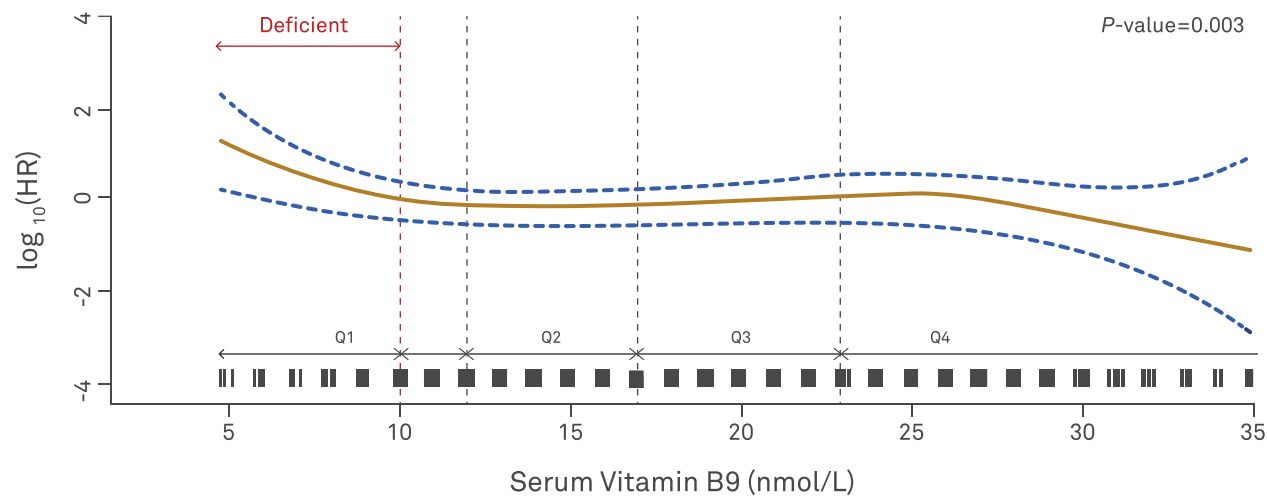


MICHAEL SINGER, MD

One of the most established mechanistic links between B vitamins and AMD is homocysteine reduction. Elevated homocysteine has been associated with vascular dysfunction, endothelial injury, and impaired microcirculation. Vitamins B6, B12, and B9 play central roles in homocysteine metabolism, and lowering those levels may have downstream vascular and retinal benefits.

Beyond that, the mitochondrial story is becoming increasingly relevant. As we deepen our understanding of dry AMD and GA, mitochondrial dysfunction continues to surface as a potential driver of cellular stress and retinal pigment epithelium compromise. If emerging dry AMD and GA therapies are targeting mitochondrial pathways, we should also consider how B vitamins may influence mitochondrial metabolism and cellular energy homeostasis.

B VITAMIN SERUM CONCENTRATIONS CORRELATE WITH REDUCED AMD RISK



Adapted from Merle BMJ, et al. *Nutrients*. 2022;14(14):2821.

B VITAMIN INTAKE CORRELATES WITH REDUCED AMD RISK

42%

reduced risk of incident early AMD with supplemental vitamin B12 intake

UPTO

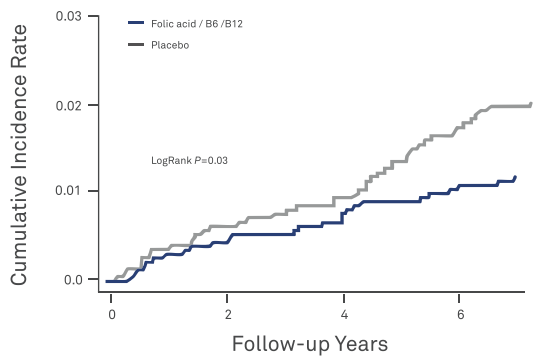
28%

reduced risk of AMD with daily doses of vitamins B5 and B6

CONTROLLED STUDIES DEMONSTRATE B VITAMIN BENEFIT

41%

reduced risk of visually significant AMD / advanced AMD with daily supplementation of folic acid (B9), B6, and B12



Adapted from Christen WG, et al. *Arch Intern Med*. 2009;169(4):335-341.

B Vitamins Are Integral to Many Aspects of Ocular Health^{3,19-21}

10% TO 20% OF THE US POPULATION MAY HAVE B VITAMIN DEFICIENCY

01 MITOCHONDRIAL DYSFUNCTION

Key driver of pathogenesis in multiple ocular diseases:

- **Vitamin B1:** Mitochondrial ATP production and molecular oxygen homeostasis
- **Vitamin B2:** Precursor to two coenzymes integral to the mitochondrial electron transport chain
- **Vitamin B3:** Can enhance NAD⁺ availability

02 OXIDATIVE STRESS

- Imbalance between ROS and neutralizing antioxidants
- Normal consequence of increase in ROS and decrease in endogenous protections that occur with age
- **Vitamins B1 and B2** can mitigate oxidative stress via antioxidant properties

03 HOMOCYSTEINE HOMEOSTASIS

- An excess of homocysteine can produce inflammation and oxidative stress
- Increasing vitamin **B6, B9, and B12** lowers homocysteine levels

04 NEUROTROPIC EFFECTS

- **Vitamin B1:** Contributes to nerve regeneration
- **Vitamin B6:** Neurotransmitter synthesis and inhibits release of neurotoxic glutamate
- **Vitamin B12:** Demonstrates nerve-regenerating effects

05 RETINAL PROTECTION

- **Vitamins B1, B2, B6, B9, and B12** have demonstrated protective effects on the retina and choroid in the context of diabetic retinopathy

Translating Emerging B Vitamin Evidence Into Clinical Practice

The emphasis on simplicity becomes especially important as clinicians consider how B vitamins may be incorporated into AMD management. In practice, recommendations will continue to be anchored by established AREDS2-based supplementation, but emerging evidence suggests that B vitamins may offer an opportunity to support patients earlier, before they progress to more advanced stages of AMD.^{2,3}

Critically, discussions around B vitamins need to distinguish the evidence already established with AREDS2 from areas where additional large, controlled, long-term data are still being generated. Future studies should help guide clinical decision-making and better define the magnitude of potential benefit.

B VITAMIN SUPPLEMENTATION MATTERS IN EARLY AMD

- Elevated homocysteine levels are associated with increased early AMD risk and faster disease progression^{4,22}
- Targeting homocysteine in early AMD provides an opportunity to intervene at an upstream biological level^{4,23}

Association Between B Vitamin Intake and Reduced Risk of AMD Progression

B Vitamins	Dietary Intake	Risk Level
B1	↑	↓ by ~45% to 60% for advanced AMD ²⁴
B6	↑	↓ for wet AMD ²⁵
B9	↑	↓ for developing GA and large drusen ^{25,26}
B12	↑	↓ for AMD by 42% ⁶
B5, B6	↑	↓ by ~28% for advanced AMD ⁵
B6, B9	↑	↓ for advanced AMD ²⁵
B1, B2, B3, B5, B6, B9, B12	↓	Observed in patients with AMD vs without AMD ^{27,28}

Observational studies suggest that higher dietary intake of specific B vitamins is associated with a lower risk of AMD and related retinal changes. Additionally, clinical studies of daily supplements containing B vitamins, often in combination with other nutrients, have reported benefits, including stabilization of atrophic AMD, improvements in retinal function, and a reduced risk of incident AMD compared with placebo.²

Daily Supplement

B2 and 13 other ingredients	Stabilized atrophic AMD ^{29,30}
B3 and 2 other ingredients	Improved a measure of retinal function ³¹
B12 + 11 other ingredients	Functional improvement of preganglionic retinal elements ³²
B6, B9, and B12	↓ risk of AMD vs placebo by ~41% ⁴

Other Considerations of Patient Supplement Use

In real-world practice, patients often take multiple supplements before receiving clinical guidance, including multivitamins and B-complex products, which can lead to questions about combining them with eye vitamins. Safety is a primary concern, particularly regarding overlapping ingredients, although B vitamins are generally well tolerated and unlikely to reach toxic levels at typical doses.^{4,31-33}

Still, supplementation is not one-size-fits-all. Patients with comorbid conditions, including hepatic or renal impairment, malabsorption, or neuropathy, may require individualized counseling, particularly when combining multiple medications and supplements.^{36,37}



MICHAEL SINGER, MD

Patients worry about safety, especially when they are using multiple products. Regarding B vitamins specifically, I explain that they are water-soluble and, when taken within established safety limits, are unlikely to reach toxic levels. That reassurance is important, especially when patients are thinking about combining supplements.



JUDY E. KIM, MD

The AREDS2 trial showed us that beta-carotene can increase the risk of lung cancer compared with lutein and zeaxanthin, demonstrating that some safety signals emerge only through rigorous study. The association with lung cancer was identified because the NEI conducted a long-term, randomized, controlled clinical trial. In exploring the potential for B vitamins to reduce AMD risk, a multicenter clinical trial would be ideal to assess various **factors**, including long-term safety, efficacy, **potential** interactions, appropriate dosages of various ingredients, and effects at different stages of AMD.



SOPHIE BAKRI, MD, MBA

We do still need nuance. Certain populations require a more individualized discussion, including patients with chronic liver or kidney disease, malabsorption syndromes, or neuropathy. We cannot assume uniform metabolism across all patients.

Balancing Innovation With Practical Care Delivery

Looking ahead, there is a clear need to balance scientific insight with practicality. Approaches such as genetic testing, baseline vitamin assessment, and metabolic profiling may refine our understanding of nutrition in AMD but may also add complexity that could limit broad supplementation practices.

Simplicity remains a key advantage of current approaches to ocular nutrition. Clinicians and patients alike will benefit from solutions that preserve ease of use as more data continue to accumulate. Lifestyle modifications coupled with nutritional supplementation remain among the most accessible strategies for reducing the risk of AMD progression.⁷ Future advances will demand rigorous study designs, including modern imaging biomarkers and thoughtful cohort selection, to help usher us into the future of nutritional supplementation for AMD.



RISHI SINGH, MD

As evidence continues to emerge, carefully designed prospective studies will be essential to better define the role of B vitamins in AMD management. Long-term clinical research across the spectrum of AMD severity will help clinicians better understand which patients may benefit most and determine how nutritional strategies should evolve over time.

Conclusion

AREDS2 remains the established foundation of nutritional management for intermediate AMD. Emerging evidence on B vitamins may help address the limited nutritional guidance available for patients with earlier-stage AMD. As clinical evidence develops, these findings may support more informed counseling from the time of diagnosis and promote greater consistency in care.

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