

# PUBLICATIONS

YEAR	TOPIC	TYPE OF STUDY	DESCRIPTION	PUBLICATION
2010	VISION	HUMAN INTERVENTION Single-Blind	This initial exploratory work with meso-zeaxanthin showed that humans respond both very well and very quickly to a supplement with the three macular carotenoids. This experiment suggested that meso-zeaxanthin may offer advantages to a supplement formulation, but more work was needed.	Augmentation of macular pigment following supplementation with all three macular carotenoids: an exploratory study. Connolly EE, Beatty S, Thurnham DI, Loughman J, Howard AN, Stack J, Nolan JM.  <a href="https://pubmed.ncbi.nlm.nih.gov/20819501/">https://pubmed.ncbi.nlm.nih.gov/20819501/</a>
2010	VISION	HUMAN DISCOVERY	This experiment discovered that about 12% of the population (sampled from Ireland) have atypical central dips in their macular pigment. Of interest, these individuals had increased risk of age-related macular degeneration (because of their risk factors). John Nolan hypothesised here that the dips in central macular pigment were uniquely due to a deficiency of meso-zeaxanthin in these individuals because this is where meso-zeaxanthin is concentrated in the macular pigment.	A Central Dip in the Macular Pigment Spatial Profile is Associated with Age and Smoking. Kirby ML, Beatty S, Loane E, Akkali M, Connolly E, Stack J, Nolan JM.  <a href="https://iovs.arvojournals.org/article.aspx?articleid=217726">https://iovs.arvojournals.org/article.aspx?articleid=217726</a>
2011	VISION	HUMAN INTERVENTION, SINGLE-BLIND, PLACEBO-CONTROLLED	This experiment followed participants over a 6-month period to again examine their response to the three carotenoids in their blood and eyes. Importantly, this re-confirmed an exceptional response when using the three carotenoids in a supplement formulation. Also, detailed testing of safety measures showed no adverse clinical implications of consuming these carotenoids.	Supplementation with all three macular carotenoids: response, stability, and safety. Connolly EE, Beatty S, Loughman J, Howard AN, Louw MS, Nolan JM.  <a href="https://pubmed.ncbi.nlm.nih.gov/21929927/">https://pubmed.ncbi.nlm.nih.gov/21929927/</a>
2012	VISION	HUMAN INTERVENTION, SINGLE-BLIND, PLACEBO-CONTROLLED	These results showed that, in healthy individuals, supplementation with all three macular carotenoids offered advantages over preparations lacking meso-zeaxanthin, both in terms of macular pigment response and visual performance enhancement (contrast sensitivity with and without glare). This work generated excitement in that this formulation may be a way to enhance vision for the general population	The impact of macular pigment augmentation on visual performance using different carotenoid formulations. Loughman J, Nolan JM, Howard AN, Connolly E, Meagher K, Beatty S.  <a href="https://iovs.arvojournals.org/article.aspx?articleid=2127668">https://iovs.arvojournals.org/article.aspx?articleid=2127668</a>
2012	VISION	HUMAN INTERVENTION, SINGLE-BLIND, PLACEBO-CONTROLLED	This research discovered how to fix (rebuild) the central macular pigment in participants with a central dip in their macular pigment. The previous hypothesis from John Nolan that meso-zeaxanthin would provide the solution was confirmed, as the only formulation to achieve the desired result had meso-zeaxanthin as part of the formulation. This is a landmark study, claimed by Dr Alan Howard as a major discovery of our time.	Macular carotenoid supplementation in subjects with atypical spatial profiles of macular pigment. Nolan JM, Akkali MC, Loughman J, Howard AN, Beatty S.  <a href="https://pubmed.ncbi.nlm.nih.gov/22652506/">https://pubmed.ncbi.nlm.nih.gov/22652506/</a>
2013	VISION and AGE-RELATED MACULAR DEGENERATION	HUMAN INTERVENTION, SINGLE-BLIND, PLACEBO-CONTROLLED	This was a detailed study of the bioavailability of carotenoid response in blood. The formulation containing all three macular carotenoids was the most effective in terms of achieving the highest combined concentration of these carotenoids in blood, thereby potentially optimising the bioavailability of these compounds for capture by the target tissue (retina).	Serum response to supplemental macular carotenoids in subjects with and without age-related macular degeneration. Meagher KA, Thurnham DI, Beatty S, Howard AN, Connolly E, Cummins W, Nolan JM  <a href="https://pubmed.ncbi.nlm.nih.gov/23211762/">https://pubmed.ncbi.nlm.nih.gov/23211762/</a>
2013	VISION DISCOVERY	REVIEW	This was a detailed scientific review of meso-zeaxanthin, where it comes from and why it is important for eye health and function. This work corrected some misconceptions relating to meso-zeaxanthin.	What is meso-zeaxanthin, and where does it come from? Nolan JM, Meagher K, Kashani S, Beatty S  <a href="https://pubmed.ncbi.nlm.nih.gov/23703634/">https://pubmed.ncbi.nlm.nih.gov/23703634/</a>

2014	METHODS (CREST)	PROTOCOL PUBLISHED BEFORE TRIAL COMMENCED	<p>This paper described the protocol for the gold standard, Central Retinal Enrichment Supplementation Trials (CREST) study. The trials were funded by the European Research Council (ERC).</p> <p>Publishing the protocol before the trial began was important as it ensured that there was no bias in either the experiment or the presentation of the results. The paper presented: the main populations of interest; the interventions to be used and the primary outcome measures. This meant that the researchers could not change the research questions or research outcomes.</p> <p>CREST was the first study to investigate the impact of supplementation with all three macular carotenoids in the context of a large, double-blind, randomized clinical trial.</p>	<p>Central Retinal Enrichment Supplementation Trials (CREST): design and methodology of the CREST randomized controlled trials. Akuffo KO, Beatty S, Stack J, Dennison J, O'Regan S, Meagher K, Peto T, Nolan JM.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4002658/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4002658/</a></p>
2014	ALZHEIMER'S (CARDS 1)	HUMAN CROSS-SECTIONAL	<p>This work, the Carotenoids and Age-Related Dementia Study (CARDS), represented the first discovery for Alzheimer's Disease relating to carotenoids. The research discovered that patients with Alzheimer's Disease are deficient in carotenoids and have poorer vision when compared to age-matched controls.</p> <p>Based upon these results, it was proposed to investigate the impact of the three carotenoids on macular pigment, visual and cognitive function in subjects with Alzheimer's disease.</p>	<p>Macular Pigment, Visual Function, and Macular Disease among Subjects with Alzheimer's Disease: An Exploratory Study; Nolan J, Loskutova E, N Howard A, Moran R, Mulcahy R, Stack J, Bolger M, Dennison J, Akuffo K, Owens N, Thurnham DI, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/25024317/">https://pubmed.ncbi.nlm.nih.gov/25024317/</a></p>
2014	VISION and AGE-RELATED MACULAR DEGENERATION (MOST 1 AMD)	HUMAN INTERVENTION, SINGLE-BLIND, HEAD-TO-HEAD	<p>This study, the Meso-zeaxanthin Ocular Supplementation Trial (MOST), showed that the formulations containing the three carotenoids resulted in improvements in visual function for patients with early age-related macular degeneration (AMD). It showed that measuring contrast sensitivity (ability to distinguish the foreground from the background) is a very good way to demonstrate these improvements.</p> <p>This paper showed results after 12-month supplementation. Further results are shown in the 2015 paper as MOST 2.</p>	<p>Supplementation with three different macular carotenoid formulations in patients with early age-related macular degeneration. Sabour-Pickett S, Beatty S, Connolly E, Loughman J, Stack J, Howard AN, Klein R, Klein B, Meuer S, Myers C, Akuffo K, Nolan JM.</p> <p>SEE SPREAD SHEET FOR LINK</p>
2014	NUTRITION	ANALYTICAL DISCOVERY	<p>This work showed the presence of meso-zeaxanthin in fish and that it may be consumed (in small quantities) as part of the human diet.</p>	<p>Verification of Meso-zeaxanthin in Fish. Nolan JM, Beatty S, Meagher KA, Howard AN, Kelly D, Thurnham DI.</p> <p><a href="https://onlinelibrary.wiley.com/doi/10.1002/ajb.201305?af=R&amp;url=https://onlinelibrary.wiley.com/doi/10.1002/ajb.201305">https://onlinelibrary.wiley.com/doi/10.1002/ajb.201305?af=R&amp;url=https://onlinelibrary.wiley.com/doi/10.1002/ajb.201305</a></p>
2014	VISION	HUMAN INTERVENTION, SINGLE-BLIND, HEAD-TO-HEAD	<p>This research investigated the impact of different amounts of the three carotenoids. The important study showed that the concentrations of meso-zeaxanthin in blood were strongly correlated with macular pigment after 8 weeks of supplementation with this carotenoid. The inclusion of lutein was also important to ensure a full response in macular pigment.</p>	<p>Macular response to supplementation with differing xanthophyll formulations in subjects with and without age-related macular degeneration. Thurnham DI, Nolan JM, Howard AN, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/25311651/">https://pubmed.ncbi.nlm.nih.gov/25311651/</a></p>
2015	VISION (MOST 2 AND)	HUMAN INTERVENTION, SINGLE-BLIND, HEAD-TO-HEAD	<p>This study followed subjects for 3 years. It showed that the longer the period of supplementation, the better the outcome for patients with early age-related macular degeneration. It highlighted the importance of continued supplementation for vision and retinal health.</p>	<p>Sustained supplementation and monitored response with differing carotenoid formulations in early age-related macular degeneration. Akuffo KO, Nolan JM, Howard AN, Moran R, Stack J, Klein R, Meuer SM, Sabour-Pickett S, Thurnham DI, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/25976647/">https://pubmed.ncbi.nlm.nih.gov/25976647/</a></p>
2015	COGNITIVE FUNCTION (CREST)	CROSS-SECTIONAL	<p>This is the first report from the Central Retinal Enrichment Supplementation Trials (CREST). The research demonstrated that macular pigment measurements provide a good indicator for cognitive health (memory and attention) in participants with no eye disease or brain disease (the healthy population).</p> <p>This was the first study in which the team used a computerized software program to assess cognitive response in subjects.</p>	<p>Cognitive Function and Its Relationship with Macular Pigment Optical Density and Serum Concentrations of its Constituent Carotenoids. Kelly D, Coen RF, Akuffo KO, Beatty S, Dennison J, Moran R, Stack J, Howard AN, Mulcahy R, Nolan JM.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/26401946/">https://pubmed.ncbi.nlm.nih.gov/26401946/</a></p>

2015	ALZHEIMER's (CARDS 2)	HUMAN INTERVENTION, DOUBLE-BLIND, PLACEBO-CONTROLLED	<p>This study, the second Carotenoids and Age- Related Dementia Study (CARDS) showed that patients with Alzheimer's disease respond positively to the supplement formulation with the 3 carotenoids for six months. It demonstrated improvements in carotenoids in blood, retina and in visual function for these patients.</p> <p>These results prompted further study to look at the impact of supplementation on cognition and visual function in subjects with Alzheimer's over a longer period of time.</p>	<p>The impact of supplemental macular carotenoids in Alzheimer's disease: a randomized clinical trial</p> <p>Nolan JM, Loskutova E, Howard AN, Mulcahy R, Moran R, Stack J, Bolger M, Coen R, Dennison J, Akuffo K, Owens N, Power R, Thurnham DT, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/25408222/">https://pubmed.ncbi.nlm.nih.gov/25408222/</a></p>
2016	VISION (CREST)	HUMAN INTERVENTION, DOUBLE BLIND, PLACEBO-CONTROLLED DATA & SAFETY MONITORING COMMITTEE MANAGEMENT OF TRIAL	<p>This is the second report from the Central Retinal Enrichment Supplementation Trials (CREST). It confirmed that supplementation with the formulation using the 3 carotenoids improves visual function for adults in the general population with low macular pigment.</p> <p>It demonstrated a way to maximize visual performance and experience, whether for professional or leisure activities.</p>	<p>Enrichment of Macular Pigment Enhances Contrast Sensitivity in Subjects Free of Retinal Disease: Central Retinal Enrichment Supplementation Trials - Report 1.</p> <p>Nolan JM, Power R, Stringham J, Dennison J, Stack J, Kelly D, Moran R, Akuffo K, Corcoran L, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/27367585/">https://pubmed.ncbi.nlm.nih.gov/27367585/</a></p>
2016	MICRO-MICELLE	ANIMAL INTERVENTION, PLACEBO-CONTROLLED	<p>This research demonstrated a way to enrich the carotenoid concentrations in the egg yolks of hens. Additionally, the greatest responses used a novel carotenoid formulation (known as micro-micelle).</p>	<p>Lutein, zeaxanthin and meso-zeaxanthin content of eggs laid by hens supplemented with free and esterified xanthophylls.</p> <p>Nolan JM, Meagher KA, Howard AN, Moran R, Thurnham DI, Beatty S.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4709836/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4709836/</a></p>
2017	VISION & AGE RELATED MACULAR DEGENERATION (CREST, AMD)	HUMAN INTERVENTION, DOUBLE BLIND, PLACEBO-CONTROLLED DATA & SAFETY MONITORING COMMITTEE MANAGEMENT OF TRIAL	<p>This is the third report from the Central Retinal Enrichment Supplementation Trials (CREST). It confirmed that supplementation over 24 months with the formulation using the 3 carotenoids improves visual function for patients with early stage age-related macular degeneration (AMD).</p> <p>This was a major finding because these patients normally lose their visual function and this confirmed that they can improve their function using supplementation with the 3 carotenoids.</p>	<p>The Impact of Supplemental Antioxidants on Visual Function in Nonadvanced Age-Related Macular Degeneration: A Head-to-Head Randomized Clinical Trial.</p> <p>Akuffo KO, Beatty S, Peto T, Stack J, Stringham J, Kelly D, Leung I, Corcoran L, Nolan JN.</p> <p>SEE SPREAD SHEET FOR LINK</p>
2017	VISION (EXIT)	HUMAN INTERVENTION, SINGLE BLIND, HEAD-TO-HEAD	<p>The Egg Xanthophyll Intervention clinical Trial (EXIT) demonstrated that consumption of the carotenoid rich eggs greatly improved blood carotenoid levels but the duration of supplementation (8 weeks) was not long enough to improve macular pigment or visual function levels.</p>	<p>Serum and macular response to carotenoid-enriched egg supplementation in human subjects: the Egg Xanthophyll Intervention clinical Trial (EXIT).</p> <p>Kelly D, Nolan JM, Howard AN, Stack J, Akuffo K, Moran R, Thurnham DI, Dennison J, Meagher K, Beatty S.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29053808/">https://pubmed.ncbi.nlm.nih.gov/29053808/</a></p>
2018	ALZHEIMER's (CARDS 3)	HUMAN INTERVENTION, SINGLE BLIND, HEAD-TO-HEAD	<p>This landmark paper identified that combining the carotenoids with omega-3 fatty acids is beneficial for patients with Alzheimer's disease.</p> <p>This formulation gave a greater carotenoid improvement in blood and also provided improvements in the quality of life for patients with Alzheimer's disease.</p> <p>This preliminary report suggested that due to the small number of patients, further study should be carried out.</p>	<p>Nutritional Intervention to Prevent Alzheimer's Disease: Potential Benefits of Xanthophyll Carotenoids and Omega-3 Fatty Acids Combined.</p> <p>Nolan JM, Mulcahy R, Power R, Moran R, Howard AN.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29945352/">https://pubmed.ncbi.nlm.nih.gov/29945352/</a></p>
2018	COGNITIVE FUNCTION (CREST)	HUMAN INTERVENTION, DOUBLE BLIND, PLACEBO-CONTROLLED DATA & SAFETY MONITORING COMMITTEE MANAGEMENT OF TRIAL	<p>This study showed, for the first time, that supplementation with the 3 carotenoids in the healthy population improves cognitive function by improving memory.</p> <p>A major strength of this study rests on its design. CREST was a double-blind, randomized clinical trial, where neither the subjects nor researchers knew which individuals were consuming the active supplement and which subjects were consuming the placebo, and where allocation to the active treatment or placebo was randomized.</p> <p>This was an important discovery for people in society that want to support brain health.</p>	<p>Supplemental Retinal Carotenoids Enhance Memory in Healthy Individuals with Low Levels of Macular Pigment in A Randomized, Double-Blind, Placebo-Controlled Clinical Trial.</p> <p>Power R, Coen RF, Beatty S, Mulcahy R, Moran R, Stack J, Howard AN, Nolan JN</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/29332050/">https://pubmed.ncbi.nlm.nih.gov/29332050/</a></p>

2019	ALZHEIMER'S & COGNITIVE FUNCTION	MAJOR REVIEW	<p>This paper was a major review to discuss and present all the available information relating to targeted nutrition using omega-3 fatty acids and carotenoids for brain health.</p> <p>Given their selective presence in the brain and their ability to slow down the development of Alzheimer's (namely oxidative damage and inflammation), these nutritional compounds offer potential for optimizing cognition and reducing the risk of Alzheimer's.</p>	<p>The Role of Nutrition for the Aging Population: Implications for Cognition and Alzheimer's Disease.</p> <p>Power R, Prado-Cabrero A, Mulcahy R, Howard AN, Nolan JM.</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/30908950/">https://pubmed.ncbi.nlm.nih.gov/30908950/</a></p>
2020	MICRO-MICELLE	HUMAN INTERVENTION, SINGLE-BLIND, HEAD-TO-HEAD	<p>This work represents the newest discovery by the research team. Here they identified a way to enhance the stability and bioavailability of the 3 carotenoids using a micromicellar formulation.</p>	<p>The Impact of Formulation on Lutein, Zeaxanthin, and meso-Zeaxanthin Bioavailability: A Randomised Double-Blind Placebo-Controlled Study.</p> <p>Green-Gomez M, Prado-Cabrero A, Moran R, Power T, Gomez-Mascaraque L, Stack J, Nolan JM</p> <p><a href="https://pubmed.ncbi.nlm.nih.gov/30908950/">https://pubmed.ncbi.nlm.nih.gov/30908950/</a></p>
2020	ALZHEIMER'S (CARES 1)	HUMAN INTERVENTION, DOUBLE-BLIND, PLACEBO-CONTROLLED	<p>The Cognitive impAIRmEnt Study (CARES) is another important interventional study using the 3 carotenoids combined with omega-3 fatty acids to improve brain health.</p> <p>Strengths of CARES Trial 1 include a comprehensive assessment of mild cognitive impairment (MCI) using sensitive and validated diagnostic measurement tools at screening, enrolment and follow-up assessments. Also the use of a consensus panel provided in-depth characterization of all the individuals taking part in the trial.</p> <p>The population studied here had an early stage of Alzheimer's disease known as mild cognitive impairment (MCI). The supplement intervention improved their memory function using the 3 carotenoids and omega-3 combined.</p>	<p>Targeted Nutritional Intervention for Patients with Mild Cognitive Impairment: The Cognitive impAIRmEnt Study (CARES) Trial 1.</p> <p>Power R, Nolan JM, Prado-Cabrero A, Coen R, Roche W, Power T, Howard AN, Mulcahy R.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7354621/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7354621/</a></p>
2020	BIOAVAILABILITY of CAROTENOIDS for HUMAN HEALTH	HUMAN INTERVENTION, DOUBLE-BLIND, PLACEBO-CONTROLLED	<p>In conclusion, Z and MZ diacetates in a micromicellar formulation presented an increased bioavailability, most likely due to improved micellarisation and absorption e</p>	<p>The Impact of Formulation on Lutein, Zeaxanthin, and meso-Zeaxanthin Bioavailability: A Randomised Double-Blind Placebo-Controlled Study. Marina Green-Gomez , Alfonso Prado-Cabrero , Rachel Moran , Tommy Power, Laura G. Gómez-Mascaraque , Jim Stack and John M. Nolan</p> <p><a href="https://www.fnhnolan.com/wp-content/uploads/2020/10/antioxidants-09-00767.pdf">https://www.fnhnolan.com/wp-content/uploads/2020/10/antioxidants-09-00767.pdf</a></p>
2022	Alzheimer's (CARES 2) Human Intervention, Double-Blind, Placebo-Controlled	HUMAN INTERVENTION, DOUBLE-BLIND, PLACEBO-CONTROLLED	<p>This study demonstrated improvements in working memory for cognitively healthy older adults, following 24-month supplementation with carotenoids, omega-3 fatty acids and vitamin E. The study showed statistically significant improvements in both tissue carotenoid concentrations and plasma omega-3 fatty acids in the active group.</p> <p>Importantly, the observed changes in nutrition levels were directly related to the observed improvements in working memory performance, as individuals with a greater increase in each nutrient made fewer errors in the working memory task.</p>	<p>Omega-3 fatty acid, carotenoid and vitamin E supplementation improves working memory in older adults: A randomised clinical trial</p> <p>Power R, Nolan John M, Prado-Cabrero A, Roche W , Coen R, Power T, Mulcahy Riona</p> <p>Journal Of Clinical Nutrition 41 (2022) 405-414</p> <p><a href="https://www.clinicalnutritionjournal.com/action/showPdf?pii=S0963-961X(22)00053-7">https://www.clinicalnutritionjournal.com/action/showPdf?pii=S0963-961X(22)00053-7</a></p>
2022	Alzheimer's (Re-MIND) Human Intervention, Double-Blind, Placebo-Controlled	HUMAN INTERVENTION, DOUBLE-BLIND, PLACEBO-CONTROLLED	<p>Exponential increases in the prevalence of AD and its relentless progressive nature is driving the need for interventions that help to ameliorate symptoms and improve quality of life in AD patients. Given the positive outcomes demonstrated in this trial, this combined micronutrient dietary supplement should be considered in the overall management of AD.</p>	<p>Supplementation With Carotenoids, Omega-3 Fatty Acids, and Vitamin E Has a Positive Effect on the Symptoms and Progression of Alzheimer's Disease.</p> <p>Nolan JM, Power R, Howard AN, Bergin P, Roche W, Prado-Cabrero A, Pope G, Cooke J, Power T, Mulcahy R.</p> <p><a href="https://www.fnhnolan.com/wp-content/uploads/2022/11/AD202506.pdf">https://www.fnhnolan.com/wp-content/uploads/2022/11/AD202506.pdf</a></p>