Understanding Nutrition of the Vitreous and the Retina: A novel way to improve patient care

NRCI Nutrition Research Centre Ireland

SETU

Prof. John M. Nolan, BSc., Ph.D.

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Disclosures

Provide educational lectures and consultancy advisory work for the following companies:

1. Stauber Nutrition
2. IOSA
3. Macul-Health LLC
4. MaculLearn
5. Heidelberg Engineering GmbH
6. Howard Foundation
7. EPAX
8. ebga-VISION GmbH
9. Supplement Certified Limited

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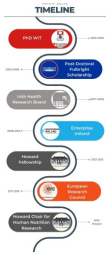
About Professor John Nolan PhD

Director of Nutrition Research Centre Ireland

Howard Chair Human Nutrition Research



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Track Record

Over 20 years of peer-reviewed, published scientific studies – 117 Peer Review Publications

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Nutrition Research Centre Ireland (NRCI)

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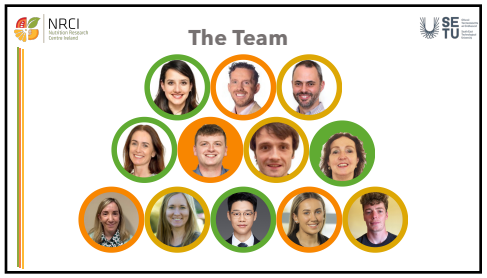
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NRCI: State-Of-The-Art Research Facility
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CLINICAL TRIALS
DIET ASSESSMENT
ANALYTICAL LAB FOR SERUM CAROTENOIDS
MP MEASUREMENT
VISUAL PERFORMANCE EVALUATION
COGNITIVE FUNCTION TESTING

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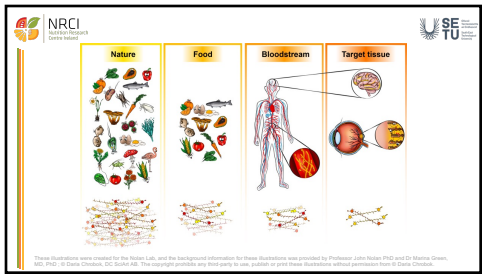
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Nature
Food
Bloodstream
Target tissue

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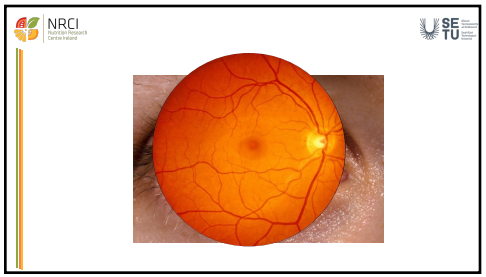
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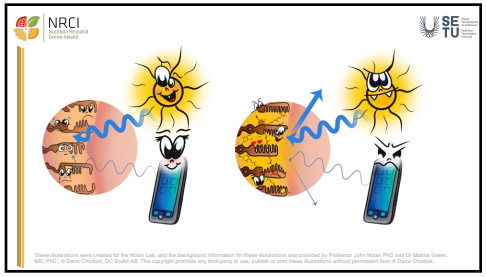
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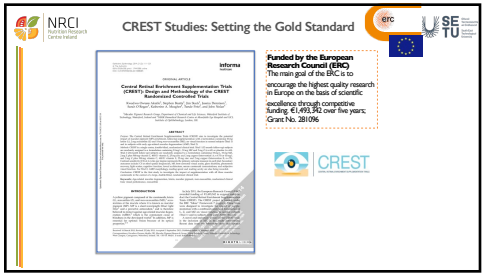
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Funded by the European Research Council (ERC)
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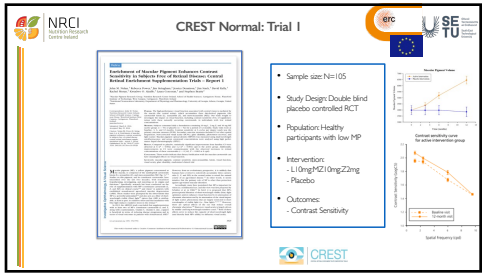

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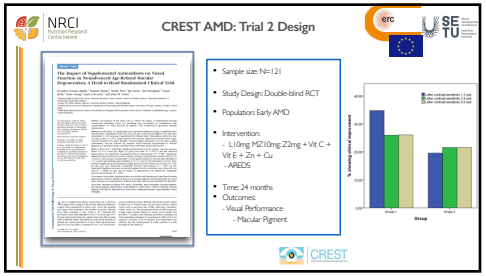

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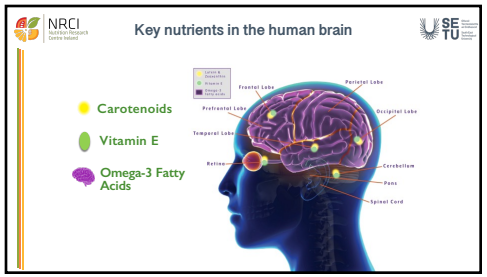

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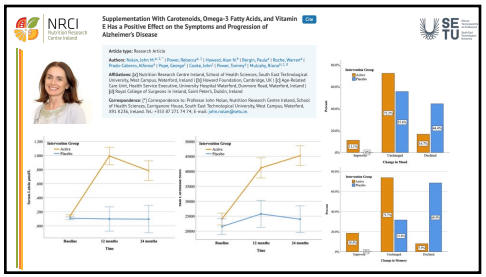

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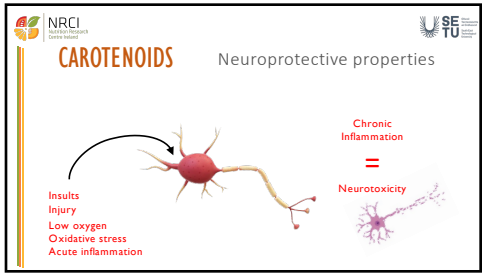

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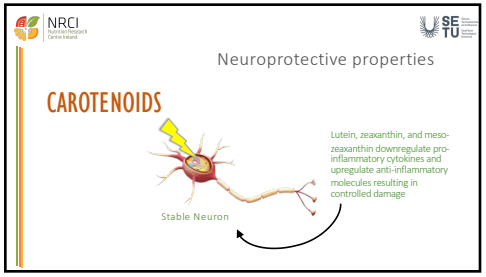

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LIFE Study Design

METHODS

- 6-month randomized, double-blind, placebo-controlled study
- Block randomization stratified by sex

ELIGIBILITY CRITERIA:

Inclusion criteria:
- Adults aged 18 to 60 years
- Informed consent

Exclusion criteria:
- Pregnancy and lactation
- Consumption of supplements
- Malabsorption
- Retinal disease

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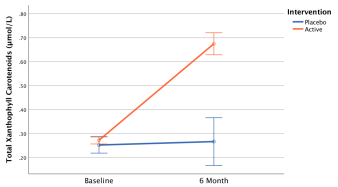
Response: Serum

RESULTS



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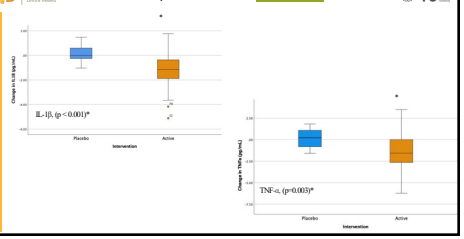
Supplementation with macular xanthophylls leads to a decrease in IL-1β and TNF- α

RESULTS



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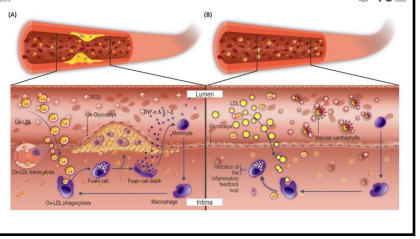
MECHANISM OF PLAQUE FORMATION



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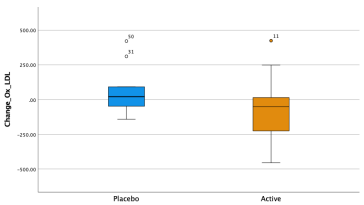
Supplementation with macular xanthophylls leads to a decrease in Oxidative LDL



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Lutein, zeaxanthin, and meso-zeaxanthin supplementation attenuates inflammatory cytokines and markers of oxidative cardiovascular processes in humans

Nicole T. Stringham, Ph.D.[1,2], Marina Green, M.D., Ph.D.[1], Warren Roche, Ph.D.[1], Alfonso Prado[1], Riona Mulcahy M.D.[1], John Nolan, Ph.D.[1]

[1]*Nutrition Research Centre Ireland (NRCI), Southeast Technical University, Waterford, Ireland*

[2]*Northern Arizona University, Flagstaff, Arizona, USA*

Keywords: Macular xanthophyll, carotenoids, oxidized LDL, IL-1β, TNF-α, atherosclerosis

Acronyms:
ELISA: enzyme linked immunosorbent assay
HPLC: high performance liquid chromatography
IL-1β: interleukin 1 beta
IL-6: interleukin 6
L: lutein
LDL: low density lipoprotein
MZ: meso-zeaxanthin
OxLDL: oxidized low-density lipoprotein
ROS: reactive oxygen species
SR-B1: scavenger receptor B1
TNF-α: tumor necrosis factor alpha
Z: zeaxanthin

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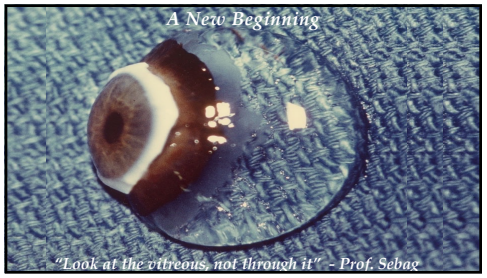

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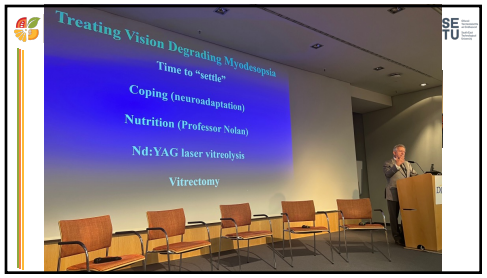

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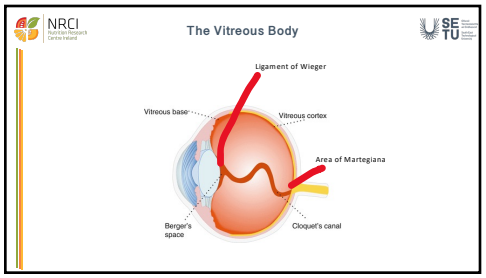

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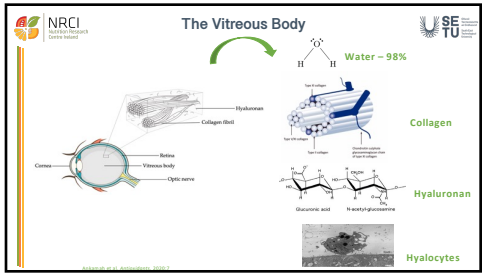

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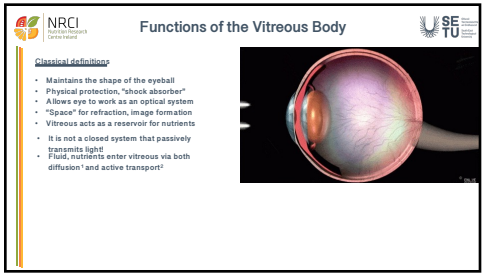

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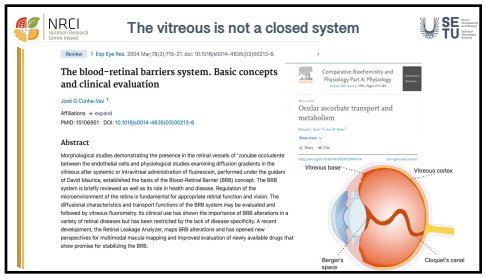

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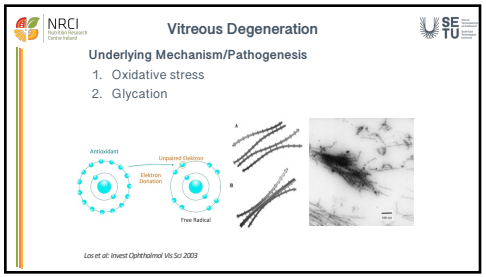

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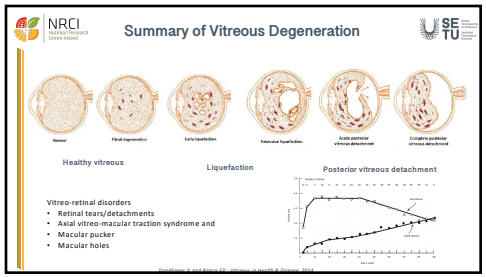

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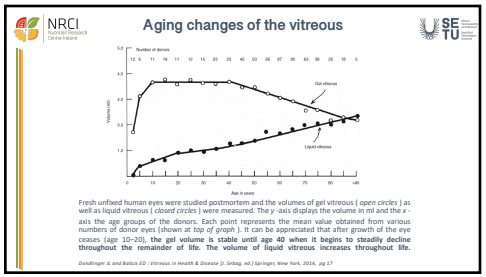

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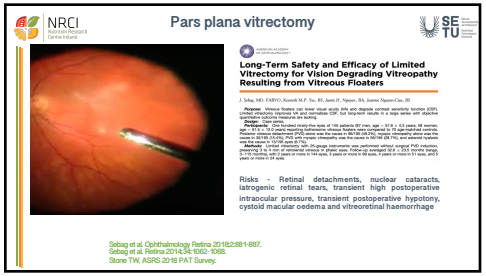

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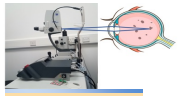
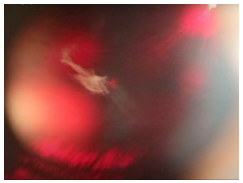
Neodymium-doped yttrium aluminium garnet (Nd:YAG) laser vitreolysis





At least 90% of retinal surgeons have never performed laser vitreolysis

Stone TW. ASRS 2018 PAT Survey.

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Treatment outcomes for vitrectomy & Nd:YAG vitreolysis

Vitrectomy	Nd:YAG vitreolysis
❖ Definitive treatment – removal of all opacities	❖ Subjective improvement: 35-100%
❖ Improved contrast sensitivity after treatment	❖ Objective improvement: 90-94%
❖ Significant reduction in vitreous echodensities on B-scan	❖ Our unpublished data: 71% subjective improvement & 90% objective improvement after 15 months follow-up

Sebag et al. Ophthalmology Retina 2018;2:881-887.
Sebag et al. Retina 2014;34:1052-1058.

Delaney et al. (2002)
Shah & Heier. JAMA Ophthalmol. 2017

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Vitreous Floaters and Quality of Life

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Vitreous Floaters and Quality of Life

- Negative impact = AMD & > glaucoma and DR
- Trade 1 year of every 10 years of their remaining life to get rid of their floaters
- Utility values of acute floaters = chronic floaters

Wagle et al: Am J Ophthalmol 152:60-5, 2011
Zou et al: Qual Life Res 22:1507-14, 2013

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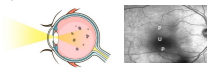
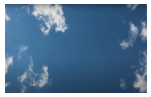
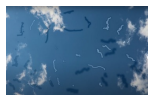
Vitreous Floaters





Healthy vitreous



Vitreous floaters

L.C. Huang et al, Vitreous in Health and Disease [J. Sebag, ed.] New York: Springer; 2014. pg.780.)

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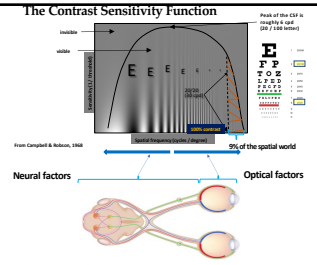
The Contrast Sensitivity Function



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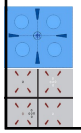
Study: Impact of floaters on contrast sensitivity

Rationale

Previous studies have shown a 51 – 91% reduction in mesopic CS @ 5cpd

Floaters are most noticeable in bright environments

No study to date studying the impact of floaters on photopic CS



Study design

- Case – control study (n = 135)
- Photopic & mesopic FCS at 10cpd
- BCVA
- Flicker sensitivity (Retinal health)
- PVD Assessment

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Table comparing the cases with controls

Variables	Cases (n = 30)	Controls (n = 85)	Sig.
Age (years)	50.87 ± 7.82	48.02 ± 6.65	0.057
Females, No. (%)	16 (53.3)	49 (57.6)	0.831
BCVA, LogMAR			
Photopic	0.06 ± 0.13	0.02 ± 0.11	0.158
Mesopic	0.30 ± 0.12	0.29 ± 0.10	0.480
Flicker threshold (%)			
Foveal	6.74 ± 2.71	6.32 ± 2.06	0.389
Parafoveal	4.36 ± 1.38	4.22 ± 1.26	0.618
FCT (%)			
Photopic	15.46 ± 9.66	11.25 ± 4.59	0.028*
Mesopic	61.48 ± 19.65	48.20 ± 15.10	<0.001*

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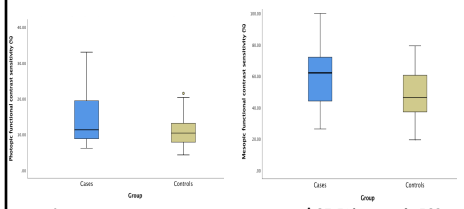
Boxplots showing the functional contrast sensitivity of cases and controls



↓37.4% photopic FCS **↓27.5% mesopic FCS**

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Healthy eye with normal CS

64% CS decline in eye with PVD

Vitreous degeneration diminish spatial contrast, especially at higher light levels when the sensitivity of the retina to contrast is high

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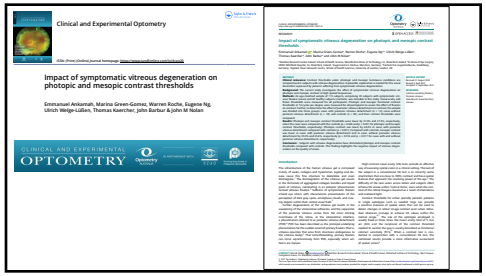

Clinical and Experimental Optometry

Impact of symptomatic vitreous degeneration on photopic and mesopic contrast thresholds

Emmanuel Ankamah, Marina Green-Gomez, Warren Roche, Eugene Ng, Ulrich Welge-Lüßen, Thomas Kaercher, John Barbur & John M Nolan

CLINICAL AND EXPERIMENTAL OPTOMETRY

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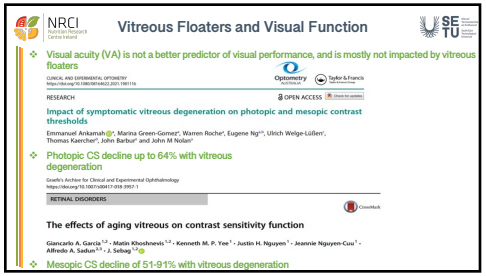

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Vitreous Floaters and Visual Function

- Visual acuity (VA) is not a better predictor of visual performance, and is mostly not impacted by vitreous floaters

CLINICAL AND EXPERIMENTAL OPTOMETRY
https://doi.org/10.1080/08164622.2021.1987116

RESEARCH OPEN ACCESS

Impact of symptomatic vitreous degeneration on photopic and mesopic contrast thresholds

Emmanuel Ankamah, Marina Green-Gomez, Warren Roche, Eugene Ng, Ulrich Welge-Lüßen, Thomas Kaercher, John Barbur and John M Nolan

- Photopic CS decline up to 64% with vitreous degeneration

Graefe's Archive for Clinical and Experimental Ophthalmology
https://doi.org/10.1007/s00417-018-3957-1

RETINAL DISORDERS

The effects of aging vitreous on contrast sensitivity function

Giancarlo A. Garcia · Matin Khoshnevis · Kenneth M. P. Yee · Justin H. Nguyen · Jeannie Nguyen-Cuu · Alfredo A. Sadun · J. Sebag

- Mesopic CS decline of 51-91% with vitreous degeneration

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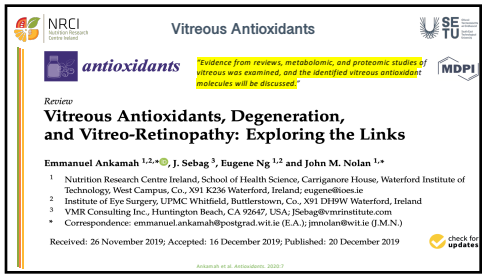

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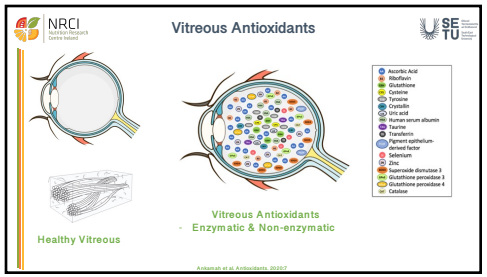

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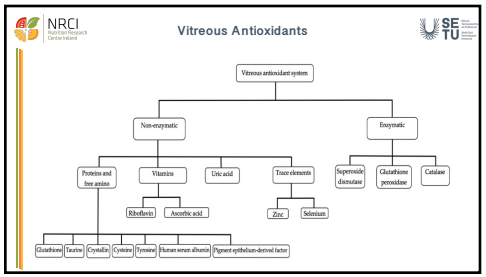

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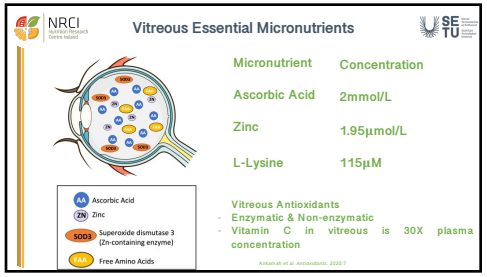

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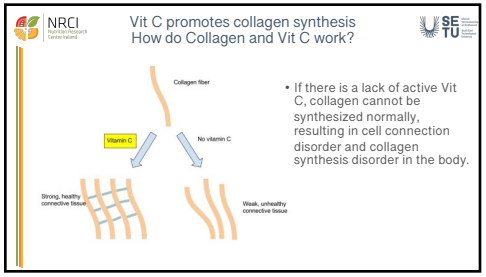

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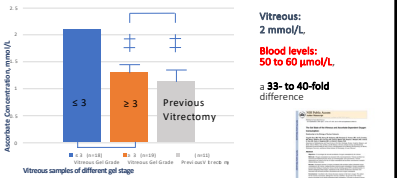
Vitamin C and the vitreous



Vitreous:
2 mmol/L,

Blood levels:
50 to 60 µmol/L.

a **33- to 40-fold** difference

Mean ascorbate concentration in vitreous samples obtained at the time of surgery. In patients who were undergoing their first vitrectomy, the gel status of the vitreous was scored on a **5-point scale**. **Vitreous that received a score of 3 or less had firmer gel; greater than 3, more liquid.** *P>.05. †P<.001.

Shui Y-B, et al. *The gel state of the vitreous and ascorbate-dependent oxygen. Arch Ophthalmol. 2010 April 1.*

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Micronutrient Formulation

Antioxidants
Vitamin C
Zinc
Citrus extract (Flavonoids)

Antiglycation
L-lysine
Citrus extract (Flavonoids)
Vitis vinifera (Grape seed) extract

Enzymatic
L-lysine
Citrus extract (Flavonoids)

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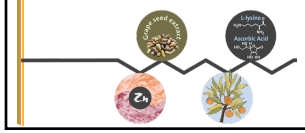
Components:

- **125 mg L-lysine**: An essential amino acid, necessary for human health, but not produced by the body. L-lysine prevents collagen glycation.
- **40 mg Vitamin C**: Guards against intraocular oxidative stress by consuming oxygen released at the vitreoretinal interface.
- **26.3 mg Vitis Vinifera:** Grapeseed extract.
  - Of which **25 mg** are **Proanthocyanidins**, which reduce glycation.
- **5 mg Zinc:** Helps reduce processes which lead to vitreal degeneration. Additionally, zinc has antioxidant and antiglycation properties.
- **100 mg Citrus Fruit Extract***
  - Of which **60 mg** is **Hesperidin**, an antioxidant



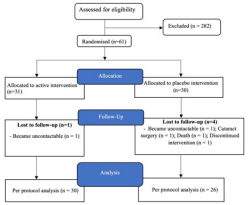
57

Scholarship no. WD_2017_43 ISRCTN15605916

HYPOTHESIS

Supplementation with vitreous antioxidants and antiglycative micronutrients improves the quality of life and visual function in patients with floaters

58



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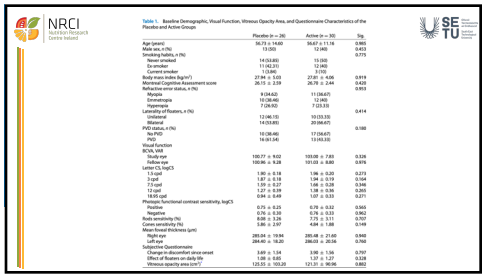
Scholarship no. WD_2017_43 ISRCTN15605916

DESIGN

- 6-month, double-blind, placebo-controlled clinical trial.
- 50:50 randomization
- Active Group (n = 31) - 125mg l-lysine, 40mg vitamin C, 25mg Vitis vinifera extract, 5mg zinc, and 100mg Citrus aurantium extract
- Placebo Group (n = 30) – microcrystalline cellulose

60



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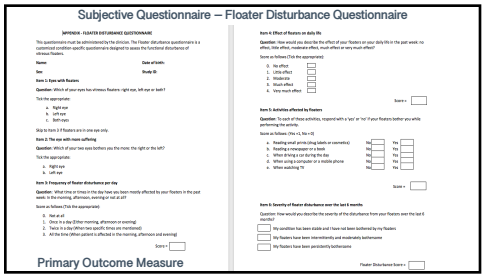

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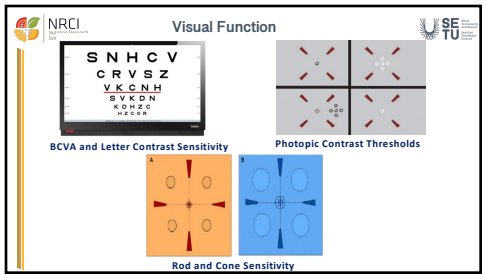

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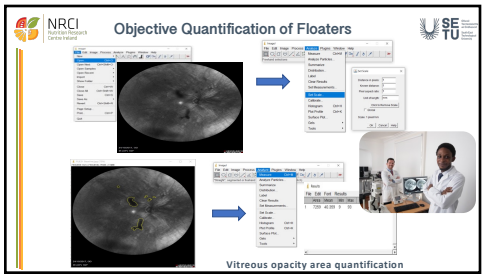

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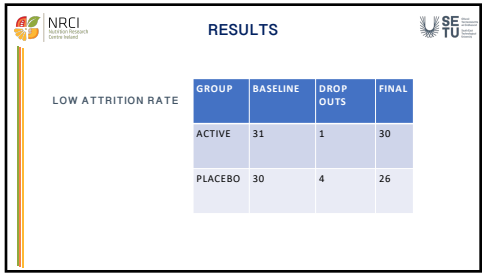

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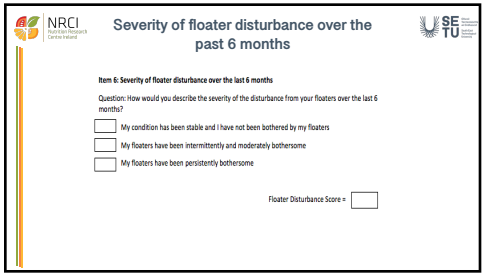

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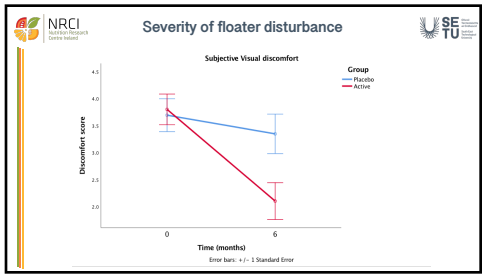

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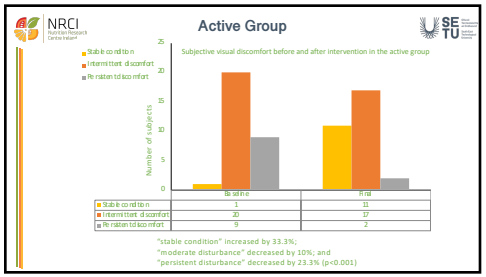

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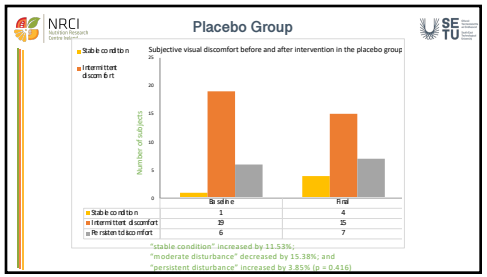

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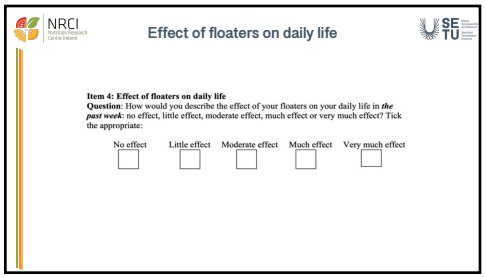

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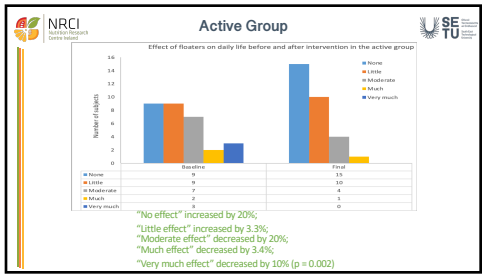

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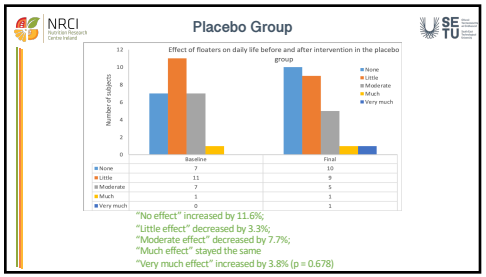

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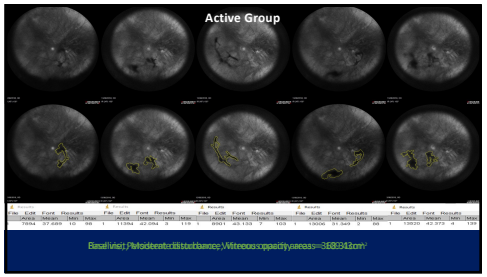

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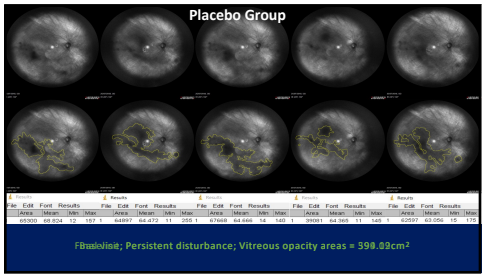

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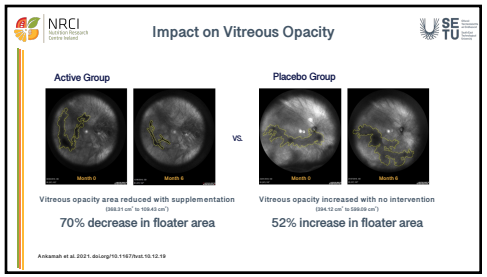

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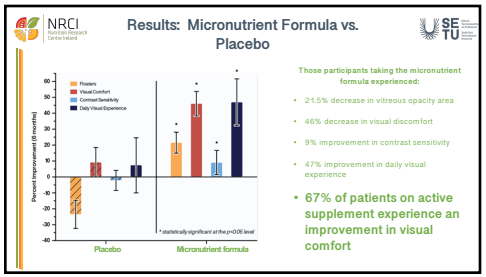

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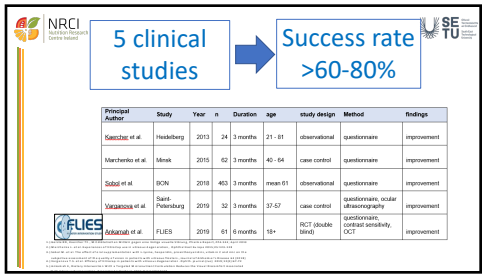

Principal Author	Study	Year	n	Duration	age	study design	Method	findings
Kaercher et al.	Heidelberg	2013	24	3 months	21 - 81	observational	questionnaire	improvement
Marchenko et al.	Minsk	2015	62	3 months	40 - 64	case control	questionnaire	improvement
Sobol et al.	BION	2018	463	3 months	mean 61	observational	questionnaire	improvement
Vargasova et al.	Saint-Petersburg	2019	32	3 months	37-57	case control	questionnaire, ocular ultrasonography	improvement
Ankamah et al.	FLIES	2019	61	6 months	18+	RCT (double blind)	questionnaire, contrast sensitivity, OCT	improvement

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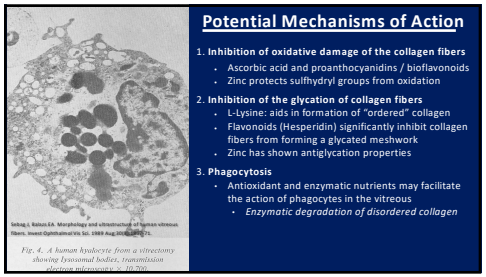

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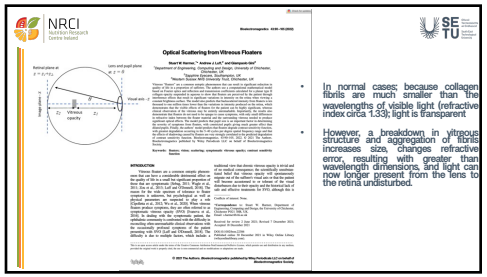
NRCI
Nutrition Research Centre Ireland
SE TU
Optical Scattering from Vitreous Floaters
In normal cases; because collagen fibrils are much smaller than the wavelengths of visible light (refractive index circa 1.33); light is transparent
However, a breakdown in vitreous structure and aggregation of fibrils increases size, changes refractive error, resulting with greater than wavelength dimensions, and light can now longer present from the lens to the retina undisturbed.

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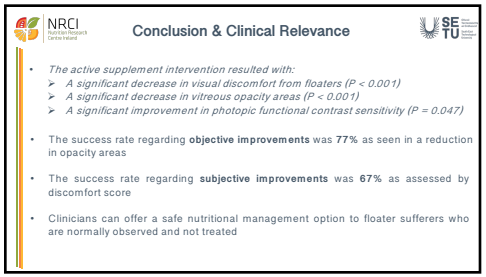
NRCI
Nutrition Research Centre Ireland
SE TU
Conclusion & Clinical Relevance
The active supplement intervention resulted with:
A significant decrease in visual discomfort from floaters (P < 0.001)
A significant decrease in vitreous opacity areas (P < 0.001)
A significant improvement in photopic functional contrast sensitivity (P = 0.047)
The success rate regarding objective improvements was 77% as seen in a reduction in opacity areas
The success rate regarding subjective improvements was 67% as assessed by discomfort score
Clinicians can offer a safe nutritional management option to floater sufferers who are normally observed and not treated

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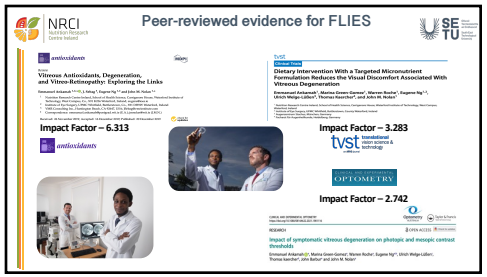
NRCI
Nutrition Research Centre Ireland
SE TU
Peer-reviewed evidence for FLIES
antioxidants
Vitreous Antioxidants, Degeneration, and Vitreo-Retinopathy: Exploring the Links
Impact Factor – 6.313
antioxidants
Impact Factor – 3.283
tvst translational vision science & technology
Impact Factor – 2.742
OPTOMETRY
Dietary Intervention With a Targeted Micronutrient Formulation Reduces the Visual Discomfort Associated With Vitreous Degeneration
Impact of symptomatic vitreous degeneration on photopic and mesopic contrast thresholds

81


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www.profjohnnolan.com
INNOVATION

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