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Prof. Justin Roberts, Ph.D, C.Sci, SFHEA, mBANT - Editor-in-Chief

Prof. Roberts is Professor in Health and Exercise Nutrition at the Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University. Justin brings to Nutrition Evidence over 25 years applied and research experience in the field of exercise nutrition and metabolism. He has published over 40 peer-reviewed, scientific articles and book chapters, and is a reviewer for numerous academic journals.

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MEET THE NED EXPERT REVIEWERS

GUEST REVIEWER

We are joined in this issue by Guest Expert Reviewer, Gilian Crowther MA (Oxon), Dip NT/ND, FBANT, CNHC reg. a fully qualified Naturopath and Nutritional Therapist. Gilian specialises in complex multisystem disorders, and finds that her core focus mitochondrial dysfunction underlies much of today's chronic disease. Gilian provides two expert reviews on EGCG and Urolithin and their effect on mitochondrial biomarkers.

EXPERT REVIEWERS IN THIS ISSUE

(In order of appearance)

Ana-Paula Agrela, MSc, BSc (Hons)

Carol Granger, DProf BSc (Hons) MSc MRSB CBiol

Clare Grundel, MSc, BA (Hons), mBANT

Gail Brady,MSc, DipION, AFMCP, mBANT, rCNHC

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Kirsty Baxter, MSc, DipION, mBANT

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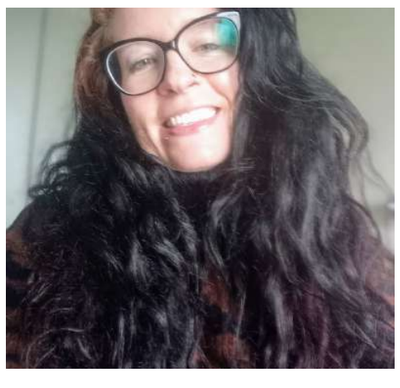
Dr Yassine Bendiabdallah, MPharm, PhD, IP, ABAAHP



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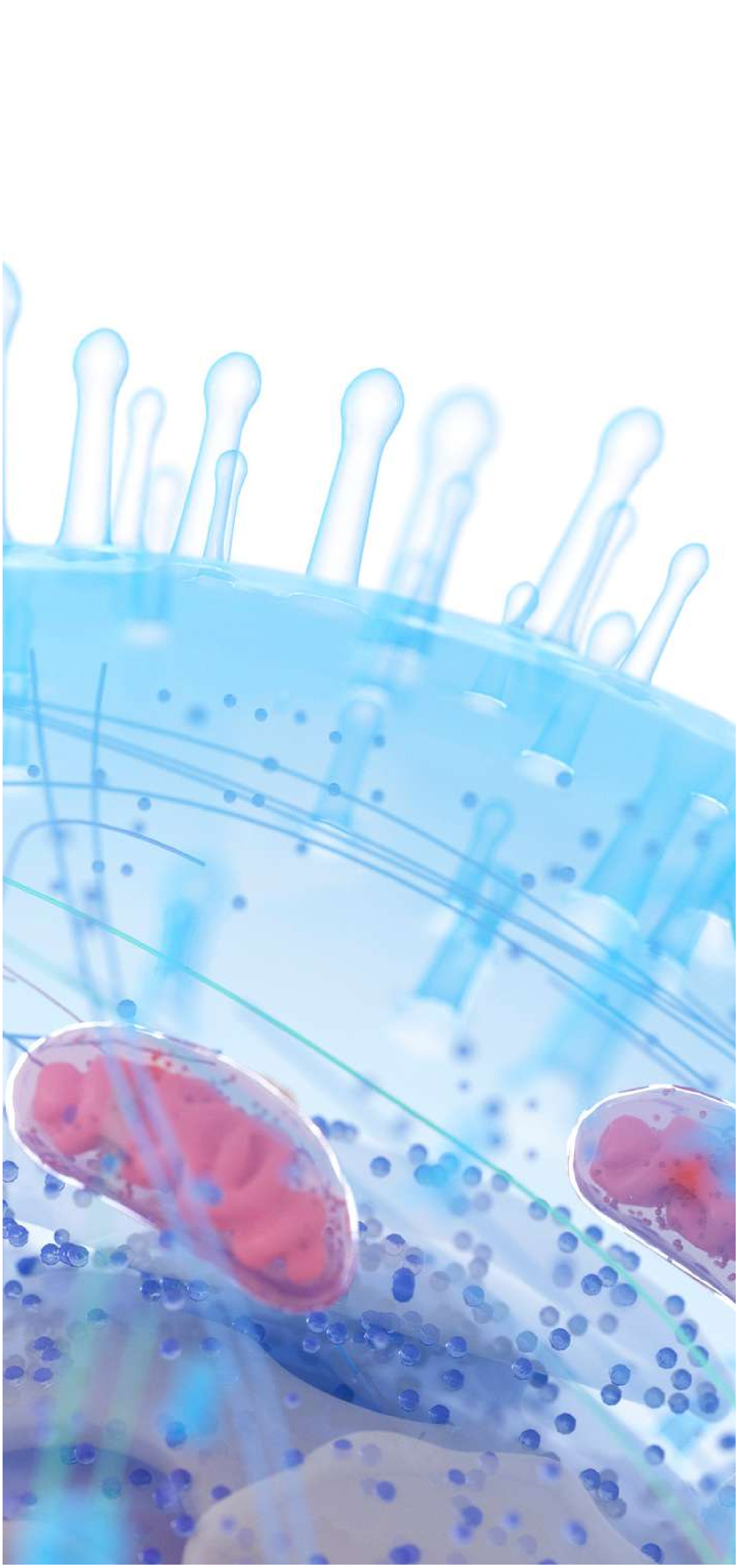
MATERIAL MEANDERS



3 REVIEWS

UROLITHIN & MITOCHONDRIA

Gillian Crowther

UROLITHIN A IMPROVES MUSCLE STRENGTH, EXERCISE PERFORMANCE, AND BIOMARKERS OF MITOCHONDRIAL HEALTH IN A RANDOMIZED TRIAL IN MIDDLE-AGED ADULTS

Singh, A ; D'Amico, D ; Andreux, PA ; Fouassier, AM ; Blanco-Bose, W ; Evans, M ; Aebischer, P ; Auwerx, J ; Rinsch, C
Cell reports. Medicine. 2022;3(5):100633

SUMMARY REVIEW:

INTRODUCTION:

- Urolithin A (UA) is a microbiome metabolite – known as a postbiotic - of elligitannins and polyphenolic compounds found in some plant foods including pomegratate, berries and walnuts.
- In animal models, UA has previously been shown to have a range of potential health benefits involving induction of mitophagy and on mitochondrial function, as well as on disease states including osteoarthritis, inflammatory bowel disease, cardiovascular disease, and neurodegenerative disorders.
- The current study sought to establish proof-of-concept of the efficacy and safety of long-term UA supplementation on physiological endpoints in middle-aged adults.

METHOD:

- The primary outcome was peak power output and secondary outcomes included a range of clinical and physiological parameters linked to muscle strength, exercise tolerance and physical performance.
- The study tested UA in 500mg and 1000 mg doses against placebo in a 3-arm randomized-controlled trial in n= 88 subjects aged 40-64y who were healthy, overweight (BMI 25.0-34.9 kg/m2), sedentary, and who had a low VO2max at study inclusion. 79 subjects completed the study.
- Subjects were assessed at baseline, midpoint (2 months) and endpoint (4 months). In addition to the UA intervention, subjects were asked to maintain low physical activity status for the duration of the trial, and avoid pomegranates and supplements known to influence muscle performance (high protein, CoQ10m vitamin B3 or L-carnitine).

RESULTS:

- **Though a difference in peak power output (primary outcome) was not observed, muscle strength improved by up to c. 12% with 500 mg daily UA (p=0.027). With 1000 mg UA daily, aerobic endurance improved by up to 15% (p=0.03), gait speed increased by 7% (p=0.004), and in the 6-minute walk test subjects improved by 7% (p=0.008) and walked on average more than 30 additional meters, indicating a clinically meaningful difference in mobility.**
- **In addition, subjects in the UA groups had improved biomarkers of cellular health. With 1000 mg UA daily, inflammation was reduced (CRP, p<0.05; IFN-γ and TNF-α, both p<0.05). In addition, biomarkers of mitochondrial efficiency were also improved with 500 mg UA daily, ling increased protein levels related to improved mitophagy, and expression of genes belonging to mitochondria.**

CONCLUSION:

- UA was deemed as safe and well tolerated at both 500 mg and 1000 mg doses for 4 months' administration.
- A strength of the study was that the groups were balanced for all physiological parameters at baseline. However, the ratio of females was 2:1, and ethnicity was mainly western European. This may limit interpretation of the findings.
- All authors except one are either employees, board members or members of the scientific advisory board of Amazentis SA, who both manufacture Mitopure, the UA supplement used, and who funded this trial.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

Mitochondrial dysfunction is associated with ageing and linked to deterioration of skeletal muscle and sarcopenia. Improving mitochondrial health may therefore help to improve muscle health as we age. Previous studies have demonstrated improvements in muscle endurance with long term UA intake in older adults (1) and the study by Singh et al. supports these findings in middle-aged adults. For middle-aged clients who are noticing a decline in muscle strength, exercise performance, or a general increase in fatigue, taking 500-1,000 mg UA daily for two to four months could lead to noticeable improvements in symptoms. The compounds from which UA is derived are also found in polyphenol-rich plant foods including pomegranates, berries and walnuts, therefore consuming these foods may be useful dietary additions for the same purpose.

These findings are likely to be relevant for younger populations too, as mitophagy, which is part of the action of UA, contributes to the removal and recycling of dysfunctional mitochondria, allowing healthier intact mitochondria to take their place.

CLINICAL PRACTICE APPLICATIONS:

- Mitophagy is an important step in improving mitochondrial health. This study demonstrates the potential of UA to activate this pathway.
- In healthy middle-aged adults who are overweight or obese, sedentary and with low physical performance, oral UA supplementation at a sufficient dose and duration may:
- increase muscle strength
- increase mitophagy proteins in human skeletal muscle, as well as various other mitochondrial markers
- increase exercise performance and aerobic exercise
- be a valuable intervention to consider in clients who are suffering from mitochondrial dysfunction

CONSIDERATIONS FOR FUTURE RESEARCH:

This study was exploratory and the sample size for some of the outcomes was very small and inadequate to demonstrate true statistical significance. Future studies of similar design are needed to confirm the findings.

Nevertheless, the study was well-structured with carefully elaborated markers. It could be used as a template for future studies.

REVIEWER: Gilian Crowther, Guest Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A - Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EGCG & MITOCHONDRIA

Gilian Crowther

COMBINED EPIGALLOCATECHIN-3-GALLATE AND RESVERATROL SUPPLEMENTATION FOR 12 WK INCREASES MITOCHONDRIAL CAPACITY AND FAT OXIDATION, BUT NOT INSULIN SENSITIVITY, IN OBESE HUMANS: A RANDOMIZED CONTROLLED TRIAL

Most, J ; Timmers, S ; Warnke, I ; Jocken, JW ; van Boekschoten, M ; de Groot, P ; Bendik, I ; Schrauwen, P ; Goossens, GH ; Blaak, EE
The American journal of clinical nutrition. 2016;104(1):215-27

SUMMARY REVIEW:

INTRODUCTION:

- This randomised controlled trial investigated the effect of 12-wk supplementation of combined epigallocatechin-3-gallate and resveratrol (EGCG+RES) on metabolic profile, mitochondrial capacity, fat oxidation, lipolysis, and insulin sensitivity.

METHOD:

- 38 overweight and obese subjects (active ingredient cohort n = 18; placebo n = 20) received 282 mg/d EGCG and 80 mg/d resveratrol; one capsule of each was taken at breakfast and dinner. Subjects were medically screened 10 times in total, including: 3 times before starting supplementation, 3 times during the supplementation period, and 3 in the last week of supplementation.
- EGCG capsules contained 94% epigallocatechin-3-gallate (141 mg/capsule) and resveratrol capsules contained 20% trans-resveratrol (40 mg trans-resveratrol in Polygonum cuspidatum extract/capsule).
- Medical screening included skeletal muscle biopsies (Vastus lateralis), with various tests done to measure oxidative capacity, X-ray absorptionmetry, a high-fat mixed meal (HFMM) test, and an insulin test via hyperinsulinemic-euglycemic clamp; meal intake before screening was standardised.
- Blood probes were also taken, and subjects completed food records; exact kcals per macronutrient were calculated.

REVIEWER: Gilian Crowther, Guest Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A - Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- 12 wks of EGCG+RES intake increased skeletal muscle oxidative capacity as well as upregulating mitochondrial pathways, which may translate into an improved metabolic risk profile over time because greater mitochondrial capacity has been associated with higher insulin sensitivity in other studies
- The fat oxidation alterations in those taking the active ingredients vs. the placebo group suggests that this intervention could lead to metabolic adaptation towards lipids instead of CHOs as a fuel source, over time.
- EGCG+RES intake attenuated the increase in plasma triacylglycerol levels during the HFMM test, while the levels were significantly increased in the placebo group after 12 wks. This suggests that the intervention may provide positive support for individuals with high triacylglcerol (triglyceride) levels
- The ratio of total cholesterol to HDL cholesterol tended to decrease after EGCG+RES supplementation but not after placebo. Increased total & HDL cholesterol marker for myocardial infarction risk, so this intervention could help with persons who have disordered cholesterol values, and perhaps contribute to reducing their MI risk over time.

🔍 CLINICAL PRACTICE APPLICATIONS:

The results of the study, which relate to clinical practice, highlight:

- 12 weeks of ECGC+RES supplementation increased mitochondrial capacity.
- EGCG+RES increased skeletal muscle oxidative capacity as well as protein expression of OxPhos complexes in skeletal muscle.
- EGCG+RES supplementation significantly affected fasting substrate oxidation, whereas fat oxidation declined in the placebo group; this suggests that it could help to improve fat metabolism.
- 12 weeks of ECGC+RES supplementation preserved fasting and postprandial fat oxidation compared with placebo.
- Plasma triacylglycerol levels were not significantly increased in the EGCG+RES cohort on being given an HFMM test after 12 wks, whereas they went up in the placebo group, indicating that this intervention preserved fasting and post-prandial fat oxidation.
- EGCG+RES group tended to decrease visceral adipose tissue mass by ~11% vs. placebo,
- These findings suggest that combined ECGC+RES supplementation might support mitochondrial function and weight loss/insulin sensitivity over a longer period of time

? CONSIDERATIONS FOR FUTURE RESEARCH:

- The EGCG+RES supplementation had no effect on postprandial glucose, insulin and FFA concentrations or local interstitial glucose and glycerol concentrations. Altering the study parameters in the future might identify changes of these markers.
- There was a tendency toward visceral adipose tissue mass decrease that was not considered significant, but altering dosage and length of time of a similar study might result in a more notable outcome related to weight loss, which was a targeted endpoint
- The combined supplements were not found to affect energy expenditure, contrary to a previous study by the same team, which was for a much shorter time period. It would be interesting to identify why this was.
- Complex and numerous gene set enrichment analyses were performed indicating that the most upregulated pathways after EGCG+RES supplementation were related to the Krebs cycle and electron transport chain, whereas pathways related to CHO metabolism were upregulated in the placebo group. This was taken to indicate that the increased mitochondrial capacity after EGCG +RES supplementation is accompanied by changes at the transcriptional and translational levels; further follow-up of this would be useful to know what clinical impact this has longer term

MITOCHONDRIAL ANTIOXIDANTS

EFFECT OF MITOCHONDRIAL-TARGETED ANTIOXIDANTS ON GLYCAEMIC CONTROL, CARDIOVASCULAR HEALTH, AND OXIDATIVE STRESS IN HUMANS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Mason, SA ; Wadley, GD ; Keske, MA ; Parker, L
Diabetes, obesity & metabolism. 2022;24(6):1047-1060

SUMMARY REVIEW:

INTRODUCTION:

- A systematic review and meta-analysis was conducted to evaluate the current evidence from randomised control trials (RCTs) in humans on the effects of mitochondrial-targeted antioxidant (mitoAOXs) on glycaemic control, cardiovascular health, and oxidative stress.

METHOD:

- 19 Randomised control trials (n= 884 participants) using mitoAOXs (including Elamipretide, MitoQ and MitoTEMPO) were included from MEDLINE-PubMed, Scopus, EMBASE and Cochrane Library databases. A Cochrane Collaboration's tool was used to assess risk bias and to grade the quality of the trials and their certainty of the evidence.

RESULTS:

- A quantitative analysis on glycaemic control found no significant effect for fasting glucose in response to MitoQ supplementation.
- A quantitative analysis on cardiovascular health related outcomes found a significant lowering effect of mitoAOXs brachial flow-mediated dilation (FMD) (standardized mean difference: 1.19, 95% CI: 0.28, 2.16; I2: 67%) and an improved blood pressure (standardized mean difference: -0.32, 95% CI:-0.95, 0.30; I2: 0%) in patients with atherosclerosis-related impairment of renal blood flow.
- A quantitative analysis on oxidative stress-related outcomes found no significant effect of mitoAOX on malondialdehyde or F2-Isoprostanes.

CONCLUSION:

While short-term studies indicate that mitoAOXs are generally well tolerated, there is limited evidence to support the use of mitoAOXs in the management of glycaemic control and cardiovascular health. Future research should focus on the effects of mitoAOXs on glycaemic control and endothelial function in target clinical population groups.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Mitochondria are a major producer of reactive oxygen species (ROS) in cells. Excess mitochondrial ROS has been implicated in the pathophysiology of various chronic diseases including Parkinson's disease, cardiovascular disease (CVD), Type 2 diabetes and cancer.
- This review reported that there is limited evidence to support the use of mitoAOXs in the management of glycaemic control and cardiovascular health. However, there are promising findings on the effect of mitoAOXs on endothelial function that warrant consideration and further investigation in target clinical population groups.

🔍 CLINICAL PRACTICE APPLICATIONS:

- The findings from this review suggest limited evidence to support the use of mitoAOX in the management of glycaemic control or cardiovascular health.
- However, there are some potential promising findings which included improved endothelial function (particularly brachial FMD) and improved blood pressure in patients with atherosclerosis-related impairment of renal blood flow.
- Based on this review, practitioners may consider recommending the use of mitoAOXs only in quite specific circumstances, namely to improve endothelial function in patients with a risk of brachial FMD or high blood pressure associated with atherosclerosis-related impairment of renal blood flow.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- The potential benefits of TRE in neurodegenerative diseases such as AD should be further investigated clinically.
- The optimal time to initiate fasting needs to be identified in future trials.
- The potential benefits of TRE in neurodegenerative diseases such as AD in the context of sleep should be further investigated.

EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None

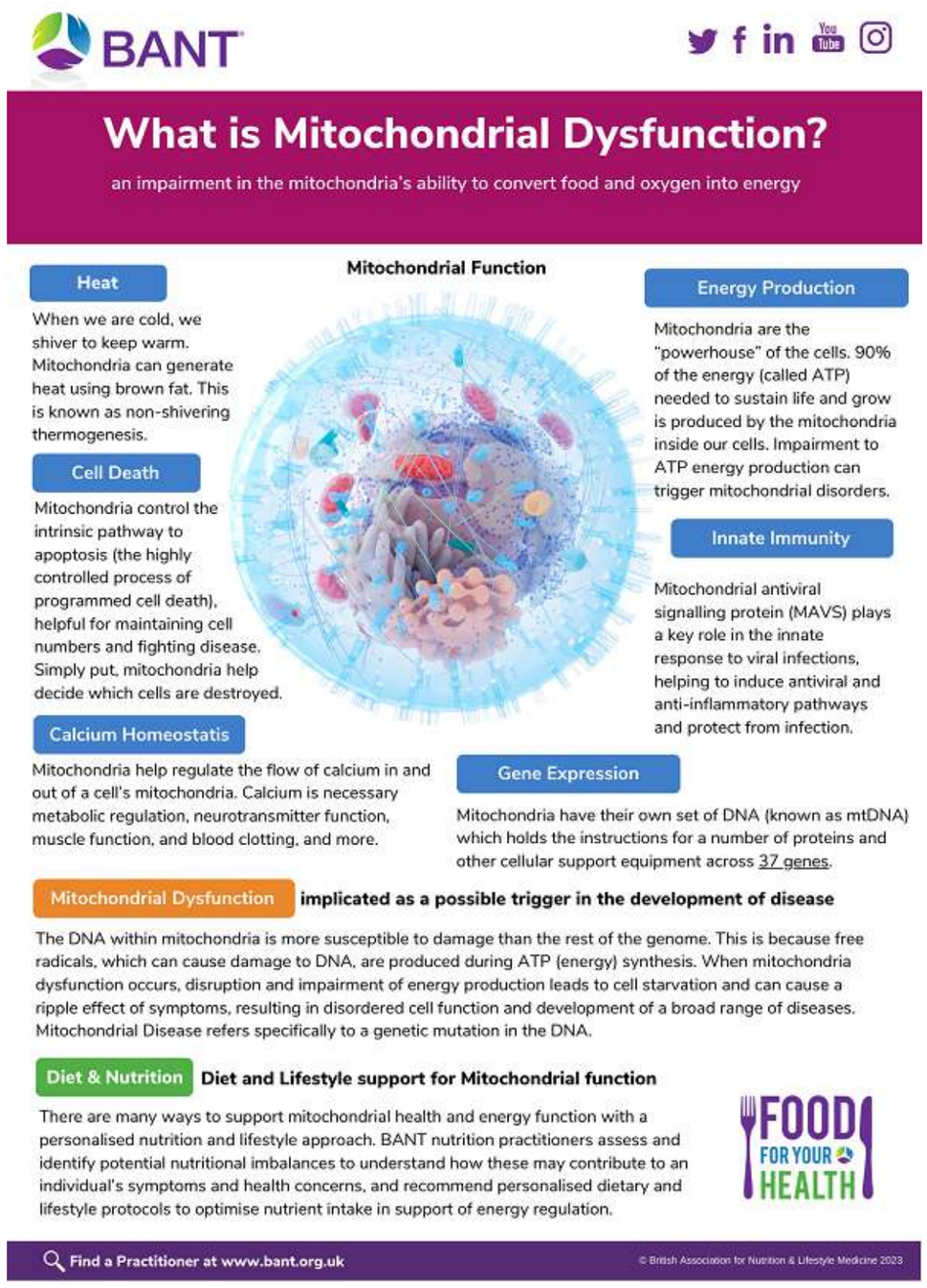
EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University and holds a Health Coaching certificate from Zest for Life. She completed her Master's degree in Holistic Health and Nutritional Education through Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

ADDITIONAL RESOURCES

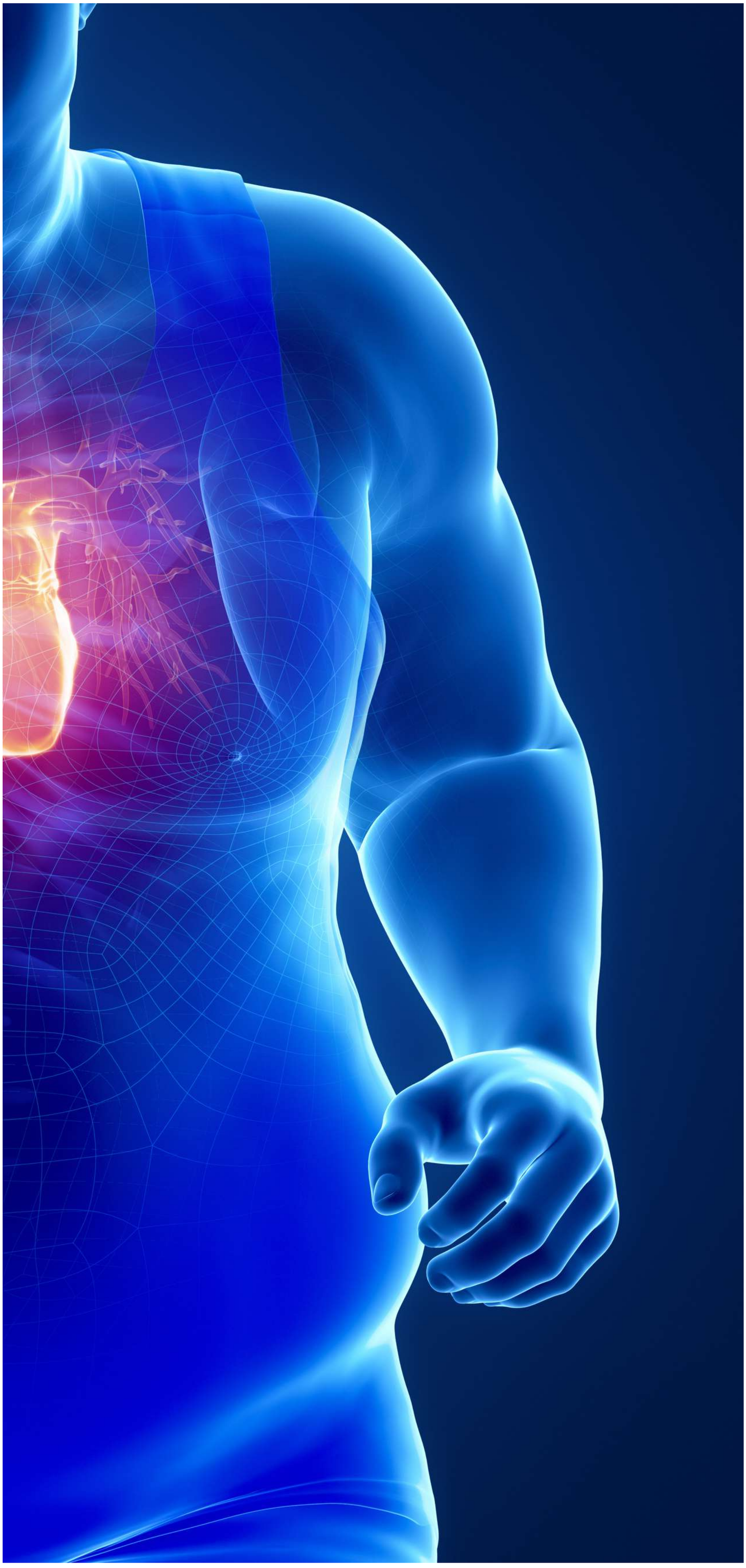
NED INFOBITES AND CLINICAL FACT SHEETS

Our monthly NED InfoBites are designed to provide quick overviews of some of the latest research available on particular health issues and nutrition topics. Designed as a one-page clinical handout, the NED InfoBites unite our editorial team's pick of the research and provide a plain-language summary suitable for sharing with nutrition clients.



NED InfoBites are supported by the BANT Fact Sheets which provide commonly accepted overviews, symptoms and explanations of risk factors for diet-induced illness and non-communicable diseases that can be supported by personalised nutrition and lifestyle medicine.

METABOLIC SYNDROME



7 REVIEWS

INTERMITTENT FASTING

EFFECT OF INTERMITTENT FASTING DIET ON GLUCOSE AND LIPID METABOLISM AND INSULIN RESISTANCE IN PATIENTS WITH IMPAIRED GLUCOSE AND LIPID METABOLISM: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Yuan, X ; Wang, J ; Yang, S ; Gao, M ; Cao, L ; Li, X ; Hong, D ; Tian, S ; Sun, C
International journal of endocrinology. 2022;2022:6999907

SUMMARY REVIEW:

INTRODUCTION:

Management of glucose and lipid metabolism can be achieved through weight reduction using dietary interventions such as very low calorie or CHO diets, which may be effective but difficult to sustain long term. An alternative approach for weight management, improved insulin resistance and subsequent prevention of comorbitities e.g. Type 2 Diabetes (T2D), Cardiovascular Disease (CVD) and cancer, is Intermittent Fasting (IF). such as time restricted or periodic fasting. This study summarises the effects of IF dietary interventions lasting less than three months in overweight and obese women with Metabolic Syndrome, defined as the presence of any metabolic dysfunction including obesity, hyperglycaemia, dyslipidaemia or hypertension.

METHOD:

The meta-anlaysis was carried out following PRISMA guidelines. A literature search in PubMed and Medline using the keywords obesity/overweight, IF diet, metabolic syndrome, RCT's and humans resulted in 10 studies with 12 types of intervention for analysis. The following outcomes were evaluated: glucose and lipid metabolism, insulin resistance, weight loss and blood pressure.Results were analysed in R software using mean differences and 95% confidence intervals, and either random or fixed effects depending on the Cochrane's Q and I(2) statistics. Funnel plots were inspected for potential bias and Egger's regression tests for publication bias.

RESULTS:

There were significant differences before and after the interventions for all glucose and lipid metabolism markers as well as body weight and systolic blood pressure :

GLUCOSE METABOLISM:

- Fasting glucose reduced by 0.15mmol/L
- Insulin plasma reduced by 13.25uUI
- HbA1c reduced by 0.08%
- HOMA-IR (insulin resistance index) reduced by 0.31 on average

LIPID METABOLISM:

- Total cholesterol reduced by 0.32mmol/L
- LDL reduced by 0.22mmol/L
- Triglyceride reduced by 0.04mmol/L

WEIGHT LOSS:

- Body weight reduced by 1.87kg
- BMI reduced by 0.8kg/m2
- Waist circumference reduced by 2.08cm

BLOOD PRESSURE:

- Systolic reduced by 2.58mmHg
- Diastolic reduced by 3.12mmHg

REVIEWER: Miranda Harris, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- IF does not require calorie restriction which may result in greater compliance
- IF does not restrict macronutrients such as CHO and fats, so may avoid the exclusion of key nutrients e.g. healthy fats and wholegrains.
- IF may have fewer adverse effects on daily routines and quality of life, which may mean adherence is easier.
- Improved glucose and lipid metabolism may prevent the development of chronic health conditions such as T2D, CVD and cancer.

🔍 CLINICAL PRACTICE APPLICATIONS:

- IF may be an effective alternative to restricted calorie or CHO diets for weight management with the associated benefits of glucose and lipid metabolism.
- IF has been shown to have therapeutic effects on individuals with impaired glucose and lipid metabolism.
- IF may be considered as a sustainable lifestyle choice rather than a ‘weight loss’ programme such as a very low calorie diet, which can result in poor quality of life and subsequent reduced adherence.
- Since it may take time for impaired glucose and lipid metabolism to progress to more serious disease states, establishing IF as an early intervention, may be considered as a prudent form of preventative medicine.
- IF has shown to have other health benefits such as reduced blood pressure and may be considered as adjuvant therapy.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Compares the effects of IF on different ethnicities, sex and age categories
- Evaluates the effect of IF on other disease states e.g. cancer, auto-immune conditions
- Assesses the response of other biomarkers e.g. inflammatory cytokines
- Compares different types and durations of IF on health biomarkers (eg periodic, time restricted)

EXPERT REVIEWER Miranda Harris

Miranda is a CNHC and BANT registered nutritionist with over 10 years clinical experience, specialising in endurance sport as well as lifestyle-related chronic health conditions. She is a senior lecturer (FHEA) focusing on research methods, dissertation supervision and sports nutrition on the Nutritional Therapy MSc course at the University of Worcester. She has recently started publishing in the field of Nutrition and Lifestyle Medicine. She is a keen triathlete and British Cycling level 3 coach.

BETA GLUCANS & LIPID PROFILE

EFFECTS OF OAT BETA-GLUCAN INTAKE ON LIPID PROFILES IN HYPERCHOLESTEROLEMIC ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Yu, J ; Xia, J ; Yang, C ; Pan, D ; Xu, D ; Sun, G ; Xia, H
Nutrients. 2022;14(10)

SUMMARY REVIEW:

INTRODUCTION:

Hypercholesterolemia is a risk factor for cardiovascular disease and a symptom of Metabolic Syndrome and commonly includes; elevated levels of total cholesterol and low-density lipoprotein cholesterol (LDL-c) and lower levels of high-density lipoprotein cholesterol (HDL-c). Conventional medical treatment for hypercholesterolemia is statins, however, statins can have a number of adverse side effects. For this reason, dietary interventions have been investigated including the use of oat beta-glucans for their potential lipid lowering effects.

The aim of this systematic review and meta-analysis was to synthesise and evaluate the evidence for the effects of oat beta-glucans on serum cholesterol and triglyceride (TG) levels in adults with hypercholesterolemia.

METHOD:

Thirteen randomised controlled trials (RCTs) published between 1999 – 2021 met the study inclusion criteria. These studies included a total population of 927 people aged between 38-76 years and from 7 different countries worldwide. The majority of participants were diagnosed with mild hypercholesterolemia.Participants were randomised into an intervention group receiving dietary sources of oat beta-glucans or food with added oat beta-glucans or a placebo control group consisting of diets without beta-glucans.

Study lengths ranged from 3 to 8 weeks with doses of oat beta-glucans between 1.5g to 6g. The studies were also broken down into sub-groups for high and low doses of oat beta-glucan and mild and moderate hypercholesterolemia.

Baseline and endpoint cholesterol (total cholesterol C, HD-c & LDL-c) and triglycerides were used to assess the effectiveness of the interventions and a weighted mean difference (WMD) calculated with a 95% confidence interval (CI).

RESULTS:

- a reduction in total cholesterol (WMD = -0.24mmol/L; 95% CI)
- a reduction in LDL-c (WMD = -0.27mmol/L; 95% CI)
- Sub-groups found that oat beta-glucans reduced serum TG levels in patients with moderate hypercholesterolemia (WMD = -0.11 mmol/L; 95% CI) but not in cases of mild hypercholesterolemia. (WMD = -0.01 mmol/L; 95% CI)
- Higher daily doses of oat beta glucans had more positive effects on TG levels, however the results were not statistically significant in this meta-analysis
- <3g WMD -0.11 mmol/L; 95% CI: -0.13 to -0.08 mmol/L
- >3g WMD -0.00 mmol/L; 95% CI: -0.16 to -0.16 mmol/L
- Greater reductions in HDL -c were found in patients with moderate hypercholesterolemia (WMD-0.06 mmol/L; 95% CI; -0.07 to -0.05 mmol/L) compared to mild cases (WMD-0.01 mmol/L; 95% CI; -0.08 to -0.10 mmol/L).

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

CONCLUSIONS:

Dietary intake of oat beta-glucans may support the reduction of total cholesterol and low density lipoprotein cholesterol, however, no significant changes were found for high density lipoprotein cholesterol or serum triglycerides. Due to the heterogeneity between studies and inconsistencies in results, more trials are needed with larger sample sizes and longer durations.

TAKE HOME MESSAGE:

- Consumption of oat beta glucans may be beneficial for improving total cholesterol and LDL-c in people with mild and moderate hypercholesterolemia
- The U.S Food and Drug Administration (FDA) recommends 3g or more of oat beta glucans per day to reap the benefits. This could be from 90g of oats (3 x 30g portions) or 1 30g portion of oats, 3 oatcakes and 1-2 tbsp of oat bran.

🔍 CLINICAL PRACTICE APPLICATIONS:

- 1.5g -6g of dietary intake of oat beta-glucans could support a reduction of TC and LDL-c in cases of mild and moderate hypercholesterolemia
- Intake of oat beta glucans >3g may reduce TG levels
- HDI -c may be improved with oat beta glucan intake of between 1.5g to 6g for clients with moderate hypercholesterolemia.

? CONSIDERATIONS FOR FUTURE RESEARCH:

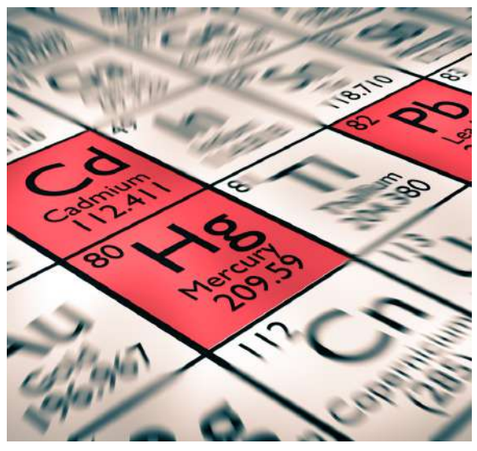
The findings of 8 of the 13 RCTs indicated that when compared to the control group, LDL-c could be lowered by oat beta-glucans whilst the other 5 trials did not. However, the cumulative results of this meta analysis found a reduction in LDL-c.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Gail Brady

Gail is a Registered Nutritional Therapy Practitioner RCNHC MBANT. She qualified is 2013 from The Institute for Optimum Nutrition in London and has since furthered her studies and completed a Master's of Science (MSc) degree in Advanced Nutrition (Research and Practice). The topic for her MSc dissertation project was menopause and potential diet and lifestyle interventions that my help to prevent weight gain. In clinical practice, Gail specialises in female health and works 1:1 with clients using a Functional Medicine framework. She also runs an online course providing a tool kit for managing perimenopause and menopause.

CADMIUM AND DIABETES RISK



CADMIUM EXPOSURE AND RISK OF DIABETES AND PREDIABETES: A SYSTEMATIC REVIEW AND DOSE-RESPONSE META-ANALYSIS.

Filippini, T ; Wise, LA ; Vinceti, M
Environment international. 2022;158:106920

SUMMARY REVIEW:

INTRODUCTION:

Cadmium exposure might occur through occupational activities, food, air pollution, and smoking. Smokers, in particular, have higher blood cadmium concentrations than non-smokers. Food is the main transmission route for non-smokers, particularly cereals, vegetables, mollusks, and offal. Females and older adults are at a greater risk due to an increased risk of iron deficiency, leading to increased absorption, as well as greater age-related bioaccumulation. Furthermore, cadmium exposure has been associated with an increased risk of diabetes in a number of studies. This systematic review and meta-analysis therefore investigates the relationship between exposure to cadmium and type 2 diabetes and prediabetes risk.

METHOD:

- The systematic review was conducted and reported in line with the PRISMA 2020 statement.
- Studies were assessed for risk of bias using the ROBINS-E tool and certainty of evidence was assessed using GRADE approach.

RESULTS:

- 42 eligible studies (case-control, cross-sectional, and cohort studies), including 814 male and female adult participants, were. Seven of the included studies were at overall high risk of bias; heterogeneity in the resulting meta-analyses was moderate to substantial. Sensitivity analyses indicated comparable results. Assessment with GRADE found no major inconsistency, indirectness or imprecision for either outcome.
- Comparing the highest versus lowest cadmium exposure concentrations associated with type 2 diabetes resulted in a RR of 1.24 (95% CI 0.96–1.59), RR 1.21 (CI 95% 1.00–1.45), and RR 1.47 (CI 95% 1.01–2.13) for blood, urinary, and toenail matrices, respectively. Concurrently, there was an elevated risk of prediabetes for cadmium levels in urine of RR 1.41 (95% CI: 1.15–1.73) and blood RR 1.38 (95% CI: 1.16–1.63), respectively.
- In the dose-response meta-analysis, a linear positive correlation between increasing urinary cadmium levels and diabetes risk was observed, with a RR 1.25 (95% CI 0.90–1.72) at concentration 2.0 μg/g of creatinine compared with no exposure. Conversely, for blood cadmium concentrations, the diabetes risk seemed to rise above 1 μg/L compared with no exposure. Moreover, prediabetes risk increased up to approximately 2 μg/g creatinine beyond which a plateau was reached with RR 1.40 (95% CI 1.12–1.76) at 2 μg/g creatinine.
- The meta-regression showed a negligible correlation between blood cadmium levels and diabetes risk. However, a positive yet imprecise association was found with increasing urinary cadmium concentrations. Similarly, no association was observed between blood cadmium concentrations and risk of prediabetes, whereas a positive relationship with urinary cadmium levels was observed.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

CONCLUSION:

A positive linear correlation between cadmium concentration (measured in multiple matrices) and risk of both type 2 diabetes and prediabetes with a dose-response relationship (moderate-certainty evidence) were observed in this systematic review and meta-analysis.

TAKE HOME MESSAGE:

Cadmium exposure through diet, occupational exposure and smoking may increase the risk of type 2 diabetes in affected individuals.

🔍 CLINICAL PRACTICE APPLICATIONS:

- To inform practitioners and clients of the risks of cadmium exposure in the diet, through occupational exposure, and through smoking.
- To advise clients on prediabetes and type 2 diabetes risk from cadmium exposure through smoking.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- As cited by the authors, future studies could incorporate stratified analysis in specific subgroups, e.g., non-smokers, or could be restricted to prospective cohort studies with more sufficient data.
- Large-scale observational studies could be conducted investigating cadmium exposure in smokers versus non-smokers.
- Clinical trials could be performed to evaluate the effect of reduction or cessation of tobacco smoking on total body cadmium concentrations.
- Continuous surveillance of dietary cadmium exposure and other heavy metals should be prioritised to inform public health.
- Dietary interventions could assess the possibility to attenuate the risk of cadmium exposure.

CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

EXPERT REVIEWER Jennifer McCarthy

Jennifer is a PhD candidate based in the Environmental Sustainability and Health Institute in TU Dublin and a freelance Scientific Editor. Her research integrates the areas of Environmental Health, Environmental Epidemiology, Food Science, Public Health, Agriculture, Microbiology, Food Safety, Risk Assessment, Mathematical Modelling and Statistics. She is a graduate member of The Nutrition Society and an associate member of the International Academy of Nutrition Educators with an MSc in Food, Nutrition and Health from UCD, MA in Translation Studies from DCU (scientific and technical writing/translation, translation technology, editing, etc.), and is a former third level Mathematics, Statistics and EAP Lecturer.

MARINE OIL IN OBESE ADULTS

ENRICHED MARINE OIL SUPPLEMENT INCREASES SPECIFIC PLASMA SPECIALIZED PRO-RESOLVING MEDIATORS IN ADULTS WITH OBESITY.

Al-Shaer, AE ; Regan, J ; Buddenbaum, N ; Tharwani, S ; Drawdy, C ; Behee, M ; Sergin, S ; Fenton, JI ; Maddipati, KR ; Kane, S ; Butler, E ; Shaikh, SR
The Journal of nutrition. 2022;152(7):1783-1791

SUMMARY REVIEW:

INTRODUCTION:

- Specialised pro-resolving mediators (SPMs) are oxylipins synthesised from omega-3 and -6 PUFAs which play a role in resolving inflammation.
- The authors highlight mouse studies have found that increasing the levels of SPMs and their metabolic intermediates can improve a range of obesity related complications. Thus, there is scientific interest in increasing the levels of SPMs in humans with diseases associated with chronic inflammation, such as obesity.
- This small non-randomised uncontrolled clinical trial of 23 individuals (13 female; 10 male) aged 50-65 years with obesity (BMI 30-40), aimed to determine the impacts of 1 month supplementation with marine oil particularly enriched with 14-hydroxydocosahexanenoic acid (14-HDHA), 17-HDHA and 18-hydroxydocosahenaenoic acid (HEPE) on:
- The change in levels of PUFA-derived oxylipins from baseline
- The change in abundance of circulating peripheral blood mononuclear cells (PBMCs)
- The change in antibody production

METHOD:

- 2g enriched marine oil (4 capsules of SPM Active provided by Metagenics, study sponsor) once daily for 28-30 consecutive days.
- Only post-menopausal women were included to reduce confounding effects of oestrogen on lipid metabolism
- Individuals were excluded if diagnosed with Type 1 or 2 diabetes, autoimmunity, liver disease, coagulopathy, uncontrolled hypothyroid or active malignancy
- Individuals were excluded if they consumed omega-3 PUFA supplements within 3 months of intervention, regularly consumed >2 servings per week of fatty fish, had a fish/shellfish allergy or were taking a predetermined list of medications.

RESULTS:

- Statistically significant increases were found in certain EPA, DPA and DHA-derived metabolites in response to supplementation relative to baseline. However, only 17-HDHA concentrations increased relative to baseline, with no effect on 14-HDHA or 18-HEPE, despite the supplement being enriched with all 3 metabolites
- Statistically significant decreases were found in arachidonic acid (AA)-derived oxylipins post supplementation relative to baseline
- Increases in immune cell populations in circulation did not reach significance post supplementation when measured by PBMCs.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Marine oil enriched with specialised pro-resolving mediators raise levels of EPA, DPA and DHA-metabolites in adult subjects with obesity
- Larger randomised, blinded and placebo-controlled trials are required to inform healthcare practitioner clinical practice decisions relating to SPM enriched marine oil supplementation
- Future research is required to determine if increased concentrations of SPMs control the resolution of inflammation in humans with obesity.

CLINICAL PRACTICE APPLICATIONS:

- Healthcare practitioners working with adults with obesity can use the results from this trial to understand that 1 month supplementation with 4g of enriched marine oil supplementation raises levels of certain EPA, DPA and DHA metabolites
- Practitioners may want to follow the research in this area as larger, controlled trials are conducted and comparisons made with non-enriched fatty acid supplements.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future clinical studies of SPM supplementation are required that are double-blind, randomised and placebo-controlled to inform scientific findings in this area
- This study was inadequately powered to assess differences between female and male participants and therefore larger trials are needed to inform the sex differences in oxylipins within the population with obesity
- Further research is required in younger subjects with obesity to assess SPMs as a possible chronic inflammation preventative strategy, due to inflammation complications over time
- Future research should take account of the heterogeneity in the population with obesity, such as microbiome profiles, food intake and baseline metabolic status
- Further studies comparing impacts of standard marine oil with enriched marine oil on chronic inflammation would inform healthcare practitioners in their clinical practice.

EXPERT REVIEWER Clare Grundel

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

Following a career in international development and finance, Ms Grundel studied for an MSc in Nutritional Therapy. Clare brings to Nutrition Evidence skills in project management developed over 20 years and more recent experience of critical appraisal of nutrition research. She is a practising Registered Nutritional Therapist based in Cambridge and focuses her nutrition practice on inflammatory arthritis and chronic pain. Clare joined the BANT team in 2017 as Science and Education Manager and manages all aspects of the Nutrition Evidence database.

T2DM & NUTRIENT SUPPLEMENTS

COMPARATIVE EFFECTS OF VITAMIN AND MINERAL SUPPLEMENTS IN THE MANAGEMENT OF TYPE 2 DIABETES IN PRIMARY CARE: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Xia, J ; Yu, J ; Xu, H ; Zhou, Y ; Li, H ; Yin, S ; Xu, D ; Wang, Y ; Xia, H ; Liao, W ; Wang, S ; Sun, G
Pharmacological research. 2023;188:106647

SUMMARY REVIEW:

OBJECTIVES:

The aim of this systematic review was to evaluate the comparative effects of vitamin and mineral supplements on managing glycemic control and lipid metabolism for type 2 diabetes mellitus (T2DM).

METHOD:

This systematic review is registered with PROSPERO and adhered to PRISMA-2020 guidelines for network meta-analysis

The Cochrane Collaboration's risk-of-bias tool was used to assess eligible randomised trials

8 prespecified markers identified and assessed in this study : 1) HbA1c (%), 2) fasting blood glucose (mmol/L), 3) total cholesterol (mmol/L), 4) triglycerides (mmol/L), 5) fasting insulin (μIU/mL), 6) HOMA-IR, 7) LDL-c (mmol/L), and 8) HDL-c (mmol/L).

RESULTS:

- 170 RCT trials of 14223 participants with T2DM treated with vitamin supplements, mineral supplements, or placebo/no treatment were included
- Low to very low certainty evidence established chromium supplements as the most effective in reducing fasting blood glucose levels and homeostasis model assessment of insulin resistance (SUCRAs: 90.4% and 78.3%, respectively)
- Vitamin K supplements ranked best in reducing glycated haemoglobin A1c and fasting insulin levels (SUCRAs: 97.0% and 82.3%, respectively), with moderate to very low certainty evidence
- Vanadium supplements ranked best in lowering total cholesterol levels with very low evidence certainty (SUCRAs:100%)
- Niacin supplements ranked best in triglyceride reductions and increasing high-density lipo-protein cholesterol levels with low to very low evidence certainty (SUCRAs:93.7% and 94.6%, respectively)
- Vitamin E supplements ranked best in reducing low-density lipoprotein cholesterol levels with very low evidence certainty (SUCRAs:80.0%).

CONCLUSION:

- Micronutrient supplements, such as chromium, vitamin E, vitamin K, vanadium, and niacin supplements, may be efficacious in managing T2DM
- It should be noted that the evidence certainty for all was low.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Clinicians could consider the adjunctive effect of micronutrients supplements, such as chromium, vitamin E, vitamin K, vanadium, and niacin supplements in a nutrition protocol to manage T2DM and slow or prevent its complications.
- The study authors state that the vitamin and mineral supplements under review had a statistically significant improvement, however they did not reach the study threshold for clinical significance. Therefore they advise caution in utilising micronutrient supplements in the management of glucose and lipid metabolism for T2DM.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Chromium plays an important role in carbohydrate and lipid metabolism and was the most effective micronutrient for decreasing fasting blood glucose, HbA1c, fasting insulin, and HOMA-IR reductions.
- Vitamin K was the top-ranked micronutrient in reducing HbA1c and fasting insulin levels. The mechanism through which Vitamin K affects glucose metabolism is proposed as activation of the AMP-activated protein kinase/sirtuin 1, that in turn increases phosphocreatine 3-kinase and glucose transporter 2 to decrease insulin resistance and fasting glucose.
- Vanadium was the top-ranked micronutrient in total cholesterol (TC) reductions. Vanadium compounds can be toxic and supplementation is only recommended in cases of deficiency,diabetes, hyperlipidemia, and hypertension, where the intake of vanadium from food should be enhanced in preference to supplementation. Careful dosage required.
- Niacin was ranked as the most effective in triglyceride (TG) reductions and increasing HDL cholesterol levels.
- Vitamin E was the top-ranked micronutrient in low-density lipo- protein (LDL) cholesterol reductions.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- New research is needed to get better insight into the efficacy of micronutrient supplements in managing T2DM.
- Selenium homeostasis, selenoprotein, insulin signaling/secretion, and carbohydrate/lipid metabolism are linked in multiple and complex ways but the authors could not explain why chromium supplementation would lower blood glucose more effectively than selenium supplementation, and suggest more research is needed to clarify this
- While vitamin K status could be an emerging treatment target in T2DM prevention and management, it remains to be determined whether vitamin K supplementation has an advantage over other nutrients in terms of hypoglycemic effect.
- The beneficial effect of vitamin E and niacin supplements regarding lipid metabolism warrant further investigation.

EXPERT REVIEWER Kirsty Baxter

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, having completed research for a Master of Science in Nutrition (Advanced Research and Practice) at the London South Bank University to support a nutritional therapy approach harnessing psychological aspects of obesity weight loss. Kirsty is currently in the process of publishing her research. She works collaboratively with a wide range of GPs and doctors, frequently giving presentations on metabolism to support awareness around the nutritional intervention for metabolic conditions.

B VITS, OMEGA 3 EFAS & CVD

DO B VITAMINS ENHANCE THE EFFECT OF OMEGA-3 POLYUNSATURATED FATTY ACIDS ON CARDIOVASCULAR DISEASES? A SYSTEMATIC REVIEW OF CLINICAL TRIALS.

Zhu, J ; Xun, PC ; Kolencik, M ; Yang, KF ; Fly, AD ; Kahe, K
Nutrients. 2022;14(8)

SUMMARY REVIEW:

INTRODUCTION:

The paper reviews whether combined supplementation of vitamin B (B2, B6, B9, and B12) and omega-3 polyunsaturated fatty acids (n3 PUFA) outweighs the individual cardiovascular benefits of each supplement. Registered in PROSPERO under CRD42018085993

METHOD:

A total of 15 clinical studies including 8,263 individuals published from December 2021, that investigated the combined effects of the supplements met inclusion criteria and were included in the review

RESULTS:

- The overall findings are inconsistent and inconclusive, yet the combined supplementation of these two nutrients may be more effective at reducing plasma homocysteine, triglyceride, and low-density lipoprotein-cholesterol than the individual components.
- The underlying mechanisms mainly include alleviating endothelial dysfunction, inhibiting atherosclerosis and lesion initiation, reducing oxidative stress, suppressing activation of pro-inflammatory cytokines, regulating endothelial nitric oxide synthase, and interfering with methylation of genes that promote atherogenesis.
- Although biologically plausible, the existing literature is insufficient to draw any firm conclusion regarding whether B vitamins can further enhance the potential beneficial effects of omega-3 PUFA intake on either primary or secondary prevention of CVD.

LIMITATIONS:

Limitations of the systematic review include different supplementation regimens, variability of study designs in terms of duration of the intervention, existence of placebo group, dosages and the inability to monitor study subjects' habitual diet.

CONCLUSION:

Although the results indicate the beneficial effects of combined supplementation in primary and secondary cardiovascular prevention, firm conclusions cannot be drawn from the existing data, and more studies are needed in this area.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Combined vitamin B and n3 PUFA supplementation might have favourable health effects
- Combined vitamin B and n3 PUFA supplementation could help in the primary and secondary prevention of cardiovascular disease
- The suggested favourable dose ranges are vitamin B6: 2.5–80 mg/day, vitamin B12: 20–1000 µg/day, folic acid: 150–10000 µg/day, and n3 PUFA 0.2–2) g/day.

🔍 CLINICAL PRACTICE APPLICATIONS:

In comparison with a single supplement alone, the combined administration of vitamin B and n3 PUFA might have:

- Hypolipidemic effects, by reducing triglycerides and LDL-cholesterol. Some of the studies indicate a lowering of LDL-c up to 13% and triglycerides up to 24%
- Anti-inflammatory effects, by reducing homocysteine. Based on some of the studies, the lowering effects might go up to 39%.

Dietary practice might benefit from the following:

- The authors highlighted food-based and healthy dietary pattern-based strategies should include food sources rich in these nutrients such as fish, vegetables, fruit, legumes, nuts, and eggs
- The authors conclude that intake of whole foods and whole diets rich in desirable foods (such as MedDiet) should be encouraged
- The supplementation dose ranges in the studies covered by the review were the following: vitamin B6: 2.5–80 mg/day, vitamin B12: 20–1000 µg/day, folic acid: 150–10000 µg/day and n3 PUFA 0.2–2) g/day

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future studies should be designed regarding the need for a uniform methodological approach in testing the combined effects of vitamin B complex and n3 PUFA supplements
- The studies should investigate supplementation strategies and dietary patterns rich in both nutrients.

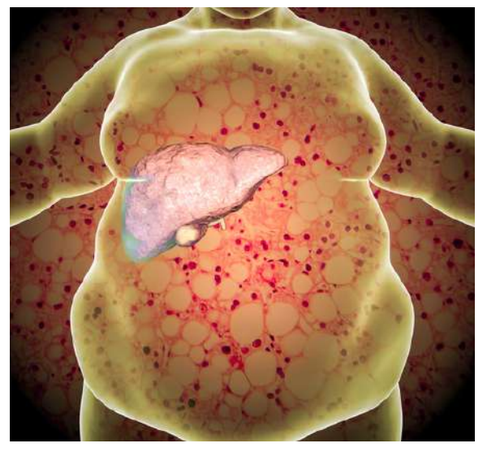
EXPERT REVIEWER Manja Zec

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

Manja is a post-doc scientist at the University of Arizona, who received her graduate and PhD degree from the University of Belgrade. During the last decade, she pursued nutrition research focused on lipid metabolism, by use of in vitro, via animal, to RCT and epidemiological studies. She is passionate about precision nutrition relying on nutrigenetics and microbiota in diverse populations. So far, she has published more than 40 peer-reviewed scientific publications, original articles and book chapters.

OMEGA 3 EFAS IN METABOLIC SYND.



EFFECTS OF OMEGA-3 FATTY ACIDS SUPPLEMENTATION ON SERUM LIPID PROFILE AND BLOOD PRESSURE IN PATIENTS WITH METABOLIC SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Liu, YX ; Yu, JH ; Sun, JH ; Ma, WQ ; Wang, JJ ; Sun, GJ
Foods (Basel, Switzerland). 2023;12(4)

SUMMARY REVIEW:

INTRODUCTION:

- This journal article presents a systematic review and meta-analysis of randomised controlled trials (RCTs) investigating the effects of omega-3 fatty acid supplementation on serum lipid profile and blood pressure in patients with metabolic syndrome. Metabolic syndrome is a cluster of conditions that increase the risk of cardiovascular disease and type 2 diabetes.

METHOD:

- This meta-analysis included 8 RCTs with 387 participants with metabolic syndrome. Participants in the intervention group took omega-3 fatty acid supplements and the outcomes included total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), systolic blood pressure (SBP), and diastolic blood pressure (DBP).

RESULTS:

- Based on a meta-analysis of data from the included trials, supplementation with omega 3- PUFAs led to no reduction in serum LDL-c level among patients with metabolic syndrome (Standardised Mean Difference (SMD) = 0.18; 95% CI: −0.18 ~ 0.53, I2 = 55%); did not increase serum high-density lipoprotein cholesterol levels (SMD = 0.02; 95% CI: −0.21 ~ 0.25, I2 = 0%); and had no reduction in serum total cholesterol level (SMD = −0.02; 95% CI: −0.22~0.18, I2 = 24%).
- On the other hand, in patients with metabolic syndrome, supplementation with omega 3- PUFAs may decrease serum triglyceride levels (SMD = −0.39; 95% CI: −0.59 ~ −0.18, I2 = 17.2%); systolic blood pressure (SMD = −0.54; 95% CI: −0.86 ~ −0.22, I2 = 48.6%); and diastolic blood pressure (SMD = −0.56; 95% CI: −0.79~ −0.33, I2 = 14.0%).
- Sensitivity analyses indicated that the pooled estimates wererobust for all outcomes.

CONCLUSION:

- The following mechanisms may explain how PUFAs may reduce the risk of metabolic syndrome. First, adequate intake of omega 3 PUFAs may reduce triglyceride and LDL synthesis in the liver. In addition, they may lower blood pressure by reducing angiotensin-converting enzyme levels in the aorta. Finally, PUFAs can increase insulin sensitivity and prevent hyperglycaemia.
- This study presents some limitations: The literature search may have some omissions. The conclusions may be hindered by the risk of bias of the trials included. No bias test was performed due to the limited number of studies.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Omega 3 PUFA may be beneficial for patients with metabolic syndrome by improving serum lipid profile and blood pressure.
- Omega-3 rich foods include fatty fish, walnuts, flaxseeds and chia seeds.
- While Omega-3 PUFA may be beneficial, they should be considered as part of a comprehensive approach to managing metabolic syndrome that include physical activity and a balanced diet.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Improved serum lipid profile: The findings from the paper indicate that omega-3 fatty acid supplementation can have a positive impact on the serum lipid profile in patients with metabolic syndrome.
- Blood pressure management: omega-3 fatty acid supplementation may help reduce blood pressure in patients with metabolic syndrome.
- Nutritional therapists can use this information to consider omega-3 supplementation as part of nutritional therapy
- Complementary approach: Nutritional therapists can utilise the findings as supportive evidence for a holistic approach to managing metabolic syndrome. By incorporating omega-3 fatty acids into personalized nutrition plans, therapists may be able to offer additional dietary or supplemental interventions for individuals with metabolic syndrome, aiming to lower triglyceride levels and manage blood pressure, alongside other lifestyle modifications.
- Patient education: Nutritional therapists can educate their patients with metabolic syndrome about the benefits of omega-3 fatty acids on lipid profile and blood pressure. By explaining the findings from the systematic review and meta-analysis, therapists can empower patients to make informed choices regarding their dietary habits and supplement use, promoting self-management and improved long-term outcomes.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research could focus on determining the optimum dosage of Omega-3 PUFAs for improving lipid profile and BP.
- More investigation is needed to analyse the long term effect of the supplements. The longest RCT was 90 days.
- Future research could explore potential variations in the effects of omega-3 fatty acids supplementation based on different patient characteristics, such as age, gender, baseline lipid profile, and blood pressure levels.
- Mechanistic studies on underlying pathways through which omega-3 fatty acids exert their effects on lipids and BP.

EXPERT REVIEWER Dr Yassine Bendiabdallah

CONFLICTS OF INTEREST: None

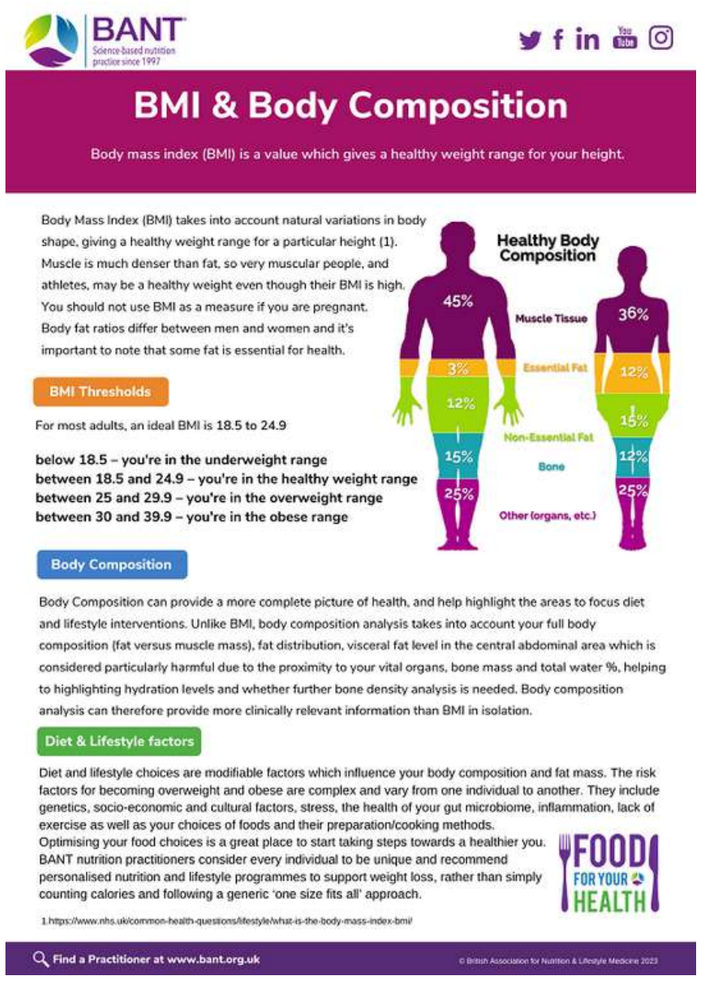
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Dr Yassine Bendiabdallah is a Functional Medicine Specialist and an expert in Bio-identical Hormone Replacement Therapy. His previous academic degree as an anticancer research scientist at Cancer Research UK at University College London, has earned him various distinctions and publications in peer-reviewed academic journals. His specialist clinical interests include personalised nutrition, aesthetics, medical treatments, travel vaccinations, health technology and the endocrine system. Yassine co-founded ZEN Healthcare, a health and wellness centre with sites in Knightsbridge, Holborn and Baker Street and is currently the managing director.

ADDITIONAL RESOURCES

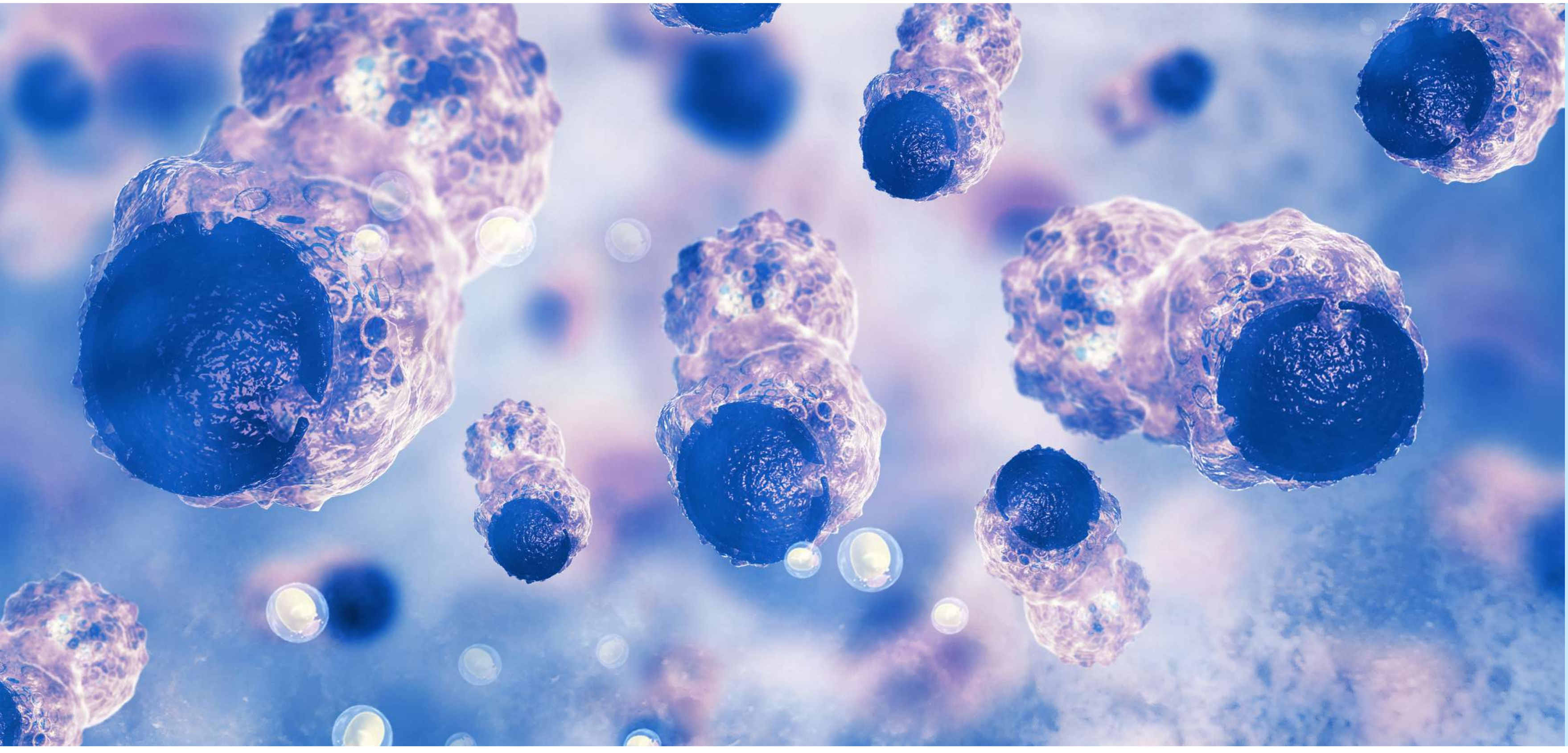
NED INFOBITES AND CLINICAL FACT SHEETS

Download the series of NED InfoBites and Fact Sheets on symptoms of metabolic syndrome including blood glucose regulation, insulin resistance, NAFLD, hypercholesteremia, hypertension, overweight and obesity, inflammation, the gut microbiome and T2DM at bant.org.uk



7 REVIEWS

CANCER & NUTRITION



LIPID INTAKE & BREAST CANCER

LIPID INTAKE AND BREAST CANCER RISK: IS THERE A LINK? A NEW FOCUS AND META-ANALYSIS

Lodi, M ; Kiehl, A ; Qu, FL ; Gabriele, V ; Tomasetto, C ; Mathelin, C
European journal of breast health. 2022;18(2):108-126

SUMMARY REVIEW:

- Among lifestyle-related breast cancer risk factors, the role of diet in breast cancer remains uncertain.
- The authors highlight a weak association between high SFA consumption and breast cancer risk in post-menopausal women.
- The authors found no association between total fat, saturated fatty-acids, mono and poly-unsaturated fatty acids and cholesterol intake and breast cancer incidence in the general population and in pre-menopausal women

OBJECTIVES:

- To determine if there is an association between total lipid intake, saturated fatty acid (SFA), Poly- and Mono-Unsaturated Fatty Acid (PUFA and MUFA) and cholesterol intake and breast cancer risk.

RESULTS:

- Forty-four articles were included in the meta-analysis, consisting of 28 case-control studies and 16 cohort studies.
- In total, this meta-analysis involved 1,185,896 women, of whom 54,553 had breast cancer.
- There was no association between total fat, SFA, MUFA, PUFA and cholesterol intake and breast cancer in the general population and in pre-menopausal women.
- In postmenopausal women, high SFA consumption was associated with increased breast cancer risk in case-control studies [relative risk (RR): 1.12; confidence interval (CI) 95%: 1.03–1.21; p = 0.006 but not in cohort studies (RR: 1.01; CI 95%: 0.85–1.19; p = 0.93).

LIMITATIONS:

- Studies included in the meta-analysis were carried out on populations from five continents with significant cultural and dietary diversity, and well as different types of oils used in the diet

CONCLUSION:

At this stage, the authors state it is not possible to establish nutritional recommendations regarding the consumption of lipids to decrease breast cancer risk.

REVIEWER: Kirsty Baxter, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

The authors found no association between total fat, saturated fatty-acids, mono and poly-unsaturated fatty acids and cholesterol intake and breast cancer incidence in the general population and in pre-menopausal women.

🔍 CLINICAL PRACTICE APPLICATIONS:

- The results of this meta-analysis does not demonstrate a statistically significant link between high consumption of total lipids, PUFA, MUFA and cholesterol and the occurrence of breast cancer.
- However, the results suggest that there is an association between SFA intake and breast cancer risk in postmenopausal women, although this was only found in case-controlled studies and not cohort studies.
- While obesity is a known breast cancer risk factor after menopause, the link between the effect of diet and the effect of obesity on the breast may be through different mechanisms.
- The authors investigated if high lipid consumption acts on breast tissue by the same mechanisms as obesity, and found the association between SFA intake and breast cancer risk in postmenopausal women must be through other biological explanations.
- The authors found that while high SFA consumption may increase breast cancer risk among post-menopausal women, biological mechanisms linking SFA and breast cancerogenesis are still unknown.
- The meta-analysis found high blood cholesterol levels appear to increase the risk of breast cancer. However, the authors could not confirm that high dietary cholesterol intake is a risk factor for breast cancer. The authors postulated this may be in part due to the low proportion of cholesterol (about 30%) in the diet, while the rest comes from the degradation of lipids and carbohydrates by the liver.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- As lipids can have different actions in the same family, studies should rather focus on specific lipid consumption.

EXPERT REVIEWER Kirsty Baxter

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, having completed research for a Master of Science in Nutrition (Advanced Research and Practice) at the London South Bank University to support a nutritional therapy approach harnessing psychological aspects of obesity weight loss. Kirsty is currently in the process of publishing her research. She works collaboratively with a wide range of GPs and doctors, frequently giving presentations on metabolism to support awareness around the nutritional intervention for metabolic conditions.

FLAVONOIDS & CANCER

CONSUMPTION OF FLAVONOIDS AND RISK OF HORMONE-RELATED CANCERS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES.

Liu, F ; Peng, Y ; Qiao, Y ; Huang, Y ; Song, F ; Zhang, M ; Song, F
Nutrition journal. 2022;21(1):27

SUMMARY REVIEW:

Hormone-related cancers (HRCs) are the most frequently diagnosed cancers globally , accounting for more than a quarter of new cancer cases worldwide in 2018. They include breast, ovarian, endometrial, prostate, testicular and thyroid cancer which share a similar carcinogenic mechanism. Diets rich in vegetables, fruit, legumes and tea may reduce cancer risk due to anticarcinogenic phytochemicals, such as flavonoids. Flavonoids are claimed to have many different physiological and pathological functions in the cancer process, including tumour cell proliferation, inflammation, angiogenesis, invasion and metastasis.. This study aimed to summarise the relationships between consumption of flavonoids with the risk of HRC.

METHOD:

The meta-analysis was carried out following PRISMA guidelines and registered on PROSPERO. A literature search in PubMed and Embase was conducted using the keywords flavonoids, flavanols and isoflavones and breast, ovarian, endometrial, prostate, testicular and thyroid cancer. 51 studies published between 1999 and 2022 consisted of 22 prospective cohort, 18 population-based and 10 hospital-based case-control studies. On the Newcastle-Ottawa Scale assessment all studies were of medium or high methodological quality.

RESULTS:

- Results were analysed using Stata 15.1 software and ORs with 95% CIs used to measure the association between flavonoid intake and HRCs risk. Statistical I2 evaluated heterogeneity among the studies.
- Funnel plots were inspected for publication bias and calculated by Begg's/Egger's regression tests. Sensitivity analyses were performed to explore the source of heterogeneity. Subgroup analysis was performed on study design and region, as well as menopausal status.
- Higher consumption of flavonoids was associated with a decreased risk of women-specific cancers but a significant elevated risk of prostate cancer as seen below.

REVIEWER: Miranda Harris, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

CONCLUSION:

Despite limitations of the meta-analysis, such as the use of observational studies and small sample sizes of the included studies, this systematic review may provide some preliminary dietary evidence for the use of flavonoids in HRCs.

TAKE HOME MESSAGE:

- Dietary flavonoids are widely available in plant-based foods such as vegetables, citrus fruits, green tea and berries
- Menopausal status may be an important consideration for flavonoid intake when considering breast cancer risk
- Differences in results for Asians and non-Asians need to be considered for the use of flavonoids in women-specific hormonal cancers and prostate cancer in men
- Caution should be exercised when considering flavones and flavanones and thyroid cancer risk until further research is available

CLINICAL PRACTICE APPLICATIONS:

- The promotion of a plant-based diet, rich in vegetables, fruits, green tea and legumes may have protective effects on women-specific cancers due to the rich presence of flavanols, flavones and isoflavones, as well as the compounds genistein, glycitein and daidzein.
- Results show no associations between total flavonoids intake and women-specific cancer however, the sub-groups of flavanols, flavones and isoflavones were associated with a decreased risk in women-specific cancers. Similar results were seen in the individual compounds of isoflavones: genistein, glycitein and daidzein. These results may guide decision-making when recommending the inclusion of these compounds for protective benefits in women-specific cancers.
- The positive association between total flavonoids and prostate cancer risk was only seen in non-Asians, and between higher consumption of flavones and flavanones and thyroid cancer risk albeit in limited studies (n=3) may provide important guidelines when considering which foods to include from a plant-based diets.

EXPERT REVIEWER Miranda Harris

Miranda is a CNHC and BANT registered nutritionist with over 10 years clinical experience, specialising in endurance sport as well as lifestyle-related chronic health conditions. She is a senior lecturer (FHEA) focusing on research methods, dissertation supervision and sports nutrition on the Nutritional Therapy MSc course at the University of Worcester. She has recently started publishing in the field of Nutrition and Lifestyle Medicine. She is a keen triathlete and British Cycling level 3 coach.

ALLIUM VEGE & CANCER

ASSOCIATION BETWEEN ALLIUM VEGETABLES AND THE RISK OF NON-DIGESTIVE TRACT CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF COHORT AND CASE-CONTROL STUDIES

Guo, L ; Yuan, X ; Yang, B ; Tang, G ; Liang, H ; Guo, F
Cancer treatment and research communications. 2022;32:100598

SUMMARY REVIEW:

- The purpose of this study was to evaluate the role of allium vegetable intake in non-digestive cancer prevention, such as lung, breast, ovarian and prostate
- This is a well-designed meta-analysis which was performed following PRISMA guidelines and included 11 cohort and 14 case-control studies of 18,070 patients
- The Newcastle-Ottawa Scale (NOS) was used to assess study quality. All included studies had NOS scores of >=7, indicating a lower risk of bias and better study quality.

RESULTS:

- **Overall, significant associations were found between higher Allium vegetable intake and lowered risk of non-digestive tract cancer (OR: 0.86; 95% CI: 0.80-0.93) in a random-effects model.**

WHEN STRATIFIED:

- By study design, statistically significant effects were observed in cohort studies (OR; 0.78, 95% CI: 0.69-0.90) but not case controlled studies (OR 0.94; 95% CI: 0.87-1.02)
- By sex, statistically significant effects were observed in both women (OR: 0.89; 95% CI: 0.81-0.98) and men (OR: 0.81, 95% CI: 0.69-0.96)
- By allium vegetable type, onion (OR: 0.81, 95% CI: 0.69-0.95) and garlic (OR: 0721, 95% CI: 0.63-0.82) were more likely to have a lower risk of non-digestive tract cancer than leek (OR: 0.88, 95% CI: 0.56-1.38)
- By study location, statistically significant correlation was found among studies in China (OR: 0731, 95% CI: 0.57-0.94) but not Europe (OR: 0.93, 95% CI: 0.85-1.02) or America (OR: 0.88, 95% CI: 0.76-1.03)
- By cancer type, statistically significant risk decreases were seen with prostate cancer (OR: 0.81, 95% CI: 0.69-0.96), marginal risk decrease with ovarian cancer (OR: 0.77, 95% CI: 0.60-1.00), whilst no statistically significance was reached with breast cancer (OR: 0.94, 95% CI: 0.83-1.05).

REVIEWER: Clare Grundel, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- The findings of this meta-analysis suggest that allium vegetable consumption is correlated with a 14% decreased risk of non-digestive tract cancer
- Of the allium vegetables studied, onion and garlic were more likely to lower the risk of non-digestive tract cancer. Due to the limited under of eligible studies and small sample sizes, the authors of this study suggest that the impact of leeks on non-digestive cancers be interpreted with caution
- Allium vegetables appear to inhibit hepatocarcinogenesis, as well as the formation of nitrosamines. They also stress the endoplasmic reticulum and the death receptor pathway, hence reducing inflammation and modulating the immune system.

LIMITATIONS:

This meta-analysis included retrospective observational studies, which may introduce recall bias.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Healthcare providers can use the results of this study to encourage the consumption of allium vegetables, in particular garlic and onion, to reduce the risk of non-digestive cancers, in particular prostate
- The results of this study could be used to encourage dietary variety, particularly in light of allium vegetables falling under the category of high-FODMAP foods. FODMAP dietary eliminations are not discussed in this paper.

? CONSIDERATIONS FOR FUTURE RESEARCH:

To build on these findings, randomised-controlled trials or high quality cohort studies are needed.

EXPERT REVIEWER Clare Grundel

Following a career in international development and finance, Ms Grundel studied for an MSc in Nutritional Therapy. Clare brings to Nutrition Evidence skills in project management developed over 20 years and more recent experience of critical appraisal of nutrition research. She is a practising Registered Nutritional Therapist based in Cambridge and focuses her nutrition practice on inflammatory arthritis and chronic pain. Clare joined the BANT team in 2017 as Science and Education Manager and manages all aspects of the Nutrition Evidence database.

CAROTENOIDS & CANCER

ASSOCIATION OF RETINOL AND CAROTENOIDS CONTENT IN DIET AND SERUM WITH RISK FOR COLORECTAL CANCER: A META-ANALYSIS

Han, X ; Zhao, R ; Zhang, G ; Jiao, Y ; Wang, Y ; Wang, D ; Cai, H
Frontiers in nutrition. 2022;9:918777

SUMMARY REVIEW:

- Colorectal cancer (CRC) is the third most common cancer worldwide, and second in terms of mortality. Diet and environmental factors may have a strong influence and causative effect. Research has linked dietary consumption and serum levels of carotenoids and retinol with CRC. However, results have been mixed.
- The aim of this meta analysis was to identify a potential association between CRC and carotenoid and retinol intake. A total of 22 cohort and case control studies published between 2000-2019 from across Europe, North America and Asia were included. The number of CRC cases totalled 19,293 from a sample of more than 450,000 people.
- Eligible studies reported data in either relative risk (RR) or odds ratios (OR) with 95% confidence intervals (95% CI). In the meta analysis, data were combined and expressed as OR with 95% CI.
- Cases and control groups were based on high or low carotenoid intake as defined by the included studies and based on dietary intake or serum concentration. Sub-group analysis was undertaken by study type, sex and tumour type. A sensitivity analysis tested the robustness of the results.
- Due to the heterogeneity between studies, adjustments were made for potential covariates and confounding factors including age, gender, a family history of CRC, smoking, alcohol consumption and levels of physical activity.
- The quality of the studies was assessed against predefined inclusion and exclusion criteria and scored using the Newcastle-Ottawa Scale (NOS).
- The nutrients studied included; beta-carotene, alpha-carotene, lycopene, lutein/zeaxanthin, beta-cryptoxanthin and retinol.

KEY FINDINGS:

- High dietary intake of beta-carotene was not associated with an increased risk of CRC in females (OR = 0.97; 95%CI 0.79-1.19), however, it may lower CRC risk in males (OR = 0.74; 95% CI 0.55-0.99).
- High dietary intake of retinol was not associated with CRC risk (OR = 0.99; 95% CI 0.89-1.10). However, the findings suggested that it may reduce CRC risk in females but increase CRC risk in males.
- There was a tendency towards a slightly decreased risk of CRC with high dietary intakes of alpha-carotene), lycopene, and beta-cryptoxanthin. The results were more pronounced in males.
- No association was found between high consumption of high lutein/zeaxanthin, retinol or total carotenoids and the risk of CRC
- Case control studies found a negative association between serum carotenoids and CRC risk. This relationship was not found in cohort studies and therefore remains uncertain

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

CONCLUSION:

This was a well-conducted meta-analysis that was not subject to any conflicts of interest. Larger, well controlled prospective studies adjusting for sex and with long-term follow-up are needed to confirm the relationship between dietary intake and serum levels of carotenoids and CRC.

TAKE HOME MESSAGE:

- Total dietary intake of carotenoids was not associated with CRC risk.
- Case control studies found that high serum carotenoids may increase CRC risk.
- There were differences in findings between males and females.
- Larger, well-controlled studies over long time frames are needed to further explore the relationship between dietary intake and serum concentrations of carotenoids and retinol with CRC. These studies should include results by sex, race and dose response.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Healthcare practitioners working with people with a family history of CRC or those who may be at increased risk may like to consider increasing carotenoid intake modestly.
- A modest increase in dietary intake of beta-carotene for males may be beneficial.
- A modest increase in dietary retinol may be beneficial for females.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Further research is needed to explore the differences between sexes for dietary intake of carotenoids and retinol and CRC risk
- Further studies are needed to investigate the relationship between serum carotenoids and CRC
- Analysis of results by race and continent may be beneficial
- Further research is needed to define dose response
- Due to heterogeneity between studies, large, well controlled studies over long time frames are needed

EXPERT REVIEWER Gail Brady

CONFLICTS OF INTEREST: None

EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

Gail is a Registered Nutritional Therapy Practitioner RCNHC MBANT. She qualified is 2013 from The Institute for Optimum Nutrition in London and has since furthered her studies and completed a Master's of Science (MSc) degree in Advanced Nutrition (Research and Practice). The topic for her MSc dissertation project was menopause and potential diet and lifestyle interventions that my help to prevent weight gain. In clinical practice, Gail specialises in female health and works 1:1 with clients using a Functional Medicine framework. She also runs an online course providing a tool kit for managing perimenopause and menopause.

LYCOPENE & LIPID METABOLISM

EFFECT OF 12-WEEK DAILY INTAKE OF THE HIGH-LYCOPENE TOMATO (SOLANUM LYCOPERSICUM), A VARIETY NAMED "PR-7", ON LIPID METABOLISM: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL-GROUP STUDY

Nishimura, M ; Tominaga, N ; Ishikawa-Takano, Y ; Maeda-Yamamoto, M ; Nishihira, J
Nutrients. 2019;11(5)

SUMMARY REVIEW:

INTRODUCTION:

- A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group study was conducted to investigate the effects of the regular and continuous intake of high-lycopene tomato, a variety named PR-7, for 12 weeks on 74 healthy Japanese subjects with low-density lipoprotein cholesterol (LDL-C) levels > 120 to <160mg/dL.

METHOD:

- The subjects were randomly assigned to either the high-lycopene tomato or placebo (lycopene-free tomato) group. Each subject in the high-lycopene group ingested 50g of semi-dried PR-7 (lycopene, 22.0-27.8mg) per day. Medical interviews were conducted, vital signs were monitored, and blood and saliva samples were taken at 0 (baseline) and at 4, 8 and 12 weeks.

RESULTS:

PRIMARY CLINICAL OUTCOMES:

- The intake of high-lycopene tomato improved LDL-C at week 12 when compared to the placebo group (Week 12: placebo, 4,1 +- 15.7mg/dL; high-lycopene tomato, -3.7 +- 13.8.mg/dL; p=0.027).
- Based on a subgroup analysis, the ingestion of high-lycopene tomato significantly decreased LDL-C in subjects with LDL-C ranging from 120–139 mg/dL at week 12 (Week 12: placebo, 4.3 15.1 mg/dL; high-lycopene tomato, +- 5.1 9.5 mg/dL; p = 0.030).

SECONDARY CLINICAL OUTCOMES:

- There were no significant differences between the high-lycopene tomato and placebo groups in terms of lipid profiles comprising of total cholesterol (TC), HDL-C, triglycerides (TG), LDL-C/HDL-C ratio, and non-HDL, and adiponectin.
- The intake of high-lycopene tomato increased lycopene levels compared to the placebo group (Week 12: placebo, +-24.2 49.3 g/dL; high-lycopene tomato, 22.7 47.9 g/dL; p < 0.001).
- In addition, beta-carotene levels increased in the high-lycopene tomato group compared to those in the placebo group at week 12 (Week 12: placebo, 0.9 13.6 g/dL; high-lycopene tomato, 12.0 24.5 g/dL; p = 0.009).

REVIEWER: Ana-Paula Agrela, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Lycopene, a carotenoid, has antioxidant effects and exhibits the highest physical quenching rate constant for singlet oxygen.
- Lycopene has also been reported to inhibit the production of serum lipid peroxide and oxidize low-density lipoprotein (LDL)
- This study reported that the intake of 50g of high-lycopene (lycopene, 22.0-27.8mg) for 12 weeks significantly decreased LDL-C in subjects with LDL-C ranging from 120–139 mg/dL.

🔍 CLINICAL PRACTICE APPLICATIONS:

- A previous meta-analysis demonstrated that LDL-C decreases when more than 25 mg per day of lycopene is ingested. The biological mechanism was associated with a reduction in 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase activity in the liver, activation of LDL-receptors, and increased expression of the ABCA1 transporter gene, the key component of HDL-C production.
- This study also suggests that there is a decrease in LDL-C at 12 weeks in subjects with LDL-C from 120–139 mg/dL.
- Based on these findings, a practitioner could therefore consider recommending 25mg of lycopene to help reduce LDL-C in patients with an LDL-C range of 120–139 mg/dL for at least 12 weeks.

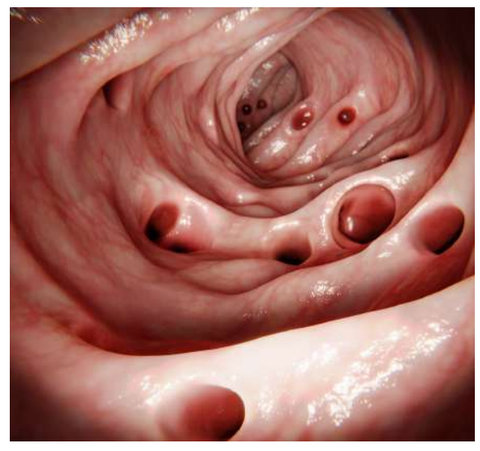
? CONSIDERATIONS FOR FUTURE RESEARCH:

- Lycopene has been reported to possess the strongest singlet oxygen scavenging ability among the eight carotenoids, as measured by the singlet oxygen absorption capacity method, and some researchers have found that lycopene and tomato display antioxidant effects. However, other reports suggest that ingesting lycopene does not affect oxidative markers. These findings suggest that further investigation is needed to evaluate the effect of lycopene on oxidative markers.
- The LOX index is a biomarker for the early risk of arteriosclerosis, cerebral infarction, and myocardial infarction. Lycopene might be ineffective against LOX-1 which is a product of the peroxidation reaction. Additional studies with a longer intake period are required to investigate the effect of lycopene on the risk of arteriosclerosis.
- The subjects in this study were asked to avoid cooking the test food (semi-dried tomato). It is, therefore, necessary to investigate the differences in the effect of the high-lycopene tomato based on various cooking methods.

EXPERT REVIEWER Ana-Paula Agrela

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University and holds a Health Coaching certificate from Zest for Life. She completed her Master's degree in Holistic Health and Nutritional Education through Hawthorn University in the United States. Ana has over 20 years' experience in researching and developing health supplements for the nutraceutical industry. She also offers group education programs and private consultations to help clients make healthier food choices and lifestyle habits.

NUTRITION ADVICE FOR COLORECTAL CANCER



INVESTIGATING THE NUTRITIONAL ADVICE AND SUPPORT GIVEN TO COLORECTAL CANCER SURVIVORS IN THE UK: IS IT FIT FOR PURPOSE AND DOES IT ADDRESS THEIR NEEDS?

Matsell, SL ; Sánchez-García, MA ; Halliday, V ; Williams, EA ; Corfe, BM
Journal of human nutrition and dietetics : the official journal of the British Dietetic Association. 2020;33(6):822-832

SUMMARY REVIEW:

INTRODUCTION:

This descriptive cross-sectional study used a survey to explore the experience of people diagnosed with colorectal cancer (CRC), regarding the information they received on nutrition.

METHOD:

- The survey used a self-administered questionnaire. This was derived from a questionnaire developed by the National Institute for Health Research (NIHR) collaboration on nutrition and cancer to explore the patient experience of those diagnosed with cancer.
- Survey participants were recruited via cancer charities, social media and support groups, and were therefore self-selected.,
- The questionnaire used open-ended and closed questions to collect quantitative and qualitative data on patient characteristics and their perspectives on nutritional needs and nutritional advice. Participants could complete the questionnaire on-line or on paper.
- Statistical analysis of numerical data used SPSS software. Text data in response to open-ended questions were analysed using reflexive thematic analysis, with two researchers independently coding the text to identify emerging themes, which were then reviewed and summarised by the research team.

PARTICIPANTS:

- 80 participants completed the survey, of which 5 were excluded due to non-CRC diagnoses. 75 eligible responses were analysed, 70 were completed by people diagnosed with CRC and 5 by a carer of a person with CRC.
- Participants came from all nine regions of the NHS, two-thirds were female, and 83% were aged 50 years and above.
- Dividing participants by stage of cancer determined that 44% had advanced cancer, the remaining being characterised as early, and tumour location at diagnosis were split equally between colon and rectum.
- For 12% of patients their diagnosis was a recurrence, and 45% had required a colostomy procedure. Stratified by treatment stage, 25% were in active treatment, 56% had completed treatment and were being monitored, and 17% were receiving symptomatic treatment only.

RESULTS:

- Detailed data on nutritional problems experienced by participants were collected, of which diarrhoea was the most common, affecting 73% participants, secondly uncertainty about what to eat affected 70% participants.
- 69% of participants reported receiving no nutritional advice regarding their cancer from their NHS cancer care team. Reasons cited were ‘not offered advice’ (69%) ‘did not know it existed’ (45%) and did not know how to access it (24%).
- Of the participants who received nutritional advice for their CRC, 56% received this from a nurse, 26% from a specialist dietitian and 35% from a general dietitian.
- Advice received at the diagnosis stage was equally likely to be around physical activity and foods to avoid, Advice received during treatment included foods to eat or avoid and general healthy eating advice.
- Participants who reported receiving no nutritional advice from their care team were asked if they received advice elsewhere. Cancer support groups provided nutrition advice to 16% respondents but 70% received no advice from any other sources. Those who sought their own advice used charity websites, recipe books and social media, including Facebook groups, and patient blogs. On-line searches for nutrition advice were commonly reported by participants.
- Comments on hospital food were also submitted by some survey participants, of which there were more than twice the number of negative comments as positive.

EMERGING THEMES:

Three main themes emerged from the qualitative data analysis derived from participants’ responses:

- Theme 1: Lack of nutritional advice
- Theme 2: Individualised aid from healthcare professionals was highly valued
- Theme 3: Treatment side-effects and bowel function impairment hinder ability of following a healthy diet

CONCLUSION:

The authors noted that less than one third of patients with a diagnosis of CRC received nutritional advice from a member of their care team, Advice received was not considered to meet expectations, being generic and unsuited to many individuals. CRC patients want individual advice, and from the professionals in their care teams, preferably from a dietitian.

REVIEWER: Carol Granger, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- People with a cancer diagnosis affecting the digestive system may be in need of personalised advice on nutrition and lifestyle at several points in their cancer journey. Appropriately skilled and experienced nutrition professionals may meet this need and improve the patient experience.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Personalised nutrition advice was considered important to the participants in this survey.
- This echoes findings of other researchers in this field, for example Penny Brohn UK, a Bristol-based charity supporting people affected by cancer.
- Evidence-based nutrition advice for people with a diagnosis of CRC may support recovery, and needs to be individualised, as a range of side effects and bowel symptoms appear to hinder recovery.
- Appropriately qualified and experienced nutrition professionals may provide this individualised advice.

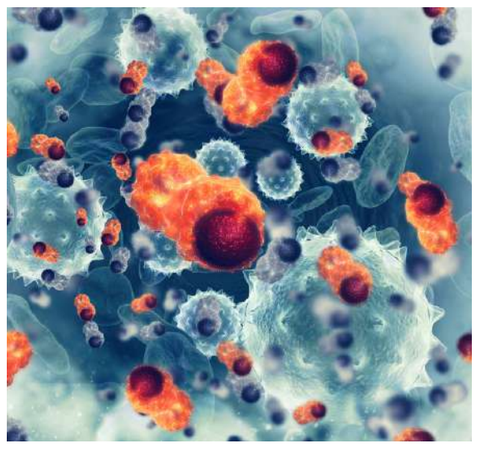
? CONSIDERATIONS FOR FUTURE RESEARCH:

- This was a small survey and the self-selected sample cannot be considered representative, therefore the findings cannot be generalised to a wider population. Further research may consider random sampling or other survey sampling techniques to produce more representative data.
- Further qualitative research could include in-depth interviews or focus groups to explore themes in more depth, for example explore the long- term impact of personalised nutritional advice on people living with and beyond CRC.
- This study did not report whether participants had consulted other nutrition professionals outside the NHS. This is an area for future research.

EXPERT REVIEWER Carol Granger

Carol is a Registered Nutritional Therapist and microbiologist. She completed research for a professional doctorate at the University of Westminster on the practice of nutritional therapy for people affected by cancer. She is a chartered biologist with a degree in biochemistry and a Master's in microbiology and brings to Nutrition Evidence her experience from a health and life sciences career over 30 years, and a personal commitment to evidence-based practice, professional regulation and inter-professional collaboration. Carol is co-chair of the Research Council for Complementary Medicine (RCCM), a director of the British Society for Integrative Oncology, and participates in the National Institute for Health Research Collaboration on nutrition and cancer.

ENDOMETRIAL CANCER & DIET



INFLAMMATORY AND INSULINEMIC DIETARY PATTERNS AND RISK OF ENDOMETRIAL CANCER AMONG US WOMEN

Romanos-Nanclares, A ; Tabung, FK ; Sinnott, JA ; Trabert, B ; De Vivo, I ; Playdon, MC ; Eliassen, AH
Journal of the National Cancer Institute. 2023;115(3):311-321

SUMMARY REVIEW:

INTRODUCTION:

This cohort study examined the incidence of endometrial cancer (EC) in women recruited to two large prospective studies in the USA. The Nurses' Health Study (NHS) and Nurses' Health Study II (NHS-II) recruited female nurses from 1984 to 2016 and 1991 to 2017 respectively. These large studies have produced significant epidemiological data, reporting associations between lifestyle factors and health outcomes across many health conditions including cancer. The two studies had combined recruitment of 237950 women and a follow up rate of 90%. This analysis applied two novel dietary indices developed and validated using cohorts within the NHS and NHS-II studies and a parallel study in male health professionals, the Health Professionals Follow-Up Study (HPFS).

METHODS:

- Researchers collected medical histories and lifestyle information using self-administered questionnaires at intervals during the study.
- In this subset analysis, 133756 women with an intact uterus were studied, representing 2823221 person years of follow up.
- Physical activity, smoking status, medication use including contraceptive use and hormone replacement therapy were recorded. Diabetes diagnosis and anthropometric data were collected.
- Dietary intakes were assessed using a semi-quantitative food frequency questionnaire (FFQ) of 116 foods items in NHS, increased to 130 food items NHS-II. The FFQ had previously been validated using 24-hour dietary recall and multi-week dietary records.

REVIEWER: Carol Granger, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

ANALYSIS OF DIETARY IMPACT:

- The empirical dietary index for hyperinsulinemia (EDIH) and empirical dietary inflammatory potential (EDIP) index were developed and validated using stepwise regression models (reported in detail elsewhere). Intakes of 39 predetermined food items within the FFQ were compared with biomarkers from three cohorts of matched cases, nested within the NHS and NHS-II studies and the HPFS, which studied male health professionals.
- Biomarkers for inflammation used to develop EDIP were plasma concentrations of IL-6, C-reactive protein (CRP), TNF-**α** receptor 2 (TNF**α**R2), and adiponectin. Validation of the EDIP identified eighteen foods of which 9 were considered anti-inflammatory and 9 proinflammatory.
- Plasma C-peptide was the biomarker for insulinemic impact for EDIH, validated to scores for intake of eighteen food groups; thirteen positively associated with C-peptide and five inversely associated.
- These indices therefore score dietary pattern, however, notably, there were some curious findings for individual foods identified as pro-inflammatory (tomatoes) and anti-inflammatory (pizza), which were noted in the publication reporting development of the EDIP.

FINDINGS:

- There were 1565 diagnoses of endometrial cancer, of which 1462 Type 1 EC were considered, discounting rare or uncertain EC subtypes.
- Associations between EDIH and EDIP scores by quintile and endometrial cancer were calculated and identified increased incidence of EC with more inflammatory and insulinemic dietary patterns. For dietary inflammatory potential assessed using EDIP, comparing highest to lowest quintile, HR = 1.46, (95% CI = 1.24 to 1.73; Ptrend < .001). For dietary insulinemic potential, comparing highest to lowest quintile, hazard ratio (HRQ5vsQ1) = 1.58, 95% CI = 1.34 to 1.87; Ptrend < .001).
- Multivariate analysis indicated a substantial effect of the combined scores on EC risk.
- However, adjusting these scores for BMI attenuated the effect, with HR close to 1 after adjustment (EDIP HR = 1.03, 95% CI = 0.87 to 1.22; EDIH HR = 1.01, 95% CI = 0.85 to 1.21). Body mass index was assessed to explain 60.4% of the association of endometrial cancer with dietary inflammatory potential as expressed as EDIP and 71.8% of inflammatory potential as expressed as EDIH. These data suggest therefore that adiposity and obesity are strongly influential in these effects.

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- Endometrial cancer is increasing in many populations, and evidence links this to rising obesity and increasing age.
- Dietary factors that increase systemic inflammation and raise blood insulin levels appear associated with the development of EC in the population of women studied.
- Women with obesity are at increased risk of developing EC, compared with women in the normal weight range, and the dietary inflammatory and insulinemic potential may contribute to this association.

🔍 CLINICAL PRACTICE APPLICATIONS:

- Endometrial cancer is increasing in incidence in industrialised countries, predicted to overtake colorectal cancer as the leading type of cancer in women in the USA by 2030.
- There is clear evidence for a link with obesity and with unopposed oestrogen. This study demonstrates the impact of dietary intake on EC risk and highlights a role for appropriate nutritional guidance to support women who may be at risk of developing EC.
- Since the association with inflammatory and insulinemic foods appears strongly influenced by obesity, measures to address body composition are important.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- Apparent anomalies in the inflammatory potential scores reman unexplained, although overall dietary pattern is more important to consider than intakes of individual food items.
- This study did not report biomarkers of insulin resistance and BMI was the only anthropometric data reported. Analysis of risk associated with body composition and adiposity would be useful. For example, waist to height ratio is considered a useful anthropometric indicator
- Further exploration of the role of dietary insulinemic impact on insulin resistance could include measurement of HbA1c in this patient group.
- As exposure to excess unopposed oestrogen is also implicated in EC, assessment of oestrogen metabolism and adiposity would also add to the understanding of this condition.

EXPERT REVIEWER Carol Granger

Carol is a Registered Nutritional Therapist and microbiologist. She completed research for a professional doctorate at the University of Westminster on the practice of nutritional therapy for people affected by cancer. She is a chartered biologist with a degree in biochemistry and a Master's in microbiology and brings to Nutrition Evidence her experience from a health and life sciences career over 30 years, and a personal commitment to evidence-based practice, professional regulation and inter-professional collaboration. Carol is co-chair of the Research Council for Complementary Medicine (RCCM), a director of the British Society for Integrative Oncology, and participates in the National Institute for Health Research Collaboration on nutrition and cancer.

ADDITIONAL RESOURCES

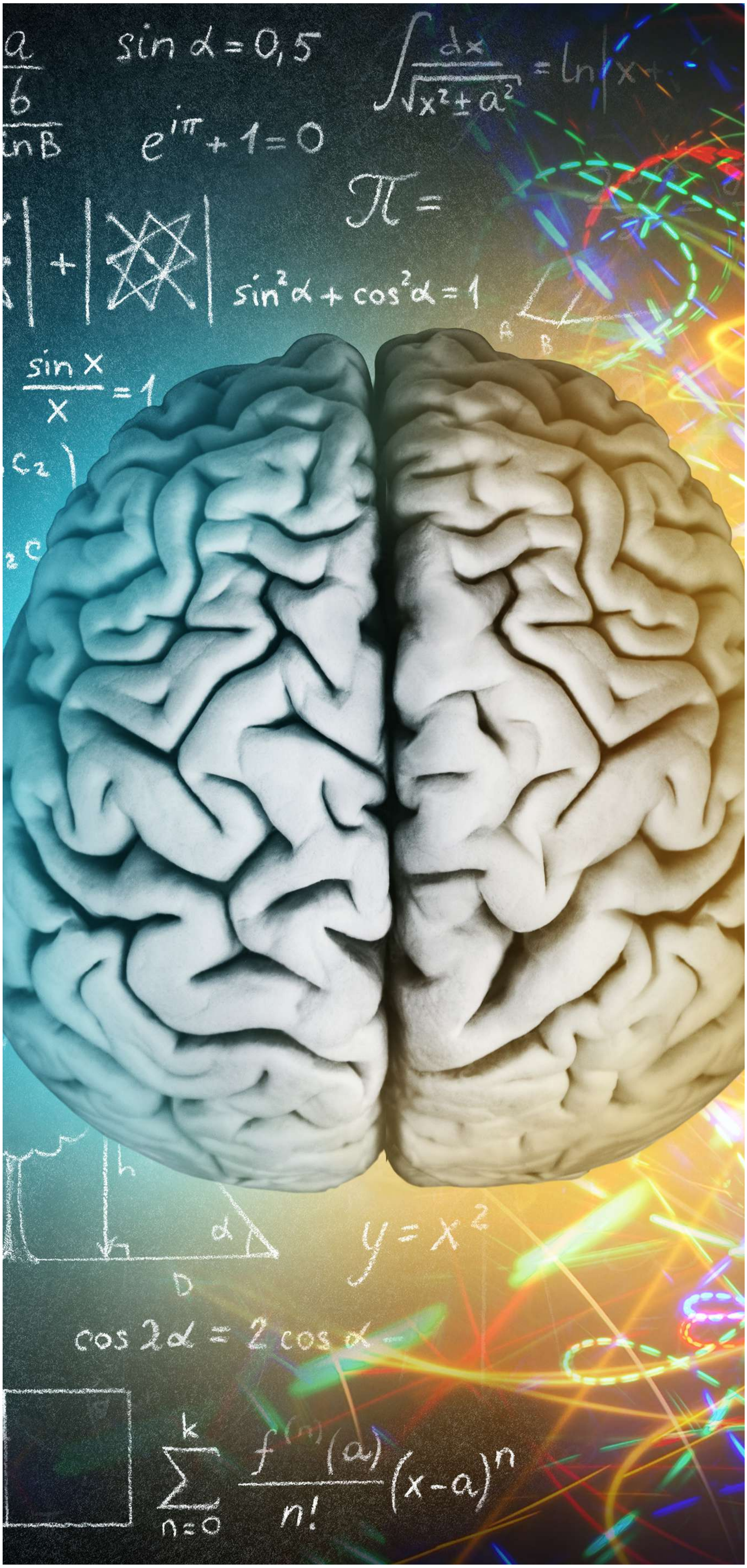
NED INFOBITES AND CLINICAL FACT SHEETS

Integrative oncology combines evidence-based nutrition & lifestyle medicine recommendations alongside traditional oncology. Identifying the exact components of a 'healthy diet' that contribute to better cancer outcomes is an area of research which is still emerging.

The boom of research into nutraceuticals – broadly defined as any product derived from food sources with extra health benefits in addition to the basic nutritional value found in foods – has improved our understanding of nutrients and dietary components and how they influence epigenetic phenomena.

Follow the latest science on phytonutrients at https://www.nutrition-evidence.com/

BRAIN HEALTH & COGNITION



2 REVIEWS

TIME RESTRICTED EATING & AD

THE EFFECTS OF TIME-RESTRICTED EATING ON SLEEP, COGNITIVE DECLINE, AND ALZHEIMER'S DISEASE

Ezzati, A ; Pak, VM
Experimental gerontology. 2023;171:112033

SUMMARY REVIEW:

- The authors highlight Alzheimer's disease (AD) is the most prevalent neurodegenerative disease affecting over 50 million aging people worldwide. While no cure is known for AD, this review proposes lifestyle interventions such as time-restricted eating (TRE) as a potential approach to delay the onset and progression of a neurodegenerative disease and could hint at autophagic mechanisms.
- TRE involves strategically limiting the eating window to 8- to 12-h with fasting—drinking only water and calorie-free coffee/tea—for 12 to 16 h within a 24-h cycle.

OBJECTIVES:

To investigate the effects of TRE on sleep and cognitive decline in healthy individuals.

RESULTS:

- Nine RCTs with varied length between one and sixteen weeks were examined
- A 5-week randomised controlled trial (RCT) showed no significant change in sleep quality between early TRE (fasting between 6 a.m.–3 p.m.), mid-day TRE (11 a.m.–8 p. m.) and control (ad lib intake) in 82 healthy subjects without obesity but the sleep quality improvement was greater in early TRE group (PSQI:Δ=−1.08±1.78vs.Δ=−0.22±2.19andΔ=−0.36±1.73, respectively).
- Sleep quality using the myCircadianClock app reported significant improvement in sleep quality (23 %) following a 12-week single arm intervention of 10-h TRE.
- Following a 16-week TRE intervention sleep duration was reported to be improved from a subjective score of 6 at base line to 8 after 36 weeks in eight overweight and obese subjects; however, the study used a subjective self-assessment survey for measuring sleep duration.
- The Pittsburgh Sleep Quality Index (PSQI) was carried out to assess sleep quality and disturbances in six trials but no trial reported significant improvement in sleep quality using the PSQI survey with TRE.

REVIEWER: Kirsty Baxter, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

CONCLUSION:

Authors highlight TRE as promising for its potential to reduce the markers of aging and neurodegenerative disease.

TAKE HOME MESSAGE:

To highlight the potential benefits of time-restricted eating (TRE) as a potential preventative approach to delay the onset and progression of neurodegenerative disease such as AD.

🔍 CLINICAL PRACTICE APPLICATIONS:

- To inform practitioners of the potential benefits of TRE that involves limiting the eating window to 8- to 12-h with fasting—drinking only water and calorie-free coffee/tea—for 12 to 16 h within a 24-h cycle.
- TRE may improve regulation of circadian rhythm and autophagy through aligning food intake with circadian rhythm, which coordinates metabolism and physiological functions including glucose, insulin sensitivity, lipid levels, energy expenditure, inflammation, sleep and cognitive function.
- TRE activates a metabolic switch which occurs 12–36 h after fasting is initiated and free fatty acids are released into the blood.
- TRE improved sleep quality and sleep duration, where a longer fasting period in TRE approach (≥12 h fasting) was associated with significantly higher sleep duration.

? CONSIDERATIONS FOR FUTURE RESEARCH:

- The potential benefits of TRE in neurodegenerative diseases such as AD should be further investigated clinically.
- The optimal time to initiate fasting needs to be identified in future trials.
- The potential benefits of TRE in neurodegenerative diseases such as AD in the context of sleep should be further investigated.

EXPERT REVIEWER Kirsty Baxter

Kirsty is a BANT and Registered Nutritional Therapy Practitioner, who has been in practice since 2016, having completed research for a Master of Science in Nutrition (Advanced Research and Practice) at the London South Bank University to support a nutritional therapy approach harnessing psychological aspects of obesity weight loss. Kirsty is currently in the process of publishing her research. She works collaboratively with a wide range of GPs and doctors, frequently giving presentations on metabolism to support awareness around the nutritional intervention for metabolic conditions.

KETOGENIC DRINK AND COGNITION

A KETOGENIC DRINK IMPROVES COGNITION IN MILD COGNITIVE IMPAIRMENT: RESULTS OF A 6-MONTH RCT.

Fortier, M ; Castellano, CA ; St-Pierre, V ; Myette-Côté, É ; Langlois, F ; Roy, M ; Morin, MC ; Bocti, C ; Fulop, T ; Godin, JP ; Delannoy, C ; Cuenoud, B ; Cunnane, SC
Alzheimer's & dementia : the journal of the Alzheimer's Association. 2021;17(3):543-552

SUMMARY REVIEW:

This randomized controlled trial demonstrates that supplementation of a ketogenic drink containing medium-chain triglycerides (MCTs) is both safe and effective in improving cognitive outcomes in individuals with mild cognitive impairments (MCI), and does so through supporting energy metabolism in the brain.

METHOD:

Cognition, plasma ketone response, and metabolic profile were assessed before and 6 months after supplementation with a ketogenic drink containing medium chain triglyceride (ketogenic medium chain triglyceride [kMCT]; 15 g twice/day; n = 39) or placebo (n = 44).

RESULTS:

Free and cued recall (Trial 1; P = .047), verbal fluency (categories; P = .024), Boston Naming Test (total correct answers; P = .033), and the Trail-Making Test (total errors; P = .017) improved significantly in the kMCT group compared to placebo (analysis of covariance; pre-intervention score, sex, age, education, and apolipoprotein E4 as covariates). Some cognitive outcomes also correlated positively with plasma ketones. Plasma metabolic profile and ketone response were unchanged.

CONCLUSION:

This kMCT drink improved cognitive outcomes in MCI, at least in part by increasing blood ketone level. These data support further assessment of MCI progression to Alzheimer's disease.

REVIEWER: Marek Doyle, Expert Reviewer
CONFLICTS OF INTEREST: None
EVIDENCE CATEGORY: A: Meta-analyses, position-stands, randomized-controlled trials (RCTs)

HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

TAKE HOME MESSAGE:

- MCT supplementation is a promising strategy to rescue energy metabolism in the brain for those with MCIs by providing an alternative energy source
- Improvements in cognition were associated with increased blood ketone levels from MCT supplementation
- Practitioners should be mindful that higher intakes of MCTs (>30g/d) may lead to negative GI effects in some individuals.

CLINICAL PRACTICE APPLICATIONS:

- The results of this randomised controlled trial demonstrate that MCT supplementation (at 30g per day, split between two doses) is a viable strategy to support brain metabolism in individuals experiencing MCIs
- There was a dose-dependant response on elevated ketones and selected cognitive improvements which may have pertinent applications to therapeutic practice (either dietary or supplemental)
- The paper highlighted the involvement of energy metabolism in cognitive decline; this has potential therapeutic applications in terms of targeted nutritional support for mitochondrial function or energy signalling
- Some individuals experienced negative gastrointestinal effects when consuming MCTs at 30g/d for prolonged periods; practitioners should be mindful of this.

? CONSIDERATIONS FOR FUTURE RESEARCH:

Future research should consider:

- Whether dietary-induced ketosis can therapeutically impact MCI and support patient well-being
- Use of MCTs in those with severe cognitive impairments or those taking medication such as cholinesterase inhibitors
- The role of glucose hypometabolism to determine alternative strategies for those who have GI issues with MCTs
- Whether APOE4 status has any impact on therapeutic outcomes to MCT supplementation
- Whether adjunct nutritional support for mitochondrial function alongside MCT could further impact on MCIs.

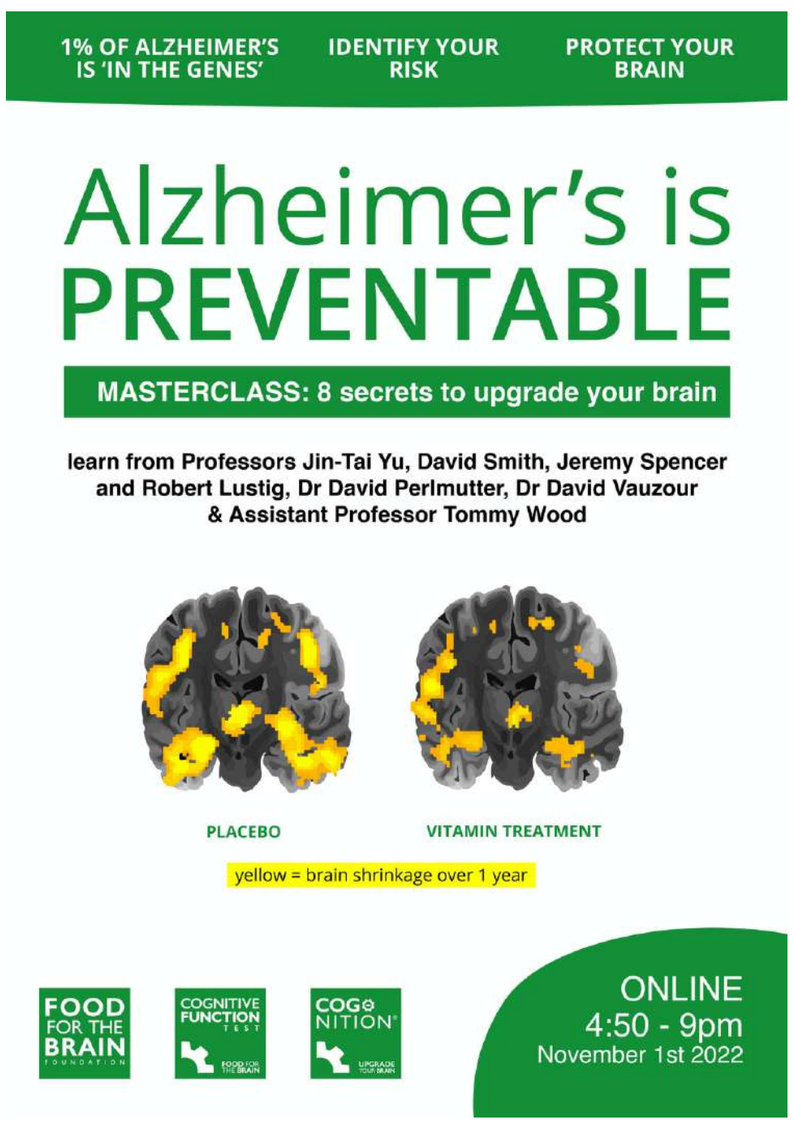
EXPERT REVIEWER Marek Doyle

Marek is a functional nutritional therapist who has spent the last 16 years building a model of personalized nutrition, based on the data of over 3,000 individual outcomes, 11,000 test results and extensive use of the scientific literature. Based in London, he offers one-to-one consultations for clients as well as training for practitioners. He holds an MSc in Personalised Nutrition.

ADDITIONAL RESOURCES

NED INFOBITES AND CLINICAL FACT SHEETS

Brain health and cognition are areas of evolving science and there is increasing evidence on the role nutrition and lifestyle medicine can play in prevention and reduction of risk factors. Download the NED InfoBite and clinical fact sheets at BANT.org.uk



SUPPORTING ALZHEIMER'S

The Food for your Brain Foundation 'Alzheimer's is Preventable Campaign' is pioneering research in this area. For more information and to take the free online Cognitive Function test and Dementia Risk Index questionnaire visit foodforthebrain.org/campaigns/alzheimers-prevention/

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