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# NED EXPERT REVIEWS

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ISSUE 4: HEALTHY AGEING & LONGEVITY JULY 2024

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# WELCOME

Clare Grundel Managing Editor



# WELCOME TO OUR EDITION ON HEALTHY AGEING AND LONGEVITY

This Edition of the NED Journal brings you a selection of articles on different aspects of ageing - including those on how to add years to your life! Longevity and Blue Zones was the theme for the inaugural NED Science Forum held at the Royal Society of Medicine on 13 May 2024 in London. Professor Justin Roberts kicked off a great evening with a presentation on some of the world's Blue Zones, which was followed by a lively and engaging debate with the audience. Justin reflects on the evening...

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NED continues to grow at pace. As a team we have enhanced functionality in our NED platform; our expert reviews have provided new avenues for practitioners to easily access academic insights and our NED Journal is already at its 4th Edition supporting evidence-based reasoning. But the journey wouldn't have been complete if we didn't have a NED Science Forum. And so our inaugural forum at the Royal Society of Medicine. From the start, what impressed me the most was the obvious passion, support and dedication from BANT members and invited guests who attended the event. The event was sold out well in advance and I even heard there was a long waiting list (note to self: make sure we book a bigger room next year).

There was a real buzz before the talks even started with plenty of networking, meeting our wonderful event sponsors and enjoying some tasty bites (thank you RSM for your hospitality). For the keynote, I wanted to provide a light-hearted insight into the global Blue Zones, comparing some of the nutritional, physical, social and environmental factors which might explain longevity. Noting that many of these cultures habitually practice simple lifestyle and dietary principles what can we learn that might impact healthspan. More importantly, I encouraged the audience to reflect on their own practice and consider the overlaps to the Blue Zones. The panel discussion that ensued was... well.... highly interesting and thought-provoking. For that I thank you, the audience, and our other panel members (Dr Michelle Barrow, Dr Jessica Rigutto, Dr Kate Lawrence and Kirsty Baxter).

The NED Science Forum provided valuable and highly pertinent insights into practitioner awareness and guided use of the NED database from Clare Grundel (NED Managing Editor). With discussion around the continued interest and on-going need for evidence-based nutrition therapy practice, Clare also discussed a new BANT initiative to consider impact data gathering to inform and enhance our profession. The importance of scientific rigour and integrity was also eloquently discussed by Dr Jessica Rigutto (NED Editorial Board Member) highlighting the fundamental need for critical reading in practice, and it was great to see some of our NED expert reviewers there to share their insights as well. The forum concluded with a fantastic discussion from Ben Brown ND on why publishing research, particularly case reports, is so important for the future of our profession, not only to develop personal growth, but to enhance professional credibility pertinent to personalised integrative practice.



Prof. Justin Roberts Editor-in-Chief,

# CONTINUED...

Clare Grundel Managing Editor



# THERE IS SO MUCH MORE TO COME FROM NED...

Whilst NED has come a very long way, there is still much to do. And so we conclude a highly successful inaugural NED Science Forum 2024, and already I'm looking forward to NED 2025. I would encourage you all to book early...



The <u>British Association of Nutrition and Lifestyle Medicine (BANT)</u> is a professional membership body for nutrition practitioners, trained in nutrition sciences and the delivery of personalised nutrition services. BANT members are reading and interpreting nutrition and lifestyle sciences such as that found in this NED Journal on a routine basis to inform their clinical decision making. You can find the BANT member practitioner listing here.

The <u>Nutrition Evidence Database</u> is one of the ways that BANT contributes to the evidence-based practice of precision nutrition. BANT is delighted to make this resource open access for all and encourages all healthcare practitioners interested in personalised healthcare to make use of the resource on a regular basis. **You can subscribe to receive monthly NED alerts** <u>here</u>.

Read previous copies of the NED Journal <u>here</u> which BANT produces and makes available open access to all. BANT aims to bring good nutrition and lifestyle sciences to the forefront of healthcare and is able to do this through its ambition, careful management and the support of sponsors and advertisers. Thanks to the organisations who have supported this edition - <u>BioNutri</u> and <u>Pure Encapsulations</u>.

Deep breath - it is time for a deep dive...

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# INAUGURAL NED FORUM



NED Editor-in-Chief, Prof. Justin Roberts provided the keynote presentation on 'People in the world's 'blue zones' live longer - what are the lessons for us in the UK?'. He was joined on stage by the NED Editorial Board comprised of Dr Michelle Barrow, Dr Kate Lawrence, Dr Jessica Rigutto, and Clare Grundel.



Dr Jessica Rigutto presented on research tools for nutritional therapists in practice, and Clare Grundel introduced NED and gathering scientific evidence.



Guest presenter Ben Brown from the Nutritional Medicine Institute (NMI) closed the evening with a session on 'the importance of research publishing, and the NMJ'.

# AN EVENING OF SCIENCE



# NED FORUM 2025

The NED Forum will return to the Royal Society of Medicine on Tuesday 13th May 2025 - stay tuned for ticket announcements and we hope to see you there!

# ABOUT NUTRITION EVIDENCE (NED)

# NUTRITION EVIDENCE DATABASE

Nutrition Evidence Database, known fondly as NED, is the UK's first scientific database of nutrition and lifestyle medicine research. It focuses on high-quality, human research and other science-supported information and is designed as a comprehensive platform for practitioners, academic researchers and students. The powerful, yet simple search functionality uses functional and lifestyle medicine filters to support evidence-based clinical decision making in personalised nutrition practice.



# UNIQUE TO NED...

- High quality human nutrition and lifestyle medicine research only.
- Useable research for Nutrition Practitioners in clinical practice.
- Categorised using functional and lifestyle medicine filters to support evidence-based clinical reasoning in personalised nutrition practice.
- Provides easy-to-use search functionality enabling searches by functional/physiological systems, modifiable lifestyle factors, laboratory test filters, as well as publication type, availability of resource and date.
- Plain language summaries and expert opinion.
- Quick assimilation of the science and access to industry leader viewpoints.
- Houses a broad range of nutrition and lifestyle medicine resources on one platform.
- Directed by an Editorial Board working in nutrition and lifestyle medicine research.



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Read our NED expert reviews to help apply the science in clinical practice.

# MEET THE NED EDITORIAL BOARD



# EDITOR IN THE SPOTLIGHT

# Dr. Jessica Rigutto - Editor, MPharm, MPH, Dr.sc., ETH Zurich, DipION, mBANT



Dr Jessica Rigutto is an independent consultant in nutrition science and a registered nutritional therapist. She is specialised in micronutrient nutrition and nutrition methodology meta-research, and leads international initiatives to support and promote standards in the science of nutrition for improved public health policy and better health outcomes.

As an external lecturer at the ETH Zürich, Switzerland, Jessica teaches diverse classes in human nutrition, as well as in nutrition research procedures and scientific integrity, and gives talks on these subjects externally.

She is widely published in the peer-reviewed, scientific press, including in Advances in Nutrition, American Journal of Clinical Nutrition, BMJ Open, European Journal of Nutrition, Nutrients, Plos One and Trends in Food Science and Technology, and has contributed to policy guidance for WHO and the OECD. Alongside her Doctor of Science in nutrition from ETH Zürich, Jessica holds master's degrees in public health and pharmacy and is currently training in Functional Medicine to support her work in clinic.

# EDITORIAL TEAM



# Dr. Michelle Barrow - Editor BSc (Hons), MSc, QTLS, DProf, fBANT

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Academic Team Director and Clinical Director at CNELM Doctorate in Professional Studies (DProf).

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Prof. Justin Roberts Editor-in-Chief, Ph.D, C.Sci, SFHEA, mBANT Professor of Nutritional Physiology applied to exercise and functional health, Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University.



# Dr Kate Lawrence - Editor, BA(Hons), PhD, FHEA

Senior Lecturer in psychology at St Mary's University. Specialises in nutritional psychology and neurodiversity, with a focus on dietary and microbiome influences on mental health and cognition.



Clare Grundel, Managing Editor MSc, BA (Hons), mBANT

Science and Education Manager, BANT

Registered Nutritional Therapy Practitioner.

# MEET THE NED EXPERT REVIEWERS



Our Expert Reviewers work within the nutrition industry in academia, research, clinical practice and wider healthcare, and provide unique and invaluable insights on the latest nutrition research to enable practitioners to apply the science to clinical practice.

Knowledge sharing is a key strategic pillar for the NED editorial team. Not only do the expert reviews get directly published on the NED database, they are further communicated via a series of monthly resources and across our BANT social media channels reaching in excess of 25,000 practitioners and followers.



# **EXPERT REVIEWERS IN THIS ISSUE**

(In order of appearance)



# Chloe Steele

Chloe has an MSc in Personalised Nutrition from the University of Middlesex, and specialises in cardiovascular disease, type 2 diabetes, and anxiety. Chloe started her career at BANT as a member of the Nutrition Evidence Database research team and now has over 5 years experience of research and writing. She has worked in several countries, and is currently in Australia, where she worked for Nutrition Australia and is currently the principal nutritionist for Heart Research Australia. She has published two papers in the Nutrition Medicine Journal, on gut microbiota and collagen. Chloe is a member of BANT and the Nutrition Society of Australia and sits on the editorial board for the Nutrition Medicine Institute in the UK.

# 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.





# **Kirsty Baxter**

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



# **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.

# **Daniel Quinones**

Daniel Quinones is a BANT and CNHC Registered Nutritional Therapist. He obtained his nutritional therapy diploma from the College of Naturopathic Medicine and MSc in Personalised Nutrition from CNELM, Middlesex University. Daniel contributes to Nutrition Evidence through his clinical experience working with weight loss clients and research into the drivers of obesity.





# Karin Elgar

Following the completion of a PhD in Physiology and a career in the pharmaceutical industry, Karin graduated as a nutritional therapist from the Institute of Optimum Nutrition in 2004. She has since been practicing in the Greater Manchester area, specialising in women's health and autoimmunity. Karin has written a number of literature reviews and carried out a variety of research and editing projects. She has also delivered CPD seminars and webinars on various topics.

# Miranda Harris

Miranda is a member of BANT and a CNHC Registered Nutritional Therapy Practitioner with over 10 years clinical experience, specialising in endurance sport. She is a senior lecturer (SFHEA) focusing on research methods, dissertation supervision and sports nutrition on the Nutrition and Lifestyle Medicine MSc course at the University of Worcester. She has recently published in the European Journal of Integrated Medicine and the Journal of Nutrition and Health and is working towards a PhD by publication. She is a keen triathlete training for Ironman.





# 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.

# SIGN UP

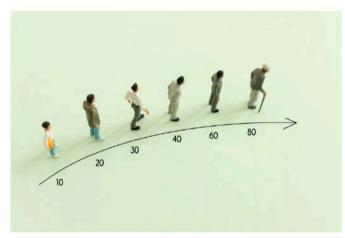


Each month we publish a dedicated Nutrition Evidence alert with our editorial team's pick of the latest research, podcasts, blog posts and expert reviews. Sign up at <u>https://www.nutrition-evidence.com</u> and have the science delivered straight to your inbox. Follow our socials for weekly posts on topics of interest.



# Nutrition Evidence Alert – July 2024 – A Focus on Foods

From our Expert Review Panel Estimating impact of food choices on life expectancy: A modeling study. in PLoS Medicine. 2022. With Expert Review from Chloe Steele. Effects of a Raisin...



# Nutrition Evidence Alert – June 2024 – Novel Therapies for Ageing and Longevity

From our Expert Review Panel Effects of whey and soy protein supplementation on inflammatory cytokines in older adults: a systematic review and meta-analysis in The British Journal of Nutrition....

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# S T E O E O S I S **6 REVIEWS**



# EXERCISE & VIT D ON BONE DENSITY



# ADDITIVE EFFECTS OF EXERCISE AND VITAMIN D SUPPLEMENTATION (WITH AND WITHOUT CALCIUM) ON BONE MINERAL DENSITY IN OLDER ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Fischer, C ; Jakob, F ; Kohl, M ; Kast, S ; Von Stengel, S ; Kerschan-Schindl, K ; Lange, U ; Thomasius, F ; Peters, S ; Uder, M ; Kemmler, W Journal of osteoporosis. 2023;2023:5570030

# INTRODUCTION:

Exercise and vitamin D supplementation are thought to have positive effects on bone mineral density (BMD) and when in combination, benefits may be enhanced. This systematic review and meta-analysis aimed to determine the effects of vitamin D and exercise combination therapy on the BMD of the lumbar spine and proximal femur.

# METHOD:

- The study looked at comparative ≥6 month vitamin D exercise trials in adults aged ≥50 years from 6 electronic databases.
- Outcome measures were BMD at lumbar spine, total hip, or femoral neck as determined by dual X-ray absorptiometry, dual photon absorptiometry, and quantitative computed tomography.

# **RESULTS:**

- Five studies with 360 participants were found to fit the entry criteria. Three were randomised control trials and two were nonrandomised.
- One study was in Caucasian men, whilst the remaining four were in postmenopausal Caucasian women.
- Two studies were for 24 months, whilst three were 12-month durations.
- Exercise regimes varied amongst studies and focused on weight-bearing and non-weight-bearing exercises.
- Vitamin D supplementation ranged from 284-2000 IU/d.
- The addition of vitamin D to exercise did not affect the BMD of the lumbar spine, femoral neck, or hip compared to exercise alone (P=0.912, P=0.675, and P=0.976 respectively), even when a trial with low vitamin D doses was excluded.



# TAKE HOME MESSAGE:

- Whilst this study failed to show additive benefits of exercise and vitamin D, dual therapy may still have some validity especially in individuals with vitamin D deficiency.
- Given the high safety and low cost of vitamin D supplementation, it might be worth recommending dual therapy to patients, especially if they are vitamin D deficient, or at high risk of osteoporosis.

# **CLINICAL PRACTICE APPLICATIONS:**

- Exercise in combination with vitamin D may have no further benefit than exercise alone on BMD of individuals who are not vitamin D deficient.
- However, this is based on only a small number of clinical trials in non-vitamin D deficient individuals.
- Combined vitamin D and exercise may still be of benefit to fracture risk in specific patients.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

• Studies should now extend to looking at exercise in combination with vitamin D supplementation on the BMD and fracture incidence of individuals with vitamin D deficiency.

# **CONCLUSIONS:**

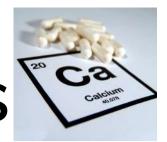
The addition of vitamin D to exercise had no additive benefits on BMD at the lumbar spine or femoral neck. However, this may be due to the trials not employing bone specific exercises and the inclusion of studies which were not performed in individuals with vitamin D deficiency.



# EXPERT REVIEWER Chloe Steele

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

# ORAL CALCIUM IN ELDERLY SUBJECTS



# EVALUATING ADHERENCE, TOLERABILITY AND SAFETY OF ORAL CALCIUM CITRATE IN ELDERLY OSTEOPENIC SUBJECTS: A REAL-LIFE NON-INTERVENTIONAL, PROSPECTIVE, MULTICENTER STUDY.

Rondanelli, M ; Minisola, S ; Barale, M ; et al. Aging clinical and experimental research. 2024;36(1):38

# **INTRODUCTION:**

A non-interventional, prospective multicentre study was conducted to evaluate the adherence, safety, and tolerability of calcium citrate supplementation in elderly osteopenic subjects.

# **METHOD:**

A total of 231 Caucasian female (91%) and male (8%) participants with a median age of 70 received 500mg of calcium citrate supplementation daily for one year. Adherence was assessed based on tolerability, compliance, and persistence. Safety evaluations included monitoring of adverse reactions (ARs), physical examinations, and clinical laboratory evaluations.

# **RESULTS:**

A total of 222 out of 231 participants (96%) completed the study. Nine subjects did not return for assessments or complete their diaries.

The primary and secondary findings of this study were as follows:

- An average adherence of 91% of oral calcium citrate supplementation was observed which was higher than the reported reference rate of 57% (p = 0.0179).
- Subjects with adherence <80% experienced a higher frequency of adverse events compared to those with adherence >80% (32/77; 42% vs 16/145%, (p = 0.0001).
- Gastrointestinal ARs were the most commonly reported, with constipation comprising 50% of all reported ARs.
- Reductions in systolic (130.7 ± 16.9 mmHg to 127.9 ± 14.5 mmHg) (p = 0.0102) and diastolic blood pressure 79.5 ± 8.7 mmHg to 77.4 ± 8.6 mmHg (baseline to V2) (p = 0.0116) were observed from baseline to the second visit.
- Positive changes were also noted in nutritional status (p = 0.0116), circulatory system disorders (p = 0.0001), and muscles/skeleton disorders (p = 0.0067) from baseline to post-baseline visit.

# TAKE HOME MESSAGE:

- The occurrence of fractures and osteoporosis are significant concerns in older adults, as ageing remains one of the primary risk factors for this condition.
- Calcium supplementation, usually with vitamin D, is a recommended complement to other specific pharmacological treatments of osteoporosis.
- This non-interventional, prospective multicentre study suggests a 91% adherence to calcium citrate supplementation over one year in elderly osteopenic patients with generally good (80%) tolerability and 4% reporting gastrointestinal adverse effects.

# CLINICAL PRACTICE APPLICATIONS:

- The prevalence of osteoporosis rises as individuals age, with approximately 10% of women at 60 years, 20% at 70 years, and 40% at 80 years.
- Calcium supplementation, usually with vitamin D, is a recommended complement to other specific pharmacological treatments of osteoporosis.
- The safety of calcium supplements remains controversial regarding an increased risk of cardiovascular events. Therefore, it is essential to investigate the safety profile of calcium in these populations.
- This study reported adherence, tolerability, and safety of calcium citrate supplementation in osteopenic elderly patients with 4% of patients reporting gastrointestinal adverse effects.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- This study was conducted on 91% Caucasian females and 8% males with a mean age of 70 years therefore, there is a need to include more male and Asian participants from various age groups in further research.
- Future studies are needed to assess the long-term impact of calcium citrate supplementation on bone density, fractures, and quality of life.

# CONCLUSION:

This study revealed a 91% adherence to calcium citrate supplementation over one year in older adults with osteopenia, Additionally, the 4% incidents of ARs reported were related to gastrointestinal disorders.



# EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

# PAGE SEVENTEEN | ORAL CALCIUM IN ELDERLY OSTEOPENIC SUBJECTS

# VIT D3 & CALCIUM ON HIP FRACTURE



# WHAT IS THE IMPACT OF DAILY ORAL SUPPLEMENTATION OF VITAMIN D3 (CHOLECALCIFEROL) PLUS CALCIUM ON THE INCIDENCE OF HIP FRACTURE IN OLDER PEOPLE? A SYSTEMATIC REVIEW AND META-ANALYSIS.

Manoj, P ; Derwin, R ; George, S International journal of older people nursing. 2023;18(1):e12492

# INTRODUCTION:

Calcium and vitamin D are integral to the bone matrix and research on their supplementation for bone health is extensive. This systematic review and meta-analysis aimed to determine the effect of calcium plus vitamin D3 supplementation on the incidence of hip fracture.

# METHOD:

- This was a systematic review and meta-analysis of 7 randomised control trials (RCTs) involving 12,620 individuals.
- Subjects were ≥65 years of age and living in the community and long-term care with or without risk of hip fracture.
- The primary outcome was the incidence of hip fracture following calcium plus vitamin D3 supplementation.
- The secondary outcomes were incidence of non-vertebral fracture, incidence of hip fracture in women, and femoral neck bone mineral density (BMD) following vitamin D3 plus calcium supplementation.

# RESULTS

- Combined vitamin D3 and calcium reduced hip fracture by approximately 25% compared to placebo (OR of 0.75; 95% Cl: 0.64, 0.87; p = .0003).
- Non-vertebral fractures were reduced by 20% following supplementation compared to placebo (0.80; 95% CI: 0.72, 0.89; p < .0001).</li>
- Higher dose combinations were the most effective and 800 IU vitamin D3 and 1200mg tricalcium phosphate reduced hip fracture by 32% (OR = 0.69, CI 95%: 0.58, 0.82; p < .0001) and non-vertebral fracture by 27% (OR = 0.73; 95% CI: 0.64, 0.84: p < .0001).</li>
- Doses of 800 IU plus 1000mg of calcium were ineffective at preventing hip fracture (OR = 1.08; 95% CI: 0.74, 1.56; p = .70) and non-vertebral fracture (OR = 0.96 95% CI: 0.81, 1.13; p = .63).
- Women reported reduced hip fracture incidence of 30% compared to placebo (OR= 0.70; 95% CI:0.59, 0.83; p < .0001).</li>
- BMD of the femoral neck was unaffected by calcium and vitamin D3 supplementation (MD = 1.21; 95% CI: -0.79, 3.20; p = .24).

#### PAGE EIGHTEEN | VIT D AND CALCIUM AND HIP FRACTURE

#### TAKE HOME MESSAGE:

• It is important to ensure that older people are receiving adequate calcium and vitamin D to prevent fractures. Supplementation of these nutrients may be an easy and effective way to ensure that older people maintain their health and independence as they age.

# CLINICAL PRACTICE APPLICATIONS:

- This study did not take into account serum calcium and vitamin D3 levels and whether fracture incidence is affected by these.
- The recommendation of 800 IU/day vitamin D3 plus 1200mg/day calcium should be considered for individuals over 65 years of age to prevent incidence of fractures.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- The influence of baseline serum vitamin D and calcium levels on incidence of fracture could aid the identification of individuals who would most benefit from supplementation.
- How different supplemental forms and doses influence fracture incidence would also be of benefit.

# CONCLUSIONS:

- Vitamin D3 plus calcium supplementation decrease the incidence of hip and non-vertebral fractures.
- 800 IU vitamin D3 and 1200mg calcium were the most effective.
- Supplementation did not affect BMD at the femoral neck.

# EXPERT REVIEWER Chloe Steele

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

#### PAGE NINETEEN | VIT D AND CALCIUM AND HIP FRACTURE

# CREATINE ON BONE HEALTH



# A 2-YR RANDOMIZED CONTROLLED TRIAL ON CREATINE SUPPLEMENTATION DURING EXERCISE FOR POSTMENOPAUSAL BONE HEALTH.

Chilibeck, PD ; Candow, DG ; Gordon, JJ ; Duff, WRD ; Mason, R ; Shaw, K ; Taylor-Gjevre, R ; Nair, B ; Zello, GA Medicine and science in sports and exercise. 2023;55(10):1750-1760

#### **INTRODUCTION:**

This study aimed to determine the effects of creatine monohydrate supplementation and exercise on femoral neck bone mineral density (BMD), lumbar spine BMD and proximal femur geometric properties in postmenopausal women over 2 years.

#### **METHOD:**

- 237 postmenopausal women (mean age, 59 yr) were randomised into 2 groups across 2 sites.
- Participant inclusion criteria: no menstrual period for 2 years, and considered at "low" and "moderate" risk of fracture.
- Treatment group (n=120) received creatine monohydrate (0.14 g/kg-1 per day-1 mixed with 0.14 g·kg-1·d-1 maltodextrin) and supervised resistance training plus partially supervised walking.
- Placebo group (n=117) received 0.28 g·kg-1·d-1 maltodextrin and supervised resistance training plus partially supervised walking.
- All participants also received 500 mg of calcium and 10  $\mu$ g (400 IU) of vitamin D per day.
- Resistance exercises and 20-30 mins of brisk walking were performed in-lab and supervised 3 days per week. 3 days of non- supervised 20-30 mins of brisk walking was undertaken outside of the lab.

# RESULTS

- Creatine monohydrate supplementation combined with resistance training and walking over 2 yr: i) had no effect on BMD at the femoral neck (P < 0.0001), total hip (P < 0.0001), or lumbar spine (P= 0.003); ii) increased lean tissue mass compared with placebo (P = 0.046); iii) preserved a number of geometric properties and may therefore help to maintain bone bending strength and cortical bending under compressive loads.
- The authors speculated that creatine supplementation stimulates remodeling of bone to alter geometric properties and whether bone formation or resorption predominates depends on the location of bone in the proximal femur.

# TAKE HOME MESSAGE:

• Creatine supplementation may have beneficial effects on bone geometry at the proximal femur when combined with a resistance training program and walking programme in postmenopausal women.

# CLINICAL PRACTICE

 Creatine supplementation is effective for increasing lean tissue mass when combined with resistance training that may allow for increased mechanical stress on bone, stimulating a net bone formation.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- Assess the mechanism of action of creatine supplementation on BMD.
- Longer term follow-up with larger sample sizes would be needed to confirm protection against hip fracture with creatine supplementation.

# **CONCLUSION:**

 2 years of creatine supplementation with resistance training and walking in postmenopausal women had no beneficial effects on BMD but did improve the proximal femur cortical thickness and section modulus bone geometry, and reduced SPW and buckling ratio that may be protective against hip fracture.

Adverse Events: The dose of creatine over 2 years resulted in minimal adverse events.

Limitation: Low compliance at 56%, and high attrition within the groups: creatine (n=86 of n=120) and placebo (n=88 of n=117) , 61% compliance for exercise sessions completed.



# EXPERT REVIEWER Kirsty Baxter

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

# PAGE TWENTY ONE | CREATINE ON POSTMENOPAUSAL BONE HEALTH

# POLYPHENOLS ON BONE METABOLISM



#### THE EFFECTS OF POLYPHENOLS ON BONE METABOLISM IN POSTMENOPAUSAL WOMEN: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROL TRIALS.

Salvio, G ; Ciarloni, A ; Gianfelice, C ; Lacchè, F ; Sabatelli, S ; Giacchetti, G ; Balercia, G Antioxidants (Basel, Switzerland). 2023;12(10)

# INTRODUCTION:

Postmenopausal, low oestrogen levels can decrease osteoclastic activity, increase osteoclastic apoptosis, and make bones more susceptible to oxidative stress, which in turn increases osteoclastogenesis and decreases osteoblastogenesis.

Polyphenols from fruits and vegetables can have an antioxidant effect. They have been shown in vitro to enhance osteoblastic activity through effects on endothelial function and have been associated with a lower risk of fractures. This systematic review and meta-analysis aimed to evaluate the effect of polyphenol supplementation on postmenopausal bone mineral density (BMD).

# METHOD:

- 21 randomised control trials were included.
- The primary outcome assessed the effect of polyphenols on BMD.
- The secondary outcome assessed the effect of polyphenols on bone turnover markers; deoxypyridinoline, osteocalcin, alkaline phosphatase, and pyridinoline.
- 18 studies reported on lumbar BMD, 12 on femoral neck BMD, and 7 on total body BMD.
- Study durations ranged from 3-36 months

# RESULTS

- Polyphenols did not affect BMD of the lumbar spine (sMD: 0.21, 95% CI [-0.08 to 0.51], p = 0.16), femoral neck (sMD: 0.16, 95% CI [-0.23 to 0.55], p = 0.42), total hip (sMD: 0.05, 95% CI [-0.14 to 0.24], p = 0.61), or whole body (sMD: -0.12, 95% CI [-0.42 to 0.17], p = 0.41). However, a sub-analysis based on studies longer than 24 months showed that lumbar BMD was improved (sMD: 1.00, 94% CI [0.19 to 1.81], p=0.02).
- Treatment duration did not affect femoral neck BMD, total hip BMD, or whole-body BMD.
- Polyphenols did not affect deoxypyridinoline or osteocalcin levels, however they did increase bone specific alkaline phosphatase (sMD: 1.27, 95% CI [1.13 to 1.42], p < 0.0001) and decrease pyridinoline (sMD: -0.58, 95% CI [-0.77 to -0.39], p < 0.0001).</li>
- There was high heterogeneity amongst the studies and 14 showed high or unclear risk of bias.

#### PAGE TWENTY TWO | POLYPHENOLS ON BONE METABOLISM



# TAKE HOME MESSAGE:

- Postmenopausal women are susceptible to decreased BMD due to lower oestrogen levels and oxidative stress.
- Although polyphenols have an antioxidant effect, supplementation does not seem to affect bone mineral density in postmenopausal women.
- Post-menopausal women should consider other lifestyle modifications to reduce the risk of osteoporosis.

# **Q** CLINICAL PRACTICE APPLICATIONS:

- A polyphenol rich diet is not recommended to improve BMD and fracture risk in postmenopausal women.
- Other lifestyle modifications with more robust research should be recommended instead.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

• Future studies would be interesting in women in perimenopause to determine if life stage affects efficacy of polyphenols.

# **CONCLUSIONS:**

Polyphenol use is not recommended as the sole preventative therapy for postmenopausal osteoporosis.



# EXPERT REVIEWER Chloe Steele

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

# ISOFLAVONES & BONE STATUS



# COMBINED BIOAVAILABLE ISOFLAVONES AND PROBIOTICS IMPROVE BONE STATUS AND ESTROGEN METABOLISM IN POSTMENOPAUSAL OSTEOPENIC WOMEN: A RANDOMIZED CONTROLLED TRIAL.

Lambert, MNT ; Thybo, CB ; Lykkeboe, S ; Rasmussen, LM ; Frette, X ; Christensen, LP ; Jeppesen, PB The American journal of clinical nutrition. 2017;106(3):909-920

# INTRODUCTION:

This was a well-constructed randomised, parallel-design, placebo-controlled, double-blind trial over 12 months. The primary aim was to determine the effectiveness of a novel fermented red clover extract (RCE) containing isoflavones and probiotics combined with traditional calcium/magnesium/vitamin D supplementation, in comparison with traditional calcium/magnesium/vitamin D supplementation, in postmenopausal women with osteopenia.

#### **METHOD:**

- The trial followed the guidelines of the Declaration of Helsinki and received ethics approval.
- Inclusion criteria: female; >=1 year postmenopause; age 60-85; and bone T score of -1 to -2.25.
- Exclusion criteria: medical treatment for osteopenia or hormone replacement therapy within the past 3 months; diet rich in or supplementation with isoflavones; supplementation with Vitamin K; medical history of stipulated conditions.
- 85 participants were eligible and randomised to either the control or treatment group.
- Treatment group received 95 mL of RCE twice daily, containing 60 mg isoflavone aglycones and probiotics, plus 1040mg calcium, 487mg magnesium and 25µg Vitamin D daily (CMD/d). Control group received masked RCE placebo plus CMD/d.

# **RESULTS:**

- The change in BMD (p=0.043) and T score (p=0.045) showed a statistically significant greater decrease in the lumbar spine, femoral neck and hip of the control group than the RCE treatment group after 12 months of treatment.
- A statistically significant reduction in one bone resorption marker was found in the RCE group compared to control (p=0.045). All other bone biomarkers failed to reach significance.
- Plasma isoflavone concentration was elevated in the RCE treatment group compared to control (p=0.0094).
- The concentration ratios of urinary oestrogen metabolites 2-OH:16αOH was significantly increased in the RCE group compared to control (p=0.026).

# TAKE HOME MESSAGE:

- Fermented red clover extract, rich in bioavailable isoflavones with selective oestrogen receptor affinity and probiotics, combined with traditional supplementation (calcium, magnesium and vitamin D) improves bone mineral density and bone turnover compared to placebo in post menopausal women with osteopenia.
- Combining probiotics with isoflavones appears to enhance intestinal isoflavone uptake and isoflavone metabolism.

# CLINICAL PRACTICE

- Healthcare practitioners working with women in postmenopause with osteopenia could consider the addition of fermented RCE with CMD/d for improved bone mineral density and bone turnover over 12 months.
- Given the positive impact of RCE intake over 12 months on 2-OH:16αOH oestrogen metabolite ratios, healthcare practitioners could consider fermented RCE when HRT is not an available option in relation to cancer risk.
- Based on these results, Nutritional Therapists working with post-menopausal women with osteopenia can focus on dietary isoflavone intake and pre and probiotic foods to support BMD, alongside supplementary options.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- Given the length of time taken in bone remodelling cycles, a clinical trial of more than 2 years would strengthen the evidence provided by DXA scan.
- All trial participants were normotensive and healthy weight. Future studies could include women with hypertension and obesity to determine effects of RCE on bone and blood pressure/lipid markers in this group.
- Controlled feeding studies to determine the dietary effects of isoflavones and pre and probiotic foods would provide additional information in this area.
- Other fermented RCE products should be trialled to replicate findings.

# **CONCLUSIONS:**

Fermented RCE with CMD/d slowed oestrogen-deficient BMD loss and improved one marker of bone turnover in postmenopausal osteopenic women. Combining RCE with CMD/d was found to be more effective in preserving bone density than CMD/d alone in this target group. Probiotics in the fermented RCE appear to enhance intestinal isoflavone uptake, metabolism, and therapeutic effect.



# EXPERT REVIEWER Clare Grundel

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

# BONE HEALTH & FOOD RESOURCES

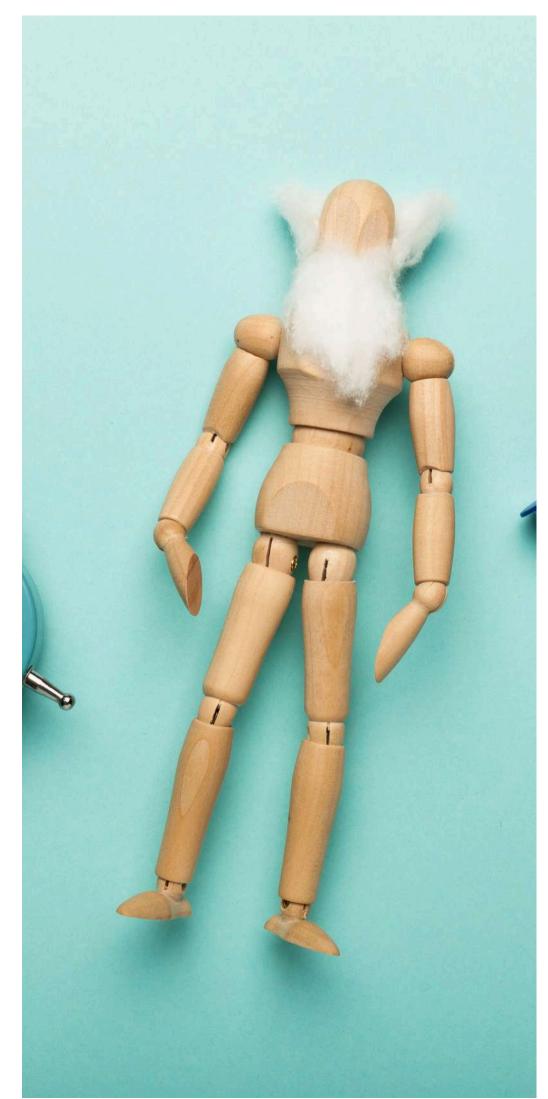
# DEDICATED RESOURCES

BANT has developed a dedicated range of resources to support practitioners to help educate on common symptoms, biological processes, and dietary and lifestyle approaches. These are suitable to share with clients in clinical consultations and group programmes.

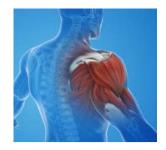


# 

**4 REVIEWS** 



# CALORIES, MUSCLE & LONGEVITY



# CALORIE RESTRICTION MODULATES THE TRANSCRIPTION OF GENES RELATED TO STRESS RESPONSE AND LONGEVITY IN HUMAN MUSCLE: THE CALERIE STUDY.

Das, JK ; Banskota, N ; Candia, J ; et al. Aging cell. 2023;22(12):e13963

# **INTRODUCTION:**

The Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE<sup>™</sup>) randomised control trial (RCT) showed that 12% caloric restriction (CR) induced muscle loss, without compromising muscle strength. This analysis of 90 individuals from that study aimed to determine the mechanisms behind this.

# **METHOD:**

- The CALERIE study was an RCT that assessed the effects of 25% CR over 2 years compared to an ad libitum control group
- This study ran alongside the CALERIE study and took skeletal muscle biopsies from a subset of 90 individuals at baseline, 12 months, and 24 months from the CR group and ad libitum control group
- This yielded 162 muscle biopsies over 2 years
- Skeletal muscle was taken from the vastus lateralis muscle and lean leg mass, and muscle strength were assessed
- In addition, RNA was extracted, and gene expression assessed.

# RESULTS

- Participants on CR lost significant amounts of weight (P=<0.001) at 12 months, with no further improvements at 2 years. Quantity or range of weight loss data was not provided
- Control participants maintained their weight over 2 years
- There were no changes in muscle strength in CR individuals despite a significant loss of muscle mass (no P value given)
- Although adjustments for change in lean leg mass resulted in less of a decline in the isokinetic muscle strength test compared to control (average power P=0.0058 and peak torque P=0.0144)
- RNA analysis showed 797 genes were overexpressed and 206 underexpressed in CR compared to control
- CR was associated with enhanced anti-ageing mechanisms with genes such as those involved in androgen receptor signalling, autophagy, circadian rhythms, DNA repair, FOXO mediated transcription, and mitochondrial biogenesis all upregulated and inflammatory genes downregulated
- These changes were responsible for the positive effect on muscle quality in individuals in the CR group.



# TAKE HOME MESSAGE:

- CR can aid weight loss and sustain losses long-term. Some lean muscle loss may also be seen, but this does not mean that muscle function has been compromised
- CR can trigger molecular and cellular mechanisms involved in skeletal muscle, sustaining functionality during a weight loss programme.

# **Q** CLINICAL PRACTICE APPLICATIONS:

- Healthcare professionals may consider a 12% CR diet for individuals who would like to lose weight and maintain its loss long-term, without compromising muscle function
- Although lean muscle mass may be lost, muscle function should not be affected, but should be monitored to ensure functionality.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

• The possible effects of combining CR with muscle strength exercises should be considered for future research to determine if muscle mass loss is prevented and whether this impacts further fat loss.

#### **CONCLUSIONS:**

It was concluded that 2 years of CR preserved muscle function despite muscle mass loss, through up-regulation of the genes involved in muscle quality and anti-ageing.



# EXPERT REVIEWER Chloe Steele

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

# ALTERNATE DAY FASTING & AGEING



# ALTERNATE DAY FASTING IMPROVES PHYSIOLOGICAL AND MOLECULAR MARKERS OF AGING IN HEALTHY, NON-OBESE HUMANS.

Stekovic, S ; Hofer, SJ ; Tripolt, N ; et al. Cell metabolism. 2019;30(3):462-476.e6

# INTRODUCTION:

Animal models have consistently demonstrated the healthspan and lifespan benefits of caloric restriction. However, chronic caloric restriction in humans has proven difficult to maintain.

Intermittent fasting may serve as a more manageable alternative to continuous caloric restriction. This randomised controlled trial and cross sectional analysis aimed to investigate the effects of alternate day fasting (ADF) on heart rate, blood pressure, cholesterol levels, CVD risk, body composition, and the metabolome and proteome of healthy, non-overweight adults (cohort median age between 48 and 52 years).

# METHOD:

Prior to the enrollment of the study a cross sectional analysis was conducted on healthy adults engaged in long term (>6 months) alternate day fasting (n=30) and a control group (n=60).

The 60 participants from the cross sectional analysis control group were then randomised to either a 4 week ADF group or a control group. In both the >6 months and 4 weeks of ADF groups, participants were instructed to eat every secondday ad libitum, but to completely exclude solid and liquid foods and caloric beverages on fasting days.

# **Results:**

Following the 4 week intervention the alternate day fasting group demonstrated:

- Reduced caloric intake from baseline vs. the control group (-37.40% vs. -8.22%, p=0.0012).
- Greater reductions in body weight (-3.5kg vs -0.2kg, p<0.0001), BMI (-1.23kg/m2 vs -0.02kg/m2, p<0.0001) and improvements in their fat to lean mass ratio (-6.3% ± 5.0 percentage points, p value < 0.0001).</li>
- Reduced systolic (-4.5mmHg, p=0.006) and diastolic (-2.5mmHg, p=0.03) blood pressure, heart rate (-4.5 b/min, p=0.0019), arterial (-3mmHg, p=0.0087) and pulse pressure (-2.5mmHg, p=0.0088) as well as pulse wave velocity (-1.538%, p=0.0362). Pulse wave velocity measures the rate at which pressure moves down the vessel wall and is a measure of arterial stiffness.
- Reduced circulating triiodothyronine (p<0.001) from baseline values.

# TAKE HOME MESSAGE:

- Short duration (<4 weeks) alternate day fasting may be an effective way to implement caloric restriction, improve body composition and reduce cardiovascular disease risk in healthy non-overweight adults.
- >6 months alternate fasting does not appear to be associated with reduced bone mass, bone mineral density of the lumbar spine region, white blood cell counts, ferritin and transferrin when compared to healthy controls.
- Both short term and long term alternate day fasting may reduce triiodothyronine in healthy adults. Low levels of fT3 without thyroid gland dysfunction has been associated with longevity in humans.
- Alternate day fasting should be performed alongside a trained clinician to reduce the risk of adverse effects due to critical medical conditions.

# $\mathbf{Q}$ clinical practice applications:

- The cross sectional analysis did not identify any differences in the long-term (>6 months) alternate day fasting group and control group in bone mass, bone mineral density of the lumbar spine region, white blood cell counts, ferritin and transferrin when compared to healthy controls. RBC counts and iron metabolism markers in the blood plasma (hematocrit, haemoglobin, iron, and transferrin saturation), were lower in the >6 months of ADF group but stayed within the reference range.
- The randomised controlled trial demonstrated that alternate day fasting may be an effective intervention to reduce caloric intake, improve body composition and reduce cardiovascular disease risk in healthy non-overweight adults within 4 weeks.
- Compliance rate was high with only 1 drop out in the alternate day fasting group of the randomised controlled trial.
- Both the 4 week intervention and long-term (>6 month) analysis identified a reduction in triiodothyronine amongst the ADF groups. Low levels of triiodothyronine in absence of thyroid gland dysfunction has been associated with longevity in humans.

# CONSIDERATIONS FOR FUTURE RESEARCH:

- Future larger studies in non-healthy and/or overweight/obese populations would be useful to determine safety and efficacy of alternate day fasting within that population group.
- Further studies comparing alternate day fasting with continuous caloric restriction would be useful to identify which intervention is most beneficial for body composition and cardioprotection.
- Subgroup analysis of diet composition and diet quality may help to identify the most appropriate/inappropriate diet to compliment alternate day fasting.
- Longer duration randomised controlled trials are needed to identify any health risks or deficiencies which may develop with long term caloric restriction and alternate day fasting.



# EXPERT REVIEWER Daniel Quinones

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

# EDUCATION ON FRAILTY MARKERS



# EFFECTS OF AN EDUCATIONAL INTERVENTION ON FRAILTY STATUS, PHYSICAL FUNCTION, PHYSICAL ACTIVITY, SLEEP PATTERNS, AND NUTRITIONAL STATUS OF OLDER ADULTS WITH FRAILTY OR PRE-FRAILTY: THE FRAGSALUD STUDY.

Casals, C ; Ávila-Cabeza-de-Vaca, L ; González-Mariscal, A ; Marín-Galindo, A ; Costilla, M ; Ponce-Gonzalez, JG ; Vázquez-Sánchez, MÁ ; Corral-Pérez, J Frontiers in public health. 2023;11:1267666

# INTRODUCTION:

- Frailty and pre-frailty increase the risk of premature mortality but are reversible
- The aim of this study was to evaluate the effects of a health education programme on frailty status in frail or pre-frail older persons.

# METHOD:

- Randomised controlled trial
- Participants: 166 community-dwelling individuals aged 65 years or over with frailty or pre-frailty living in Spain were enrolled, 163 completed the study (80 in intervention and 83 in control group)
- Four weekly group sessions which included guidelines for physical activity, nutrition and cognitive training as well as the promotion of psychological and social wellbeing, and 6 follow-up calls over 6 months versus control.

# **RESULTS:**

Baseline demographics: The educational group consisted of more women (p=0.001), had a younger average age (p=0.019), lower height (p=0.001) and a higher average education level (p=0.013) compared to the control group.

#### Effects on intervention group:

- Reductions in frailty score (p<0.05 vs baseline and change vs change in control group), with 30% of participants in the intervention group no longer being classified as frail or pre-frail in contrast to none in the control group
- Reductions in fatigue and exhaustion score (p<0.05 vs baseline and change vs change in control group)
- Increase in gait speed and improvements in various physical function tests (all p<0.05 vs baseline and change vs change in control group)
- Improvements in mini nutritional assessment (p<0.001 vs baseline and change vs change in control group)
- Improvement in sleep behaviour demonstrated by an increase in awakenings in the control group (p<0.05 vs baseline and change vs change in intervention group) whilst this parameter did not change in the intervention group.

No effects (vs control) on:

- Anthropometric parameters/unintended weight loss
- Other sleep parameters
- Physical activity expenditure and physical activity score
- Hand grip strength.



# TAKE HOME MESSAGE:

To improve frailty and physical functioning, a comprehensive programme may be effective, which includes:

- Nutrition
- Physical exercise
- Cognitive training
- Promotion of social and psychological wellbeing.

# **Q** CLINICAL PRACTICE APPLICATIONS:

- A comprehensive programme, encompassing not only nutrition, but also exercise, cognitive training and a focus on social and psychological wellbeing may be most effective in improving frailty and physical functioning
- Nutrition intervention, alongside other lifestyle interventions, may have benefits for nutritional status in older adults, even if this is not reflected in a change in anthropometric parameters, such as weight.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

• Studies with longer-term follow-up would help evaluate whether/for how long the benefits are sustained.

# **CONCLUSIONS:**

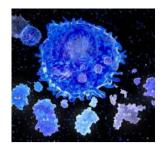
This affordable and simple health education programme is effective in reducing frailty in elderly and may contribute to healthy ageing.



# EXPERT REVIEWER Karin Elgar

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

# WHEY AND SOY ON CYTOKINES



# EFFECTS OF WHEY AND SOY PROTEIN SUPPLEMENTATION ON INFLAMMATORY CYTOKINES IN OLDER ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Prokopidis, K ; Mazidi, M ; Sankaranarayanan, R ; Tajik, B ; McArdle, A ; Isanejad, M The British journal of nutrition. 2023;129(5):759-770

# **INTRODUCTION:**

- A decline in muscle mass and physical capacity, known as sarcopenia, may start in the fourth decade with accumulation of adiposity, resulting in elevated circulating proinflammatory cytokines.
- Systematic and local elevation of oxidative stress and reactive oxygen species accumulation may accelerate agerelated muscle wasting, however may be mitigated with antioxidant nutrients.
- This SR and MA evaluated whey and soy proteins effects on interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF- $\alpha$ ) and C-reactive protein (CRP) in older adults.

# **METHOD:**

SR followed PRISMA guidelines, was registered on PROSPERO and included 31 RCT studies published in English between 2004-21. Intervention group received soy/whey supplements and comparator group received a placebo; circulating levels of CRP, IL-6 and/or TNF- $\alpha$  were assessed. MA used random-effects to calculate the pooled effects. Overall quality of evidence was rated as moderate.

#### **RESULTS:**

#### Whey protein:

- IL-6 levels were reduced significantly (Number of studies (k) = 12, Mean Difference (MD): -0.79, 95 %
   Confidence Interval (CI): -1.15, -0.42, p< 0.01), however, high heterogeneity was observed (I2 = 96 %).</li>
- Treatment duration  $\leq 8$  weeks showed a significant reduction in serum CRP (k = 4, MD: -0.30, 95 % CI: -0.39, -0.21, I2 = 0 %) compared with > 8 weeks (k = 6, MD: 0.13, 95 % CI: -0.13, 0.40, I2 = 9 %), whereas TNF- $\alpha$  and IL-6 remained unaltered.
- Individuals with sarcopenia and pre-frailty displayed a significant reduction of IL-6 (k = 3, MD: -0.98, 95 % CI: -1.56, -0.39, I2 = 0 %) but no benefits were observed for CRP or TNF.

#### Soy protein:

- There was a significant reduction in TNF- $\alpha$  (k = 6, MD: -0.16, 95 % CI: -0.26, p<0.05).
- The addition of isoflavones demonstrated a significant decrease in TNF-α (k = 5, MD: -0.20, 95 % Cl: -0.31, -0.08, I2 = 34 %) but an increase in CRP (k = 7, MD: 0.53, 95 % Cl: 0.12, 0.94), however high heterogeneity was observed in the latter (I2 = 91 %).

# TAKE HOME MESSAGE:

- Nutritional strategies such as whey and soy protein supplementation may be regarded as safe and effective to attenuate adverse changes in muscle mass with ageing, however need to be considered alongside individual dietary intake and health status.
- Consider optimising protein intake and quality of protein through diet as an alternative or first line strategy.

# CLINICAL PRACTICE

- Consider whey and/or soy protein supplementation in older adults particularly those reported with pre-frailty and sarcopenia as an effective and safe strategy to attenuate low-grade inflammation and associated risks.
- Soy isoflavones may have additional antioxidant benefits for older adults although further research is needed to confirm this due to high heterogeneity found.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

Future research could:

- Evaluate other factors which influence the inflammatory profile such as nutrient density, vitamins and minerals supplementation and exercise.
- Include those with co-morbidities and healthy populations with placebo comparator groups.
- Evaluate dose and type of soy isoflavones on circulating inflammatory markers and the effect of combined whey and soy protein.

#### **CONCLUSIONS:**

 The study found a significant reduction in IL-6 following whey protein with effects augmented in those with frailty and sarcopenia and a significant reduction in TNF-α following soy protein with effects augmented by additional soy isoflavones, possibly due to antioxidant effects.

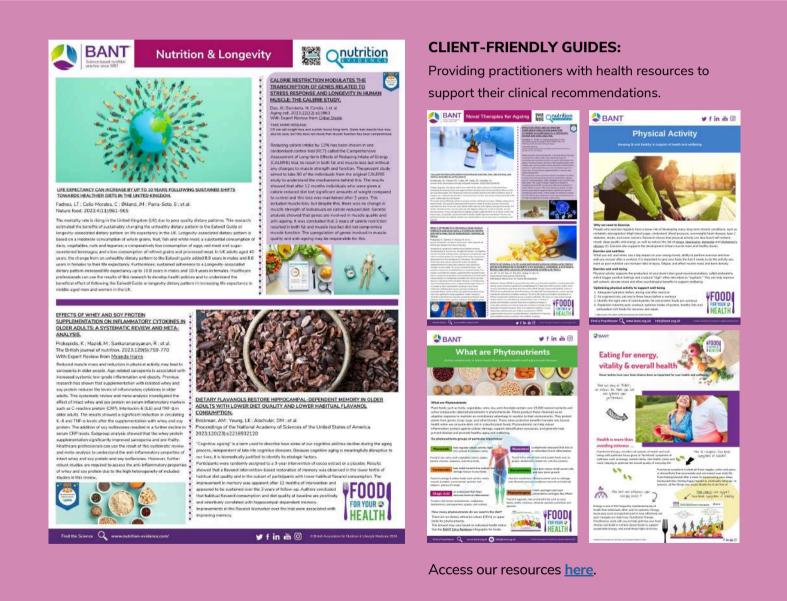
# **EXPERT REVIEWER** Miranda Harris

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

# LONGEVITY & BLUE ZONES RESOURCES

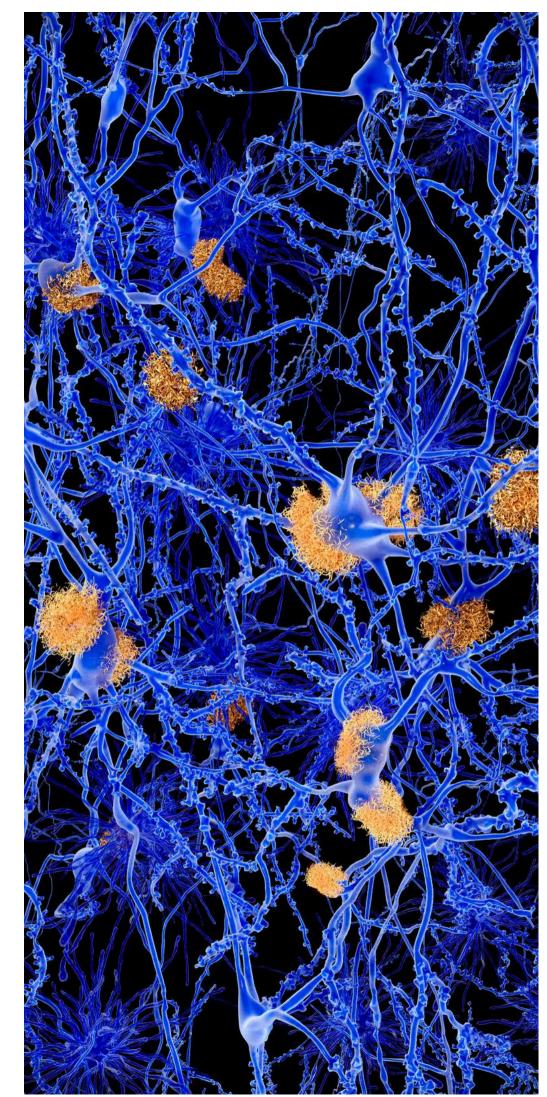
# DEDICATED LONGEVITY RESOURCES

BANT has developed a dedicated range of resources to support practitioners to help educate on common symptoms, and dietary and lifestyle approaches. These are suitable to share with clients in clinical consultations and group programmes.



# D N N N N N H A M A M M A M M

**5 REVIEWS** 



# MULTIDOMAIN INTERVENTION



### A MULTIDOMAIN INTERVENTION AGAINST COGNITIVE DECLINE IN AN AT-RISK-POPULATION IN GERMANY: RESULTS FROM THE CLUSTER-RANDOMIZED AGEWELL.DE TRIAL.

Zülke, AE ; Pabst, A ; Luppa, M ; et al. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2024;20(1):615-628

### INTRODUCTION:

The aim of this study was to evaluate the effectiveness of the AgeWell.de programme which targets modifiable risk factors for dementia.

### METHOD:

- Cluster-randomised, controlled trial (clustered by participating general practitioners).
- Intervention: nutritional counselling (based on the guidelines by the German Society for Nutrition), enhancement of physical and social activity, cognitive training, and the management of cardiovascular risk factors (overweight, smoking). Baseline individual face-to-face session with study nurse, followed by contact with the nurse after 2, 4 and 8 months, second face-to-face session with the nurse at 12 months and further contacts at 16 and 20 months. Endpoint assessments at 24 months.
- Controls: standard care.
- Sample size: 1030 adults aged 60-77 at increased risk of dementia, of which 819 completed the study and were included in the analysis.
- Primary outcome: global cognitive performance (GCP)
- Secondary outcomes: mortality, nursing home placement, activities of daily living (ADL), instrumental activities of daily living (IADL), quality of life (QOL), health-related (QOL), depressive symptoms, and social inclusion.

### **RESULTS:**

- No significant difference in GCP, p=0.874. No difference in ADL (p=0.374), IADL (p=0.746), QOL (p=0.964), depressive symptoms (p=0.090) and social inclusion (p=0.495).
- Improvement in health-related QOL (AME = 0.198, 95% CI: 0.069, 0.328, p=0.003).
- Results for mortality and nursing home placement are not reported.
- Part of the study took place during the COVID-19 pandemic. More participants (9%) than controls (3.7%) reported perceived COVID-19-related restrictions with regards to nutrition (p=0.004). No such difference was observed for perceived restrictions regarding physical activity (p=0.328), cognitive activity (p=0.262) or social activity (p=0.192).



### TAKE HOME MESSAGE:

Nutrition counselling based on the guidelines of the German Society for Nutrition, in association with other lifestyle counselling and optimisation of medication, does not improve GCP.

### **Q** CLINICAL PRACTICE APPLICATIONS:

• Nutrition counselling based on the guidelines of the German Society for Nutrition, in association with other lifestyle counselling and optimisation of medication, does not improve GCP.

### **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- Studies using more intensive and individualised interventions may evaluate whether such strategies are more beneficial for improving GCP.
- Studies of specific subgroups, e.g. based on lifestyle or medical risk factors, may help find more specific populations and interventions to help improve GCP.

### **CONCLUSIONS:**

The authors concluded that the multidomain intervention had no beneficial effects on GCP and that higher-intensity interventions and more ambitious goals may be needed.



# EXPERT REVIEWER Karin Elgar

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

# MED. DIET & ALZHEIMER'S



# MEDITERRANEAN DIET AND STRUCTURAL NEUROIMAGING BIOMARKERS OF ALZHEIMER'S AND CEREBROVASCULAR DISEASE: A SYSTEMATIC REVIEW.

Gregory, S ; Pullen, H ; Ritchie, CW ; Shannon, OM ; Stevenson, EJ ; Muniz-Terrera, G Experimental gerontology. 2023;172:112065

### **INTRODUCTION:**

Changes in hippocampal volume (HV) and white matter intensity volume (WMIV) have been identified as structural neuroimaging biomarkers of neurodegenerative disease such as Alzheimer's Disease (AD) and Cerebrovascular disease (CVD) respectively. Evidence has shown adherence to the Mediterranean Diet (MedDiet) has been associated with reduced risk for strokes. This review evaluated the MedDiet in relation to HV and WMIV.

### **METHOD:**

The review followed PRISMA guidelines and was registered on PROSPERO. Literature searching resulted in seven studies published between 2012 and 2022, which met the inclusion criteria. Six studies analysed cross-sectional data and one analysed longitudinal data. The NIH Quality Assessment Tool for Observational and Cross-Sectional Studies was used to assess risk of bias.

Overall, the studies were rated as low-risk of bias with details of the research question, participant group exposure and outcome variables included. Due to moderate to high heterogeneity in some studies, a meta-analysis was deemed unsuitable and narrative synthesis was conducted to present the results.

### **RESULTS:**

Mean participant age ranged from 53.19 to 80.3 years and volunteers were healthy or had subjective cognitive decline and a few participants had dementia (n=46).

### **Hippocampal Volume:**

Four studies included 20,077 participants and found no significant associations between MedDiet adherence and hippocampal volume. All four studies were cross-sectional from larger cohort studies. To establish causative relationships longitudinal and RCT trials are required.

### White Matter Hyperintensity Volumes:

Four studies included 1938 participants. Two studies found a significant negative association between MedDiet and WMHV, demonstrating higher Mediterranean Scores were associated with lower level of WHMV. The other two studies found no significant associations.

### TAKE HOME MESSAGE:

Due to inconclusive results on the associations between MedDiet adherence and AD and cerebrovascular related structural neuroimaging findings, specific recommendations for the MedDiet cannot be made on the basis of this study until further research has been completed.

### **Q** CLINICAL PRACTICE APPLICATIONS:

There were no significant associations between MedDiet adherence and HV, which was surprising given the evidence stating adherence to the MedDiet is associated with a lower incidence of dementia and stroke. However all four studies were cross-sectional studies and in order to detect causal associations, longitudinal and RCT's are needed. Two studies did show a significant association between higher MedDiet adherence and lower WMHV, whereas two studies reported no significant associations.

Caution needs to be taken when recommending the MedDiet specifically for a reduction in HV and WMHV until further research has been undertaken.

# **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger cohorts and participants from the Mediterranean region where lifelong adherence to the MedDiet is more likely.
- Looking at other risk factors to include obesity, lack of activity, poor sleep quality and stress.
- Evaluating different socio-economic status, which has been shown to impact dietary behaviour.
- Alternative imaging outcomes such as cortical thinning, PET amyloid and tau.
- Gold standard for methodology in particular dietary analysis and scanning and outcome derivation.

### **CONCLUSIONS:**

Overall, these results are inconclusive on the associations between the MedDiet and HV and WMHV, and identify a gap in the knowledge, therefore further research such as RCT's remains a priority to further understand the impact diet may have on neuroimaging markers of AD and CVD.

# EXPERT REVIEWER Miranda Harris

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

# 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

### **INTRODUCTION:**

- 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.

### 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

- 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.

### CONCLUSION:

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



# EXPERT REVIEWER Kirsty Baxter

CONFLICTS OF INTEREST: None EVIDENCE CATEGORY: C: Non-randomized trials, observational studies, narrative reviews

# POLYPHENOLS & FUNCTION



### POLYPHENOL SUPPLEMENTATION AND EXECUTIVE FUNCTIONING IN OVERWEIGHT AND OBESE ADULTS AT RISK OF COGNITIVE IMPAIRMENT: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Farag, S ; Tsang, C ; Murphy, PN PloS one. 2023;18(5):e0286143

### **INTRODUCTION:**

A systematic review and meta-analysis were undertaken to investigate the impact of polyphenol supplementation on executive functions (cognitive functions which constitute part of the working memory and decision-making processes) among overweight and/or obese populations.

### **METHOD:**

A comprehensive literature search was conducted using four electronic databases: PubMed/Medline, PsycInfo, Scopus and the Cochrane Trials Library. Inclusion criteria encompassed primary research studies which investigated the impact of polyphenols versus placebo on executive function in overweight or obese adults.

The review comprised a total of 23 randomised controlled trials (RCTs), incorporating a participant pool of N = 1,976 individuals. The mean ages of participants in all 23 studies receiving polyphenol supplementation were 62.92 years (SD = 8.06 years) and the mean BMIs ranged from 25.5 kg/m2 to 33.7 kg/m2.

Various dietary polyphenols were investigated in the studies, with the main groups being isoflavones, flavonoids, resveratrol, phenolic acid, curcumin, walnuts and blueberry powder.

- The JADAD scale was employed to assess the methodological quality of the incorporated studies
- Hedges g, accompanied by 95% confidence intervals (CI) for endpoints, was computed utilising a random effects model whenever applicable
- Various statistical methods were considered for potential application in evaluating publication bias
- Sensitivity analysis was conducted to assess the robustness of the obtained results.

### **RESULTS:**

- Meta analysis of the 23 primary studies produced a non-significant effect of polyphenol supplementation on executive function (g = 0.076, Cl = -0.018 to 0.170)
- A double-blind, randomised, placebo-controlled parallel study reported significant benefits in 60 participants (mean age 67 years) taking 80mg of curcumin over placebo for digital vigilance and serial subtraction tasks (p=0.041)
- A double-blind, randomised, placebo-controlled parallel intervention trial showed significant benefits in 79
  patients (mean age of 61 years) taking 150mg of resveratrol for visuospatial working memory double span
  and trail making test (p= 0.012).

### TAKE HOME MESSAGE:

- Overweight and obesity have increasing evidence that indicates a link to compromised executive functions such as memory and decision-making processes and cognitive impairment
- This meta-analysis revealed a non-significant effect of polyphenol supplementation on executive functions among overweight and/or obese populations with a susceptibility to cognitive impairment.

### **CLINICAL PRACTICE APPLICATIONS:**

- Research has documented the association between compromised executive functions and obesity/overweight, emphasising neuroinflammation and oxidative stress as potential mechanisms
- A plausible intervention involves the utilisation of polyphenols, known for their antioxidant and anti-inflammatory properties
- This systematic review and meta-analysis revealed a non-significant effect of polyphenol supplementation on executive functions
- A potential beneficial impact for 80mg of curcumin and 150mg of resveratrol was revealed in younger populations (mean ages of 67 and 61 years).

### **?** CONSIDERATIONS FOR FUTURE RESEARCH:

- A potential beneficial impact of 80mg of curcumin and 150mg of resveratrol supplementation was revealed in a younger population (mean ages of 67 and 61 years), highlighting the necessity for in-depth exploration in subsequent studies
- The diversity in tasks employed for assessing executive functions and the comprehensive reporting of the phenolic composition of supplements had limitations that warrant consideration in future research
- The exact constituent and dose of supplementation needs to be described as this is necessary for the identification of the potential beneficial compounds for cognitive health and to support clinical practice.

### CONCLUSION:

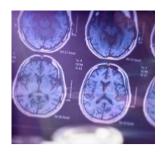
This meta-analysis revealed a non-significant effect of polyphenol supplementation on executive functions among overweight and/or obese populations.



# EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None
• EVIDENCE CATEGORY: B: Systematic reviews including RCTs of limited number

# MED. & WESTERN DIETS ON AD



### MEDITERRANEAN AND WESTERN DIET EFFECTS ON ALZHEIMER'S DISEASE BIOMARKERS, CEREBRAL PERFUSION, AND COGNITION IN MID-LIFE: A RANDOMIZED TRIAL.

Hoscheidt, S ; Sanderlin, AH ; Baker, LD ; et al. Alzheimer's & dementia : the journal of the Alzheimer's Association. 2022;18(3):457-468

### INTRODUCTION:

Epidemiological studies have associated a Western diet (West-diet) with an increased risk of Alzheimer's disease (AD) and other dementias. This study aimed to examine the impact of a Mediterranean-diet (Med-diet) versus a West-diet on AD pathology, cognition, vascular function and metabolic markers in middle aged adults with normal cognitive (NC) function compared to adults with mild cognitive impairment (MCI).

### **METHOD:**

N=41 NC adult females completed the Med-diet and N=43 adult females with MCI completed the West-diet arm of this study. The average age of the participants was 56y. All participants received isocaloric diets which were either high or low in saturated fat, sodium and glycaemic index (GI) for 4 weeks. Statistical analyses were conducted per dietary arm as well as per cognitive function (NC vs MCI).

### **Results:**

- NC Participants were found to have decreased cerebro-spinal fluid (CSF) biomarkers (p=.026) following the Med-diet and increased levels following the West-diet. Whereas, cerebral perfusion increased following the med-diet and decreased after the West-diet (p=.003). These results indicate a reduced AD risk. The MCI group showed no changes to CSF or cerebral perfusion for either dietary group.
- Cognition tended to improve for the NC Med-diet and remain the same for the NC West-diet group. No changes were found for the MCI groups.
- Total cholesterol levels were increased following the West-diet and decreased following the Med-diet for both groups (p=0.0001).
- Glucose and HbA1C were unchanged in the NC group following the Med-diet, increased for the West-diet (p=.049) and decreased for the MCI group (p=<.001). whereas fasting insulin was increased in the NC Med-diet group and decreased in the MCI Med-diet (p=.0.12) and West diet groups.



### TAKE HOME MESSAGE:

A Med-diet may be beneficial for supporting brain health, cognitive function. metabolic health and reduce the risk of an AD pathology in middle-aged adults with normal cognitive function.

### $\mathbf{Q}$ clinical practice applications:

A Med-diet may be beneficial for supporting brain health, cognitive function, metabolic health and reducing the risk of an AD pathology in middle-aged adults with normal cognitive function but not for those with MCI.

### ? CONSIDERATIONS FOR FUTURE RESEARCH:

The authors acknowledged several limitations to this study.

These results require further confirmation through longer and larger studies, particularly the surprising finding that a West-diet may confer beneficial effects on metabolic and brain health for middleaged adults with MCI.

### **CONCLUSION:**

The results of this study found that diet may modulate AD pathology, cognitive and metabolic function in middle-aged adults. A West-like diet may increase risk of AD through its effects on impairing cognitive function, reducing cerebral infusion and negatively influencing metabolic health in NC adults. Conversely, A Med-diet may promote brain function and metabolic health. However, surprisingly, in this study the results were reversed for MCI middle aged adults, the results showed improvement in metabolic and cerebrospinal fluid biomarkers for the West-diet. These results require further confirmation.



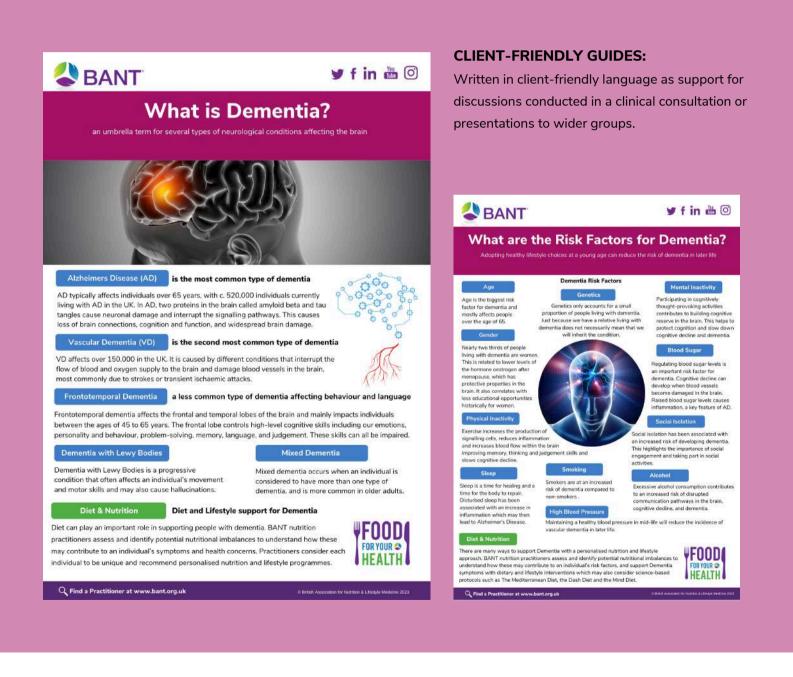
### EXPERT REVIEWER Gail Brady

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

# SYMPTOMATOLOGY FACT SHEETS

### CLINICAL FACT SHEETS

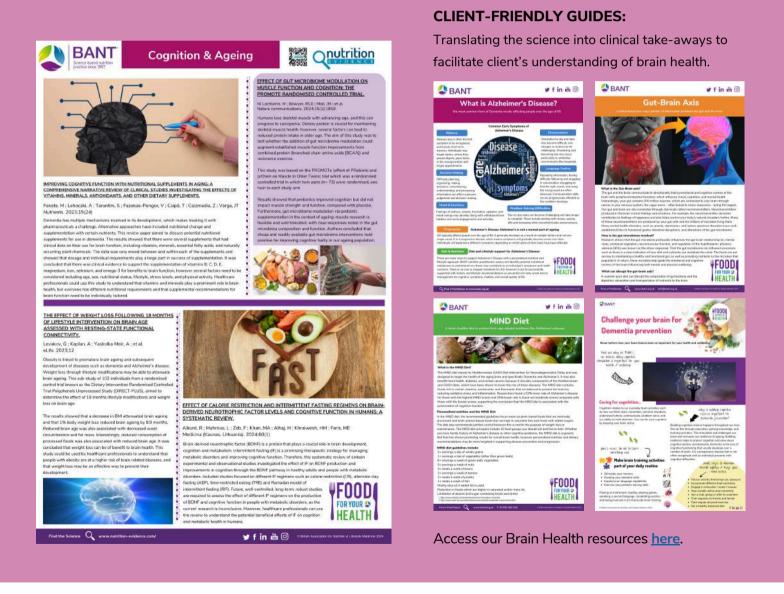
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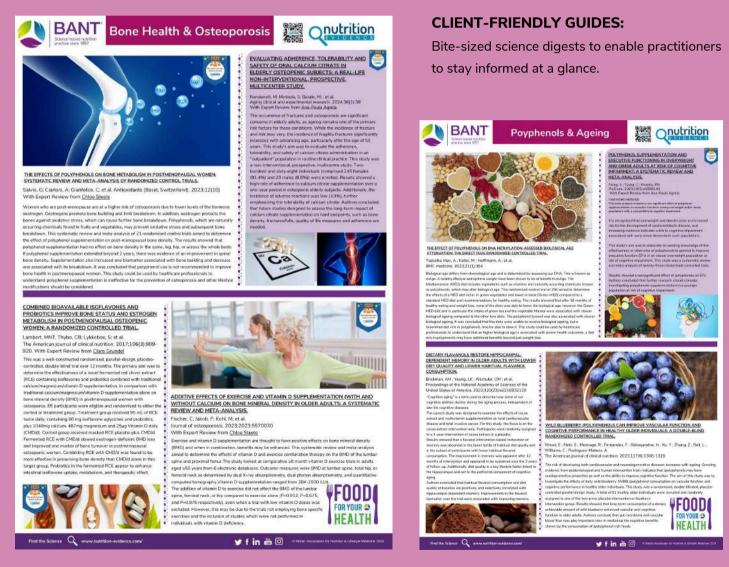


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