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# nutrition EVIDENCE

## NED EXPERT REVIEWS

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**ISSUE 2: MALE HEALTH, STRESS & ADHD**  
**NOVEMBER 2023**





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## Nutritional Therapy Practitioners & Lifestyle Medicine

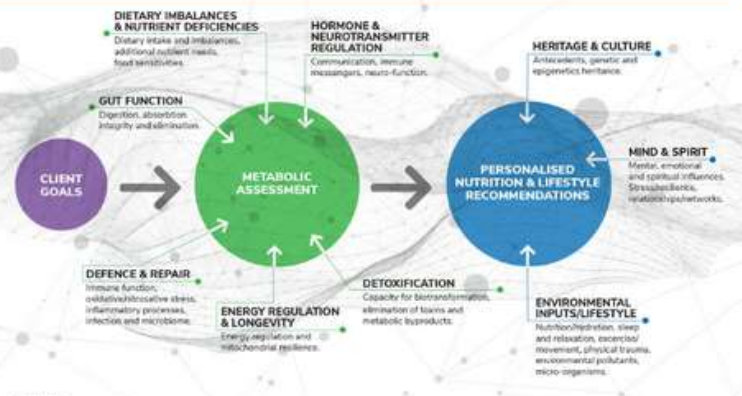
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The British Association for Nutrition and Lifestyle Medicine (BANT) is the professional body for over 3,500 BANT nutrition practitioners. Its primary function is to assist its members in attaining the highest standards of integrity, knowledge, competence, and professional practice, in both clinical and non-clinical settings.

# WELCOME



## WELCOME BACK TO BANT'S NED EXPERT REVIEW JOURNAL

We were thrilled with the response to our first Edition – which you can access [here](#) in case you missed it – and are delighted to bring Edition 2 to your attention, with a new set of expert reviews covering Stress and Adrenals, ADHD and Male Health.

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The [British Association of Nutrition and Lifestyle Medicine \(BANT\)](#) 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](#).

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So get the kettle on and curl up for a decent read. You will not be disappointed!

**Clare Grundel, Managing Editor**

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# WHAT'S NEW IN NED



Nutrition Evidence Database (NED) is growing fast and becoming the go-to platform for nutrition practitioners seeking the latest nutrition science.

The NED Editorial team are continuously exploring new ways to diffuse the science, making it easier for nutrition practitioners to apply the science in clinical practice.

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**2022 Circulating levels of maternal vitamin D and risk of ADHD in offspring**

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## Editor-in-Chief

Prof. Justin Roberts, Ph.D, C.Sci, SFHEA, mBANT



Dr Roberts is a Professor of Nutritional Physiology applied to exercise and functional health within the Cambridge Centre for Sport and Exercise Sciences, Anglia Ruskin University. He is a BANT Registered Nutritionist, and Editor-in-Chief for the Nutrition Evidence Database (the only scientific database which specialises in nutrition and lifestyle medicine to support an evidence-based approach to practitioner clinical-decision making). He has published over 65 peer-reviewed, scientific articles and book chapters, and is a reviewer for numerous academic journals including: European Journal of Clinical Nutrition; International Journal of Sport Nutrition and Exercise Metabolism; Nutrients; Medicine and Science in Sport and Exercise; Frontiers in Nutrition; and the Journal of the International Society of Sports Nutrition. His research focuses on nutritional strategies to promote metabolic flexibility and adaptive recovery in relation to exercise, including polyphenol and protein-targeted approaches, along with interests in pre-probiotic and food-based strategies to support gastrointestinal function.



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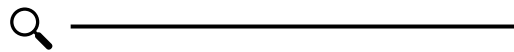
Science and Education Manager, BANT

# 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 alphabetical order from top left to right, bottom left to right)

Ana-Paula Agrela, MSc, BSc (Hons)

Gail Brady, MSc, DiplON, AFMCP, mBANT, rCNHC

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Jessica Rigutto, MPharm, MPH, Dr.sc., ETH Zurich, DiplON,

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Kirsty Baxter, MSc, DiplON, mBANT

Michelle Barrow, BSc (Hons), MSc, QTLS, DProf, fBANT

Nicky Ester, MSc, RNutr



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## Nutrition Evidence Alert – October 2023 – Sleep & Insomnia

Sleep, Insomnia and Circadian Rhythms From our Experts Dose-response relationship between weight loss and improvements in obstructive sleep apnea severity after a diet/lifestyle interventions:...



## Nutrition Evidence Alert – September 2023 – Neurodiversity & ADHD

Neurodiversity & ADHD – Your Monthly Alert From our Experts Circulating levels of maternal vitamin D and risk of ADHD in offspring: results from the Vitamin D Antenatal Asthma...

## Bionutri AUTUMN WEBINARS

Join the hundreds of healthcare professionals that visit our free weekly 11-12 Wednesday webinar. A wide range of topics covered plus interactive Q and A. Extensive back catalogue of recorded CPD webinars available. In November **Bionutri** will be focusing on the respiratory system.

### Respiratory Health Part 1 Wednesday 8<sup>th</sup> November 11am-12noon Sue McGarrigle ND

With winter approaching and confined spaces with people sneezing and coughing, damp and cold, lack of sunlight, combine that with stress of some kind, poor sleep, an underlying health problem or some kind of infection or inflammation and our body's defence mechanisms are taxed to the max. This first webinar will be looking at the nutrition needed for supporting upper and lower respiratory health conditions which tend to manifest in the winter months.

### Respiratory Health Part 2 Wednesday 15<sup>th</sup> November 11am-12noon Rosie Rayner ND

Following on from part 1, we will dive deep into other breathing issues that we often see in clinic and discover how immunity has a big influence on lung health. Join us and learn how to best support your clients nutritionally, with their chronic or seasonal breathing difficulties.

### Herbs for Respiratory Health Wednesday 22<sup>nd</sup> November 11am-12noon Edward Joy

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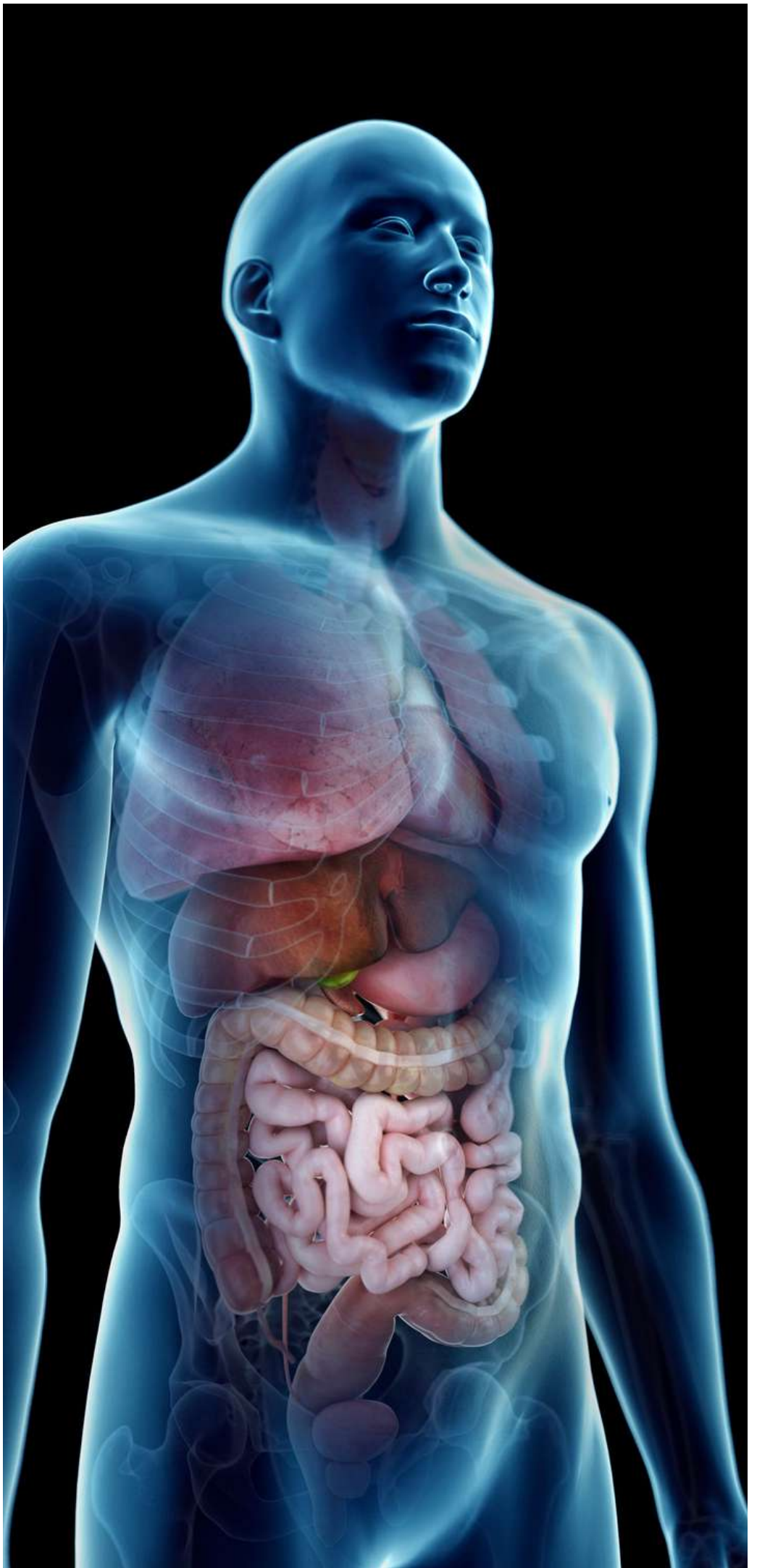
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# MALE HEALTH

4 REVIEWS



# DIET & MALE SEMEN QUALITY



## THE EFFECT OF HEALTHY DIETARY PATTERNS ON MALE SEMEN QUALITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Cao, LL ; Chang, JJ ; Wang, SJ ; Li, YH ; Yuan, MY ; Wang, GF ; Su, PY  
Asian journal of andrology. 2022;24(5):549-557

### INTRODUCTION:

This study aimed to determine the effects of healthy dietary patterns on semen quality.

### METHOD:

- This meta-analysis was performed following PRISMA guidelines and included 6 cross-sectional studies with 1244 participants
- The included cross-sectional studies examined the influence of the Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and prudent diet patterns on semen quality parameters.
- In 4 of the studies participants were divided into groups based on their scores for the Mediterranean diet from low to high adherence.
- 2 studies examined the DASH diet and the prudent diet and used food frequency questionnaires to compare high consumption with low consumption of healthy dietary patterns.
- The PICOS (Participants, Intervention, Comparison, Outcomes, and Study design) criteria that were used to structure the research question.
- 11 Checklists were used to assess the quality of included studies

### RESULTS:

By comparing high consumption with low consumption of healthy dietary patterns, the results showed:

- significantly higher sperm concentrations (mean difference [MD] =  $6.88 \times 10^6 \text{ ml}^{-1}$ , 95% confidence interval [CI]:  $1.26 \times 10^6 \text{ ml}^{-1}$ – $12.49 \times 10^6 \text{ ml}^{-1}$ ;  $P < 0.05$ )
- significant increase in total sperm count (MD =  $16.70 \times 10^6$ , 95% CI:  $2.37 \times 10^6$ – $31.03 \times 10^6$ ;  $P < 0.05$ )
- significant increase in progressive sperm motility (MD = 5.85%, 95% CI: 2.59%–9.12%;  $P < 0.01$ ) but there was no significant correlation between healthy dietary patterns and total sperm motility (MD: 6.86%, 95% CI: –0.25%–13.96%;  $P > 0.05$ ).
- there was no significant association between a healthy dietary pattern and normal sperm morphology (MD: 0.28%, 95% CI: –0.33%–0.90%;  $P > 0.05$ )
- there was no significant association between a healthy dietary pattern and semen volume (MD: 0.04 ml, 95% CI: –0.20 ml–0.28 ml;  $P > 0.05$ ).

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- This Systematic Review and Meta Analysis showed that healthy dietary patterns had beneficial effects on sperm concentration, total sperm count, and progressive sperm motility in males, which affect male fertility.
- Authors concluded that healthy dietary patterns may promote male reproductive health and thus improve semen quality in the population.
- Healthy dietary patterns meant the Mediterranean diet for 4 out of 6 studies. All healthy diet patterns were determined by the authors to be rich in plant-based foods, where saturated fats provide only a small percentage of the total energy intake.

## LIMITATIONS:

- Included studies were all cross-sectional studies, and it is impossible to determine the causal relationship between the high intake of healthy dietary patterns and semen quality.
- The number of studies included was small, and there was not enough literature to support drawing reliable conclusions.
- No comparison was made between specific diets such as dash vs Mediterranean.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- The authors concluded that dietary interventions should be considered in clinical work as part of the therapies improving male semen quality.
- Dietary interventions for men should be included as part of preconceptional clinical management,
- Dietary interventions for men should also be considered in infertility clinical management.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

Randomised Clinical Trials should be conducted to build on these findings.



## EXPERT REVIEWER Dr. Michelle Barrow

CONFLICTS OF INTEREST: None

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

Dr Michelle Barrow is the Academic Team Director and Clinical Director at CNELM. Michelle completed a Doctorate in Professional Studies (DProf) in 2019, titled "Leading transformation in Personalised Nutrition Practice". Her doctoral research included the construction of clinical tools to enable the development of a new evidence base for personalised nutrition practice in obesity management. She strives to develop the evidence base to support personalised nutrition practice through her academic work, research supervision, post-doctoral research, and publication.

# VIT E, OMEGA 3 ON REPRODUCTION



## THE INFLUENCE OF VITAMIN E AND OMEGA-3 FATTY ACIDS ON REPRODUCTIVE HEALTH INDICES AMONG MALE WORKERS EXPOSED TO ELECTROMAGNETIC FIELDS

Mohammadi, H ; Golbabaeei, F ; Dehghan, SF ; Imani, H ; Ramezani Tehrani, F ; Khodakarim Ardakani, S  
American journal of men's health. 2022;16(1):15579883221074821

### **INTRODUCTION:**

A block-randomized, double-blind, placebo-controlled study was conducted to investigate the effects of using vitamin E and Omega 3 fatty acid supplementation on reproductive indices among workers in an automobile parts manufacturing facility. The effect of exposure to electromagnetic fields on sex hormones and sperm parameters was also assessed.

### **METHOD:**

92 married males between the ages of 20-50 were deployed into 4 groups. The first group was given vitamin E (100 mg) accompanied by a placebo capsule. The second group was given Omega 3 fatty acids (180 mg eicosatetraenoic acid [EPA] and 120 mg docosahexaenoic acid [DHA]) accompanied by a placebo capsule. The third group was given vitamin E along with Omega 3 fatty acids. Finally, the fourth group acted as a placebo group and was given 2 placebo capsules. The semen parameters of the participants were analysed before and after three months of consuming the supplements. Sex hormones within the blood serum were also analysed after the 3-month supplement period. At the endpoint, 80/92 subjects completed the study.

### **RESULTS:**

- Certain demographic parameters had significant effects on sluggish and full sperm motility: age ( $B = -1.344$ ,  $p = .034$ ); employment duration ( $B = -1.863$ ,  $p = .022$ ); and smoking ( $B = -94.24$ ,  $p = .003$ ).
- The difference in the level of testosterone before and after the intervention was not statistically significant.
- The difference in follicle-stimulating hormone (FSH) and Luteinizing Hormone (LH) before and after the intervention were not statistically significant for any of the supplement groups.
- There was a statistically significant effect on sperm count and sperm with full motility before and after the intervention in the vitamin E + Omega 3 group,  $p = .016$ .
- The effect of supplement use on sperm morphology was significant in the vitamin E + Omega 3 group ( $B = -4.961$ ;  $p = .001$ ).
- The effect of supplement use on full and sluggish sperm motility was also significant in the vitamin E + Omega 3 group ( $B = 72.211$ ,  $p = .021$ ).
- Electric fields had the largest effect on the percentage of immotile sperm amongst the exposure variables ( $B = 9.541$ ;  $p = .053$ ).

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Vitamin E and Omega 3 fatty acids have been reported to influence sperm morphology and sperm motility.
- This study reported that the intake of 100 mg of vitamin E accompanied by Omega 3 fatty acids (180 mg eicosatetraenoic acid [EPA] and 120 mg docosahexaenoic acid [DHA]) had a significant improvement in sperm morphology and motility after 3 months.
- In addition, this study also reported that electric magnetic fields may have a negative effect on sperm morphology and motility.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Prior studies have reported on the antioxidant effects of vitamin E and the effect of Omega 3 fatty acids on the testicles and the hypothalamic-pituitary-gonadal axis.
- This study concluded that participants increased their normal sperm morphology by 16% and their sperm motility by 12% over a 3-month period by supplementing with vitamin E and Omega 3 fatty acids.
- Based on these findings, a practitioner could therefore consider recommending 100 mg of vitamin E accompanied by Omega 3 fatty acids (180 mg eicosatetraenoic acid [EPA] and 120 mg docosahexaenoic acid [DHA]) for at least 3 months to help support the reproductive health of their male patients struggling with sperm morphology and/or sperm motility.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- In this study vitamin E and Omega 3 did not show significant effects on certain sex hormones (testosterone, FSH and LH) therefore, there is a need to investigate if a higher dosage or longer consumption of the supplements could make a difference to these outcomes.
- There are mixed findings on the potential effects of electric magnetic fields on male reproductive indices and therefore there is a need for further clinical studies to be done using the same type of frequency, intensity, and exposure protocols to draw further conclusions.

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## 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.

# EXERCISE & MALE INFERTILITY



## EFFECTIVENESS OF EXERCISE TRAINING ON MALE FACTOR INFERTILITY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

Hajizadeh Maleki, B ; Tartibian, B ; Chehrazi, M  
Sports health. 2022;14(4):508-517

### **INTRODUCTION:**

The World Health Organisation estimates that infertility affects 10% to 15% of couples in industrialised countries. Approximately 50% of all infertility cases are attributed to male-related factors, in particular, poor semen quality (called male factor infertility). The aim of this study was to evaluate the effectiveness of exercise training on male factor infertility and seminal markers of inflammation.

### **METHOD:**

- The forms of exercise: moderate-intensity continuous training (MICT), resistance training (RT), combined aerobic and resistance training (CET), high-intensity continuous training (HICT), and high-intensity interval training (HIIT).
- 7 RCTs representing 18 groups (11 exercise (supervised, not home-based), 7 non-intervention control [NON-EX]) and 2641 participants and/or patients (1429 exercise, 1212 NON-EX). All the RCTs were conducted in Iran involving healthy adult participants and/or infertile patients (with doctor-diagnosed male factor infertility). The intervention period was  $\geq 10$  weeks with a follow-up period.

### **RESULTS:**

#### **Compared with a non-intervention control group, the top ranking interventions for pregnancy rate:**

Combined aerobic and resistance training (CET) ( $p=0.89$  relative risk [RR] = 27.81), moderate-intensity continuous training (MICT) ( $p=0.87$ , RR = 26.67), resistance training (RT) ( $p=0.61$ , RR = 12.54), high intensity continuous training (HICT) ( $p=0.34$ , RR = 5.55), and high-intensity interval training (HIIT) ( $p=0.28$ , RR = 4.63).

#### **For live birth rate:**

MICT ( $p=0.82$ , RR = 10.05), RT ( $p=0.70$ , RR = 4.92), HIIT ( $p=0.66$ , RR = 4.38), CET ( $p=0.45$ , RR = 2.20), and HICT ( $p=0.30$ , RR = 1.55)

#### **The following parameters/markers rank the 5 exercise strategies in order of effectiveness:**

- Semen quality parameters were significantly improved after the following types of exercise interventions as compared with the non-intervention group [NON-EX]: CET > MICT > HICT > RT > HIIT
- The following training strategies were significantly better at improving seminal markers of oxidative stress: CET > MICT > HIIT > HICT > RT
- The following training strategies were significantly better at improving seminal markers of inflammation: CET > MICT > HIIT > RT > HICT
- The following training strategies were significantly better at improving measures of body composition and VO<sub>2</sub> max: CET > HICT > MICT > HIIT > RT
- There was insufficient evidence of a difference for the selected types of exercise interventions versus NON-EX group for pregnancy and live birth rates in healthy participants.

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- For couples with male factor infertility, this review recommends moderate intensity-aerobic exercise in combination with strength training to be the intervention with the highest probability of being the best approach for reproductive health benefits.
- A conservative interpretation of the findings is required because they were based on single studies.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- In light of these findings, it is reasonable to propose that infertile men and at-risk populations take part in the top-ranking interventions identified in this analysis.
- For substantial reproductive health benefits, one should consider doing all of the selected types of exercise interventions (CET, MICT, RT, HICT, and HIIT); however, moderate intensity-aerobic exercise and strength training in combination would generally be more favourable to lend clinically significant improvements.
- To add to this, exercise can offer a myriad of other health benefits, is a possibly safe activity and a cost-effective treatment strategy for male factor infertility.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- There was only a small number of relevant trials available for comparison suggesting the need for additional studies.
- Further trials are needed to analyse the dose-response impacts of exercise modalities on male reproductive function.
- The results propose several domains for development in the reporting of RCTs addressing the impacts of interventional exercise studies on male reproductive function.
- Heterogeneity of some findings and discrepancy across the included studies was significant. For example, variations in the characteristics of training programs. Future analyses should aim to continue to address this.
- There is a concern that this study may not relate to already active patients with male factor infertility which future studies should address.



## EXPERT REVIEWER Georgie Murphy

CONFLICTS OF INTEREST: None

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

Georgie is a Registered Nutritional Therapist and BANT member. She studied Nutritional Therapy at CNM in London. Prior to this she completed her MSc in Nutrition at King's College London and BSc in Biomedical Science from University College Dublin. Georgie brings experience working as the Head of Nutrition at a personalised nutrition start-up. She has experience in supplement development, clinical research, biotech and early-stage clinical trials. Her areas of specialism include gut health and how it affects skin health.

# LOW CARB DIETS & TESTOSTERONE



## LOW-CARBOHYDRATE DIETS AND MEN'S CORTISOL AND TESTOSTERONE: SYSTEMATIC REVIEW AND META-ANALYSIS

Whittaker, J ; Harris, M  
Nutrition and health. 2022;28(4):543-554

### INTRODUCTION:

A systematic review and network meta-analysis was conducted on the effects of low-carbohydrate (LC) versus high-carbohydrate (HC) diets on men's testosterone and cortisol.

The review was registered with PROSPERO and reported using PRISMA 2020 checklists.

### METHOD:

A comprehensive search strategy was used to find intervention studies looking at healthy adult males and LC diets of <35% carbohydrate. Studies were assessed for quality using the Cochrane Risk of Bias tool. Sub-group analyses was conducted for diet duration, protein intake and exercise duration.

### RESULTS:

The literature search resulted in 27 studies with a total of 309 healthy adult male participants, age:  $27.3 \pm 4.7$  (to minimise variation in steroid hormone metabolism), body mass:  $78.6 \pm 7.1$ kg and BMI:  $24.8 \pm 1.6$ . 12 randomised and 15 non-randomised controlled trials were analysed. 21 studies were considered low risk bias, 5 medium and 1 high risk.

- Short-term (<3 weeks) LC diets moderately increased resting cortisol (0.41 [0.16, 0.66],  $p < 0.01$ ) when compared to HC diets.
- Long-term ( $\geq 3$  weeks) LC diets had no consistent effect on resting cortisol
- LC diets resulted in higher post-exercise cortisol, after long-duration exercise ( $\geq 20$  min): 0 h (0.78 [0.47, 1.1],  $p < 0.01$ ), 1 h (0.81 [0.31, 1.31],  $p < 0.01$ ), and 2 h (0.82 [0.33, 1.3],  $p < 0.01$ ).
- The overall results for resting total testosterone (TT) showed a significant decrease on LC versus HC diets (SMD =  $-0.48$ ,  $p = 0.01$ ). However, subgroup analyses revealed this effect to be limited to high-protein (HP) LC diets, which yielded a large decrease in TT (SMD =  $-1.08$ ,  $p < 0.01$ ; 5.23 nmol/L), albeit in a small sample ( $n = 26$ ).
- Moderate protein (MP) (<35%), low-carbohydrate diets had no consistent effect on resting total testosterone, however high-protein ( $\geq 35\%$ ), low-carbohydrate diets greatly decreased resting ( $-1.08$  [ $-1.67$ ,  $-0.48$ ],  $p < 0.01$ ) and post-exercise total testosterone ( $-1.01$  [ $-2$ ,  $-0.01$ ]  $p = 0.05$ ).
- There was no overall effect of LC versus HC diets on 0 h post-exercise TT (SMD =  $-0.03$ ,  $p = 0.95$ ). However, subgroup analysis showed 0 h post-exercise was non-significantly higher on long-term LC versus HC diets (SMD = 0.44,  $p = 0.18$ ), and much lower on short-term LC versus HC diets (SMD =  $-1.01$ ,  $p = 0.05$ )



# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Short-term LC-diets cause a moderate increase in resting and post-exercise cortisol however this effect is not seen in LC-diets followed for greater than 3 weeks.
- HP-LC diets caused a statistically significant decrease in resting TT, suggesting caution in relation to endocrine effects of LC diets.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

The results of this review suggest that exercising whilst following a LC diet can increase cortisol in the short term, but not long-term. This suggests a period of diet adaptation. The effects of long-term LC diets on cardiovascular disease risk is uncertain and healthcare practitioners should monitor client responses and keep up-to-date with new research.

Since HP-LC diets were found to significantly decrease resting testosterone it highlights the need to ensure that protein intake does not exceed the urea cycle's capacity due to potential adverse endocrine effects.

For clients where there is a desire to increase strength, power and hypertrophy, a MP-LC diet could be of benefit, as it showed potential to signal an increased anabolic state post exercise..

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Since LC diets have been shown to have a positive effect on health – decreased triglycerides, increased high density lipoprotein cholesterol and weight loss - future studies would benefit from including these markers so any positive and negative impacts can be monitored directly.
- Despite extensive analysis including sensitivity analysis to reduce bias and heterogeneity of the results, the paper highlights a need for further research to ensure consistency in key parameters e.g., exercise duration and intensity, carbohydrate supplements inclusion and period of dietary intervention. Since it was identified that HP-LP diets impact post exercise and resting TT, follow up studies would benefit from consistency in participants diets. This would help to reduce any potential confounding results.



## EXPERT REVIEWER Nicky Ester

CONFLICTS OF INTEREST: None

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

Nicky received her Masters in Nutrition from University College Cork in Ireland. She also has a diploma in nutritional medicine and has trained as Natural Chef. She brings with her over 20 years' experience of working within the Health and Wellbeing sector, 10 years of which were spent in her own private clinical practice. Throughout her career she has given lectures to help increase the awareness of nutrition and its importance in relation to optimal health and well-being. She is passionate about empowering individuals to understand the role they play in their health in order to create meaningful and lasting change.

# ADDITIONAL RESOURCES

## NED INFOBITES AND CLINICAL FACT SHEETS

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### Male Infertility & Nutrition

**COMPARISON OF L-CARNITINE VS. COQ10 AND VITAMIN E FOR IDIOPATHIC MALE INFERTILITY: A RANDOMIZED CONTROLLED TRIAL**  
Ma L, Sun Y  
European review for medical and pharmacological sciences. 2022;36(13):4098-4704

The World Health Organization (WHO) defines infertility as the inability to conceive after more than one year of regular unprotected intercourse. Male infertility has several different causes, ranging from genetic alterations to lifestyle choices to general medical diseases, medications, or even drugs.

The aim of this study was to compare the efficacy of L-carnitine versus coenzyme Q10 (CoQ10) and Vitamin E in improving outcomes in patients with idiopathic male infertility, such as sperm count, sperm morphology, and testosterone levels. It was concluded therefore that L-carnitine may be superior to the combination of CoQ10 and Vitamin E in improving sperm parameters. Authors conclude that future studies should examine clinical pregnancy rates in order to strengthen and warrant their findings.

**THE EFFECT OF HEALTHY DIETARY PATTERNS ON MALE SEMEN QUALITY: A SYSTEMATIC REVIEW AND META-ANALYSIS**  
Cao, LL, Chang, JJ, Wang, SJ, Li, YH, Yuan, MY, Wang, GF, Su, PF  
Asian Journal of Andrology. 2022;24(5):549-557  
With Expert Review from **Michelle Bacon**

Infertility has been identified by the World Health Organization as a worldwide problem. The analysis of semen quality is key in assessing male fertility. The aim of this study was to explore the effect of healthy dietary patterns on male semen quality. This study is a systematic review and meta-analysis of six articles. The six articles were cross-sectional studies involving 1244 subjects, from which 706 subjects with the lowest and highest adherence to a healthy dietary pattern were included in the meta-analysis. Healthy dietary patterns meant the Mediterranean diet for 4 out of 6 studies. All healthy diet patterns were determined by the authors to be rich in plant-based foods, where saturated fats provide only a small percentage of the total energy intake. Results show that the sperm concentration, progressive sperm motility, and total sperm count were significantly higher in the group with high consumption of a healthy dietary pattern than those in the group with low consumption; however, there wasn't a clear relationship between normal sperm morphology, total sperm motility, and serum volume. Authors concluded that healthy dietary patterns may promote male reproductive health and thus improve semen quality in the population.

**THE IMPACT OF DIABETES MELLITUS TYPE 1 ON MALE FERTILITY: SYSTEMATIC REVIEW AND META-ANALYSIS**  
Falcone, P, Di Lodovico, E, De Barbato, A, et al.  
Andrology. 2022;30(3):426-440

The relationship between type 2 diabetes mellitus and male hypogonadism is well known, whereas the impact of type 1 diabetes mellitus (DM1) on male fertility and testis functions has been less studied. The aim of this study was to systematically review and discuss the available evidence evaluating pregnancy rate, male genital axis, and sperm parameters in men with DM1.

**EFFECTIVENESS OF EXERCISE TRAINING ON MALE FACTOR INFERTILITY: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS**  
Halizadeh Maleki, B, Tazirlikian, B, Chaharati, M  
Sports Health. 2022;14(4):508-517

Male factor infertility is characterized by the existence of suboptimal sperm parameters in the male partner of childbearing age and is presently defined as the inability to conceive a child with frequent and unprotected sexual intercourse in the fertile phase of the menstrual cycles for a year or longer. The main aim of this study was to evaluate the effectiveness of 1 or more of the selected types of exercise interventions (aerobic-intensity continuous training (ICT), resistance training (RT), combined aerobic and resistance training (CRT), high-intensity continuous training (HICT), and high-intensity interval training (HIT)) in the prevention and treatment of male factor infertility. This study is a systematic review and meta-analysis of seven randomized controlled trials representing 18 groups (11 exercise, 7 non-intervention control (NON-INT) and 2N4), participants, and/or patients (129 exercises, 1212 NON-INT). Results show that in the setting of couples with male factor infertility, when compared with the NON-INT group, selected types of exercise interventions improved the relative risk of pregnancy rate in the following order: CRT > MICT > RT > HCT > HIT. The top-ranking interventions for live birth rate were for MICT, RT, HIT, CRT, and HCT. In addition, the interventions with the highest probability of being the best approach out of all available options in improving semen quality parameters were for CRT, MICT, HICT, RT, and HIT. Authors conclude that when clinicians are formulating clinical recommendations for preventing and treating male factor infertility, the findings of this study should be considered.

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### Benign Prostatic Hyperplasia

**CAUSAL RELATIONSHIP BETWEEN OBESITY, LIFESTYLE FACTORS AND RISK OF BENIGN PROSTATIC HYPERPLASIA: A UNIVARIABLE AND MULTIVARIABLE MENDELIAN RANDOMIZATION STUDY**  
Wang, YB, Yang, L, Deng, YQ, Yan, SY, Luo, LS, Chen, P, Zeng, XT  
Journal of Translational Medicine. 2022;20(1):495

Benign prostatic hyperplasia (BPH) is a common benign disease in middle-aged and elderly men which is often underestimated and undiagnosed. If patients are not treated in time, it may lead to serious complications, such as urinary retention, renal insufficiency and renal failure. The aim of this study was to evaluate the possible causal associations of abdominal obesity (measured as waist circumference), overall obesity (measured as body mass index), lifestyle factors (alcohol intake, smoking, alcohol drinking, and sedentary behavior) with risk of BPH. This study is a univariable and multivariable mendelian-randomized study. Results show that genetic predisposition to higher waist circumference and sedentary behavior are independently and causally associated with the risk of BPH. However, there isn't conclusive evidence that genetic predisposition to relative carbohydrate, fat intake, and sugar intake, smoking and alcohol drinking are causally associated with the risk of BPH. Authors conclude that further studies are needed to identify comprehensive risk factors on BPH and develop freely accessible prediction models for the BPH. These will help to identify individuals at particular risk and provide decision-making supports for individualized intervention.

**IMPACT OF DIABETES MELLITUS ON LOWER URINARY TRACT SYMPTOMS IN BENIGN PROSTATIC HYPERPLASIA PATIENTS: A META-ANALYSIS**  
Ho, C, Fan, H, Wu, J, Hu, J, Sun, X, Liu, G  
Frontiers in Endocrinology. 2022;12:74748

Benign prostatic hyperplasia (BPH) is a disease that causes lower urinary tract symptoms (LUTS). Age, sex hormones, diet, alcohol, obesity, and genetic factors are closely related to the occurrence of BPH.

The aim of this study was to investigate the impact of diabetes mellitus on LUTS in BPH patients. This study is a systematic review and meta-analysis of eight articles (consisting of 1685 cases and 4653 controls).

Results show that the International Prostate Symptom Score of the diabetic BPH group was significantly higher than that of the non-diabetic BPH group, indicating that diabetes mellitus may aggravate the LUTS of BPH patients. Authors conclude that LUTS in BPH patients is increased in patients with diabetes mellitus compared with controls.

**SYSTEMATIC REVIEW AND META-ANALYSIS OF CANDIDATE GENE ASSOCIATION STUDIES OF BENIGN PROSTATE HYPERPLASIA**  
Lin, L, Li, P, Liu, X, Xie, X, Liu, L, Singh, AK, Singh, HN  
Systematic reviews. 2022;11(1):60

Benign prostatic hyperplasia (BPH) is a non-malignant enlargement of the prostate which can cause urinary dysfunction and may affect the quality of life of patients. Polymorphism in several genes has been linked to the high susceptibility of BPH.

The aim of this study was to analyze genetic variations in important genes towards the susceptibility of BPH. This study is a systematic review and meta-analysis of twenty-three case-control studies (13 for CYP17 gene, 10 for VDR, vitamin D receptor [a member of the steroid/thyroid hormone receptor family], and 4 for ACE-angiotensin-converting enzyme [component of the renin-angiotensin system] polymorphisms). The sample size in each study ranged from 22 to 105 participants. Results show that genetic polymorphism in the ACE gene was significantly associated with the risk of BPH when compared with control subjects. Whereas there was a negative association for the polymorphism located in VDR and CYP17 genes with the risk of BPH. Authors conclude that larger studies with prospective data and larger sample sizes are required.

**TESTOSTERONE DOES NOT AFFECT LOWER URINARY TRACT SYMPTOMS WHILE IMPROVING MARKERS OF PROSTATITIS IN MEN WITH BENIGN PROSTATIC HYPERPLASIA: A RANDOMIZED CLINICAL TRIAL**  
Rastrelli, G, Cipriani, S, Lotti, F, Cella, I, et al.  
Journal of Endocrinological Investigation. 2022;45(7):1413-1425

Benign prostatic hyperplasia (BPH) — also called benign prostatic enlargement — is frequent in aging populations, with a 40 - 50% prevalence in men aged 50-60 years and up to 90% in men older than 80 years. The aim of this study was to verify whether testosterone therapy (TT) in men with BPH, metabolic syndrome (MetS) and low testosterone is able to improve lower urinary tract symptoms (LUTS) and inflammatory inflammation. This study is a double-blind, randomized 24-week clinical trial in men with low testosterone and MetS and a candidate for prostate surgery for BPH. Patients (n=146) were centrally randomized 1:1 to one of the two groups: TT or placebo.

Results show that TT administered for 24 weeks is a safe option and it improves prostatic inflammatory markers that ameliorating one of the pathogenic components of BPH. However, there were no differences in improvements of the urinary symptoms between both groups (TT and placebo).

Authors conclude that decreased inflammation is not accompanied by a significant improvement in urinary symptoms, and that their findings show the safety of TT in subjects with BPH of surgical significance.

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# ADHD & NEURODIVERSITY

5 REVIEWS



# IMPULSIVENESS IN ADHD CHILDREN



## IMPULSIVENESS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AFTER AN 8-WEEK INTERVENTION WITH THE MEDITERRANEAN DIET AND/OR OMEGA-3 FATTY ACIDS: A RANDOMISED CLINICAL TRIAL

San Mauro Martin, I ; Sanz Rojo, S ; González Cosano, L ; Conty de la Campa, R ; Garicano Vilar, E ; Blumenfeld Olivares, JA  
Neurologia. 2022;37(7):513-523

### **INTRODUCTION:**

A randomized, cross-sectional study was conducted to investigate the effects of a Mediterranean diet and Omega-3 supplementation on the impulsiveness in children with attention-deficit/hyperactivity disorder (ADHD).

### **METHOD:**

76 Children ages 6-16 years of either sex, with a diagnosis of ADHD, were divided into 4 groups, with a control group and 3 intervention groups. Group 1 (controls) followed their usual diet. Group 2 (Mediterranean diet) adopted a Mediterranean diet according to a series of recommendations. Group 3 (omega-3) received omega-3 fatty acid supplements. Group 4 (Mediterranean diet + omega-3) adopted the same diet as group 2 and also received omega 3 fatty acid supplements.

Dieticians provided a tailored Mediterranean diet for each participant. The Omega-3 supplement comprised of 550mg EPA and 225mg of DHA sourced from deep-sea sardines and anchovies.

The Barratt Impulsiveness Scale (BIS-11c) was administered to every child individually to evaluate impulsiveness. The KIDMED questionnaire was administered to evaluate the participant's adherence to the Mediterranean diet. The study was conducted over 8 weeks. At the endpoint, 60/76 subjects completed the study.

### **RESULTS:**

- Children in the omega-3 supplement group showed a significant drop in the Barratt Impulsiveness Scale score after the intervention (from 49 to 45.10;  $p = .049$ ).
- Children in the Mediterranean diet and supplement group showed higher cognitive scores (from 2.758 to 2.631).

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- The results from this study show no statistically significant differences between groups, except for the group of children receiving omega-3 supplementation.
- Patients with ADHD receiving omega 3 fatty acids (550 mg eicosatetraenoic acid [EPA] and 225 mg docosahexaenoic acid [DHA]) daily presented with less impulsive behaviour than controls with ADHD and patients who adopted a Mediterranean diet.
- EPA/DHA supplements may be considered for paediatric patients with ADHD, particularly those with the predominantly hyperactive-impulsive subtype.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Approximately 20%-40% of patients with ADHD do not respond to pharmacological treatment therefore there is a need for alternative options.
- Based on these findings, a practitioner could therefore consider recommending 550mg of eicosatetraenoic acid (EPA) and 225mg of docosahexaenoic acid (DHA) sourced from deep-sea sardines and anchovies for at least 8 weeks to help reduce impulsiveness and improve cognitive function in patients with a hyperactive-impulsive subtype of ADHD.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- This study included combined types of ADHD therefore further investigations are needed on each type of ADHD using different interventions to establish which intervention works best.
- Assessment of diet and omega status before intervention was not conducted, which may have affected outcomes in this study. Further research could consider gathering this data at baseline.
- Larger studies are also needed to determine the relationship between BIS scores and treatments to deepen our understanding of this topic.
- Conflict of interest statement: This study was fully funded by the manufacturer of the provided Omega 3 supplement.

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## EXPERT REVIEWER Ana-Paula Agrela

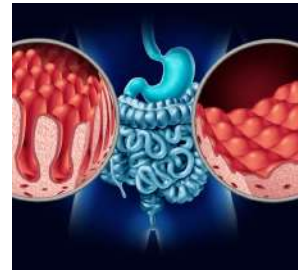
CONFLICTS OF INTEREST: None

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. She completed her Master's degree in Holistic Health and Nutritional Education at 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.



# ADHD & COELIAC IN CHILDREN



## THE ASSOCIATION BETWEEN ADHD AND CELIAC DISEASE IN CHILDREN

Gaur, S  
Children (Basel, Switzerland). 2022;9(6)

### **INTRODUCTION:**

Untreated coeliac disease (CeD) can be accompanied by an array of neurological symptoms. Some of these symptoms are similar to those observed in attention deficit hyperactive disorder (ADHD), like an inability to focus, lack of mental alertness, physical under-activity and clinically measurable under-activity in particular brain regions. The mechanism of such symptoms is not fully understood but is thought to be linked to low-grade inflammation in the brain as a result of permeability in the gut and blood-brain barrier, which could contribute to the presentation of ADHD-like symptoms. This systematic review explored the association between coeliac disease (CeD) and attention deficit hyperactive disorder (ADHD).

### **METHOD:**

The review was conducted following the PRISMA reporting guidelines.

Inclusion criteria for the search:

- Search terms of ADHD and CeD
- Participants < 18 years.

52 papers were retrieved and screened

23 met inclusion/exclusion criteria

### **RESULTS:**

- **13 studies (out of the 23) demonstrated an association between ADHD and CeD**
- **Most studies reporting a positive association were published post 2015**
- **The largest study reported (112,240 patients with CeD) demonstrates that ADHD showed an association of OR = 1.75 in in CeD.**
- **The study was limited by several factors including study design of the studies included in the review, which were mostly observational and some without control.**

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- There is an association between celiac disease (CeD) and attention deficit hyperactive disorder (ADHD).
- Some children with ADHD may respond well to gluten-free diet.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Evidence from across the literature suggests that children with untreated or newly diagnosed CeD may find that following a gluten-free diet can help improve some symptoms associated with ADHD
- The author suggests that there may be a behavioural phenotype of ADHD that responds to a gluten-free diet. If this is the case, it suggests that screening of ADHD patients for celiac disease may be important.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- The number of studies were relatively small and varied in design. Further large-scale studies would help further inform the understanding of the association and potential therapeutic benefits of gluten-free diet.
- It would be interesting to further explore how different subtypes of ADHD, especially the inattentive subtype, may be associated with CeD.
- In particular, it might be useful to consider how the clinical construct of sluggish cognitive tempo (SCT) is associated, since SCT symptoms overlap with the neurological manifestations of CeD.

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## EXPERT REVIEWER Dr. Kate Lawrence

CONFLICTS OF INTEREST: None

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

Dr Lawrence is a Senior Lecturer in psychology at St Mary's University, Twickenham. Kate's research specialises in neurodevelopmental disorders, with a particular focus on dietary and microbiome influences on mental health and cognitive function. She is published in many scientific journals, including Frontiers in Psychology, Neuropsychology, Neuropsychologia, Brain and Cognition.

# Q10 & VITAMINS IN NEURO DISORDERS



## EFFICACY AND SAFETY OF Q10 UBIQUINOL WITH VITAMINS B AND E IN NEURODEVELOPMENTAL DISORDERS: A RETROSPECTIVE CHART REVIEW

Cucinotta, F ; Ricciardello, A ; Turriziani, L ; Mancini, A ; Keller, R ; Sacco, R ; Persico, AM  
Frontiers in psychiatry. 2022;13:829516

### **INTRODUCTION:**

A retrospective chart review study was conducted on the clinical efficacy and safety of metabolic support therapy (MST) with Q10 ubiquinol, vitamin E and complex-B vitamins in various neurodevelopmental disorders.

59 patients (49 Children and 6 Adults) between the ages of 2.5–39 years old diagnosed with Autism Spectrum Disorder (n=17), Autism Spectrum Disorder with co-morbid Intellectual Disability (n=19), Intellectual Disability or Global Developmental Delay (n=15), Attention-Deficit/Hyperactivity Disorder (n=3), and Intellectual Disability in Phelan-McDermid syndrome due to chr. 22q13.33 deletions (n=5) were included in the study.

### **METHOD:**

- Participants received 50-100mg Q10 ubiquinol, 30-60mg of vitamin E, 5.5mg-11mg of nicotinamide, 3mg-6mg of dexpanthenol, 0.45mg-0.09mg of riboflavin-5'-sodium phosphate, 5mg-10mg of inositol, pyridoxine hydrochloride, and 0.07mcg -1.40mcg of cyanocobalamin for three months. Different dosage levels were administered based on the participant's body weight and the maximum daily allowance. Patients remained on their prescribed medications.
- The Clinical Global Impression of Severity (CGI-S) scale, as well as the Clinical Global Impression of Improvement (CGI-I) scale was assessed by experienced Child and Adolescent or Adult Psychiatrists. The clinical diagnosis was further confirmed using the Autism Diagnostic Observation Schedule – 2nd ed (ADOS-2) and the Autism Diagnostic Interview-Revised (ADIR) for ASD, the Griffiths Mental Development Scale (GMDS) for GDD, a cognitive test (Leiter-R, WPPSI-III, WISC-IV, WAISIV) for ID, the Conners Parent Rating Scale (CPRS) also in Teacher version (TRF) and the Batteria Italiana per l'ADHD (BIA) for ADHD.

### **RESULTS: 45/59 (76.2%) of the subjects completed the study.**

- **Most widespread improvements were recorded in cognition (n=26 44,1%), adaptive functioning (n=26 44,1%) and social motivation (n=19 32.2%).**
- **45/59 (76.27%) patients responded to MST according to Clinical Global Impression of Severity scores.**
- **One 13-year-old boy with an intellectual disability, gained over 20 IQ points after consuming metabolic support therapy for 6 months.**
- **Mild side effects of hyperactivity and insomnia were reported in 18/59 (30%) of patients.**



# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Oxidative stress and mitochondrial dysfunction are reported to play a role in brain and neurological disorders.
- This retrospective chart review suggests that metabolic support therapy with Q10 ubiquinol, vitamin E and complex-B vitamins is well tolerated and produces some improvement in most patients with neurodevelopmental disorders, especially in the presence of intellectual disability.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Pharmacological treatments are prescribed to correct comorbid symptoms like sleep disorders, aggressiveness, and irritability in neurodevelopmental disorders like ASD. The efficacy of these treatments displays great interindividual variability depending not only on the treatment approach, therapist experience, and therapeutic setting but also on the genetic background of the patient.
- Oxidative stress and mitochondrial dysfunction have been described in many different brain and neurological disorders.
- Minimising the mitochondrial dysfunction produced by oxidative stress damage in brain disorders, while not directly correcting the primary mechanism responsible for the pathology, may nonetheless help to improve the clinical condition, acting as an indirect therapy.
- This study provides preliminary evidence of the efficacy and tolerability of a 'metabolic support therapy' encompassing Q10- ubiquinol, Vitamin E and complex-B vitamins in patients with different neurological disorders.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- This study was based on a retrospective design using a small sample size.
- Randomised controlled trials for each single neurodevelopmental disorder are needed to conclusively demonstrate the efficacy of mitochondrial bioenergetic and antioxidant agents and to estimate their therapeutic effect size.



## EXPERT REVIEWER Ana-Paula Agrela

CONFLICTS OF INTEREST: None

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

Ana is a Nutrition Consultant, and Health Coach who graduated with a BSc. (Hons) in Nutritional Science from Middlesex University. She completed her Master's degree in Holistic Health and Nutritional Education at 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.

# VITAMIN D STATUS & RISK OF ADHD



## CIRCULATING LEVELS OF MATERNAL VITAMIN D AND RISK OF ADHD IN OFFSPRING: RESULTS FROM THE VITAMIN D ANTENATAL ASTHMA REDUCTION TRIAL

Chu, SH ; Huang, M ; Kelly, RS ; Kachroo, P ; Litonjua, AA ; Weiss, ST ; Lasky-Su, J  
International journal of epidemiology. 2022;51(3):910-918

### **INTRODUCTION:**

**Background:** This paper describes a secondary data analysis from an RCT that looked at the effect of prenatal vitamin D supplementation on risk of childhood asthma in offspring. Enrolled women aged 18–39 years with a history of asthma, eczema or allergic rhinitis, or whose partner (biological father of child) had a history of the aforementioned condition, received either 400 IU or 4400 IU vitamin D daily for the duration of their pregnancy. Offspring follow-up is still ongoing.

**Aims:** The current study aims were twofold: (i) to determine the association between maternal vitamin D levels in trimesters 1 and 3 and the risk of attention deficit/hyperactivity disorder (ADHD) in offspring diagnosed by age 6 years or later; and (ii) to identify potentially sensitive periods during gestation in which vitamin D levels may be especially important for reducing risk of ADHD.

### **METHOD: ADHD STATUS WAS ASSESSED THROUGH PARENTAL REPORTING BETWEEN AGES 6-9**

The analytical sample included 679 mother-child pairs, from the original sample of 876 participating mothers. No sample size calculation was reported, though the sample was considered representative of the overall RCT study population.

Maternal vitamin D (serum 25(OH)D) was classified as follows:

Highly deficient <12 ng/mL » Deficient 12 ng/mL to 19.9 ng/mL » Insufficient 20 ng/mL to 29.9 ng/mL » Sufficient ≥30 ng/mL

### **RESULTS:**

No baseline associations between a vitamin D sufficient status and offspring ADHD in maternal samples collected during trimester 1 were observed (OR 1.06, 95% CI 0.51–2.19; P.0.871), though this association became statistically significant at trimester 3 (OR 0.47, 95% CI 0.26–0.84; P.0.011). This translated to a 53% less chance of having a child with ADHD at age 6 or later among mothers with vitamin D sufficiency compared with children of mothers with vitamin D deficiency. There was also a linear trend in the protective association of vitamin D sufficiency (≥30 ng/mL) on reduced risk of offspring ADHD at age 6 years or later in data from trimester 3. Stratified analyses revealed a protective association for sufficient maternal vitamin D status and offspring ADHD among males (OR 0.47, 95% CI 0.23–0.94).

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Ensure that women in pregnancy, and possibly also those seeking to conceive, have adequate vitamin D status in order to reduce the risk of ADHD in offspring.

## CLINICAL PRACTICE APPLICATIONS:

- Ensuring a sufficient vitamin D status by the 3rd trimester of pregnancy may help to lessen the risk of ADHD in offspring. Nutritional therapists and other clinicians working with pregnant women or women looking to conceive should consider checking vitamin D status and providing corrective supplementation and lifestyle advice to augment vitamin D levels where indicated.

## CONSIDERATIONS FOR FUTURE RESEARCH:

- The authors of this study postulated that the statistically significant protective association between vitamin D at trimester 3 and ADHD in offspring was not significant in trimester 1 due to a low observed variability in vitamin D status (>75% of women were vitamin D insufficient), and thus the statistical test being underpowered to see difference between groups with sufficient or insufficient status.
- Further research could expand upon this hypothesis to test whether vitamin D status in trimester 1, or preconceptually, may offer a protective association for ADHD and other related neurological conditions that may manifest in early life.

CONFLICTS OF INTEREST: None

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

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## EXPERT REVIEWER Dr.sc. Jessica Rigutto

Dr Rigutto is a Senior Assistant and Lecturer at the Human Nutrition Laboratory, Institute of Food, Nutrition and Health, of ETH Zürich. Following an early career in pharmacy, Jessica obtained a Master of International Public Health at the French School of Public Health and a Doctor of Science in Human Nutrition from ETH Zürich. Jessica is co-creator of the OpeN-Global knowledge hub on nutritional biomarkers for global health research, hosted by King's College London. Her research specialises in addressing micronutrient deficiencies through novel applications and supporting public health policy.

# MICRONUTRIENTS FOR ADHD



## MICRONUTRIENTS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN YOUTHS: A PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL

Johnstone, JM ; Hatsu, I ; Tost, G ; Srikanth, P ; et al.

Journal of the American Academy of Child and Adolescent Psychiatry. 2022;61(5):647-661

### **INTRODUCTION:**

Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric condition that can result in low educational performance and achievement. Around 5-7% of children are believed to be affected. Alongside inattention and hyperactivity, emotional dysregulation is a common feature of ADHD. Psychiatric problems can continue into adulthood and an increased risk of incarceration and substance abuse have been reported.

Treatment with prescription medications may improve symptoms of ADHD, however, potential side effects include mild growth suppression, and mood and emotional dysregulation. Non-pharmacological treatments are being investigated.

Previous research on single nutrients have shown mixed results for emotional dysregulation and mood issues in ADHD. The aim of this study was to test whether supplementation with a multi-nutrient could be beneficial to children aged 6-12 years with ADHD and irritability.

### **METHOD: THE TRIAL WAS BLINDED TO ALL PARTICIPANTS, PARENTS AND STUDY STAFF.**

126 unmedicated children from North America with ADHD (mean age 9.8 years) completed this 8-week study. All participants had at least 1 symptom of anger, irritability, peer conflict or Disruptive Mood Dysregulation Disorder (DMDD).

Randomisation was into an intervention (n=71) or placebo (N=55) group with a 3:2 ratio to promote enrolment. Participants were required to take 6-12 capsules daily, depending on age and tolerance, of micronutrients or a placebo. Micronutrient dosages were above the recommended dietary allowance (RDA). Outcomes were measured using clinician and parent rated assessments and by a further adult who knew the child well.

### **RESULTS:**

**The clinician-rated results found 54% of the micronutrient group and 18% of the placebo group had improvements in irritability symptoms (Risk ratio =2.97, 97.5% CI: 1.5, 5.90, p<0.001). This was not replicated in the parent/adult rated results. Children in the micronutrient group grew on average 6mm more than the placebo group (p=0.002). No serious adverse treatment effects were reported. Adherence to protocol was met by >74% of participants (n=93).**

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- This fully-blinded RCT of micronutrients addresses several concerns related to existing ADHD treatment, including the possibility of counteracting height suppression and treating associated irritable mood, emotional dysregulation, and aggression.
- Although further research is needed, multinutrient supplementation should be considered for children with ADHD.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Multinutrient supplementation including vitamins, minerals, amino acids, and antioxidants may support height growth in children who take pharmacologic treatment
- Multi nutrient supplementation may also help with irritable mood, emotional dysregulation, and aggression in ADHD children
- Micronutrients given at doses between the Recommended Dietary Allowance and Upper Tolerable Intake Level appear safe and may be developed into an alternative or complementary treatment for ADHD.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Further large scale research is needed into the potential benefits of micronutrients for children with ADHD and irritability.

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 in 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 may 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.

# ADDITIONAL RESOURCES

## NED INFOBITES AND CLINICAL FACT SHEETS

All BANT resources are provided as free downloads on our website enabling practitioners to utilise them in clinic and group settings. They are purposefully written in client-friendly language so that they can be shared as handouts to clients as support for discussions conducted in a clinical consultation or presentations to wider groups.

**BANT** Nutrition & ADHD

### Attention Deficit Hyperactivity Disorder

ADHD is a disorder that is defined through analysis of behaviour

**Inattention**

Difficulty paying attention to or holding attention to tasks, following instructions, organising tasks & activities, failure to finish tasks, making careless mistakes, does not seem to listen when spoken to directly.

**Reluctance**

General reluctance to do, or avoidance of things that dislike or that require mental effort over a long period of time.

**Forgetfulness**

Often easily distracted or forgetful in daily activities.

**Defined Criteria for ADHD**

**Hyperactivity**

Often "on the go" acting as if powered by a motor, talks excessively, is frequently agitated and impatient and has trouble waiting their turn.

**Impulsivity**

Often blurts out an answer before a question has been completed or intrudes on others. Moves about in situations where it is not appropriate

**Restlessness & Fidgeting**

Fidgets with or taps hands or feet, squirms in seat, leaves seat in situations when remaining seated is expected.

**ADHD Characteristics** The definition for ADHD is defined by a list of criteria

People with ADHD show a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with day-to-day functioning and/or development. Diagnosis can only be done by a medical professional. ADHD can carry through into adulthood where symptoms might look different at older ages reflecting both the changing maturity of the individual and the changing circumstances and expectations on them.

**UK Statistics** More common in boys than girls with an average incidence rate of <5% Current data indicates a UK childhood incidence rate of 5% and an adult incidence rate of 3-4%, providing a total estimate of 2.6million people in the UK with ADHD (This breaks down to c.694,000 children with a gender split of roughly 4:1 boys:girls, and 1.9 million adults).

**Diet & Nutrition** Diet and Lifestyle support for ADHD

Research shows that diet and lifestyle modifications, can play an important role in supporting individuals with ADHD to manage certain symptoms. An individualised approach to this condition is important as every person with ADHD responds differently.

More information available at <https://adhduk.co.uk/>

Find a Practitioner at [www.bant.org.uk](http://www.bant.org.uk)

**BANT** Nutrition & ADHD

### THE ASSOCIATION BETWEEN ADHD AND CELIAC DISEASE IN CHILDREN: EXPERT REVIEW FROM KATE LAWRENCE

Unresolved celiac disease (CeD) can be accompanied by an array of neurological symptoms. Some of these symptoms are similar to those observed in attention deficit hyperactive disorder (ADHD), like an inability to focus, lack of mental alertness, physical under-activity and clinically measurable under-activity in particular brain regions. The mechanism of such symptoms is not fully understood but is thought to be linked to low-grade inflammation in the brain as a result of permeability in the gut and blood-brain barrier, which could contribute to the presentation of ADHD-like symptoms.

This is an updated systematic review including 23 studies of children and young adults, which found an association between ADHD and CeD. In contrast to previous reviews that found no clear association. This review paid particular attention to the diagnostic criteria of ADHD and its subtypes, highlighting the need to examine the linkages of ADHD in future studies. Specifically, the inattentive subtype may be a behavioural ADHD phenotype that could respond to a gluten-free diet. The authors advocate screening ADHD patients for CeD and encourage the consideration of neuro-neurological symptoms in the assessment of ADHD to identify potential CeD cases.

**IMPAULSIVENESS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AFTER AN 8-WEEK INTERVENTION WITH THE MEDITERRANEAN DIET AND/OR OMEGA-3 FATTY ACIDS: A RANDOMISED CLINICAL TRIAL WITH EXPERT REVIEW FROM ANA-PAULA AGRELA**

San Mauro Martín, I.; Sanz Rogo, S.; González Casano, L.; et al. *Neurologia*. 2022;37(7):513-523

The aim of this 2022 randomised clinical trial was to analyse changes in the Barratt Impulsiveness Scale (BIS-11) scores in children with ADHD after an 8-week intervention with the Mediterranean diet, omega-3 fatty acid supplementation, or Mediterranean diet plus omega-3 fatty acid supplementation, as compared to a control group. Participants (>60) were divided into 4 groups, with a control group and 3 intervention groups. Results show that participants with ADHD taking n-3 PUFA supplements (500 mg EPA and 325 mg DHA daily) showed significantly lower levels of impulsiveness than those adopting a Mediterranean diet and controls. These participants also scored lower on all subscales of the BIS (cognitive, motor, and lack of planning). However, there weren't any differences in impulsive behaviour between participants taking n-3 PUFA supplements and those taking supplements and adhering to the Mediterranean diet. Authors conclude that omega-3 rich (EPA/DHA) supplements should be considered for paediatric patients with ADHD, particularly those with the predominantly hyperactive-impulsive subtype.

**MICRONUTRIENTS FOR ATTENTION-DEFICIT / HYPERACTIVITY DISORDER IN YOUTH: A PLACEBO-CONTROLLED RANDOMIZED CLINICAL TRIAL WITH EXPERT REVIEW FROM GAIL BRADY**

Johnstone, JM.; Habbu, I.; Tsai, G.; et al. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2022;61(5):647-661

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental condition that affects about 3-7% of children. This eight-week randomised placebo-controlled clinical trial evaluated the effects of a multi-nutrient supplement in 135 children with ADHD, aged 6-12 years, focusing specifically on inattentive mood symptoms. The multi-nutrient formula contained vitamins, minerals, amino acids, and antioxidants. Outcomes were measured by scores rated by clinicians (Clinical Global Impression-Improvement aka CGI-I) and scores rated by parents (ADHD and Attention Symptom Inventory-5 aka CASI-5). The multi-nutrient formula showed overall benefits in the blinded clinician rating but not by parental reports. According to the parents, level of improvement was reported both in the placebo and intervention groups. The supplement was well tolerated with good adherence and the measured blood markers demonstrated safety of use.

**CIRCULATING LEVELS OF MATERNAL VITAMIN D AND RISK OF ADHD IN OFFSPRING: RESULTS FROM THE VITAMIN D ANTENATAL ASTHMA REDUCTION TRIAL WITH EXPERT REVIEW FROM JESSICA RIGUTTO**

Chu, SH.; Huang, M.; Kelly, RS.; Kothano, P.; Litarjova, AA.; Weiss, ST.; Lasky, Su.; International Journal of Epidemiology. 2022;51(3):910-918

Vitamin D has been found to play a critical role in neurodevelopment across sensitive periods in utero, infancy and early childhood. Among neurodevelopmental and behavioural disorders in early life, attention-deficit/hyperactivity disorder (ADHD) is the most common among children worldwide. Low levels of circulating 25-hydroxy-vitamin D [25(OH)D] have been shown to associate with greater ADHD. The aims of this study were to (i) determine the association between maternal vitamin D levels in the first and third trimesters of pregnancy and the risk of offspring ADHD by age 8 years or later, and (ii) identify potential sensitive periods in utero during which vitamin D levels might be most important for reducing risk of ADHD. This is an ancillary study of the Vitamin D Antenatal Asthma Reduction Trial (VDAART). The VDAART was a randomised, double-blind, multicentre clinical trial in which 876 participating mothers were recruited between 10-18 weeks of gestation and assigned to receive either 4000 or 400 IU/day of vitamin D throughout pregnancy. Results show positive associations between maternal 25(OH)D sufficiency in the third trimester and child ADHD, but not at baseline. At baseline and in the third trimester, there were higher odds of ADHD in male offspring compared with female offspring in 25(OH)D insufficient mothers (1st small sample size). Authors conclude that higher levels of maternal vitamin D during pregnancy may play a protective role against risk of ADHD in offspring.

**VITAMIN D3**

**FOOD FOR YOUR HEALTH**

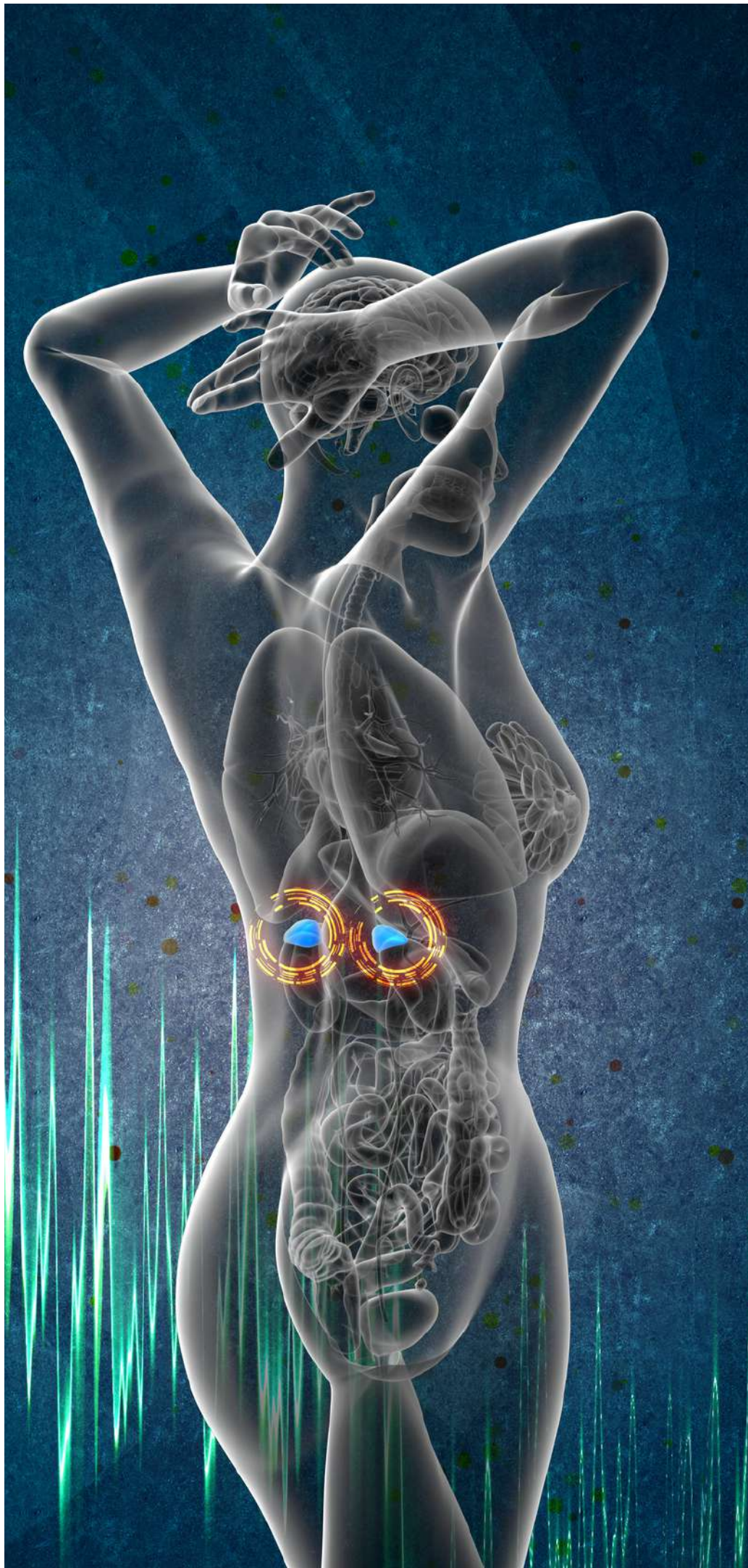
Find the Science [www.nutrition-evidence.com/](http://www.nutrition-evidence.com/)

Download the fact sheet [here](#)

Download the NED InfoBite [here](#)

# STRESS & ADRENALS

5 REVIEWS



# FEED MICROBES FOR STRESS



## FEED YOUR MICROBES TO DEAL WITH STRESS: A PSYCHOBIOITIC DIET IMPACTS MICROBIAL STABILITY AND PERCEIVED STRESS IN A HEALTHY ADULT POPULATION

Berding, K ; Bastiaanssen, TFS ; Moloney, GM ; Boscaini, S ; et al.  
Molecular psychiatry. 2022

### INTRODUCTION:

This RCT explored the impact of a psychobiotic diet, compared to a control diet, on perceived stress, sleep and gut microbiota. A high psychobiotic diet is one high in prebiotic and fermented foods. In this study, a psychobiotic diet included daily recommended consumption and servings of the following:

- High prebiotic fruit & veg (6-8)
- Grains (5-8)
- Fermented foods (2-3)
- Legumes (3-4 per week)

### METHOD:

- A single-blind, randomised, controlled study
- 45 healthy adults (18-59 years) with poor dietary habits
- Sample size determined by previous microbiome research - target not reached due to introduction of covid restrictions
- Active intervention (n=24) received dietitian advice to follow psychobiotic diet
- Control intervention (n=21) received dietitian advice largely based on the Irish Healthy Eating Guidelines food pyramid
- Intervention duration 4 weeks.
- Assessed on questionnaire measures of perceived stress and sleep, pre and post-intervention (no primary outcome defined)
- Shotgun microbiome analysis on stool samples, pre and post-intervention

### RESULTS:

- **Perceived stress improved in the psychobiotic diet group**
- **Subjective sleep quality improved in the psychobiotic diet group**
- **Only subtle changes in microbial composition and function**
- **More stable microbiota throughout the study (regardless of diet) was correlated with greater changes in perceived stress**
- **Neither cortisol awakening response nor measured immune markers were affected by dietary intervention**



# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Eating foods known to have a positive influence on gut microbial composition could elicit benefits in terms of reducing perceived stress and improving sleep quality.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Providing advice on dietary intake of foods known to positively impact gut microbiota may be helpful for individuals affected by stress or sleep problems
- The inclusion of the following foods may be helpful:
  - High prebiotic fruit & veg (6-8 per day)
  - Grains (5-8 per day)
  - Fermented foods (2-3 per day)
  - Legumes (3-4 per week)

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Important to replicate these results in a larger sample
- It might be helpful to investigate individual aspects of the diet separately, to assess their individual impact
- Objective measures of sleep (such as actigraphy recordings) might provide additionally useful findings
- It would be interesting to explore the effect of the psychobiotic diet in other conditions
- Chronobiology or chrononutrition - i.e. looking at timing of the foods proposed in the section above

CONFLICTS OF INTEREST: None

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



## EXPERT REVIEWER Dr. Kate Lawrence

Dr Lawrence is a Senior Lecturer in psychology at St Mary's University, Twickenham. Kate's research specialises in neurodevelopmental disorders, with a particular focus on dietary and microbiome influences on mental health and cognitive function. She is published in many scientific journals, including Frontiers in Psychology, Neuropsychology, Neuropsychologia, Brain and Cognition.

# BIFIDOBACTERIUM & STRESS



## BIFIDOBACTERIUM LONGUM SUBSP. LONGUM REDUCES PERCEIVED PSYCHOLOGICAL STRESS IN HEALTHY ADULTS: AN EXPLORATORY CLINICAL TRIAL

Boehme, M ; Rémond-Derbez, N ; Lerond, C ; et al.  
Nutrients. 2023;15(14)

### INTRODUCTION:

A randomised, placebo-controlled, two-arm, parallel, double-blind exploratory clinical trial was conducted to investigate the effect Bifidobacterium longum (BL) strain NCC3001 on stress-related psychological and physiological parameters and acute stress in healthy adults who typically experience mild-to-moderate-levels of stress.

### METHOD:

- 47 Participants between the ages of 25-65 years old with mild-to-moderate psychological stress received  $1 \times 10^{10}$  CFU of Bifidobacterium longum (BL) strain NCC3001 daily or a placebo for 6 weeks.
- Participants completed the Perceived Stress Scale (PSS), the Hospital Anxiety and Depression Scales (HAD-A and HADS-D), the Gastrointestinal Symptom Rating Scale (GSRA), the Pittsburgh Sleep Quality Index (PSQI) questionnaire, the Positive and Negative Affect Schedule (PANAS), the State Trait Anxiety Inventory (STAI-6), the Maastricht Acute Stress Test (MAST) and the Visual Analog Scales (VAS, which measures pain intensity) during the clinical study. The Depression, Anxiety and Stress Scale (DASS-42) questionnaire was also used to depict the progression of the participants through the study.
- Faecal samples were taken at baseline and 6 weeks and awakening saliva samples were taken at baseline, 2, 4, 6 and 8 weeks. At the endpoint, 45/49 (91%) of the subjects completed the study. One participant reported an adverse event and the other withdrew without an explanation. Two participants were excluded from the full analysis.

### RESULTS:

- **After 6-week of the probiotic intervention, there was a significant decrease in perceived stress in the probiotic group (21.4%) compared to the placebo group (-10.2%),  $p = 0.017$ .**
- **There was a significant improvement in subjective sleep in the probiotic group compared to the placebo group ( $p = 0.037$ ).**
- **There was a significant decrease in the positive PANAS change score from the pre-stressor stage in the probiotic group compared to the placebo group ( $p = 0.01$ ).**
- **There were lower pain values (VAS) scores from pre-stressor to post-stressor in the probiotic group compared to the placebo group ( $p = 0.05$ ).**
- **There was no significant difference between groups in anxiety (HADS-A) and Depression (HADS\_D).**

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- There is mounting evidence to suggest that nutritional interventions can influence our stress responses. One of the routes by which nutrition can influence physiological and psychological stress responses involves the microbiota–gut–brain-axis.
- This exploratory trial suggests that supplementation with *Bifidobacterium longum* (BL) strain NCC3001 leads to a beneficial effect on stress relief and improves subjective sleep quality in a healthy adult population reporting moderate levels of psychological stress.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- While the mechanism underlying the correlation between the microbiota and the gut-brain-axis is not fully understood, it is thought to play a critical role in the links between the microbiota, mood, stress, and brain health.
- This exploratory trial additionally supports the potential of specific probiotics being used to reduce perceived stress and improve subjective sleep quality in healthy adults.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger, powered clinical trials are needed to provide further insights into the mechanisms underlying the stress-relieving and sleep-improving effect of *Bifidobacterium longum*.
- Furthermore, the dosage and duration of the probiotics need further investigation in a larger healthy population.
- Comparative research is needed to help investigate the effect of different probiotic strains on stress relief and sleep quality.



## 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. She completed her Master's degree in Holistic Health and Nutritional Education at 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.

# AEROBIC EXERCISE & CORTISOL



## EFFECT OF AEROBIC EXERCISE, SLOW DEEP BREATHING AND MINDFULNESS MEDITATION ON CORTISOL AND GLUCOSE LEVELS IN WOMEN WITH TYPE 2 DIABETES MELLITUS: A RANDOMIZED CONTROLLED TRIAL

Obaya, HE ; Abdeen, HA ; Salem, AA ; et al.  
Frontiers in physiology. 2023;14:1186546

### INTRODUCTION:

- Stress, a key factor for Type 2 diabetes mellitus (T2DM), stimulates the hypothalamus-pituitary-adrenal gland (HPA) and triggers parasympathetic nerve withdrawal, leading to increased circulating cortisol levels and higher levels of blood glucose. Exercise is a key intervention that can modulate the HPA axis and help manage stress.

### METHOD:

- Fifty-eight women (aged between 40-50), diagnosed with T2DM for at least 5 years but medically stable with moderate to high stress scores were randomised to either aerobic training (AT) or aerobic exercise combined with slow deep breathing and mindfulness meditation (DMM) training three times weekly over 6-weeks.
- 
- AT group performed aerobic exercise on a treadmill at an intensity of 60%– 75% of the maximum heart rate for a total of 40 min, including a 5 minute warm up and 5 min cool down.
- 
- AT + DMM group performed a combination of aerobic exercise as per the AT group followed by a total of 10 minutes of diaphragmatic slow, deep breathing; and mindfulness meditation.

### RESULTS:

- **Both groups showed a change from baseline in serum cortisol to  $p < 0.0001$**
- **At 6 weeks in the AT + DMM group, the primary outcome of serum cortisol (nmol/L) levels was 12.59 nmol/L [95% CI 4.45-6.52] a decrease of 30.29% and the fasting blood glucose levels (secondary outcome) was 136.37mg/dl (95% CI: 9.19–2.6) a decrease of 14.54%**
- **In the AT group performing only aerobic exercise decreased serum cortisol levels by 20.16% and FBG levels decreased by 9.97%.**

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Practitioners could consider slow deep breathing and mindfulness meditation, added to aerobic exercise, as potentially useful components of the T2DM management program for stressed women.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- Consider a combined therapy approach with diaphragmatic breathing exercises and aerobic exercises that targets both the endocrine and autonomic nervous systems, as this may have a synergistic effect to assist with maintaining normal blood sugar levels and cortisol levels in individuals with T2DM.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Future research is needed to determine the most effective combination of therapies for managing both FBG and serum cortisol levels in individuals with T2DM.

## CONCLUSION:

This study showed that combining slow deep breathing and mindfulness meditation with aerobic exercise reduced the serum cortisol ( $p = 0.01$ ) and FBG levels ( $p = 0.001$ ) in women with T2DM compared to only aerobic training.

CONFLICTS OF INTEREST: None

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



## EXPERT REVIEWER 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.

# LACTOCOCCUS & THE HPA AXIS



## EFFECTS OF LACTOCOCCUS LACTIS SUBSP. CREMORIS YRC3780 DAILY INTAKE ON THE HPA AXIS RESPONSE TO ACUTE PSYCHOLOGICAL STRESS IN HEALTHY JAPANESE MEN

Matsuura, N ; Motoshima, H ; Uchida, K ; Yamanaka, Y  
European journal of clinical nutrition. 2022;76(4):574-580

### INTRODUCTION:

Lactococcus lactis subsp. cremoris (YRC3780), which is isolated from kefir, has been associated with anti-allergic effects in humans. However, it remains unknown whether daily intake of YRC3780 attenuates the response to psychological stress in humans in parallel with changes to the gut microbiome. We examined the fundamental role of YRC3780 in the gut microbiome, stress response, sleep, and mental health in humans.

### METHOD:

Effects of daily intake of YRC3780 on the hypothalamic-pituitary-adrenal (HPA) axis response to acute psychological stress were investigated in a double-blind, placebo-controlled clinical trial involving 27 healthy young men (mean age and body mass index: 23.5 years and 21.5 kg/m<sup>2</sup>) who were randomly assigned to placebo (n = 13) or YRC3780 (n = 14) groups. The HPA axis response to acute psychological stress, the diurnal rhythm of HPA axis activity, and gut microbiome were assessed and compared between the two groups.

### RESULTS:

**The results showed that daily intake of YRC3780 significantly lowered morning salivary cortisol levels compared with placebo. In addition, salivary cortisol levels following a social stress test significantly decreased +40 min after beginning the TSST in the YRC3780-treated group compared to placebo. There were no significant differences between the two groups in terms of actigraphy-based sleep quality, but the subjective sleep quality and mental health were significantly improved in the YRC3780-treated group compared to placebo.**

### CONCLUSION:

Our study suggests that daily intake of YRC3780 improves the HPA axis response to acute psychological stress, which might be associated with a decrease in morning cortisol levels.

# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Research indicates a bidirectional interaction between the gut microbiome and the central nervous system, affecting the functions of the brain and spinal cord.
- This clinical trial suggests that daily intake of *Lactococcus lactis* subsp. *cremoris* (YRC3780) may enhance the HPA axis response to acute psychological stress, potentially linked to a reduction in morning cortisol levels.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- The precise mechanisms underlying the correlation between the gut microbiota and the gut-brain axis remain incompletely understood, emphasising the need for further research.
- This clinical trial demonstrated that daily intake of YRC3780 decreased morning salivary cortisol levels at 6 and 8 weeks and reduced the salivary cortisol response to acute psychological stress.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

- Larger, adequately powered clinical trials are required to provide deeper insights into the mechanisms responsible for the stress-reducing and sleep-improving effects of *Lactococcus lactis* subsp. *cremoris*.
- Furthermore, investigations into optimal dosage and duration of probiotic supplementation are warranted for a more comprehensive understanding, particularly in diverse demographic groups.
- Comparative research is needed to explore the effects of various probiotic strains on objective stress responses.

CONFLICTS OF INTEREST: None

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



## 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. She completed her Master's degree in Holistic Health and Nutritional Education at 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.

# TRE STRATEGIES & STRESS HORMONES



## THE WINDOW MATTERS: A SYSTEMATIC REVIEW OF TIME RESTRICTED EATING STRATEGIES IN RELATION TO CORTISOL AND MELATONIN SECRETION

Chawla, S ; Beretoulis, S ; Deere, A ; Radenkovic, D  
Nutrients. 2021;13(8)

### INTRODUCTION:

This systematic review aimed to examine the effects of two patterns of Time Restricted Feeding (TRE): (1) traditional TRE, and (2) Ramadan fasting, on two markers of circadian rhythm: (1) cortisol and (2) melatonin.

### METHOD:

- A search was performed on PubMed, and Web of Science (all databases) up to December 2020 using search terms relating to “time-restricted eating”, “intermittent fasting”, “cortisol”, “melatonin”, and “orexin”.
- 14 randomised controlled trials and observational studies that met the criteria were included.
- Quality assessment of all studies was performed

### RESULTS:

**14 studies met the inclusion criteria. 10 of the studies used TRE in the context of Ramadan (total n=242) whilst 4 followed non-Ramadan TRE protocols (total n=124). Of the 14 studies identified in the literature review, 13 reported results on cortisol, and 4 on melatonin.**

- **All 4 melatonin studies found a statistically significant reduction of melatonin ( $p < 0.05$ ) during Ramadan.**
- **2 of 3 studies assessing 24-h serum cortisol changes during Ramadan noted an “abolishing” of the circadian rhythm of cortisol ( $p < 0.05$ ), meaning there was a flattening of cortisol levels during the fasting month compared with the non-fasting month.**
- **All 13 cortisol studies recorded a cortisol shift in response to time restricted eating, albeit over different time frames and different cortisol recording methods.**
- **1 randomised 4-day crossover study (n=11) found skipping dinner resulted in significantly reduced evening cortisol ( $p=0.03$ ) and non-significantly raised morning cortisol. Skipping breakfast resulted in significantly reduced morning cortisol ( $p=0.10$ ).**
- **1 observational study of females aged 18-45 (n=65) found that skipping breakfast demonstrated decreased morning (waking) cortisol, elevated midday cortisol, and no significant evening cortisol differences compared to the control group.**



# HOW TO BRING THIS RESEARCH INTO YOUR CLINICAL PRACTICE

## TAKE HOME MESSAGE:

- Other human and animal studies have highlighted the benefits of restricting the feeding window for longevity and metabolic health.
- Whether one chooses early or late TRE may help to determine the optimal time of alertness and sleep.
- Early TRE, which involves skipping dinner, may allow for greater alertness in the morning as the lower levels of cortisol at night can improve sleep quality and higher morning cortisol raises alertness, optimising wakefulness and productivity.

## 🔍 CLINICAL PRACTICE APPLICATIONS:

- The mechanisms behind these findings are not well understood, but are likely to include: the complex endocrine interplay with insulin response and glucocorticoid secretion.
- Caution must be taken in terms of generalisability due to the small sample size of the included studies

Early or late TRE can determine the optimal time of alertness and sleep:

- Early TRE (eating 8am-2pm / skipping dinner), may allow for greater alertness in the morning as the lower levels of cortisol at night can improve sleep quality and higher morning cortisol raises alertness, optimising wakefulness and productivity.
- Late TRE (skipping breakfast) may provide greater alertness mid-day, due to an intensified cortisol response mid-day.

## ? CONSIDERATIONS FOR FUTURE RESEARCH:

Further larger studies should be conducted to:

- Examine TRE during the inactive and active phases of the circadian rhythm under controlled conditions.
- Exclude studies relating to pregnancy, pathology, and athletic status.
- Ensure sufficient control for confounding factors that can affect serum parameters, including sleep duration and timing, total energy expenditure, and light exposure



## EXPERT REVIEWER Dr. Michelle Barrow

CONFLICTS OF INTEREST: None

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

Dr Michelle Barrow is the Academic Team Director and Clinical Director at CNELM. Michelle completed a Doctorate in Professional Studies (DProf) in 2019, titled "Leading transformation in Personalised Nutrition Practice". Her doctoral research included the construction of clinical tools to enable the development of a new evidence base for personalised nutrition practice in obesity management. She strives to develop the evidence base to support personalised nutrition practice through her academic work, research supervision, post-doctoral research, and publication.

# ADDITIONAL RESOURCES

## CLIENT FOOD & LIFESTYLE GUIDES

In addition to NED resources we also provide a range of food and lifestyle guides suitable to share with clients as an introduction to generic healthful habits. The science behind these can all be found on [nutrition evidence](#)

**BANT** Twitter Facebook LinkedIn YouTube Instagram

### Adrenal Glands & Stress Hormones

The gateway to a cluster of symptoms including stress and anxiety, fatigue, disrupted sleep, weight imbalances and more...

**Adrenal Hormones** A finely-tuned protection system until it gets disrupted

The adrenal glands, located above the kidneys, are directly involved in regulating the body's stress response by secreting the steroid hormones adrenaline and cortisol. Hormones are chemical messengers that interact with each other in three ways; permissibly, synergistically and antagonistically, to control many metabolic processes. These two hormones act in unison to protect the body against short term stressors, often called the 'fight or flight response'. Once a perceived threat has passed, adrenaline and cortisol levels return to normal. The long-term activation of the stress response system, from psychological and mental stressors, and the overexposure to cortisol can disrupt almost all your body's processes. Cortisol curbs functions that would be nonessential or harmful in a fight-or-flight situation. It alters immune system responses and suppresses the digestive system, the reproductive system and growth processes. Over time, it triggers inflammation and puts you at increased risk of many health problems.

**Adrenalin** ↑

Adrenalin rapidly responds to stress by increasing your heart rate, elevating blood pressure to increase blood flow to the muscles and brain, and boosting energy supplies by helping to convert glycogen to glucose in the liver (glycogen is the liver's storage form of glucose.)

**Cortisol** ↑

Cortisol, the primary stress hormone, increases blood sugar levels (glucose) in the bloodstream and regulates metabolism. It enhances your brain's use of glucose and increases the availability of substances that repair tissues. It also regulates the inflammatory response, and immune function.

**Diet & Nutrition**

Diet can play an important role in supporting adrenal hormones, moderating the nervous system response to stressors and reducing inflammation. BANT nutrition practitioners assess and identify potential nutritional imbalances to understand how these may be contributing to adrenal imbalances and will optimise the diet accordingly to restore balance.

**FOOD FOR YOUR HEALTH**

Find a Practitioner at [www.bant.org.uk](http://www.bant.org.uk) © British Association for Nutrition & Lifestyle Medicine 2022

## CLIENT-FRIENDLY GUIDES:

Translating the science into clinical take-aways for clients to integrate into their daily routine.

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### Excessive stress can be harmful for health

Never before has your food choices been so important for your health and wellbeing.

Is stress overly affecting your life?

**Fight or flight response**

**FOOD FOR YOUR HEALTH**

**BANT** Twitter Facebook LinkedIn YouTube Instagram

### Learn to breathe better to live better

Never before has your food choices been so important for your health and wellbeing.

Are you breathing as well as you could?

**shallow breathing & stress**

**FOOD FOR YOUR HEALTH**

**BANT** Twitter Facebook LinkedIn YouTube Instagram

### Are you embracing enough natural light?

Never before has your food choices been so important for your health and wellbeing.

We are reliant on a daily cycle of light.

**Are for 10-20 minutes / daily to help you make Vitamin D**

**FOOD FOR YOUR HEALTH**

**BANT** Twitter Facebook LinkedIn YouTube Instagram

### Relax more and access your inner calm

Never before has your food choices been so important for your health and wellbeing.

Take charge of your everyday life.

**rest and digest response**

**FOOD FOR YOUR HEALTH**

[Download the fact sheet here](#)

[Download the guides here](#)

# FOLLOW US



Keep your finger on the pulse by following us on socials for weekly nutrition science and clinical resources.

Tune in on Tuesdays to our weekly pick of the science



## BANT on Social Media



BANT is committed to promoting the nutritional therapy profession across all channels so if you're not yet following us on social media, please come and join the conversation. The more you engage, like, comment, and share our BANT content, news and resources, the more we can grow our nutritional credibility and drive awareness of our profession.



You can influence your **HEALTH & WELLBEING**



### MODIFIABLE risk factors

**Do you get enough quality sleep?**  
Sleep hygiene, routine, fatigued vs. restored, day vs. night.

Sleep



Stress

**How stressful is your daily life?**  
Wired and tired, anxious, adequate support at work and at home.

Physical Activity



Microbiome

**How beneficial are your bacteria?**  
Digestive issues, nutrient absorption, immune tolerance.

**Do you exercise regularly?**  
Exercise type, frequency, duration, cardio vs. strengthening.



Toxic Environment

**How toxic is your everyday environment?**  
Chemicals and pollutants at home, at work, in food, in the air.

**How balanced is your diet?**  
What and when, food variety, special diets, intolerances, hydration.

Diet



**Nutritional therapy is the application of nutrition and lifestyle medicine to inform individualised recommendations for optimal health and wellbeing.**





Nutrition Evidence 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.

[www.nutrition-evidence.com/](http://www.nutrition-evidence.com/)



**BANT**<sup>®</sup>  
Science-based nutrition  
practice since 1997

