Building Capacity for Evidence Synthesis among Complementary and Integrative Medicine Learners: The Neurotrauma Evidence Synthesis Training (NEST) Program

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Introduction

- Traumatic brain injury (TBI) presents a significant global burden, with 69 million cases annually.
- The last decade has seen an increase in the quantity of systematic reviews and meta-analyses; however, the quality of existing reviews is low in a range of disciplines.
- There is a need for training in the conduct of high-quality evidence synthesis.

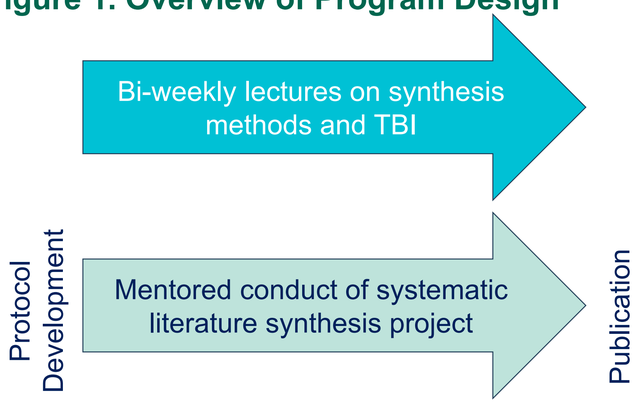
Objectives

The Neurotrauma Evidence Synthesis Training (NEST) program seeks to address this gap by building research capacity in evidence synthesis, particularly within complementary and integrative medicine (CIM) environments.

Methods

- "Train-the-trainer" model for structured mentorship in evidence synthesis and TBI-specific content.
- Trainees work in group on systematic evidence synthesis projects from protocol development to publication; some include topics beyond TBI.
- Education is delivered through synchronous and asynchronous online content and hands-on training.
- Evaluation includes both quantitative and qualitative measures to assess changes in evidence synthesis and TBI knowledge and evidence-based practice attitudes; completed spring 2024 and will be repeated after 1 year.

Figure 1. Overview of Program Design



Results

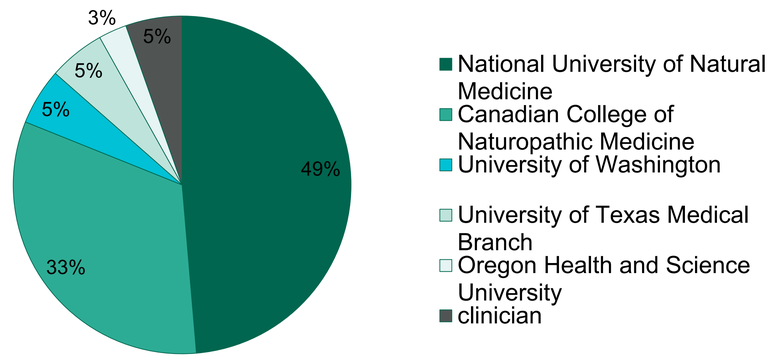


Figure 2. Educational institution affiliation for NEST participants

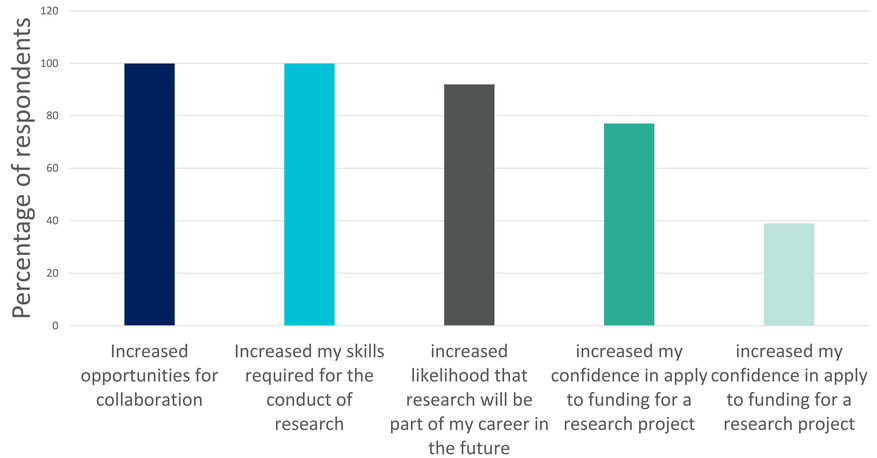


Figure 3. Participant responses about NEST experience

I've done other types of research in the past, like bench research, but I found that this was an opportunity that better aligns with my interest and also to learn more about evidence synthesis and the process of generating systematic reviews which I thought was better suited with my interest compared to bench research."

Figure 4. Quote from a NEST participant

NEST Projects	Status
The role of olive oil and its constituents in mental health: a scoping review	Published
The effects of supplemental curcumin on anxiety symptoms in adults: A systematic review and meta-analysis	Manuscript in preparation
The effect of Rosmarinus officinalis on depression, anxiety and psychological stress in adults: A systematic review and meta-analysis	Analysis in progress
Allium sativum and mental health: A scoping review	Data extraction in progress
Dietary protein and anxiety symptoms and disorders: A scoping review	Screening in progress
Convergence insufficiency after traumatic brain Injury: A S=systematic review	Iterative title/ abstract screening
Polyphenols	Data extraction in progress
Cognition, brain fog, and the microbiome: an overview of reviews	Data extraction in progress
Growth hormone	Data extraction in progress
Post-Traumatic epilepsy	Data extraction in progress
Mind-body practices for multiple sclerosis: An umbrella review	Search in progress

Discussions

- There is a high degree of interest among National University of Natural Medicine and Canadian College of Naturopathic Medicine students in learning about evidence synthesis.
- Early evaluation suggests that participants report benefits of participation.
- Several projects are underway and making progress, suggesting feasibility of this program in facilitating the conduct of systematic literature synthesis projects.

Conclusions

NEST addresses a critical gap in the field of neurotrauma research and provides a replicable model for building capacity in evidence synthesis.

Funding

Research reported in this publication was supported by the National Center for Complementary & Integrative Health of the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Mind Mood and Motherhood: Exploring CBT, Omega-3, and Yoga for Perinatal Depression: A Narrative Review

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Introduction

- Perinatal depression (PND) is a mood disorder that can occur during pregnancy and postpartum, affecting maternal well-being and fetal development.
- PND has been associated with complications such as preterm birth, low birth weight, prolonged labor, and an increased likelihood of cesarean delivery.
- Pharmacological treatments, including second-generation antipsychotics, are commonly used but have been linked to potential risks such as cardiovascular malformations and neonatal adaptation syndromes.
- Research into non-pharmacological treatment options is ongoing to identify effective and safe alternatives for managing PND and improving maternal and infant health outcomes.

Objectives

The objective of this study was to evaluate the effectiveness of non-pharmacological interventions for managing perinatal depression, exploring alternative approaches that may support maternal mental health and improve pregnancy outcomes.

Search Methods

- A systematic search was conducted in PubMed, Cochrane Library, and ScienceDirect for randomized controlled trials (RCTs) and meta-analyses on non-pharmacological interventions for perinatal depression.
- Studies were selected based on the PICO framework, including perinatal adult women with depressive symptoms, interventions involving yoga, omega-3 supplementation, or cognitive behavioral therapy (CBT), and a placebo control group. Depression outcomes had to be measured using the Edinburgh Postnatal Depression Scale (EPDS) or Beck's Depression Inventory (BDI).
- Non-randomized trials, studies with incomplete data, and RCTs already included in meta-analyses were excluded to maintain data integrity and prevent duplication.
- The search identified 174 studies—29 on yoga, 82 on omega-3 supplementation, and 63 on CBT—providing a broad evidence base for assessing the effectiveness of these interventions.

Table 1: PICO framework

Population	Intervention	Outcome
Perinatal adult women.	Yoga, omega-3, or CBT.	Changes in EPDS or BDI scale.

Results

Table 2: Yoga

Author	Interventions	Control	Result
Newham, J. J., et al. (2014)	8-week antenatal yoga course for women in the second/early third trimester.	Treatment-as-usual (TAU) control group.	. No significant difference in depression scores between groups, but yoga showed a preventative statistically significant effect against increased depressive symptoms.
Lin, I.-H., et al. (2022)	Meta of 9 prenatal yoga studies varying dosage (4-12 weeks total duration, 1-3 sessions per week, 30-75 minutes per session).	Various control conditions (non-yoga interventions or no treatment).	Prenatal yoga significantly reduced depression scores in women with diagnosed depression but not in those without depression.
Rong, L., et al. (2021)	12-week yoga intervention (60 min, 3x per week) for first-time pregnant women.	Routine prenatal care.	The yoga intervention did not result in a statistically significant difference in depression scores compared to the control group after the 12-week intervention.

Table 3: CBT

Author	Interventions	Comparison	Results
Yazdanimehr, R., et al. (2016)	Mindfulness-integrated Cognitive Behavior Therapy (MiCBT) for pregnant women(8 weeks, once per week, led by a psychologist).	Standard prenatal care.	Significant reduction in depression (EPDS scores decreased from 16.83 to 9.03 at follow-up).
Pettman, D., et al. (2023)	Meta-analysis of 26 RCTs on CBT-based interventions for perinatal depression (varied dosage:4-16 weeks total duration, 1-2 sessions per week, session length not consistently reported).	Studies using control conditions such as waiting list, treatment-as-usual, or other interventions.	CBT was found to have a medium effect size and be statistically significant in reducing depression (Hedge's g = -0.54). Large effect sizes for parenting self-efficacy and social support.
Zemestani, M., & Fazeli Nikoo, Z. (2019)	Mindfulness-Based Cognitive Therapy (MBCT) for pregnant women with comorbid depression & anxiety(8 weeks, once per week, group therapy format).	No treatment control group.	Significant decrease in depression (BDI-II) with large effect sizes. Increased psychological well-being and improved emotional regulation. Effects were maintained at follow-up.

Table 4: Omega 3

Author	Investigation	Comparison	Results
Mozurkewich, E.L., et al. (2013)	Omega-3 supplementation during pregnancy From 12-20 weeks gestation to 6-8 weeks postpartum, daily Omega-3 (EPA or DHA-rich).	Placebo group.	No significant reduction in depressive symptoms (BDI scores unchanged).
Zhang, M.M., et al. (2020)	Meta-analysis of 8 RCTs on Omega-3 for perinatal depression(4-16 weeks total duration, daily Omega 3 supplementation doses varied per study).	Placebo groups from included studies.	Moderate effect on reducing depression (SMD = 0.65, p = 0.02). Stronger effect for postpartum depression (SMD = 1.59, p < 0.001) than pregnancy depression. Both of these findings were statistically significant Shorter intervention duration (<8 weeks) was more effective. Higher EPA/DHA ratio (≥1.5) was more beneficial.
Vaz, J.D.S., et al. (2017)	Omega-3 supplementation (1.8g/day, EPA 1.08g + DHA 0.72g) for pregnant women at risk of postpartum depression.	Placebo.	No significant effect on overall depressive symptoms (EPDS scores). Women with a history of depression saw a greater reduction in EPDS scores (p = 0.038).

Discussions

Strengths

- All studies included were high-quality randomized, controlled trials and 3 of the 9 were meta-analyses.
- All 3 interventions were well tolerated and had good safety profiles.

Limitations

- Significant heterogeneity in intervention methodologies, particularly regarding dosage, duration, and delivery formats across studies.
- Adherence issues were noted in Omega-3 trials due to nausea and taste aversion, leading to high dropout rates in some studies.
- Many studies within the systematic reviews used a small sample size, contributing to large but non-significant effect sizes.
- The EPDS/BDI is a self-reported assessment, which can create social desirability bias.

Mechanism of Action

- Yoga: Lowers cortisol and enhances relaxation via parasympathetic activation. It boosts serotonin and dopamine for mood regulation.
- CBT: Helps reframe negative thought patterns and encourages positive behavioural changes and social engagement.
- Omega 3: Enhances serotonin and dopamine activity and reduces neuroinflammation.

Further Research Needed

- Research is needed to determine whether combining these therapies enhances their effectiveness compared to using them individually.
- Strategies to reduce dropout rates in Omega-3 trials, such as improved formulation, shorter duration, and taste modifications, require further investigation.
- The effectiveness of CBT across different delivery methods— in-person, virtual, or self-guided—needs to be systematically evaluated to identify optimal outcomes.
- Further studies are necessary to establish the ideal duration, dosage, and frequency of these treatments for maximum efficacy.

Conclusions

Based on the available evidence, CBT, yoga, and omega-3 supplementation may serve as effective interventions for perinatal depression. These interventions have minimal adverse effects and can be integrated into prenatal care to enhance maternal mental health. Further research is needed to address the use of these interventions in combination.

For references or further questions, please email: nstanley@ndnet.ccnm.edu

The Teaching Kitchen Landscape in Canada & the United States: a scoping review

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Introduction

Public health researchers have concretely established the role of diet and nutrition in disease prevention and management across all population levels. While many programs aim to enhance the nutrition literacy of their participants, there is a role for food skill instruction to equip individuals with skills needed to translate nutritional knowledge at a practical level. Teaching kitchens (TK) provide "*hands-on culinary instruction with concurrent education of nutritional concepts, exercise, mindfulness, and behavioral change*". This scoping review study aims to provide a foundation to inform future implementation practices of such initiatives, in improving health outcomes, food literacy, and food agency in program participants.

Objectives

- To map the extent of TK utilization in Canada & the United States.
- To identify common implementation methods used in TK programs.
- To identify potential benefits at both the individual and population level.
- To build a foundation of evidence to inform future research.

Methods

Table 1: Arksey and O'Malley Framework Stages

Identify the research question	• What does the existing body of literature reveal on the use of teaching kitchens, and how they are implemented to improve cooking skills, food literacy, and health outcomes?
Identify relevant studies	• A preliminary search of key databases (PubMed, CINAHL) was undertaken to identify articles on the topic. • All identified keywords and index terms adapted for each information source and included searches on PubMed, MEDLINE, CINAHL, and Cochrane databases. • Studies published only in English, from 2011-2021, involving hands-on instruction, and conducted in Canada and the United States were included.
Study selection	• All identified citations were collected and exported to an online screening (Covidence) and duplicates removed. • Title and abstracts screened by two independent reviewers for assessment against inclusion/exclusion criteria. • Full text review was completed by two reviewers.
Chart the data	• Data extracted using extraction tool developed by reviewers including study information, participant details, and concept, context, methods, and key findings relevant to the review question.
Collect, summarize, and report the results	• Extracted data to be charted and presented in narrative summary and descriptive analysis will be conducted to report on variety of implementation strategies, methods, objectives, and context of delivered programs.

Screening Protocol

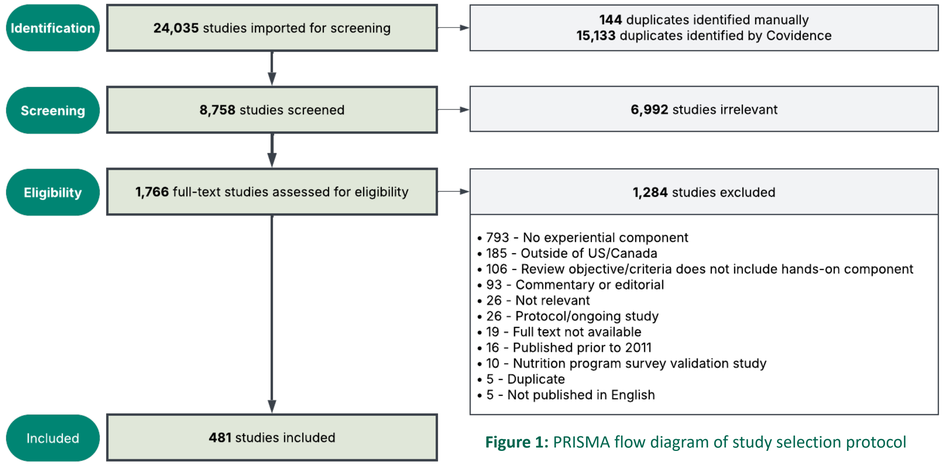


Figure 1: PRISMA flow diagram of study selection protocol

Results

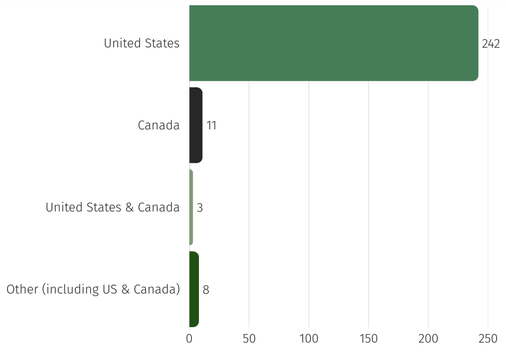


Figure 2: Program locations by country (n=264)

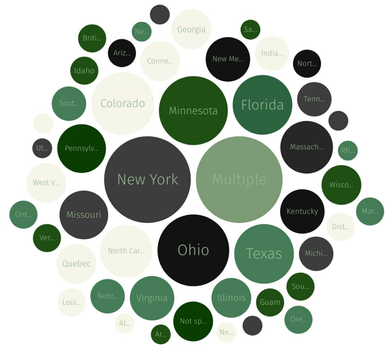


Figure 3: State/province of program (n= 237)

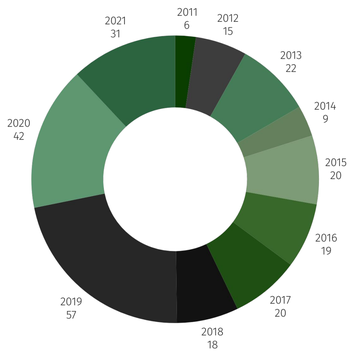


Figure 4: Year of study publication (n=259)

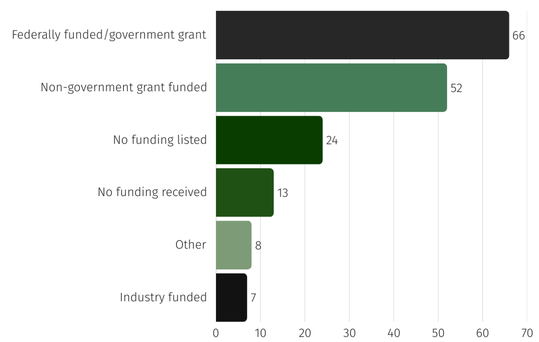


Figure 5: Study funding (n=154)

Results cont'd

Figure 6: Program target audience – many programs target multiple demographics (n=134)

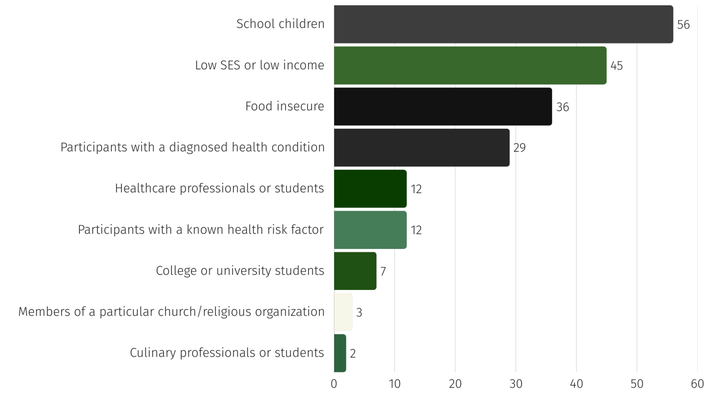
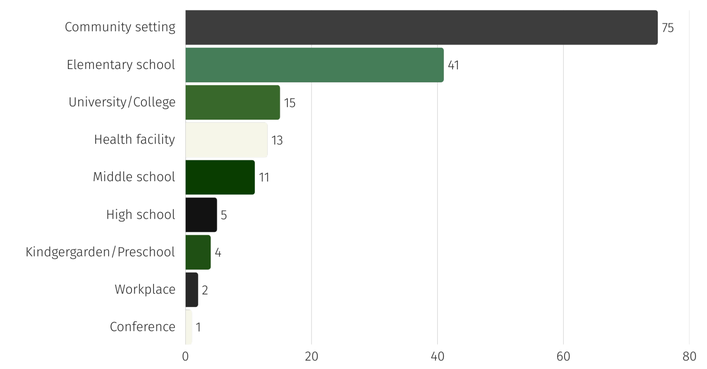


Figure 7: Program setting (n=167)



Current Stage in Review

- Over 50% of data extracted by two independent reviewers and consented on.
- Remaining articles have been extracted and currently being reviewed by one reviewer.
- Next steps involve cleaning up raw data, and reporting on results.

Conclusions

Preliminary findings suggest that TK programs are being researched and utilized in Canada and the United States in a variety of contexts. The results obtained through this scoping review may assist in guiding programs and initiatives to identify the impact of TK programs, and provide a useful tool for collaboration and advancement within the field.

For references or further questions, please email: ginavbrown8@gmail.com

Investigating the effect of nicotinamide mononucleotide (NMN) supplementation on aging maternal oocytes: A narrative review

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Introduction

- The proportion of mothers of 35 years of age or older is increasing yearly in Canada. In 2021, a quarter of all live births were by mothers over the age of 35.
- The quality of oocytes deteriorates with age, contributing to reproductive challenges in older women.
- NMN, a precursor to nicotinamide adenine dinucleotide (NAD), may enhance mitochondrial function by boosting NAD+ levels, improving energy production, and reducing oxidative damage.

Objectives

The purpose of this review was to analyze existing evidence on whether NMN is associated with oocyte quality and age-related chromosomal abnormalities in mothers of advanced maternal age.

Search Methods

- PubMed and The Cochrane Library were used to search for available literature with the following inclusion criteria:
  1) Female mammals (animals or humans)
  2) Treatment of aged oocyte with NMN as a sole intervention
  3) Control group without treatment (placebo/untreated)
  4) Analysis of oocyte quality as an outcome
  5) Experimental studies
  6) Peer-reviewed article
- The search string "(Nicotinamide mononucleotide OR NMN) AND aging oocytes" was used.
- The search yielded 13 studies, of which 8 studies met the inclusion criteria and included 7 experimental animal studies (6 *in vivo*, 1 *in vitro*), and 1 *in vitro* human study.

Table 1. PICO Framework

Population	Intervention	Comparison	Outcomes
Female mammals	NMN supplementation	Placebo or untreated	Oocyte quality or other measures relating to oocyte & reproductive health

Results

Table 2. Summary of Evidence

Author	Intervention	Control	Key Results
Miao et al., 2020	68-week-old mice injected with NMN (200 mg/kg body weight) daily for 10 consecutive days.	Young (6 weeks old) & aged (68 weeks old) mice injected with PBS (200 mg/kg body weight) daily for 10 consecutive days.	↑ ovulation rate ↑ mitochondria function ↑ oocyte quality ↑ fertilization ability ↓ apoptosis ↓ oocyte DNA damage from ROS
Bertoldo et al., 2020	12-month-old female mice treated with NMN in drinking water (2 g/L water) daily for 4 weeks.	12-month-old female mice without NMN in drinking water for 4 weeks.	↑ ovulation rate ↑ blastocyst quality ↑ live births ↑ litter size ↓ meiotic defects ↓ pregnancy loss
Huang et al., 2022	40-week-old female mice treated with NMN (0.5g/ml water) daily for 20 weeks.	4, 8, 12, 24 and 40-week-old mice female treated with saline daily for 20 weeks.	↑ condition of estrous cycle ↑ endocrine function ↑ # of follicles & corpus luteum ↑ mitochondria ↑ protease activity ↑ autophagy level ↓ aging & inflammation ↓ P16 in ovaries
Liang et al., 2024	**Short-term:** 12-month-old female mice injected with NMN (500mg/kg body weight) daily for **10 consecutive days** **Long-term:** 12-month-old female mice treated with NMN in drinking water (2g/L water) daily for **8 weeks.**	**Short-term:** 2-month-old (young) and 12-month-old (aged) female mice injected with saline daily for **10 consecutive days** **Long-term:** 2-month-old (young) and 12-month-old (aged) female mice without NMN in drinking water for **8 weeks.**	↑ serum anti-aging effects ↑ ovarian health & reserve ↑ oocytes & quality ↑ mitochondrial function ↑ energy metabolism ↓ ovarian atrophy ↓ ovarian inflammation (IL-1β & TNF-α)
Li et al., 2023	Matured oocytes cultured in porcine Zygote Medium with NMN (1µmol/L, 10µmol/L, 100µmol/L) for 24h or 48h at 38.5°C with 5% CO_2.	Matured oocytes cultured in porcine zygote medium without NMN.	↑ antioxidant genes (SOD1 & Cat) ↑ mitochondrial membrane potential ↑ anti-apoptotic gene (BCL-2) ↑ development ability ↑ blastocyst synthesis rate ↑ pluripotent genes ↓ ROS levels ↓ pro-apoptotic gene (Bax)
Yang et al., 2020	6-week-old Mut/Mut*** mice treated with NMN in sterile drinking water (900mg/kg body weight) daily for 2 weeks.	6-week-old Mut/Mut*** mice treated without NMN in sterile drinking water daily for 2 weeks.	↑ NADH/NAD+ ratio (↓ infertility) ↑ stem cell mitophagy ↑ cell function recovery (-) mtDNA point mutations of follicles (-) primordial & mature follicles (-) mitophagosomes
Habibalahi et al., 2022	Aged (12-month-old) female mice treated with NMN in drinking water (2g/L water) daily for 4 weeks.	Aged (12-month-old) & young (4- to 5-week-old) female mice treated without NMN in drinking water daily for 4 weeks.	↑ oocyte morphological properties
Urrutia et al., 2022 ***Human *in vitro* study**	Germinal vesicles of older females (>35 years old) and young females (≤35 years old) treated with 100µM of NMN.	Germinal vesicles of older females (>35 years old) and young females (≤35 years old) without NMN.	**Older females:** ↑ time to 1st polar body extrusion ↑ duration of MI ↑ germinal vesicle competence **Young females:** ↑ cytoplasmic competence ↑ duration of MI ↓ permanence of germinal vesicles

Discussions

Most studies found improvements in: levels of NAD+/NADPH, mitochondria/function, meiotic competence, fertilization capacity, oocyte yield, developmental potential of embryo, and ovarian inflammation. Morphological and metabolic properties were also commonly comparable to those of younger counterparts.

Strengths

- Most studies used similar methods for administration method (NMN in drinking water or injected), dosing strategies for intervention and comparison groups, and ages for 'young' and 'aged' mice.
- Administration timelines varied across studies, illustrating broad benefits across a range of strategies.

Limitations

- 12 out of 13 studies investigated animal populations (mice or pigs), limiting the generalization of these findings to humans.

Clinical Application

- Given the consistency of these preclinical findings, it is possible that NMN supplementation may have a positive effect on the health of aging oocytes in humans.

Future Directions

- Additional clinical evidence on humans is needed to strengthen these prospective insights and perhaps assist in addressing fertility challenges in mothers of advanced maternal age.

Conclusions

Exposure to NMN provides favourable improvements to animal oocyte and reproductive quality in preclinical studies. Additional clinical evidence on humans is needed to determine whether NMN can reduce fertility challenges in mothers of advanced maternal age.

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Pilot testing of a diet cost calculation process for the EASe-GAD (Eating and Supplementation for the treatment of Generalized Anxiety Disorder) Study

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Introduction

- Emerging evidence demonstrates a positive effect of dietary counselling on mental health outcomes, including generalized anxiety disorder.
- A barrier to dietary counselling is patient and clinician perception that these recommendations will be associated with a higher cost.
- There is insufficient data to determine the effect of dietary interventions on total food costs.
- There are limited methods that have been developed for the calculation of cost difference between diets.

Objectives

To develop and pilot test a diet reporting tool for the collection of information necessary for the calculation of dietary costs.

Methods

- Draft diet reporting tool and instructions were developed.
- Participants from previous EASe-GAD study were recruited and asked to record food intake for 7 consecutive days.

Figure 1. Diet Reporting Tool Sample

Day 1 Date: ___Example_____ Participant ID #: ____01____

Time	Foods Eaten	Individual Ingredients (for prepared items)	Portion	Brand or Menu Name of Item	Store/restaurant where purchased	Any Additional Notes (optional)
9am	Breakfast sandwich		2 whole sandwiches	Egg McMuffin	McDonalds	
	Coffee with oat milk		1 grande	Mocha	Starbucks	
11am	Apple		1 whole	Gala	Food Basics	
1pm	Peanut butter		2 Tbsps	Skippy	No Frills	
	White bread		2 slices	Wonder	Sobeys	
6pm	Chicken stir fry	Chicken	4 oz	President's choice	No Frills	
		Red pepper	1 whole		Sobeys	
		Rice	1 cup	Uncle Bens	Food Basics	
		Teriyaki stir fry sauce	1 Tbsp	VH	Sobeys	

- Participants provided feedback on experience during a qualitative interview to:
  - Assess acceptability
  - Guide modifications
- Diet diary data is being analyzed to assess:
  - cost per item
  - weekly total food expenditure
  - Feasibility of tool (based on percentage of items that cost data can be determined for).

Results

Figure 2. Qualitative and Quantitative Study Outcomes

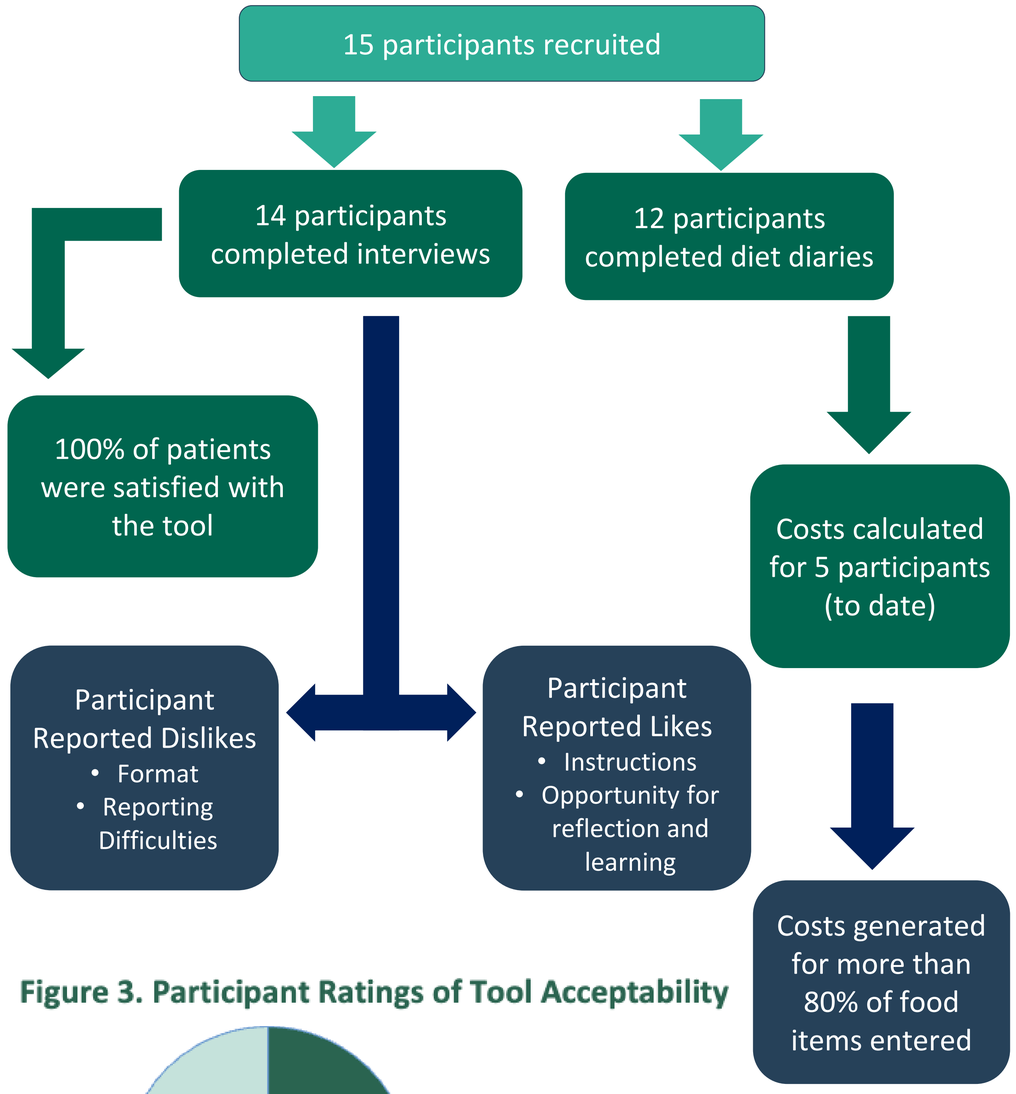
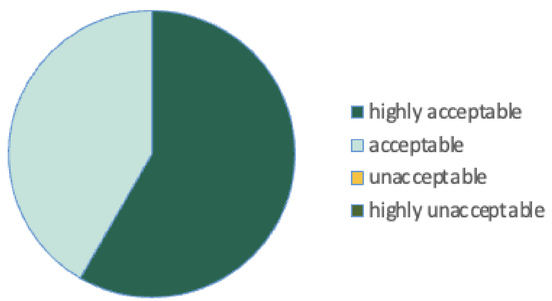


Figure 3. Participant Ratings of Tool Acceptability



Discussions

Findings

- Cost analyses suggest data acquired through tool is sufficient to determine diet cost.
- Cost calculation labour ranged from 2.5 to 6 hours per participant per week.
- Areas of challenge: missing store data, local stores without websites.

Next Steps

- Modifications to improve tool instructions.
- Modifications to tool format to increase acceptability and ease of use.

Table 1: Recommended Diet Tool Template Modifications

Change	Rationale
Format	Barrier free access and ability to record data on phone increase accessibility
Instruction Clarification	Provide greater detail on how to record restaurant meals, batch recipes or homemade foods to ensure participant reporting of information is accurate and relevant
Repeat a meal feature	Reduce repetition and reporting burden
Tool training	Training may minimize common errors and clarify understanding
Collect price data for restaurant items	Participants were aware of the price of the meal and willing to record this information

Conclusions

Early findings of this pilot study suggest that the creation of a diet tool for collecting data needed for diet cost calculation is both feasible and acceptable.

Funding Acknowledgement

Research reported in this publication was supported by the National Center for Complementary & Integrative Health of the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

For references or further questions, please email: nyoannou@gmail.com

A Narrative Review on the Efficacy of Creatine Monohydrate, Caffeine, and Nitrate on Athletic Performance

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Introduction

This narrative review was conducted to investigate the efficacy three of the most common physiological ergogenic aids - creatine, caffeine, and nitrate - in enhancing 1-repetition maximum (1-RM) strength in bench press and squat variations. Ergogenic aids, categorized into mechanical, psychological, physiological, pharmacological, and nutritional types, are widely used to improve athletic performance. With a significant economic impact and history of usage, these aids require informed, evidence-based recommendations by healthcare professionals to ensure appropriate use and maximal impact.

Objectives

To investigate the efficacy of creatine monohydrate, caffeine, and nitrate in improving strength measurements in back squat and/or bench press 1-RMs

Search Methods

- Search parameters: Article Type: Full Text, Clinical Trial, Meta-Analysis, Randomized Control Trial, Systemic Review, Humans, from 2018/1/1 – 2023/9/30

Table 1: PICO framework

Population	Intervention	Outcomes
• >/ 18 years old • Experienced in squat & bench press variations • Have been engaged in a regimented training program for at least 3 months • Had not taken the investigated aid within the last month • Free from injury, pathology, anti-inflammatory medications, and dietary supplements which may impact muscular performance or biology	• Creating supplementation + training 4-20g for 4-6 weeks • Caffeine supplementation + training 250mg to 750mg 48hours to 7 weeks • Nitrate supplementation + training 400mg/70mL to 12mmol for 3- 4 weeks	Primary: • Percent increase in 1-RM strength Secondary: • Biomarkers of muscle damage • Body composition

Results

11 articles were included to determine the impact of creatine, caffeine, & nitrate in the enhancement of muscle strength & performance as displayed by a 1-RM contraction in a squat variation and/or bench press.

CREATINE:

- Compared to placebo, creatine (20g x6 days, 2g x 22 days and 4g/day) showed a significantly greater increase in back squat & bench press 1-RM.
- After 4 weeks, a combination of resistance training and creatine supplementation (20g x6 days, 2g x 22 days) significantly increases back squat 1-RM compared to resistance training alone.
- After 6 weeks, 4g to 10g/day of creatine elicited significant increase in leg press, back squat, & bench press 1-RM compared to baseline.

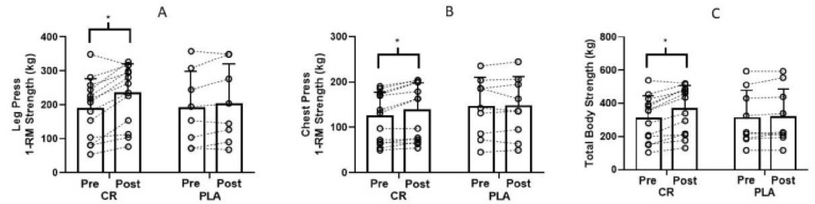

Figure 1. Impact of creatine on leg press, chest press, & total body strength 1-RM.

CAFFEINE:

- Compared to 300mg caffeine, coffee (8.9g dehydrated) elicited a significantly greater improvement in leg press 1-RM.
- Compared to baseline, coffee (8.9g dehydrated) elicited a significantly greater improvement in leg press 1-RM.
- Subgroup-analyses revealed a significant increase in maximal upper body muscle strength associated with caffeine consumption, however no significant differences were noted in maximal lower body strength.
- Compared to placebo, ~472mg of caffeine 60 minutes prior to exercise elicited a significant improvement in bench press 1-RM.
- Compared to control, ~472mg of caffeine 60 minutes prior to exercise elicited a significant improvement in bench press & back squat 1-RM.
- No significant effect was observed in 1-RM performance following 250mg, 500mg, or 750mg doses of oral caffeine rinse.

NITRATE:

- 12mmol/140mL 2.5 hours prior to exercise elicited no difference in back squat 1-RM performance compared to placebo.
- Subgroup analysis indicates that there is an increase in back squat 1-RM performance following nitrate supplementation, however there is a relationship between efficacy and the dosing regime followed.
- At 50% back squat 1RM, 400mg/70mL 120 minutes prior to exercise elicited an increase in mean velocity, mean power, and peak power.

Discussions

- Creatine enhances ATP production for high-intensity exercise and may reduce delayed-onset muscle soreness (DOMS).
- Caffeine boosts performance by reducing perceived exertion and mobilizing fatty acids. Studies show liquids may outperform capsules, with potential added benefits from coffee's bioactive compounds. While some ergogenic effects may be placebo-driven, chronic caffeine use could still enhance training volume and strength.
- Nitrate supplementation may aid in blood flow and oxygen delivery to muscles, however its efficacy as an ergogenic aid may be inferior to that of creatine or caffeine.
- Future research may wish to control for dietary intake of creatine, ensuring all individuals studied have equal familiarity with technique & execution of exercises, and increasing number of female subjects in study populations for transferability to general practice.

Clinical Application

- Creatine has been shown to elicit significant improvements in muscular strength within a 4-to-6-week timeframe when combined with a resistance training program consisting of a minimum of 2 to 4 sessions per week compared to placebo. A general guideline for creatine dosing should follow 5g/day, taken intra- or post-workout on training days.
- Caffeine dosing is generally recommended at a rate of 3-9mg/kg, to be consumed approximately 1-hour prior to initiating exercise.

Conclusions

Creatine and caffeine have strong evidence for improving athletic performance, while nitrate supplementation may be a secondary consideration.

For references or further questions, please email: segan@ndnet.ccnm.edu

The Effects of Supplemental Curcumin on Anxiety Symptoms in Adults: A Systematic Review and Meta-Analysis

Katherine Kartusch [1], Zoe Beal [1], Laura LaChance [2], Joshua Goldenberg [3], Monique Aucoin, ND [1,2]

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Introduction

- Anxiety disorders are the world's most common mental disorders and can have a profound impact on an individual's daily life.
- Evidence suggests that curcumin, which has been shown to have antioxidant, anti-inflammatory and neuroprotective properties, may aid in the alleviation of depression symptoms.
- Less is known about the impact on anxiety symptoms.

Objectives

To conduct a systematic review and meta-analysis of the human experimental studies assessing the impact of curcumin on anxiety symptoms.

Search Methods

- PubMed and Web of Science databases were searched.
- Title and abstract screening and full text screening were completed in duplicate.
- Data was extracted independently in duplicate.
- Planned subgroup analyses includes baseline anxiety severity (moderate/severe vs. low BAI score) and standard vs. enhanced-bioavailability curcumin.

Table 1: Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
1. >/ 18 years old	1. Observational studies, review articles, opinion papers, editorials, letters, case studies, case reports, book chapters, and non-human studies
2. Controlled or uncontrolled human experimental trials	2. Studies not published in English
3. Any delivery method of curcumin at any dose	3. Studies that combine curcumin with other interventions
4. Report impact of curcumin on anxiety symptom severity	

Results

- 329 articles identified; 14 studies met the inclusion criteria for the systematic review (12 RCTs for the meta-analysis, total n = 980).
- Curcumin doses ranged from 80mg-4500mg, and the duration ranged from 4 to 12 weeks.

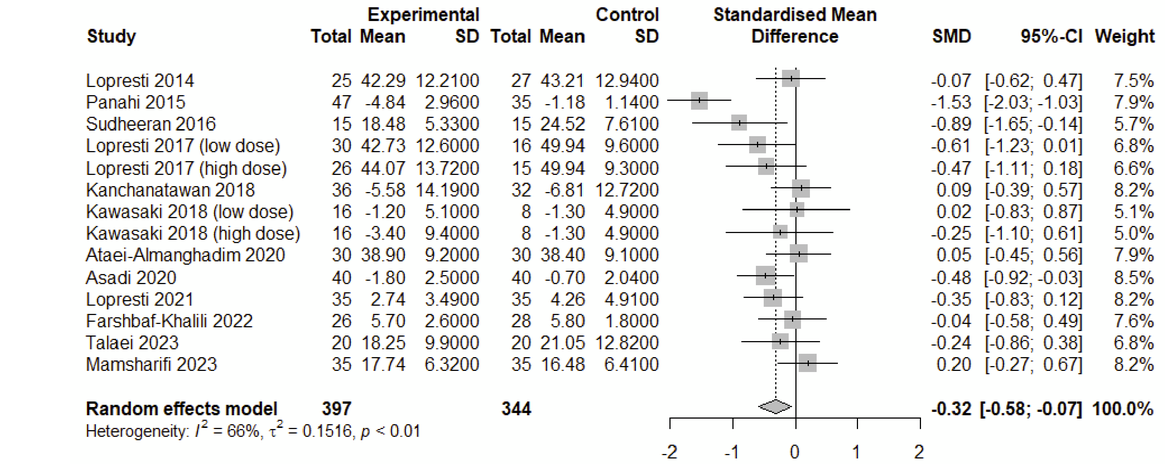

Figure 1. Effect of curcumin supplementation on anxiety symptom severity. SMD -0.32 (95% CI -0.58;-0.07) I^2 66%.

Certainty assessment							№ of patients		Effect		Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	curcumin	placebo	Relative (95% CI)	Absolute (95% CI)	
Anxiety symptom severity (follow-up: range 4 weeks to 12 weeks; assessed with: various)											
12	randomised trials	serious[a]	not serious[b]	not serious	serious[c]	none	397	344	-	SMD **0.33 SD lower** (0.58 lower to 0.07 lower)	⨁⨁◯◯ Low[a,b,c]
Anxiety Symptom severity (low risk of bias)											
10	randomised trials	not serious	not serious	not serious	serious[c]	none	335	294	-	SMD **0.17 SD lower** (0.33 lower to 0)	⨁⨁⨁◯ Moderate[c]
Anxiety Symptom severity (BAI)											
12	randomised trials	serious[a]	not serious	not serious	serious[c]	none	397	344	-	MD **2.89 lower** (5.13 lower to 0.64 lower)	⨁⨁◯◯ Low[a,c]
Anxiety Symptom Severity (BAI, low risk of bias studies)											
10	randomised trials	not serious	not serious	not serious	serious[c]	none	335	294	-	MD **1.36 lower** (2.42 lower to 0.3 lower)	⨁⨁⨁◯ Moderate[c]

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. 12 of 14 studies were low risk of bias using ROB2, subgroup analysis does suggest a significant test of interactions (p<0.01)
b. Potentially significant heterogeneity (I2=66%, p<0.01) was explained by a single study. Removal of this study resulted in I2=10%, p=0.34.
c. Based on new GRADE guidance these finding as rated as imprecise because the lower confidence interval equates to a clinically meaningless change in symptoms.

Figure 2. GRADE

Sub-analyses

- "Leave one out" sensitivity analysis: excluding Panahi (2015) reduced heterogeneity to 10%.
- Participants in 10 of the studies had moderate to severe baseline anxiety; no difference on sub-analysis.
- Eight studies used enhanced-bioavailability curcumin, trend towards greater impact on anxiety among studies using enhanced form.
- Meta-regression did not identify an effect based on dose.

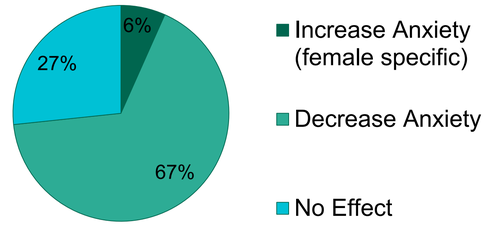

Figure 3. Effect of curcumin supplementation

Discussions

Possible Mechanism of Actions

- Curcumin's antioxidant properties may counteract ROS-induced neuroinflammation, neurodegeneration and anxiety.
- Curcumin can enhance DHA synthesis, potentially mitigating DHA deficiency-linked anxiety.
- Curcumin has been shown to upregulate BDNF, offering neuroprotection against the anxiety risk factor BDNF Val66Met SNP.

Clinical Significance

- Findings suggest a potential clinically meaningful change in anxiety symptom score, however, the lower bound of the confidence interval includes a clinically meaningless effect.

Limitations

- Four studies measured anxiety as a secondary outcome.
- Lack of studies with a duration > 12 weeks.

Future Research

- Long-term randomized controlled trials focusing on anxiety as a primary outcome.
- Consideration of absorption and bioavailability.

Conclusions

The findings of this systematic review and meta-analysis suggest that supplementation of curcumin may be associated with a reduction in anxiety symptoms.

Funding

Research reported in this publication was supported by the National Center for Complementary & Integrative Health of the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health

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Case Report on Short-Term Fasting During FOLFOX Chemotherapy in a Stage IV Colorectal Cancer Patient

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Introduction

- Colorectal cancer is the fourth most diagnosed malignancy in Canada.
- Colorectal cancer tends to have worse outcomes in men despite affecting both sexes evenly.
- Chemotherapy is often part of the prescribed antineoplastic regimen.
- FOLFOX is the first line chemotherapeutic combination for advanced stage IV disease.
- Chemotherapeutic side effects are the reason for treatment pauses, delays and discontinuation.
- This contributes to poorer outcomes and increased cancer mortality.
- As a result, there has been great interest in adjunct dietary interventions to help mitigate these events.
- Short term fasting is one of the researched approaches.

Case Presentation

- RB is a 63-year-old Caucasian male diagnosed with early-stage colorectal cancer via colonoscopy in April 2021.
- He declined all treatment, including surgery, from his initial diagnosis (2021) to June 2023.
- In June 2023, he presented to emergency with a bowel obstruction due to tumor bulk and a subsequent bowel resection was performed with stoma creation.
- At this time, he was upstaged to Stage IV disease, as it was discovered that RB had liver and lung metastases.
- RB presented to the Integrated Cancer Clinic at the Canadian College of Naturopathic Medicine in August 2023, prior to starting FOLFOX chemotherapy.
- He was seeking adjunct therapies to help him prepare for chemotherapy and mitigate anticipated side effects.
- At the initial appointment, he was recommended short-term fasting surround his chemotherapy treatments.

Intervention

- RB chose to fast for 72 hours total surrounding his chemotherapy.
- Specifically, he fasted 24 hours before the infusion, the day of the infusion and 24 hours post infusion, as 5-Fluorouracil is given over 48 hours.

Day -2	Day -1	Infusion Day	Day +1	Day +2
Normal Diet	FASTING			Normal Diet

Results

Table 1. Patient's Progress During Treatment

Visit Date	Weight (lbs), BMI	Objective Findings	Subjective Report
10-Aug-2023	111.9 BMI: 18.1	• Sunken in facial appearance • Generalized pallor and frailty noted • Cachexic appearance • Height: 5'6"	• Fatigue interferes with daily function • Anxious to start chemotherapy
14-Sep-2023	125 BMI: 20.2	• Looks well • Facial tissue has filled in • Weight gain visibly noted from first visit	• Started short-term fasting • Reports very mild and tolerable neuropathy post infusion • States has more energy • Able to re-introduce more foods
7-Dec-2023	125 BMI: 20.2	• Appears well • Weight stable from last visit	• Short-term fasting continued • Reports minimal side effects of chemotherapy • States imaging showed 50% reduction in liver metastases and shrinkage of primary tumor • Being considered for stoma revision
15-Feb-2024	127 BMI: 20.5	• Appears well • Weight increased from last visit	• Short-term fasting continued • Continues to experience minimal side effects from FOLFOX

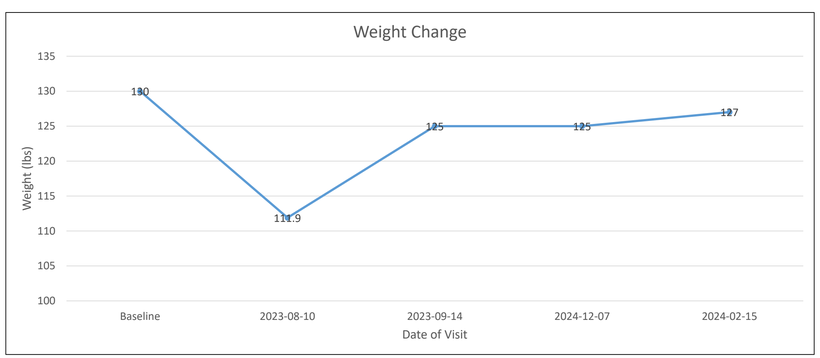

Figure 1. Patient's Weight Changes

Discussions

- The proposed mechanism of action for short-term fasting during cancer treatment is the exploitation of the Warburg Effect.
- Cancer cells rely solely on glycolysis to produce energy and can not switch their metabolic mechanism to accommodate for higher energy needs in times of stress.
- This makes cancer cells particularly vulnerable during short-term fasting as there is a lack of nutrients while normal cells protect themselves via switching metabolic pathways to meet energy needs.
- As a result, chemotherapeutic agents are more effective in targeting malignant cells leading to better tumor response with mitigation of side effects.
- In this case report, the patient was able to tolerate FOLOX with minimal side effects and regain weight while implementing a 72 hour fast surrounding his chemotherapy infusions.
- More research is needed to establishing safety and efficacy of short-term fasting in late-stage colorectal cancer patients undergoing chemotherapy.
- The findings of this case report can not be generalized as it presents a positive outcome in only one patient.

Conclusions

- This case report presents a positive outcome of short-term fasting (72 hours) surrounding FOLFOX chemotherapy by improving tolerance of the agent, reducing side effects and aiding in weight restoration in a stage IV colorectal cancer patient.
- Large scale studies are needed to establish short-term fasting as a mainstream intervention for improving chemotherapy tolerance and response.
- Naturopathic oncology providers should continue to consult relevant research prior to recommending any type of fasting in late-stage cancer patients receiving chemotherapy.

For references or further questions, please email: ocalderon@ndnet.ccnm.edu

Allium sativum and Mental Health: A Scoping Review

Vanessa Eedy, CCNM student [1],Hisham Al Osh, CCNM student [1], Rudo Duri, NUNM student [2] , Laura LaChance, ND [1] , Joshua Goldenberg, ND[2], Monique Aucoin, ND [1,3]

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Introduction

- The prevalence of mental illnesses remains high.
- Recent research has begun to examine the potential of dietary interventions as therapeutic strategies.
- Garlic has antioxidant and anti-inflammatory properties; inflammation and oxidative stress are implicated in mental illness pathogenesis.
- Garlic intake is associated with positive outcomes for cardiovascular disease, metabolic disease, and cancer; but less is known about the impact on mental health.

Objectives

To systematically search for and synthesize the research on garlic and mental health in a scoping review.

Search Methods

- PubMed, Embase (Ovid), Web of Science (Core Collection), CINAHL, and grey literature were searched.
- Titles and abstracts and full text articles were screened independently by two reviewers.
- Two authors independently extracted data from articles and final data were checked by another author.
- Data were analyzed qualitatively to identify patterns and trends as well as gaps in the existing literature.

Table 1: Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
· Human experimental or observational studies, animal studies, systematic reviews, meta-analyses · Intake assessment or delivery of garlic or one of its constituents (such as allicin/diallyl thiosulfonate, alliin/S-allyl-cysteine sulfoxide) · Assessment of any mental health outcome (validated mental health questionnaires, diagnostic criteria of mental disorders, and/or self-reported measures) · Any year of publication, language or publication status	· Narrative reviews, editorials, opinion articles, cell culture studies.

Results

- The search yielded 5,637 results. After abstract screening, 46 results remained. After full-text screening, 32 studies were eligible for inclusion.

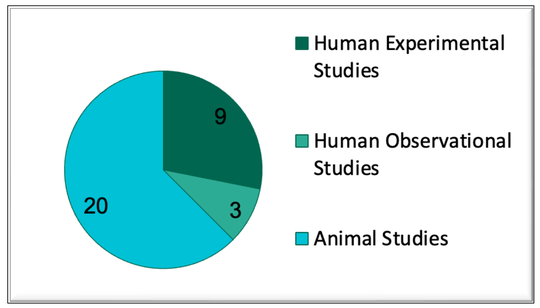

Figure 1. Number of each study design eligible for inclusion

Table 2: Human Experimental Studies

Study	Design	Participants	Sample size	Intervention/ duration	Outcome	Result
Jafari, 2021	RCT	Women with PMS	129	Garlic, 12 weeks	Mood symptoms	Improved
Nishimatsu, 2014	RCT	Men with symptoms of aging	49	Garlic + combo herbal product, 26 weeks	Depression, psychological symptoms	No difference in depression, improved psychological symptoms
Peleg, 2003	RCT	Adults with primary hypercholesterolemia	33	Garlic + dietary counselling, 16 weeks	Depression, impulsivity	No difference
Wahyudi, 2022	RCT	Chronic kidney disease patients	40	Garlic, 6 weeks	Quality of life, mental health	Improved
Kade, 1993*	RCT	Unspecified	39	Garlic + gingko, 1 week	Well-being	Improved
Nagata, 2017*	RCT	Healthy adults	49	Garlic, 4 weeks	Mood, stress	Improved
Nakasone, 2015*	RCT	Workers with mild work stress	54	Garlic + egg yolk, 8 weeks	Perceived mood	Improved
Ohiro, 2013*	Un-specified	Active workers with insomnia and fatigue	17	Garlic, 8 weeks	Mood	Improved
LarijaniV, 2012*	RCT	Male firefighters at risk for coronary artery disease	65	Garlic + CoQ10, 52 weeks	Perceived mental stress	Improved

*unable to access full text article

Animal Studies

- Most animal studies reported an improvement in anxiety-like behaviours. Additional analysis in progress.

Discussions

Strengths

- Multiple databases were used, including a grey literature search.
- Defined eligibility criteria and duplicate screening reduced bias in selecting studies for inclusion.

Limitations

- Few human experimental and observation trials eligible for inclusion.
- Some studies used combination interventions.
- Dose and duration of garlic varied between studies.
- Several studies could not be accessed in full text form.

Possible Mechanism of Action

- Many studies suggest garlic's impact on mental health may be attributed to its antioxidant and anti-inflammatory properties. Some studies also suggest garlic has an impact on levels of monoamine neurotransmitters in the brain, namely serotonin and dopamine.

Further Research

- More human randomized controlled trials are necessary to assess the potential benefits of garlic for mental health.

Conclusions

Garlic may have a beneficial impact on mental health; however, human experimental studies using garlic as a monotherapy are needed.

Funding

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For references or further questions, please email: veedy@ndnet.ccnm.edu

The effect of *Rosmarinus officinalis* on depression, anxiety and psychological stress in adults: A systematic review

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Introduction

- Mental health is key to well-being, shaping emotions, quality of life and relationships.
- *Rosemarius officinalis* (Rosemary), a Mediterranean plant, is know for many therapeutic properties.
- Rosemary's effects may be linked to its influence on the nervous system, modulation of noradrenergic, dopaminergic and serotonergic pathways.
- No previous systematic reviews have assessed the impact of Rosemary on mental health symptoms or disorders.

Objectives

To systematically assess the effects of *Rosmarius officinalis* on depression, anxiety and psychological stress in adults through the conduct of a systematic review and meta-analysis.

Search Methods

- PubMed, Ovid, Core Collection, and CINAHL databases were searched.
- Screening was done independently and in duplicate for title/abstract level and subsequently reviewed on a full-text level with reasons for exclusion noted.
- Data were extracted using piloted templates. Extraction was completed in duplicate.
- Descriptive analysis is presented. Meta-analysis is in progress.
- A subgroup analysis will be conducted to assess if baseline severity symptoms impact outcomes.

Table 1: Eligibility Criteria

Inclusion Criteria	Exclusion Criteria
1.Randomized controlled trials 2.Adult population 3.Delivery of Rosemary in any form including essential oil, capsules, tea, aromatherapy, inhalation or topical application. 4.Assessment of depression, anxiety, and/or psychological stress symptoms as outcomes 5.Placebo, other active comparison or no treatment 6.Any year of publication, language, publication status	1. Uncontrolled studies, non-experimental, observational, animal studies, cell lines, reviews. 2. Delivery of rosemary combined with other herbs or other therapies

Results

- The literature search yielded 1564 studies after duplication. Thirteen studies met criteria for inclusion, including a total of 851 participants.

Table 1. Descriptive summary of thirteen studies included in the systematic review

Population	Participants with existing psychiatric disorders - *2 studies*	Participants with no existing psychiatric disorders - *11 studies*
Duration of Study	Long term duration of 4-8 weeks - *6 studies*	Short term duration of 5-30 minutes - *7 studies*
Method of Rosemary Administration	Inhaled Rosemary administration - *9 studies*	Oral Rosemary administration - *4 studies*
Dose of Rosemary	1 to 4 drops of rosemary was inhaled	700mg to 4g of rosemary was taken orally
Comparison Intervention	Placebo - *9 studies*	Active treatment - *2 studies* No treatment -*2 studies*

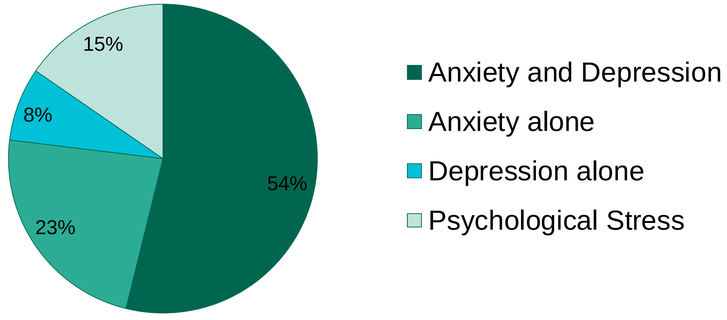

Figure 1. Anxiety, Depression and Stress as outcome measures across all studies

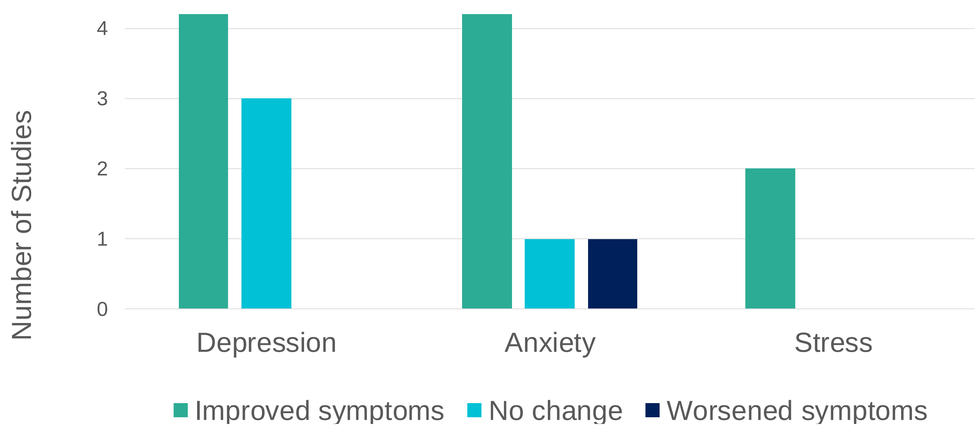

Figure 2. Changes to Anxiety, Depression and Stress outcomes across all studies

Discussions

A constituent in Rosmarinus officinalis, 1,8-cineole, affects serotonin and dopamine, while also decreasing neuroinflammation by inhibiting TNF-α and IL-1β. Additionally, the inhalation of rosemary compounds activates the olfactory pathway, directly stimulating the limbic system.

Strengths and Limitations

A key strength of this systematic review is that all studies analyzed were randomized controlled trials. Screening and data extraction were performed independently and in duplicate.

There was significant methodological variation between studies in terms of method of administration (oral, inhaled), dose, duration and outcomes.

Conclusions

Based on early analysis of findings, *Rosmarinus officinalis* may improve symptoms of depression, anxiety, and psychological stress. However, inconsistencies in study design and administration methods call for further investigation.

Funding

Research reported in this publication was supported by the National Center for Complementary & Integrative Health of the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health

For references or further questions, please email: maucoin@ccnm.edu

Medical Comorbidities in Adults with Neurodevelopmental Conditions: A Retrospective Medical Record Review Study

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Introduction

- Neurodevelopmental disorders (NDDs), such as Autism Spectrum Disorder (ASD), Attention-Deficit/Hyperactivity Disorder (ADHD), are increasingly recognized for their complex, multisystem presentations.
- Recent research has shown growing interest in the bidirectional relationship between psychiatric and physical symptoms in individuals with NDDs, as well as their association with lesser-known conditions, including connective tissue disorders such as hypermobile Ehlers-Danlos Syndrome (hEDS) and complex chronic conditions like fibromyalgia and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).
- These associations are complex and often overlooked in the primary care setting, leading to elevated symptom burden and a reduced quality of life for adults with NDDs.

Objectives

- To systemically examine the prevalence of medical comorbidities in adults with NDDs using patient record data from naturopathic teaching clinics and compare descriptively to population prevalence rates.

Search Methods

- A retrospective medical record review was conducted at the Schad Naturopathic Clinic (SNC) and affiliated Canadian College of Naturopathic Medicine (CCNM) satellite clinics.
- Electronic medical records (on the MedAccess database) from May 2019 to December 2023 were obtained for patients with neurodevelopmental disorders (NDDs) using the following ICD-10 codes: F90.9, F84.0, F81.0, R48.0, F95.9, F81.2, F82, and F80.9. This study was approved by the Canadian College of Naturopathic Medicine's Research Ethics Board.

Table 1: Eligibility Criteria for Patient Records

Inclusion Criteria	Exclusion Criteria
1.Documented NDD diagnosis (charts that contain the abovementioned ICD-10 codes) 2.Age ≥18 years at first visit. 3.At least two recorded visits (to ensure sufficient information) 4.Signed informed consent for allowance of medical records to be reviewed by the CCNM and the SNC health professionals and students for learning outcomes	1.Age <18 years 2.No signed informed consent for allowance of medical records to be reviewed by the CCNM and the SNC health professionals and students for learning outcomes 3.Records contributed to by the researchers

Results

Table 2: Gender Breakdown

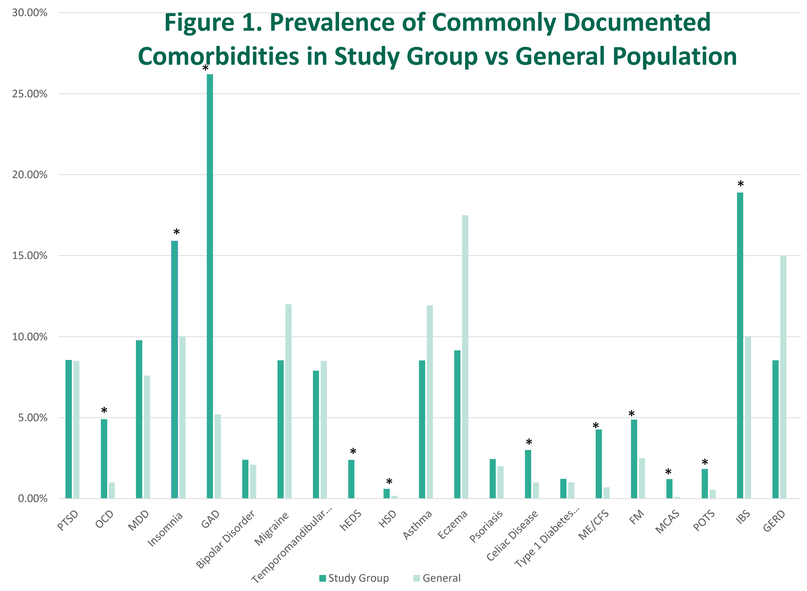
Patients Analyzed	N=164
Female, %,	67
Mean age, years	37
Standard deviation, SD	12.42
Male, %	29.3
Mean age, years	34
Standard deviation, SD	12.8
Non-binary, %	3.6
Mean age, years	30
Standard deviation, SD	12.44
Total mean age, years	36
Standard Deviation, SD	12.44

Table 3: Prevalence of NDDs

NDD	%
ADHD total	89.6
ADHD only	81.7
ASD total	16.5
ASD only	9.1
Both ADHD and ASD	7.3
Developmental Dyslexia total	1.9
Developmental dyslexia only	1.2

ADHD, Attention-Deficit/Hyperactivity Disorder
ASD, Autism Spectrum Disorder

Figure 1. Prevalence of Commonly Documented Comorbidities in Study Group vs General Population



"*" denotes a statistically significance increase in prevalence between groups at p<0.05 based on the Chi-square test.

- Preliminary analyses of 164 eligible charts suggest an increased prevalence of certain comorbidities within this adult population diagnosed with neurodevelopmental disorders (NDDs) compared to national rates. Notably, higher rates were observed for celiac disease, connective tissue disorders like hypermobile Ehlers-Danlos Syndrome (hEDS), and related conditions including Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Syndrome (MCAS). Additionally, chronic pain and fatigue syndromes such as FM and ME/CFS, as well as well-established psychiatric comorbidities including Generalized Anxiety Disorder (GAD), Obsessive Compulsive Disorder (OCD), and Post-traumatic Stress Disorder (PTSD) , were more prevalent. Interestingly, some of the more common disorders—such as asthma, eczema, and GERD—were observed at lower rates in this study population compared to general North American population estimates reported in recent literature.

Discussions

Strengths:

- **First study** to investigate the multisystemic nature of NDDs by analyzing existing patient records from naturopathic teaching clinics. It examines a broad range of potential comorbidities, including autoimmune, metabolic, gastrointestinal, and connective tissue disorders, going beyond well-established psychiatric comorbidities.
- While ASD has been recognized as a comorbidity in hypermobile Ehlers-Danlos Syndrome (hEDS), research on the link between ADHD and connective tissue disorders remains limited. The data shows an increased prevalence of hEDS and Hypermobility Spectrum Disorder in adults with ADHD (predominantly female), highlighting the need for further research into the interplay between these two multisystemic spectrum disorders.

Limitations:

- Relatively small sample size, limiting our ability to generalize findings to broader populations.
- The retrospective design relies on existing patient records, which are subjective in nature and do not always provide streamlined or standardized data.
- Data was collected solely from naturopathic teaching clinics, which may not reflect trends in other primary care healthcare settings.

Clinical Application: Understanding the multisystemic nature of NDDs can enhance clinician awareness of commonly co-occurring conditions, enabling earlier recognition and intervention.

Further Research: A prospective study examining the connections between NDDs and their comorbidities is encouraged to further explore prevalence patterns and pathophysiological links. Such research could help inform the development of enhanced screening tools and diagnostic criteria for underrecognized conditions, ultimately allowing for improved clinical detection and care strategies. Expanding this work into larger, more diverse populations will also strengthen the understanding of these complex interactions and guide future integrative treatment approaches.

Conclusions

Significant multisystem comorbidities exist in the NDD patient population at CCNM-affiliated clinics. Addressing these complexities in clinical and research settings can lead to better screening protocols, more comprehensive treatment approaches, and ultimately, improved long-term outcomes for adults with NDDs.

For references or further questions, please email: etoprak@ndnet.ccnm.edu

Investigation the Effect of Nutraceuticals on Incidence and Severity of Chemotherapy-Induced Peripheral Neuropathy: A Narrative Review

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Introduction

- Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating side effect experienced by cancer patients.
- CIPN is a major dose-limiting side effect of treatments with platinum and taxane chemotherapy agents, like paclitaxel, cisplatin and oxaliplatin.
- The most common symptoms of CIPN include numbness, tingling, paresthesia, dysesthesia and a burning pain in a stocking-glove distribution.
- Current pharmacologic CIPN management include gabapentin, tramadol, glutathione or tricyclic antidepressants.
- 68% patients report developing CIPN within the first month but only 30% will see a reduction after 6 months.
- Neuroprotective nutraceuticals like omega-3 fatty acids, glutamine, and melatonin can help reduce oxidative stress and neuroinflammation.

Objectives

This study aims to assess various well-researched nutritional supplements, including omega-3 fatty acids, glutamine, and melatonin, to determine their efficacy in preventing and mitigating CIPN symptoms.

Search Methods

- A thorough search was done on PubMed, using key words such as “CIPN”, “nutraceuticals”, “orthomolecular”, “omega-3 fatty acids”, “glutamine”, and “melatonin”
- Exclusion criteria included:
  - Narrative reviews
  - Animal studies
- Inclusion criteria included:
  - Human studies
  - Randomized, double-blind, placebo-controlled trials
  - Chemotherapy done with platinum and taxane agents
- Primary outcomes evaluate the incidence and severity of CIPN
- Agents will be compared via parameters such as reductions in incidence in CIPN, neuropathic pain and improvements in nerve conduction, to identify the most promising candidates.

Results

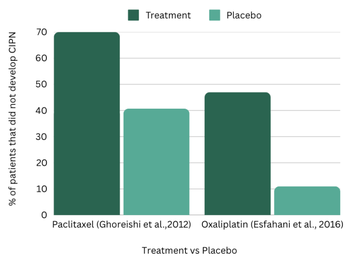

Figure 1. When on paclitaxel treatment, 70% (n=30) of patients did not develop CIPN in the omega-3 fatty acids supplemented group, while 40.7% (n=11) did not develop CIPN in the placebo group (p=0.029). When on oxaliplatin treatment, 47% (n=17) of patients did not develop CIPN in the omega-3 fatty acids, while 11% (n=4) did not develop CIPN in the placebo group (p=0.002).

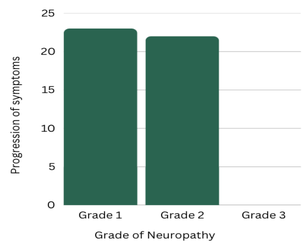

Figure 2. When supplemented with 21 mg of melatonin, 45% of patients (n=10) developed neuropathy. Of the 45%, 23% reported grade 1 neuropathy and 22% developed a grade 2 neuropathy. No patients reported grade 3 neuropathy. 55% of patients (n=12) reported no neuropathy.

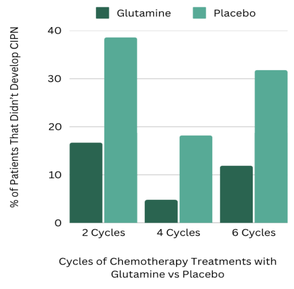

Figure 3. Compared to placebo, a lower percentage of grade 1-2 peripheral neuropathy was observed in the glutamine group (16.7% vs 38.6%, p=0.04) after two cycles of treatment, and a significantly lower incidence of grade 3-4 neuropathy was noted in the glutamine group after four cycles (4.8% vs 18.2%, p=0.05) and six cycles (11.9% vs 31.8%, p=0.04).

Authors	Interventions	Comparison	Results
Ghoreishi et al., 2012	**Intervention Group:** Participants received omega-3 fatty acid capsules, 640 mg three times daily, during chemotherapy and for one month after completing treatment.	**Control Group:** Participants received a placebo following the same schedule.	The study found that 70% of patients in the omega-3 group did not develop peripheral neuropathy, compared to 40.7% in the placebo group. This difference was statistically significant, with a p-value of 0.029.
Esfahani et al., 2016	**Intervention Group:** Patients received 640 mg of n-3 PUFAs three times daily (totaling 1,920 mg per day) during their chemotherapy regimen with oxaliplatin and continued for one month after completing chemotherapy.	**Control Group:** Patients received placebo capsules following the same schedule.	This difference was statistically significant, with a p-value of 0.002. The severity of neuropathy, assessed using the reduced Total Neuropathy Score (TNSr), was significantly lower in the n-3 PUFA group compared to the placebo group (p = 0.001).
Nahleh et al., 2010	**Intervention Group:** All participants received 21 mg of melatonin daily at bedtime throughout their taxane chemotherapy regimen and continued for an additional 28 days post-chemotherapy.	**Control Group:** This was a single-arm study without a placebo or control group. The outcomes were compared to historical data on the incidence of taxane-induced neuropathy.	**Incidence of Neuropathy:** 45% of patients (10 out of 22) developed neuropathy: Grade 1: 23% (5 patients) Grade 2: 23% (5 patients) No cases of Grade 3 or higher neuropathy were reported. **No Neuropathy:** 55% of patients (12 out of 22) did not experience any neuropathy. **Quality of Life:** The median score on the FACT-Taxane quality of life assessment remained stable, with only a 0.5-point median decline from baseline to the end of the study, suggesting that melatonin did not adversely affect quality of life.
Wang et al., 2007	**Intervention Group:** Patients received 15 grams of oral glutamine twice daily (totaling 30 grams per day) for seven consecutive days, starting on the day of each oxaliplatin infusion.	**Control Group:** Participants did not receive glutamine supplement.	**Impact on Daily Activities:** Interference with daily activities due to neuropathy was reported by 16.7% of patients in the glutamine group, compared to 40.9% in the control group. (p-value=0.017). **Oxaliplatin Dose Reduction:** Dose reductions due to neuropathy were necessary in 7.1% of patients in the glutamine group, compared to 27.3% in the control group (p-value=0.024).
Stubblefield et al., 2005	**Intervention Group:** Participants received 10g of glutamine three times daily for 4 days starting 24 hours after completing paclitaxel treatment.	**Control Group:** Participants did not receive glutamine supplement.	**Weakness:** Patients who received glutamine experienced significantly less weakness compared to those in the control group (p = 0.02). **Loss of Vibratory Sensation:** The glutamine group had a significantly lower incidence of vibratory sensation loss compared to the control group (p = 0.04). **Toe Numbness:** Patients receiving glutamine reported significantly less toe numbness than those who did not receive glutamine (p = 0.004).

Discussions

Possible Mechanism of Action

- Omega-3 fatty acids integrate into neuronal cell membranes, influencing signal transduction, ion transport, receptor function, and neurotransmission.
- Omega-3-fatty acids help reduce neuropathic pain by directly modulating nerve activity and inhibiting proinflammatory cytokines such as IL-1β, IL-6, TNF-α.
- The mechanism of neuroprotection by glutamine is unclear yet evidence suggests it may offer neuroprotection by upregulating nerve growth factor (NGF), which declines as neuropathy worsens. NGF administration prevents paclitaxel-induced neuropathy in mice, and glutamine has been shown to increase NGF mRNA in animal models. Additionally, high systemic glutamine may reduce glutamate conversion, potentially contributing to symptom relief.
- Melatonin suppression of free radical generation plays a role in mediating the toxic effects of chemotherapy.

Strengths and Limitations

- A limitation is the lack of human trials.
- Lack of quality studies, such as small sample size and lack of control group in the Melatonin study

Further Research

Further studies can include research on the mechanism of action of these nutraceuticals to deeper understand their neuroprotective potential. Additionally, trials comparing these nutraceuticals to one another using the same methods would allow for establishing superiority of one therapy. Including more outcome measures in further research, such as CIPN incidence, severity, and specific nerve conduction parameters would allow for a more holistic view of the nutraceuticals effect. Future research should include more large-scale randomized human trials, and further explore supplement safety, efficacy, and underlying mechanisms to establish integrative protocols for neuropathy prevention in cancer patients. More melatonin studies could also allow for a greater understand of its effectiveness and mechanism of action.

Clinical Application

These nutraceuticals hold promise for CIPN management. CIPN can often be so debilitating that individuals may require a reduction in chemotherapy dose or even stopping before completing the planned course. Therefore, addressing CIPN via reducing its frequency and severity potentially has implications on the efficacy of cancer treatment and overall patient outcomes, as patients may be able to complete their course of treatment at the prescribed dose.

Conclusions

Omega-3 fatty acids, glutamine and melatonin, when used individually, reduced the incidence and severity of chemotherapy induced neuropathic pain, while supporting nerve function.

For references or further questions, please email: achandrakumar@ndnet.ccnm.edu

Effects of CAM interventions on PTSD in Veterans and Veteran family members: a rapid systematic review and meta-analysis

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Chronic Pain Centre of Excellence for Canadian Veterans

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Introduction

- Post-traumatic stress disorder (PTSD) is more common among Veterans, with Veterans Affairs Canada reporting a 10% prevalence in combat Veterans and peacekeepers. In the U.S., 10% of male Veterans and 19% of female Veterans are diagnosed with PTSD, compared to 6% of civilians.
- PTSD in Veterans is often caused by combat, witnessing death, other war-related traumas, and Military Sexual Trauma, all of which can differ significantly from the causes of PTSD in civilians.
- Nearly 50% of U.S. Veterans and active-duty personnel use at least one Complementary Alternative Medicine (CAM) therapy, and understanding the efficacy of CAM has been identified as a research priority by Veterans and their families.
- Although the 2023 VA/DoD treatment guidelines for PTSD include recommendations on CAM interventions, the guidelines indicate that at the time of publication, there was insufficient evidence for their effectiveness in alleviating PTSD symptoms. The reviews cited lacked an assessment of quality of the studies or attempts to pool data.

Objectives

Synthesize evidence on the efficacy of all CAM interventions in improving mental health & quality of life outcomes for Veterans and their families living with PTSD in Five Eyes countries.

Search Methods

- We searched MEDLINE, PsycINFO, and AMED for studies that enrolled Veterans with PTSD and/or their families from Five Eyes countries from 2013 - December 2023, evaluated CAM interventions, and assessed changes in mental health outcomes using validated scales. Reference lists of relevant articles were hand searched to identify grey literature.
- The search strategy was defined and pilot tested with support from established search language and descriptions of CAM by the NCCIH. Articles were screened in duplicate at title/abstract and fulltext using Covidence software. Data extraction was done by one reviewer and verified by a second using standardized forms.
- Randomized controlled trials (≥10 participants/arm) and observational studies (≥30 participants) in veterans or families, with diagnosis of PTSD at baseline, that assessed changes in PTSD, depression, anxiety, quality of life and/or cost outcomes were included.
- Cochrane risk of bias tool 2 and ROBINS-I tools were used to assess risk of bias.
- Estimates of efficacy and effectiveness were pooled when reported by > 1study and assessed certainty of evidence using the GRADE approach. Reporting was guided by PRISMA recommendations.

Results & Discussion

Figure 1. PRISMA Flow Chart

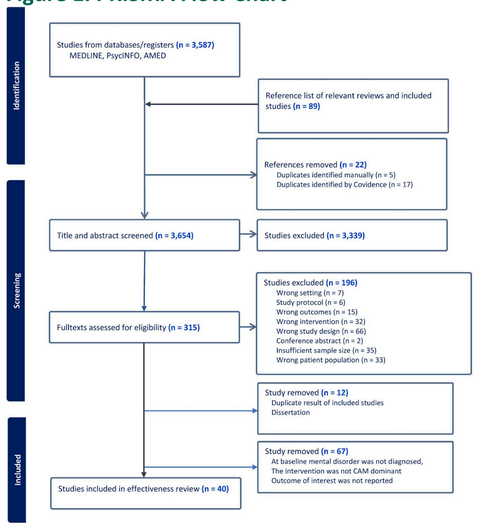

Figure 2. Risk of Bias 2 (RCTs)

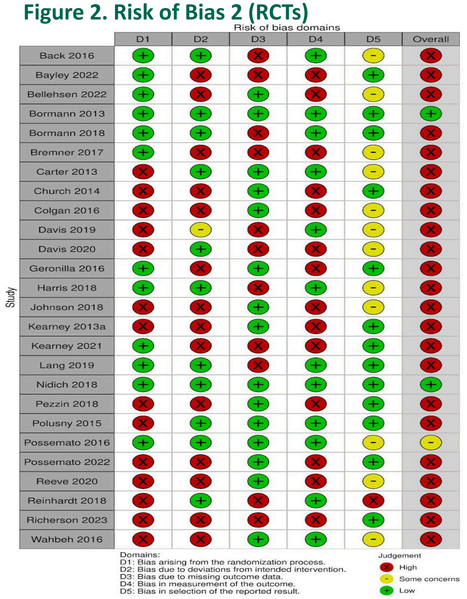

Table 1. GRADE Assessment of Evidence

CAM intervention	PTSD Severity-CAPS	PTSD Severity-PCL	Depression	Anxiety	Quality of life
Mantram Repetition	WMD of change scores from baseline: -8.53 (-13.61 to -3.45) CAPS (scale 0-136)	WMD of change scores: -4.09 (-7.22 to -0.95) PCL-Civilian, (scale 17-85)	WMD of change scores: -2 (-3.53 to -0.47) PHQ-9 (scale 0-27)	MD of change scores: -0.72 (-2.59 to 1.15) Anxiety -Brief Symptom Inventory–18 (BSI-18)	MD of change scores: 2.87 (0.04 to 5.70) Short Form?? _ Mental Component (scale 0-100)
Meditation	WMD of end scores: -11.08 (-18.71 to -3.45) (CAPS-IV), (scale 0-136)	WMD of end scores follow up: -10.66 (-15.00 to -6.32) PCL-Military (scale 17-85)	SMD, Cohen's d: -0.57 (-0.83 to -0.32)	SMD, Cohen's d: -0.59 (-1.08 to -0.10)	MD of post-test adjusted for baseline 9.14 (-0.41 to 18.7) (Q-LES-Q-SF) (scale 14-70)
Breathing-Based Intervention	MD of change score from baseline: -14.2 (-25.67 to -2.73) CAPS (0-88)	MD of change score from baseline: -20.50 (-28.81 to -12.19) PCL-Civilian, (scale 17-85)	MD of change score from baseline: -8.72 (-12.63 to -4.81) BDI 0-63		MD of change score from baseline: 0.1 (-3.991 to 4.19) WHOQoL-BRIEF, 1-130
MBSR	WMD of change scores: -9.32 (-21.08 to 2.45) CAPS (scale 0-136)	WMD of change scores: -4.29 (-5.44 to -3.14) PCL-Civilian (scale 17-85)	WMD of change scores: -2.77 (-3.34 to -2.21) PHQ-9) (scale 0-27)		MD of change score from baseline: 5.22 (1.73 to 8.71) WHOQOL-BRIEF) (scale 0-130)
Emotional Freedom Techniques		MD of change score: -27 (-32.09 to -21.91)	MD of change score: -10 (-13.38 to -6.62)	MD of change score: -12 (-16.08 to -7.92)	
Music		Adjusted MD: -9.7 p=0.01 PCL-Civilian (scale 17-85)	Adjusted MD: −6.3, p = 0.02 BDI)-II (scale 0-63		Adjusted MD:0.03, p = 0.75 EuroQoL (scale 0-100)
Antioxidant Therapy (N-Acetylcysteine)	β linear regression =- 0.127, P value=NS [a] Crude MD between end scores: -19.5 CAPS (scale 0-136)	β linear regression =- 0.355, P value <0.01a Crude MD between end scores: -10.7 PCL-Military (scale 17- 85)	β linear regression = -0.325, P value <0.05a Crude MD between end scores: -9.4 Beck Depression Inventory (BDI)-II (scale 0-63)		
Service Animals		Adjusted MD end scores: -4.6 (-9.10 to -0.10) PCL-5 (scale 0-80)	Adjusted MD end scores: -1.19 (-2.78 to 0.39)	MD of change score from baseline: -3.3 (-5.56 to -1.04) Trauma Symptom Inventory-2: Anxiety subscale (highest 15)	Adjusted MD of end scores: 1.35 (-1.79 to 4.49) VR-12 MCS (Scale 0-100) Adjusted MD of end scores: -0.90 (-3.78 to 1.99) VR-12 Physical Component Score (Scale 0-100)
Healing Touch		MD: -12.54 (-22.06 to -3.02) On PCL-5 (scale 0-80)			
Animal-Assisted Interventions	MD: -11.86 (-14.45 to -9.27) CAPS (scale 0-80)	WMD change scores(before-after): -11.59 (-13.77 to -9.41) PCL-Military (scale 17-85)	WMD change scores(before-after): -7.44 (-9.79 to -5.08) (BDI)-II (scale 0-63)	MD: -4.62 (-14.05 to 4.81) Burns Anxiety Inventory: 0-99	Cohen's d= 0.36, p =0.016
Mixed Meditation	Hedges' g = -0.32 (-0.62 to -0.01) CAPS (scale 0-80)	Hedges' g = -0.39 (-0.67 to -0.11) PCL-Specific (scale 17-85)			
Mindful Movement (Yoga+Tai Chi)	WMD of endscore: -3.52 (-10.44 to 3.40) CAPS (scale 0-136)	WMD of change scores from baseline: -1.86 (-7.29 to 3.58) PCL (scale 17-85)	SMD Cohen's d: -0.35 (-65 to -0.06)	SMD Cohen's d: -0.30 (-59 to -0.01)	MD: 51.70 (18.80 to 84.60) Short Form 36 Quality of Life Instrument (scale not reported)
Spiritual	MD of change score from baseline: 5.86 (-3.34 to 15.06) CAPS (scale 0-136)	MD of change score from baseline: 1.71 (-4.07 to 7.49) PCL-Civilian (scale 17-85).			

Significant Improvement	High-Quality Evidence	Moderate Quality Evidence	Low-Quality Evidence	Very Low-Quality Evidence
No significant improvement	High-Quality Evidence	Moderate Quality Evidence	Low-Quality Evidence	Very Low-Quality Evidence

- Twenty-six RCTs and 14 observational studies with 3,321 participants (84.4% male, median age 51.4 years)
- Thirty-eight of 40 studies (95%) of studies were conducted in the USA; 92% were conducted in outpatient clinics. No studies were on Veteran family members.
- High risk of bias: 23 (88%) of 26 RCTs; 100% of observational studies ≥ 1 domain.
- **Moderate-quality evidence** suggests **meditation** (WMD: -10.66, 95% CI: -15.00 to -6.32), Emotional Freedom Technique (EFT) (MD: -27.00, 95% CI: -32.09 to -21.91), and **Sudarshan Kriya Yoga (SKY)** (MD: -20.50, 95% CI: -28.81 -12.19) reduces PTSD symptoms greater than the minimal important difference (MID).
- Meditation and EFT improves depression and anxiety, while SKY improves depression greater than one MID.
- For CAM interventions informed by small- to medium-sized trials, **moderate-quality evidence suggests that music therapy, NAC, and service animals** can improve self-assessed PTSD symptoms and depression, albeit by less than one MID. Additionally, **moderate quality evidence indicates that healing touch improves PTSD** symptoms above one MID, but evidence for its effect on depression and anxiety is lacking. We found **very low quality evidence**, which results in uncertainty regarding the impact of **animal-assisted interventions, mixed meditation and mindful movement** on PTSD symptoms, depression, anxiety and quality of life. Thus, more rigorous research is needed for these interventions before being strongly considered for clinical practice or health system integration.

Strengths

- This is the first systematic review and meta-analysis synthesizing current evidence for the effectiveness of different CAM interventions in reducing PTSD symptoms, depression, anxiety, and improving quality of life in Veterans. Additional strengths of this review include use of a comprehensive search strategy without language restrictions, explicit eligibility criteria, assessments of risk of bias, and utilizing the GRADE approach to assess the quality of evidence.

Limitations

- A focused definition of CAM from NCCIH, restrictions to studies of Veterans in Five Eyes countries over the past decade from three bibliometric databases, contributing to selection bias, and findings indicating many CAM interventions lacked robust evidence as these were often supported by only a single study.
- Most studies focused on predominantly male, white/Caucasian participants over 50 years old in the US, thus limiting the generalizability of findings to diverse Veteran populations, with no investigations into the impact of CAM on Veterans' families.

Conclusions

Meditation, EFT and SKY may result in clinically meaningful reductions in PTSD, depression and anxiety. Further rigorous research is warranted to better understand effectiveness of CAM interventions for Veterans with PTSD.

This project received funding from the Atlas Institute for Veterans and Families

For references, forest plots figures or further questions, please email: kcooley@ccnm.edu

Utilization of Naturopathic Medicine amongst People Living with Systemic Sclerosis: Perspectives, Expectations and Factors in Decision-making

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Introduction

Systemic sclerosis (SSc, also known as scleroderma) is a chronic, multi-organ system rheumatic autoimmune disease characterized by the fibrosing of connective tissue.

Pathophysiological events in SSc include endothelial cell inflammation resulting in cell dysfunction and inflammatory infiltrates, chronic fibroblastic activity resulting in continuous collagen synthesis and angiogenesis, as well as damage to blood vessels and organs.

SSc is distinguished by phasic small artery vasospasms (Raynaud's phenomenon), symmetrical fibrosing, tightening of the skin, insoluble calcinosis commonly of the metacarpophalangeal and metaphalangeal joints, microstomia, gastroesophageal reflux disease, telangiectasia, and gastrointestinal manifestations.

Diagnostic autoantibodies on blood work include:

- Anti-centromere (ACA)
- Anti-topoisomerase I (SLE-70).

Other common biomarkers include:

- Positive antinuclear antibodies (ANA)
- Rheumatoid factor (RF)
- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR)
- Echocardiography
- Pulmonary function testing (PFT).

Systemic sclerosis can have severe implications for quality of life by impacting physical ability, gastrointestinal issues, respiratory problems, pain, and emotional challenges, including reduced self-confidence due to craniofacial and other appearance-related changes. There is no cure for scleroderma, and the prognosis for individual patients varies greatly.

Introduction

The utilization of naturopathic medicine in many patient populations is **unknown.**

There is growing evidence to suggest that Complementary Alternative Modalities (CAM), such as naturopathic medicine are of interest to many people living with chronic illness.

There is no cure for SSc, and the prognosis for individual patients varies greatly. Several evidence-based naturopathic strategies have been used to treat chronic rheumatic diseases such as SSc.

No well-designed studies have evaluated the usage, decision-making process, or perceived efficacy of naturopathic medicine in SSc.

Bridging this gap in the literature could enhance naturopathic doctors' knowledge of treating chronic disease patients from a psycho-social standpoint to better manage expectations. Thus, we are currently conducting a cross-sectional survey study evaluating the use of naturopathic modalities in SSc patients.

Objectives

(1) Assess if people living with SSc are currently using or have previously used naturopathic medicine, including modalities defined under naturopathic medicine;

(2) Assess why people with SSc decide to seek out adjunct modalities defined under naturopathic medicine;

(3) Evaluate the perceived efficacy of these modalities.

Design & Methodology

Participant eligibility & recruitment

Participants living with SSc will be recruited through the SPIN Cohort and via patient organizations and social media. The SPIN Cohort is a large-scale global group of people with clinically diagnosed scleroderma that have been considered for SPIN research participation by their rheumatologist. The cohort is comprised of approximately 1400 people from 7 different countries. Eligible participants will be people diagnosed with SSc that are fluent in English, French or Spanish who have access to an online device to complete online surveys. Participants will be recruited through email announcements to the SPIN Cohort. Interested participants will follow a survey link to ensure their eligibility and consent to being contacted further.

Measures

This will be a cross-sectional study, where participants will report important descriptive demographics including current location, SSc subtype, sex, gender, race or ethnicity, age, educational status, occupational status, age at diagnosis, family history, and associated SSc-related symptoms. Participants will also have completed a Health Assessments Questionnaire-Disability Index (HAQ-DI) to provide valuable insights on disability status.

Survey items

The survey items will be constructed of both newly formulated questions and adapted questionnaire items. In order to accurately represent patient demographics for statistical analysis, SSc demographic questions will be adapted from previous studies. Other survey items will capture what naturopathic services people with SSc patients use, what they use it for, and what resources encourage or deter patients from using naturopathic modalities. Survey items will aim to use mostly ratings and multiple-choice questions to avoid qualitative discrepancy for purposes of statistical analysis. We have adapted survey items from the 2012 NHIS Questionnaire – Adult CAM Adult Alternative Health/Complementary and Alternative Medicine. Newly formulated questionnaire items will be created and edited by SPIN researchers, and CCNM naturopathic medical experts.
The survey will be disseminated online over Qualtrics, where participants can provide informed consent, and complete the survey.

Data processing & analysis

The survey will be analyzed through descriptive statistics, and correlational analysis. For correlational analysis, non-modifiable characteristics (age, sex, ethnicity, etc.) and modifiable demographics (location, educational and occupational status) will be compared. If there is a sufficient sample size, exploratory analysis using correlational analysis will be used to determine whether certain characteristics are more indicative of specific outcomes pertaining to the questionnaire. Data will be analyzed in regard to geographic location, underscoring the differences between regulated and unregulated areas of practice, safety and scope of practice under naturopathic medicine.

Discussion, Results & Conclusion

This survey is in progress. The findings of this study may enhance our understanding of the use of naturopathic medicine among patients living with systemic sclerosis. The information from this survey will help guide future research and provide a nuanced perspective on the importance of naturopathic medicine for SSc patients.

Funding: This project received funding from the CCNM Student Innovation Fund.
For references or further questions, please email: vcook@ndnet.ccnm.edu

Use of Antimicrobial Herbs for Rectal Resection induced Diarrhea in Patient with Colorectal Cancer: A Case Report

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Introduction

- Colorectal cancer is the second leading cause of death among men and women in Canada following lung cancer.
- Rectal resection is a commonly performed surgical procedure when tumor cells invade the pelvic peritoneum with sigmoid colon and/or rectum being involved.
- Diarrhea after rectal resection is a common side effect due to altered bowel motility, changes in gut microbiome, malabsorption of bile and electrolytes.
- Antimicrobial herbs such as berberine and garlic have been studied to fight infections and address gut dysbiosis, however, they have not been previously studied for the treatment of rectal resection induced diarrhea.

Objectives

The aim of this case report is to document a case in which antimicrobials were used as a treatment for rectal resection induced diarrhea in a patient diagnosed with colorectal cancer.

Case Presentation

- A 68-year-old female with a history of stage IV rectosigmoid mucinous adenocarcinoma diagnosed in March 2019, underwent a rectal tumour resection as part of her cancer treatment, therefore has an ostomy bag.
- Following the rectal resection, she struggled with severe diarrhea causing her to change her bag 8-10 times in the day
- No identifiable infection or other complications based on stool testing.
- Different interventions were given to the patient such as fiber, probiotic, prebiotics, L- glutamine and digestive enzymes, all failed to manage diarrhea related symptoms.
- Further testing using the GI Map test revealed dysbiosis caused by high *Morganella* and *Pseudomonas* opportunistic bacteria.
- A 3-month protocol using antimicrobial herbs such as oregano, berberine, and garlic were used while simultaneously healing the gut lining using fiber and L-glutamine and addressing underlying emotional stress.
- The patient reported reduced bowel movement and bulking of the stool to a type 4 on the Bristol stool chart.

Case Presentation

Timeline:

- March 2019: Diagnosed with stage 4 rectosigmoid mucinous adenocarcinoma
- August 2019: Simultaneous rectal tumor resection and hepatic resection – reports on and off diarrhea since resection (8-10 watery bowel movements per day when it is severe)
- December 2019: neo-adjuvant FOLFOX with chemoradiation
- July 2024: GI map testing - high *Morganella* and *Pseudomonas* opportunistic bacteria, high IgA anti-gladin and IgA secretory
- July 2024: Celiac testing conducted but patient did not eat enough gluten, thus, may be a false negative. Troubleshooting with patient when to run another test to not interrupt improved bowels
- July 2024: Started protocol below: 4-6 bowel movements per day and Type 4 on Bristol stool chart after one to two month on the protocol below
- August 2024: Stool testing – No pathogens present (ruled out any infectious cause)

Table 1. Supplement introduction, dosage and indications to address dysbiosis

Recommendation	Dose	Indication
		Killing Phase (3 Months)
Oregon Grape/ Berberine/Garlic	750-1000mg (1 month course of each)	Antimicrobial herb that contains the extract berberine used to kill unwanted microbes in the gut
		Simultaneous healing phase (3 Months)
L-glutamine	15g	Studied to protect and repair the cells of the GI tract, reduce inflammation and promote a healthy gut immune response
Butyrate	1750mg	Supports a healthy microbiome by reducing inflammation in the gut as well as strengthening the gut barrier by increasing mucus production and tight junction.
		Long term Management
Soluble Fiber	10g	Helps heal the gut, promote GI motility and regularity, bulk up the stool and supports long term prevention of colorectal cancer
Betaine HCL	520mg with food	Long term stress reduces stomach acid. HCL is used to increase stomach acid, support digestive function and promote the absorption of nutrients

Discussions

We hypothesize the following causes of the patient's diarrhea following rectal resection:

- Potential movement of healthy bacteria further up in the GI tract due to surgery
- Long term stress as an outcome of stage 4 cancer diagnosis which caused sympathetic dominant nervous system. This results in reducing stomach acid which affects proper digestion of nutrients.
- Celiac or gluten sensitivity which was reflected on GI Map test based on high IgA markers.

Anti-microbial herbs have been studied in the context of treating gut infections and overgrowths including SIBO, SIFO (small intestinal fungal overgrowth), and *H. pylori.* It also has shown positive effects in killing opportunistic bacteria in the gut through mechanisms of cell membrane damage, inhibiting protein and nucleic acid synthesis, and modifying the metabolism of pathogens. In this patient's case, addressing gut dysbiosis at the pathogenic level was not enough as long-term stress was a key player in dysbiosis through increasing inflammation, reducing gut motility and digestion as well as increasing gut sensitivity. Thus, addressing the patients gut dysbiosis holistically improved symptoms.

Conclusions

This case illustrates that the use of antimicrobial herbs in conjunction of gut healing interventions and long-term management of stress may improve frequency and consistency of bowel movements after rectal resection in a patient with colorectal cancer. Further research is warranted.

For references or further questions, please email: nnafisa@ndnet.ccnm.edu

Dietary Protein and Anxiety Symptoms & Disorders: A Scoping Review

Kyla Lamb, CCNM student [1], Jensen Pletch, CCNM student [1], Jamie Menzel, MScN CNS [2], Melissa A Murphy, PhD RDN [3,4], Laura LaChance, MD MSc [1], Ann Sze, MLIS [1], Monique Aucoin, ND MSc [1,5]

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Introduction

- Anxiety and psychological stress are increasingly prevalent, with dietary factors emerging as potential modifiable risk factors.
- Protein intake may have an impact on mental health by modulating neurochemical pathways and the microbiota-gut-brain axis.
- Despite growing interest, there has been no systematic investigation of dietary protein's role in anxiety and stress disorders.

Objectives

This scoping review seeks to address this gap by systematically investigating the impact that the quality or quantity of dietary protein has on the development or progression of anxiety or psychological stress symptoms or disorders.

Search Methods

- Medical databases searched include Medline (PubMed), EMBASE (OVID) Web of Science (Core Collection), and CINAHL.
- Search strings were built upon text words and, where relevant, subject heading terms (e.g., MeSH, Emtree terms), based on the core search terms of “Anxiety,” “Stress,” and “Dietary Protein”.
- The initial search string was created for PubMed and then translated using the Polyglot Search Translator. Translations and the full strategy were reviewed by an experienced medical librarian.
- No language, date, peer-review, or publication status restrictions were applied.

Table 1. Inclusion and Exclusion Criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Inclusion of human clinical trials, observational studies, pre-clinical studies, systematic reviews, and meta-analyses	Perinatal studies examining maternal diet effects on offspring
Studies must assess dietary protein or amino acid intake/adequacy using any method (e.g., FFQ, diet recall, food diaries, urine analysis, etc.)	Research primarily focused on amino acid metabolism rather than dietary intake or levels
Studies must evaluate the presence/absence of anxiety disorders or changes in anxiety symptoms (including perceived emotional stress)	Studies examining phenylketonuria (PKU) or other rare genetic conditions

Results

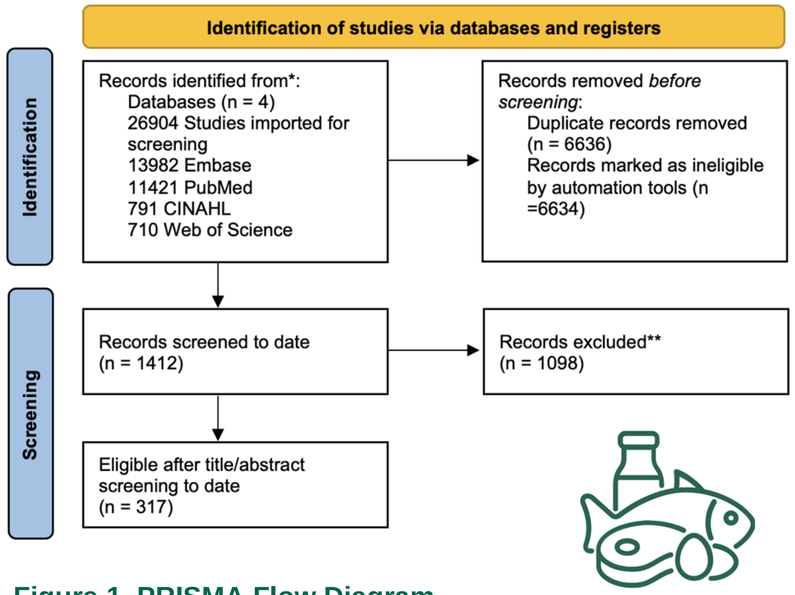


Figure 1. PRISMA Flow Diagram

Table 2. Study Designs Identified in Screening To Date

Study Designs Frequently Identified	Study Designs Infrequently Identified
Tryptophan depletion studies	Studies assessing the impact of changing total dietary protein quantity
Supplementation of bioactive peptides	Studies assessing the impact of protein quality
Observational studies comparing high and low protein intake	Longitudinal studies assessing protein intake and anxiety outcomes over time
Studies administering L-arginine, a precursor for nitric oxide (NO)	

Discussions

Strengths

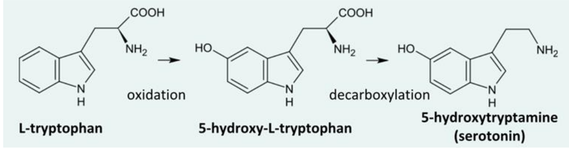
- This review features an extensive search and duplicate screening to minimize bias or the omission of relevant research.

Limitations

- Limited research directly addressing the study question.

Mechanism of Action

- Essential amino acids are used in the synthesis of neurotransmitters.
- **Tryptophan** is an essential amino acid and **precursor to serotonin**, which regulates mood, anxiety, and stress.
- Serotonin impacts **emotional stability**, **sleep**, and **cognitive function**.
- Many studies focus on **tryptophan depletion models**, which reduce serotonin synthesis to study mood and anxiety.



Conclusions

This project is in progress. Early assessment of the findings suggest that there is a need for more human clinical trials that modify total dietary protein quantity or quality and assess the impact on anxiety symptoms.

Funding

Research reported in this publication was supported by the National Center for Complementary & Integrative Health of the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

For references or further questions, please email: maucoin@ccnm.edu

Characterizing Lifestyle, Nutritional Habits, and Mental Health Outcomes in Students of Complementary and Integrative Health

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Introduction

The International Cohort on Lifestyle Determinants of Health Study (INCLD) is a longitudinal cohort study composed of complementary and integrative health students (CIH) from the National University of Natural Medicine.

Measures include:
•Anthropometrics
•Serum and salivary biomarkers of cardiovascular risk, reproductive hormones, and cortisol
•Nutritional intake using digital food frequency questionnaires
•Microbiota sequencing
•Validated surveys to explore participants' mood, stress levels, and stress management practices.

Research on the health and lifestyle of CIH students remains underrepresented in the current literature, highlighting a gap in understanding this population's unique characteristics and needs.

Objectives

To characterize the demographics of CIH students, including lifestyle, nutrition, and mental health outcomes.

Methods

Cleaning the Dataset
•Standardized inconsistent formats (i.e. dates, text)
•Checked for outliers and anomalies, addressing them appropriately

Coding the Dataset
•Created new variables to enhance analysis
•Implemented categorical variables for easier interpretation
•Ensured data integrity by validating coded variables against the original dataset

Summarizing the Dataset
•Summarized findings in summary tables for interpretation
•Generated descriptive statistics to provide an overview of the dataset

Figure 1. INCLD health study participant attendance metrics

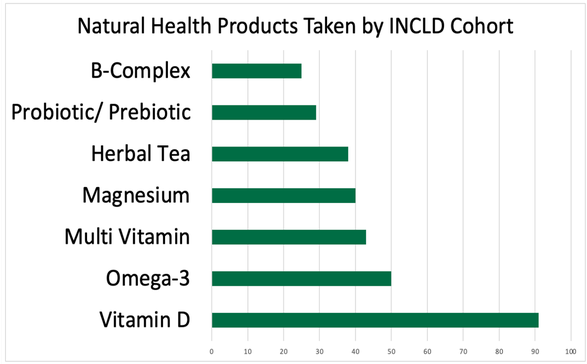
Results

General Demographics

Demographic breakdown: 86% female, 65% aged 21-30, 77% White/Caucasian, 73% at a healthy weight, 73% menstruating without hormonal contraceptives, 58% studying Naturopathic Medicine, and 24% studying Nutrition.

Natural Health Products (NHP) Use & Perceived Mental Health

86% consume NHP regularly



	N	%
Perceived Stress Scale		
Low Stress (≤13)	65	(37.1)
Moderate Stress (14-26)	102	(58.3)
High Perceived Stress (27-40)	8	(4.6)
Major Depression Inventory		
No Indication of Depression	140	(81.9)
Mild Depression	16	(9.4)
Moderate Depression	9	(5.3)
Severe Depression	6	(3.5)

Figure 2. Most frequently consumed NHP Figure 3. Perceived mental health status

Mind Body Practices & Physical Activity

Approximately 40% of the cohort classified themselves as active. Nearly 80% engage in meditation, over 40% practice it 2-3 times a week, and yoga is the second most common mind-body practice, with other stress management activities including walking, reading, and exercising.

Dietary Practices

	Mean (SD)
Estimated Dietary Intake	
Total Calories (cal)	1646.6 (667)
Total Carbs (g)	177.33 (74.6)
Total Protein (g)	62.8 (29)
Total Fat (g)	78 (35.7)
Total Dietary Fibre (g)	27.2 (11.9)

Figure 4. Estimated dietary intake

	N	%
Most Commonly Consumed Foods/Day (≥3-4 x/ week)		
Organic Produce	135	(78.9)
Local Produce	88	(51.5)
Dark Leafy Greens	127	(74.7)
Coffee	93	(54.4)
Garlic	122	(72.2)
Onion	123	(72.9)
Extra Virgin Olive Oil	91	(53.8)
Avocado Oil	68	(40.0)
Prepared Own Meals from Scratch	158	(92.9)

Figure 5. Commonly consumed foods

Discussions

CIH students exhibit higher rates of health practices like NHP use, healthy eating, and mindfulness, likely due to the focus on nutrition, NHP education, and preventative care in CIH programs. These findings suggest a need for further research on the link between integrative healthcare education and student health, including the long-term impact of these practices on well-being in students and healthcare practitioners.

Next Steps & Future Applications

We are currently in the process of analyzing relationships between the following variables of interest for each category:

Dietary Data (Independent Variables)
1) Ratio of dietary consumption of omega-3 to omega-6 intake
2) Fermented food intake
3) Percentage of organic sourced foods

Microbial Data (Dependent Variables)
1) Alpha (Shannon Index)
2) Beta Diversity
3) Abundance of different phyla, specifically Firmicutes and bacteroidetes and their butyrate-producing members (i.e. Roseburis (firmicute phylum))

Mental Health Data (Dependent Variables)
1)PROMIS 29-depression scores
2)PROMIS 29-anxiety scores
3)MDI scores

Conclusions

This research highlights basic demographics and lifestyle practices of CIH students in the INCLD study. Further studies will evaluate the impact of these practices on mental and physical wellbeing and the gut microbiome.

For references or further questions, please email: jpletch@ndnet.ccnm.edu

Naturopathic approaches to atopic dermatitis: a cross-sectional audit of patient care at a naturopathic teaching clinic

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Introduction

- It is estimated that up to 17% of Canadians will suffer from atopic dermatitis (AD) at some point in their lives.
- In Ontario specifically, patients with AD have an average of 3.6 publicly funded doctors visits per year to assess and treat their AD.
- The total cost of AD in Canada is estimated to be 1.4 billion Canadian dollars annually.
- Given this burden, there is a growing interest in the use of complimentary and alternative medicines (CAM) as an adjunct to conventional treatment for AD.
- In fact, up to 34% of patients will seek out and use CAM therapies at some point to treat their AD, however, less is known about the nature of the care that is being provided by CAM professionals, including naturopathic doctors.

Objectives

This study aims to describe the different therapies used by naturopathic doctors (NDs) to support patients with AD. This research may provide useful information in the development of standards of care and practice guidelines for the holistic treatment of AD.

Search Methods

- Electronic medical charts from the Schad Naturopathic Clinic (SNC) were reviewed for demographics, treatments, compliance, and response to treatment.
- Charts were selected by searching the electronic medical record system of the SNC between May 1st, 2019 and Dec 31st, 2022 for patients with atopic dermatitis in their charted assessment (ICD9 Code 691 and 691.8).
- Records were excluded if they did not have at least 3 visits during the date range specified or were under 18 years of age at the time of their first appointment.
- Manual extraction was done by four individuals using a pilot-tested template to describe the nature of the conditions, laboratory investigations and treatments provided.
- This study was approved by the Canadian College of Medicine's Research and Ethics Board.

Results

Demographics

- **Age:** Ages ranged from 23 to 80; mean = 39.
- **Gender:** Female (n = 125); Male (n = 22); Not Charted (n = 10).

Average Number Of Visits

- Number of visits ranged from 3 to 52; mean = 12.

Conventional Treatments

- See 'Figure 2. Conventional Treatments'.

Naturopathic Treatments

- See 'Figure 3. Naturopathic Therapies By Modality'.
- See 'Figure 4. Nutraceuticals and NHPs'.

Nutraceuticals and NHPs

- **Omega-3s:** Daily doses ranged from 250mg of EPA and 300mg of DHA to 3380mg of EPA and 866mg DHA.
- **Vitamin D:** Daily doses ranged from 800IU to 5000IU.
- **Probiotics:** All options recommended were multi-strain products. Daily doses ranged from 7 billion CFUs to 25 billion CFUs.

Botanicals (Topical)

- An oatmeal bath or paste was recommended in 18 of 157 charts (11%); calendula cream in 11 of 157 charts (7%); St. Francis' Skin Healing Salve in 9 of 157 charts (6%); and chickweed cream in 6 of 157 charts (4%).

Nutrition

- A diet diary was completed in 51 of 157 charts (32%).
- The elimination diet was the most popular dietary intervention recommended (40 of 157 charts (25%)).
- **General nutrition themes:** increase water intake; increase consumption of healthy fats; increase fruit and veg consumption; increase fiber intake; follow an anti-inflammatory diet

Education

- Skin hygiene and bathing education was provided in 13 of 157 charts (8%); Education on hypoallergenic/fragrance-free detergents & personal care products in 8 of 157 charts (5%); ceramide moisturizers in 14 of 157 charts (9%).

Figure 2. Conventional Treatment

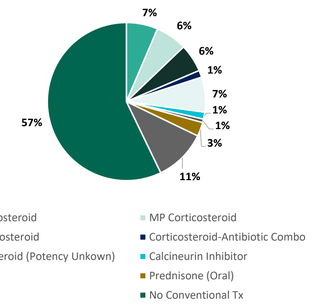


Figure 3. Naturopathic Therapies By Modality

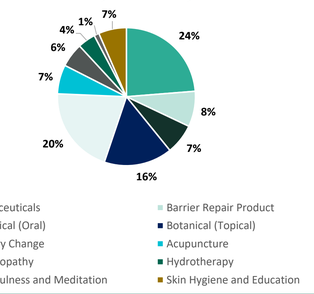
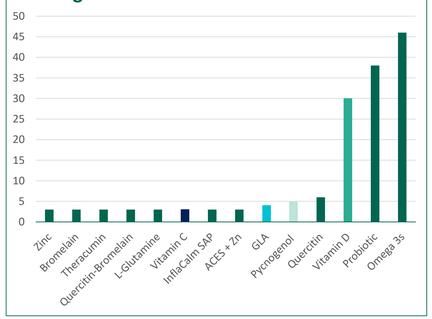


Figure 4. Nutraceuticals and NHPs



Discussions

This discussion highlights key interventions used by NDs at the SNC, including nutritional, topical, and dietary strategies, and examines the available literature on their role in managing AD severity and symptoms.

Omega-3s:

- High dose Omega-3s yield statistically significant reductions in SCORAD scores compared to controls in adults with AD. RvE1 which is derived from eicosapentaenoic acid (EPA) suppresses T cell production of IL-4 and IFN-γ, as well as decreasing serum IgE levels.

Vitamin D:

- There is no standardized dosage of vitamin D for reducing the SCORAD index in AD. Instead, the key factor is achieving sufficient serum 25(OH)D levels. Research indicates that patients with serum 25(OH)D levels of ≥20 ng/mL, whether through supplementation or other sources, tend to have lower SCORAD scores and reduced disease severity.

Probiotics:

- Probiotics are a therapeutic option for AD in adults, showing significant SCORAD improvements. However, their impact on quality of life is unclear, and small study sizes limit generalizability. Beneficial strains vary, with *Lactobacillus salivarius, Lactobacillus acidophilus, Bifidobacterium animalis subsp. lactis,* and *Bifidobacterium breve* showing the most promise.

Topical Oatmeal:

- Topical oat preparations have consistently shown benefit in improving skin barrier function and symptomatic management of AD. Studies support the use of a 1% OTC topical oat preparation as both an independent and adjunctive therapy to conventional treatments for mild-to-moderate AD.

Topical Calendula:

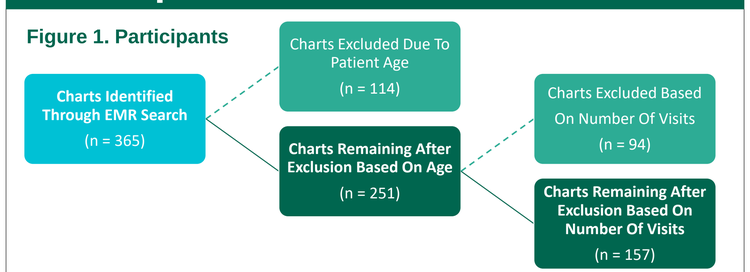
- Consistent evidence suggests that calendula is generally well tolerated when applied topically, making it a safe option for individuals seeking natural remedies. No studies have examined the independent effects of *Calendula officinalis* for the treatment of AD, but studies on infantile diaper rash and post-radiation dermatitis, suggesting potential efficacy for AD.

Elimination Diet:

- There is insufficient evidence to support strict dietary elimination in the vast majority of adults with AD. The elimination diet may result in a minimal but likely unimportant improvement in severity, pruritus, and sleeplessness in patients with mild-to-moderate AD. However, a select subgroup of patients with clinically relevant food allergies may benefit from its usage, highlighting the importance of specific IgE mediated allergy testing prior to recommendation.

Participants

Figure 1. Participants



Conclusions

The findings of this audit suggest potential roles for various naturopathic treatments in managing atopic skin presentations, including omega-3 fatty acids, topical oat preparations, vitamin D supplementation, and specific probiotic strains. Evidence from literature suggests that omega-3 fatty acids may help reduce inflammation, while topical oat preparations can support skin barrier function in mild-to-moderate atopic dermatitis. Vitamin D supplementation that is tailored to individual serum levels may correlate with improved clinical outcomes, while probiotics such with *Lactobacillus salivarius, Lactobacillus acidophilus, Bifidobacterium animalis subsp. lactis,* and *Bifidobacterium breve* show promise with no reported adverse effects. Conversely, treatments such as calendula and the Elimination Diet lack sufficient evidence to recommend their routine use, with the latter potentially increasing the risk of food allergies and gastrointestinal issues.

These findings provide preliminary insights into naturopathic management strategies, but further high-quality research is needed to confirm efficacy, establish best practices, and inform clinical guidelines for practitioners treating AD.

For references or further questions, please email: bdedecker@ccnm.edu