# Naturopathic Approaches and Training for Utilizing Research Evidence Informed Practice Skills (NATURES): A Mixed Methods Study

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## Introduction

- Evidence-based practice incorporates the best available evidence along with clinician expertise and patient values.
- Naturopathic medicine programs include EBP curricula.
- Alongside curriculum changes, there has been a commensurate change in ND acceptance of EBP.
- A recent cross-sectional study in Canada assessed EBP skills, attitudes, and use among Canadian NDs.
  - Results for all three domains were high or favourable
  - Participants expressed interest in educational opportunities to refresh or improve these skills

## Objectives

1. Assess current attitudes, skill, use, barriers/facilitators of EBP among North American NDs at the AANP conference.
2. Identify EBP educational topics of most interest.
3. Assess impact of an EBP workshop on attitudes, skill, & use.
4. Assess participant views about the EBP workshop.

## Methods

**Table 1. Study Design Elements**

| | |
|---|---|
| **Design** | Cross-sectional design to capture data at 2 timepoints (before and after workshop). |
| **Participants** | Naturopathic doctors or naturopathic medical students practicing or studying in the United States who were registered to attend the AANP 2024 conference. |
| **Data Collection** | • First survey was distributed 4 weeks before the conference (registered attendees were invited to complete via email)<br>• Second survey was sent to individuals who attended the EBP workshop 4 weeks after the conference via email |
| **EBP Workshop** | • 2-hour workshop during 2024 AANP convention<br>• Various EBP topics discussed (e.g., using PICO to ask a clinical question, searching scientific literature, limitations & biases, basic statistics)<br>• Time to practice applying the skills taught |
| **Analysis** | • Frequencies, correlations, bivariate analyses (t-tests, ANOVA), & linear regression (quantitative)<br>• Thematic analysis (qualitative) |

## Results

- Pre-conference survey: n= 47, primarily women (72%), age 30-49 (62%).
- Interest in educational topics: applying EBP to naturopathic medicine (70%), critical appraisal (51%), identifying sources of bias (47%).

**Table 2. EBASE Scores at Baseline**

| | |
|---|---|
| **EBP Use** | Median: 14.2<br>Indicates a moderate-high level of use of evidence |
| **EBP Skills** | Median: 40.5<br>Indicated a predominantly average to somewhat advanced level of skill |
| **EBP Attitudes** | Median 32.7<br>Indicated a predominantly agree to strongly agree |

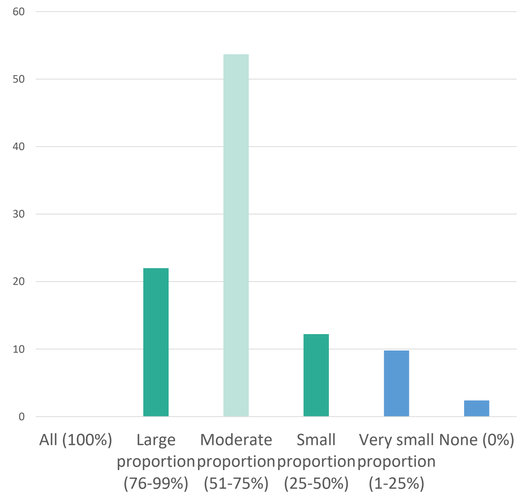


**Figure 1. Percentage of participating naturopathic doctors' clinical practice based on evidence from clinical research (n=41)**

### Accurate understanding of EBP

"Using research, patient preference, and clinical experience to guide and optimize patient care and outcomes"

### Positive views about EBP

"I think it's vital to good patient care." "Naturopathic medicine needs Evidence-informed practices"

### Barriers & Facilitators to EBP Use

- Limited availability of naturopathic-specific research
- Insufficient skill in locating, interpreting, appraising, and applying research & lack of time to do these things
- Access to the internet, online databases, full-text journal articles, and pre-synthesized evidence facilitators

### Post-Conference Survey

- Low participation (n=8), unable to assess for change in scores
- Relevancy, adequacy, effectiveness and impact of the workshop all rated highly

## Discussions

### Overall Findings

- First study to quantitatively assess EBP attitudes, skill, and use as well as interest in EBP educational opportunities among American NDs.
- American NDs seem to have a largely favourable **view of EBP**, average to somewhat advanced **skill use**, and moderately high **use of EBP.**
- Unable to assess workshop's potential impacts on EBP attitudes, skill, or use.

### Strengths & Limitations

+ Use of a validated instrument (EBASE questionnaire).

+ Demographics similar to those seen in the ND profession.

- Small sample size relative to licensed NDs in America.

## Conclusions

- Overall, our findings suggest American NDs are generally supportive of EBP and have a moderately high level of self-reported skill and use.
- Attendees at an EBP workshop reported that the delivered continuing education in EBP was relevant, effective, and impactful.

## Acknowledgements

We wish to thank the American Association of Naturopathic Physicians (AANP) and the Naturopathic Doctors who participated in this research.

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

# The effect of Myo-Inositol supplementation in reducing the risk of developing gestational diabetes mellitus (GDM) in overweight and obese woman: a narrative review

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## Introduction

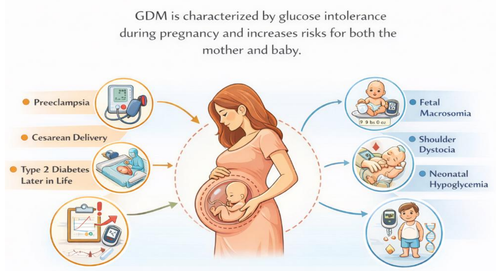


Figure 1: GDM consequences for the mother and fetus. Note: Image generated using Open AI (Chat GPT 5.2), Feb. 13, 2026, from the prompt: create a simple diagram for this information "GDM is characterized by glucose intolerance that develops during pregnancy and is associated with increased risks for the mother, including preeclampsia, cesarean delivery, and progression to DM type 2 later in life. GDM also increases the risk of fetal macrosomia, shoulder dystocia, neonatal hypoglycemia, and long-term metabolic disorders"

Myo-inositol (MI) is a structural component of cell membranes and a mediator of insulin signaling. MI supplementation may reduce insulin resistance and lower the risk of GDM and improve outcomes.

However, few studies have specifically examined its effects on maternal insulin resistance (mIR), a key underlying mechanism in GDM development.

## Objectives

This narrative review aimed to evaluate the consistency of existing findings on the use of myo-inositol for GDM prevention in overweight and obese women.

## Search Methods

This review used PubMed database using these inclusion criteria:

| Category | Description |
|---|---|
| Study design | Randomized controlled trials (RCTs) |
| Population | Overweight and obese pregnant women (BMI>24 kg/m2) |
| Intervention | Myo-Inositol supplementation |
| Intervention timing | Early to mid-pregnancy (before 28 weeks of gestation) |
| Control | Folic Acid, Standard of Care, or Placebo |
| GDM assessment | 75g of oral glucse tolerance test (OGTT) at 24-28 weeks' gestation |
| Primary outcomes | Development of gestational diabetes mellitus (GDM) |
| Secondary outcomes | Gestational hypertension, newborn birth weight |

## Results

| Author (Year) | Study Type | Participants (n) | Intervention (MI) | Control | Duration of treatment |
|---|---|---|---|---|---|
| Santamaria et al. (2015) | Open-label RCT | Obese pregnant women (BMI ≥30), n=220 | Myo-inositol 2 g + folic acid 200 µg twice daily (4 g/day total) | Folic acid | 12–13 weeks' gestation → delivery |
| Esmaeilzadeh et al. (2023) | Double-blind RCT | Overweight women (BMI 25–<30), n=60 | Myo-inositol 2 g + folic acid 400 µg once daily | Placebo + folic acid | 14 → 24 weeks (≈10 weeks) |
| Moini et al. (2025) | Open-label RCT | High-risk pregnancy, mean BMI ≈28, n=150 | Myo-inositol 4 g + folic acid 400 mg once daily | Folic acid alone | 11–14 weeks → +14 weeks |
| Amaefule et al. (2022) | Double-blind pilot RCT | High-risk; >⅓ obese, n=198 | Myo-inositol 2 g + folic acid 200 µg twice daily | Placebo | 12–15+6 weeks → delivery |
| Asimakopoulos et al. (2024) | Open-label RCT | Mean BMI 23 (intervention), 25 (control), n=200 | Myo-inositol 4 g + folic acid 400 µg once daily | Standard care | 11–13+6 weeks → 26–28 weeks |
| D'Anna et al. (2013) | Open-label RCT (authors state placebo-controlled) | BMI <30; n=220 (99 MI / 98 placebo completed) | Myo-inositol 2 g + folic acid 200 mg twice daily (4 g/day) | Folic acid 200 mg twice daily | 12–13 weeks → delivery |
| D'Anna et al., 2015 | Open-label RCT | Obese pregnant women (BMI ≥30), n=220 | Myo-inositol 2 g + folic acid 200 µg twice daily (4 g/day) | Folic acid | 12–13 weeks → delivery |
| Vitale et al. (2021) | Open-label RCT | Overweight women (BMI 25–<30), n=223 | Myo-inositol 2 g + folic acid 200 mg twice daily | Folic acid | 12–13 weeks → 3 weeks postpartum |
| Farren et al. (2017) | Open-label RCT | Family-history risk; mean BMI 26, n=240 | Myo-inositol 1.1 g + D-chiro-inositol 27.6 mg + folic acid 400 mg once daily | Placebo | 10–16 weeks → 24–28 weeks |
| Matarrelli et al. (2013) | Double-blind pilot RCT | Non-obese (sample size NR) | Myo-inositol (dose NR) | Placebo | Throughout pregnancy |

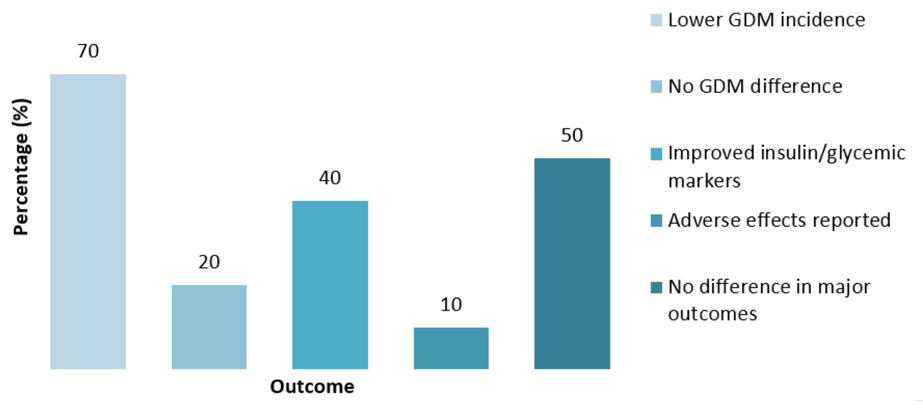


**Figure 2. Percentage of RCTs reporting outcome**

## Discussions

- Most studies reported a statistically significant reduction in GDM incidence with myo-inositol supplementation.
- Improvements in mIR support a role in the insulin signaling pathway, although findings were not consistent across all trials.

### Mechanism of Action

1. Insulin binds the insulin receptor.
2. This activates the PI3K–Akt pathway.
3. Myo-inositol → inositol phosphoglycans (IPGs) act as second messengers.
4. IPGs amplify insulin signaling
5. GLUT4 translocates to the membrane.
6. Glucose uptake increases
7. ↓ Hepatic gluconeogenesis and ↓ circulating insulin levels.

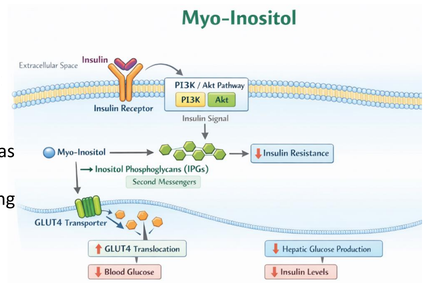


Figure 3: MI mechanism of action. Note: Image generated using Open AI (Chat GPT 5.2), Feb. 13, 2026, from the prompt: create a diagram showing how myo-inositol improves insulin signaling and reduces insulin resistance.

### Clinical Application

- Given the limited preventive pharmacologic options in pregnancy, MI may represent a safe strategy to target a key pathophysiologic mechanism underlying GDM.
- No serious adverse effects were reported with MI supplementation; however, one trial reported vomiting.

### Study Limitations

- Further research may benefit from including articles not published in English or in other databases. Findings from some included studies may not account for participant expectation, or confounding variables, particularly when open-label study designs were used. Our study did not assess risk of bias.
- Studies used heterogenous interventions (egs. dose timing, and co-administered substances) and populations which limits interpretability of findings.

## Conclusions

The use of myo-inositol supplementation is a promising treatment option to prevent GDM in overweight and obese women.

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

# Investigating the Effect of Photobiomodulation on Fertility Outcomes: A Narrative Review

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## Introduction

- Infertility affects approximately 1 in 6 couples in Canada.
- Reproductive health challenges often stem from issues related to impaired gamete quality and cellular function.
- Photobiomodulation (PBM), a non-invasive light therapy, could be relevant to reproductive health based on evidence that it may enhance cellular metabolism and nitric oxide levels, which may be important for maintaining optimal reproductive cell function and supporting sperm motility.

## Objectives

The purpose of this review was to examine existing literature on the effects of PBM on fertility outcomes in males and females.

## Search Methods

- PubMed and The Cochrane Library were used to search for available literature with the following inclusion criteria:
  1) Humans
  2) PBM in any form
  3) Control group without treatment (control or untreated)
  4) Analysis of markers for fertility (e.g., sperm motility, successful pregnancy) as an outcome
  5) Experimental studies
  6) Peer-reviewed article
  7) English language
- The search string (photobiomodulation OR PBM OR PBMT) AND (fertility OR infertility OR sperm count OR sperm motility).
- The search yielded 41 studies, of which 12 studies met the inclusion criteria. An additional 3 studies were identified from the reference list analysis of included articles (n=15).

**Table 1. PICO Framework**

| Population | Intervention | Comparison | Outcomes |
|---|---|---|---|
| Humans | PBM in any form | Control or untreated | Markers for fertility |

## Results

**Table 2. Summary of Evidence**

| | Category | PBM Wavelengths | Key Results | Sources |
|---|---|---|---|---|
| Males | Sperm Motility & Energetics | • Red laser (650 nm) & NIR (980 nm)<br>• PBM (650 nm)<br>• Red light (660 nm) & NIR (810 nm, 830 nm)<br>• LED (multiple)<br>• PBM (610 nm)<br>• LLLT (830 nm) | • Stimulates mitochondrial respiratory chain to activate tail movements required for fertilization<br>• ↑ energy consumption for better passage through the female genital system = ↑ pregnancy probability<br>• ↑ motility & viability in fresh & asthenozoospermic samples | • Ahmed et al. (2024)<br>• Saylan et al. (2023)<br>• Ban Frangez et al. (2015)<br>• Safian et al. (2020)<br>• Stigliani et al. (2024)<br>• Salman Yazdi et al. (2014) |
| | Sperm Health Integrity & Treatment Protocol Optimization | • Pulsed-wave light (655 nm)<br>• LLLT (905 nm)<br>• LLLT (810 nm) & LED (660 nm & 850 nm) | • Preserves DNA & acrosome integrity<br>• Dose-dependent response present in sperm motion characteristics<br>• Fresh sperm responds more robustly to specific energy levels compared to frozen | • Espey et al. (2022)<br>• Firestone et al. (2013)<br>• Gabel et al. (2018) |
| | Cryo-preservation (ART) | • 810 nm PBM Pre-conditioning (Pre-thaw/ Post-thaw) | • Acts as a "protective shield" that safeguards sperm against the mechanical & thermal damage of freezing<br>• Application timing (pre- vs. post-thaw) differentially impacts motion parameters in normozoospermic men | • Safian et al. (2021)<br>• Safian et al. (2022) |
| Females | Female Fertility & Uterine Health | • 632 nm laser<br>• He-Ne laser Pretreatment<br>• LLLT (635 nm)<br>• IR & NIR (between 600-1000 nm) | • Repairs uterine structure & ↑ function (ameliorates IUAs) after mechanical injury by activating cAMP/PKA pathway<br>• ↑ endometrial receptivity & preparation for frozen-thawed embryo transfer in recurrent implantation failure patients<br>• ↑ long-term reproductive health markers (e.g., full-term pregnancy) in 9-month follow-ups | • Zheng et al. (2024)<br>• Tsai et al. (2020)<br>• El Faham et al. (2018)<br>• Phypers et al. (2024) |

## Discussions

Studies conducted in males showed positive effects in sperm motility and function, improved regulation of mitochondrial energetics, and nitric oxide levels. In females, a higher rate of successful pregnancies and positive fertility tests was observed.

### Strengths

- Emphasis on human studies improves the clinical relevance of the findings.

### Limitations

- Lack of studies focusing on long-term reproductive outcomes (i.e., birth rates).
- Current literature is male-dominant.
- Considerable variability in protocols (wavelengths, treatment duration, dosage), study populations, and outcome measures.
- Most studies are limited to ART and are clinically applied, limiting access with significant costs associated.

### Clinical Application

- Given the consistency of these preclinical findings, it is possible that PBM may have a positive effect on fertility outcomes in humans.

### Future Directions

- Additional clinical evidence on humans is needed to strengthen these prospective insights and perhaps assist in addressing fertility challenges in men and women.

## Conclusions

PBM therapy demonstrated favorable reproductive outcomes in the available studies. Given that the majority of the included experimental studies focused on males, further randomized trials are needed to strengthen these prospective insights and potentially assist in addressing fertility challenges in both men and women.

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

# Building the Comprehensive Research Evidence Synthesis Training (CREST) Center: A Process Evaluation of a Virtual Systematic Review Training Center for Complementary and Integrative Health Trainees

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## Introduction

- Systematic reviews are the foundation of evidence-based practice (EBP) guidelines
- However, most systematic reviews in the field of complementary and integrative health (CIH) are of critically low quality.
- There is a need for training in the conduct of high-quality evidence synthesis.

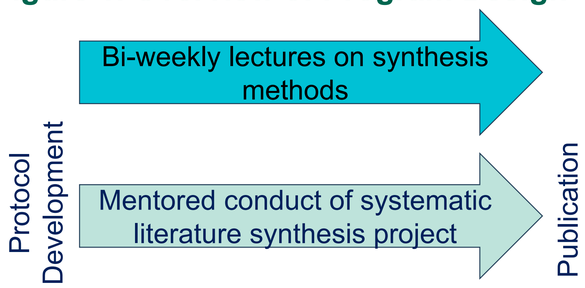
## Objectives

The Comprehensive Research Evidence Synthesis Training (CREST) Center was developed as a virtual, mentorship-driven training center that explicitly includes CIH institutions and learners. This poster reports on a process evaluation of CREST's first two years, highlighting its design, participant characteristics and outputs.

## Methods

- Trainees work in group on systematic evidence synthesis projects from protocol development to publication.
- 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 evidence-based practice attitudes; completed spring 2024 and repeated after 1 year.
- Assessments: Evidence-Based practice Attitude and Utilization Survey (EBASE) questionnaire (EBP attitudes), Assessing Competency in Evidence Based Medicine (ACE) Questionnaire (EBP knowledge)

**Figure 1. Overview of Program Design**




## Results

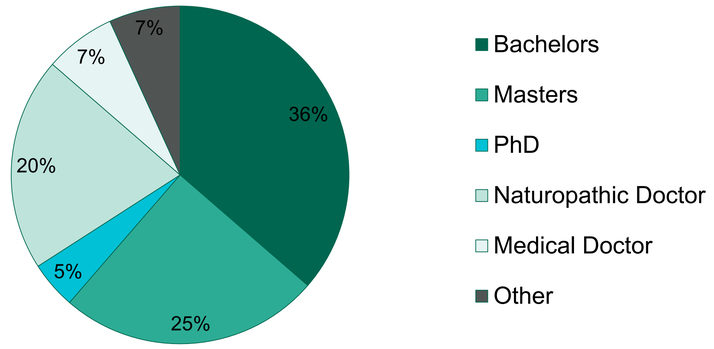



**Figure 2. In-progress and complete degrees obtained by CREST participants**

- **Baseline EBASE Attitudes Score**: 35.3 (SD 2.59) corresponding to "predominantly agree to strongly agree"
- **Baseline ACE questionnaire**: 9.2 out of 15

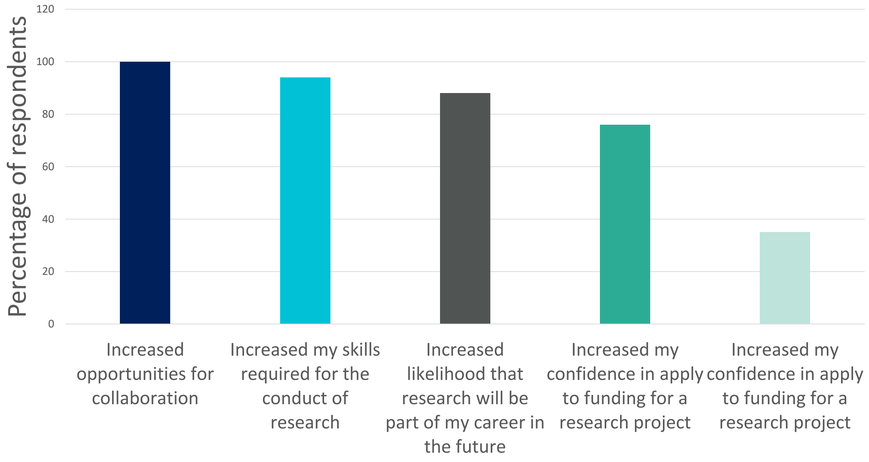



**Figure 3. Participant responses about CREST experience**

## Funding

Research reported in this publication was supported by the National Institutes of Health under Award Number U24AT012549 through the RAND REACH Center as well as R25DK130848, K12NS130673, T32-AT002688. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. This project also received support from a RAND REACH Center pilot grant funded by the NCMIC foundation.

**Table 1. List of current projects**

| CREST Projects | Status |
|---|---|
| The role of olive oil and its constituents in mental health: A scoping review | Published |
| Allium sativum and mental health: A scoping review | Published |
| The effects of supplemental curcumin on anxiety symptoms in adults: A systematic review and meta-analysis | Under review |
| The effect of Rosmarinus officinalis on depression, anxiety and psychological stress in adults: A systematic review and meta-analysis | Manuscript in progress |
| Dietary protein and anxiety symptoms and disorders: A scoping review | Manuscript in progress |
| Dietary glycemic index and glycemic load and anxiety: A systematic review | Data extraction |
| Convergence insufficiency after traumatic brain Injury: A systematic review | Quality assessment |
| Cognition, brain fog, and the microbiome: An overview of reviews | Manuscript in progress |
| The cumulative incidence of post-traumatic epilepsy after mild traumatic brain injury: A systematic review | Data extraction |
| The impact of recombinant growth hormone on quality of life for adult growth hormone deficiency: A systematic review and meta-analysis | Data extraction |
| Guidelines for the diagnosis of testosterone deficiency in adult males: A systematic review and critical appraisal | Manuscript in progress |
| Natural versus sugar & artificial sugar substitutes on postprandial glycemia and metabolic parameters: A systematic review | Manuscript in progress |
| The impact of Artemisia Annua and Artemisia Afra on fibrosis: A scoping review | Data extraction |
| Intermittent fasting and pain: A systematic review | Screening |
| Movement-based mind-body practices for multiple sclerosis: An Umbrella review | Published |
| Microbial-derived polyphenol metabolites and gut microbiota: A scoping review of clinical studies | Under Review |
| Microbial-derived phytoestrogens in health and disease: A scoping review | Data extraction |

## Discussions

- There is a high degree of interest among CIH students in learning about evidence synthesis.
- Early evaluation suggests that participants report benefits of participation (Figure 3).
- Several projects are underway and making progress, suggesting feasibility of this program in facilitating the conduct of systematic literature synthesis projects.

## Conclusions

CREST addresses a critical gap in the field of CIH evidence synthesis and provides a replicable model for building capacity.

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

# The Role of Nutrition in Mental Health Care in North America: A Qualitative Study

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## Introduction

- The emerging field of 'nutritional psychiatry' explores the interplay between nutrition and mental health.
- In observational and clinical trials, high-quality, nutrient-rich diets are associated with decreased risks of depression and anxiety, while ultra-processed diets are linked to an increased risk of mental health disorders.
- Despite this growing evidence, implementation of dietary counselling in mental health care is limited.

## Objectives

1. Explore North American mental health professionals' perceptions of and experiences with incorporating nutrition into clinical mental health practice
2. Identify perceived barriers and facilitators to discussing or integrating nutrition within routine clinical care
3. Explore differences and similarities in perspectives across professional roles and between practitioners in the United States and Canada

## Methods

### Table 1: Study Design

| Population | Data Collection | Outcomes |
|---|---|---|
| • Regulated mental health practitioner<br>• Practicing in the United States or Canada | • 60–90-minute virtual focus groups<br>• Semi-structured interview methodology<br>• Analysis using Kuckartz content analysis method | • Assessment and identification of themes that mental health practitioners have surrounding using nutrition in clinical practice |

**Recruitment:** Social media, professional email listservs, and word of mouth; snowball sampling used to expand reach.

**Analysis Plan:** Kuckartz qualitative content analysis using deductive theme development (based on existing literature) and inductive subtheme generation.

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

## Results

**Participant Characteristics**

- Twenty-four participants, predominantly female and mid-career mental health professionals, with an average age range of 35–44 years.
- Canadian sample (N = 21) was larger and more professionally diverse. Most participants hold master's degrees in social work, with a mean of 13.45 years in practice.
- U.S. sample (N = 3) included psychologists, social workers, and counsellors holding graduate or doctoral degrees, with a mean of 6 years in practice.
- Largely based in private practice, with additional representation in other sectors, such as hospital and community mental health settings.

**Themes** Using Kuckartz content analysis, the following themes were identified, with supporting quotes from focus group participants:

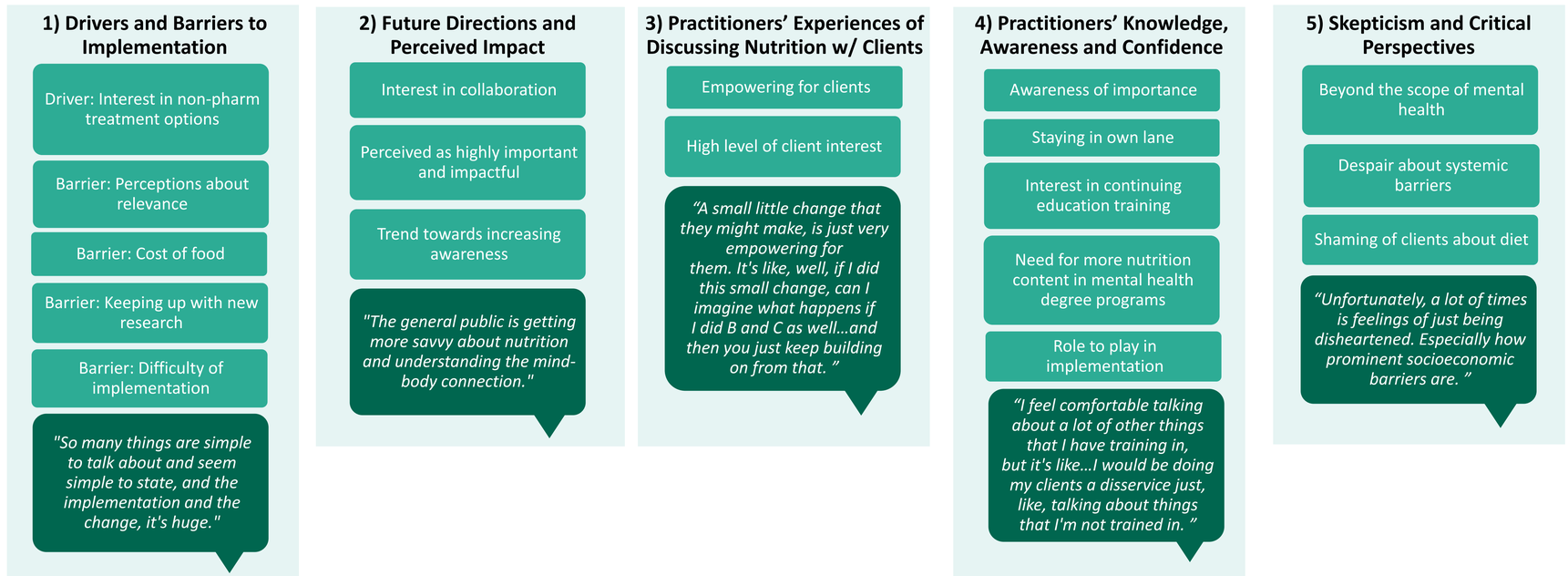


**Figure 1. Themes and subthemes identified in focus groups and supporting participant quotes**

## Discussions

**Strengths**

- Inclusion of multiple mental health disciplines captured diverse interprofessional perspectives.
- Use of Kuckartz's framework supported both theory-driven and emergent theme analysis.
- Systematic qualitative approach enhanced analytic rigor.

**Limitations**

- Findings should be interpreted with caution when generalizing to broader populations.
- Likely selection bias—participants generally held favorable views towards nutrition.
- Perspectives may not reflect clinicians with neutral or negative views.

## Conclusions

Mental health care practitioners report a high level of interest in the role of nutrition in mental health care. They recognize it as an important component of care but also acknowledge the presence of barriers and the need for additional training and support.

# Quercetin for the treatment of dermatographic urticaria with angioedema: A case report

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## Introduction

- Dermatographia urticaria is an allergic skin condition marked by itching and raised red marks that appear after scratching. It can occur in combination with angioedema, characterized by swelling beneath the skin.
- These conditions are common and results in significant discomfort. Not all patients respond to the available treatment options.
- Quercetin is a flavonoid with anti-allergic and anti-inflammatory effects.

## Case Presentation

A 31-year-old white female sought naturopathic care for intermittent allergy-like symptoms experienced over the past six months. Symptoms included generalized itching, dermatographia urticaria ("skin writing"), facial flushing, periorbital swelling, ear fullness, dizziness and lightheadedness. Flushing episodes occurred approximately every 2 days and lasted several hours. She had known allergies to dust and penicillin and was diagnosed with dermatographia in 2022 following a severe bee sting reaction. Her symptoms worsened in 2025, and an allergist suggested a possible food chemical allergy after testing returned negative. Antihistamines were recommended but not initiated.

Her medical history included reactive hypoglycemia, well managed through a low-glycemic index diet with adequate protein and fiber. She had a history of anxiety and depression managed with psychotherapy, exercise-induced asthma treated with salbutamol as needed, and previous bloating and nausea that improved after eliminating gluten. At the start of naturopathic care, she was taking vitamin D (1000 IU daily), omega-3 (1300 mg daily), salbutamol as needed and used an IUD for contraception.

### Diagnostic Assessment:

- Based on the patient's description of her symptoms, a diagnosis of dermatographia urticaria and angioedema was considered to be most likely.

### Therapeutic Intervention:

- Quercetin 500mg (increasing to 1000 mg/day after 1 week) and 2000mg vitamin C/day for allergy symptoms
- Increase Vitamin D from 1000 IU/day to 2000 IU/day to prevent deficiency and support overall health

## Results

**Figure 1. Dermatographia urticaria**

"Dermographism in child", created by Gzzz, 2021, https://commons.wikimedia.org/wiki/File:Dermographism_in_child.jpg, Wikimedia Commons, Creative Commons Attribution-Share Alike 4.0 International.

### 1st follow up (3 weeks from baseline):

- Significant improvement in symptom frequency and severity.
- She had not had an episode of flushing in the prior 2 weeks.
- She also did not have any episodes of dizziness.

### 2nd follow up (6 weeks from baseline):

- Only 2 episodes of flushing since previous visit which were related to stressful situations.
- She had experienced no episodes of skin writing, despite provocation, and reported decreased ear congestion.

### 3rd follow up (10 weeks from baseline):

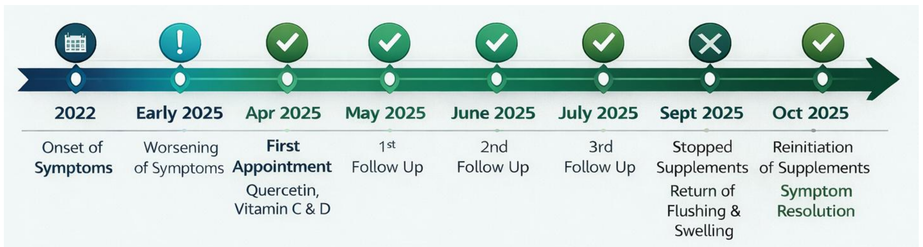
- No flushing, no itching at all, energy was great.

### 5th follow up (27 weeks from baseline):

- The patient had been referred to another allergist for a second opinion. As directed, she stopped the supplements a few days prior to the appointment. She noticed a return of her facial flushing symptoms.
- She restarted her supplements after the appointment and within 2 weeks, the symptoms subsided.
- The allergist diagnosed her with chronic idiopathic urticaria and angioedema and prescribed 2 antihistamine medications.

The patient reported that she took the supplements consistently. She was queried about adverse or unanticipated effects of the treatment at each visit, but none were reported.

**Figure 2. Timeline of Milestones**




## Discussions

- Quercetin may reduce urticaria/angioedema by stabilizing mast cells and decreasing release of histamine and inflammatory mediators, reducing wheal formation and tissue swelling.
- Preclinical and limited human evidence supports quercetin's role in reducing allergic symptoms; vitamins C and D were added based on clinical experience.

### Strengths

- Inadvertently included a natural experiment whereby the patient's symptoms returned upon stopping the prescribed supplements and again subsided once she was resumed supplementation. This adds strength to the hypothesis that the resolution of the patient's symptoms was the result of the supplements.

### Limitations

- The experience of a single patient, and the outcome may not be generalizable.
- Other changes or factors, besides the treatment described, may have been responsible for the reported improvement.

### Clinical Application

- While studies have previously reported a decrease in certain allergic symptoms following supplementation with quercetin, no clinical trials have assessed the effects on dermatographia urticaria or angioedema.

## Conclusions

Quercetin and vitamin C supplementation may improve symptoms of dermatographia urticaria, idiopathic urticaria and angioedema in this case. Further research involving randomized controlled trials is warranted to establish clinical efficacy and safety of quercetin in human populations.

**For references or further questions, please email: mbagnato@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) is a Mediterranean plant, is know for many therapeutic properties.
- Rosemary is known to influence the nervous system, modulation of noradrenergic, dopaminergic and serotonergic pathways.

## 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 and risk of bias assessment was completed in duplicate.
- Results were pooled in a meta-analysis using a random-effects inverse variance model
- A priori subgroup analysis was conducted based on method of administration.

**Table 1: Eligibility Criteria**

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

## Results

- The literature search yielded 1564 studies after duplication. Fourteen studies met criteria for inclusion, including a total of 865 participants.
- Risk of bias was "high" or "some concerns" in five and six studies, respectively
- Primary analysis: No impact of rosemary supplementation on depression, anxiety or stress symptoms. In sub-analysis, there was a beneficial effect of oral supplementation on anxiety symptoms.

**Table 1. Characteristics of Included Studies**

| | |
|---|---|
| **Population** | Participants with existing psychiatric disorders or symptoms (n=3)<br>Participants with no existing psychiatric disorders (n=11) |
| **Duration of Study** | Long term duration of 4-8 weeks *(n=7)*<br>Short term duration of 5-30 minutes (n=7) |
| **Method of Administration** | Inhaled Rosemary (n=9), Oral Rosemary (n=5) |
| **Dose of Rosemary** | 1 to 4 drops of rosemary was inhaled<br>700mg to 4g of rosemary was taken orally |
| **Comparison Intervention** | Placebo (n=9), Active treatment (n=2), No treatment (n=2) |

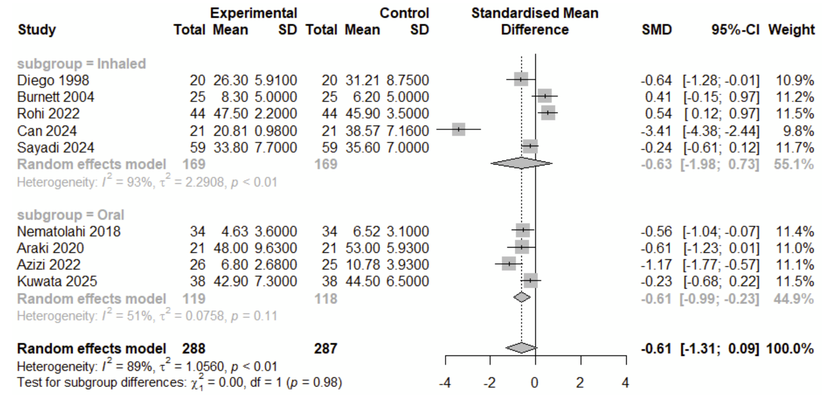


**Figure 1. Meta-analysis of the studies assessing the impact of rosemary supplementation on anxiety symptoms - subanalysis based on method of administration.**

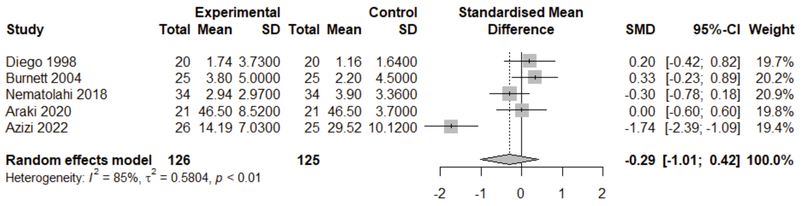


**Figure 2. Meta-analysis of the studies assessing the impact of rosemary supplementation on depression symptoms**

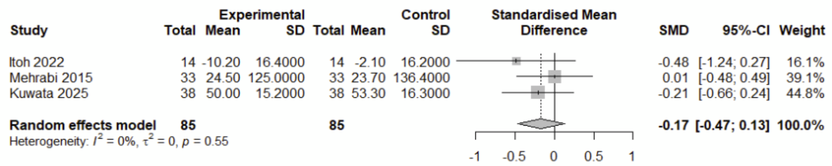


**Figure 3. Meta-analysis of the studies assessing the impact of rosemary supplementation on stress symptoms**

## Discussions

- It is possible that oral dosing may be more effective than inhaled for treating anxiety.
- 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

- Screening and data extraction were performed independently and in duplicate.
- Significant methodological variation between studies in terms of method of administration (oral, inhaled), dose, duration and outcomes.

## Conclusions

It is uncertain if rosemary supplementation improves anxiety, depression and psychological stress outcomes. More research on the impact of oral rosemary supplementation for four to eight weeks is warranted.

## 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 This project also received support from a RAND REACH Center pilot grant funded by the NCMIC foundation.

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

# Dietary glycemic index/load, insulin index/load and anxiety: A systematic review and meta-analysis

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## Introduction

- Anxiety disorders are the most prevalent psychiatric conditions worldwide, yet many affected individuals report that the available treatment options are not fully accessible, tolerable, or effective.
- Diet has been increasingly recognized as a key determinant of mental health conditions, and the post-prandial glycemic effects of foods may alter biological pathways linked to anxiety.
- Dietary glycemic index and dietary insulin index are measures of the post-prandial glycemic effects of food relative to standard reference foods; higher value denote a larger increase in blood sugar.
- Dietary glycemic load and dietary insulin load take into account both the glycemic effect and the quantity of food consumed.

## Objectives

Conduct a systematic review and meta-analysis on the impact of dietary glycemic index/load and/or dietary insulin index/load on anxiety symptoms and disorders.

## Search Methods

- A search was conducted using PubMed, Embase, Web of Science, and CINAHL using controlled vocabulary and free-text terms.
- Duplicate, independent screening is complete and data extraction is in progress.
- Standardized risk of bias assessments will be performed in duplicate.
- The study results will be pooled in a meta-analysis using a random effects inverse variance model.

**Table 1. Eligibility Criteria**

| | |
|---|---|
| Population | Adults (18+ years of age) |
| Exposure/ Intervention | Measurement or change of dietary glycemic index/load and/or dietary insulin index/load |
| Outcome | Anxiety symptoms or disorders |
| Study Design | Observational or Experimental |

## Results

- 9181 studies were identified after deduplication.
- After title and abstract screening, 43 studies were included.
- After full text screening, 12 studies met criteria for inclusion (Figure 1).

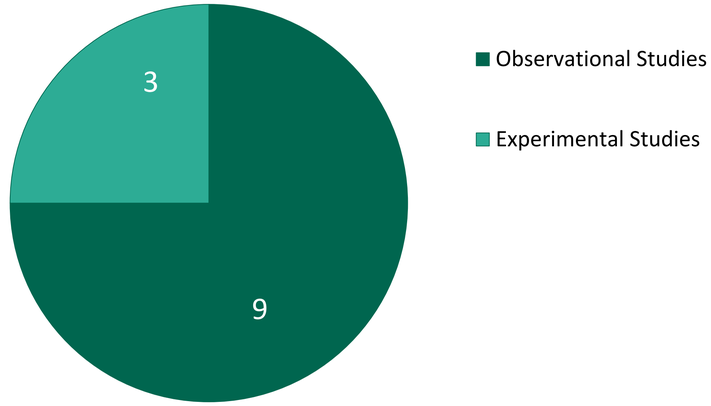


**Figure 1. Design of included studies**

### Observational Studies

- All used a cross-sectional design.
- Sample size ranged from 398 to 7574.
- Participants included community samples of adults, elderly adults and body builders.
- Studies assessed exposure using food frequency questionnaires.
- Anxiety symptoms were assessed using the Hospital Anxiety and Depression Scale, the Beck Anxiety Inventory, and the Depression Anxiety and Stress Scale-21.
- Two studies reported a statistically significant increase in anxiety symptoms among participants consuming a higher glycemic index diet or lifestyle index for insulin resistance.

### Experimental Studies

- Data extraction is currently in progress

## Discussions

### Possible Mechanisms

- High glycemic index foods can cause reactive. hypoglycemia which shares many symptoms with anxiety
- Dietary glycemic index can impact the availability of substrates for the gut microbiome; health of the gut microbiome impacts mental health.
- Glycemic balance can alter activation of the hypothalamic-pituitary axis and the stress response.
- High glycemic index diets may be low in other nutrients important for mental health.

## Conclusions

Understanding how dietary glycemic/insulin index and load may influence anxiety could provide new insight into the plausible role of diet patterns and blood sugar regulation 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. This project also received support from a RAND REACH Center pilot grant funded by the NCMIC foundation.

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

# The Effect of Dietary Protein on Anxiety and Stress Symptoms: A Scoping Review

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## Introduction

- Anxiety and psychological stress are common and increasing, prompting interest in modifiable lifestyle factors such as diet
- 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 to other databases. Translations and the full strategy were reviewed by an experienced medical librarian.
- No language, date, peer-review, or publication status restrictions were applied, though these sources will be noted in the evidence summary.
- Data extraction was completed using a piloted template. Qualitative analysis is underway.

### 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

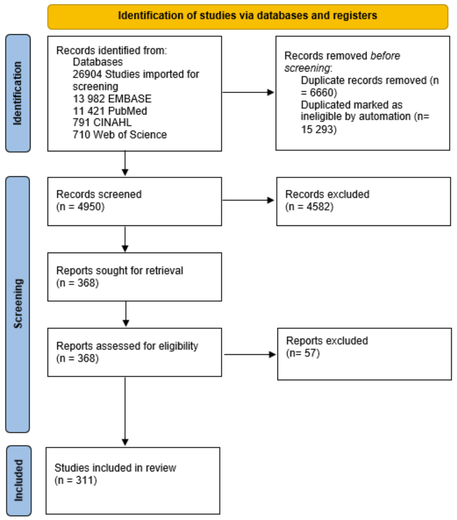


**Figure 1. PRISMA Flow Diagram**

### Table 1. Summary of Included Studies by Category, Population and Outcome Measured

| Category | Human (n) | Animal (n) | Results |
|---|---|---|---|
| Dietary protein intake | Exp: 29<br>Obs: 35 | Exp: 31 | **Exp**: Most studies report improvements in anxiety or stress outcomes with higher protein intake<br>**Obs**: Most studies report an association between less protein and more anxiety or stress |
| Amino acid supplementation | Exp: 19<br>Obs: 11 | Exp: 41 | **Exp**: Most studies report an association between increased methionine and more anxiety or stress. Most report an association between increased arginine, lysine, phenylalanine, tyrosine, and/or tryptophan and less anxiety or stress.<br>**Obs**: most studies report an association between less amino acid intake and more anxiety or stress |
| Tryptophan modification | Exp:<br>Obs:12 | Exp:<br>Obs:2 | **Exp**: Tryptophan depletion studies showed mixed results. Studies using tryptophan supplementation primarily reported a reduction in anxiety and stress symptoms.<br>**Obs**: Lower tryptophan levels associated with higher stress and anxiety symptoms |
| Individual Foods | Exp: 7 | Exp: 13 | **Exp**: Most interventions improved anxiety or stress related outcomes or biomarkers with mixed effects on subjective anxiety measures |

Exp: Experimental, Obs: Observational

## Discussions

### Key Findings

- Evidence linking dietary protein to anxiety and stress is broad but methodologically heterogeneous
- The literature is largely mechanistic with relatively few human trials isolating dietary protein intake

### Research Gaps

- Clinically relevant human data are limited, particularly for whole-protein foods
- Key gaps remain regarding the effects of protein quality, source, and dose on anxiety and stress outcomes

### Implications for Future Research

- Future research should prioritize well-controlled human trials examining realistic dietary protein interventions and clinically meaningful outcomes


**Figure 2. Summary of possible mechanisms**

## Conclusions

There is an association between dietary protein and anxiety or stress; however, further research, including well-controlled human intervention studies examining protein quality and source is warranted.

## Funding

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

# A Case Report on Self-Directed Recovery of Gu Syndrome: Reversal of Multisystem Dysfunction via Microbiome Restoration and Subconscious Guided Protocols

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## Introduction

- Gu syndrome, in Traditional Chinese Medicine (TCM) , is a chronic inflammatory condition caused by pathogens, toxins, and parasites, and it encompasses both digestive and neurological symptoms. In this case, this condition involved significant microbiome disruption, presenting as Candida overgrowth, dysbiotic flora consistent with small intestinal bacterial overgrowth (SIBO), mold toxicity, intestinal hyperpermeability and chronic multisystem involvement.
- This case illustrates novel integration of subconscious-driven or intuitive recovery with integration of microbiome-focused therapeutic protocols.

## Case presentation

**2014-2018:** A 38-year-old male developed multiple symptoms after a trip to a developing country. His symptoms included weight gain, excessive fatigue, anxiety, low mood, brain fog, constipation, bloating, slow urination and nocturia. Initial lab tests run by an endocrinologist in Oct 2014 ruled out anemia, hypothyroidism and infection. The patient had stool analysis that tested positive for Candida in Aug 2015 and for dysbiotic flora consistent with SIBO in Dec 2016, ordered by a functional medicine doctor and an ND, respectively.

**2019-2022:** The patient was diagnosed with Gu syndrome in Apr 2020 by a Chinese medicine doctor based on his clinical presentation. His symptoms were gradually resolving, although urinary symptoms persisted. He tested positive for leaky gut on an intestinal antigenic permeability test in Aug 2020 and for mold toxicity on a visual contrast sensitivity test in Jan 2022, both self-ordered.

**Table 1. Intervention phases in different stages of healing**

| Phase | Intervention |
|---|---|
| Pathogen elimination | Botanicals: oregano, berberine, garlic, caprylic acid; Candida diet, FODMAP diet, restrictive diets |
| Detoxification | Binders: Activated charcoal, chlorella, N-acetyl cysteine |
| Gut repair, mucosal regeneration | Slippery elm, marshmallow root, glycine, L-glutamine |
| Microbiome rebuilding | Inulin, human milk oligosaccharides, acidic foods, spirulina |

## Lab Results

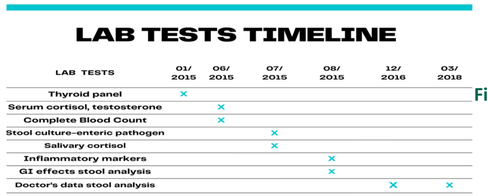


Figure 1. Timeline of lab tests done between 2015 and 2019

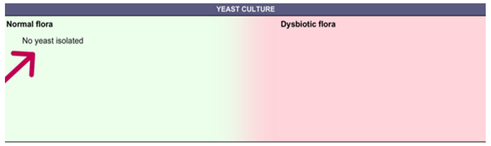


Figure 2. Comprehensive stool analysis (Doctor's Data) after treatment with Candida protocol (sample collected on 12/05/2016)

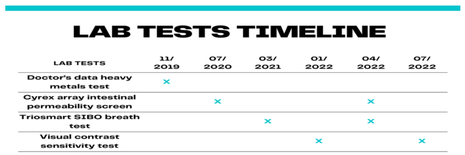


Figure 3. Timeline of lab tests done between 2019 and 2022.

| Gases | Expected | Observed | Normal/Abnormal |
|---|---|---|---|
| $H_2$ | <24.96 ppm | 4.78 | Normal |
| $CH_4$ | <10.00 ppm | 0.90 | Normal |
| $H_2S$ | <3.00 ppm | 2.16 | Normal |

Figure 4. TrioSmart breath test after treatment with the SIBO protocol (sample collected on 04/24/ 2022)

| TEST | | | RESULT | |
|---|---|---|---|---|
| Array 2 – Intestinal Antigenic Permeability Screen | IN RANGE (Normal) | EQUIVOCAL* | OUT OF RANGE | REFERENCE (ELISA Index) |
| Actomyosin IgA ** | 7.89 | | | 0.0-20.1 |
| Occludin/Zonulin IgG | 1.09 | | | 0.3-1.6 |
| Occludin/Zonulin IgA | 0.61 | | | 0.1-1.6 |
| Occludin/Zonulin IgM | 0.72 | | | 0.0-1.8 |
| Lipopolysaccharides (LPS) IgG | | 1.94 | | 0.0-2.6 |
| Lipopolysaccharides (LPS) IgA | | | >2.80 | 0.0-1.8 |
| Lipopolysaccharides (LPS) IgM | 1.50 | | | 0.0-2.1 |

Figure 5. Cyrex array intestinal antigenic permeability screen after treatment with leaky gut protocol (sample collected on 04/20/2022)

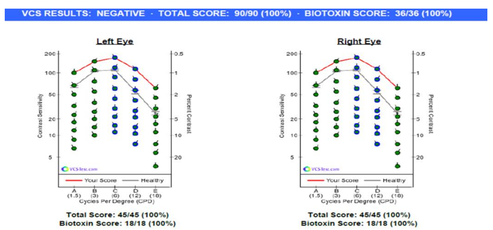


Figure 6. Visual contrast sensitivity test after treatment with mold protocol (Sample collected on 07/25/2022)

## Discussions

### Mechanism of action

- Dr. Heiner Fruehauf's diagnostic criteria for Gu syndrome involve both digestive and neurological symptoms that are unexplained by conventional medicine and usual patterns of TCM. The case met the diagnostic criteria, and the patient had fungal and bacterial overgrowth as the cause of his symptoms.
- The subconscious-driven approach was based on the patient's intuition about his health, and tracking progress for extended periods of healing with changes in anthropometric measures and physical performance. The patient restored balance in his system or terrain, by changes in diet and nutrition which was confirmed by the lab results.

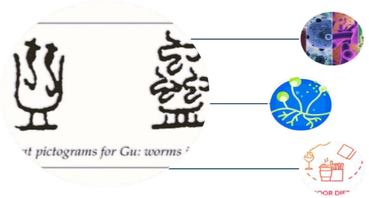


Figure 7. Pathogenesis of Gu syndrome

**Strengths:** This case is unique because it shows lab-confirmed normalization of Candida, dysbiotic flora consistent with SIBO, mold, leaky gut, and systemic Gu syndrome with dietary interventions, supplementation, and minimal use of pharmaceuticals.

**Limitations:** A patient-driven, subconscious approach may lead to inconsistent supplement dosing and selection of lab tests that were not gold standard, causing false positive results. Patient was not under constant medical supervision, and the differentiation between adverse effects due to Jarisch Herxheimer and non-Herxheimer can be highly subjective, based on subconscious guidance

## Conclusions

This is a single, novel case, and the results would be generalizable only through future research. Future research should evaluate subconscious-driven models as a therapeutic strategy for chronic inflammatory conditions.

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

# A case report on polyarthralgia with rash following Parvovirus manifesting as a sequela of Streptococcal infection

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## Introduction

- Parvovirus is associated with clinical syndromes such as the fifth disease, arthritis, aplastic crisis, and hydrops fetalis. Polyarthralgia and arthritis linked to Parvovirus are more common in adults (50-80%) than in children (8%).
- This case report demonstrates that Parvovirus can cause polyarthralgia and polyarthritis in adults, which may resemble the sequelae of Group A streptococcal infection, such as acute rheumatic fever (ARF) or acute post-streptococcal reactive arthritis (PSRA).

## Case presentation

**Visit 1:** A 36-year-old Caucasian female followed up after an ER visit for polyarthralgia starting 4 days prior, and rash the week before polyarthralgia. She had 3 courses of antibiotics for Group A Streptococcal (GAS) infection within the last 5 months. A physical examination showed moderate swelling and tenderness in the hands, feet, and knees bilaterally, with pain on active movement. Labs were ordered to rule out different causes of arthritis.

**Visit 2:** The patient noticed an 80% improvement in joint pain after 1 week. She noticed facial erythema for 2 days and on her arms on the day of the visit. Given her ongoing chest pain with deep inhalation, an EKG revealed a slow sinus rhythm, but within normal limits.

**Visit 3:** The patient had been exposed to a parvovirus outbreak at a preschool where she worked as a teaching assistant. Parvovirus testing was ordered.

**Interventions:**

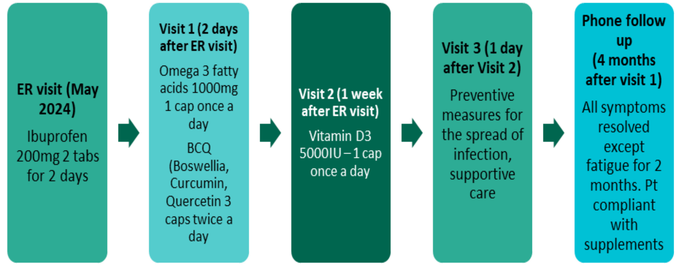


**Figure 1. Interventions given in different visits**

## Results

**Table 1. Differential diagnosis and laboratory tests**

| DDx | Lab tests | Results |
|---|---|---|
| Infectious arthritis - Lyme, viral | Lyme disease serology<br>Parvovirus B19 antibodies | Negative – Lyme serology<br>Positive- IgM and IgG Parvovirus antibodies |
| Postinfectious reactive, Rheumatic fever | Anti-streptolysin (ASO) | Not done |
| Rheumatoid arthritis | Rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP) | Negative |
| Osteoarthritis | X-ray hands, knees | Negative |
| Systemic rheumatic illnesses | Anti-nuclear antibodies (ANA) | Negative |
| Vitamin D deficiency | Vitamin D levels | 26.9 ng/ml |

ER note - CBC, CMP, ESR, PT/PTT, Uric acid were within normal limits except Hematocrit 34.5 (low), absolute Lymphocyte count .73 (low).

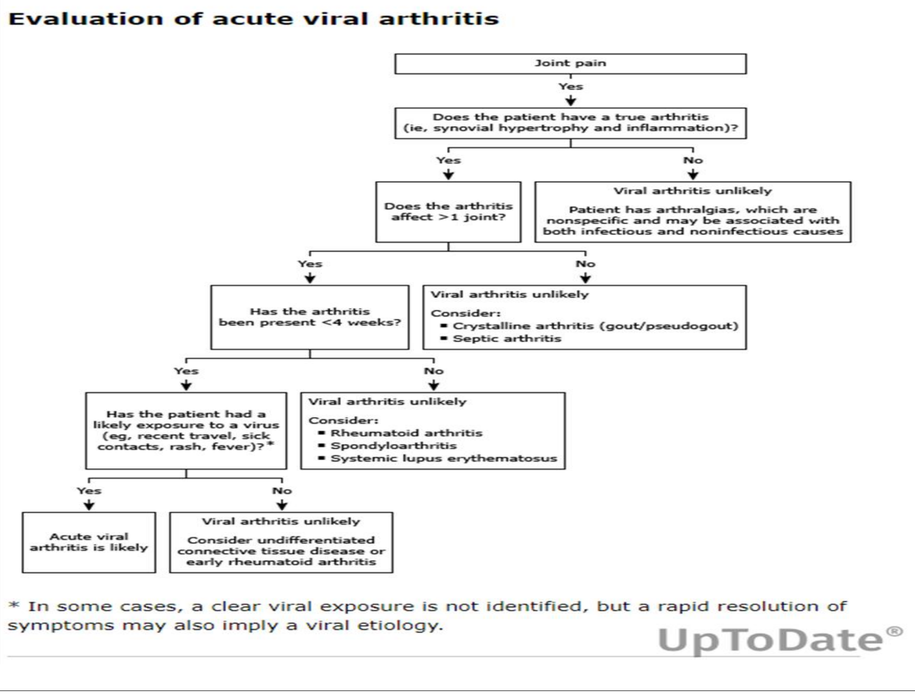


**Figure 2. Algorithm for the evaluation of acute viral arthritis.**

Moore T, Syed R, Calabrese C. Viral arthritis: Causes and approach to evaluation and management. UpToDate. Updated: 31 Mar, 2025. Accessed 22 Feb, 2026. https://www.uptodate.com/contents/viral-arthritis-causes-and-approach-to-evaluation-and-management.

## Discussions

The patient's acute presentation, followed by rapid symptom resolution, supports the diagnosis of viral arthritis. A mild decline in hematological parameters such as hemoglobin, hematocrit, mean corpuscular volume, mean cellular hemoglobin, and mean hemoglobin concentration is associated with parvovirus infection, along with a reduction in the total number of lymphocytes in viral infections.

The timeline does not fall within the typical ARF and PSRA window period. Antibiotic treatment further reduces the risk of progression to ARF, which has led to a decline in its incidence in developed countries.

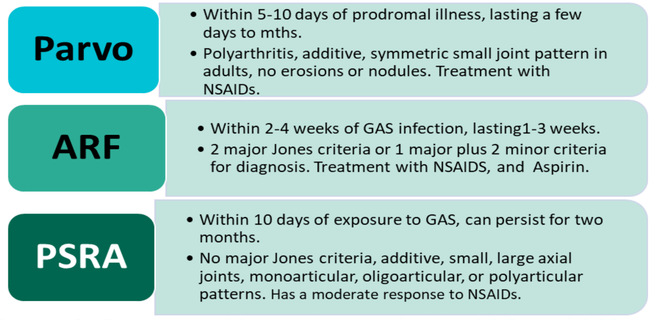


**Figure 3. Features of Parvovirus arthritis, ARF, and PSRA**

**Strengths:** The bacterial and viral causes of arthritis can share features; timely laboratory testing can establish an accurate diagnosis. An integrative approach can yield favorable outcomes in acute arthritis cases.

**Limitations:** Lab testing for anti-streptolysin titers could not be performed as the presentation and resolution of the case were acute. The extent of streptolysin response can be altered by antibiotics, age, season, and the number of infection episodes.

## Conclusions

Acute clinical awareness and laboratory testing are required to distinguish between bacterial and viral causes of arthritis. This will facilitate correct clinical diagnosis and formulation of a management plan.

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

# Combined Use of Berberine and Probiotics for Glycemic Management in Type 2 Diabetes Mellitus: A Narrative Review

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## Introduction

- In 2021, diabetes affected approximately 537 million people worldwide, representing over 10% of the global population. By 2045, diabetes prevalence is expected to increase to 783 million individuals.
- Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, hyperglycemia, and increased cardiovascular risk.
- Standard glycemic therapies (e.g., metformin, insulin) are effective but can have tolerability or adherence issues.
- Berberine, a plant derived alkaloid, has demonstrated glucose- and lipid-lowering effects comparable to first line agents.
- Probiotics support gut microbiome balance, and are commonly used to improve gastrointestinal health and metabolic function.
- Despite variable probiotic outcomes, enrichment of beneficial genera following antidiabetic therapy suggests that adjunctive probiotic use with berberine may enhance metabolic effects. A growing interest exists in gut microbiome modulation as a therapeutic target in metabolic diseases, and gut microbiome-mediated mechanisms of Berberine.

## Objectives

The objective of this narrative review is to evaluate and synthesize the current clinical evidence on the combined use of berberine and probiotics for glycemic management in individuals with type 2 diabetes mellitus, with a focus on glycemic outcomes, gut microbiota modulation, potential synergistic effects, and existing gaps in the literature.

## Search Methods

- Databases used to search included PubMed, Cochrane Library, CINAHL, MEDLINE.
- The inclusion criteria included human randomized controlled trials (RCTs), systematic reviews and meta-analyses, with studies investigating combined berberine (BBR) and probiotic interventions

**Table 1. PICO framework**

| Population | Intervention | Outcomes |
|---|---|---|
| • >18 and <70 years old<br>• Diagnosed hyperglycemia or type 2 diabetes<br>• BMI >19 and <35 kg/m$^2$ | • Berberine alone<br>• Probiotics alone<br>• Berberine + Probiotics<br>• Placebo or standard care | Primary-Glycemic control markers:<br>• HbA1c<br>• Fasting plasma glucose<br>• Post-prandial glucose<br>• HOMA-IR<br>Secondary- Gut microbiota changes |

## Results

- Two randomized controlled trials (RCTs) met inclusion criteria and were included in the final synthesis.
- Berberine (BBR) significantly reduced HbA1c, fasting plasma glucose, and post-prandial glucose compared with placebo.
- Probiotics alone did not produce significant improvements in glycemic outcomes in either RCT.
- Combination therapy (BBR + probiotics) achieved glycemic improvements comparable to berberine alone.
- Improvements in HOMA-IR were observed only when probiotics were combined with berberine.
- Berberine alone did not consistently improve insulin resistance measures.
- Berberine induced marked alterations in gut microbiota composition.
- Probiotics alone did not significantly alter gut microbial composition.
- The addition of probiotics did not consistently enhance glycemic outcomes beyond berberine alone.
- Combination therapy demonstrated selective benefit for insulin sensitivity and microbiome modulation.
- Gastrointestinal adverse effects were more frequently reported in berberine-containing intervention groups.

**Table 2. Differential effects of berberine and probiotics on glycemic, insulin resistance, and gut microbiota outcomes in randomized controlled trials**

| Characteristic | Zhang et al., 2020 | Ming et al., 2021 |
|---|---|---|
| **Study Design** | Multicenter, randomized, double-blind, placebo-controlled | Multicenter, randomized, placebo-controlled |
| **Population** | Newly diagnosed T2DM patients | Newly diagnosed hyperglycemia |
| **Sample Size** | 409 participants | 300 participants |
| **Intervention Arms** | BBR; Probiotics; BBR + Probiotics; Placebo | BBR; Probiotics; BBR + Probiotics; Placebo |
| **Duration** | 12 weeks (after antibiotic run-in) | 16 weeks |
| **Primary Glycemic Outcomes** | ↓ HbA1c, fasting glucose, post-load glucose with BBR ± probiotics | ↓ FPG and HbA1c primarily in BBR and combination groups |
| **Probiotics Alone** | No significant glycemic benefit | No significant glycemic benefit |
| **Insulin Resistance (HOMA-IR)** | Improved **only** in BBR + probiotics group | Modest improvement in combination group |
| **Microbiome Effects** | Significant BBR-induced shifts; ↓ *Ruminococcus bromii*; altered bile acid metabolism | BBR altered microbiota; probiotics alone showed minimal changes |
| **Safety** | GI side effects more common with BBR | GI symptoms more frequent with BBR |

## Discussions

### Possible of Mechanism of Action

Berberine may reduce abundance of taxa involved in secondary bile acid production (e.g., Ruminococcus bromii), potentially shifting bile acid pools toward more insulin-sensitizing profiles. Berberine influences GLP-1 secretion and metabolic signaling pathways via gut–liver axis mediators such as FXR and FGF19. Berberine improves insulin resistance and glucose regulation by modulating host gene expression through microbial metabolites. Probiotics may produce short-chain fatty acids with insulin-sensitizing effects. Probiotics may support BBR's metabolic effects as depicted in Figure 2.

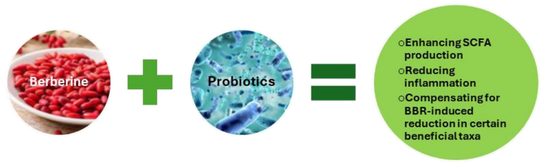


**Figure 1: Metabolic effects of Probiotics and Berberine**

### Strengths and Limitations

- Strengths: Highlights a novel therapeutic paradigm beyond standard pharmacotherapy.
- Limitations: Few high-quality RCTs exist; sample sizes are moderate and heterogeneity in probiotic strains limits generalizability.

### Future Research & Clinical Application

- Future research should look into what the strain-specific effects of probiotics are when combined with BBR, as well as if this combination produces sustained glycemic improvements over long-term follow-up.
- Clinical Application: Adjunctive use of BBR with probiotics may improve glucose control, especially in patients intolerant or unresponsive to standard therapies. Could be considered for early or mild T2DM as a complementary support strategy.

## Conclusions

There is insufficient evidence to assess the effect of the combination of BBR and probiotics on glycemic control in T2DM. Further high-quality research is required.

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

# Developing Clinical Practice Guidelines for Natural Products in Oncology: Results from a Database Coverage Analysis

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## OVERVIEW

- Clinical practice guideline development begins with a systematic literature search.
- Conducing systematic searches for natural health products (NHPs) poses challenges, including the diversity of products, varied terminology, and inconsistent indexing.
- The optimal combination of databases to search for comprehensive coverage for NHP-related topics is unknown.
- Beyond traditional databases, the Knowledge in Integrative Oncology Website (KNOW) is a curated repository of clinical research on natural agents in cancer compiled from MEDLINE and Embase. KNOW could be a viable alternative or adjunct to librarian-conducted searches.
- In this project, we evaluated which bibliographic databases are necessary for comprehensive coverage, the added value of KNOW, and the potential of KNOW to replace traditional searches.

## METHODS

**Search Strategy**

Two systematic search strategies for NHPs for chemotherapy-induced peripheral neuropathy (CIPN) were developed.

(1) "Patterson Search" - Developed with a medical librarian for MEDLINE, Embase, Allied and Complementary Medicine Database (AMED), Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature (CINAHL)

(2) "KNOW Search" – developed for KNOW database

The Patterson search string included controlled vocabulary (e.g., MeSH and database-specific equivalents) and keywords related to cancer, CIPN, and NHPs. Database-specific searches were developed using the Ovid platform. The KNOW search used the side effect tag "peripheral neuropathy" and the keywords neuropathy, neuropathic, and neurotoxicity.

Both searches were conducted from database inception to March 31st, 2025. Articles underwent de-duplication and were screened by two independent reviewers. Conflicts were resolved internally among the reviewers.

## METHODS (CONT)

**Study Eligibility Criteria**

**Inclusion Criteria**

(1) Peer reviewed and published meta-analyses, clinical trials, and observational studies in English

(2) Adult cancer population

(3) Evaluating the prevention or treatment of peripheral neuropathy from systemic anticancer treatments (e.g., chemotherapy, targeted agents, immunomodulatory drugs)

(4) Intervention is an NHP or combination of NHPs

**Exclusion Criteria**

(1) Grey literature, case reports, systematic reviews without a meta-analysis, narrative reviews and overviews of meta-analyses, meeting abstracts, interim analyses

(2) Meta-analyses with inappropriate methodology

(3) Neuropathy caused by non-systemic treatments (e.g., surgery)

(4) Multimodal interventions (e.g., NHP + nutrition)

**Analysis**

Database coverage was assessed by calculating the proportion of included studies retrieved from each database and by comparing the KNOW search to the full Patterson search.

## RESULTS

From the Patterson search, we obtained 3547 articles. 1017 duplicates were removed, leaving 2530 for screening. In KNOW, we found 502 articles. 189 duplicates were removed, leaving 313 for screening. From the combined six databases, we found a total of **91 unique relevant articles** that met eligibility criteria.

72 articles (79%) were found by more than one database. KNOW retrieved the most unique articles (10, 11%), followed by Embase (7%), MEDLINE (2%) and CINAHL (1%). AMED and Cochrane Library did not retrieve any unique articles.

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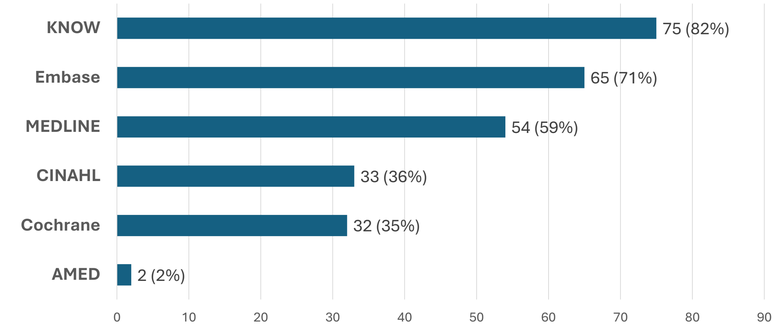
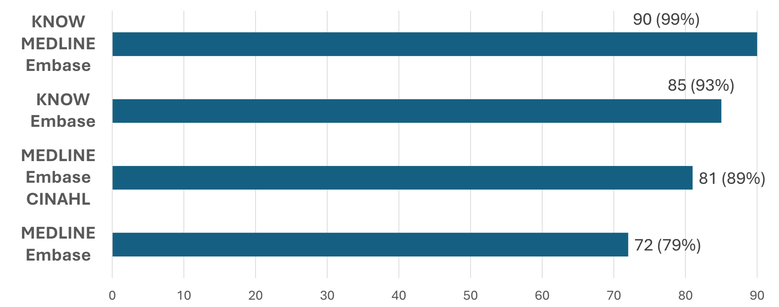
## RESULTS (CONT)

**Relevant articles from each database**




The entire Patterson search retrieved 81 relevant articles (89%) and the KNOW search retrieved 75 (82%). Consequently, there were 10 KNOW articles that were not found in the Patterson search, and 16 Patterson articles not found in KNOW.

**Relevant articles across database combinations**




Cochrane and AMED did not yield any additional articles to MEDLINE and Embase. CINAHL yielded one article not found in MEDLINE, Embase, or KNOW.

## CONCLUSION

This analysis highlights the importance of searching multiple databases despite overlapping coverage. The KNOW database alone is insufficient to replace traditional literature searches; however, it adds value in conjunction with MEDLINE and Embase for systematic searches for NHPs in cancer care. AMED, CINAHL, and Cochrane Library offered minimal value, contributing only one unique citation collectively.