Clinical Practice Guidelines for Natural Products in Oncology

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OVERVIEW

The growing research base for natural health products (NHPs) in cancer care presents a challenge for clinicians to integrate emerging findings. Clinical practice guidelines (CPGs) aim to support integration of best evidence into practice, reduce clinician workload, and enhance patient outcomes. Limited guidelines have been created for integrative oncology, leaving substantial gaps. This project aims to: (1) develop rigorous, transparent, and feasible methodology for the creation of CPGs for NHP use in cancer care; and (2) create a series of CPGs to help manage cancer-related symptoms using NHPs.

RATIONALE

NHPs are commonly used by people with cancer and recommended by integrative health care providers (HCPs). However, the medical community often expresses concern regarding their safety and efficacy. Existing guidelines are insufficient to inform the use of NHPs.

Limitations to Existing Guidelines

- Guideline panels rarely include practitioners knowledgeable in the use of NHPs
- Traditional knowledge is usually not considered
- Guideline methodology not adherent to established frameworks (e.g., GRADE, AGREE II, AMSTAR)

Given how patients value NHPs and they are commonly recommended by integrative HCPs, guidance is needed. Adapted guideline methodology is needed to accommodate the unique aspects of NHP research and practice.

END USERS AND GUIDELINE TEAM

Target users: Integrative HCPs (primary); all HCPs (secondary)
Target population: Adults with cancer

Development Team (DT): Oversees and manages the project
Advisory committee (AC): Provides independent oversight
Expert panel: Formulates recommendations

Funding: OncANP Research Grant; CCRF Grant; Patterson Institute

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METHODS

Adheres to GRADE principles, AGREE II, and AMSTAR.

Define Scope and Clinical Questions

PICO criteria and outcomes selected by development team; approved by advisory committee

Inclusion Criteria

(1) Clinical trials, observational studies, or meta-analyses
(2) Adult cancer population
(3) Systematic measurement of a guideline outcome
(4) Intervention is an NHP or combination of NHPs

Exclusion Criteria

(1) Case reports, narrative reviews
(2) Retracted studies
(3) Multimodal interventions (e.g., NHP + nutrition)

Literature Search

Databases: MEDLINE, Embase, Cochrane library, KNOW

Certainty of Evidence (COE)

Represents **our confidence in the effect estimate.** Determined for each guideline outcome. following data extraction and quality appraisal.

COE	Starting criteria
High	• Randomized controlled trials
Moderate	• N/A
Low	• Non-randomized studies of interventions (NRSIs) with a control group
Very Low	• Studies without a control group

All evidence can be **downgraded** for:

(1) Risk of Bias – systematic error distorting the effect estimate
(2) Imprecision – wide confidence intervals or small sample sizes
(3) Inconsistency – lack of agreement or uniformity in results
(4) Indirectness – mismatch in PICO criteria
(5) Publication bias – under publication of studies due to their results

Bodies of evidence consisting of NRSIs can be **upgraded** based on:

(1) Large magnitude of effect
(2) Presence of a dose-response gradient

METHODS (CONT.)

Grade of Recommendation

Expert panel assigns a recommendation grade for each clinical question (i.e., prevention or treatment of the symptom), indicating how strongly they recommend for or against the use of an NHP in that scenario. Recommendation grade is based on the certainty of evidence, balance of desirable and undesirable effects (net effect), and patient values. **Desirable effects** are benefits/advantages of an intervention; **undesirable effects** are harms/disadvantages.

We adopt a 5-level system (as opposed to GRADE's 4-level system) to distinguish between therapies with reasonably certain benefits that most patients would consider (grade B) and those with limited but supporting evidence that a minority would consider (grade C)

Grade	Description
A	There is confidence that the desirable effects strongly outweigh its undesirable effects. The panel recommends the intervention.
B	The desirable effects probably outweigh the undesirable effects with some uncertainty. The panel suggests using the intervention.
C	The desirable and undesirable affects are closely balanced, or confidence in the evidence is very low, resulting in substantial uncertainty. The panel suggests the intervention may be used in select patients.
D	The undesirable effects probably outweigh the desirable effects with some uncertainty. The panel suggests against using the intervention.
E	There is confidence that the undesirable effects outweigh its desirable effects. The panel recommends not using the intervention.
I	There is insufficient evidence to determine the direction of effect or to judge the balance of desirable and undesirable effects. The panel cannot make a recommendation for the intervention.

SIGNIFICANCE AND NEXT STEPS

The development of guidelines using this methodology is novel in the field of naturopathic and integrative oncology. The dissemination of CPGs may reduce knowledge gaps, promote the application of evidence in patient care, strengthen interdisciplinary collaboration, and enhance patient outcomes. The first CPG is for chemotherapy-induced peripheral neuropathy. The expert panel has been assembled, and data extraction is underway.