Anorexia Evaluation Table 2023: Cannabinoids and Derivatives

Systematic Review

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations	Quality and Nursing Implications
Hammond, S., Erridge, S., Mangal, N., Pacchetti, B., & Sodergren, M.H. (2021). The effect of cannabis-based medicine in the treatment of cachexia: A systematic review and meta-analysis. *Cannabis and Cannabinoid Research, 6*(6), 474–487. https://doi.org/10.1089/can.2021.0048	**Design:** Systematic review and meta-analysis **Method:** Evidence search was conducted in Medline®, Embase®, Cochrane, and Web of Science® Core Collection (gray literature) databases; Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) methodology was used for quality of evidence; and Cochrane Risk of Bias (ROB) tool and heterogeneity assessment were used. **Sample:** 5 studies with 934 participants with mean age of 53 years were included. 2 studies focused on HIV and wasting, 3 studies focused on patients with advanced cancer and self-reported unexplained weight loss of more than 5% or more than 2.3 kg. The majority of participants were male with exception of female majority in 1 study. Participants had Eastern Cooperative Oncology Group (ECOG) performance status scores of 0–2 in cancer studies; all had washout of 1 month for any previous use of appetite stimulants (e.g., corticosteroids, all cannabis products); all patients were able to tolerate oral intake.	**Independent Variable(s)**: Cannabis-based medicine (dronabinol, cannabis extract, tetrahydrocannabinol [THC], nabilone) with or without active treatment (megestrol) for cachexia **Dependent Variable(s)**: Appetite, weight, quality of life (QOL), adverse events (AEs) **Intervention:** Cannabis-based medicine (dronabinol, cannabis extract, THC, nabilone) with or without active treatment (i.e., megestrol) for cachexia	Appetite change measured with visual analog scale (VAS) scored from 0 to 10. Weight measured in kg. QOL measured with different instruments: Functional Assessment of Anorexia-Cachexia Therapy (FAACT) Global Health Status Score European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire–Core 30 (EORTC QLQ-C30) AEs	Change in appetite favored control group (mean change = –1.79, 95% CI [–3.77, 0.19]), but was not statistically significant (p = 0.08). Change in weight was pooled for 2 studies (mean change = –4.26 kg, 95% CI [–12.28, 3.76], p = 0.30, I^2 = 95%). QOL was measured with different instruments, but pooled results were insignificant (mean QOL = –0.14, 95% CI [–0.32, 0.03], p = 0.11). In one study, AEs in experimental arm were 43% compared with control of 13% (p < 0.001), most commonly dizziness, euphoria, and drowsiness. In two studies there was no difference in AEs between cannabis and megestrol groups. One study found increased incidence of impotence in the megestrol group compared with the dronabinol group (p = 0.002). Three studies reported no differences in frequency of AEs in cannabis versus placebo groups.	Limited number of studies with high heterogeneity in change in weight studies and low-quality ratings across all studies Missing outcome data noted due to attrition Small sample sizes Limited applicability of findings	Review methods were sound. The differences in cannabis-based medicine dosing and combinations with active treatment across studies, along with limited study duration (max 12 weeks) and mixed populations, make it difficult to apply findings to population of interest. Diverse types of cannabis-based medicines were studied in the literature. Some were combined with and without active treatment for anorexia/cachexia (i.e., megestrol) in different populations namely patients with HIV-related anorexia/cachexia and cancer-related anorexia/cachexia. This systematic review with meta-analysis did not have significant findings for the use of these medicines for appetite improvement, weight improvement, or QOL improvement. More research is needed to understand the role of this intervention in the treatment of anorexia/cachexia in patients with cancer.

Razmovski-Naumovski, V., Luckett, T., Amgarth-Duff, I., & Agar, M.R. (2022). Efficacy of medicinal cannabis for appetite-related symptoms in people with cancer: A systematic review. *Palliative medicine, 36*(6), 912–927. https://doi.org/10.1177/02692163221083437	**Design:** Systematic review **Methods**: A meta-analysis was used for all studies that included the necessary outcome-related information and were homogenous. Narrative synthesis was completed for other studies. Data extraction from the literature was performed by one of the reviewers and verified by a second reviewer. The Cochrane ROB tool was used. **Sample:** 5 studies with total of 847 participants with various cancers on active treatment with chemotherapy or radiation therapy were included. Majority of participants were male and older than age 50 years.	**Independent Variable(s):** Medicinal cannabis, including nabilone, dronabinol, cannabis extract, THC, megestrol acetate, or a combination of the above **Dependent Variable(s):** Appetite-related symptoms including weight, food/caloric intake, body mass index, taste and smell, food preferences, chemosensory alterations, toxicities related to intervention **Intervention:** Medical cannabis intervention (varied) compared to placebo (4 studies) or megestrol (1 study)	North Central Cancer Treatment Group (NCCTG) questionnaire FAACT EORTC QLQ-C30 VAS for appetite Macronutrient Preference Checklist Common Terminology Criteria for Adverse Events (CTCAE) for reaction reporting with cannabis Nutritional habit and consumption evaluation system (Sistema de Evaluación de Hábitos Nutricionales y Consumo de Nutrimentos [SNUT]) Satiety-labeled intensity magnitude (SLIM) Weight gain (defined as 10% or greater gain during treatment)	NCCTG questionnaire on appetite (1 study) found that use of megestrol plus dronabinol compared to megestrol alone was not statistically significant. Compared to dronabinol, there was an increase in appetite with megestrol use ($p = 0.0001$). Nabilone (1 study) showed no significant increase in appetite when measured using an independent questionnaire ($p = 0.3295$). Compared with placebo group in 1 study, dronabinol group showed an improvement in appetite ($p = 0.05$) and in pre-meal appetite ($p = 0.05$). With the FAACT (3 studies) measure, there was no significant improvement in appetite when using a cannabinoid ($p = 0.929$ for nabilone; $p = 0.7$ for dronabinol; $p = 0.3$ for the combination arm; $p = 0.003$ for dronabinol versus megestrol *favoring megestrol*). On the VAS, there was no significant difference in results when comparing cannabis extract, THC, and placebo ($p = 0.068$). For chemosensory perception (1 study): Dronabinol group had enhanced perception of food ($p = 0.018$) and improved taste and smell ($p = 0.026$); megestrol acetate group reported increased taste perception ($p = 0.0003$). Satiety as measured by SLIM (1 study): Increased satiety relative to baseline with dronabinol ($p = 0.03$) compared to placebo ($p = 0.05$) Weight gain (4 studies): Greater than 10% increase in weight during treatment with megestrol acetate ($p = 0.02$) with no change in cannabinoid arms compared with placebo Food intake (4 studies): Dronabinol group increased protein intake ($p = 0.008$) and had increased preference for pre-meal protein using the Macronutrient Preference Checklist ($p = 0.063$). Increase in caloric intake with dronabinol was not significant when compared to placebo ($p = 0.637$). Nabilone group had increased carbohydrate intake ($p = 0.040$) as measured by SNUT. Increased caloric intake was not significant in the nabilone group ($p = 0.123$); megestrol group had increased food intake ($p < 0.0001$).	Limited number of studies included Limited number of cannabinoids studied All trials allowed participants who were receiving active treatment, possibly impacting their appetite-related symptoms. Net global benefit was not used to assess outcomes in any of the studies that were included.	The results are feasible and relevant to practice; however, the multifactorial process associated with appetite-related symptoms must be considered. The methodology was sound and rigorous, including a two-reviewer, multistep process if studies were not part of the meta-analysis. Bias for each study was assessed using the Cochrane ROB tool and reported in this article. Depending on the evaluation tool, some trials showed an increase in appetite when nabilone or megestrol acetate was used. When prescribing cannabinoids, dosing, dose titration, and the impact of chemotherapy and radiation therapy on appetite-related symptoms must be considered. Key aspects of patient education include dosing, self-administration, tracking, and adherence to therapy. Additional studies are necessary to determine the efficacy of medicinal cannabis for increasing appetite and improving appetite-related symptoms. Information related to food intake, including timing of meals/snacks, types of food, food perceptions, and whether the food was filling, may be difficult to track but is necessary to help identify the efficacy of interventions on increasing food intake.

Simon, L., Baldwin, C., Kalea, A.Z., & Slee, A. (2022). Cannabinoid interventions for improving cachexia outcomes in cancer: A systematic review and meta-analysis. *Journal of Cachexia, Sarcopenia and Muscle, 13*(1), 23–41. https://doi.org/10.1002/jcsm.12861	**Design:** Systematic review and meta-analysis **Method:** Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). Database search was conducted of Ovid Medline®, Embase®, PubMed® and clinical trials in progress databases for studies of cannabinoids or synthetic derivatives compared to active or inactive controls. ROB and quality of evidence assessments were performed. **Sample:** Systematic review consisted of 10 studies: 4 randomized controlled trials (RCTs) and 6 nonrandomized studies of interventions (NRSIs) with 804 total patients (RCTs: n = 647, NRSIs: n = 157; study sample range = 6–311). Sample consisted of adult patients with cancer (mean age range = 47.3–67 years) with confirmed cachexia.	**Independent Variable(s):** Cannabinoid interventions **Dependent Variable(s):** Weight change, appetite change, QOL **Intervention**: Cannabinoid-based interventions in multiple forms and synthetic cannabinoids	Appetite: Validated scales, validated questionnaires, and self-evaluations Weight: self-or physician-reported QOL: EORTC QLQ-C30, self-reported questionnaires	**Appetite:** Very low-quality evidence in 3 studies included in meta-analysis (n = 297) suggested no significant benefits of cannabinoids for appetite compared with control (standard mean deviation [SMD] = –0.2; 95% CI [–0.51, 0.46], p = 0.93). Patient-reported observations from 7 NRSIs suggested improvements in appetite. **Weight:** 1 RCT reported greater weight gain with megestrol during the intervention, 1 RCT reported no difference in weight between groups, 4 NSRIs reported small improvement in weight gain with cannabinoids measured in separate ways (mean gain = 0.3 kg, median gain = 1.0-1.3 kg, percent weight increase range = 7.7–21.6%), 1 NRSI reported a decrease in weight in cannabinoid groups, and 1 NRSI reported a decrease in weight with higher doses of dronabinol (very low-quality evidence). **QOL** Meta-analysis of moderate-quality evidence (5 studies, n = 545) showed that cannabinoids were significantly less efficient than active or inactive control on QOL (p = 0.007). **AEs:** 9 of 10 studies reported on AEs. 2 showed no difference in severity between intervention and control groups, 1 reported 4 AEs and 1 serious AE related to the intervention, and 2 RCTs showed no significant differences.	The Cochrane Library was not searched because of previous comprehensive work (Wang et al., 2019). Single-reviewer initial screening suggested a potential for missed studies. Available evidence consists heavily of observational reports lacking comparison and relies on subjective outcomes. High heterogeneity with interventions between studies	No recommendations can be made to support the use of cannabinoids alone to improve symptoms and outcomes. Anorexia is a symptom of cancer-associated cachexia. This systematic review and meta-analysis demonstrated that cannabinoids alone used for appetite stimulation do not show significant benefit. Higher-quality studies utilizing multimodal therapies may be needed.

General Evidence

Citation	Design/Method Sample/Setting	Variables and Intervention	Outcome Measures	Results/Analysis	Limitations	Quality and Nursing Implications
Turcott, J.G., Del Rocío Guillen Núñez, M., Flores-Estrada, D., Oñate-Ocaña, L.F., Zatarain-Barrón, Z. L., Barrón, F., & Arrieta, O. (2018). The effect of nabilone on appetite, nutritional status, and quality of life in lung cancer patients: A randomized, double-blind clinical trial. *Supportive Care in Cancer, 26*(9), 3029–3038. https://doi.org/10.1007/s00520-018-4154-9	**Design:** Double-blinded placebo- controlled RCT **Method:** Patients were randomized to nabilone or placebo with evaluation of outcome measures at weeks 4 and 8. **Sample:** Patients with stage III and IV non- small cell lung cancer (NSCLC) (n = 47). **Setting:** Outpatient thoracic oncology unit in Mexico City	**Independent Variable(s):** Nabilone **Dependent Variable(s):** Nutritional status, QOL, appetite, biometrics of weight, body mass index (BMI), platelet and albumin levels **Intervention**: Dose of 0.5 mg nabilone (a synthetic THC derivative approved for chemotherapy-induced nausea and vomiting [CINV] or placebo) for 2 weeks, increased to 1 mg daily for remaining 6 weeks of studies Patients were evaluated at weeks 4 and 8.	Anorexia Cachexia Scale (AC/S) VAS measuring appetite and weight loss FAACT tool EORTC QLQ-C30 and QOL Questionnaire–Lung Cancer 13 (QLQ-LC13) CTCAE	Baseline characteristic differences: Nabilone group had worse performance status (p = 0.010), older age (p = 0.042), and greater weight loss in previous 6 months (p = 0.032). No statistically significant differences in control group and experimental group at 4 weeks for appetite and biometric variables. After 8 weeks, each group had improvement in appetite on the AC/S without differences between groups. Experimental group reported improvement on VAS for anorexia (0.006). Experimental group had higher intake of carbohydrates (−42.4 g versus +21.8 g, p= 0.040) and statistically significantly improved QOL measures in role functioning, emotional functioning, social functioning, and pain. Control group had drop in energy consumption at 8 weeks (p = 0.041) but the difference between groups was not significant. Control group had decrease in CINV (p = 0.043) on health related QOL scale. Intervention group had no decrease in CINV from baseline.	Small sample size Attrition: 47 patients were initially randomized, but at week 4 only 33 remained in the study, and at week 8 only 22 remained in the study. Attrition was due primarily to clinical deterioration requiring hospitalization, death, or loss to follow up. Baseline characteristic differences were noted: nabilone group had worse performance status, older age, and greater weight loss in the previous 6 months.	Methodology appears sound, results were reported with reliability, but due to small sample size, considerable attrition and use in only 1 type of cancer and over a 2-year period in 1 institution, findings may not be generalizable. Patients with advanced NSCLC with confirmed anorexia have a poorer prognosis in general, which could explain the number of deaths that occurred during the 8 weeks of the study.

General Evidence: Review of Multiple Interventions

Citation	Design/Method	Sample/Setting	Significant Findings	Limitations	Quality of Evidence/Worth to Practice	Nursing Implications
Saeteaw, M., Sanguanboonyaphong, P., Yoodee, J., Craft, K., Sawangjit, R., Ngamphaiboon, N., . . . Chaiyakunapruk, N. (2021). Efficacy and safety of pharmacological cachexia interventions: Systematic review and network meta-analysis. *BMJ Supportive and Palliative Care, 11*(1), 75–85. https://doi.org/10.1136/bmjspcare-2020-002601	**Design:** Systematic review and network meta-analysis **Method** The PubMed®, Embase®, Cochrane, and ClinicalTrials.gov databases were searched for RCTs studying pharmacologic interventions for cachexia with weight, appetite, and adverse event measures. Dual reviewer extraction and risk of bias assessment completed.	**Sample:** 80 RCTs reviewed representing 10,579 patients of which 7220 had a cancer diagnosis.	49 studies assessed total body weight from baseline to 8 weeks with 13 interventions. Total body weight was improved compared to placebo in steroid, megestrol, medroxyprogresterone, ghrelin mimetic, and androgen groups. Mean weight differences ranged from 1.5 to 6.45 kg. 19 studies assessed appetite score changes from baseline to at least 8 weeks (n = 2,632). Compared to placebo, megestrol and androgen had significant improvements in appetite scores, with mean differences ranging from 0.44 to 1.83. 14 studies (n = 1,333) had appetite scores measured earlier than 8 weeks from baseline. Compared with placebo, ghrelin improved appetite scores (mean difference = 1.11) 24 studies assessed lean body weight differences compared to baseline at 8 weeks, finding that growth hormone, androgen, and ghrelin mimetic (anamorelin) significantly improved lean body weight, with mean differences ranging from 1.38 to 2.54 kg. Adverse events were significantly increased in growth hormone, dronabinol, and megestrol groups compared to control (23 studies, 2,329 participants). There was no significant increase in serious adverse events compared to placebo across other interventions.	Studies in some interventions were small, particularly for melatonin and olanzapine interventions. Authors report one-third of the included trials had high risk of bias, so findings should be interpreted cautiously. Nutritional supplements were not studied.	Quality rating in primary outcome of total body weight studies was moderate. Quality rating for other outcomes studied was low to moderate.	This network meta-analysis provides findings consistent with current cachexia guidelines. Dronabinol does not show clinical benefit and increases overall adverse events. Megestrol improved total body weight and appetite scores without serious adverse events. High dose megestrol (greater than 400 mg/day) showed increased adverse events after treatment but not serious adverse events. Androgen groups had improved appetite scores. Corticosteroid use had positive findings for total body weight, and anamorelin showed improvements in appetite, total body, and lean body weight without adverse events.

Clinical Practice Guidelines

Guideline Citation	Purpose	Sample/Setting	Significant Recommendations	Limitations	Quality and Nursing Implications
Arends, J., Strasser, F., Gonella, S., Solheim, T.S., Madeddu, C., Ravasco, P., . . . Ripamonti, C.I. (2021). Cancer cachexia in adult patients: ESMO Clinical Practice Guidelines☆. *ESM O Open, 6*(3), 100092. https://doi.org/10.1016/j.esmoop.2021.100092	To provide answers to questions regarding the diagnosis and treatment of cachexia-related physical and psychological problems, relying on evidence-based information whenever possible.	Adult patients with cancer cachexia	1. Regular nutritional screening and nutritional support is recommended based on expected survival (weighing burden to patient). Screen and assess nutritional metabolic status and risk. Rescreen for those not at risk every 3 months. 2. Anorexia/cachexia interventions include: • Ensuring adequate intake for energy, protein requirements, and muscle training; • Using pharmacological agents to increase appetite; and • Engaging in psychosocial interactions to alleviate distress. 3. Pharmacologic interventions include: • Corticosteroids and progestins may improve appetite for brief periods of time and must be weighed against potential risk. • There is moderate evidence for olanzapine use. • Cannabinoids showed no significant effect on appetite or QOL, and safety data is lacking. • There is insufficient evidence to support use of NSAIDs. • Ghrelin receptor agonist anamorelin is approved in Japan but showed only modest effects in the ROMANO study in Europe and is not currently recommended. 4. Cachexia care should be delivered using a combination of nutrition; physical activity; psychological, oncologic, and palliative/supportive/rehabilitative care; and oncologist competencies. 5. Comprehensive assessment and patient-centered approach to care includes consideration of cost effectiveness, availability, multitargeted and multimodality treatment options.	1. Level and strength of evidence not reported for each article. 2. Search strategy not defined. 3. Adults only 4. Overall aim of the guideline was cachexia, therefore limited focus was given to anorexia.	Search strategy per European Society for Medical Oncology standard operating procedures for clinical practice guidelines. Findings and recommendations are feasible and relevant for cancer-related anorexia. Strong evidence is provided with numerous recommendations for cachexia, of which anorexia is one subjective component. Care must be multimodal, interprofessional, and patient- and family-centered. Pharmacologic interventions such as corticosteroids and progestins may improve appetite for brief periods of time and must be weighed against potential risk. There is moderate evidence for olanzapine use. Nursing education regarding the management of patients considering pharmacologic interventions is necessary and should include financial review.

Roeland, E.J., Bohlke, K., Baracos, V.E., Bruera, E., Del Fabbro, E., Dixon, S., . . . Loprinzi, C.L. (2020). Management of cancer cachexia: ASCO Guideline. *Journal of Clinical Oncology, 38*(21), 2438–2453. https://doi.org/10.1200/JCO.20.00611	Provide an evidence-based clinical guideline for the management of cancer cachexia in adult patients with advanced cancer.	Sample: Adult patients with advanced cancer and one or more of the following: loss of body weight, lean body mass, and/or appetite	1. Guidelines are moderately in favor of nutritional support and counseling with a registered dietitian. 2. Considerations for pharmacologic interventions for cancer cachexia include: • Moderately in favor of recommending short trials of progesterone analogs or corticosteroids, weighing risk and benefit for patient. Megestrol improves appetite and body weight (adipose not skeletal mass) but has risk of thromboembolic events, adrenal suppression, and edema. • No recommendation was made for anamorelin, which was FDA-reviewed but not approved. It is not commercially available in the U.S. • Cannabinoids and derivatives did not show improvement in appetite, weight change, or QOL alone or in combination with megestrol. Guideline panel ranks strength as weak against use of this intervention. • Olanzapine data is lacking to make a recommendation on use in cachexia. • No recommendation on use of thalidomide because of low strength of evidence and low benefit with side effects of somnolence and constipation. • Exercise was not included in any eligible trials related to cachexia in patients with advanced cancer.	Small sample sizes High rates of patient dropout reported in several studies. The majority of the RCTs had risk of bias assessed as intermediate or high.	The methodology was valid and rigorous. A panel of experts reviewed the literature, developed the draft guideline, and allowed public comment prior to finalizing the guideline. A thorough process was followed for the finalization, publication, and implementation of the guideline. The recommendations ranked "moderately in favor" are feasible, relevant, and can be applied to the patient population of interest. Nurses work collaboratively with interprofessional colleagues to manage patient symptoms; awareness of the interventions, the harm versus benefit grading, and the strength of the recommendation will enable the nurse to actively participate in discussions regarding the management of cachexia. The guideline also provides key information regarding how to reduce patient and caregiver frustration related to changes in eating habits, nutritional intake, and physical manifestations associated with cachexia. Nurses will be able to use this information in addition to information related to out-of-pocket costs and health disparities when caring for patients with cancer-related cachexia.