

Rationale and Study Protocol for the Academy of Nutrition and Dietetics' Outpatient Oncology Outcomes Feasibility Study

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CANCER REPRESENTS A SUBSTANTIAL health and economic burden in the United States. As the second most common cause of death, cancer kills approximately 1,670 people per day.¹ Nearly 1.74 million people will be diagnosed with cancer in 2018.¹ Direct medical costs associated with cancer were estimated to be \$80.2 billion in 2015, with roughly 52% of those costs for hospital outpatient or office-based provider visits.¹ This represents a substantial shift to managing cancer treatment and its side effects in the outpatient vs inpatient setting. Approximately 90% of oncology patients now receive treatment in outpatient cancer centers and clinics.²

It is important to consider the optimal composition of the outpatient care team to improve patient outcomes. As many as 50% of oncology patients are at nutrition risk when they present for diagnosis and/or treatment of their disease,³ indicating the need to include registered dietitian nutritionists (RDNs) on the patient care team. In a classic study by Dewys and colleagues,⁴ malnutrition in cancer patients negatively impacted response to treatment and survival. In addition, cancer treatment itself can increase nutritional risk, with chemotherapy- and radiotherapy-induced toxicities causing multiple side effects that commonly reduce oral intake, leading to weight loss, loss of lean body mass, and poor nutritional status.⁵⁻⁷ Untreated nutrition-related treatment side effects also increase

health care costs, with an average incremental cost increase of \$1,575 for patients with uncontrolled vs controlled chemotherapy-induced nausea and vomiting.⁸

An upcoming Academy of Nutrition and Dietetics feasibility study, described in this article, will 1) determine the feasibility for RDNs to collect registry data on aspects of the usual nutrition care process and for a third-party honest broker (neutral third party, who is not part of the research team) to conduct a chart review of treatment and medical outcomes for oncology patients in outpatient settings; and 2) collect information that will improve power calculations for five tumor types and estimates of intraclass correlation coefficient across sites. These data will be used to inform a future, larger study that is designed and adequately powered to estimate the impact that provision of RDN nutrition care has on oncology patients' medical and economic outcomes in the outpatient setting.

Nutrition interventions initiated by RDNs help mitigate the side effects of the disease and treatment to improve outcomes for the patient. For example, there is compelling evidence that early nutrition intervention, along with a multidisciplinary approach to nutrition care involving RDNs, results in less weight loss, greater radiotherapy completion rates, and fewer unplanned hospital admissions and emergency department visits, with decreased length of stay for patients with esophageal and head and neck cancer^{5,9-11} than for those who receive delayed nutrition care only after progressive weight loss is identified. Furthermore, a recent systematic review and meta-analysis by de van der Schueren and colleagues¹² identified the

particular importance of nutrition interventions that mitigate lean body mass loss and systemic inflammation during cancer therapy. Nutrition screening should begin upon initiation of oncology services and continue routinely throughout treatment because the patient may develop nutrition problems and be at risk for malnutrition during later phases of treatment. Early identification and management of malnutrition risk improves and protects nutrition status and quality of life, which leads to improved outcomes.¹³ RDNs routinely intervene for patients at nutritional risk in inpatient settings. However, in many outpatient settings, RDNs are understaffed and unable to meet demands to see oncology patients at nutritional risk.¹⁴ This understaffing is due, in part, to insufficient evidence to support the impact that RDN nutrition care can have on oncology patient's medical and economic outcomes in the outpatient setting.

PROJECT DEVELOPMENT

The feasibility study objectives will be accomplished via two separate studies: an Academy of Nutrition and Dietetics Health Informatics Infrastructure (ANDHII) registry study and a medical chart review. The [Figure](#) provides a pictorial representation of the feasibility study.

Treatment Centers and Participants

This feasibility study will include six outpatient cancer treatment centers. To be considered eligible, a facility must have a policy and procedures in place to screen all patients for nutrition risk and use an electronic medical record. A total

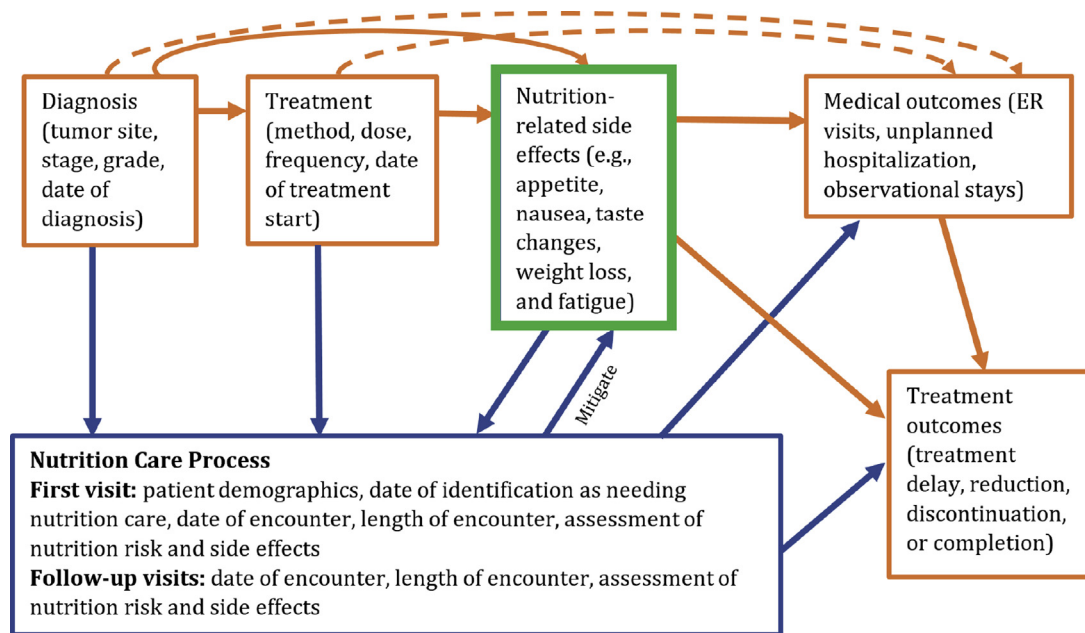


Figure. Representation of data that will be collected in the registry study (blue: Nutrition Care Process, nutrition-related side effects) and medical chart review (orange: diagnosis, treatment, medical and treatment outcomes, nutrition-related side effects). Green box: data collected in both parts of the study. Dashed lines indicate paths that will be controlled for with disease severity adjustment.

of 42 randomly selected adult patients with an active diagnosis of lung, esophageal, colon, rectal, or pancreatic cancer will be included in the registry study. Additional inclusion criteria for the registry study are that the patient resides in the United States; has active or intended cancer treatment with one or a combination of different therapies, such as chemotherapy, radiation, chemoradiotherapy, immunotherapy, or targeted therapy in the outpatient setting; screened and found to be at nutrition risk; and receives nutrition care from a participating RDN within 2 weeks of being screened. Patients currently enrolled in a clinical trial will be excluded from the registry study. A medical chart review will be conducted for all of the patients in the registry study, and for an additional 42 patients, matched to the registry patients by primary tumor type, who screened positive for nutrition risk and who never received nutrition care from an RDN. All other patient inclusion and exclusion criteria are the same for the registry study and the medical chart review.

Ethical Approval

The University of New Mexico Health Sciences Center's Human Research Protections Office (#18-173) approved all aspects of the research protocol. All

participating sites with an Institutional Review Board (IRB) or affiliated IRB will defer to the University of New Mexico Health Sciences Center's Human Research Protections Office via an IRB Authorization Agreement or conduct local IRB review and approval of the study protocol. If a site does not have an IRB, they will provide a letter of support deferring oversight to the University of New Mexico Health Sciences Center's Human Research Protections Office.

Registry Study

One RDN from each facility will be asked to complete an anonymous survey to gather information on their qualifications and experience and the outpatient facility characteristics. Each RDN will then be oriented to the basic study methodology and trained to enter data into the ANDHII registry via an introductory webinar and online tutorials. The RDN will be currently providing nutrition care to oncology patients in an outpatient setting and committed to entering de-identified patient data into the ANDHII registry for seven patients.

A registry study does not involve human subjects, as defined in the Office for Human Research Protections Guidance on Research Involving Coded

Private Information or Specimens.¹⁵ To meet the standards for registry research, our protocol ensures that the identities of the individuals whose data are collected are protected from disclosure to the investigators. ANDHII prevents the entry of any of the 18 patient identifiers listed in The Health Insurance Portability and Accountability Act of 1996 safe harbor de-identification standard.¹⁶ This is accomplished by using a structured data collection form that provides no fields for the entry of identifiers and validation that the data lacks potentially identifying data (eg, age older than 89 years) before transmission from the user's computer to the server.

Each patient record in ANDHII is assigned a randomly generated re-identification code. This code permits the RDN who recorded the data to re-identify patients in ANDHII to submit follow-up data for a patient, and to facilitate chart access for the honest broker/abstractor during the medical chart review. Each RDN will store the re-identification code solely in their progress note for the encounter within the patients' medical records and use it for no other purpose. This creates a code key for each patient that exists within their medical record, allowing RDNs to re-identify records, while simultaneously creating a legal obligation

under The Health Insurance Portability and Accountability Act of 1996 that prevents RDNs from releasing this key to the investigators per registry research standards.

Using this registry approach to data collection facilitates accurate estimates of current practices and outcomes by removing nonparticipation bias, while protecting the patients involved from the risks, such as breach of confidentiality, that are inherent to human subjects research.

Once they have identified a patient who meets the study inclusion criteria, the RDNs will use the true random number generator feature on random.org to determine whether the patient should be entered into ANDHII or not. RDNs will be instructed on how to randomly generate a number “0” or “1,” and to enter patient data if a “1” is generated but not if a “0” is generated. This procedure has been included to minimize RDN bias in patient selection. RDNs will do this until they have identified and entered usual nutrition care data for seven patients. The categories of data to be collected include general, nonidentifiable demographics, anthropometrics, nutrition risk (based on each site’s nutrition assessment policy), diet history, nutrition-focused physical findings related to nutrition risk and side effects, and details regarding the nutrition care encounter. The variables within these categories are merely suggested, and the RDN can choose to enter these variables or additional variables within ANDHII based on her or his usual nutrition care. They will complete this entry for the initial patient visit, as well as for any follow-up encounters that take place during a 180-day timeframe.

Medical Chart Review

The medical chart review will be conducted by an honest broker to cover the time from the first oncology visit through 180 days after the start of treatment for all participants. This timeframe corresponds to the period of care provided by the RDN. Briefly, the data abstractor(s) will collect information on patient diagnosis and treatment; on treatment outcomes (dose reduction, treatment delay, discontinuation or completion); nutrition-focused physical findings related to nutrition risk and side effects; and medical outcomes for

patients in the registry study and for additional patients who screened at nutrition risk and who never received nutrition care from an RDN, matched to the registry patients by primary tumor type. The extracted data will not contain personal identifiers, and there will be no permanent link created between the extracted data and the patient chart because it will not be necessary to go back to any specific patient chart once the data have been extracted. Abstraction tool data will be collected and managed using the Research Electronic Data Capture (REDCap) tool hosted at University of New Mexico.¹⁷ REDCap is a secure, web-based application designed to support data capture for research studies. Range checks/validation and skip functions will be included in the REDCap version of the abstraction tool to improve data quality.

The participating sites will provide the honest broker with the selected patient medical records to review through a secure web portal via a process that will be determined by each site. Records from patients included in the registry study will be identified by the RDN as outlined in the registry study section. To identify the comparison charts from patients who never received nutrition care from the RDN, the RDN will review census lists for the same period during which the registry study was conducted at their facility and identify patients who were not seen by the RDN (ie, no RDN note in the medical chart). The RDN will then enter the total number of patients not seen during this timeframe into random.org by tumor types, and the randomizer will indicate which charts should be reviewed for that tumor type, based on a random integer generator.

The data abstractors will be professionally trained and experienced in data collection from medical records. They will work remotely and access records electronically via a secure portal. Inter-rater reliability will be performed before commencing abstraction. An inter-rater reliability agreement rate of 90% will be required before abstraction begins. Every mismatch will be used as a training opportunity for all data abstractor(s). In addition, during the course of the data collection, the lead data abstractor will re-abstract five randomly selected records per auditor, and the results will be compared and used for training.

Statistical Analysis

The primary purpose of this study is to determine the feasibility of data collection procedures and to gather the information needed for sample size calculations in a larger study. Descriptive analyses will be conducted to preliminarily examine the relationship between the provision of nutrition care and medical and treatment outcomes, adjusting for disease severity and stratified by tumor type, but we do not anticipate having the power to draw any substantive conclusions with this feasibility study.

ISSUES AND OUTCOMES

Anticipated Issues

There are some anticipated challenges for this feasibility study. Ideally, we would like to have representation from different types of outpatient oncology facilities (eg, associated with academic medical centers, community-based clinics, or freestanding clinics) and from facilities in different geographic regions. However, enrollment of facilities for the study will likely depend on meeting the basic inclusion criteria and site interest. This is partly because feasibility studies are constrained in terms of time frame and budget, and we will aim to address this shortcoming in the larger follow-up study. We also anticipate that there may be challenges encountered with entering data into ANDHII, with accessing the electronic medical records, and with variable quality of record keeping and record structure, as there may be six different electronic medical records systems. The goal is to identify and develop solutions to common issues that are encountered during the registry study and medical chart review as part of this feasibility study.

Expected Outcomes

The results of the study are expected to inform the design of a future, larger study that is designed and adequately powered to estimate the impact that the provision of RDN nutrition care has on an oncology patient’s medical, treatment, and economic outcomes in the outpatient setting, and to better justify improved RDN staffing in outpatient oncology treatment settings.

References

- American Cancer Society. *Cancer Facts & Figures 2018*. Atlanta, GA: American Cancer Society; 2018:76.
- Halpern MT, Yabroff KR. Prevalence of outpatient cancer treatment in the United States: Estimates from the Medical Panel Expenditures Survey (MEPS). *Cancer Invest*. 2008;26(6):647-651.
- Halpern-Silveira D, Susin LRO, Borges LR, Paiva SI, Assunção MCF, Gonzalez MC. Body weight and fat-free mass changes in a cohort of patients receiving chemotherapy. *Support Care Cancer*. 2010;18(5):617-625.
- Dewys WD, Begg C, Lavin PT, et al. Prognostic effect of weight loss prior to chemotherapy in cancer patients. *Am J Med*. 1980;69(4):491-497.
- Odelli C, Burgess D, Bateman L, et al. Nutrition support improves patient outcomes, treatment tolerance and admission characteristics in oesophageal cancer. *Clin Oncol (R Coll Radiol)*. 2005;17(8):639-645.
- Arrieta O, Michel Ortega RM, Villanueva-Rodríguez G, et al. Association of nutritional status and serum albumin levels with development of toxicity in patients with advanced non-small cell lung cancer treated with paclitaxel-cisplatin chemotherapy: A prospective study. *BMC Cancer*. 2010;10:50.
- Marshall KM, Loeliger J, Nolte L, Kelaart A, Kiss NK. Prevalence of malnutrition and impact on clinical outcomes in cancer services: A comparison of two time points [published online ahead of print May 2, 2018]. *Clin Nutrition*. <https://doi.org/10.1016/j.clnu.2018.04.007>.
- Carlotto A, Hogsett V, Maiorini E, Razulis J, Sonis S. The economic burden of toxicities associated with cancer treatment: Review of the literature and analysis of nausea and vomiting, diarrhoea, oral mucositis and fatigue. *Pharmacoeconomics*. 2013;31(9):753-766.
- Capuano G, Grosso A, Gentile PC, et al. Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemoradiotherapy. *Head Neck*. 2008;30(4):503-508.
- Brown TE, Banks MD, Hughes BGM, Lin CY, Kenny LM, Bauer JD. Comparison of nutritional and clinical outcomes in patients with head and neck cancer undergoing chemoradiotherapy utilizing prophylactic versus reactive nutrition support approaches. *J Acad Nutr Diet*. 2018;118(4):627-636.
- Lewis SL, Brody R, Touger-Decker R, Parrott JS, Epstein J. Feeding tube use in patients with head and neck cancer. *Head Neck*. 2014;36(12):1789-1795.
- de van der Schueren MAE, Laviano A, Blanchard H, Jourdan M, Arends J, Baracos VE. Systematic review and meta-analysis of the evidence for oral nutritional intervention on nutritional and clinical outcomes during chemo(radio)therapy: current evidence and guidance for design of future trials. *Ann Oncol*. 2018;29(5):1141-1153.
- Thompson KL, Elliott L, Fuchs-Tarlovsky V, Levin RM, Voss AC, Piemonte T. Oncology evidence-based nutrition practice guideline for adults. *J Acad Nutr Diet*. 2017;117(2):297-310.e47.
- National Academies of Sciences, Engineering, and Medicine. *Examining Access to Nutrition Care in Outpatient Care Centers: Proceedings of a Workshop*. Washington, DC: The National Academies Press; 2016.
- US Department of Health and Human Services. Coded Private Information or Specimens Use in Research, Guidance (2008). <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/research-involving-coded-private-information/index.html>. Updated October 5, 2018. Accessed November 14, 2018.
- US Department of Health and Human Services. Methods for de-identification of PHI. <https://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/index.html>. Updated November 6, 2015. Accessed September 10, 2018.
- Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-381.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

FUNDING/SUPPORT

This work was supported by the Commission on Dietetic Registration.

ACKNOWLEDGEMENTS

The authors are grateful to Rosa Hand, PhD, RDN, LD, FAND, and William Murphy, MS, RDN, formerly of the Academy of Nutrition and Dietetics, for their initial contributions to the development of the feasibility study protocol. This research used the facilities or services of the Behavioral Measurement and Population Sciences Shared Resource, a facility supported by the State of New Mexico and the UNM Comprehensive Cancer Center (#P30CA118100; principal investigator: C. Willman).

AUTHOR CONTRIBUTIONS

D. D. Guest, T. Cox, A. Coble Voss, A. Nguyen, K. McMillen, V. Williams, J. Lee, P. Beck, K. Lenning, T. Titus-Howard, and E. Yakes Jimenez collaboratively developed the protocol. D. D. Guest and E. Yakes Jimenez wrote the first draft of the manuscript. All authors reviewed and commented on subsequent drafts of the manuscript.