Pre-Application Webinar for RFA-CA-21-031, Exercise and Nutrition Interventions to Improve Cancer Treatment-Related Outcomes (ENICTO; U01 Clinical Trial Required) and RFA-CA-21-032, (ENICTO Coordinating Center; U24 Clinical Trial Not Allowed)

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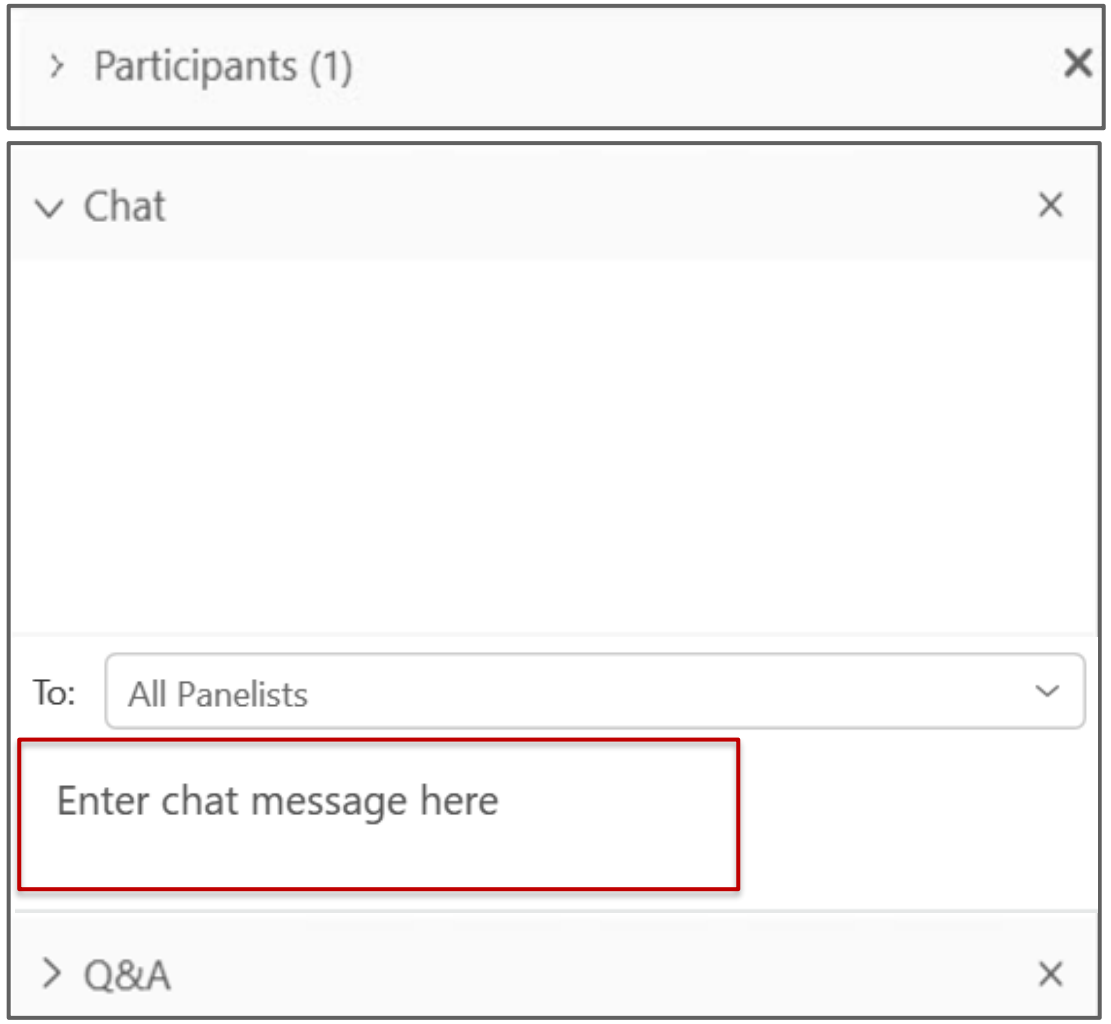
Using WebEx and Webinar Logistics



- All lines will be in listen-only mode
- Submit comments at any time using the **Q&A** feature and select All Panelists
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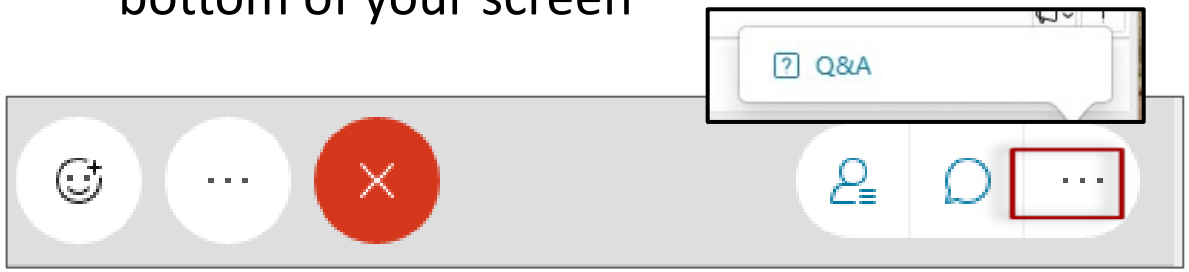

- Closed captioning is available as a link in the Chat Box
- This webinar is being recorded

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Purpose of RFAs (U01 & U24)

U01 Project Sites (Anticipated 3 -5 awards)

- To understand how exercise and nutrition interventions (alone or combined) affect treatment-related outcomes for curative/life-extending therapies

- Treatment-related outcomes include:
  - Treatment completion (e.g., dose interruption, reduction, or delays)
  - Related healthcare utilizations (e.g., hospital admissions, surgeries, length of stay, ED visits)
  - Severe adverse events (e.g., CTCAE ≥ 3, dose-limiting and organ-specific toxicities)

- To address research gaps concerning specific exercise and nutrition interventions across cancer sites, treatment protocols, and among adults or children

- Awardees will participate in an Exercise and Nutrition to Improve Cancer Treatment-Related Outcomes (**ENICTO**) in Cancer Survivors Consortium that include, but are not limited to, pilot project participation

Purpose of RFAs (U01 & U24)

U24 Coordinating Center (CC) (1 Award)

- CC's primary mission will include:
  - Collaborative scientific contribution
  - Administrative responsibilities
  - Communication responsibilities

- The CC will also develop and execute a platform to monitor progress and facilitate evaluation of the initiative across U01 project sites

- The CC awardee will participate in the (ENICTO) Consortium, that include, but are not limited to, pilot project participation

Required Elements of RFA (U01)

- Propose an exercise, medical nutrition, or a combined intervention approach
- Specify the knowledge gap addressed, justify the cancer survivor population under study, and biological plausibility of the intervention to affect the treatment-related outcome(s)
- Employ an appropriately powered NIH clinical trial design with a treatment-related outcome as the identified primary endpoint and include a patient-reported outcome as a secondary outcome
- The trial must be initiated before or during cancer treatment
- Include plan to capture robust treatment data - planned and delivered dose and type for all treatment modalities, and where appropriate, supportive care measures

Required Elements of RFA (U01) Continued

- Include validated measures of body composition, diet, general physical activity, and where appropriate, metabolic biomarkers
  - These data are required to leverage the opportunity provided by a cooperative agreement and data capture for possible cross-site pilot projects
  - At minimum two assessments must be taken- at baseline and at one or more post-intervention timepoints
- Cooperate with Coordinating Center in identification of common data elements and standardization procedures

Required Elements of RFA (U01) Continued

- Requirements: Studies with Exercise Intervention Component
  - Specify details of exercise prescriptions (e.g., FITT criteria)
  - Include validated measure of exercise adherence (e.g., percentage of participants completing exercise as prescribed as well as average adherence level)
  - Include exercise-related biomarkers relevant to treatment outcomes (e.g., change/maintenance of CRF, strength, or functional status)

- Requirements: Studies with Medical Nutrition Component
  - May focus on dietary patterns, macronutrients, timing of intake (e.g., intermittent fasting), body composition, and/or weight control/maintenance
  - Must use validated measures of diet that are appropriate for the selected population

Required Elements of RFA (U01) Continued

- Required Expertise
  - Experience, expertise, and ability to organize, manage and implement the proposed clinical trial and to meet proposed timelines
  - Transdisciplinary teams: It is anticipated that each award will support transdisciplinary teams of investigators

Required Elements of RFA (U24)

- Describe plan to develop and implement a platform for U01 sites to report data elements involving exercise, physical activity, medical nutrition, diet, cancer treatment delivery metrics, and cancer treatment-related and patient-reported outcomes across U01 sites

- Describe plan for implementation of a platform for U01 sites to report intervention protocol elements and sample population geographic and demographic characteristics

- Describe plan for devising methods to identify, harmonize, and analyze common data elements across U01 sites

- Describe plan for enhancing communication and collaboration across U01 sites

Required Elements of RFA (U24) Continued

- Required Expertise
  - **Scientific administration, coordination, and evaluation expertise**: Experience with coordination of NIH initiatives
  - **Exercise and nutrition clinical trials**: expertise in the methods used to collect and analyze these longitudinal data
  - **Cancer treatment and clinically related outcomes**: The CC must have familiarity and expertise in the patient-reported and clinical assessments routinely assessed as part of cancer care
  - **Collection and analysis of novel data related to implementation and cost evaluation**

Cooperative Agreement Structure and Pilot Projects

- **The ENICTO Steering Committee** is the initiative's main governing board (voting)
  - One representative from each ENICTO-U01 awardee site
  - One representative from the ENICTO-U24 Coordinating Center
  - One representative from the NCI
- **Pilot Projects and Collaborative Activities**
  - Steering committee may form ENICTO cross-site scientific interest groups
  - The ENICTO awardees and NCI project scientists may participate in initiative-wide activities and cross-site pilot project collaborations
  - Pilot project funding must be approved by the Steering Committee
  - Projects may derive from common data collection across sites or from approved novel data collection across sites
- Projects supported by $35K/year in years 2 – 5 from budgets of each U01 and the CC awardees

Questions

The slide deck and Q&A document will be archived on the following webpage in approximately 1-2 weeks:
https://cancercontrol.cancer.gov/brp/events/exercise-nutrition-interventions

Q: Who is considered a cancer survivor for the purposes of this RFA?

A: We use the current NCI definition for this RFA- "An individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life. There are many types of survivors, including those living with cancer and those free of cancer. This term is meant to capture a population of those with a history of cancer rather than to provide a label that may or may not resonate with individuals."
https://cancercontrol.cancer.gov/ocs#:~:text=Welcome%20to%20the%20Office%20of,of%20cancer%20and%20its%20treatment.

Questions Continued

Q: Is it acceptable to propose studies with patients with metastatic disease?

A: Yes. Projects including patients with metastatic disease are permitted as long as they are receiving cancer treatment with curative or life-extending intent.

Q: Is it acceptable to propose studies with patients with poor prognosis?

A: Yes. Projects proposing patients with aggressive cancers or disease sites with poor prognosis are permitted as long as they are they are receiving cancer treatment with curative or life-extending intent.

Questions Continued

Q: Are there cancer treatment-related endpoints beyond those listed examples that can be used?

A: The Primary endpoint must be among those *categories* specified in the RFA (treatment completion, healthcare utilization, severe adverse event). For example, a biomarker for CIPN may not be the primary endpoint, but it could be included in a study that also measures severe adverse events such as CTAE ≥ 3 or dose-interruption affecting treatment completion. Applicants must justify how the identified primary endpoint fits into one of the categories.

Questions Continued

Q: Are collection of cancer treatment-related outcomes limited to the before/during treatment timepoint?

A: No. Applicants may propose to follow participants beyond the completion of primary cancer treatment (for curative and life-extending intent) to capture treatment-related outcomes as deemed appropriate to the research question within the timeframe of the grant period.

Questions Continued

Q: How long is the clinical trial and follow-up period?

A: The trial length and follow-up period are investigator-determined but must be justified to consider the target population, cancer treatment, and the selected primary endpoint and other secondary outcomes as appropriate within the timeframe of the grant period.

Questions Continued

Q: Does the range of intervention timing extend to prehabilitation-type approaches?

A: Yes. The intervention timing may include prehabilitation-type approaches, but it is not required. The intervention timing period should be justified for the selected primary endpoint and other secondary outcomes as is appropriate.

Questions Continued

Q: May I take an approach comparing exercise prescription to general physical activity recommendation?

A: Applications proposing an exercise intervention trial, alone or in combination with medical nutrition, that only compares a general physical activity guideline (PAG) approach to a control condition are non-responsive. Trials that include a PAG approach in comparison to a fully articulated exercise prescription are responsive.

Questions Continued

Q: Do applications proposing an exercise intervention have to measure adherence to the exercise program or only physical activity?

A: In addition to describing elements of the exercise prescription, interventions with an exercise component must use valid measures of exercise adherence to the prescribed program, and document related exercise effects (e.g., change in CRF, strength, or function). Interventions should also include a general measure of physical activity, but it is not sufficient alone.

Questions Continued

Q: Does a medical nutrition intervention have to manipulate macronutrients and timing of intake?

A: No. Studies may include a broad array of nutritional factors, including a focus on dietary patterns, macronutrients, timing of intake (e.g., intermittent fasting), body composition, and/or weight control/maintenance.

Q: Does a medical nutrition intervention have to take place in a hospital setting?

A: No. Interventions must be well-measured but may take place anywhere. All proposed interventions must be justified by strong scientific evidence.

Questions Continued

Q: Are measures of body composition required for studies where body composition might not be part of the protective pathway?

A: Yes. As a general requirement to fulfill the terms of the cooperative agreement, all studies must include at least one validated measure of body composition for the purposes of collecting common data constructs across studies for possible use in cross-sites analyses.

Questions Continued

Q: Are measures of physical activity required for studies where exercise is not an element of the intervention approach?

A: Yes. As a general requirement to fulfill the terms of the cooperative agreement, all studies must include at least one validated measure of physical activity for the purposes of collecting common data constructs across studies for possible use in cross-sites.

Questions Continued

Q: What is the minimum number of assessment-timepoints required if a measure of body composition, diet, or physical activity is only being proposed for the purposes of fulling a general requirement as opposed to being integral to an intervention approach?

A: Assessments conducted only to fulfill general requirements for physical activity, diet, and body composition must be measured at pre-intervention baseline and at one or more post-intervention timepoints.

Questions Continued

Q: Should possible pilot projects emanating from common data in the consortium be described in the application?

A (U01 Applications): No, U01 applications should not describe any pilot project. With submission, applicants acknowledge and agree to the terms of the cooperative agreement, which describe possible pilot projects, but they should not be proposed at the time of application.

A (U24 Applications): No, U24 applications should not describe any pilot project, but should list possible avenues for pilot project research. The ENICTO consortium structure provides the opportunity to pool data across research sites, collect new data, and to pursue research questions collectively that could not be pursued by individual U01 research sites. U24 applicants should list the areas/possible directions for pilot studies are anticipated.

Questions Continued

Q: Who approves pilot projects?

A: The ENICTO Steering Committee must approve use of collective data for pilot projects and use of funds set aside for these purposes.

Questions Continued

Q: Can we have a foreign component and plan to recruit survivors in foreign countries?

A: Foreign components are allowed for U01 applications; however, they are not allowed for U24 applications. The PI should carefully consider how the nature of the foreign involvement impacts the trial approach, significance, and translational potential of the project.

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