Cancer Prevention and Control Planning Grant Program (Clinical Trials Optional)
R34 PAR-22-173
U34 PAR-22-174

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NIH NATIONAL CANCER INSTITUTE

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Session Agenda

1. *Planning Grants for Cancer Prevention and Control Clinical Trials (R34 and U34 Clinical Trials Optional)*
   - *Brandy Heckman-Stoddard, PhD, MPH*
2. *Planning Grants for Behavioral Interventions in Cancer Prevention and Control*
   - *Susan Czajkowski, PhD*
3. *Q&A*
   - *Brandy Heckman-Stoddard, PhD, MPH*
   - *Susan Czajkowski, PhD*
   - *Ann Geiger, PhD, MPH*

Prior Structure for Funding for Clinical Trials

R21	Exploratory, Phase I-II
R01	All trials except Phase III clinical trials that test the efficacy of cancer-related medical (oncologic) interventions or Phase III clinical trials of cancer imaging (or other diagnostic) modalities
Network Funding	Early Phase and Late Phase trials developed through network infrastructure

What is a R34 or U34?

From OER definition of grant mechanisms (R34 and U34):

For clinical trials, the planning grant is designed to:

- permit early peer review of the rationale and concept for the proposed clinical trial;
- support development of essential elements of a clinical trial
- lead to an application for support of a full-scale trial, based on elements developed under the planning period

History of R34 and U34 at NIH

- R34 currently used by NIDA, NIDDK, NIAAA, NIMH, NIAID, NEI, NINDS, NCATS, and NHLBI
- U34 currently used by NCATS and NIDDK
- Not previously used by NCI

Example U34- U34DK124174-01(Sachin Wani)

Background: Endoscopic eradication therapy (EET) is the standard of care for patients with Barrett's Esophagus (BE) and high-grade dysplasia (HGD) or mucosal esophageal adenocarcinoma.

Primary aim: Determine if BE patients with low-grade dysplasia (LGD) benefit from EET.

Planning aims:

- Compare the two approaches using the primary endpoint of neoplastic progression rate (progression to HGD or mucosal or invasive EAC).
- Compare defined patient-centered outcomes such as health-related quality of life between the two treatment groups.
- Compare the performance of molecular (TissueCypher and p53 immunohistochemistry) and imaging (wide-area transepithelial sampling – WATS) biomarkers to conventional histologic assessment of dysplasia via forceps biopsy to improve risk-stratification in BE with LGD patients

Why planning grants are needed for DCP and DCCPS late phase trials?

Cancer Prevention and Control trials :

- Often do not have pharmaceutical or industry support
- Involve multi-disciplinary teams that may not have worked together previously including primary care physicians and other specialists.
- Often challenging statistical issues about best study design, control group, endpoint, etc.
- Feasibility of recruitment and acceptance of randomization
- Design better trials that are more successful

Purpose of Planning Grant

- Through this Funding Opportunity Announcement (FOA), the National Cancer Institute (NCI) intends to facilitate well planned clinical trials across the cancer prevention and control spectrum aimed at improving prevention/ interception, cancer-related health behaviors, screening, early detection, healthcare delivery, management of treatment-related symptoms, supportive care, and the long-term outcomes of cancer survivors.
- Yield information that is both scientifically necessary and also sufficient to permit final decisions about the design or conduct of the large Phase II or beyond clinical trial.
- Application must include a summary of the future planned clinical trial
- Enhance rigor while saving time and cost to ensuring future trial success.
- Planning grant is not a prerequisite for an R01 funding clinical trial or a large trial through a network.

Examples of research needs include but are not limited to the following:

- Identify the appropriate control or comparison group to use in the subsequent clinical trial.
- Standardize and evaluate feasibility of the intervention or outcome across multiple sites.
- Feasibility and plan for development of a placebo
- Standardize and validate survey instruments.
- Standardize and test effectiveness of training tools.
- Adapt and test an intervention or outcome instrument for a population that differs culturally from the population for which the instrument was originally designed.
- Modeling data to support trial assumptions in the study design.
- Statistical planning and design
- Perform studies to refine the appropriate study population, intervention, outcome, and/ or study endpoint.

Due Dates

Application Due Dates			Review and Award Cycles		
New	Renewal / Resubmission / Revision (as allowed)	AIDS	Scientific Merit Review	Advisory Council Review	Earliest Start Date
October 25, 2022	October 25, 2022	January 07, 2023 *	March 2023	May 2023	July 2023
February 24, 2023	February 24, 2023	May 07, 2023 *	July 2023	October 2023	December 2023
June 26, 2023	June 26, 2023	September 07, 2023 *	November 2023	January 2024	April 2024
October 25, 2023	October 25, 2023	January 07, 2024 *	March 2024	May 2024	July 2024
February 27, 2024	February 27, 2024	May 07, 2024 *	July 2024	October 2024	December 2024
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June 25, 2025	June 25, 2025	September 07, 2025 *	November 2025	January 2026	April 2026

NIH standard due dates marked with an asterisk.

Funding Period and Budget

- Planning grant support can be requested for a maximum of 3 years.
- Application budgets are limited to $225,000 per year and $450,000 in direct costs over the 3-year project period without a clinical trial.
- Applications that include a pilot/feasibility clinical trial are limited to $225,000 per year and $600,000 in direct costs over the 3-year project period.
- There are no set aside funds.

Required Attachments

- Milestone Plan
- Stakeholder Engagement Plan
- Future Clinical Trial Description

Milestone Plan

- The filename "Milestone Plan.pdf" should be used and the attachment should not exceed 2 pages.
- Detailed information and timelines for completing all necessary planning activities. Milestones should be easily measurable and realistic.
- These milestones will be negotiated at the time of the award, as appropriate.
- The Milestone plan is a separate document from the Study Timeline.

Stakeholder Engagement Plan

- The Filename "Stakeholder Engagement Plan.pdf" should be used and the attachment should not exceed 2 pages.
- The application must describe multi-level stakeholder engagement activities already conducted and how these activities influenced the development of the protocol or proposed study conduct, including recruitment.
- The application should also describe any stakeholder engagement efforts planned during the planning period and how these activities will be used.

Future Clinical Trial Description

- The filename "Future Clinical Trial Description.pdf" should be used and the attachment may not exceed 3 pages.
- Provide a description to the extent known of the *future* clinical trial to provide context for information sought in the Planning award.
- The summary should not describe the pilot/feasibility trial that may be conducted during the Planning period of award.

Letters of Support

- Provide all appropriate letters of support, including any letters necessary to demonstrate the support of consortium/site participants, cores, laboratories, pharmacies, and other collaborators, including cost-sharing by NIH resources, in the case of intramural collaborators.
- If co-funding or in-kind support is planned from any source (non-NIH sources or NIH sources), letter(s) outlining details of the commitment (e.g. type, amount, and source of support), signed by a business official on organization letterhead, must be included.
- Letters of support should also be provided from individuals or organizations that have been or will be involved in stakeholder engagement efforts.

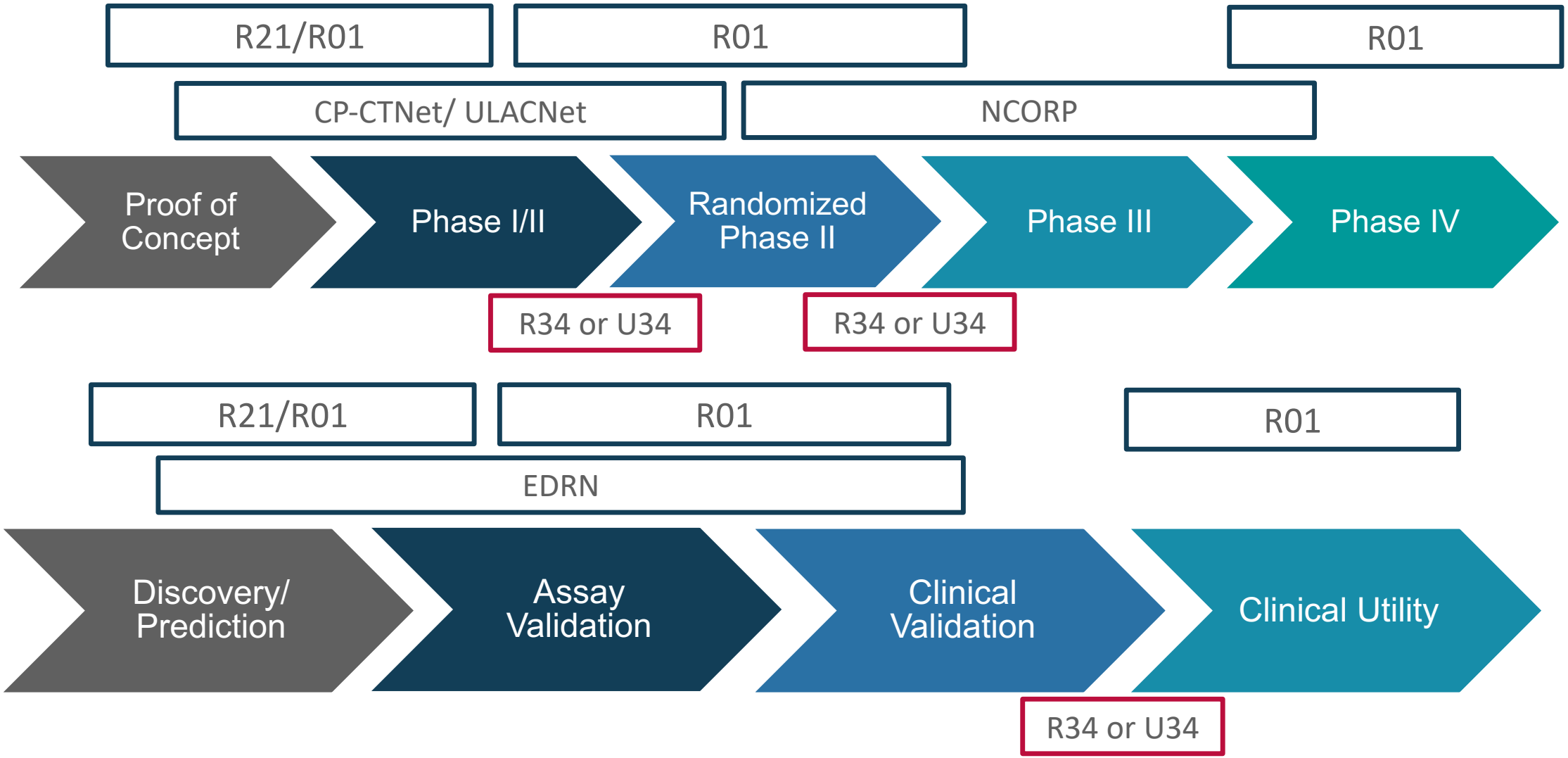
PHS Human Subjects and Clinical Trials Information

- Description of the feasibility/ pilot study that will be conducted as part of the planning award
- **2.5 Recruitment and Retention Plan**
- **2.7 Study Timeline (Directly relates to the pilot/ feasibility study vs. the milestone plan which captures the all the work in the planning grant.)**
- **4.3 Statistical Design and Power**

Comparing and contrasting the R34 vs U34

Investigator-initiated R34	Network facilitated U34
Preparatory to Phase II/III, but specific pathway undetermined	Preparatory to large Phase II/III within specified network
“Necessary and sufficient”; No scientific requirements	Required activities – network engagement, adhere to existing rules for concept and protocol review
R	U
1-3 Years	1-3 years
Followup study potentially funded through R01	Followup study potentially funded through CP-CTNet, ULACNet, NCORP, etc.

Funding through the intervention vs. biomarker pipeline



Using an NCI Network to Conduct Research

- Research must be conducted via Network sponsorship
- Researcher contacts Research Base, Partnership Center, Lead Academic Organization to secure sponsorship
- Lead network site must notify NCI Program Director if plan to submit federally funded grant application (R01, U34, etc.)
  - Study chair, Lead network site PI, and NCI PD discuss aims, population, rationale/feasibility, timeline/budget considerations
  - Determine if within scope of program and there is no overlap with other projects in the pipeline or active

NCORP Symptom Management Example #1
Funded R34 - R34HL146927 NCORP Trial EAQ191 (Bonnie Ky)

Background: In non-cancer populations, SPRINT demonstrated that intensive systolic blood pressure (SBP) lowering to a target <120mmHg substantially reduces the rate of cardiovascular (CV) events and all-cause mortality.

Primary aim: tolerability of intensive SBP control that limited application of guidelines for aggressive SBP targets in clinical practice for oncology patients.

<u>Planning Grant Activities</u>

- Perform a retrospective analysis to define the distributions of SBP, CV risk scores, incidence of CV events, and all-cause mortality rates in cancer patients
- Perform a 60-patient prospective pilot study using a site-based cluster randomization design amongst 4 ECOG-ACRIN sites comparing ‘Intensive SBP Control’ with ‘Usual Care.’ This will be facilitated by a centralized BP Advisory Core, and will inform the SBP trajectories, safety and tolerability of Intensive SBP control, and participant and site burden.

NCORP Symptom Management Example #2

Primary aim: To compare the effect of prophylactic anti-HBV therapy versus upon indication anti-HBV therapy on time-to-adverse liver outcomes of liver failure or liver- related death in patients with chronic HBV infection (HBsAg+ and anti-HBc+) receiving anti-cancer therapy for solid tumors.

Patient population: diagnosed with stage I-III solid tumor planning to receive systemic anti-cancer therapy

Possible Planning Grant Activities

- The prevalence of chronic HBV infection is reported to be 0.3%, and the prevalence of past HBV infection is 4.6% though these rates may be underreported
  - Conduct a survey within NCORP to understand the prevalence within the network
  - Conduct site and physician assessment of feasibility
- Develop a process to identify patients including developing a relationship with infectious disease/gastroenterologists currently treating this patient population
- Develop and test a recruitment plan

NCORP Cancer Care Delivery Research Example #1

Primary Aim:	compare 8-week post-operative function among elderly patients between sites randomized to implement a toolkit to assess and manage frailty with or without implementation coaching, compared to usual care
Patient Eligibility:	elderly patients requiring major surgery for cancer who are assessed as frail using a standard measure
Practice Setting:	surgical practices that conduct a minimum number of major cancer surgeries

<u>Possible Planning Grant Activities</u>

- Pilot procedures for data collection that require direct observation of surgeons and staff in clinical settings
- Assess how frailty assessment can be incorporated into existing clinical workflows
- Formally evaluate physician and practice interest and capacity for implementation activities, including toolkit development

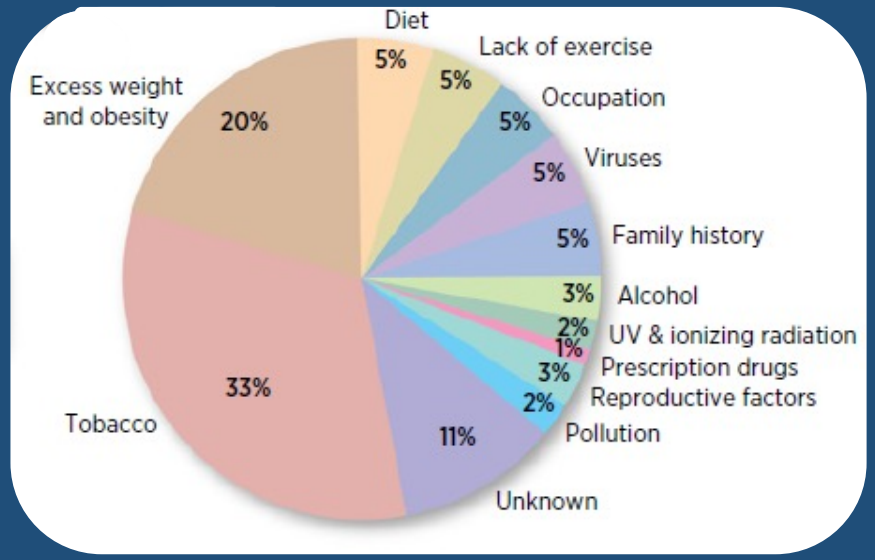
NCORP Cancer Care Delivery Research Example #2

Primary Aim:	compare the effectiveness of virtual learning collaborative versus technical assistance on uptake of an existing palliative care program
Patient Eligibility:	diagnosed within the last 90 days with an advanced cancer
Practice Setting:	medical oncology

<u>Possible Planning Grant Activities</u>

- Determine feasibility and uptake of virtual nurse training program
- Assess time commitment and staffing considerations for practice participation in technical assistance and virtual learning collaborative
- Develop and evaluate Spanish version of existing program and outcome measures

Up to 50% of Cancers May Be Preventable through Health Behavior Change

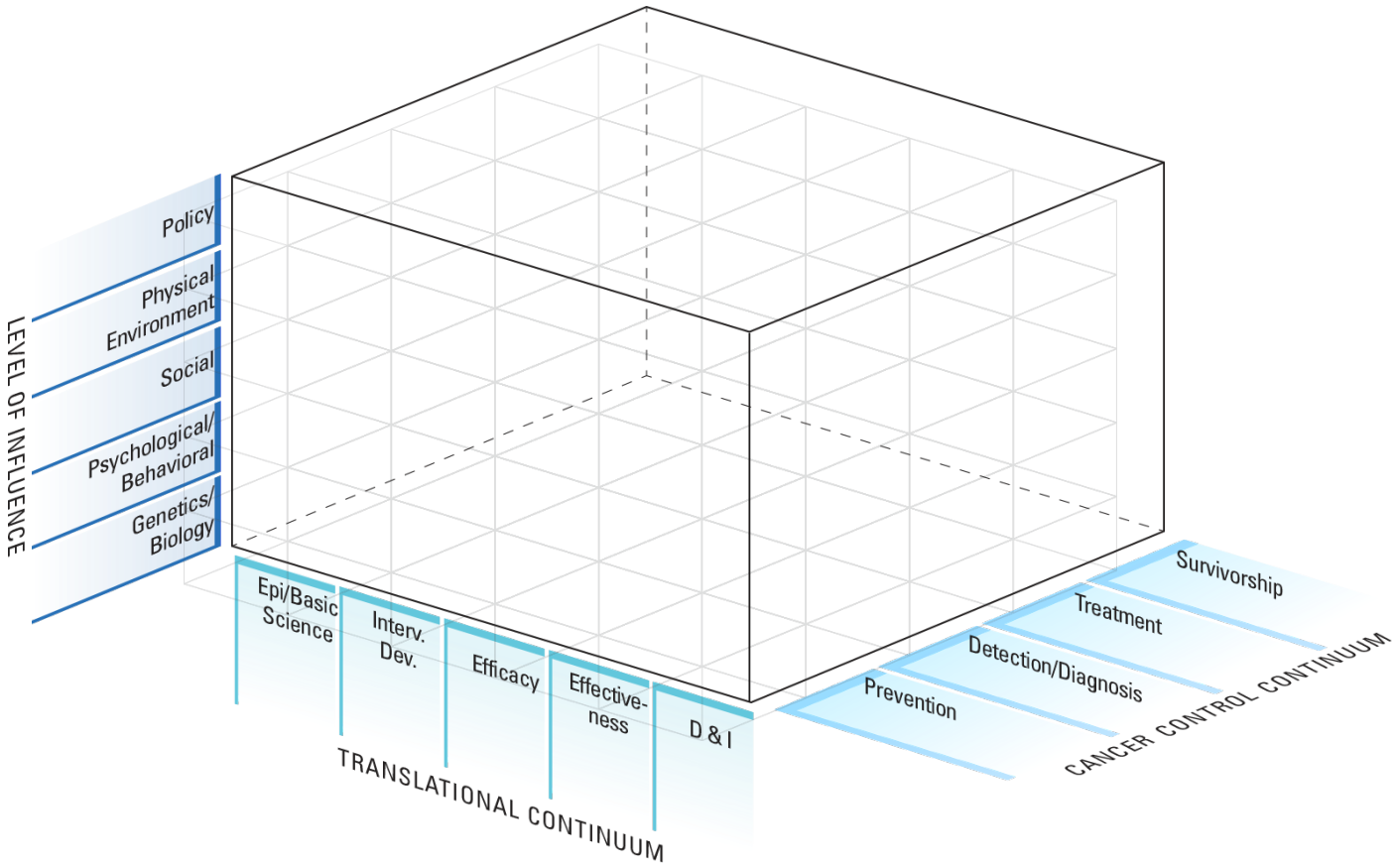


NCI's Behavioral Intervention Priorities

Cancer-related Behavioral Risk Factors of Interest

- Energy balance
- Alcohol use
- Diet
- Obesity
- Sleep and circadian dysfunction
- Physical activity and sedentary behavior
- Sun safety and tanning
- Adherence to cancer-related medical and behavioral regimens
- Other emerging cancer risk behaviors

NCI supports behavioral clinical trials that span multiple levels of analysis and all phases of the translational spectrum and cancer control continuum



https://cancercontrol.cancer.gov/brp/hbrb/strategy.html

Planning grants for behavioral intervention studies – relevant topics

- ***Behavioral research in cancer prevention and control*:** development and testing of interventions addressing risk behaviors such as: tobacco use, energy balance, or sun exposure; vaccine uptake; immune function; screening behavior; treatment adherence; biopsychosocial processes of cancer-related behavior; communication, decision science, environmental modifications and policy changes aimed at altering cancer-related health behaviors and/or preventing or improving cancer-related risks and outcomes.
- ***Healthcare delivery:*** single and multi-level interventions addressing the organization and/or delivery of cancer care (e.g., team-based care; novel use of electronic health records; new organizational mechanisms/staffing such as patient navigation; new models of specialized services such as palliative care or survivorship programs).
- ***Cancer survivorship:*** interventions addressing the physical, psychological, social, and financial burden of cancer and its treatment among survivors of cancer and their families (e.g., social functioning, caregiver adaptation).
- ***Implementation science*:** strategies to promote the adoption, implementation, and sustainability of evidence-based intervention into routine healthcare and public health settings or the deimplementation of ineffective interventions.

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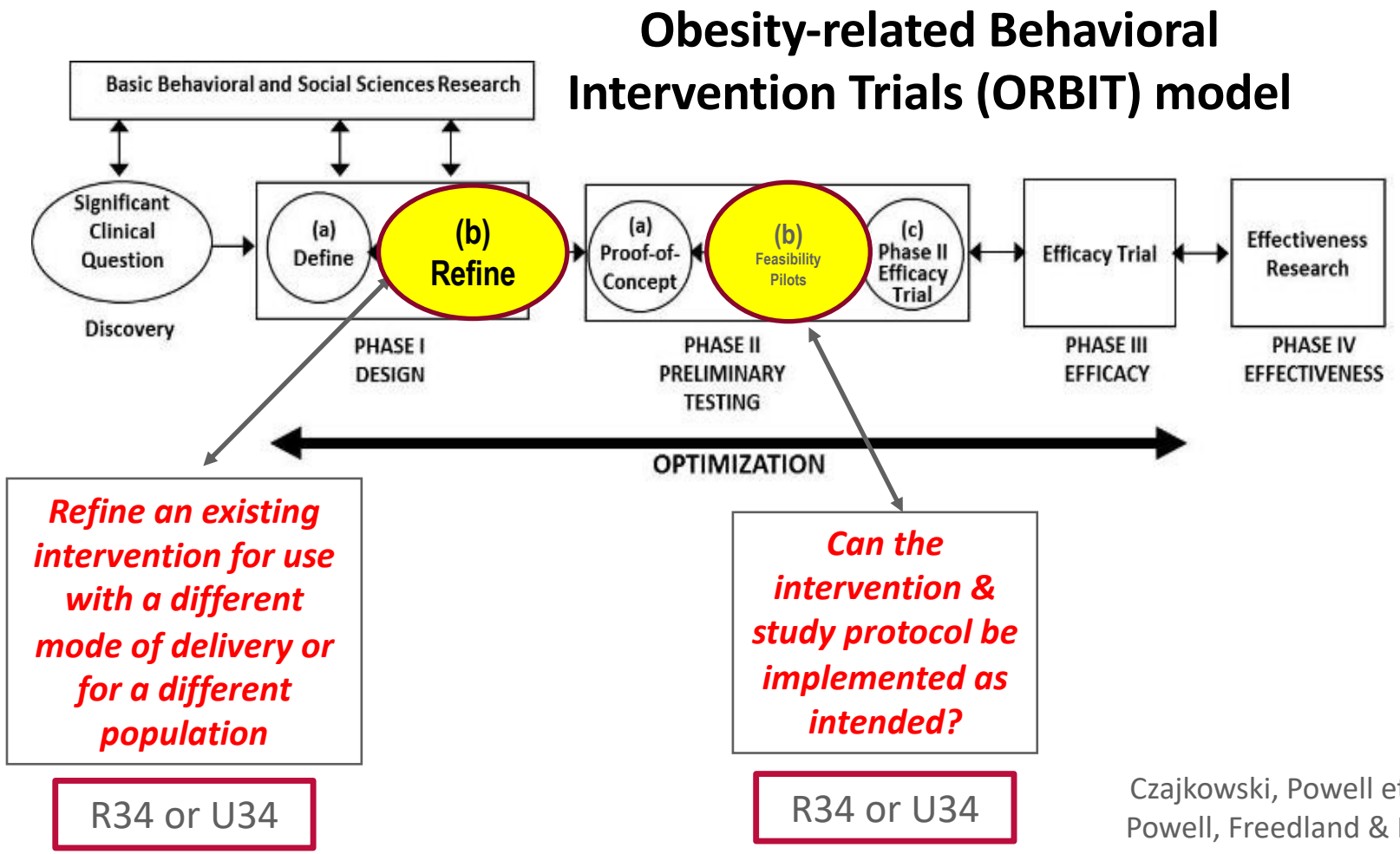
There are 2 phases on the behavioral intervention development & testing pipeline where a planning grant may be useful



Czajkowski, Powell et al., *Health Psychology* 2015; Powell, Freedland & Kaufmann, *Behavioral Clinical Trials for Chronic Diseases,* 2021

Examples of research needs relevant to behavioral clinical trials in cancer prevention and control

- Perform studies to refine the appropriate study population, intervention, outcome, and/or study endpoint.
- Collect information necessary to identify appropriate recruitment methods and estimate available populations, screening-to-enrollment yield, attrition rate, or response rate and ensure a diverse and adequate study population.
- Identify the appropriate control or comparison group to use in the subsequent clinical trial.
- Standardize the intervention or outcome across multiple sites.
- Test the feasibility of an outcome or intervention in the field &/or determine acceptability of the intervention to study participants.
- Determine whether adequate adherence to an intervention is achievable.
- Standardize and validate survey instruments.
- Statistical planning and design.

Perform studies to refine the appropriate study population, intervention, outcome, and/or endpoint

- Example:
  - A Phase III clinical trial is being planned to test a weight loss intervention on invasive disease-free survival in women with breast cancer
  - Prior research has established the ability of an in-person intervention to achieve the desired degree of weight loss in this population

  Possible Planning Grant Activities

  - Test whether a *telehealth* intervention using the same elements as the in-person intervention can achieve similar results in the same study population used in prior research
  - Test whether a version of the in-person intervention *that is adapted for use with a different population* can achieve similar results as in the original study

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Collect information necessary to identify appropriate recruitment methods, screening-to-enrollment yield, attrition rate, adherence, feasibility/acceptability

- Example:
  - A Phase III clinical trial is being planned to test a weight loss intervention on invasive disease-free survival in women with breast cancer
  - The large sample size needed requires the use of multiple recruitment sites to achieve adequate power for determining effects on the endpoint of interest

  <u>Possible Planning Grant Activities</u>

  - Determine whether the specific sites being considered for the larger trial can achieve specified recruitment goals in timely fashion
  - Determine the screening-to-enrollment yield for use in the larger planned study
  - Determine retention rate, degree of adherence to the intervention, and feasibility/acceptability of the intervention to the population of interest

Scientific contacts:

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Thank you!

Questions?