Lessons Learned from the National Cancer Institute's Community-Based Clinical Trials

Society of Clinical Trials- May 16,2022

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Division of Cancer Prevention

NIH NATIONAL CANCER INSTITUTE

NIH NATIONAL CANCER INSTITUTE Community Oncology Research Program (NCORP)

Setting the Stage

- **Over 80% of cancer care takes places in community settings**
- **Only 3-5% of patients in the US participate in cancer clinical trials**
- **Clinical trials are designed to advance cancer prevention, screening, treatment, and survivorship by providing scientific evidence**
- **"Without adequate rates of participation by patients and physicians, it is unlikely that important research questions with the potential to improve patient outcomes will be answered efficiently and effectively"** ***A National Cancer Clinical Trials System for the 21st Century, IOM***
- **Commemoration of the 50th Anniversary of the National Cancer Act**

NCI's Community-Based Clinical Trials: Today's Discussion

- History of NCI's Community-Based Programs
- NCORP Community Oncology Research (NCORP)
- Community-Based Clinical Trials: Informing Public Health Policy with Compelling Evidence
  - Trials
  - Successes
  - Challenges
- Future Directions of Clinical Trials in Community Settings

History of NCI Community-Based Clinical Trials

A Journey Continues!

Community Clinical Oncology Program (CCOP) -1983
Minority-Based CCOP – 1990

NCI Community Cancer Centers Program (NCCCP) - 2007

NCI Community Oncology Research Program (NCORP) 2014

Community & Minority-Based Clinical Oncology Programs (CCOPs & MB-CCOPs)

- 30-40% of treatment accrual to the NCI Cooperative Groups
- Chemoprevention Trials:

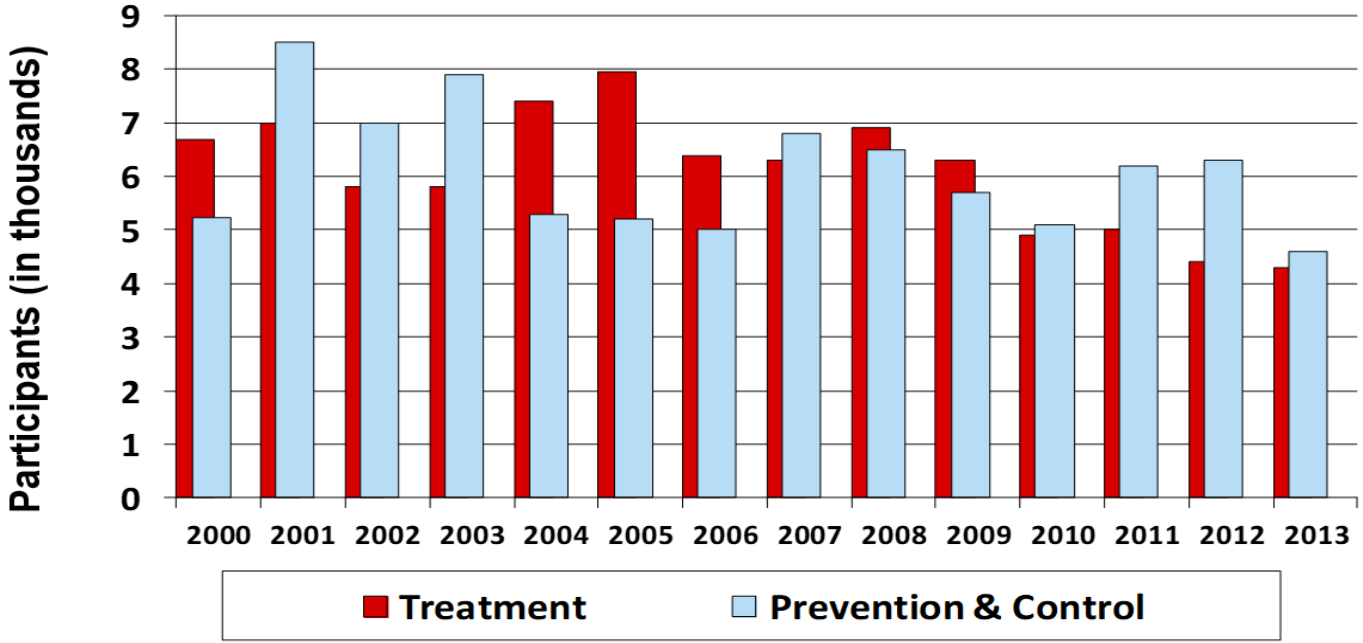
The Breast Cancer Prevention Trial (P-1) n=13,388	FDA Approval of Tamoxifen
Prostate Cancer Prevention Trial (PCPT), n=18,882	Finasteride reduced the risk of prostate ca. by 30%
Study of Tamoxifen and Raloxifene (STAR), n=19,747	FDA Approval of Raloxifene
Selenium and Vitamin E Cancer Prevention Trial (SELECT) n=35,533	No reduction in prostate ca.; increase in ca. In the Vitamin E arm

- Introduced symptom management into the clinical trials network

NCI Community Clinical Oncology Program Network Accrual 2000 – 2013

Minority accrual:
MB-CCOPs: 62%
CCOPs: 10%

Total accrual 170,685
(40% to NCTN treatment)



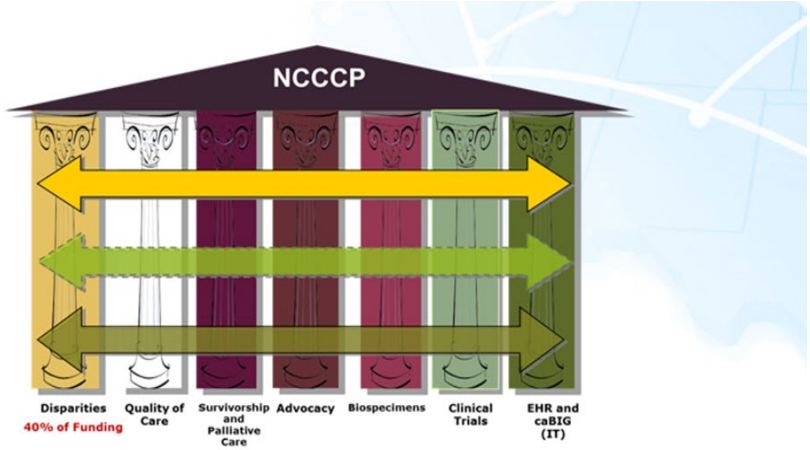

SELECT
(Estudio del Selenio y la Vitamina E para Prevenir el Cáncer)
Dr. Jaime Claudio-Investigador Afiliado 787-791-9026
Multivitamínico y suplementos del estudio gratis por 12 años
¡Pregunte hoy sobre como participar en el más grande estudio clínico de prevención del cáncer de próstata jamás realizado!
Dr. Jaime Claudio
Profesor Ad-Honorem
Medicina de Familia-UPR-Ciencias Médicas
SELECT
SELECT
SELECT

CCOPs & MB-CCOPs Cont'd: Lessons Learned

- Enthusiasm for RCT and contributors to trials, e.g., breast and bowel adjuvant
- Community physicians who participate in trials more rapidly adopt state-of-the-art care
- Partnerships with industry for chemoprevention – enhance recruitment efforts
- Targeted practices needed to enhance racial/ethnic minorities
- Challenges from local IRBs
- Essential role of Community and Participant Advisory Boards

NCI Community Cancer Centers Program (NCCCP)

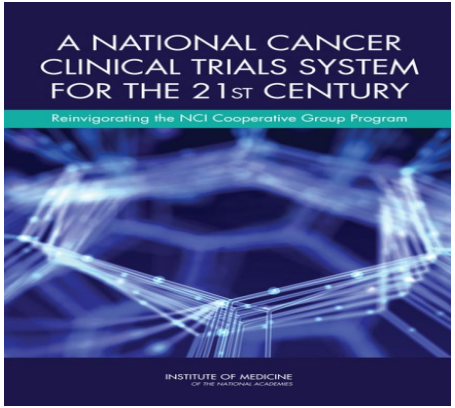
- **Pilot Program of 21 Sites**
  - ❖ **Reduce cancer health disparities**
  - ❖ **Increase participation in clinical trials**
  - ❖ **Improve quality of cancer care**
  - ❖ **Enhance cancer survivorship and palliative care services**
  - ❖ **Promote collection of high-quality biospecimens**



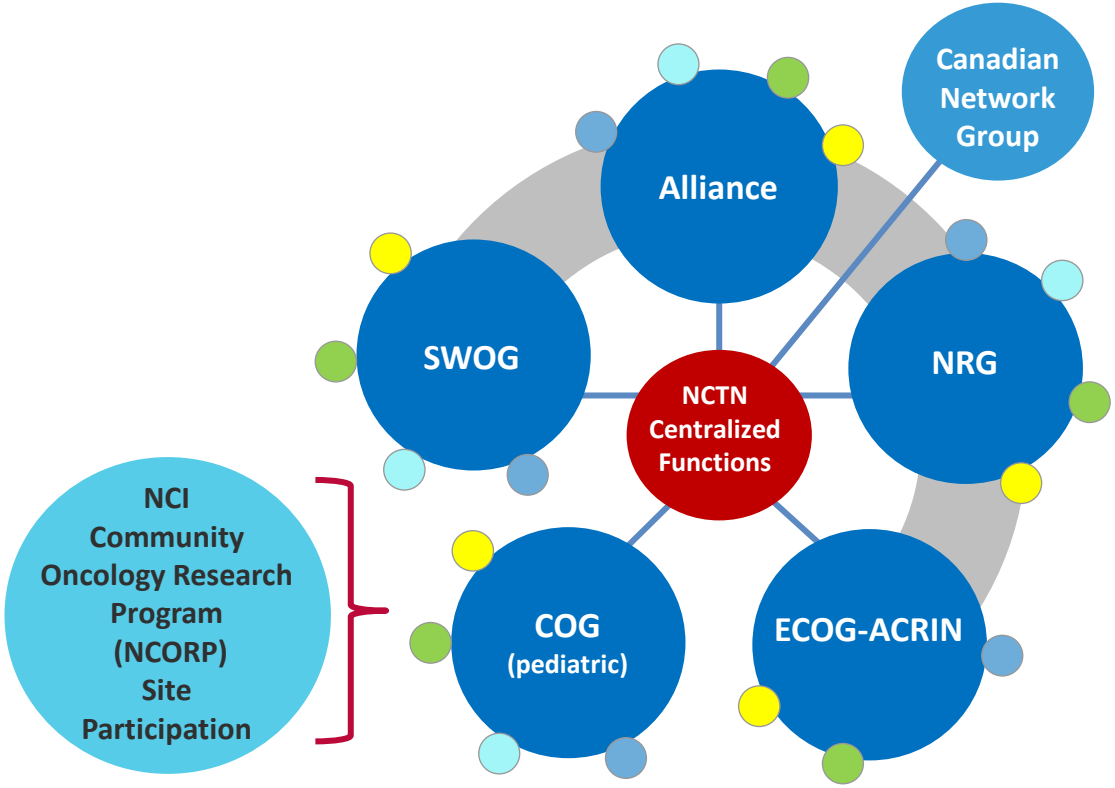
NCI Community Oncology Research Program (NCORP)

Revamping NCI Clinical Trials

1. Improve the speed and efficiency of the design, launch, and conduct of trials
2. Incorporate innovative science and trial design into trials
3. Improve the means of prioritization, selection, support, and completion of trials
4. Incentivize the participation of patients and physicians in trials



Organization and Infrastructure for the NCTN



≈ 2,200 enrolling sites across North America plus international sites

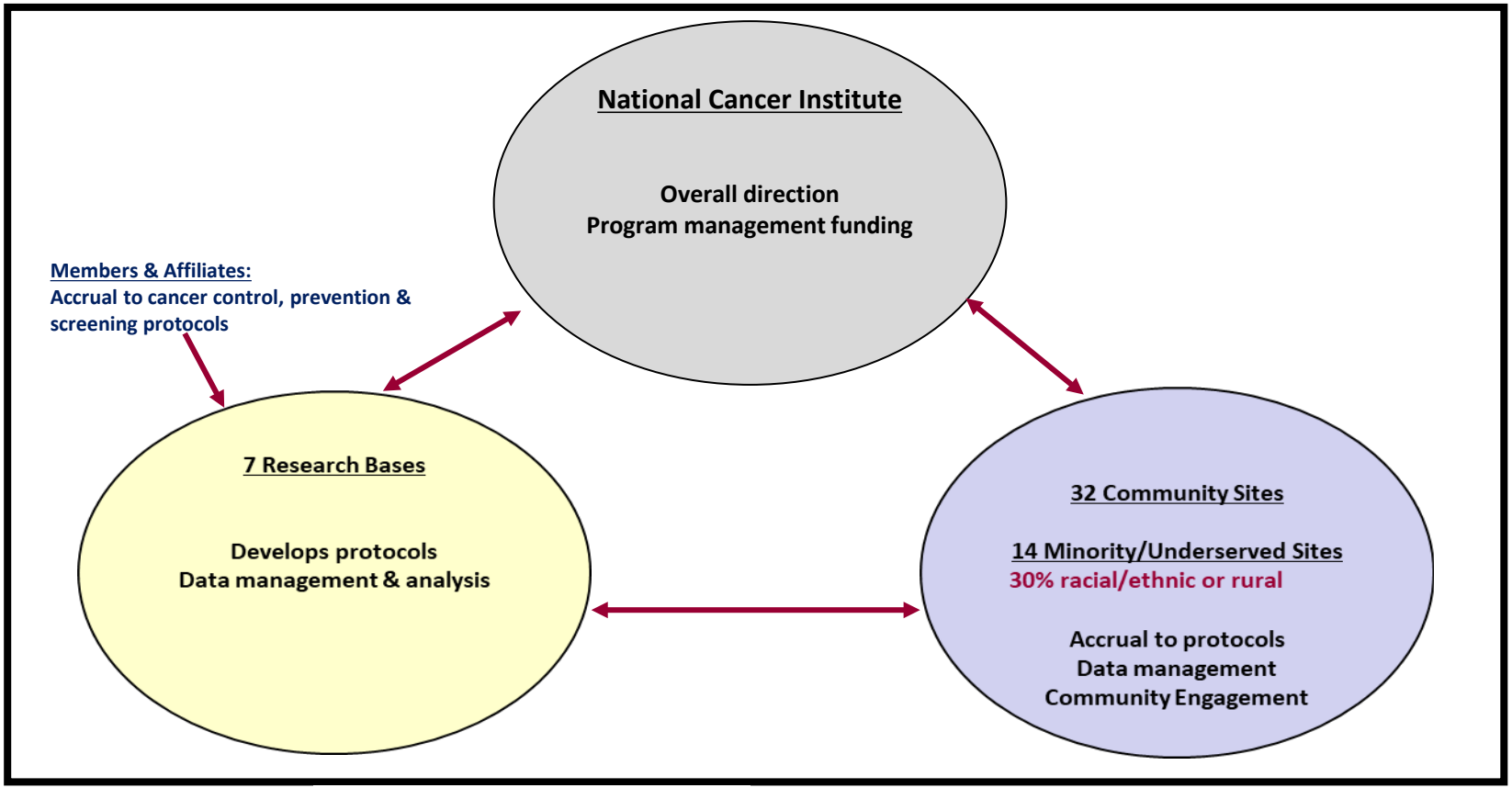
LEGEND:

- **Centralized Functions:**
  - NCI IRB with 4 Boards
  - Cancer Trials Support Unit
  - RT/Imaging Core Center
  - NCI Disease-Specific Steering Committees
  - Common Data Mgt with System Central Hosting
- **Lead Academic Participating Sites (LAPS)**
- **Operations Centers**
- **Statistics & Data Management**
- **Tumor Banks**

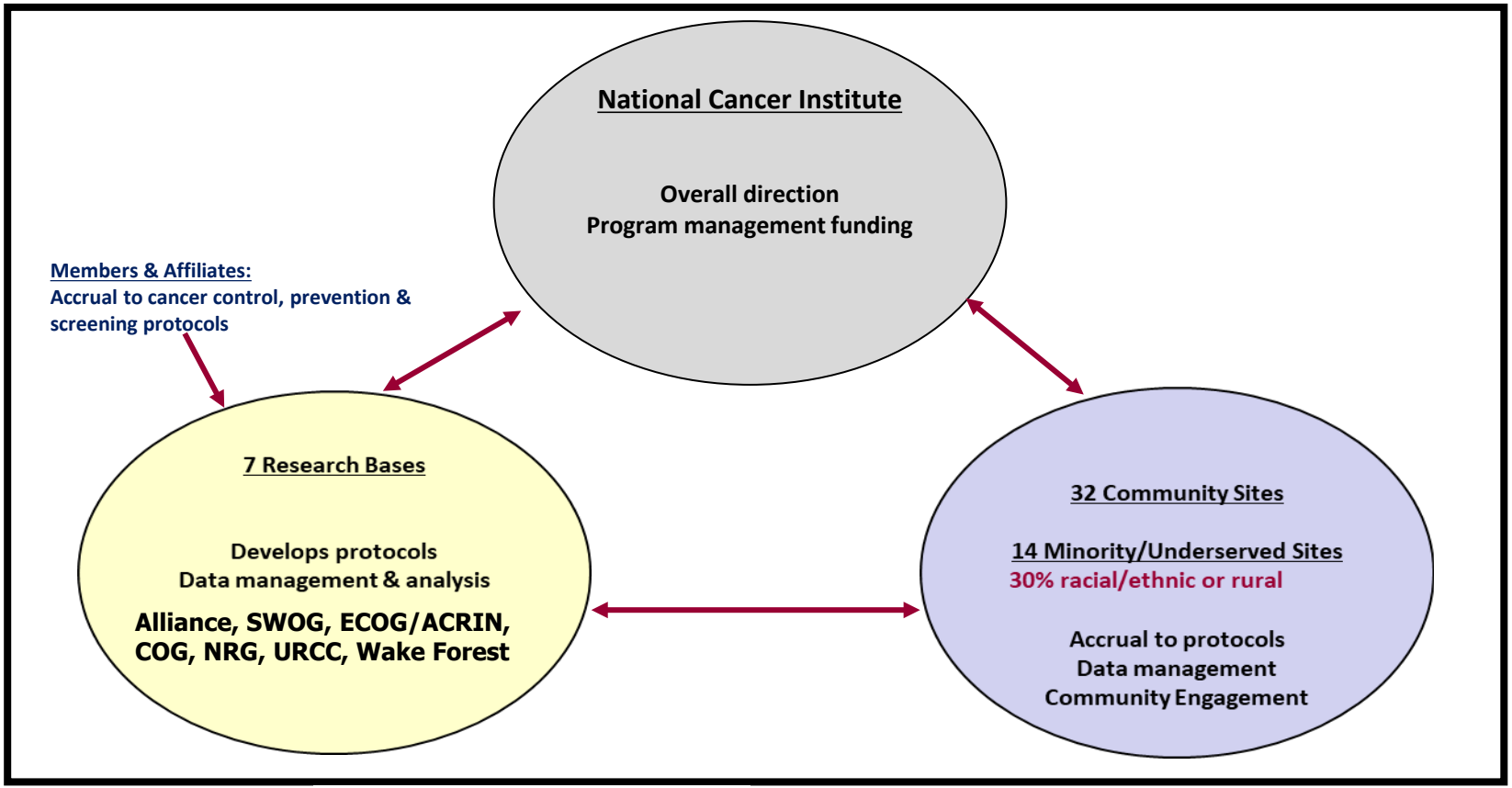
NCORP: Community/Academic Partnership

- Clinical Trials/Studies:
- Accrual to symptom management, palliative care, prevention, surveillance, screening, and QOL embedded in treatment trials
- Accrual to National Trials Network(NCTN): treatment, advanced imaging trials, and tissue acquisition studies
- Accrual of patients, clinicians, & organizational factors that influence care delivery through cancer care delivery research (CCDR) trials and studies
- Cancer disparities research incorporated into clinical trials and CCDR
- Biobanks and Imaging Radiation Oncology Core to support the research portfolio

NCORP Organizational Relationships

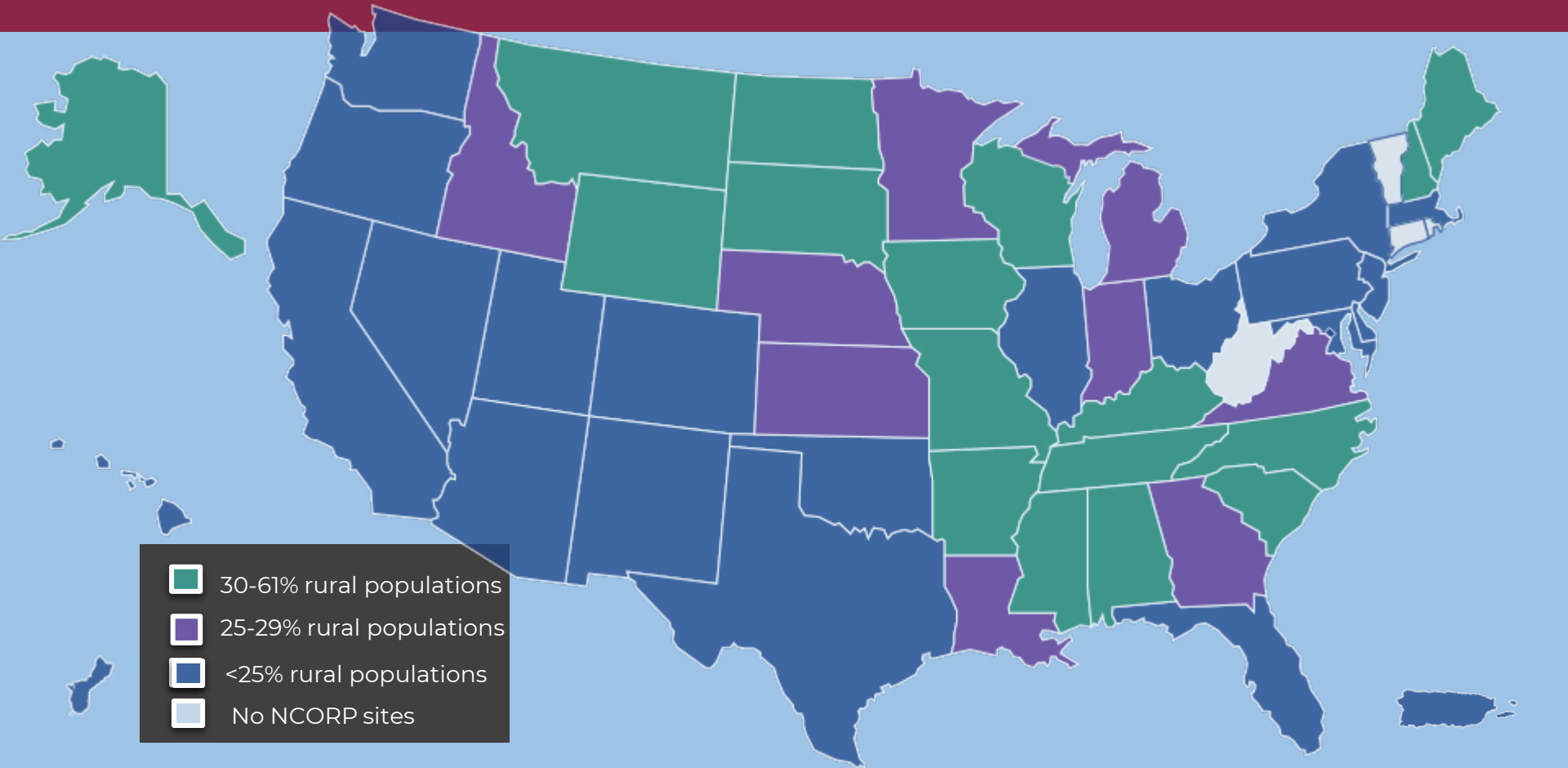


NCORP Organizational Relationships

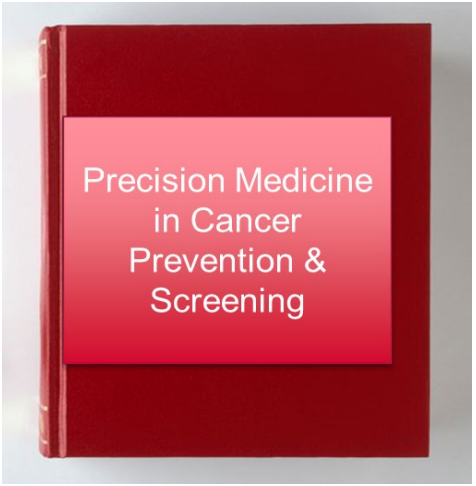


NCI Community Oncology Research Program (NCORP)
Community and Minority/Underserved Sites, 1000+, 4000+ investigators

Rural Population by State, Territory



✓ Design and conduct cancer prevention, control, and screening/post-treatment surveillance clinical trials



Cancer Moonshot Biobank

Longitudinal biospecimens: Blood and/or tissue samples with two or more time points including: archival, baseline, on treatment, & progression

NCORP ACCRUAL
August 1, 2014 – April 30, 2022, N=71,184

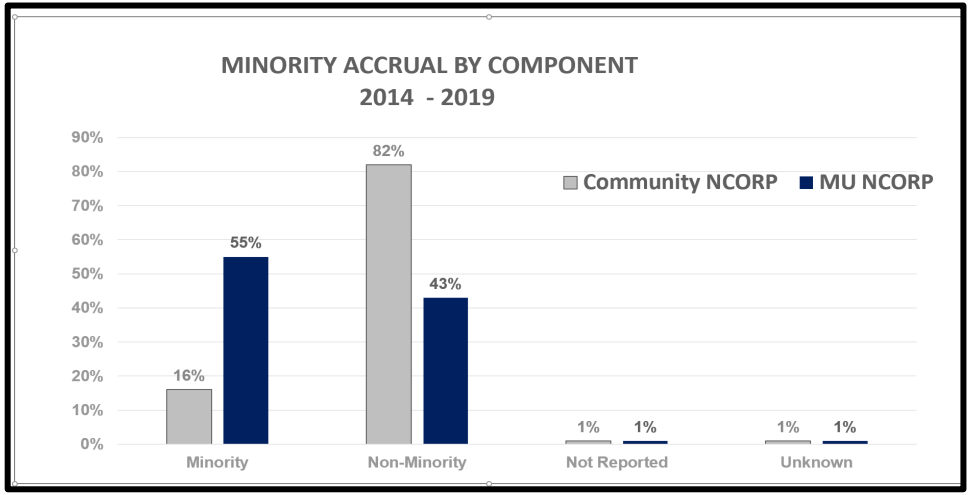
	2014 CPC / TX	2015 CPC / TX	2016 CPC / TX	2017 CPC / TX	2018 CPC / TX	2019 CPC / TX	2020 CPC / TX	2021* CPC / TX
ALL NCORPs	**2763 /3911 6,674**	**3822/5058 8,880**	**3603/4523 8,126**	**4649/3627 8,336**	**6353/3712 10,065**	**6603/3306 9,868**	**7483/4284 11,743**	**4777/2715**
Community NCORPs	2430/3261	3384/3848	3187/3543	3939/2916	5015/3000	5174/2456	5784/3209	3729/1982
Minority NCORPs	333/650	438/1210	416/980	710/711	1338/712	1429/850	1699/1075	1048/733

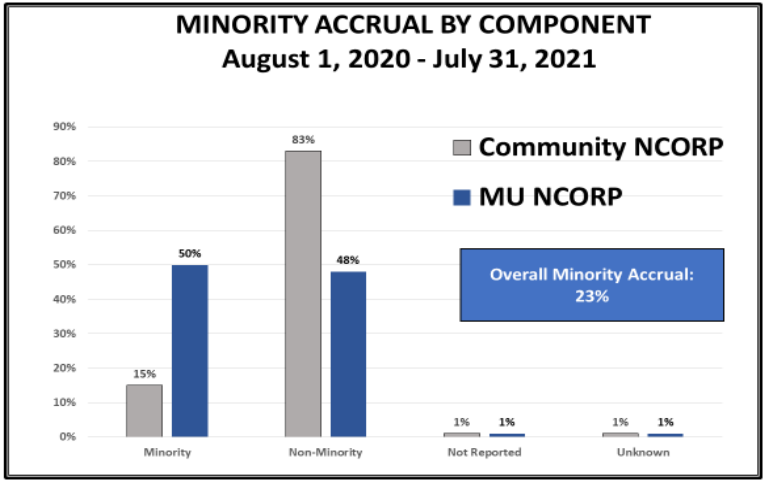
*** 9 Month Data**

NCORP Minority/Underserved Sites (affiliates)

Baptist Health (12)	Ark, MS, TN
Columbia University (2)	NY, FL
GaCares (10)	GA
Gulf South (49)	LA, MS
Hawaii (24)	HI, Guam
Kansas U (16)	KS, MO
Medical University of South Carolina (14)	SC
Montefiore (6)	NY
National Capital (Georgetown) (2)	DC
U of New Mexico (16)	NM
Puerto Rico (18)	PR
Stroger/Cook County	IL
Texas Pediatric (2)	TX
Virginia Commonwealth University (18)	VA

Minority Accrual

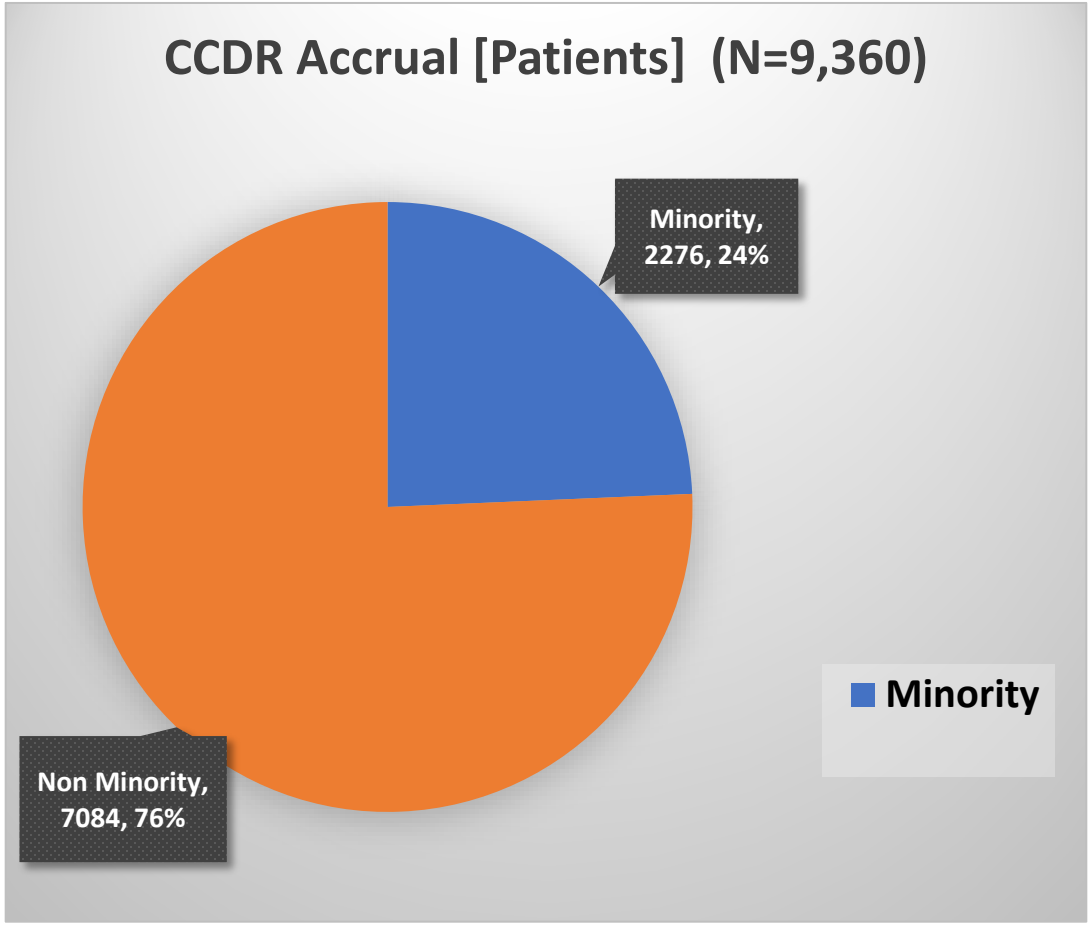




CCDR Minority Accrual

- **Total Accrual – 9,360 patients**

  (Aug. 1, 2014 – Mar. 31, 2022)
  - **24% minority accrual**
  - **MU Sites contribute 61% of total minority accrual**



Data Source: DCP Dashboard/OPEN

Lessons from the NCORP Network

- Majority of cancer care is provided in the community; however, there are major practice changes
- Access to diverse “real world” healthcare delivery settings
- Access to an increasingly diverse patient populations across the US
- Tests feasibility of implementing new interventions and processes in the community setting
- Enhances potential that outcomes will be broadly applicable in practice
- Accelerates the uptake of new interventions and processes into routine practice

NCI Community Oncology Research Program (NCORP)

New Generation of Clinical Trials

Precision Medicine Trials

The term precision refers to prospects for enhanced molecular resolution, mechanistic clarity, and therapeutic cogency that may accompany clinical implementation of genomics technologies.

Precision medicine's more individualized, molecular approach to cancer will enrich and modify but not replace, the successful staples of oncology – prevention, diagnostic, some screening methods and effective treatments – while providing a framework for accelerating the adoption of precision medicine in other spheres.

NCI Community Oncology Research Program
Molecular Analysis for Therapy Choice (MATCH)

43.3% 2770/6391 of Patients Registered for Screening are from NCORP Community and Minority Community Sites

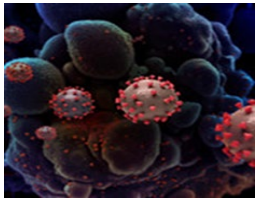
Since 2021: 40% 37/92

NCI Cancer Moonshot™ Initiatives within NCORP

Goal: To Evaluate Sensivity and Drug Resistance to FDA Approved Moleculary Targeted Agents Used in Standard of Care.

- **NCI Protocol 10231: To procure and bank formalin-fixed, paraffin-embedded (FFPE) tissue (& snap-frozen as well), blood (for cell-free DNA analysis), and nucleic acids from patients (n = 150) with advanced solid cancers prior to 1st-line standard targeted therapy and at 1st recurrence.**
- **NCI Biobank Protocol 10323: To support investigations through the procurement & distribution of multiple longitudinal specimens and data. Including a central biorepository; clinical tumor biomarker testing; e-consent; sub-studies on patient engagement and ethical, legal, social implications, and a biobank website for participants and providers to access to biomarker reports, and educational resources.**

Biospecimens: Baseline, on treatment, and at disease-progression.



Research Priorities in Cancer & Treatment Related Toxicities

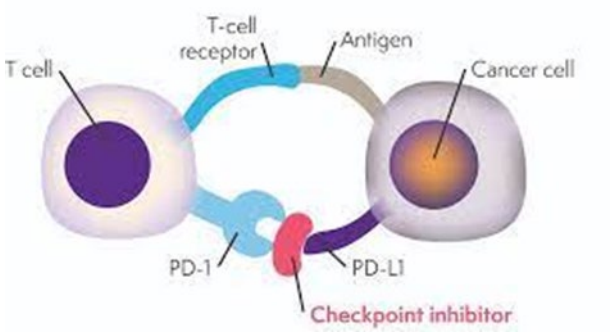
1. Cognitive Impairment

2) Neurotoxicity

3) Cardiovascular Toxicity

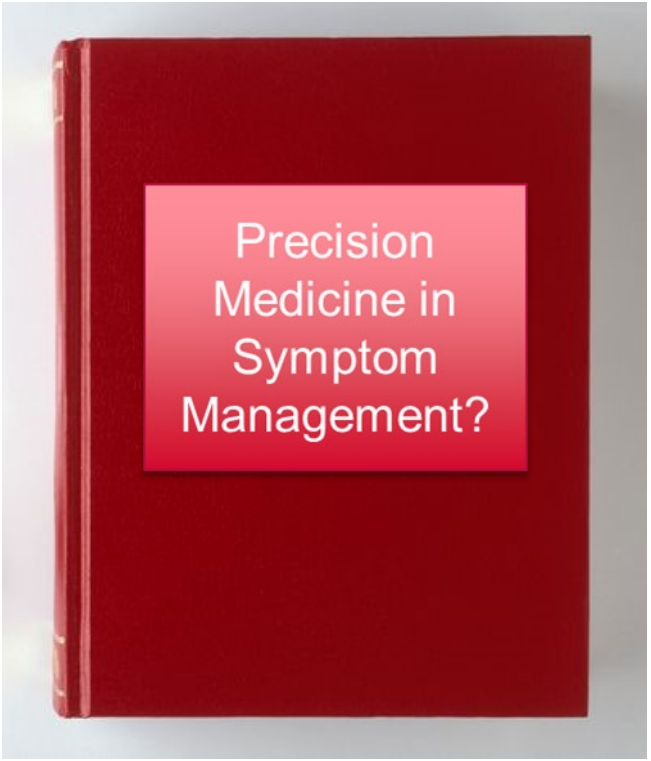
4) Fatigue

5) Cancer Specific Pain



Strategies Toward Precision Medicine in Symptom Management

- Longitudinal Studies
- Preclinical Models
- Establishing Biobanks to support
- Establishing industry relationships
- Working with Early Detection Network to study biomarkers of risk prediction and response



- **NRG-C003 Randomized Phase II/III Trial of Prophylactic cranial irradiation w/wo Hippocampal avoidance for SCLC**

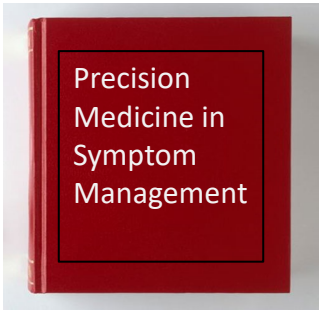
Disparities Research in Symptom Management

- **Targeted populations with across Research Base pooled analyses**

  - ❖ **URCC-21038: Disparities in REsults of Immune Checkpoint Inhibitor Treatment (DiRECT): A Prospective Cohort Study of Cancer Survivors Treated with anti-PD-1/anti-PD-L1 Immunotherapy in a Community Oncology Setting**

  - ❖ **Patient Reported Outcomes language translations**

  - ❖ **EAZ171 Prospective validation of taxane therapy and risk of chemo-induced peripheral neuropathy in African American women**



✓Accelerating the translation of knowledge gained from clinical trials into clinical practice

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting

Rudolph M. Navari, M.D., Rui Qin, Ph.D., Kathryn J. Ruddy, M.D., Heshan Liu, Ph.D., Steven F. Powell, M.D., Madhuri Bajaj, M.D., Leah Dietrich, M.D., David Biggs, M.D., Jacqueline M. Lafky, M.S., and Charles L. Loprinzi, M.D.

ABSTRACT

BACKGROUND
We examined the efficacy of olanzapine for the prevention of nausea and vomiting in patients receiving highly emetogenic chemotherapy.

METHODS
In a randomized, double-blind, phase 3 trial, we compared olanzapine with placebo, in combination with dexamethasone, aprepitant or fosaprepitant, and a 5-hydroxytryptamine type 3–receptor antagonist, in patients with no previous chemotherapy who were receiving cisplatin (≥70 mg per square meter of body-surface area) or cyclophosphamide–doxorubicin. The doses of the three concomitant drugs administered before and after chemotherapy were similar in the two groups. The two groups received either 10 mg of olanzapine orally or matching placebo daily on days 1 through 4. Nausea prevention was the primary end point; a complete response (no emesis and no use of rescue medication) was a secondary end point.

RESULTS
In the analysis, we included 380 patients who could be evaluated (192 assigned to olanzapine, and 188 to placebo). The proportion of patients with no chemotherapy-induced nausea was significantly greater with olanzapine than with placebo in the first 24 hours after chemotherapy (74% vs. 45%, P=0.002), the period from 25 to 120 hours after chemotherapy (42% vs. 25%, P=0.002), and the overall 120-hour period (37% vs. 22%, P=0.002). The complete-response rate was also significantly increased with olanzapine during the three periods: 86% versus 65% (P<0.001), 67% versus 52% (P=0.007), and 64% versus 41% (P<0.001), respectively. Although there were no grade 5 toxic effects, some patients receiving olanzapine had increased sedation (severe in 5%) on day 2.

CONCLUSIONS
Olanzapine, as compared with placebo, significantly improved nausea prevention, as well as the complete-response rate, among previously untreated patients who were receiving highly emetogenic chemotherapy. (Funded by the National Cancer Institute; ClinicalTrials.gov number, NCT02116530.)

From Indiana University School of Medicine–South Bend, South Bend (R.M.N.); Alliance Statistics and Data Center, Mayo Clinic (R.Q., H.L.), and Mayo Clinic (K.J.R., J.M.L., C.L.L.), Rochester, MN; Sanford NCORP (National Cancer Institute Community Oncology Research Program) of the North Central Plains, Sioux Falls, SD (S.F.P.); Illinois Cancer Care–Peoria, Peoria (M.B.); Gundersen Lutheran Medical Center, La Crosse, WI (L.D.); and Delaware–Christiana Care NCORP, Newark, DE (D.B.). Address reprint requests to Dr. Navari at 4518 Crown Point Ln., Mount Olive, AL 35117, or at rmnavari@gmail.com.

N Engl J Med 2016;375:134-42.
DOI: 10.1056/NEJMoa1515725
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Research

JAMA Oncology | Brief Report

Olanzapine for the Treatment of Advanced Cancer–Related Chronic Nausea and/or Vomiting
A Randomized Pilot Trial

Rudolph M. Navari, MD; Cameron M. Pywell, MD; Jennifer G. Le-Rademacher, PhD; Patrick White, MD; Andrew B. Dodge, MS; Costantine Albany, MD; Charles L. Loprinzi, MD

IMPORTANCE Nausea and vomiting, unrelated to chemotherapy, can be substantial symptoms in patients with advanced cancer.

OBJECTIVE To evaluate the utility of olanzapine for treating chronic nausea/vomiting, unrelated to chemotherapy, in patients with advanced cancer.

DESIGN, SETTING, AND PARTICIPANTS This study is a double-line, placebo-controlled, randomized clinical trial conducted from July 2017 through April 2019, with analysis conducted in 2019. Eligible participants were outpatients with advanced cancer who had persistent nausea/vomiting without having had chemotherapy or radiotherapy in the prior 14 days. Chronic nausea was present for at least 1 week (worst daily nausea numeric rating scores needed to be greater than 3 on a 0-10 scale).

INTERVENTIONS Patients received olanzapine (5 mg) or a placebo, orally, daily for 7 days.

MAIN OUTCOMES AND MEASURES Patient-reported outcomes were used for study end points. Data were collected at baseline and daily for 7 more days. The primary study end point (the change in nausea numeric rating scores from baseline to the last treatment day) and the study hypothesis were both identified prior to data collection.

RESULTS A total of 30 patients (15 per arm) were enrolled; these included 16 women and 14 men who had a mean (range) age of 63 (39-79) years. Baseline median nausea scores, in all patients, were 9 out of 10 (range, 8-10). After 1 day and 1 week, the median nausea scores in the placebo arm were 9 out of 10 (range, 8-10) on both days, compared with the olanzapine arm scores of 2 out of 10 (range, 2-3) after day 1 and 1 out of 10 (range, 0-3) after 1 week. After 1 week of treatment, the reduction in nausea scores in the olanzapine arm was 8 points (95% CI, 7-8) higher than that of the placebo arm. The primary 2-sided end point *P* value was <.001. Correspondingly, patients in the olanzapine arm reported less emesis, less use of other antiemetic drugs, better appetite, less sedation, less fatigue, and better well-being. One patient, on the placebo, stopped treatment early owing to lack of perceived benefit. No patients receiving olanzapine reported excess sedation or any other adverse event.

CONCLUSIONS AND RELEVANCE Olanzapine, at 5 mg/d, appeared to be effective in controlling nausea and emesis and in improving other symptoms and quality-of-life parameters in the study population.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03137121

Visual Abstract
Supplemental content

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JAMA Oncol. 2020;6(6):895-899. doi:10.1001/jamaoncol.2020.1052
Published online May 7, 2020.

Few Older Adults Included in Registration Studies

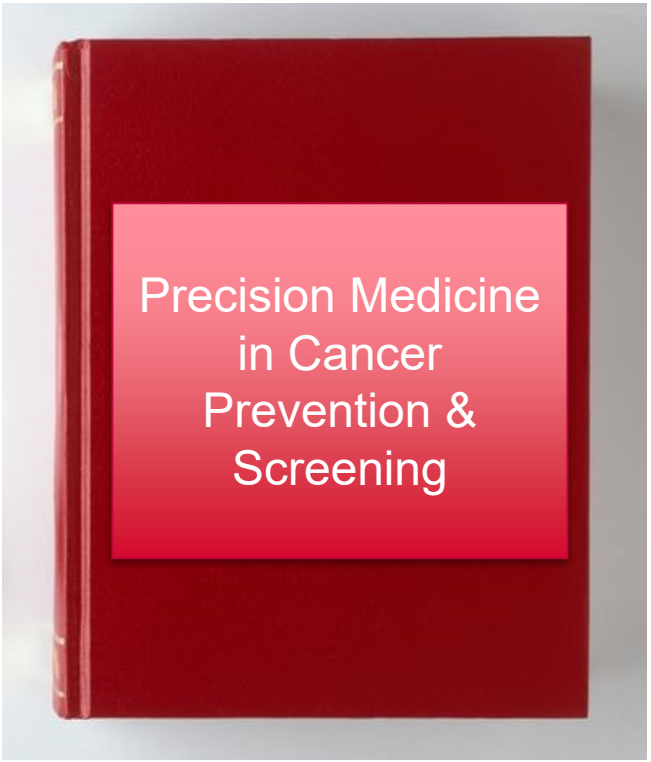
Breast Cancer as an Example

Agent Name	Approval	N	Age ≥ 65	N	Age ≥ 75
Abemaciclib	09/2017	154	35%	39	9%
		42	32%	10	8%
Neratinib	07/2017	172	14%	25	2%
Ribociclib	03/2017	150	45%	35	11%
Palbociclib	2/2015	181	41%	48	11%
		86	25%	27	8%
Ado-Trastuzumab Emtansine	2/2013	65	13%	11	2%
Everolimus	7/2012	290	40%	109	15%
Pertuzumab	6/2012	60	15%	5	1%
Eribulin Mesylate	11/2010	121	15%	17	2%
Lapatinib	1/2010	34	17%	2	1%
		282	44%	77	12%
Ixabepilone	10/2007	45	10%	3	<1%
		32	13%	6	2.5%

Package Insert, "Geriatric Usage" section

✓ Facilitating the participation of minorities and other underserved populations across all study types and settings

- **A171601: A Phase II Trial Assessing the Tolerability of Palbociclib in Combination with Letrozole or Fulvestrant in Patients Aged 70 and Older with Estrogen Receptor-Positive, HER2-Negative Metastatic Breast Cancer**
  - **Primary Objective: To estimate the safety and tolerability (adverse event rate) of the combination of palbociclib and letrozole or fulvestrant in adults age 70 or older with estrogen receptor-positive, HER2-negative metastatic breast cancer.**
  - **Primary Endpoint: Primary Endpoints: The primary endpoint is the adverse event rate at 6 months, defined as the proportion of patients with documentation of grade 3 - 5 toxicity**



CANCER PREVENTION RESEARCH | COMMENTARY

Establishing a Primary Care Alliance for Conducting Cancer Prevention Clinical Research at Community Sites

Bernard W. Parker[1], Barbara L. McAneny[2], Edith P. Mitchell[3], Ana María López[3], Sandra A. Russo[1], Pamela Maxwell[3], Leslie G. Ford[1], and Worta McCaskill-Stevens[1]; for the National Cancer Institute PARTNRS Planning Committee[4]

ABSTRACT

In September 2020, the National Cancer Institute convened the first PARTNRS Workshop as an initiative to forge partnerships between oncologists, primary care professionals, and non-oncology specialists for promoting patient accrual into cancer prevention trials. This effort is aimed at bringing about more effective accrual methods to generate decisive outcomes in cancer prevention research. The workshop convened to inspire solutions to challenges encountered during the development and implementation of cancer prevention trials. Ultimately, strategies suggested for protocol development might enhance integration of these trials into community settings where a diversity of patients might be accrued. Research Bases (cancer research organizations that develop protocols) could encourage more involvement of primary care professionals, relevant prevention specialists, and patient representatives with protocol development beginning at the concept level to improve adoptability of the trials within community facilities, and consider various incentives to primary care professionals (i.e., remuneration). Principal investigators serving as liaisons for the NCORP affiliates and sub-affiliates, might produce and maintain "Prevention Research Champions" lists of PCPs and non-oncology specialists relevant in prevention research who can attract health professionals to consider incorporating prevention research into their practices. Finally, patient advocates and community health providers might convince patients of the benefits of trial-participation and encourage "shared-decision making."

Rationale for a Primary Care Alliance in Cancer Prevention Studies

Clinical detection of both cancer and premalignant conditions exists within the domain of primary care professionals, who in this respect are the "first responders" and medical "gate-keepers" of the healthcare system (1). Traditionally, they comprise family physicians, internists, pediatricians, obstetrician–gynecologists, nurse practitioners, and physician assistants (2). Yet, the subsequent active consultation and management of frank disease and pre-cancer that has been detected early necessitates involvement by medical oncologists, general surgery or surgical subspecialists (e.g., colorectal surgeons, urologists, gynecologists), radiologists (e.g., diagnostic and interventional), and other specialists (e.g., dermatologists, geneticists, etc.) (3). As such, accruing participants to cancer prevention trials is highly dependent on primary care professionals and the numerous specialists engaged in prevention, detection, and management of premalignant conditions, as well as on the people themselves who are at risk for cancer (4). However, the recognized gulf in professional communication and coordination between primary care professionals and oncologists of multiple specialties—surgical, radiological, and pharmacological—indicates the overdue need for relational change in these clinical practice settings (5). Moreover, the chasm between the groups can impede clinical oncology research, although primary care professionals, particularly Black and Latino physicians, have indicated they are interested in learning more about cancer clinical trials (6). Experiences conducting cancer prevention studies through the National Cancer Institute Community Oncology Research Program (NCORP) are affected by the accrual challenges within this cancer care delivery system, and thus led to the concept and inaugural workshop called "PARTNRS: The Primary Care Alliance in Research Trials Involving NCORP Sites."

Purpose of the PARTNRS Workshop

The PARTNRS workshop, convened on September 18, 2020, was developed to improve participant accrual to NCORP-

[1]National Cancer Institute, Division of Cancer Prevention, Bethesda, Maryland. [2]New Mexico Cancer Center, Albuquerque, New Mexico. [3]Sidney Kimmel Cancer Center of Jefferson Medical School, Thomas Jefferson University, Philadelphia, Pennsylvania. [4]See note and listing at end of the article.

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Cancer Prev Res 2021;14:977–82

doi: 10.1158/1940-6207.CAPR-21-0019

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NRG-CC005 – FORTE (Five- or Ten-Year Colonoscopy for 1-2 Non-Advanced Adenomatous Polyps)

Primary Objective

1. To examine colorectal cancer incidence in participants with 1 to 2 non-advanced adenomas randomized to surveillance colonoscopy at 10 years compared to participants randomized to surveillance colonoscopy at 5 and 10 years.

Secondary Objectives

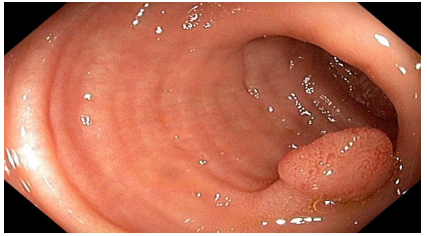
1. **To examine advanced adenoma incidence in participants with 1 to 2 non-advanced adenomas randomized to surveillance colonoscopy at 10 years compared to participants randomized to surveillance colonoscopy at 5 and 10 years.**
2. **To examine colorectal cancer mortality in participants with 1 to 2 non-advanced adenomas randomized to surveillance colonoscopy at 10 years compared to participants randomized to surveillance colonoscopy at 5 and 10 years.**

Exploratory Objective

1. **Collection of blood, stool, and tissue samples for purposes of the NRG-CC005 study and for future unspecified research.**

Trial Design: The sample size of 9,500 participants randomized 1:1 will achieve 90% power to detect a non-inferiority margin difference of 0.387% at alpha 5% one-sided.

➢ **Accrual Goal – 9,500**



ECOG/ACRIN 1151: Tomosynthesis Mammographic Imaging Screening Trial (TMIST)

Primary Objective

1. To determine whether the cumulative rate of advanced breast cancer in women undergoing screening with tomosynthesis + digital mammography (TM) is reduced compared to digital mammography (DM) alone

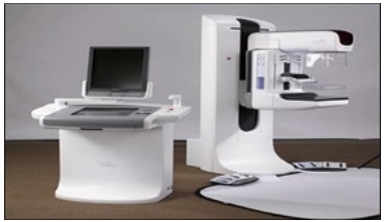
Secondary Objectives

1. To compare the diagnostic performance of TM and DM
2. To compare the recall rates and biopsy rates for TM versus DM
3. To compare the rate of interval cancers for TM and DM
4. To examine the correlation between BIRADS imaging features and histologic and genetic features
5. To estimate and compare breast-cancer-specific mortality between the two study arms
6. To estimate and compare the prevalence of breast cancer subtypes and classify histologically malignant, pre-malignant and benign lesions using PAM 50.

Trial Design: Occurrence of advanced cancer at any time up to 7 years from randomization (time-to-event endpoint, comparison via log rank test) and powered at 85% for a 20% relative reduction in advanced cancer at 4.5 years from randomization

Biorepository: Biopsy tissue, blood, and buccal cell biospecimens

- **Accrual Goal: 69,297/128,905**
- **Current Enrollment: 20.4 AA; 5.9 Hispanic; 1.8, Asian, 0.3, AI/AN; NH/PI 0.2**



Non-treatment/IND Investigators

- **Current registration process places unnecessary burden on researchers that wish to exclusively participate on non-treatment and/or non-IND studies.**

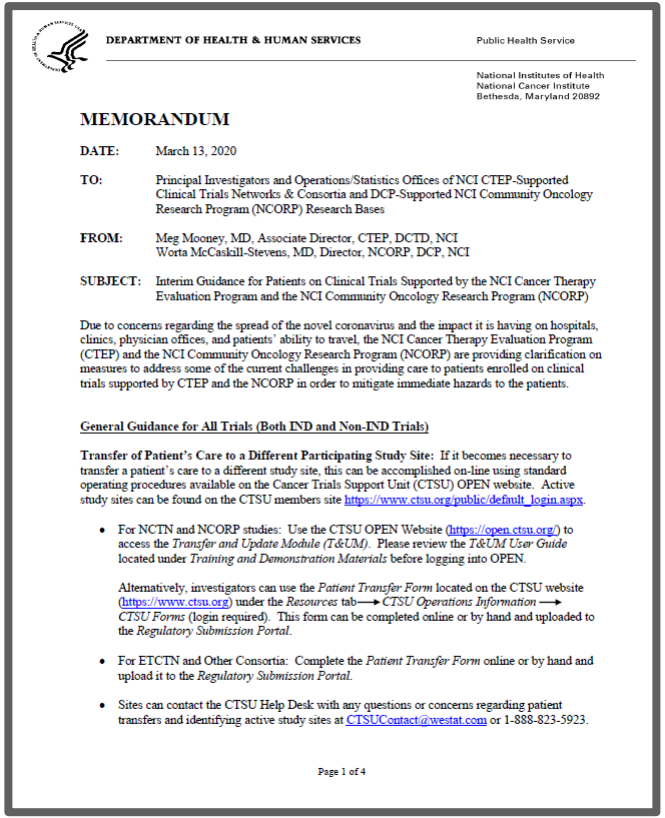
Documentation Required	IVR	NPIVR	NONIVR	AP	A	AB
FDA Form 1572 / International Investigator Statement (IIS)	✔	✔				
Financial Disclosure Form	✔	✔		✔		
NCI Biosketch (education, training, employment, license, and certification; includes GCP training)	✔	✔	✔	✔		
Agent Shipment Form (if applicable)	✔					
CV (optional)	✔	✔	✔	✔		

IVR = Investigator; NPIVR = Non-physician Investigators; NONIVR = Non-treatment/Non-IND Investigator; AP = Associate Plus; A = Associate; AB = Associate Basic

NCI Community Oncology Research Program (NCORP)

Challenges

COVID-19: Past, Current & Future Impact



DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

MEMORANDUM

DATE: March 13, 2020

TO: Principal Investigators and Operations/Statistics Offices of NCI CTEP-Supported Clinical Trials Networks & Consortia and DCP-Supported NCI Community Oncology Research Program (NCORP) Research Bases

FROM: Meg Mooney, MD, Associate Director, CTEP, DCTD, NCI
Worta McCaskill-Stevens, MD, Director, NCORP, DCP, NCI

SUBJECT: Interim Guidance for Patients on Clinical Trials Supported by the NCI Cancer Therapy Evaluation Program and the NCI Community Oncology Research Program (NCORP)

Due to concerns regarding the spread of the novel coronavirus and the impact it is having on hospitals, clinics, physician offices, and patients' ability to travel, the NCI Cancer Therapy Evaluation Program (CTEP) and the NCI Community Oncology Research Program (NCORP) are providing clarification on measures to address some of the current challenges in providing care to patients enrolled on clinical trials supported by CTEP and the NCORP in order to mitigate immediate hazards to the patients.

General Guidance for All Trials (Both IND and Non-IND Trials)

Transfer of Patient's Care to a Different Participating Study Site: If it becomes necessary to transfer a patient's care to a different study site, this can be accomplished on-line using standard operating procedures available on the Cancer Trials Support Unit (CTSU) OPEN website. Active study sites can be found on the CTSU members site https://www.ctsu.org/public/default_login.aspx.

- For NCTN and NCORP studies: Use the CTSU OPEN Website (https://open.ctsu.org/) to access the *Transfer and Update Module (T&UM)*. Please review the *T&UM User Guide* located under *Training and Demonstration Materials* before logging into OPEN.

  Alternatively, investigators can use the *Patient Transfer Form* located on the CTSU website (https://www.ctsu.org) under the *Resources* tab⟶*CTSU Operations Information*⟶*CTSU Forms* (login required). This form can be completed online or by hand and uploaded to the *Regulatory Submission Portal*.

- For ETCTN and Other Consortia: Complete the *Patient Transfer Form* online or by hand and upload it to the *Regulatory Submission Portal*.

- Sites can contact the CTSU Help Desk with any questions or concerns regarding patient transfers and identifying active study sites at CTSUContact@westat.com or 1-888-823-5923.

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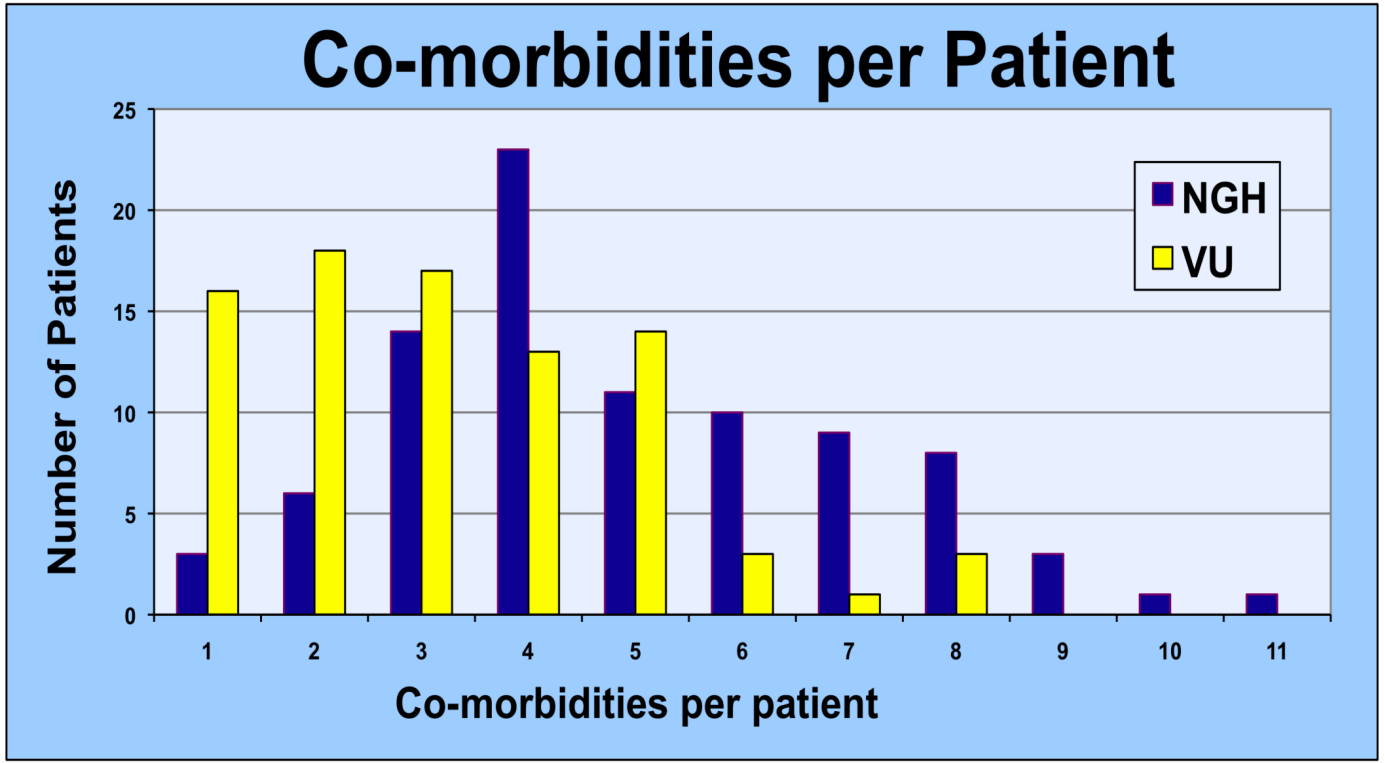
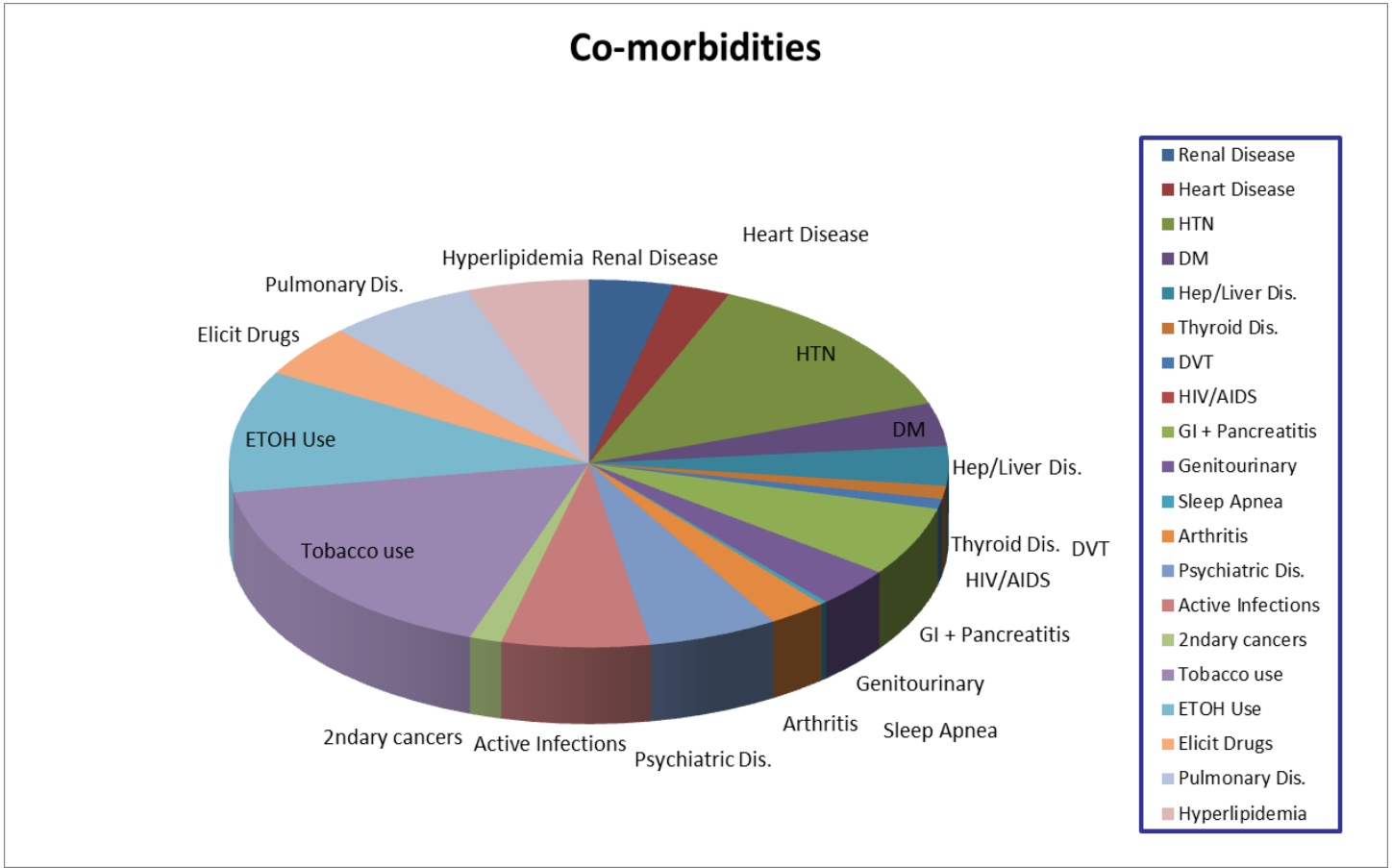
- **Are there specific trials more affected than others?**
- **Are there specific populations more affected others?**
- **Are there specific institutions more affected than others?**

Patients at the Nashville General Hospital
Meharry Minority CCOP/Vanderbilt



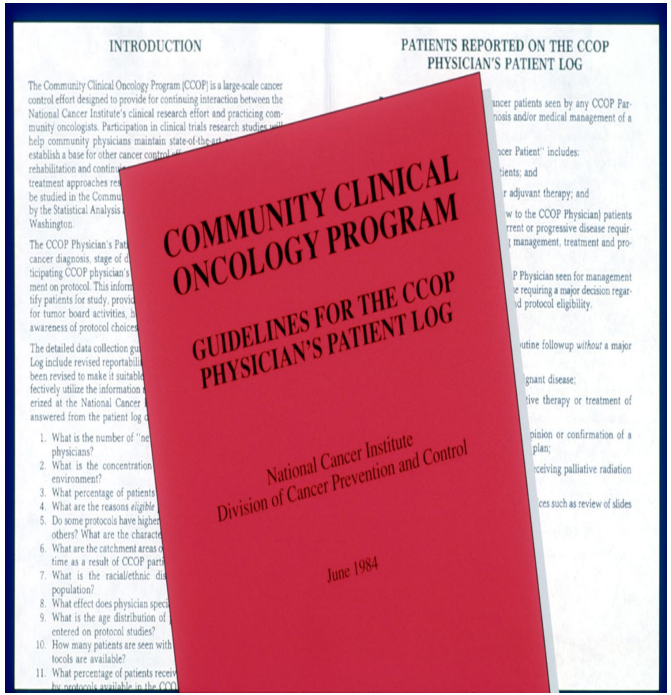
Patients at the Nashville General Hospital



Among the most important factors are social determinants of health, which are defined by the NCI as the conditions in which people are born, grow, live, work, and age, including the health system.

Division of Cancer Control & Population Sciences, National Cancer Institute, NIH. https://cancercontrol.cancer.gov/

Expanded Data Collection to Characterize Trial Participants



NCORP Clinical Trial Screening Adult CRF: DCP-001

OPEN PROTOCOL ENROLLMENT

Please Note: The following four questions pertain specifically to DCP-001

1. **Has informed consent been signed** *(select only one)*:
   ☐ Yes *(Answer 1a.)* ☐ No *(If NO, click Continue three times: DO NOT answer additional questions)*
   1 a. **If yes, was consent obtained in** *(select only one)*:
   ☐ Writing *(Answer 1 b.)* ☐ Verbally by phone *(Answer 1 b.)*
   1 b. **Was patient previously enrolled** *(select only one)*:
   ☐ Yes *(Answer 1 c.)* ☐ No *(Skip to question 2.)*
   1 c. **If yes, provide previous Patient ID #(s):** *Specify (Alpha-numeric Character Limited Text)*

OPEN DEMOGRAPHICS

2. **Ethnicity** *(select only one)*: ☐ Hispanic or Latino ☐ Not-Hispanic/Latino ☐ Not Reported ☐ Unknown
3. **Gender** *(select only one)*: ☐ Male ☐ Female ☐ Unknown
4. **Race** *(select all that apply)*: ☐ American Indian or Alaska Native ☐ Native Hawaiian or Other Pacific Islander ☐ Asian ☐ Black or African American ☐ White ☐ Not Reported ☐ Unknown

ADDITIONAL DEMOGRAPHICS

5. **Screening completion date** *(ex. MM/DD/YYYY)*: *Specify (Numeric Character Limited Text and/or Calendar Field)*
   (Only respond if patient is being screened for a DCP Clinical Trial (Cancer Control/Prevention/CCDR)
6. **Is the patient enrolled on a treatment clinical trial** *(select only one)*: ☐ Yes *(Answer 6a.)* ☐ No *(Answer 7)*
   6 a. **If the patient is enrolled on a treatment clinical trial, indicate the sponsor** *(select only one)*:
   ☐ NCI ☐ Pharma ☐ Other Sponsor

Please Note: If the patient is less than 18 yrs. of age, complete questions 10-18 with primary caregiver's status

7. **Age** (ex 43): *Specify (Numeric, Character Limited Text)*
   7 a. **If patient is an infant, indicate whether age is in days, weeks or months** *(select only one)*:
   ☐ Days ☐ Weeks ☐ Months
8. **Foreign Born** *(select only one)*: ☐ Yes ☐ No ☐ Not Reported ☐ Prefer not to Answer
9. **Geographic Ethnic Group** *(Other than Hispanic or Latino)* *(select only one)*:
   (If patient selected Hispanic or Latino in question 2 (Ethnicity), do not answer and skip to question 10)
   Asian: ☐ Central Asian ☐ Northeastern Asian ☐ Southern Asian ☐ Southeastern Asian ☐ Western Asian
   African Descent: ☐ African Descent/Caribbean ☐ African Descent/Sub-Saharan ☐ African descent/Other
   European: ☐ Eastern European ☐ Northern European ☐ Southeastern European ☐ Western European
   ☐ Unknown/Don't Know
10. **Primary language spoken at home** *(select only one)*: ☐ English ☐ Spanish ☐ French ☐ Chinese ☐ Filipino ☐ Vietnamese ☐ Arabic ☐ Korean ☐ Other
11. **How often does the patient have someone help when reading hospital materials** *(select only one)*:
    ☐ Always ☐ Often ☐ Sometimes ☐ Occasionally ☐ Never
12. **Marital Status** *(select only one)*: ☐ Married ☐ Never Married ☐ Separated ☐ Widowed ☐ Divorced ☐ Domestic Partnership
13. **Rural** *(select only one)*: ☐ Yes, defined by provider shortages ☐ Yes, lack of proximity to Cancer practice/center ☐ No
14. **Highest Level of Education** *(If patient/caregiver refuses, skip to question 15)* *(select only one)*: ☐ No formal education ☐ Grade school ☐ Not high school graduate ☐ High school graduate (including equivalency) ☐ Graduate or professional degree ☐ Some college or associate degree ☐ Bachelor's degree ☐ Master's degree ☐ Doctoral degree or professional degree
15. **Employment Status** *(select only one)*: ☐ Employed 32 hrs or more per week ☐ Employed less than 32 hrs per week ☐ Full-time student ☐ Part-time student ☐ Homemaker ☐ Retired ☐ Unemployed ☐ Only temporarily laid off, sick leave or maternity leave ☐ On medical leave ☐ Disabled ☐ Unknown

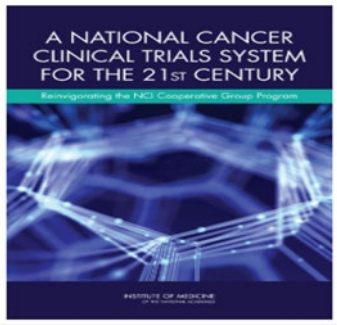
Use of a Clinical Trial Screening Tool to Address Cancer Health Disparities in (NCORP)

Of the 19,373 individuals invited to participate in an NCORP/CTEP trial within NCORP

16,095 (83%) provided informed consent

11,902 (74%) enrolled onto a clinical trial

Not-enrolled: 50% were ineligible; 47% were eligible but declined



"Without adequate rates of participation by patients and physicians, it is unlikely that important research questions with the potential to improve patient outcomes will be answered efficiently and effectively"

NCORP 2020: Cancer Prevention & Primary Care

- **Changes in NCORP Institutions:**
  - ❖ **Community Sites: 10 integrated health systems, 6 non-integrated health systems, and 16 hospital practices,**
  - ❖ **Minority/Underserved Community Sites:1 safety net hospital,1 health system, 3 academic/safety net, and 9 academic**
  - **9 Veterans Administration Hospitals**
- **Increased complexity of trials**
- **Increased co-existing comorbidities, different restricted referral patterns, closed systems**

THE GREAT MIGRATION

THE GREAT RESIGNATION!!!

NCORP Trial Enrollments by NPIVRs (APPs)*

**NCI DCP/DCCPS Guideline permitting APPs to enroll participants to NCORP trials/studies released 10/14/20*

1,007 NPIVR's listed in NCORP-SYS as members of NCORP's (as of 4/1/22)

- 948 are fully active
- 55 are awaiting rostering to a NCORP Research Base
- 4 pending approval

	8/1/19 – 7/31/20	8/1/20 – 7/31/21	8/1/21 – 2/28/22**
NCORP Clinical Trials	0	458	342 *(annualized = 586)*
NCORP CCDR Studies	0	24	88 *(annualized = 151)*
Total	0	482	430 *(annualized = 737)*

** Reflects 7-months

Overall Challenges

- **Co-morbidities**
  - **ASCO- NCI, Kim, et al., Clin Cancer Res 2021 May 1;27(9):2394-2399.**
- **Culture of some populations and clinical disciplines**
- **Cost to the patients and practices**
- **Staffing**

❖**New NCI Advanced Practice Providers Policy**

NCORP: Cancer Disparities Strategies

Early Onset Malignancy Initiative: Eligibility- Newly Diagnosed Patients

Cancer Sites	Age Cut Offs
Breast	≤45
Colon	≤55
Liver	≤55
Multiple Myeloma	≤50
Prostate	≤55
Renal*	≤50

Tumor and nl tissue sample: early dx pts
Molecular characterizations
Host immune status w immunophenotype

A collaboration between the Division of Cancer Prevention (DCP), Center for Cancer Genomics (CCG), and Center for Research Strategy (CRS)

Populations:
African-American, Caucasian, Hispanic, Native American
***Renal in Native Americans Only**

Focus on Health Disparities: Which Pandemic?

…The COVID-19 pandemic has shone a bright and deeply distressing light on just how much health inequity persists in our society**. We need to look at this unflinchingly, and embrace that challenge, enlisting the vision of the talent all around us**." Francis Collins, NIH, June 2020

"***During these unprecedented times, I do take comfort in knowing that our mission includes and benefits everyone, regardless of race, socio-economic status, education, geographic location or access to care. The events taking place today only strengthen our resolve to help eliminate these injustices."*** Ned Sharpless, NCI, June 2020

Health equity is the aspirational goal of optimal health for all.

.... **U.S. Department of Health and Human Services The Secretary's Advisory Committee on National Health Promotion and Disease Prevention Objectives for 2020. Healthy People 2020;2008.**

NCORP Disparities-Focused Portfolio

- **S1417CD is the first national prospective cohort study to measure the financial impact of cancer diagnosis and treatment on patients (and caregivers)**
- **To estimate the cumulative incidence of self-reported major financial hardship (MFH) at 12 months in patients age ≥ 18 within 120 days of mCRC diagnosis on systemic chemo or biologic tx.**
- **One of more of the following:**
  - **New debt accumulation**
  - **Selling/refinancing home**
  - **≥ 20% income decline**
  - **Borrowing money/Loans to pay for cancer treatment**

NCORP Disparities-Focused Portfolio

S1417CD

N=368 eligible patients (73% alive at end of 12 mo)

Median age: 60.2 (21.2, 89.3); Gender: Male (62%)

Race: White (78%); Black (13%); Asian (4%)

Marital status: Married (59%)

Insurance: Private (46%); Medicare (39%); Medicaid (12%); Uninsured (2%)

Annual household income: ≤ $50K (58%)

Education: ≤ high school graduate (40%)

Employment (pre-diagnosis): Employed (62%); Retired (26%); Disability (7%)

NCORP Disparities-Focused Portfolio

- **S1417CD Conclusions:**
- **Patients are willing to participate in research that aims to address their financial concerns.**

- **MFH accumulates over time. Nearly 75% of pts experienced MFH at 12 mo despite access to health insurance. Lower income and assets increased risk for MFH.**

- **Clinical and policy interventions are needed to protect cancer patients from financial devastation during and after treatment**

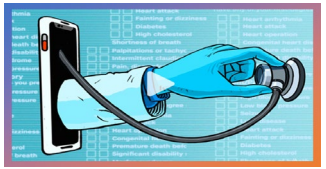
Disparities Research Approaches to Move toward Equity:

- **Clinical Trials: Integration/Partnerships**
  - ❖ Pooling and sub-analyses of data from completed studies or DCP-001
  - ❖ Enrich data to analyze sub-groups in new studies
  - ❖ Add disparities research questions to existing concepts
  - ❖ Initiatives to engage primary care physicians
  - ❖ Convene Research Base statisticians to explore trial designs

Considerations?

- **Implementation of Medicaid Coverage**

  New Law Requires Medicaid Coverage of Clinical Trial Participation. Effective Jan. 1, 2022, Clinical Treatment Act expands clinical trial access to more than 41.6 million Medicaid beneficiaries



NCI CTAC Strategic Planning Working Group – Nov 2020

Re-assess strategic vision for clinical trials system for 2030 and beyond

Review and address necessary clinical trials infrastructure

Developed
15 recommendations &
3 operational initiatives

Themes:

Trial Complexity and Cost

Decentralized Trial Activities

- ❑ Local/Remote Conduct of Study Procedures
- ❑ Telehealth Use in Clinical Trials

Promoting Accrual and Access

- ❑ Broaden Eligibility Criteria
- ❑ Conduct Trials to Support Minority & Underserved Pt Needs

New Data Collection Approaches

- ❑ Limit Data Elements Collected
- ❑ Using EHRs to Support Clinical Trials

PRO Data for Clinical Trials

Operational Burden

Statistical Issues

Workforce Outreach and Training

In Conclusion:

- **Community-Based NCI Clinical Trials Network supports unique research studies that complement treatment**
- **Community-Based NCI Trials Network supports trials that are moving toward precision medicine**
- **Experiences from community investigators and practices inform all components of trial design and the conduct of those trials ----necessary before influencing policy**
- **Cancer care is primarily in the communities in which individuals live, community networks are at the helm as contributors of identifying and reducing cancer health disparities**

NCI NCORP Team

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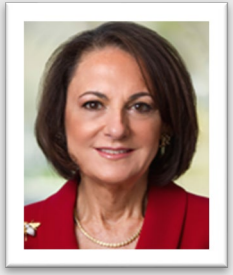

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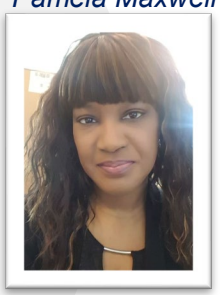

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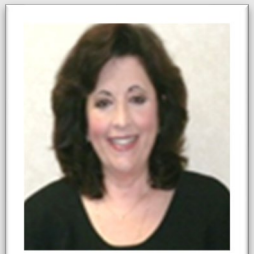

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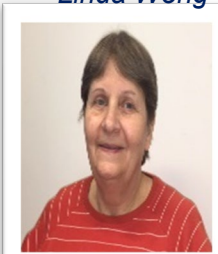

Questions/Comments?