March 2022

CP-CTNet NEWSLETTER

Cancer Prevention Clinical Trials Network

We all wondered if winter would ever come to an end and now spring is finally here! Join us in finally packing away our mittens, hats, scarves, and boots until next winter (or next week for those of us in the Midwest). New crocuses and daffodils will soon be pushing up from the soil and reaching for the sunlight. Have you seen any flowers yet? We are cautiously optimistic that the world will soon return to a "new normal" and we truly are counting the days until we can collaborate in person again! And of course, we are all looking forward to the network springing ahead with exciting new protocols and new advancements in our cancer prevention mission.

FUN FACTS

The first day of spring is called the vernal equinox. The term vernal is Latin for "spring" and equinox means "equal night."

The first spring flowers are typically lilacs, irises, lilies, tulips, and daffodils.

Spring fever is a real syndrome which includes symptoms of restlessness and daydreaming. When the temperature rises during the warm spell after a long winter, our blood vessels dilate so blood can be carried to the body surface where heat can be expelled quickly. People experience an energetic feeling when this happens.

"Spring work is going on with joyful enthusiasm." -John Muir

IN THIS ISSUE

DMACC Updates

DATA MANAGEMENT AND REPORTING UNIT

Sue Siminski, MS, MBA – Unit Director; DMACC sub-PI
Kayla Denson, PhD, MBA – Unit Co-Manager
Kelly Dunn, MPH, CCRP – Unit Co-Manager
Alex Krolikowski, MS – Training Specialist

SVAR Process

During this quarter, DMACC continued to work with LAOs to develop System Variable Attribute Reports (SVARs) as per the procedure outlined in **SOP 02-03** *Electronic Case Report Form Development*. DMACC looks forward to assessing the impact of the updated SVAR process once it has been completed in its entirety with one or more SVARs. In addition, DMACC plans to slightly adjust the SVAR process to incorporate a virtual meeting between DMACC and the LAO study team after the receipt of DCP's comments on the first version of the protocol. The goal of these meetings will be to foster close communication between DMACC and the LAOs about protocol-specific eCRFs and any associated nuances (e.g., dose modifications, tissue histology, repeating procedures, etc.).

DMACC is working with the LAOs to create SVARs for nine studies in development:

- UMI21-05-01 (Obeticholic Acid-Barrett's Esophagus)
- INT21-05-01 (Tri-Ad5-Colon)
- UWI20-04-01 (RG1-VLP)
- UWI21-06-01 (GCC Agonists-Duodenum)
- UAZ21-06-01 (BSSE-Lung)
- UAZ21-07-01 (Metformin-Oral Cancer)
- MDA21-06-01 (Nous-209-Lynch Syndrome)
- NWU21-08-01 (Iloprost-Lung)
- UWI20-00-01 (STEMVAC-Breast)

There are two studies in the DCP/PIO eCRF review process, including:

- MDA20-01-01 (Obeticholic Acid-FAP)
- MDA20-02-01 (Metformin-Breast/TEAM)

Study Builds in Rave

Work is ongoing on the study builds for UWI20-00-01 (STEMVAC-Breast), MDA20-01-01 (Obeticholic Acid-FAP), MDA20-02-01 (Metformin-Breast/TEAM), and MDA21-06-01 (Nous-209-Lynch Syndrome). The NWU20-04-01 (Metformin-Lung) study build was pushed to production on February 25, 2022.

COVID-19 eCRFs

CP-CTNet COVID-19 eCRFs were updated to include additional vaccination and booster information. These eCRFs were added to existing studies this February and all new studies will include these eCRFs in Rave.

Pre-Screening and Screening eCRFs

CP-CTNet Pre-screening and Screening eCRFs were updated to capture information about informed consent during pre-screening, instead of screening. These updated eCRFs were added to existing studies throughout February and all new studies will include these eCRFs in Rave.

Protocol Deviations

CP-CTNet Protocol Deviation Notification eCRFs were added to existing studies during February as well. All new studies will include these eCRFs in Rave. Additional documentation, educational materials, and training sessions will be available to support LAOs, AOs, and DCP with the new protocol deviation reporting process.

Virtual Specimen Repository

The Virtual Specimen Repository Group met on January 18, 2022 and March 21, 2022.

DMACC met with UAZ, NWU, UWI, and MDA to conduct initial Laboratory Data Management System (LDMS) implementation calls, where study-defined preloads were outlined. UAZ and NWU started utilizing their LDMS database to log specimen inventory for their ongoing studies. Their data are funneling to DMACC in real time. Along with this implementation, the DMACC LDMS training team conducted a detailed LDMS introductory training for NWU on January 25, 2022. On the March call, several example visualizations were presented to the group.

Meetings

DMACC, UAZ, DCP, and MRI Global met on February 9, 2022, to discuss the workflow for randomization, treatment assignments, and study agent shipping for UAZ's two blinded studies, UAZ21-06-01 and UAZ21-07-01. The teams plan to meet again on March 30, 2022 for further discussion.

The third Cross-Network Collaboration (CNC) meeting was held on February 28, 2022. DCP, LAOs, and DMACC discussed several topics including the new CP-CTNet project management workflow, eligibility checklist review process, LAO oversight of AOs, and I-SCORE Think Tank agenda items. The next CNC meeting is scheduled for May 2, 2022.

Documentation

The DMACC Documentation Team added and updated the following documentation on the *Program Resources* page:

- **SOP 01-03** *Site Activation*: Rewritten to clarify the site activation process.
- *CP-CTNet Site Activation Checklist for LAOs*: Rewritten to align with SOP 01-03.
- **SOP 01-01** *Regulatory Documents*: Updated the list of essential site regulatory documents. Added clarification about Form FDA 1572, the Delegation of Tasks Logs (DTLs), and the Central Institutional Review Board (CIRB)- or Independent Ethics Committee (IEC)-approved Informed Consent Document (ICD).
- **REFGD05** *CP-CTNet Genomic Data Sharing Guidance*: Added clarification about who is responsible for completing and signing the Genomic Data Sharing Plan (GDSP).
- **REFGD08** *CP-CTNet Public Website/DMACC Portal Gateway Overview and User Registration Guide*: Updated to reflect the most recent release of the CP-CTNet DMACC public website and Portal Gateway, including the process for requesting new and updated user access.
- **REFGD11** *LAO Resource Submission Procedures*: A new document that details the procedures that LAOs follow when requesting the addition, update, or removal of resources on the *LAO Resources* page on the *CP-CTNet DMACC public website*.

The DMACC Auditing Unit is working closely with DCP to update two SOPs in response to feedback received during the first two audits, including **SOP 01-01** *Regulatory Documents* and **SOP 03-03** *LAO Oversight of AOs*.

DMACC also continued to work with the DCP Nurse Consultants this quarter to update the *AQuIP Toolkit*.

Educational Content

The DMACC Education and Training team offered 12 training sessions for LAOs and AOs during January, February, and March of this year. Training session topics included: *Completing the Recruitment Journal in Rave*, *Rave Reports for Quality Assurance*, and *Determining Treatment Assignments for CP-CTNet*.

LAOs, AOs, and DCP can access registration links for upcoming training sessions via the *Training Registration* page on the Portal Gateway. The Education and Training team continuously develops regular training sessions for LAOs, AOs, and DCP on CP-CTNet procedures and systems. If you have ideas for new sessions or materials, please reach out to the Education and Training team at *Training_CP-CTNet@frontierscience.org*.

Project Management

DMACC implemented a commercial project management software tool to streamline our project tracking workflow. This tool allows DMACC to receive action item and project requests from CP-CTNet members and provide real-time updates throughout the request completion process. The status of each project or action item will be shared with CP-CTNet members at meetings and upon request via system-generated data visualizations from the time that the request is submitted until the request is completed.

CLINICAL TRIALS AUDITING UNIT

Julie Chang, MD – Unit Director
Holly Shaw, MS, CCRP – Unit Co-Manager
Barbara Wollmer, BSN, RN – Unit Co-Manager
Meredith Kissel, MPH – Clinical Trials Auditor

The Auditing Unit participated in the previously-mentioned CNC meeting on February 28. The LAO Coordinators and Investigators provided valuable insight and feedback regarding managing network activities within their own institution, as well as their AOs. We look forward to continued discussion on the topics of monitoring AOs/LAO oversight, as well as assisting the LAOs and DMACC Data Management and Reporting Unit in providing any resources that might be helpful for these activities.

To this end, the Auditing Unit is in the process of revising several SOPs to support auditing activities within the network. The Targeted Source Data Verification (TSDV) module in Rave is being configured for all studies (presently configured for UAZ20-01-02, NWU20-04-01, and NWU20-01-03). This module will be incorporated into all future study builds as well.

Another focus of the Auditing Unit is to revise the *Audit System* application that was released at the end of October 2021. We anticipate being able to offer training and demonstrations of the system shortly after the updates are implemented. Stay tuned!

ADMINISTRATIVE AND COORDINATING UNIT

KyungMann Kim, PhD – Unit Director; DMACC Principal Investigator
Kelly Miller, BS, CCRC – Unit Manager
Bridget Dermody, BS – Administrative Specialist

Planning for the 2022 I-SCORE Meeting has definitely been a team effort. Registration for the meeting opened on February 8. So far, 174 people have registered for the virtual meeting scheduled for March 31 through April 1, 2022 via WebEx. If you haven't done so already, please *register online* and be sure to share the meeting information with all of your collaborators. We want to set a record for attendance this year! Registration ends: March 30, 2022.

Please visit *https://events.cancer.gov/dcp/iscore* to view the updated agenda and speaker biographies. We look forward to virtually seeing everyone who plays a vital role in the success of CP-CTNet. We realize work commitments and clinic schedules may prevent attendees from listening in on all of the presentations for both days, but please join us whenever your availability allows. We hope you find the meeting engaging and inspiring. An electronic survey will be issued at the end of the meeting; please take a moment to complete it. Your feedback is valuable and important to the planning committee, especially if your suggestions can improve the overall experience of attendees.

Some slides may be accessible after the meeting, if speakers grant their approval for sharing. The planning team includes: Dean Brenner (UMI), Goli Samimi (NCI DCP), Eileen Dimond (NCI DCP), Mela Asefa (NCI DCP), Perquita Perry (NCI DCP), Bridget Dermody (DMACC), and Kelly Miller (DMACC). We would like to thank all the speakers, moderators, registrants, and, of course, IT support staff in advance. If you have questions, please contact us at: *Admin_CP-CTNet@frontierscience.org*.

WEBSITE AND PORTAL GATEWAY UPDATE

Bob Starkweather, MS – Deputy Director of Software Engineering
David Goss, MA – Software Engineering Business Analyst

DMACC is always working to keep *CP-CTNet-DMACC.org* updated with the latest information for CP-CTNet sites, network colleagues, collaborators, and the public. Since December, several new funding opportunities, news posts, and document resources have been added. We added a new page for *LAO resources*, updated the interactive CP-CTNet map to reflect the far-reaching collaborative effort of LAOs and AOs, and enhanced the *Trials* page to include active and DCP-approved trials.

We have also been making updates to the DMACC Portal Gateway. New access request features were made available to Portal Gateway users in February 2022. Users are now able to request access to additional resources or updates to their accounts directly from the Portal Gateway. Many links and resources have been updated as well.

As the CP-CTNet program grows, more data visualization options and reports will be added to the Portal Gateway to monitor study progress and key metrics. Users can expect to see the addition of file size and file type information for available resources on the public website and Portal Gateway in the coming months.

The Website Review Committee met monthly in 2022 on January 12, February 16, and March 16. The next meeting is scheduled for April 20, 2022.

Staff Spotlight

NEW STAFF

Amy Selegue, BA, BSN, MLS. Amy is the new Manager of Cancer Prevention Clinical Research at the University of Arizona Cancer Center (UACC) and is responsible for overall project management of prevention trials at UACC. Amy was previously employed at the UACC Clinical Trials Office as a Senior Program Coordinator, working closely with the National Clinical Trials Network (NCTN) program and overseeing Clinical Trials Reporting Program (CTRP) and *ClinicalTrials.gov* reporting requirements. She has bachelor's degrees in communication and nursing, and last year received her master's degree in legal studies with an emphasis in health law and policy from the University of Arizona College of Law. She is passionate about cancer research and is thrilled to be working with the UACC prevention group and CP-CTNet to help manage their many exciting collaborations.

Brian Cholewa, PhD. Dr. Cholewa is a Senior Toxicologist and Program Director for the DCP Chemopreventive Agent Development Research Group (CADRG) of the NCI. At CADRG, he oversees the CCS Associates regulatory contract following Dr. Dan Boring's retirement, and currently leads regulatory efforts for DCP in support of CP-CTNet. He also serves as the primary toxicologist for agent development in the PREVENT program. Dr. Cholewa completed his PhD in Molecular and Environmental Toxicology at the University of Wisconsin, Madison, followed by a Postdoctoral Fellowship at Vanderbilt University. Prior to joining NCI, Dr. Cholewa spent nearly four years at the FDA in the Division of Hematology Oncology Toxicology in the Office of Oncologic Diseases as a Pharmacology/Toxicology reviewer.

Lanni Aquila, BS, MS. Lanni recently transferred from the AIDS Clinical Trials Group (ACTG) Network to CP-CTNet as a DMACC Data Manager. Lanni is a born and raised Buffalonian. She earned her BS degree in Biology from Canisius College and her MS degree in Cancer Sciences from SUNY at Buffalo. She also previously worked at Roswell Park Comprehensive Cancer Center in Buffalo, where her research focused on using epigenetic modifiers to overcome chemotherapy resistance in ovarian cancer.

Shanker Gupta, PhD. Dr. Gupta (DCP CADRG) will oversee the MRI Global drug repository contract following Dr. Dan Boring's retirement.

Shehnaz K. Hussain, PhD, ScM. Dr. Hussain is a Professor in Public Health Sciences at the UC Davis School of Medicine and the Associate Director for Population Sciences at the UC Davis Comprehensive Cancer Center. Dr. Hussain earned an MS in Epidemiology from Johns Hopkins University and her PhD in Epidemiology from the University of Washington. She completed a postdoctoral fellowship in genetic epidemiology at the Karolinska Institute in Sweden, and a second fellowship in cancer prevention and control at UCLA. Dr. Hussain's research program stems from a long-standing interest in the etiology, prevention, and early detection of infection-associated cancers. She has over a decade of leadership experience in the design, implementation, conduct, analysis, and reporting of multi-center longitudinal cohort studies, case-control studies, and clinical trials. She has developed a particular interest in studying biomarkers that relate to, or modulate, the immune response including serum immune markers, intestinal microbiome, and immunogenic microbial components and metabolites. Dr. Hussain's current research program is largely focused on the disease continuum from non-alcoholic fatty liver disease (NAFLD) to hepatocellular carcinoma (HCC). Key components of this research program include racial/ethnic disparities, the interplay of diet, microbiome, and metabolome in HCC etiology, primary and secondary HCC prevention with statins, diet modification in NAFLD, and HCC early detection with imaging biomarkers. Additionally,

aligned with her long-standing interests in infectious causes of cancer, she is also actively conducting research on EBV- and HPV-associated cancer etiology and prevention, particularly in the setting of severe immunosuppression (chronic HIV infection and solid organ transplantation). Dr. Hussain serves on the CP-CTNet Steering Committee.

PROMOTIONS

Kayla Denson, PhD, MBA. Kayla is now Co-Manager of the Data Management and Reporting Unit. She has a BS degree in Biology from York College of Pennsylvania, an MBA in Management from Frostburg State University, and a PhD in Cell and Molecular Biology from SUNY at Buffalo. Kayla completed her PhD thesis work in a Cancer Genetics lab at Roswell Park Comprehensive Cancer Center and focused on cell signaling in mammary gland development and tumorigenesis. Kayla joined Frontier Science in 2017 and worked as a Protocol Data Manager and a Coordinating Data Manager for the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Network. Kayla joined CP-CTNet as a Senior Data Manager in 2020.

Kelly Dunn, MPH, CCRP. Kelly is the other Co-Manager of the Data Management and Reporting Unit and is responsible for the day-to-day operations of the unit, including coordinating SVAR development and review as well as management of clinical trials data. She has a BS degree in Psychology and an MPH degree in Community Health and Health Behavior. Prior to rejoining Frontier Science in November 2021, Kelly worked at Roswell Park Comprehensive Cancer Center as a Clinical Research Quality Assurance Coordinator. In her clinical trials career, she has also worked in regulatory, site coordinator, grants coordinator, and data management roles.

RETIREMENTS

Lynette Blacher, MLS. Lynette began her career at Frontier Science as a Data Manager for the International Breast Cancer Study Group (IBCSG) and within three years, she became Director of Data Management for that group. Lynette and the IBCSG team at Frontier Science collaborated with over 1500 centers and 40 collaborative groups to conduct clinical trials in breast cancer. Their research has included Phase Ib-III treatment, surgical, interventional, observational, and registrational trials for early and metastatic breast cancer. Many of these trials have also included quality of life and translational research components. Lynette also worked on trials studying rabies vaccines.

In 2019, Lynette became Project Lead for the Data Management and Reporting Unit for DMACC. In her role for the network, she oversaw the establishment of the Cancer Prevention Clinical Trials Network, working closely with the University of Wisconsin-Madison DMACC team and DCP. She was responsible for the establishment of DMACC, collaborating with multiple universities to provide clinical trial support for the efficient conduct of early-phase clinical trials, as well as the development of documentation and training for the project.

Over the years, Lynette was involved in several Frontier Science initiatives, including the SUNY at Buffalo Intern Program, grant proposal writing, and the development of monitoring procedures. She was also a member of the Federal Information Security Management Act (FISMA) Group and Compliance Committee, and coordinated the Cancer Projects Oversight Group.

Valerie Butler, RN, CCRP. A long, long time ago Valerie Butler began her nursing career in southern California. After many years in nursing (including medical, surgical, urgent care, and occupational health), she found her niche in clinical research working at the University of Arizona College of Medicine coordinating industry sponsored trials. In 2003, she was offered the position of Associate Director for Tucson Clinical Research, a free-standing, multi-specialty, dedicated research facility where she supervised the day-to-day clinical operations of their satellite facility. In 2005, she became Director of Clinical

Research managing the business operations of the company as well as overseeing the clinical operations of multiple employees. Valerie was recruited back to the University of Arizona to join the Early Phase Cancer Chemoprevention Consortium program as Site Coordinator in February of 2010 and has been delighted to work with Dr. Sherry Chow and the cancer prevention team ever since. On February 28, Valerie retired from the University of Arizona to pursue other interests and open a new chapter in her life. She is grateful for the opportunities afforded her by the University of Arizona and most especially, Dr. Chow.

*If your team has any staffing changes, please reach out to *Admin_CP-CTNet@frontierscience.org*. We appreciate it!

NWU LAO STAFF SPOTLIGHT

Dr. Seema Khan (NWU Principal Investigator) and Kelly Benante (NWU LAO Coordinator)

What sparked your interest, and how long have you been involved with clinical research?

Dr. Khan: Well, I'm basically a clinician. I did not have any exposure to research of any kind as a medical student. As a resident, my main exposure was to read the results of clinical research studies, so I had very little understanding of how research findings were generated. Then, I was exposed to a change in clinical practice driven by research. This was the conversion from mastectomy as the unquestioned treatment for all breast cancer patients, to the possibility of conserving the breast. I saw this play out in real time as a surgical oncology fellow. The findings of the trial were met with great skepticism by many surgeons, but I did read the paper by Fisher and although I didn't understand all of it, I was impressed by the fact that doctors were able to pose a question, and answer it, for the benefit of women diagnosed with breast cancer.

Also, as a fellow, I gained some real exposure to research and was heavily influenced by a close friend who was already established as junior faculty in the medical oncology program at Roswell Park. She was passionate about research and drew me into her projects and helped me realize that I too could approach a problem, propose a way to address it, persuade my colleagues that this was a worthwhile effort, and get an answer.

Kelly: I first became interested in clinical research during an undergraduate internship at a local cancer center. I worked with a really passionate group of women including research nurses and a cancer registry coordinator who showed me that research was a valuable component of clinical care and patient well-being.

I've also worked as a Clinical Research Coordinator for the AIDS Malignancy Consortium at the Ruth M. Rothstein CORE Center in Chicago and have been with the Northwestern Cancer Prevention Consortium as a Quality Assurance Monitor and Senior Project Administrator for over 5 years.

What is your role in the CP-CTNet Program?

Dr. Khan: I lead the Northwestern Cancer prevention clinical trials network.

Kelly: As the Senior Project Administrator for our program, I manage the administrative team for the Northwestern University LAO. I really enjoy this work because I'm able to do a little bit of everything throughout the lifespan of our trials, and I get to serve as a liaison between our group, NCI DCP, and the really interesting PIs and research teams at other sites.

What challenges/advantages do you see within the CP-CTNet Program?

Dr. Khan: **Challenges:** This is an early phase clinical trials network. Early phase trials are very important in the development of new strategies for both treatment and prevention. But because event rates are far less frequent in a high-risk population than recurrence in a cancer population, and most biomarkers are imperfect surrogates, the size of the trials that we can propose and complete within CP-CTNet is a real limiting factor. I believe that our success of conversion from early to later phase trials would be higher if our early phase trials were larger, and therefore more robust. But that would take bigger budgets.

Advantages: This is a hugely exciting space to be working in. It is the best job in the world for a clinician wanting to make a difference in cancer prevention. It allows us the opportunity to explore new ideas, to trans-germinate ideas, and to gain from the insights and experience of our colleagues at DCP. The fact that the early phase clinical trials program is now in its third funding cycle means that there is a critical mass of experience and abilities that have been gathered together under one big roof. In this environment, given the wide range of initiatives that are being pursued, from immunoprevention to alternative dosing to creative repurposing of agents proven to be safe in the noncancer setting, I expect that in the next decade we will see a surge of new preventive options for people at high risk for cancer.

Kelly: **Challenges:** As with any grant, we are limited by funding and timelines. Almost every investigator we work with wants a larger trial with more biomarkers. We have also found that study startup and recruitment take longer than anticipated, further stretching our limited resources including time and effort.

Advantages: I think the CP-CTNet program is especially appealing to and advantageous for mid- or early-career investigators. Every step of the way, there is a lot of support and feedback for investigators to develop their trials. This comes from the LAO PI and their administrative teams and directly from the assigned NCI DCP group. I don't know if this is a unique feature to our program, but I think it's an excellent way to set the stage for further cancer prevention research and collaborations.

What advice do you have for other members of CP-CTNet who share your job title and/or responsibilities?

Dr. Khan: My fellow LAO PIs are an amazingly talented and accomplished group. We talk fairly frequently and bring our individual perspectives to the discussion. We often see things similarly, but there is usually a slightly different angle (I call that stereotactic vision) that makes things clearer in terms of how we can better collaborate and help each other. We also discuss how best to use the resources that are allotted to us under this funding mechanism, and how to meet the expectations that come with the funding. We usually see some level of mismatch between those two sides of the equation, but by combining our talents to spot solutions, we manage to move forward, and enjoy the process!

Kelly: Ask questions and don't reinvent the wheel. Another major advantage to the network structure is that we can work together across LAOs, share best practices, and learn from each other's challenges. This also goes for working with our colleagues at NCI DCP and DMACC, who I've found to be very receptive to our feedback and responsive to our questions.

In terms of managing trials, I would also advise them to invest more time in accrual site selection. We've found that there are a lot of factors besides having a target population that make a successful site. As a result, we're spending more time looking at a potential site's relationship with the study PI, experience working with the NCI CIRB, ability to accrue diverse populations, clinical trials infrastructure, etc.

What challenges have you experienced within the CP-CTNet program and how have you overcome them?

Dr. Khan: The challenge is mainly related to the initiation of trials. It is very exciting to have a concept approved for development, but then the trial initiation process begins. With the switch from the contract mechanism to the UG1 grant mechanism, we expected that initiation time would shorten, but various other hurdles have replaced the contractual delays, and the overall start time is not appreciably different. This is a real difficulty since the study teams lose momentum and enthusiasm during a lengthy startup process. It also increases the cost of the trial and decreases productivity. I think we will overcome this problem as the new system settles into place, but it is a work in progress.

Kelly: I agree, study startup continues to be our greatest challenge. It's been difficult to navigate new systems for collecting regulatory documents, new databases, etc. Thanks to lots of communication, the process is becoming smoother with each new trial we open.

In addition, now that we have trials open, we are starting to face recruitment challenges. I am fortunate to manage a resourceful and dedicated team who works closely with our accrual sites to devise strategies for increasing accrual. In some cases, this means a protocol amendment, for others it's developing online recruitment materials, and sometimes it's a matter of supporting coordinators with more protocol training and opportunities to share best practices with one another.

Where did you go to college?

Dr. Khan: Nazareth College for Women in Hyderabad, Pakistan and Dow Medical College in Karachi, Pakistan.

Kelly: I went to Illinois Wesleyan University in Bloomington, IL for my BA degree in Biology. After undergrad, I spent 3 years in Malawi as a United States Peace Corps Volunteer. I earned my MPH from the University of Illinois at Chicago, where I focused on Community Health Sciences and Maternal and Child Health.

What are your hobbies/interests out of work?

Dr. Khan: I like to read, walk, and travel.

Kelly: I have a 3-year-old and an almost 2-year-old, so they occupy just about all of my time outside of work! I try to be outside as much as possible and enjoy traveling, baking, and learning about new places.

What is the best advice you've been given?

Dr. Khan: Tell it like it is, but be gentle about it.

Kelly: Be present. It's easy to become distracted with many competing deadlines and priorities, but it's important to always focus on the task at hand and give it the full attention it deserves.

Featured Articles

ENGAGING OLDER ADULTS IN CLINICAL RESEARCH

By: Diane St. Germain, RN, MS – Program Director of the Community Oncology & Prevention Trials Research Group (DCP NCI)

Background

Cancer is a disease of older adults, though participation in clinical trials does not reflect this. Over 60% of cancers occur in older adults but only 33% of older adults participate in clinical trials[1]. The barriers contributing to low clinical trial accrual are well documented in the literature and include patient, physician, and system barriers. Table 2 lists those specifically impacting older adults [2-4]. Despite these known barriers, there is a paucity of evidence-based strategies to overcome them. Sedrak's[4] systematic review of barriers and interventions identified only one intervention study which was an educational intervention geared toward physicians that when compared to receipt of standard information, did not demonstrate an increase in accrual[5]. To understand research personnel's perspective on strategies that would increase accrual of older adults to clinical trials, Freedman et al[6] conducted a survey in Alliance for Clinical Trials in Oncology. The top four strategies included: 1) develop more dedicated trials for older adults 2) minimize exclusion criteria focused on comorbidities, 3) consider different strategies by age (> 65 versus > 70 years of age), and 4) require that trials have an expansion cohort of older adults.

Physicians remain one of the key factors to a patient's decision to enroll in a clinical trial. Age bias exists and physicians tend to err on the side of less aggressive treatment. They are often challenged when determining whether an older patient is "fit" to receive standard therapy as part of routine care or to enroll onto a trial. Often this determination is intuitive, relying on the clinician's non-evidence-based assumptions. In routine care, this can lead to either under- or over-treatment of older patients. In clinical research, this can lead to reduced opportunities for older adult participation in clinical trials.

Geriatric Assessment (GA) may play a role in evaluating fitness for trial participation; however, there is no consensus in the research community about how best to implement GA in clinical trials. As a result, current use of GA in NCI-funded trials is varied. Additionally, despite excitement in the medical community about the role of GA for older adult patients as a part of routine care, uptake has been low. This is likely in part due to limited evidence from clinical trials identifying specific treatment situations in which GA should be used and variability in studies regarding which components of geriatric assessments are needed. For instance, the National Comprehensive Cancer Network (NCCN) provides general guidelines for Older Adult Oncology, including reasons to use GA, but GA is not typically integrated in the disease specific NCCN Guidelines.

There has been a call to design clinical trials specifically for older adults though it is not clear when it is appropriate to include age specific designs. But the lack of participation of older adults in any clinical trial persists, resulting in data that is not applicable to the heterogeneity of this population, leaving clinicians without clear information regarding how to treat older adults, particularly those with comorbidities and frailty.

Efforts to Date

In addition to several meetings that have brought increased attention to older adults and cancer[7-9], there has been several key impactful efforts. In 2017 the American Society of Clinical Oncology (ASCO), Friends of Cancer Research, and NCI broadened eligibility criteria to increase representation on clinical trials[10] which is contributing to efforts to modify eligibility and increase enrollment of older adults. In 2021, a second round of recommendations were published focused on performance status and functionality[11]. ASCO has also published recommendations regarding the gaps in treating older adults with cancer[12] and guidelines regarding integration of GA into oncology clinical care[13].

NCI has seen efforts to design age specific trials in patients with leukemia, lymphoma, and lung cancer. For example, in the last several years the NCI Community Oncology Research Program (NCORP) funded 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" (NCT03633331). In addition, NCORP has formed a Disparities Integration Emphasis Group to increase disparities related research in the network and enhance accrual of underrepresented populations to NCI sponsored clinical trials.

The NIH has expanded the Inclusion of Children Policy to now include all age groups, including older adults. Researchers applying for NIH funding must now justify if certain age groups are excluded from their research and once funded, annually report participation by age in addition to race and ethnicity[14].

In 2020 the FDA released draft guidance for the pharmaceutical industry regarding the inclusion of older adults in trials. The guidance document specifically states, "Sponsors should prospectively consider information that should be collected for older adults that will be clinically informative and will provide an understanding of clinical outcomes in older adults. For example, in addition to collection of age and performance status, elements from geriatric assessment tools, such as functional status and cognitive function, or frailty measures and a comprehensive assessment of comorbidities should be considered during trial design"[15].

1. Lastly, in 2021 NCI conducted a meeting to address accrual of older adults to NCI supported trials. The meeting, sponsored by Cancer Moonshot℠, was held virtually for two days, and gathered experts from various related fields, including oncologists, nurse scientists, advance practice nurses, gerontologists, statisticians, clinical trialists, and patient advocates. The goals of the workshop were to:
2. Engage physicians to address barriers to enrollment of older adults to clinical trials.
3. Engage patients to enhance our understanding of the barriers to enrollment of older adults to clinical trials and discuss ways to overcome them.
4. Develop consensus regarding the research priorities for the use of geriatric assessment to enhance precision enrollment and treatment of older adult patients on NCI-sponsored clinical trials
5. Build consensus around the methods to integrate CGA in future trials, with the long-term objective of having these trial results provide evidence to use CGA to inform decision-making for cancer treatments in older adults, both in routine care and in future trials.

Three working groups were formed to address study design, needed infrastructure to increase accrual of older adults, and stakeholders' wishes (see Table 1). The work of these groups is ongoing and will be reported in the literature in the future.

Table 1. Cancer Moonshot℠ Accrual Meeting Working Groups

Study Design	Infrastructure	Stakeholders
Consider trial designs that promote enrollment of older adults (e.g., cohort designs, extended cohorts, parallel cohorts, less fit older adults), stratification by vulnerability/frailty	Development of a roadmap from conceptualization of research question to dissemination of results • Necessary resources • Consideration of the older adult through the process	Identify modifiable accrual barriers from each stakeholder perspective
Use of geriatric assessment in clinical trials	Infrastructure needs to perform comprehensive geriatric assessment	Identify interventions that can address the identified barriers to enhance accrual of older adults to NCI sponsored clinical trials
	Use of technology/telehealth to engage older adults in clinical research	Address clinician biases toward enrolling older adults to clinical trials
		Identify patient needs and concerns and develop interventions to address

Summary

In summary, there is a significant need to identify strategies to increase accrual of older adults to clinical trials. There are several opportunities to develop strategies within the NCI Clinical Trials Program including trial design, providing the infrastructure needed to support accrual, and using a screening tool to identify trial and site-specific barriers. There is a large investigator community passionate about the care of older adults with cancer and the importance of including older adults in clinical research so they may have access to state of the art care and trial results can be applicable to patients of all ages.

Barriers to Clinical Trial Enrollment of Older Adults[2-4]

- Comorbidities restricting trial eligibility
- Limited trials designed explicitly for older adults
- Inclusion of treatments that may be too toxic for older adults
- Clinician bias
- Decreased functionality
- Concern that older adults would have decreased capacity to process information and comply with assigned treatment
- Psychosocial issues such as transportation, financial burden, lack of social support, time commitment
- Patient concern about efficacy/toxicity; concerned they are too old
- The extra time and resources needed to enroll older adults

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14. *https://grants.nih.gov/policy/inclusion/lifespan.htm*

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About the Author

Diane St. Germain is a Nurse Consultant and Program Director in the Community Oncology and Prevention Trials Research Group in the NCI Division of Cancer Prevention. In this position, she manages a grant portfolio focused on symptom management and palliative care; serves as a Program Director in the NCI Community Oncology Research Program (NCORP), overseeing oncology practices conducting clinical research in community settings; and, is the Program Director for the Alliance NCORP Research Base. Areas of interest include patient reported outcomes, cancer related cognitive impairment, use of non-pharmacologic approaches to pain and symptom management, health care disparities, and clinical trial accrual particularly of underrepresented populations.

She is the NCI representative to the Symptom Management and Quality of Life Steering Committee, co-chair of the NCORP Disparities Integration Working Group, scientific lead for the Cancer Moonshot℠ project, "Translations and Validation of Patient Reported Outcome Measures: Addressing and Accrual Barrier to Minority and Underserved Participation in Symptom Clinical Trials", and co-creator of the NCORP Clinical Trials Screening Tool.

In addition, she is a member of the NCI Health Equity Council Communications and Outreach Working Group and the Trans-NCI Cancer and Aging Coordinating Committee.

DCP COVID-19 COMMITTEE

The COVID-19 pandemic caused profound operational challenges for both our medical and research communities. Quarantine mandates, clinic and lab closures, abrupt transition to telework, staff and patient illness, and limited drug availability required the medical and research communities to quickly adopt novel and more flexible approaches to health care delivery and clinical trial conduct.

Similarly, the pandemic required swift action from the DCP Early Phase Clinical Trials Program. DCP staff convened several emergency meetings to develop and implement clinical trial contingency plans to ensure safety and continuity of care for its clinical trial participants in compliance with FDA and NCI CIRB COVID emergency guidance.

Although such unforeseen circumstances presented many challenges, a unique opportunity to reevaluate the current clinical trial model became clear. In fact, some of the emergency practice measures so efficiently and effectively streamlined clinical trial operations that DCP formed the Clinical Trials Simplification Committee (CTSC).

The goals of the committee were to identify challenges related to early phase cancer prevention clinical trial efficiency during the pandemic, to assess the effectiveness of clinical trial safeguards, and to propose innovative approaches to minimize clinical trial challenges moving beyond the pandemic. The deliverables included a report to the DCP Cancer Prevention Clinical Trials Network (CP-CTNet) Steering Committee, and the dissemination of the findings. A manuscript summarizing the recommendations has been accepted for publication in Cancer Prevention Research.

The Committee established three working groups with a focus on the following areas: 1) trial design and implementation; 2) participant safety and convenience; and, 3) trial oversight and regulatory issues. The specific recommendations of the Committee are listed in Table 2.

While the COVID-19 pandemic has illuminated the need to move away from complex and cumbersome clinical trial processes and develop innovative participant-centric trial designs, studies may be needed to evaluate the effectiveness of these innovations.

We want to take this opportunity to thank the Committee members* for their dedication and hard work. We also wish to acknowledge all DCP Early Phase Clinical Trials Program staff (DCP, contractors, and grantees) for their heroic efforts to keep our trial participants safe and our studies moving forward during this unprecedented crisis.

***Committee members include:** Bridget Dermody, Bruce F. Kimler, Eduardo Vilar, Eva Szabo, Goli Samimi, Katina DeShong, Kelly Benante, Leslie Ford, Lisa Bengtson, Margaret House, Sue Siminski, Troy Budd, and Vikrant Sahasrabuddhe.

Table 2. Clinical Trial Simplification Committee Recommendations

Clinical Trial Element	Recommendation	Ready for Implementation	
		Yes	No
Study visits	- Minimal in-person visits for agents with established safety - Incorporate study visits with SOC in-person or telehealth visits - Extend clinic hours / allow alternative visit locations	- Yes, for some visit types - Discuss at concept level with DCP and other study team members	More complex visits considered in conjunction with FDA Guidance, CIRB, and local institutional requirements
Safety assessments and safety labs	- Virtual safety/AE checks - Safety labs/imaging collected at local sites	- Yes - Discuss at concept level	
Procedure types and timing (SOC v non-SOC)	Design study around SOC biopsies or procedures	- Yes - Discuss at concept level	
Receipt of study agent and participant instructions	Mail study agent and phone follow-up to verify receipt, and to give instructions for administration and storage, and use of diary and AE forms	Yes – for some agents	For other agents, confer with agent repository and institutional pharmacy on shipping/handling requirements
Participant-centric sampling and home-based technologies	Examples: - Blood collection used Neoteryx Mitra Cartridge - Cervical/vaginal sample collected with Evalyn Brush - Home blood pressure cuff - Wearable technology (continuous glucose monitor)	Yes, in some cases	- In conjunction with FDA Guidance, and CIRB / local institutional requirements - Laboratory – sample kits, shipping labels, etc. - Participant training on sample collection
Protocol review / eligibility criteria	- Virtual PIs and DCP staff meeting to review/edit protocol documents in real-time - Limit eligibility criteria and schedule of event items to most essential	- Yes - Collaboration between study PIs and DCP study staff	
Remote/virtual informed consent (IC)	- Sent electronically before consenting process - Via phone, conference call, video, telemedicine, or other mode, and include a witness - Create SOP / IC template for remote process - Webinar to educate staff about remote process		Consider FDA Guidance, CIRB, and local institutional requirements
Remote trial auditing/monitoring	Obtain information about site capabilities for HIPAA compliant document sharing platforms, electronic health record access, pharmacy policies and procedures, and capacity for remote visits	Yes	
Protocol deviation reporting	- Minor Deviations to be reported quarterly - Moderate and Major Deviations reviewed and graded as received	Yes	

UPCOMING EVENTS

Mar 31: Quarterly CP-CTNet Steering Committee Meeting (virtual)

I-SCORE Meeting (virtual)
March 31-April 1, 2022

Apr 8: *American Association for Cancer Research*
AACR Annual Meeting
in New Orleans, LA (hybrid)
April 8-13, 2022

Jun 3: *American Society of Clinical Oncology*
ASCO Annual Meeting
in Chicago, IL (hybrid)
June 3-7, 2022

Jul 29: Quarterly CP-CTNet Steering Committee Meeting
(virtual/possibly in person)

Cycle #	Steering Committee Date	Concept Solicitation Date	Concept Due Date
10	January 28, 2022	February 4, 2022	April 4, 2022
11	March 31, 2022	April 20, 2022	June 20, 2022
12	July 29, 2022	August 5, 2022	October 5, 2022
13	October 28, 2022	November 4, 2022	January 9, 2023

CP-CTNET STUDIES

ACTIVE STUDIES

UAZ - University of Arizona Cancer Prevention Clinical Trials Network

- **UAZ20-01-02.** An Extended Follow-up Study of the HPV Vaccine Delayed Booster Trial
  Enrolling Sites: LAO – UAZ, AO – UCLA
- **UAZ20-01-01.** Bioactivity of Apalutamide in Prostate Cancer Patients Scheduled for Prostatectomy
  Enrolling Sites: LAO – UAZ, AO – Johns Hopkins

NWU - Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Northwestern Cancer Prevention Consortium

- **NWU20-01-03.** Role of Lisinopril in Preventing the Progression of Non-Alcoholic Fatty Liver Disease (NAFLD): Relief-NAFLD
  Enrolling Sites: AOs – Cedars Sinai Medical Center, Duke, Mt. Sinai Hospital
- **NWU20-02-01.** Surgical Window of Opportunity Study of Megesterol Acetate and Metformin for Endometrial Intraepithelial Neoplasia
  Enrolling Sites: LAO - NWU, AOs - University of Colorado, Duke
- **NWU20-02-02.** A Randomized and Placebo-Controlled Phase II Trial Targeting Dominant-Negative Missense Mutant p53 by Atorvastatin for Reducing the Risk of Longstanding Ulcerative Colitis-Associated Cancer
  Enrolling Sites: LAO/AO - NWU
- **NWU20-04-01.** Metformin for Chemoprevention of Lung Cancer in High Risk Obese Individuals
  Enrolling Site: AO - Roswell Park Cancer Center

STUDIES IN THE PIPELINE

UAZ - University of Arizona Cancer Prevention Clinical Trials Network

- **UAZ21-06-01.** Phase II Randomized, Placebo-Controlled Trial of Broccoli Seed and Sprout Extract (BSSE) to Evaluate Sustained Detoxication of Tobacco Carcinogens in Heavy Smokers (BSSE)
- **UAZ21-07-01.** M4OC-Prevent 2.0: Phase IIb Trial of Metformin for Oral Cancer Prevention

NWU - Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Northwestern Cancer Prevention Consortium

- **NWU21-08-01.** A Phase II Trial of Oral Iloprost for the Precision Chemoprevention of Lung Cancer

MDA - University of Texas MD Anderson Cancer Center, iCAN-PREVENT: International Cancer Prevention Clinical Trial Consortium

- **MDA20-01-01.** A Phase IIa, Placebo-Controlled, Randomized Study of Daily Obeticholic Acid (OCA) to Reduce Intestinal Polyp Burden in Familial Adenomatous Polyposis (FAP)
- **MDA20-02-01.** Time Restricted Eating and Metformin (TEAM) in Breast Cancer (BC) and Adjacent Intraepithelial Neoplasia (IEN). A Randomized, Phase IIb, Window of Opportunity PreSurgical Trial. (TEAM Trial)
- **MDA21-06-01.** A Phase Ib Clinical Trial of Nous-209 for Recurrent Neoantigen Immunogenicity and Cancer Immune Interception in Lynch Syndrome Patients

UWI - MW Chemoprevention Network - University of Wisconsin and the Mayo Clinic

- **UWI20-00-01.** A Phase II Trial of the Immunogenicity of a DNA Plasmid Based Vaccine (STEMVAC) Encoding TH1 Selective Epitopes from Five Antigens Associated with Breast Cancer Stem Cells (MDM2, YB1, SOX2, CDH3, CD105) In Patients with Early-Stage Triple Negative Breast Cancer
- **UWI20-04-01.** A Dose Escalation Phase I Trial of the Safety and Immunogenicity of RG1-VLP, A Candidate Broadly Protective Vaccine for the Prevention of HPV-Associated Cancer
- **UWI21-06-01.** Pilot Study of GCC Agonists to Identify a Cyclic-GMP Signal in Duodenal Tissue of Healthy Volunteers

UMI – University of Michigan, Early Phase Clinical Cancer Prevention Consortium (ClinCaP)

- **UMI21-05-01.** Obeticholic Acid for Chemoprevention in Barrett's Esophagus
- **UMI22-09-01.** Phase IIA Trial of Acolbifene vs Low Dose Tamoxifen in Pre-menopausal Women at High Risk for Development of Breast Cancer
- **UMI22-09-02.** ONC201 for Chemoprevention in Colorectal Cancer (BrUOG 399)

CP-CTNet Cross-Network

- **INT21-05-01.** Phase II Clinical Trial of the Multitargeted Recombinant Adenovirus 5 (CEA/MUC1/Brachyury) Vaccine (Tri-Ad5) in Lynch Syndrome
- **INT22-09-01.** Randomized Trial of Apalutamide in Non-Muscle Invasive Bladder Cancer

Research Funding Opportunities

GRANTS & AWARDS

- Chan Zuckerberg Initiative - Science Diversity Leadership Award *https://tinyurl.com/bdzxxxkc*
- NCI Administrative Supplement Opportunity for Strategies to Optimize Recruitment and Retention of Cancer Prevention and Symptom Management Clinical Trial Participants *https://grants.nih.gov/grants/guide/notice-files/NOT-CA-21-070.html*
- Administrative Supplements to Recognize Excellence in Diversity, Equity, Inclusion, and Accessibility (DEIA) Mentorship *https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-057.html*
- The Funding Opportunity Announcement (FOA) PAR-22-114: Administrative Supplements to Support Cancer Disparity Collaborative Research has just been published. *https://grants.nih.gov/grants/guide/pa-files/PAR-22-114.html*

HOW TO REACH US

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Other Links

DMACC website
DCP CP-CTNet website

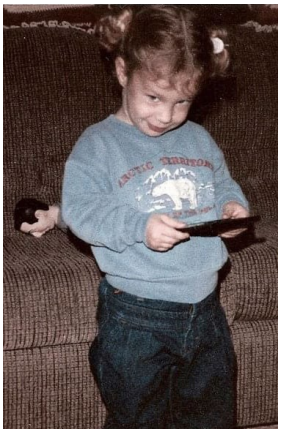
THE NAME GAME

Our last contestant on the name game was Kelly Miller of DMACC and Maggie House and Barbara Wollmer both guessed correctly!

Can you name the CP-CTNet team member in this photo?

Hint: She is playing with a calculator in this photo.

Submit your guesses to *DMACC_Newsletter_Editors@frontierscience.org*. The answer will be revealed in the next newsletter!



Please submit your favorite childhood photo to *Our Editorial Team* to be used in future editions.

Do you have questions, comments, or newsletter content suggestions? Please *email us*.

NCI Cancer Prevention Clinical Trials Network
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