

The Cancer Research Network Connection

Ed's Corner of the World

News from the CRN PI

At the 2009 Fall CRN Steering Committee meeting, I announced that I wanted to step down as CRN PI at the end of CRN3 (2012) to spend more time on research and writing. The Steering Committee formed a CRN4 PI Search Committee that met regularly from September 2010 to January 2011. The Search Committee's charge was to recommend to the Steering Committee a single candidate for PI to lead the CRN through the competitive renewal process and into the future. The Committee developed and disseminated a call for applications and a job description, solicited applications, interviewed candidates and spoke

with their references. The candidates were highly qualified, with distinguished careers, and had years of cancer research and leadership experience. While the decision was difficult, the CRN4 PI Search Committee recommended Larry Kushi, ScD from KPNC for CRN4 PI. Larry is an internationally respected nutritional epidemiologist, who has led many successful collaborations among HMOs, academic and community organizations. Larry has accepted this new role and is looking forward to leading us into CRN4. The CRN will be in very good hands!

- Ed Wagner (GHC)

News from NCI

Update from the CRN Program Director

On December 2-3, 2010, A Conference on Methodological Challenges in Comparative Effectiveness Research took place at the NIH Natcher Center in Bethesda. The conference was co-sponsored by NIH and AHRQ. The conference agenda and many of the conference presentations are available at: <http://conferences.thehillgroup.com/CERDecemberConference/agenda.html>. The conference was organized around clinical case studies. Two of these were relevant to cancer: a session on comparative effectiveness of surgical and radiotherapy treatments for prostate cancer and a session on evaluating the benefits and consequences of imaging

strategies for diagnosing and monitoring cancer. Other sessions that may be of interest to CRN investigators include methods to address confounding in observational studies and Value of Information analysis. I also found the talk by Christopher Forrest, in the session on learning healthcare systems, of interest. While it concerned a research network established to study pediatric gastroenterology, many of the principles of a learning healthcare system which Forrest described and elaborated are highly reminiscent of the CRN. See Terry Field's article on page 5 of this newsletter for more information about the session.

-Martin Brown (NCI)



The Cancer Research Network (CRN) is a collaboration of 14 non-profit HMOs committed to the conduct of high-quality, public domain research in cancer control. The CRN is a project of NCI and AHRQ.

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CRN Site Profile: Kaiser Permanente Northern California

DIVISION OF RESEARCH

Founded in 1945, Kaiser Permanente Northern California (KPNC) is one of the oldest and largest not-for-profit HMOs in the U.S. At the end of 2009, KPNC covered a population of 3,223,235 members. Headquartered in Oakland, CA, its service area comprises



Larry Kushi

the counties surrounding the San Francisco Bay Area and the Central Valley from the Sacramento Area to Fresno. It has 21 hospitals and numerous outpatient facilities, and serves almost 30 percent of the population in its service area. KPNC is one of eight regions through which Kaiser Permanente provides health care, and comprises an alliance among the Kaiser Permanente Health Plan, Kaiser Foundation Hospitals, and The Permanente Medical Group.

The Division of Research (DOR) is the KPNC entity that conducts public-domain, externally-funded research. It was founded in 1961 as the Department of Medical Methods Research. The DOR has 55 scientists and approximately 550 employees. Organizationally, it is a part of The Permanente Medical Group, although the vast majority of grants that provide its funding are channeled through the Kaiser Foundation Research Institute (KFRI), a part of the Kaiser Foundation Hospitals. KFRI also houses the Institutional Review Boards that oversee KPNC research activities.

In addition to hosting the KPNC VDW, the DOR has other resources that help facilitate cancer research. These include the KPNC Cancer Registry that meets the SEER Program standards,

and which reports to the San Francisco Bay Area and California Cancer Registries. We are the home of the KPNC biospecimen and pathology committee, which, among other tasks, oversees use of clinical pathology specimens for research purposes. Over

1,500 in situ and invasive cancer cases are diagnosed monthly, and their associated blocks and slides are stored indefinitely. One example of the use of this pathology resource is a retrospective nested case-control study with 10-year mortality follow-up that is one of the principal validation studies on oncotype DX® in breast cancer care, led by Laurie Habel.

In recent years, there has been an effort to consolidate organizationally research activities in KPNC. We incorporated the KP Oncology Clinical Trials (KPOCT) under the DOR administrative umbrella this past year. While KPOCT activities continue to be led by Lou Fehrenbacher of the KP-Vallejo Medical Center, where the administrative offices of KPOCT are located, there is greater interaction between DOR researchers and KPNC oncologists and trialists. Through KPOCT, KPNC is a full member of the Southwest Oncology Group (SWOG) and National Surgical Adjuvant Breast and Bowel Project (NSABP) cooperative groups. KPNC is also pending full membership in the Radiation Therapy Oncology Group (RTOG).

KPNC investigators have been involved in several CRN-affiliated research projects. Some examples include Dr. Habel, who leads an ongoing prospective examination of DCIS

as one of the CRN's core research projects, and Carol Somkin, who leads studies related to recruitment of participants to clinical trials. Stephen Van Den Eeden leads the KPNC component of a case-control study of pancreatic cancer, led by Meg Mandelson (GHRI.) We are also active participants in two of the three CRN-related NCI-funded comparative effectiveness GO grants, working on projects led by Deb Ritzwoller (KPCO), Jane Weeks (Dana-Farber Cancer Institute), and Katrina Goddard and Evelyn Whitlock (KPNW).

The DOR is also involved in many other cancer research projects. Examples include studies of cancer risk among people infected by HIV led by Mike Silverberg; prescription medication use and cancer risk led by Laurie Habel; Medicare Part D and disparities in cancer and diabetes care led by Alyce Adams; prospective cohort studies of lifestyle factors and breast cancer prognosis led by Larry Kushi (the Pathways Study) and Bette Caan (the LACE Study); studies of Barrett's esophagus and colorectal cancer screening led by Doug Corley; and studies in skin cancer led by Maryam Asgari, who also holds the distinction of being a former CRN Scholar. These and other studies often involve collaborations with other institutions, from across the Bay to across the country.

In addition to our research setting, we are blessed with the opportunity to live and work in one of the truly beautiful and dynamic metropolitan areas in the United States. We look forward to continuing to play a role in furthering research activities in the CRN.

- Larry Kushi (KPNC)



What's New with the CRN Scholars?

In this installment of the CRN Scholar profile series, we learn about the investigator development opportunities afforded by the CRN to Chyke A. Doubeni, MD, MPH (UMass/Meyers), a participant in the 2007-09 CRN Scholar program.

Q How has the CRN research environment fostered your career goals?

A The CRN has provided the ideal environment and community for my research training by providing access to research collaborators and data on large, diverse, and stable populations. I have been able to

look at a wide range of data, from Medicare to multiple outcomes along the entire continuum of cancer care to mortality.

Q What research activities were you able to undertake with CRN support?

A Since joining the CRN in 2004, I have had the good fortune of building a substantial portfolio of research activities, starting with a



Chyke Doubeni

CRN administrative supplement for underrepresented minorities from the NCI Center to Reduce Cancer Health Disparities. This support led to a successful application for a career development award that was funded on its first submission. I also participated in the innovative CRN Scholars Program, which enabled me to broaden my network of collaborators and work with renowned mentors and content experts. These training opportunities provided the pilot data as well as operational experience needed for two independent awards, which are currently underway.

Chyke's Career of Cancer Prevention Research in the CRN

Career Development

2004-2007: CRN Administrative supplement for under-represented minorities

Study target: A cohort of about 800 women from 4 CRN sites during the five-year period after treatment for breast cancer in 1996 or 1997.

Findings: Surveillance mammography rates were surprisingly low and fell off over time. Women with a history of visits to gynecologists or primary care physicians had a higher likelihood of having surveillance mammograms when compared to those without a record of such visits. (Doubeni et al. *Cancer* 2006;106:2482-8)

2007-2012: K01 "Understanding Racial and Ethnic Differences in Survival from Colorectal Cancer"

Study target: About 14,000 patients with new-onset colorectal cancer (CRC) from 6 CRN sites using the VDW.

Findings: After adjusting for age, gender, diagnosis year, and study site, blacks had a 17% higher risk of CRC-specific death compared to whites. This statistically significant gap was accounted for mainly

by differences in tumor stage at diagnosis and receipt of surgical treatment. These findings were consistent with subsequent analyses performed using data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) and Medicare Current Beneficiary Survey data, which suggest that CRC racial disparities are due mostly to differences in exposure to and use of health care services, rather than the result of inherent biological or genetic risks. (Doubeni et al. *Cancer* 2007;109:612-20)

CRN Scholars Program

2007-2009: CRN pilot project "Socioeconomic Diversity in Integrated Healthcare Delivery Systems"

Study target: Within 3 health plans, we identified more than 50,000 members who were 50-75 years of age, had no record of having had a CRC test in 2000. We followed the patients through 2007 to identify the sequence of CRC tests.

Preliminary findings: During the 8 years of follow-up, 40% of members had no record of having had a CRC test, compared to 18% who had fecal occult blood test (FOBT), and

28% who had colonoscopy as their first tests. Analyses of these data on the associations with testing are underway.

Current Independent Research Awards

2009-2011: GO grant "Cancer Screening Effectiveness and Research in Community-based Healthcare (SEARCH)" (Co-PI with Diana Buist, GHC)

Study target: To conduct studies in colorectal and cervical cancer screening with the aim of developing methodological expertise in cancer screening comparative effectiveness research within the CRN.

2010-2015: R01 "Effectiveness of Screening Colonoscopy in Reducing Deaths from Colorectal Cancer" (Co-PI with Robert Fletcher, HPHCI)

Study target: A study by a trans-disciplinary team of investigators on the effectiveness of screening colonoscopy in preventing deaths from colorectal cancer, especially for cancers arising in the right colon.

- Chyke Doubeni (MPCI), Sarah McDonald, Leah Tuzzio (GHC)

Dissemination & Implementation Science and the CRN: An Interview with Russ Glasgow

One of CRN's own investigators, Russell E. Glasgow, PhD, was recently appointed as the Deputy Director for Dissemination and Implementation Science, Division of Cancer Control and Population Sciences, National Cancer Institute. (http://cancercontrol.cancer.gov/od/leadership_glance.html). Russ graciously agreed to be interviewed by Deb Ritzwoller to describe his new position and discuss potential opportunities for future CRN research endeavors.

Q What was your background prior to moving to NCI?

A My dissertation was on smoking cessation as it applied to individually based interventions. This led to more work in worksites and communities. My second line of research was around chronic disease self-management. I also conducted diabetes research for a long time – both individual and group interventions. This work then led to research collaborations with Kaiser Permanente Northwest. I also worked with Ed Wagner and his group on collaboratives to improve chronic illness care, including the implementation of the Chronic Care model in community health care settings. I moved to Colorado 12 years ago, serving as a Senior Scientist at both AMC Cancer Center and the KPCO Institute for Health Research (2002). I served as a co-investigator on CRN HIT II and in 2008 I began serving as

co-investigator and Director of the Dissemination Core of the NCI-funded CRN Center of Excellence in Cancer Communication Research (<http://crn.ccr.org>).

Q What's your new role at NCI?

A The Dissemination and Implementation (D&I) Science office is undergoing strategic planning, but our key role is to:

- 1) Advance the science of D&I. Examples include pragmatic trials, use of simulation modeling, and other rapid learning initiatives.
- 2) Support investigators looking for funding, for example, through the NIH trans-disciplinary Research on Dissemination and Implementation in Health awards (see Program Announcements PAR-10-038 (R01), PAR-10-039 (R03) and PAR-10-040 (R21) at <http://grants.nih.gov>.)
- 3) Serve as a liaison and an 'influencer' to large trials to promote early planning for eventual translation of the study results into practice and policy.
- 4) Serve as a "connector" or liaison. If a particular program is not right for the investigator or study, my role is to identify and connect them to other NCI programs.
- 5) Help build the field. Promote collaborations within and across other NIH institutes, across governmental and public/private initiatives, and collaborations with international entities.

Tools and resources provided by NCI and Russ' office:

- 1) Cancer control PLANET (<http://cancercontrolplanet.cancer.gov>). This is a website for planning strategies that could be used by HMO prevention departments or

community benefit groups to find cancer rates by state or city to find health disparities statistics, and to select evidence-based interventions and evaluation plans appropriate for implementation research. It also provides tips from investigators on how to design their research for effective dissemination.

- 2) Cancer Trends Progress Report offers the key measures in cancer prevention and survivorship.
- 3) Comprehensive list of references on dissemination, implementation and diffusion.
- 4) Training webinar series on issues related to bringing researchers and practitioners together. In 2011, a week-long summer training program on D&I science, coordinated by the Office of Behavioral and Social Science Research.

Q What tips or lessons could you share with us?

A First, embrace technology! Patient-centered medicine is the future. CRN members need to leverage their access to patient portals within their EMRs. The VA, other health plans and European health systems are currently employing patient-reported outcomes within research. We can learn from and leverage these initiatives. Second, think about the extent to which the CRN learnings and findings can generalize to other settings, populations and contexts. Think about making it an empirical question by partnering with practice based research networks (PBRNs), community health settings, VA and others. Last, consider attending the NIH D&I annual meeting in Bethesda on March 21 & 22 or the D&I summer training program.

- Russ Glasgow (NCI), Debra Ritzwoller (KPCO)

The CRN Connection is a publication of the CRN intended to inform and occasionally entertain CRN collaborators. It is produced with oversight from the Communications & Collaborations Committee.

Please send comments and suggestions on this newsletter to Sarah McDonald, mcdonald.sj@ghc.org

A Rapid Learning Healthcare System...

“... is one that uses advances in information technology to continually and automatically collect and compile from clinical practice, disease registries, clinical trials, and other sources of information, the evidence needed to deliver the best, most up-to-date care that is personalized for each patient....A Rapid Learning Healthcare System ensures that this data-rich system learns routinely and iteratively by analyzing captured data, generating evidence, and implementing new insights into subsequent care.”¹

During the past few years there has been increased interest in the potential for implementing rapid learning systems in oncology and cancer care, culminating in a workshop conducted by the Institute of Medicine in October, 2009. The workshop summary is available online (<http://iom.edu/Reports/2010/A-Foundation-for-Evidence-Driven-Practice-A-Rapid-Learning-System-for-Cancer-Care.aspx>).

The sites in the Cancer Research Network are among very few organizations in the US with all of the components needed for developing and supporting an oncology rapid learning healthcare system (RLHS). Although such a development appears to be a natural outgrowth of the CRN, how we would structure such a system has not been obvious. During the recent symposium on comparative effectiveness sponsored by NIH and AHRQ, we received some clues. Dr. Christopher Forrest from PEDSnet (a pediatric EHR data sharing network) presented details of a prototype RLHS project focused on children with inflammatory bowel disease (IBD.) The project is based within Improve Care Now which includes 29 pediatric GI practice sites, 27 physicians and 10,000 children with IBD. The primary clinical issues addressed in the project arose from

clinician interest in better defining the optimum time for introducing biologics during care of these children. The clinicians determined the minimum dataset required to answer their questions, giving them a vested interest in actually entering the required data during patient care. In addition, they played a critical role in defining important potential confounding variables by providing information on the clinical factors that influence their decisions on the use of biologics. All of these core data elements are collected during patient visits through paper forms or via modification of the sites' EHRs. Data is entered/transferred into local i2b2 databases and federated queries are conducted using SHRINE. In the future, children and parents will directly enter outcomes into the data system using the NIH PROMIS network. A sophisticated analytic approach has been designed to cope with the varying patterns of care under the primary treatment strategies and to handle important confounders that may also be intermediaries during a course of treatment. The team is considering issues related to the timing of analyses and approaches for feeding results back to clinicians without explicitly standardizing care. The PowerPoint presentation from Dr's Forrest and Joffe is available online (<http://conferences.thehillgroup.com/CERDecemberConference/agenda.html>). It is also possible to view the presentations at <http://videocast.nih.gov/Summary.asp?File=16319> (fortunately, the relevant presentations are toward the beginning of that file!).

Despite differences in the clinical content, this prototype provides some important insights for a possible CRN-based RLHS. Clinician commitment is crucial, suggesting that the system must focus on those clinical questions

they consider most important. The data required to answer these questions may not be adequately captured in existing systems, particularly data elements related to the indications for therapeutic decisions. The team supporting an RLHS should include specialists in a number of areas with sophisticated capabilities in information technology and study design and analysis. The design of approaches for feeding results into the ongoing systems of care requires particular attention and the involvement of clinicians.

It is evident that the CRN's multi-site collaborative teams, parallel data structures, and the capacity to conduct federated queries could provide solid support for an oncology RLHS. Are we ready to take on this challenge?

- Terry Field (MPCI)

1. Murphy S, Patlak M rapporteurs. A foundation for evidence-driven practice: a rapid learning system for cancer care: workshop summary. Washington, DC: The National Academies Press. 2010.

CRN News

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process means fewer IRB reviews for your multi-site study.

Originally limited to just data-only studies, the revised SOP can be used for all research except clinical trials (i.e., drug, device and biologics). As before, your home IRB always retains the right to choose to do in-house review in lieu of the facilitated process.

The updated SOP, application cover sheet, FAQs, and process flowchart are already integrated into the HMORN Collaboration Toolkit, available at www.hmorn.org. Access these and other multi-site IRB tools online today!

CRN News and Milestones

Former CRN Scholar moves on

Nirav Shah, MD, MPH, a participant in the 2007-09 CRN Scholar program, was named Commissioner of the New York State Department of Health by Governor-elect



Nirav Shah

Andrew Cuomo. Nirav has been on the faculty at Geisinger Center for Health Research and the NYU School of Medicine. In addition to his participation on the CRN Scholar program, he has been an active member of the CRN Communications & Collaborations Committee (producers of this newsletter!) The CRN's loss is New York's gain. Best of luck, Nirav!

CRN Meetings at HMORN Conference

The 2011 HMORN Conference is rapidly approaching! Mark your calendars for March 22-25 in Boston, MA. Check out the conference agenda at www.hmorn.org.

Several CRN study teams will present their findings and works in progress during the open sessions. All are welcome and encouraged to attend the CRN Pilot Project Seminar on **Thursday March 24, 5:30-7:00 pm**.

Those interested in developing new research collaborations may wish to attend any of the open Scientific Interest Group (SIG) sessions. For example, the Cluster Randomized Trials (CRT) SIG is holding its inaugural meeting on **Wednesday March 23, 12-1pm**. The CRT SIG is for anyone interested in the conduct and

methodology of CRTs in the HMORN. All perspectives are welcome, including IRB, ethics, biostatistics, investigators, etc. If interested but unable to attend the session at HMORN, email Dr. Elizabeth Loggers at loggers.e@ghc.org to be included in ongoing email conversations.

Facilitated IRB review for HMORN studies – now better than ever

Next time you are putting together a multi-site study, be sure to check out the HMORN standard operating procedure (SOP) for IRB Review of Multi-Site Research. The SOP explains how to coordinate IRB review at multiple HMORN institutions and how one IRB can serve as lead IRB for the overall project. This streamlined

See *CRN News*, page 5

Recent Findings from CRN Scientists

Ed Wagner (GHC) led the CRN-funded study "Quality of Patient-Centered Cancer Care." The study team reported in the December 2010 issue of *Quality and Safety in Health Care* that cancer patients and their families have urgent needs for information and support especially early in their course. These findings informed the development of the intervention trial "Testing an Optimal Model of Patient-Centered Cancer Care (Nurse Navigator)", funded through the CRN Cancer Communication Research Center (CCRC).

Ruth McCorkle (Yale), a consultant on the Nurse Navigator project, published a review of self-management interventions in the January 2011 issue of *CA: A Cancer Journal for Clinicians*. The review concluded that oncology practices can now build strong relationships with

their patients and formulate mutually agreed upon care plans that enable and empower patients to care for themselves in the way they prefer.

Kathy Mazor (Meyers/UMass) leads the CRN-funded study "Health Literacy: Do People Understand What They Hear?" The study team reported in the December 2010 issue of the *Journal of Health Communication* that variability in the public's ability to understand spoken media messages may limit the effectiveness of both public health campaigns and provider-patient communication.

Jessica Chubak (GHC) led an analysis on the CRN-enabled pharmacoepidemiologic study "Medications and Colorectal Cancer Risk", published in the January 2011 issue of the *International Journal of Cancer*. The authors reported that

their data support findings from previous epidemiologic and animal studies that suggest antidepressants may reduce the risk of colorectal cancer.

The Multiplex Initiative, funded by CRN and NHGRI, evaluated consumers' responses to online direct-to-consumer marketing of genetic susceptibility tests. In the September 2010 issue of the *Journal of Medical Internet Research*, **Kimberly Kaphingst** (Washington University) reported that the healthy adults in this study perceived Web-based genomic information presented using evidence-based communications approaches to be helpful in supporting both decisions to test and not to test. The authors recommend additional research to ensure these results generalize to target groups with lower literacy and less Internet savvy.