December 2009

The Cancer Research Network

Connection

Did you know?

GHS = Geisinger Health System
GH = Group Health
HPHC = Harvard Pilgrim Health Care
HPRF = HealthPartners Research Foundation
HFHS = Henry Ford Hospital System
KPCO = Kaiser Permanente Colorado
KPGA = Kaiser Permanente Georgia
KPH = Kaiser Permenente Hawaii
KPNC = Kaiser Permanente Northern California
KPNW= Kaiser Permanente Northwest
KPSC = Kaiser Permanente Southern California
LCF = Lovelace Clinic Foundation
MCRF = Marshfield Clinic Research Foundation
MPCI = Meyers Primary Care Institute

The HMO CRN Cancer Research Network

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.

News from Ed, Larry, and Mark

Update from the CRN Executive Committee

We had a productive Fall Steering Committee meeting in Rockville on November 3-4. Attendees included the CRN Steering Committee, the Academic Liaison Committee, and colleagues from the NCI, the National Institute of Mental Health (NIMH), the National Heart, Lung and Blood Institute (NHLBI) and the Agency for Health Research and Quality (AHRQ). The meeting began with a discussion to identify synergies among CRN-related projects, people, and data areas. Colleagues from NCI and NIMH discussed some upcoming collaborative projects under development; one is a possible agreement between NIMH and NCI to use the CRN Cooperative Agreement as a model for an HMO-based Mental Health Research Network. Of course, CRN scientists were excited about possible research studies in psycho-oncology.

Perhaps most importantly, we started brainstorming what the future of the CRN could look like if the NCI funded an infrastructure-only grant, possibly supporting data resources, collaborations, and training. One suggested scenario was to establish a block of funding restricted to projects that involve a couple of CRN sites and at least one NCI Cancer Center (academic or community). CRN scientists have become successful in obtaining R01 and R21 awards, so our research program has expanded far beyond the core projects in the U19 cooperative agreement. We also discussed how the CRN can become a laboratory to conduct pragmatic, prospective comparative effectiveness trials, and concluded the meeting with a discussion on ways the CRN sites can learn to implement innovations in clinical care.

- Ed Wagner (GH), Mark Hornbrook (KPNW), Larry Kushi (KPNC)

News from NCI

Update from the CRN Program Director

For several days in November, several of us from NCI – me, Robin Yabroff and Marsha Reichman – visited the Center for Health Research in Honolulu, Hawai'i. In addition to having the chance to enjoy the wonderful island of Oahu (I climbed Diamond Head and toured the Lyon Arboretum, Robin went swimming with the spinner dolphins and sea turtles, Marsha saw the North Shore events in the Triple Crown of surfing), this was a very productive scientific visit and a chance to get to better know the research staff and clinicians who contribute so much to the CRN's research laboratory. On Friday, November 13, we met with CRN and Hawai'i SEER staff about a project that is being led

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Developing a cancer research collaboratory: two case studies

The CRN encourages new and continued partnerships in the scientific community, including linkages with researchers from outside organizations such as comprehensive cancer centers, academic institutions and the NIH. A successful collaboration involves:

- sharing ideas
- aligning with CRN priority areas of research
- developing an innovative research proposal or paper

Two such relationships developed in 2007-09, through CRN's established collaborations mechanisms.

Improving breast cancer surgery effectiveness through establishment of an electronic cancer surgery database

Collaboration timeline

1) October 7, 2007: Ted James, MD, Assistant Professor of Surgery at University of Vermont gives a presentation on Quality Indicators in Breast Cancer Surgery at a Breast Cancer Surveillance Consortium (BCSC) meeting. Erin Bowles (GH) has an informal discussion with Dr. James after his presentation about potential project ideas and informs CRN PI Office of CRN collaboration opportunity.

2) January 14, 2008: University of Vermont and Group Health investigators submit a proposal to the CRN Pilot Funds Program. Proposal is not funded. CRN Executive Committee identifies Ed Wagner as a senior mentor to help the investigators identify other sources of funding.

3) July 2008 – March 2009: Incubation of concept and ongoing conference calls with investigators at University of Vermont, Group Health, and NCI.

4) March 25, 2009: Collaboration Inquiry form submitted by Larry McCahill, MD, Van Andel Research Institute (formerly on faculty at University of Vermont).

5) April 7, 2009: Proposal submitted to CRN New Proposals Committee.

6) April 27, 2009: Proposal submitted to NCI in response to Challenge Grant RFA.

7) September 30, 2009: Project is funded. PI: Larry McCahill. CRN sites involved are KPCO (PI Heather Feigelson), GH (PI Erin Bowles), MCRF (PI Adedayo Onitilo).

Project abstract

This project will extend the University of Vermont's electronic breast cancer surgical outcomes database to three CRN sites. The study investigators will use this database to develop and assess measures of surgical quality by examining variation in outcomes of initial breast cancer surgery at patient-, surgeon-, hospital-, and geographic-levels. In addition, the project team will develop protocols and data capture tools that can be implemented elsewhere in order to extend this data network to additional CRN sites. The development of such a clinical data network will allow comparative effectiveness research to be conducted, particularly as related to current controversies in the management of breast cancer, such as an appropriate pathologic margin of clearance in partial mastectomies. Improved understanding of surgical quality can potentially diminish wide variability in outcomes and healthcare costs associated with breast cancer surgery.

Chronic Immune Stimulation and Lymphomagenesis

Collaboration timeline

1) May 30, 2008: Jill Koshiol, PhD, NCI Cancer Prevention Fellow submits Collaboration Inquiry form (http://www.crn.cancer.gov). CRN Executive Committee assesses concept proposal for feasibility and fit with CRN priorities.

2) June-September, 2008: CRN Executive Committee has preliminary discussions with Dr. Koshiol and CRN investigators involved in lymphoma research to ensure synergy with other active and nascent projects and to guide development of the concept proposal.

3) September 12, 2008: Concept proposal is shared with CRN investigators via Opportunities email list.

4) September 30, 2008: Investigators from six CRN sites participate in an initial conference call to discuss the proposal. Bob Greenlee and Paul Hitz (MCRF) agree to write and distribute a VDW program.

5) January 8, 2009: NCI Intramural pilot funds awarded.

6) March 6, 2009: Bob Greenlee (MCRF) agrees to be the lead CRN investigator.

7) March – November, 2009: VDW data are collected at five CRN sites (MCRF, HFHS, KPCO, KPNW, LCF).

8) November 4, 2009: At CRN annual meeting, Dr. Koshiol presents preliminary data and a plan to conduct a validation study in two sites (MCRF and KPCO).

Project abstract

The primary aim of this study is to assess the association between chronic immune stimulation and risk of lymphomas and related precursor conditions. Secondary aims are 1) to evaluate the association between chronic immune stimulation and survival after diagnosis of lymphoma; and 2) to explore risk factors for progression from precursor to malignancy. Conducting this study in the CRN would improve on previous studies because it is more generalizable to the US population and better able to capture exposures through use of both inpatient and outpatient data (a limitation of many previous studies). Incorporation of laboratory, medication, and survival data should also give us a more comprehensive picture of lymphomagenesis than previous studies and identify patients who are at particular risk of developing lymphoma or of dying from their lymphoma after diagnosis. The CRN may also provide a unique opportunity for future molecular studies of lymphoma since many sites have access to archived tissues that could be used to biologically evaluate observed associations.

"[Identifying a lead CRN investigator] was key because it gave me one person to come to with questions and really helped move things along."

- Jill Koshiol, PhD

Those interested in collaborating with the CRN should visit NCI's CRN Web site at www.crn.cancer.gov. Potential research partners can use the Collaboration Inquiry form to connect with the CRN PI's office. The CRN PI's office will assess interest level and feasibility for the research ideas and will facilitate and track the progress of the collaboration.

Another way to get to know CRN investigators in your area of research interest is by joining a Scientific Interest Group (SIG). SIGs are initiated and led by investigators with shared interests in emerging areas of high priority research. SIGs enable investigators at different institutions to meet virtually, share ideas, problem solve and develop manuscripts and/or grant proposals. Visit NCI's CRN Web site for information on active SIGs and how to join. For questions about CRN SIGs, contact Leah Tuzzio (tuzzio.l@ghc.org) in the PI's Office.

Visit NCI's CRN Web site for a listing of national cancer meetings, calls for abstracts and papers and other opportunities relevant to CRN's scientific priorities.

Expanding research data capacity by structuring Epic, an electronic medical record

Beginning in 2007, David Greenstein, MD, Kaiser Permanente Georgia's Chief of Gastroenterology, adapted Epic tools (e.g. SmartNotes, SmartPhrases) to facilitate structuring of digitized progress notes for all colonoscopies. His goal was to be able to monitor the department and individual provider performance on a set of colonoscopy quality measures recommended by the American Society of Gastroenterology. For example, withdrawal time is recommended to be at least seven minutes after reaching the cecum in order to obtain an adequate view of the colon wall for detection of polyps.

Doug Roblin, PhD (KPGA) wrote a SAS algorithm that consisted of string searches for phrases identifying these quality measures (e.g. "WITHDRAWAL TIME WAS") and for extracting relevant information. For example, the algorithm extracts "7" from the phrase "WITHDRAWAL TIME WAS 7 MINUTES". The first iteration of the algorithm faced several challenges, the most daunting being the fact that the key phrases could be located at any point in a progress note text line and could be split across lines. Dr. Greenstein subsequently re-structured the colonoscopy progress notes so that the key phrases indicating the measures always begin with the first character of a progress note line.

"...clinicians and researchers are now able to electronically abstract reason for a colonoscopy...by a simple and accurate SAS algorithm."

Thus, clinicians and researchers are now able to electronically abstract reason for a colonoscopy (e.g. routine screening or for examination of reasons for specific symptoms such as irritable bowel symptoms) and key clinical quality indicators (e.g. withdrawal time, numbers of polyps biopsied, biopsy method) by a simple and accurate SAS algorithm. This provides a unique research and quality indicator data asset that can be linked to the individual patient for evaluation of whether individual- or provider-level differences in quality of the colonoscopy procedure contribute to favorable or adverse patient outcomes. In the process of developing this algorithm and other algorithms for abstraction of data from digitized progress notes, we discovered that some types of visits are more easily structured than others. Screening and diagnostic services, which frequently follow a relatively consistent protocol, are more easily structured than health risk appraisals which assess a range of health information often specific to an individual patient (for example, imagine the numerous ways in which types of leisure physical activity might be documented).

- Doug Roblin (KPGA)

Scholar Profile: Reina Haque, PhD

Success Story from a CRN Scholar Program Graduate

A team of investigators from KPSC (Reina Haque & Virginia Quinn), KPNC (Laurie Habel) and HPHC (Suzanne Fletcher) will soon embark on a new project, "ABC: Antidepressants and Breast Cancer Pharmacoepidemiology." The main goal of this cohort and nested case-control study is to examine the drug interaction between antidepressants and tamoxifen in a group of nearly 25,000 women. This study proposal received an excellent score (1st percentile), and there were several key reasons for this highly successful application:

- Timely issue that addresses an important but understudied area among survivors. Most of the existing studies were based on *in vitro* data with small numbers, suggesting some antidepressants may interfere with tamoxifen's protective effect preventing breast cancer recurrence
- Diversity and numbers of patients included in the analysis
- Group of investigators from various disciplines who collaborate on CRN affiliated breast cancer projects
- Mentoring from experts and grant writing tips through the CRN Scholars Program
- Enthusiasm from the set of initial reviewers who provided concrete suggestions
- Advice from NCI program officials early in the proposal process
- Use of pilot data to enhance the impact of the research question
- Perseverance through the lengthy application and re-application process. We had preliminary data to effectively address every single critique.

This three-year study will begin in early 2010. As antidepressants remain the cornerstone of depression treatment among survivors, establishing the safety of concurrent use of tamoxifen and antidepressant medication has the potential to improve breast cancer survivors' quality of life, and indirectly, their breast cancer outcomes.

- Reina Haque (KPSC)

Kaiser Permanente Center for Effectiveness and Safety Research (CESR)

In March 2009, Kaiser Permanente's National Research Council approved a proposal to create a Center of Excellence for Evaluation of the Effectiveness and Safety of Drugs, Devices and Biologics" (CESR). In response, the KP Program Office made available up to $5 million over an 18-month period across the eight Kaiser Permanente regions for initial CESR infrastructure development.

The mission and vision of CESR are to conduct and disseminate high-quality, high-priority, translational comparative effectiveness and safety research that is of importance in both the public domain and within Kaiser Permanente, in order to improve the public's health and influence the delivery of health care. CESR will accomplish this using the unique assets of this inter-regional, Kaiser Permanente program-wide resource and collaboration with non-KP partners through the HMORN to answer critical internal and external health care questions.

The CESR "kick-off" meeting was held in Oakland, in July. Several CESR sub-groups were formed including the Administrative Network led by Stan Watson (KFRI) and Sac Carreathers (KPSC), the Investigator Network led by Joe Selby (KPNC), and the Data Network led by Mary Durham (KPNW). Oversight of CESR will be under the purview of the CESR Steering Committee, which is made up of the regional research directors and is led by John Steiner (KPCO). The Data Coordinating Center (DCC), a sub-group within the Data Network Committee, will be located at KPNW. The DCC is led by Don Bachman at KPNW, with support from regional data coordinators (TBN), with Deb Ritzwoller (KPCO CRN site PI) serving as the investigator liaison. Recruitment for a permanent national director of CESR will be led by Steve Jacobsen (KPSC). This individual will be a senior scientist with expertise in the study of drug, vaccine, and/or device safety and effectiveness. The Director will lead a network of researchers and analysts based in Kaiser Permanente's eight regional research centers in building and using Kaiser Permanente's national drug safety/effectiveness resource.

The VDW will be the primary data source for CESR. CESR resources will be used to continue the VDW development work that has been completed over the past eleven years via the CRN, HMORN and other funding sources. Specifically, the DCC will work in tandem with the HMORN and CRN. CESR DCC staff will work in concert with other network partnerships to advance VDW content and quality across all KP regions, and ultimately the entire HMORN/CRN. Currently, the DCC is very busy. To date, the DCC has distributed, and has received results from seven of the eight regions for a meta data survey. This survey captures region or site specific information associated with all data content areas. In addition, Don Bachman and regional site specialists have developed and distributed enhanced data quality assurance programs that are being run at the six existing VDW KP regions. The survey and the updated programs are available on the CRN portal, with the plan that these programs will be distributed in the near term to all HMORN/CRN sites.

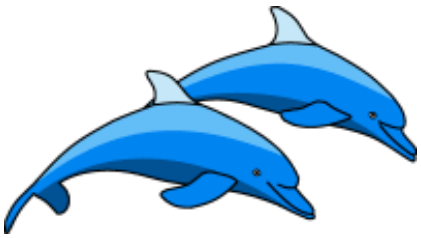
From its inception, CESR was designed to promote collaboration rather than competition with other sites in the CRN and the HMORN. The funding invested by KP in CESR will help the eight KP regions develop the data infrastructure, investigator networks, administrative systems and governance principles that are also the goals of the CRN, the HMORN Governing Board, and its Asset Stewardship Committee.

-Deb Ritzwoller (KPCO)

News from NCI *continued from page 1*

by Marsha, Mark Hornbrook and Andrew Williams, that is designed to demonstrate the capacity to link Kaiser Permanente Hawai'i's electronic data on comorbidity directly to SEER cancer cases. If this is shown to be feasible and scaleable in other types of healthcare delivery systems, it would greatly enhance the usefulness of SEER data. We also visited the Kaiser Hawai'i hospital and met with the practicing oncologists, pathologist and nurse, who described their current research interests and activities. On Monday and Tuesday we participated in a Cancer Summit, sponsored and organized by the three Kaiser members (Hawai'i, Northwest and Georgia) of the Center for Health Research. Presentations and discussions addressed a wide variety of research topics, including biobanking, genomic and prognostic markers, cancer screening, informatics, ethnicity, nutrition and cancer, assessing preventive care, economic analysis and comparative effectiveness research. Upon my return to Rockville, I shared the material from the Summit with our Division Director, Bob Croyle, because I know he will find it to be an exemplary, but only partial, description of the important ongoing work of CRN.

- Martin Brown (NCI)



New findings from CRN scientists

The **CRN Ovarian Diffusion Administrative Supplement study** team reported on the accuracy and complexities of using automated clinical data from seven CRN health plans for capturing chemotherapy administrations. The manuscript, led by Erin Bowles (GH), was published in the October 2009 issue of *Medical Care*. The study team evaluated the sensitivity and specificity of chemo administrations from three automated clinical data sources (Health Care Procedure Coding System, National Drug Codes, and International Classification of Diseases) compared with tumor registry data and medical chart data. We found that clinical codes used in combination are useful in capturing chemotherapy more comprehensively than tumor registry and without the need for costly medical record abstraction.

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The CRN's **Clinical and Pathologic Predictors of Ductal Carcinoma in Site (DCIS) study** team, led by Laurie Habel (KPNC), reported in the November 2009 issue of *Breast Cancer Research* that recurrence declined among DCIS patients treated with breast-conserving surgery (BCS). Through reviewing medical charts and reviewing slides for histopathologic features, they aimed to examine the use and impact of therapies on risk of recurrence of DCIS patients diagnosed between 1990 and 2001 at three CRN health plans. They concluded that "the marked increase in the 1990s in the use of adjuvant therapy for DCIS patients treated with BCS in the community setting only partially explains the 50% decline in risk of recurrence risk. Changes in pathology factors have likely also contributed to this decline."

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The **Breast Cancer Treatment Effectiveness in Older Women (BOW) study** team identified factors associated with delayed radiotherapy (RT) among older women with early-stage breast cancer. Heather Gold (Cornell University), led the recent manuscript that was published in the November 2009 issue of *American Journal of Managed Care.* The study team concluded that timely RT should be facilitated through physician and patient education, navigation, and notification programs to improve quality of care.

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Little is known about the risk of recurrence more than five years after diagnosis among older breast cancer survivors. The **BOW study** team analyzed data from a community-based population to identify some associations for late recurrence. Jaclyn Bosco (Boston University), led a manuscript that was published in the November 2009 issue of *Cancer Epidemiology, Biomarkers & Prevention.*

- Leah Tuzzio (GH)

Update on projects funded through the American Recovery and Reinvestment Act (ARRA)

CRN investigators were very successful in receiving funding from the ARRA-related NIH Stimulus grants. In particular, when the request for Grand Opportunity (GO) Comparative Effectiveness Research (CER) applications was issued last April, the CRN Steering Committee decided to submit three applications, in the areas of screening, therapy, and genomics. All three of these GO grants were funded. These grants are led, respectively, by Diana Buist (GH) and Chyke Doubeni (MPCI); Deb Ritzwoller (KPCO) and Jane Weeks of the Dana-Farber Cancer Institute (DFCI); and Katrina Goddard and Evelyn Whitlock (KPNW) with support from Larry Kushi (KPNC). Each grant is multi-institutional, and across the three grants, just about every CRN site is represented. These GO grants demonstrate the growing importance of CER in the era of health care reform, and the particular suitability of our integrated health care settings for conducting such research.

Even as the activities under these grants are underway, the NCI will be convening a two-day meeting January 5-6 to facilitate collaborations among the funded CER GO grants and to discuss future directions to build upon and sustain the momentum that this stimulus-funding provides. In addition to these GO grants, the CRN and HMORN received a number of other ARRA-funded Challenge grants and administrative supplements to ongoing grants.

Congratulations to all on your success in receiving stimulus-related NIH support for your research ideas and projects.

-Mark Hornbrook (KPNW), Larry Kushi (KPNC) and Ed Wagner (GH)

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

Oversight ... Martin Brown, Alyssa Grauman, Reina Haque, Terry Field, Deb Ritzwoller, Cheri Rolnick, Leah Tuzzio, Nirav Shah, Ed Wagner, Robin Yabroff

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