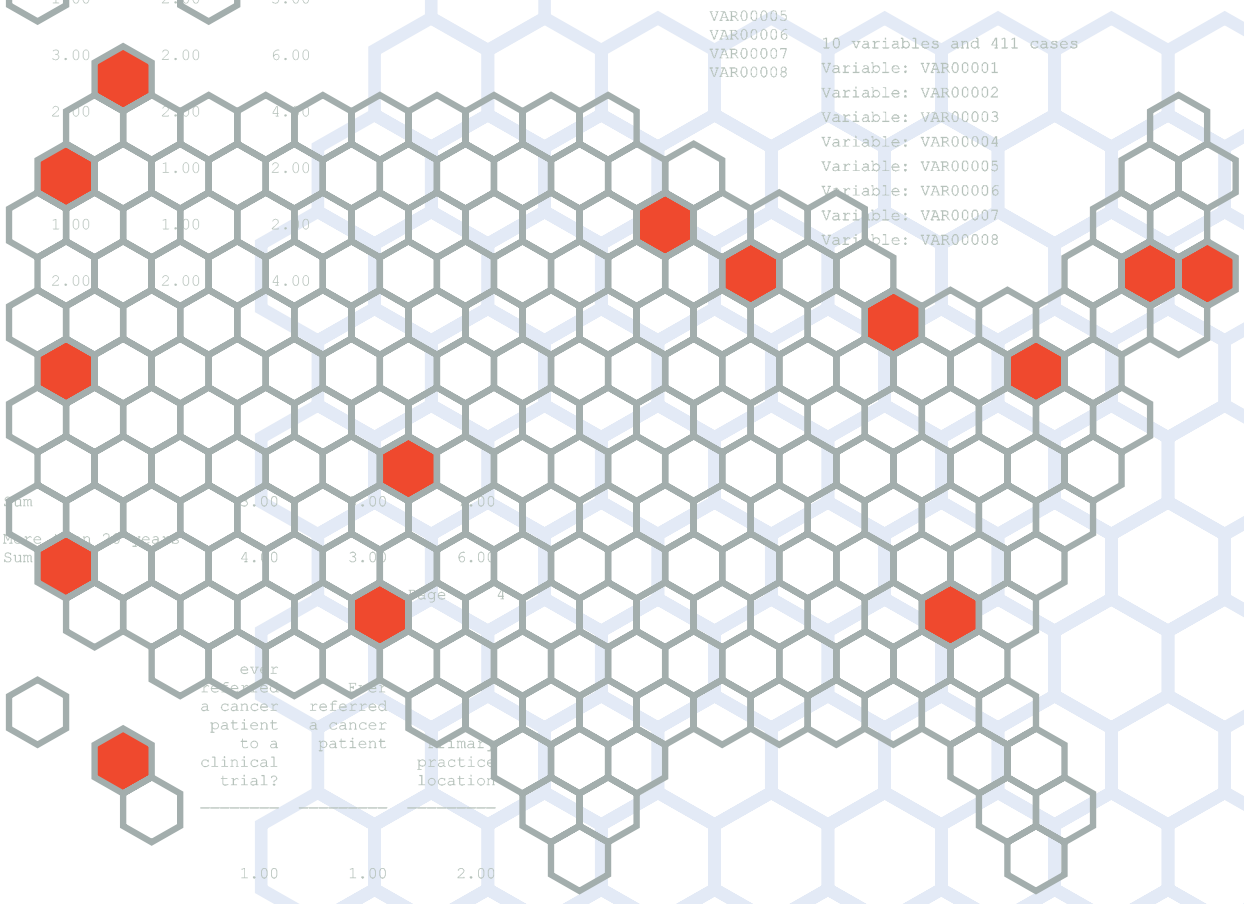
National Cancer Institute

The HMO Cancer Research Network



CAPACITY, COLLABORATION & INVESTIGATION

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

The HMO Cancer Research Network

CAPACITY, COLLABORATION & INVESTIGATION

1 Foreword

2 Overview

3 History

6 Research Themes

8 Collaborating with the CRN

10 Capacity

13 Data Sources

14 Informatics & Research Tools

16 Organizational Structure

18 Site Principal Investigators

20 Contact Information

22 CRN Research & Project Portfolio

24 Scientific Studies & Selected Accomplishments

28 New Directions for CRN 3

32 Publications by Project 1999–2008

FOREWORD

The utilization of health care systems as a platform for basic, clinical, and population sciences research is a central component of NCI's strategic vision. In the 10 years since the HMO Cancer Research Network (CRN) was initiated as a cooperative agreement, the network has provided a framework for leading and working with others to address some of the most perplexing cancer research challenges.

CRN has evolved to encompass research organizations affiliated with 14 large health care delivery systems covering nearly 11 million individuals, conducted dozens of joint research projects, and published over 100 peer-reviewed papers. It has become a national cancer research resource by increasing support for data standardization and dissemination that facilitates collaboration with researchers outside the network.

Originally conceived as a "population laboratory" centered in community-based health care systems, the CRN is able to harness these organizations' data and health informatics systems to conduct cancer etiology, epidemiology, and health services research. It allows for large, multi-center, multidisciplinary intervention research that addresses the spectrum of cancer control, including studies of prevention, early detection, treatment, survivorship, surveillance, and end-of-life care. The CRN is also uniquely positioned to study the quality of cancer care in community-based settings.

The generation of new research ideas is a core value of the CRN, and partnership is at the heart of every project. Through innovative research initiatives, strong leadership, and teamwork with top cancer experts across the country, the network has come to stand as a model for data sharing and collaborative research.

This publication was conceived as an important tool for ensuring that the CRN meets its challenges and goals. Its first main goal is to describe the CRN's research agenda, accomplishments, capacity, and future research potential. Secondly, it aims to serve as a "user's guide" for potential collaborators. It is our hope that readers will gain a greater understanding of how to become partners in this scientific community, how to work successfully with CRN members, and how to utilize CRN's unique research resources and scientific expertise. Readers will then have a greater capacity to undertake research projects that will both benefit the research community and advance knowledge crucial to the progress of cancer control in the United States.

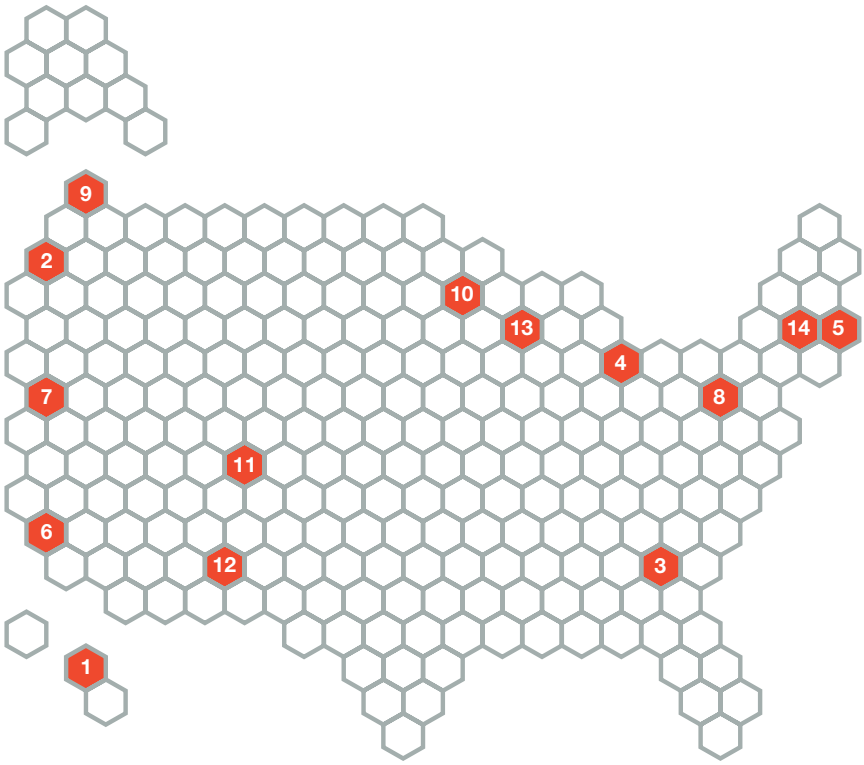
I thank the many colleagues and investigators involved in the CRN, and our partner, the Agency for Healthcare Research and Quality, for their expertise, dedication, and enthusiasm in ensuring that the CRN continues to respond to NCI's priorities for the diffusion of cancer care innovations into practice and health services.

Robert T. Croyle, Ph.D.

Director, Division of Cancer Control and Population Sciences
National Cancer Institute

OVERVIEW

Cancer Research Network Sites & Participating Delivery Systems



1 **Center for Health Research-Hawaii**, Kaiser Permanente Hawaii

2 **Center for Health Research-Northwest**, Kaiser Permanente Northwest

3 **Center for Health Research-Southeast**, Kaiser Permanente Georgia

4 **Department of Research,** Henry Ford Hospital and Health System

5 **Department of Ambulatory Care and Prevention**, Harvard Pilgrim Health Care

6 **Department of Research and Evaluation**, Kaiser Permanente Southern California

7 **Division of Research**, Kaiser Permanente Northern California

8 **Geisinger Center for Health Research**, Geisinger Health System

9 **Group Health Center for Health Studies**, Group Health Cooperative

10 **HealthPartners Research Foundation**, HealthPartners

11 **Institute for Health Research**, Kaiser Permanente Colorado

12 **Lovelace Clinic Foundation**, Lovelace Health System

13 **Marshfield Clinic Research Foundation,** Marshfield Clinic

14 **Meyers Primary Care Institute,** Fallon Community Health Plan

The Cancer Research Network (CRN) is a consortium of 14 nonprofit research centers based in integrated health care delivery organizations. Collectively, these organizations provide care to nearly 11 million individuals.

To achieve its scientific goals, the CRN fosters collaborations among CRN investigators and with investigators and research institutions outside of the CRN member organizations.

The CRN is funded through a National Cancer Institute (NCI) cooperative agreement grant, which ensures substantive NCI involvement in attaining research goals and catalyzing new collaborations. The Agency for Healthcare Research and Quality (AHRQ) also supports the CRN.

CRN research focuses on the characteristics of patients, clinicians, communities, and health systems that lead to the best possible outcomes in cancer prevention and care. The CRN also develops and makes good use of standardized approaches to data collection, data management, and analysis across health systems.

HISTORY

Beginnings

In 1997, the National Cancer Institute (NCI) issued a Request for Applications (RFA) entitled "Cancer Research Network Across Health Care Systems." In doing so, it acknowledged the need for data from representative populations, with lengthy follow-up periods, and a comprehensive range of patient information, to examine important questions about care, long-term outcomes, costs, and other issues important to cancer care delivery and cancer patients. By virtue of their organized care structures, defined populations, and extensive data systems, health maintenance organizations (HMOs) were seen as promising venues and as a strategic resource to address unmet research needs. NCI recognized the important contribution of information garnered from large clinical trials and other databases such as the Surveillance Epidemiology and End Results (SEER)-Medicare linked data for non-HMO cancer patients aged 65 and older. But NCI also acknowledged the limitations of such selective information sources and envisioned a research network that would include population data for people younger than 65, and those at risk for cancer. NCI gave highest priority to studies that addressed the distribution of risk factors and disease in the population, translation of research findings into practice, and the impact of organizational factors on access to and quality of cancer prevention and care. The CRN response to the RFA grew out of discussions among leaders of the established HMO Research Network (www.hmoresearchnetwork.org). The CRN now includes 14 of the 15 HMO Research Network members, all of which have an established program in cancer research and are based in integrated health care delivery systems.

CRN 1: 1999–2003

CRN 1 aimed to improve the effectiveness of cancer prevention and treatment through research identifying system, provider, and patient factors affecting outcomes. The CRN's initial research projects focused on three areas paramount to cancer control: effectiveness of breast and cervical cancer screening in community practice; extent of adherence to tobacco control guidelines at the system, provider, and patient levels; and efficacy of prophylactic mastectomy and early screening among women at increased risk for breast cancer. Several administrative supplements, R01 grants, and other funded projects added to the CRN's initial research portfolio. These diverse

We haven't known about the survival benefit of surveillance mammography in older women before, because older women were not included in large numbers in the original screening trials of mammography, and no one has ever tested the effectiveness of screening after breast cancer in older women. Observational research is a very important tool when you have a well-defined population that can fill in the gaps from clinical trials. And given the tight research budgets, such health services research becomes a cost-effective means of answering questions.

Tuma R. Surveillance Mammography Extends Overall Survival in Older Breast Cancer Survivors. *Oncology Times* 2007; 29(20):24-25. [commenting on findings from the CRN-affiliated research project, Breast Cancer in Older Women (BOW).]

studies included investigations of end-of-life care for prostate cancer, barriers to HMO participation in clinical trials, lung and colon cancer outcomes, medications and risk of colorectal cancer recurrence, and breast cancer treatment effectiveness in older women. CRN 1 included 10 funded sites and one affiliate site.

CRN 2: 2003–2007

Research projects included in CRN 2 broadened the scope of the original investigations to include randomized trials examining the use of electronic medical records (EMRs) to improve adherence to tobacco control guidelines and the effectiveness of an individually tailored, Web-based program to promote daily fruit and vegetable consumption. A third project studied the clinical and pathologic predictors of recurrence among women with ductal carcinoma *in situ* (DCIS). As with the previous grant, several supplements, R01 grants, and pilot funds augmented the core research, including a multicenter study of pancreatic cancer etiology and several information technology studies aimed at improving the research capacity of the CRN's data and informatics resources. Indeed, CRN 2 responded to NCI's call for efforts to create widely accessible, uniform health informatics resources and tools for conducting population-based cancer research. Priorities during this time included further developing and leveraging standardized approaches to data collection, management, and analysis; and enhancing the ability of the CRN to respond to NCI priority areas related to rare cancers and to translating research into practice. The Virtual Data Warehouse (VDW), a pivotal tool to facilitate multi-site cancer research, was a key product of CRN 2. In addition, the DCIS and pancreatic cancer projects expanded CRN's scientific agenda to include linking of biomarker examinations with population-based studies. During this period, CRN sites also continued to collaborate in several large studies initiated outside the CRN RFA, including the Cancer Care Outcomes Research and Surveillance Consortium; the Michigan Center for Health Communications Research; and the study of Multiplex Genetic Susceptibility Testing, supported by the National Human Genome Research Institute. CRN 2 also was

1997

- Request for Applications, "Cancer Research Network Across Health Care Systems"

1999

- First Cancer Research Network grant (**CRN 1**) funded through cooperative agreement

2002

- Second competitive Request for Applications issued

2003

- Second Cancer Research Network grant (**CRN 2**) funded
- AHRQ becomes co-sponsor of CRN initiative

2005

- Compendium of CRN papers published as a *Journal of the National Cancer Institute* Monograph
- CRN featured at NCI Summit on Delivery Systems as Research Platforms

marked by increased efforts to support the professional development of junior investigators, including a tailored mentoring workshop for this purpose and the initiation of CRN pilot funds to support small studies. CRN 2 included 11 funded sites and two affiliate sites.

CRN 3: 2007–2012

CRN investigators are embarking on a new generation of activities for CRN 3. Responding to recommendations from an independent, external evaluation committee, CRN 3 activities involve increasing collaboration with external researchers, research institutions, and networks outside the CRN member organizations; further development of data resources in collaboration with the NCI cancer Biomedical Informatics Grid (caBIG™) and other Department of Health and Human Services (DHHS) initiatives in this area; increased support for junior investigators; more research on dissemination; and studying the implementation of strategies to increase enrollment in clinical trials. Comprehensive infrastructure support and enhancement remain the primary focus of CRN 3. In addition, three new studies will:

- Investigate the economic burden of cancer, focusing on the impact of age, stage, comorbidities, and benefits
- Develop and test measures of oral health literacy through the lens of cancer prevention messages
- Examine the potential for EMRs to improve cancer control by developing a specific, standardized utility: the Cancer Prevention Index.

Several ancillary studies also are underway. CRN 3 includes 14 funded sites.

2006

- External, independent evaluation conducted
- Third competitive Request for Applications issued

- CRN recognized by NIH Roadmap Inventory & Evaluation of Clinical Research Networks (IECRN) as a "Best Practices" site

2007

- Third Cancer Research Network grant (**CRN 3**) funded

RESEARCH THEMES

In 2008, staff from the National Institutes of Health and CRN research staff, advisors, non-CRN cancer researchers, and patient advocates participated in a concept mapping process to identify scientific priorities for the CRN. The eight CRN priority research themes that emerged from this exercise, although not exclusive, include most of the CRN's current work, as well as areas of particular interest for future research. Themes are described in this section.

Data Resources and Infrastructure

CRN member organizations have electronic medical record systems, patient Web sites, and rich arrays of current and historical electronic data on enrollee populations. A major priority is the continued improvement of the CRN standardized data infrastructure, and the development and testing of research, surveillance, and medical practice innovations built upon electronic medical records, patient Web portals, computer-based physician order entry systems, and automated records of complete health service utilization.

Enhancing Cancer Communication and Decision-making

With its extensive data on patients and providers, a key CRN strength is the capacity to examine and optimize the quality of patient communication and decision making about cancer screening, diagnosis, treatment, and survivorship in diverse populations. CRN studies in this area examine a wide range of issues—from shared clinical decision making to Web-based consumer information.

Improving the effectiveness of cancer prevention, control, and care through research that identifies system, provider, treatment, and patient factors affecting outcomes

Health Care Delivery, Quality, Costs, and Outcomes

Examining the influence of alternate health care processes on quality, cost, and outcomes is a key foundation of managed care research centers. Studies in this area address the nature and quality of cancer prevention services, screening, treatment, supportive care, and survivorship care, and their impacts on health outcomes and costs. The relatively large number of clinical sites and the size and diversity of CRN patient populations facilitate studies of practice variation, disparities in care and outcomes, and intervention studies.

Health Insurance Benefit Design and Patterns of Care Utilization

Improvements in care and benefit structure can be advanced with research that examines the relationship between patients' benefit design, in the form of cost sharing or out-of-pocket costs for medical services (e.g., copayments, coinsurance, and deductible rates) and their use of cancer screening and treatment services. Patients who have higher cost sharing for medical services typically are less likely to use recommended medical care services. Moreover, cost sharing has disproportionate effects on low income populations.

Cancer Epidemiology, Prevention, and Health Promotion

The CRN provides large and diverse populations for conducting cross-sectional, case-control, cohort, and intervention studies to examine numerous cancer-related conditions, including health disparities and rare outcomes. Studies of health promotion strategies, lifestyle change, and risk factor assessment and identification benefit from the HMO setting. This setting enhances the ability to define populations to facilitate recruitment and follow-up, work with the health care system to enhance retention of study participants, and have available detailed information on medical care covariates and comorbid conditions that may impact research outcomes of interest.

Psychosocial Factors and Burden of Cancer

Factors such as education, financial assets, literacy, psychosocial distress, and costs of treatment impact cancer care, patient outcomes such as quality of life, and patient care experiences. This research theme emphasizes studies to characterize these effects better, and to identify interventions to ameliorate them. Examining disparities in cancer access, outcomes, and treatment, and the effectiveness of psychosocial interventions for cancer patients, are priority research areas.

Research Translation and Patterns of Screening, Treatment, and Care

The CRN's population size, diversity, and data resources provide rich opportunities to study cancer prevention and care in different care settings, patient populations, and regions of the country over time. Of particular interest are studies of the introduction and diffusion of new diagnostic and treatment modalities into practice, and the conduct of pharmaco-epidemiologic and pharmaco-genomic studies of the effectiveness of cancer drugs.

Building Capacity to Support Emerging Areas of Cancer Control Research

CRN investigators and health care organizations have tremendous potential to advance research activities to develop, enhance, and test health informatics, database, and biospecimen tools and resources to support research in areas such as cancer risk assessment and modeling; studies of behavioral, environmental, and genetic factors; and personalized health care approaches to preventive care, screening, diagnosis/prognosis, and treatment. In addition, the CRN aims to develop activities to increase the timeliness, efficiency, and effectiveness of recruitment to phase 2 and phase 3 prevention and treatment trials.

COLLABORATING WITH THE CRN

Getting Started

Visit the CRN Web site (*http://crn.cancer.gov*) to familiarize yourself with the CRN data sources and research priorities to see how well they fit your research interests and data needs. The Principal Investigator's office will connect you with appropriate partners at one or more CRN sites or affiliates to determine whether your interests and/or data needs align with CRN. Complete the Web inquiry form to describe:

- Any current or previous involvement with the CRN
- A statement of your main research questions and hypotheses
- The nature of the data needed from the CRN to address your research questions
- A description of your project team or potential collaborators
- An estimated timeline for proposal development and submission
- The type of proposal you are planning to submit (e.g., an NIH R01), and whether it is in response to a particular Request for Applications (RFA) or Program Announcement (PA)

Resources to Ensure a Productive Collaboration

- The CRN New Proposals Committee has outlined policies and procedures for reviewing and submitting new collaborative proposals. The Committee assesses feasibility, potential for overlap with existing projects, and appropriateness of the CRN as the setting to answer your research questions.
- Experienced CRN investigators are available for direct involvement in all aspects of the research, including research design, conduct, analysis, and dissemination.
- CRN sites contributing data to your project will review and comment on your research proposal.
- The CRN Publications Committee has outlined policies and procedures for authorship and publication of CRN-related research.

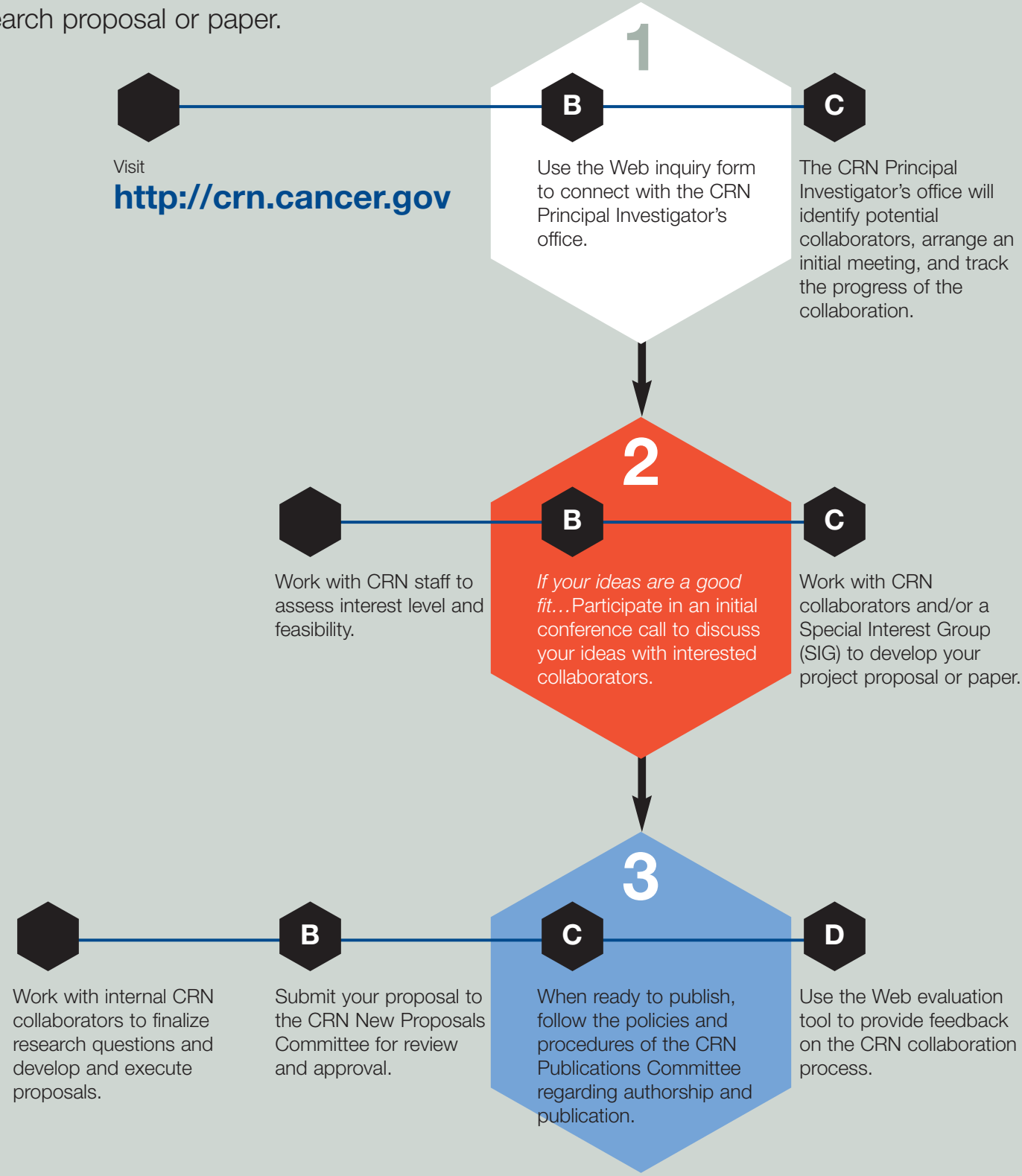
This has been an outstanding opportunity to broaden our collaborations with researchers beyond the University and to connect our faculty to populations for the study of cancer. From the Cancer Center's perspective, our clinicians (in particular) will have new opportunities to study various aspects of cancer prevention, early detection, treatment, and survivorship questions.

DeAnn Lazovich, Ph.D.,
Associate Professor
Division of Epidemiology
and Community Health
University of Minnesota

Visit the HMO Research Network (www.hmoresearchnetwork.org) to familiarize yourself with the various research centers and networks, including the CRN, to see which fits best with your research interests.

Collaboration at a Glance

A successful collaboration involves sharing ideas, aligning with CRN priority areas of research, and developing an innovative research proposal or paper.



Community Linkages

With 14 research centers based in integrated health care delivery organizations nationwide, the CRN is heavily influenced by its proximity to and familiarity with the day-to-day provision of cancer care. All CRN sites are longstanding organizations with a stable presence in their communities. They also have research centers and investigators who understand their enrollee populations, the organization and delivery of care, and the associated data systems.

Population Coverage

CRN member organizations have a combined population of nearly 11 million enrollees. The age and sex distributions of enrollees collectively reflect those of the general U.S. population, although individual plans vary widely. The CRN includes population centers with a high percentage of African American enrollees (Henry Ford Hospital and Health System, Harvard Pilgrim Health Care, and Kaiser Permanente Georgia); Asian Americans (Kaiser Permanente Hawaii, Kaiser Permanente Northern California, and Kaiser Permanente Southern California); and Hispanics (Lovelace Health System, Kaiser Permanente Southern California, Kaiser Permanente Northern California, and Kaiser Permanente Colorado). Racial and ethnic diversity is an important strength of the CRN, which permits studies emphasizing effectiveness research focused on those subpopulations.

QUICK FACTS

> Between 1999 and 2008, CRN researchers published more than 100 peer-reviewed journal articles.

> CRN partnerships and affiliations include the HMO Research Network, many NCI-designated Cancer Centers, and several federal agencies, including NCI, the National Heart, Lung, and Blood Institute (NHLBI), the National Human Genome Research Institute (NHGRI), and the Agency for Healthcare Research and Quality (AHRQ).

> The CRN has significantly leveraged its core funding since the original grant to develop and receive 12 infrastructure or core research grants; 17 administrative or minority supplements; and 7 pilot studies.

> The CRN has participated in other funded work, including 12 R01, U01, and P50 grants; 9 NCI, CDC, AHRQ, and pharmaceutical company contract studies; and three training grants and career awards.

Characteristics of the CRN Research Centers

	GHC	GHS	HPHC	HPRF	HFHS	KPCO	KPG	KPH	KPNC	KPNW	KPSC	LCF	MCRF	MPCI
Year Established	1983	2003	1969	1989	1948	1987	1998	1991	1961	1964	1975	1990	1959	1996
2007 Funding, Millions	28.1	3.8	24	10.2	66.9	14.7	1.6	4.0	62.7	30	19	2.3	29	1.2
% Extramural	89	90	80	75	85	63	75	90	93	90	63	100	42	70
# Full-time M.D./Ph.D. -level staff	29	14	45	13	81	15	3	2.5	52	54	14	6	25	10
# Programmers	25	2	12	10	24	17	3.5	2	76	24	22	3	10	2
Total Staff	269	118	130	78	500	106	12	31	467	250	90	31	190	23
Research Facilities														
Survey Research	●	●	●	●	●	●		●	●	●			●	●
Clinical Center	●	●	●	●	●		●	●	●	●			●	●
Chart Abstraction	●	●	●	●	●	●	●	●	●	●	●	●	●	●

Key (table column heads, pages 11–13)

GHC = Group Health Cooperative (Group Health Center for Health Studies)

GHS = Geisinger Health System (Geisinger Center for Health Research)

HPHC = Harvard Pilgrim Health Care (Department of Ambulatory Care and Prevention)

HPRF = HealthPartners (HealthPartners Research Foundation)

HFHS = Henry Ford Hospital and Health System (Department of Research)

KPCO = Kaiser Permanente Colorado (Institute for Health Research)

KPG = Kaiser Permanente Georgia (Center for Health Research-Southeast)

KPH = Kaiser Permanente Hawaii (Center for Health Research-Hawaii)

KPNC = Kaiser Permanente Northern California (Division of Research)

KPNW = Kaiser Permanente Northwest (Center for Health Research-Northwest)

KPSC = Kaiser Permanente Southern California (Department of Research & Evaluation)

LCF = Lovelace Health System (Lovelace Clinic Foundation)

MCRF = Marshfield Clinic (Marshfield Clinic Research Foundation)

MPCI = Fallon Community Health Plan (Meyers Primary Care Institute)

Characteristics of the Health Plans

	GHC	GHS	HPHC	HPRF	HFHS	KPCO	KPG	KPH	KPNC	KPNW	KPSC	LCF	MCRF	MPCI
Year Established	1947	1985	1969	1957	1960	1969	1985	1958	1945	1942	1947	1973	1916	1977
Structure, %														
Staff/Group	80	90	20	64	65	100	90	100	100	100	100	52	85	53
Independent Phys. Assn.	20	10	80	0	30	0	10	0	0	0	0	48	15	46
Preferred Provider	0	0	0	36	5	0	0	0	0	0	0	0	0	1
Clinic Sites	30	1,234	14	34	70	17	10	17	159	27	103	21	41	20
Hospitals	2	84	21	84	10	2	3	1	19	1	11	4	4	53[1]
Total enrollment, x 1,000[2]	540	210	805	620	295	462	286	225	3,260	487	3,190	221	175	171
1-year retention	80	82	79[3]	77	84	83	87	85	87	82	85	85	88	95[4]
3-year retention	63	54	55	57	68	66	67	72	75	66	71	N/A	73	92
5-year retention	51	41	—	44	56	56	54	63	66	57	61	N/A	68	92
Age, Years, %														
<=24	30	27	33	36	30	30	32	32	32	31	34	34	31	29
25-44	24	26	31	29	26	27	34	28	28	27	27	29	23	24
45-64	33	30	29	27	31	29	27	28	28	30	27	26	26	27
65-74	7	8	4	4	7	8	4	6	7	7	7	7	9	9
>=75	6	9	3	4	6	6	3	5	6	5	5	5	10	11
Female, %	53	51	52	52	55	53	52	51	52	52	53	52	53	51
Race, %														
White	82	96	75	85	67	75	63	25	51	84	38	55	97	87
African American	3	<1	16	6	28	6	33	<1	8	3	8	1	<1	2
Asian American	6	0	5	5	2	2	<1	63	17	5	10	1	<1	3
American Indian	1	<1	<1	<1	<1	1	<1	<1	<1	1	<1	2	<1	<1
Hispanic	4	1.4	4	4	1	15	<1	3	19	6	41	38	<1	8
Other	3[5]	<1	0	0	2	1	4	17	5	1	<1	0	<1	0

1 = Includes affiliated hospitals

2 = Total enrollment, all sites combined: 10,966,000 members

3 = 1-year retention is for Dec 2002 cohort

4 = Retention among cancer survivors only

5 = Includes persons reporting >1 race

NOTE: Information last updated in 2006

DATA SOURCES

CRN sites have a rich array of legacy data systems that date back many years. The table below summarizes data systems available from each participating CRN site. These data systems have been used for research for decades for both single and multi-site studies. The number of collaborating sites and the complexity of CRN research questions required the CRN to create a more efficient and standardized approach to data aggregation. The CRN chose to create a Virtual Data Warehouse (VDW), consisting of databases with a common set of standardized variables in each CRN site. The variability of the legacy data systems has made developing the VDW the CRN's most formidable challenge.

Year of Availability for Key Data Resources

	GHC	GHS	HPHC	HPRF	HFHS	KPCO	KPG	KPH	KPNC	KPNW	KPSC	LCF	MCRF	MPCI
Automated Medical Record	2005	1995	1969	2004	1988	1997	2006	2004	2005[P]	1997	2004	N/A	1994	2006
Administrative Data														
Membership	1988	1999	1969	1990	1980	1992	1995	1958	1976	1982	1988	1996	1986	1987
Outside Claims	1979	1999	1990	1990	1991	1993	1995	1995	1992	1986	1991	1996	1985	1987
Patient Scheduling	1984	1997	N/A	1990	1988	1992	1995	1992	1987	1985	1993	N/A	1991	1987
Deaths	1972	N/A	1983	N/A	1990	1988	1995	1985	1970	1979	1988	N/A	1992[P]	N/A
Cost	1998	1999	1990	1990	1990	1997	1995	1995	1996	1998	1996	1999[P]	1985[P]	1988
Automated Clinical Data														
Outpatient Visits	1992	1996	1969[P]	1990	1988	1992	1995	1995	1995	1987	1993	1996	1991	1987
Hospitalizations	1979	1993	1990[P]	1990	1989	1991	1995	1988	1976	1965	1981	1996	1991	1987
Emergency Room	1992	1993	1990[P]	1990	1988	1994	1995	1988	1995	1985	1993	1996	1991	1987
Pharmacy	1977	1985	1988[P]	1990	1992	1993	1995	1992	1994	1986	1992	1996	1992	1987
Laboratory	1988	1995	1969[P]	1994	1995	1994	1995	1988	1994	1993	1991	2000[P]	1985	1990
Long-term Care	1992	N/A	1990[P]	1990	1995	1994	1995	1995	N/A	1986	1995	N/A	N/A	1999
Home Health Care	1992	N/A	1990[P]	1990	1995	1994	1995	1995	2002	1987	1995	N/A	N/A	1999
Radiology	1986	1994[P]	1969[P,T]	1990T	1988[P]	1992	1995	1991	1997	1989	1994	N/A	1974	1996
Pathology	1996	1987[P]	1969[P,T]	1990T	1988[P]	1994	1995	1995	1998	1970	N/A	N/A	1995	1996
Cancer Registry	1974	1980	1997	N/A	1972	1987	2004	1973	1973	1960	1988	1999	1960	N/A

Key

P = Partial T = Text with search capability N/A = Information not available in a single comprehensive datafile

INFORMATICS & RESEARCH TOOLS

The HMOs affiliated with the CRN have an ethical and legal obligation to safeguard the confidentiality of medical information of their individual members. Thus, it is natural that CRN scientists and their home organizations have long been concerned about the sensitivity of health system data, especially medical information about individuals and also data related to quality or delivery of care and prices paid for medical care inputs. HMO leaders have legitimate concerns that without careful stewardship, such data could be compromised or misrepresented. Because of these concerns, the CRN Steering Committee rejected the notion of establishing a centralized repository of generic data on the enrollees of each HMO for use in current and future studies. However, the CRN proposed developing standardized data resources to increase the quality and efficiency of research using automated data: the Virtual Data Warehouse, cancer counters, electronic medical records, and natural language processing. The CRN also operates under an NIH Certificate of Confidentiality as well as statutory provisions of the Agency for Healthcare Research and Quality that further shield CRN research information containing patient or provider identification from third party discovery.

Emerging Partnerships with caBIG™

The CRN is coordinating its informatics with NCI's cancer Biomedical Informatics Grid (caBIG™) to facilitate collaboration. One project is identifying strategies for increasing enrollment in NCI clinical trials by linking the CRN to the Cancer Text Information Extraction System (caTIES), an open-source natural language processing system available from the caBIG Web site. caTIES facilitates extraction, coding, and querying attributes referenced in free-text pathology reports. A standard, caBIG-compliant version of caTIES is planned for the CRN's VDW. The aim of the caBIG collaboration is to use caBIG tools to improve the VDW's compatibility and interoperability with national standards. Where reasonable and feasible, the CRN will contribute candidate data elements for consideration in the caBIG Data Standards Repository.

The CRN also is an active contributor to the caBIG Population Sciences Special Interest Group and the cross-cutting Data Sharing and Intellectual Capital Workspace. Both groups are working on strategies to facilitate multi-site collaboration, data collection, and stewardship—topics that are well-aligned with the CRN's extensive experience.

The Virtual Data Warehouse (VDW)

The VDW is a distributed data warehouse, a federated database that is comprised of standardized datasets stored behind separate security firewalls at each participating CRN site. The data sets include variables with identical names, formats, and specifications (including definitions, labels, and coding). Person-level data at each CRN site remains under local control at that site. The VDW is supported by a set of informatics tools—hardware and software—facilitating storage, retrieval, processing, and managing VDW datasets; a set of access policies and procedures governing use of VDW resources; and documentation of all elements of the VDW.

Cancer Counters

To facilitate efficient study planning, CRN staff developed virtual data marts or "counters." The Cancer Counter includes summarized de-identified data that can produce counts of patients with cancer aggregated by tumor site, morphology, stage, health plan, vital status, race, gender, and Hispanic ethnicity, and allows users to select one- and two-way frequencies of these variables. The Cancer Counter has proven to be invaluable for estimating study population sizes for new cancer research proposals.

Electronic Medical Records (EMRs) and Natural Language Processing (NLP)

More CRN sites use EpicCare® than any other EMR system. EMRs allow researchers to manipulate and standardize free-text clinical data such as clinical assessment findings, image interpretations, pathology evaluations, hospital discharge summaries, and consultant evaluations. In addition to the standard physician user-interface, many of the EMRs also have a patient interface, where patients can view items in their medical record (such as visit summaries and laboratory test results), send secure messages to their physicians, and enter information into a health risk assessment survey or other survey instrument. This provides the CRN with opportunities for innovative interventions. Natural language processing (NLP) helps investigators to identify the variety of sentences, clauses, words, symbols, and abbreviations that represent synonyms for a concept of research interest. CRN informaticists developed an NLP tool called MediClass® to collect standardized information about tobacco control counseling in "Using Electronic Medical Records to Measure and Improve Adherence to Tobacco Treatment Guidelines in Primary Care."

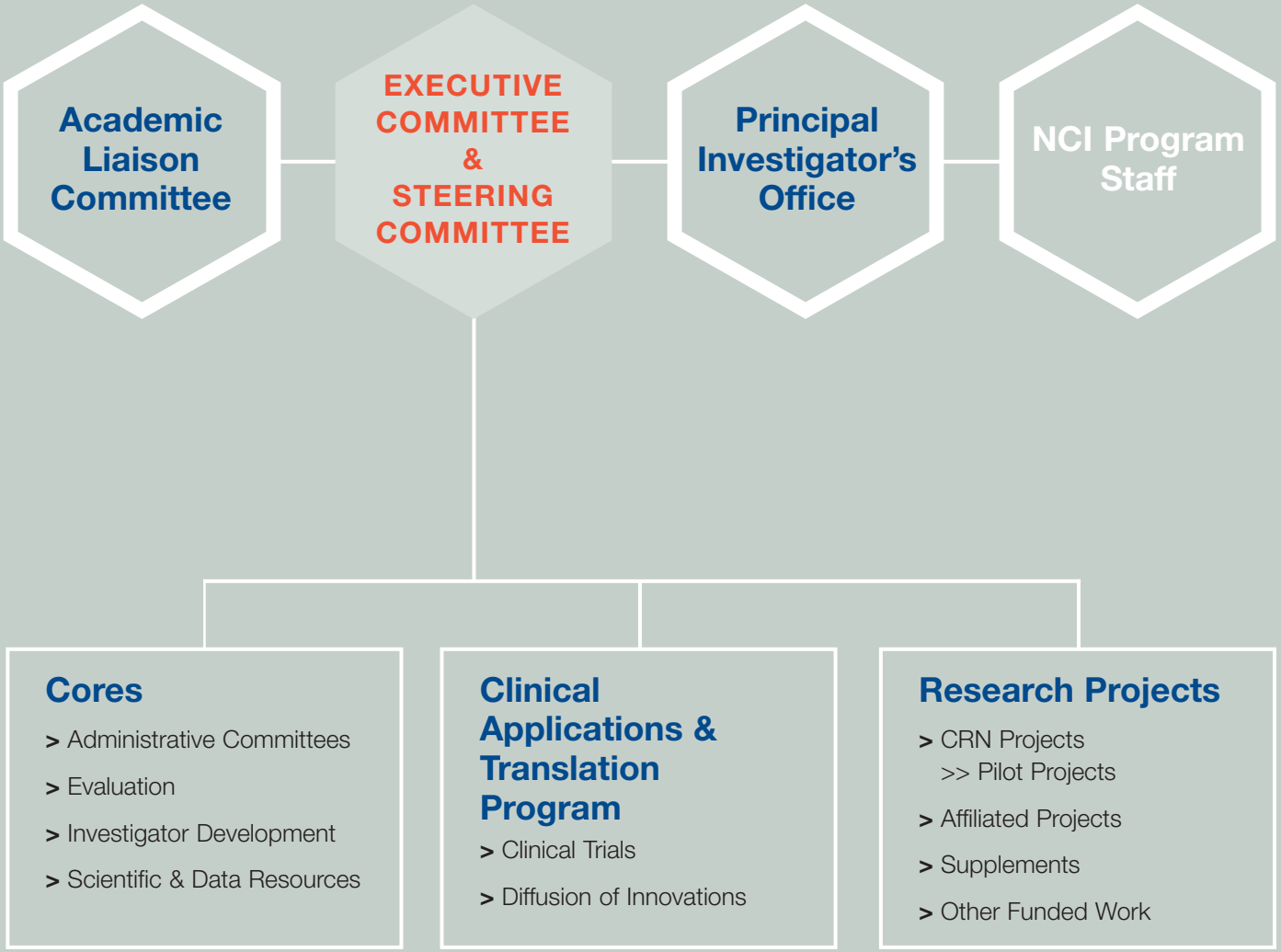
ORGANIZATIONAL STRUCTURE

The CRN is overseen by Academic Liaison, Executive, and Steering Committees. As a cooperative agreement grant, there is also active collaboration between the CRN Principal Investigator's Office and NCI program staff. The CRN's administrative structure includes four cores, a Clinical Applications and Translation Program, and research projects.

The four cores include an Administrative Core, an Evaluation Core, a Scientific and Data Resources Core, and an Investigator Development Core. The Clinical Applications and Translation Program emphasizes work in two major areas: improving enrollment in cancer clinical trials and studying diffusion of innovations in cancer prevention and care. Scientific Interest Groups (SIGs) are initiated and led by investigators with shared interests in emerging areas of high-priority research.

CRN SCIENTIFIC INTEREST GROUPS (SIGs)

- > Obesity
- > Family History
- > Cancer Survivorship
- > Pharmacovigilance
- > Others


Academic Liaison Committee
EXECUTIVE COMMITTEE & STEERING COMMITTEE
Principal Investigator's Office
NCI Program Staff
Cores
> Administrative Committees
> Evaluation
> Investigator Development
> Scientific & Data Resources
Clinical Applications & Translation Program
> Clinical Trials
> Diffusion of Innovations
Research Projects
> CRN Projects
>> Pilot Projects
> Affiliated Projects
> Supplements
> Other Funded Work

SITE PRINCIPAL INVESTIGATORS

Group Health Center for Health Studies, Group Health Cooperative

Edward H. Wagner, M.D., M.P.H.
CRN Principal Investigator

Senior Investigator, Group Health Center for Health Studies

Director, MacColl Institute

Research Interests: studies of interventions to reduce disability in seniors and to enhance the care of persons with chronic illness

Division of Research, Kaiser Permanente Northern California

Lawrence H. Kushi, Sc.D.
CRN Co-Principal Investigator

Associate Director for Etiology and Prevention Research

Research Interests: role of diet and nutrition in the etiology of coronary artery disease and breast and other cancers

Center for Health Research-Northwest, Kaiser Permanente Northwest

Mark C. Hornbrook, Ph.D.
CRN Co-Principal Investigator

Senior Investigator and Chief Scientist, Kaiser Permanente Northwest Center for Health Research

Research Interests: health care cost and utilization analysis, economic evaluation methods, patient classification methods, health status measurement, predictive modeling, and health-based payment systems

Meyers Primary Care Institute, Fallon Community Health Plan

Terry S. Field, D.Sc.
Associate Director, Meyers Primary Care Institute

Associate Professor of Medicine, University of Massachusetts Medical School

Research Interests: providing safe and effective health care for adults who are disabled, chronically ill, or elderly

Marshfield Clinic Research Foundation, Marshfield Clinic

Robert T. Greenlee, Ph.D., M.P.H.
Marshfield Epidemiologic Study Area Lead Scientist, Marshfield Clinic Research Foundation

Research Interests: cancer surveillance and control; sociodemographic disparities in prevention, early detection, and treatment; and clinical epidemiology of cardiovascular disease, particularly arrhythmias and conduction disorders

Geisinger Center for Health Research, Geisinger Health System

Robert D. Langer, M.D., M.P.H.
Director, Outcomes Research Institute, Geisinger Center for Health Research

Adjunct Professor of Epidemiology, University of Pittsburgh Graduate School of Public Health

Research Interests: preventing chronic diseases, with a focus on the effects of age, gender, and culture/ethnicity as they affect the development and course of these conditions

Lovelace Clinic Foundation, Lovelace Health System

Margaret J. Gunter, Ph.D.
President and Executive Director, Lovelace Clinic Foundation

Research Interests: disease management, quality improvement, racial and ethnic disparities, guideline implementation, and the use of information technology to improve practice

Center for Health Research-Southeast, Kaiser Permanente Georgia

Douglas W. Roblin, Ph.D.
Senior Investigator, Kaiser Permanente Southeast Center for Health Research

Adjunct Assistant Professor of Health Policy and Management, Rollins School of Public Health at Emory University

Research Interests: organizational and financial characteristics of health care systems affecting patient outcomes, such as medical services use and cost, visit satisfaction, and quality of chronic disease care

Department of Ambulatory Care and Prevention, Harvard Pilgrim Health Care

Suzanne W. Fletcher, M.D., M.Sc.
Professor Emerita of Ambulatory Care and Prevention, Harvard Medical School and Harvard Pilgrim Health Care

Research Interests: prevention, especially related to breast cancer screening, DCIS, and quality of life issues

HealthPartners Research Foundation, HealthPartners

Cheri J. Rolnick, Ph.D., M.P.H.
Associate Director of Research, HealthPartners Research Foundation, HealthPartners

Research Interests: women's health issues, cancer, evaluation, and health behaviors

Department of Research, Henry Ford Hospital and Health System

Christine Cole Johnson, M.P.H., Ph.D.
Senior Staff Scientist

Associate Chair for Research, Department of Biostatistics and Research Epidemiology

Director, HFHS Josephine Ford Cancer Center's Epidemiology, Prevention, and Control Program

Director, HFHS Center for Allergy, Asthma, and Immunology Research

Research Interests: cancer prevention and the etiologies of allergy and asthma

Institute for Health Research, Kaiser Permanente Colorado

Debra P. Ritzwoller, Ph.D.
Investigator, Health Care Economist, Institute for Health Research, Kaiser Permanente Colorado

Research Interests: costs and cost-effectiveness of behavioral interventions, the uninsured, disease management interventions, vaccine effectiveness, public health surveillance systems, physician compensation, comorbidities, cost estimation, and cost-effectiveness

Center for Health Research-Hawaii, Kaiser Permanente Hawaii

Rachel Novotny, M.S., Ph.D.
Senior Investigator, Science Director, Center for Health Research-Hawaii

Assistant Program Director for Bionutrition, The Center for Health Research

Research Interests: the impact of diet, physical activity, and body size on health and disease; and how periods of rapid growth affect overall health

Department of Research and Evaluation, Kaiser Permanente Southern California

Virginia P. Quinn, Ph.D.
Research Scientist

Department of Research and Evaluation, Kaiser Permanente Southern California

Research Interests: lifestyle and health behavior change, prevention, screening and adherence, adolescents and depression, and quality of cancer-related care

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CRN RESEARCH & PROJECT PORTFOLIO

Project Title	Funding Source	Year Funded
HMO Cancer Research Network: Infrastructure	NCI CRN Infrastructure	1999
Program Testing Early Cancer Treatment & Screening (PROTECTS)	NCI CRN1 Project	1999
HMOs Investigating Tobacco (HIT)	NCI CRN1 Project	1999
Detecting Early Tumors Enables Cancer Therapy (DETECT)	NCI CRN1 Project	1999
Evaluation of End-of-Life Care for Prostate Cancer in the Managed Care Environment	CDC Task Order	2000
Pilot Study to Identify Organizational Barriers to HMO Participation in Clinical Trials	NCI Administrative Supplement	2000
Design, Implementation & Analysis of a Clinician Survey (DETECT supplement)	NCI Administrative Supplement	2000
Lung/Colon Cancer Outcomes: The Cancer Research Network (CanCORS)	NCI Cooperative Agreement	2001
Patient-oriented Outcomes of Prophylactic Mastectomy	NCI R01 Grant	2001
Colon Cancer Survivors—Medications and Risk of Recurrence	NCI R01 Grant	2001
Investigating Medical Patient Records & Administrative Data in Case Identification and Treatment (IMPACT)	NCI R01 Grant	2001
A Pilot Study of Disenrollment among HMO Patients with Cancer	NCI Administrative Supplement	2001
Enrolling Vietnamese and Chinese Women in Breast Cancer Treatment and Prevention Trials	NCI Administrative Supplement	2001
The Impact of Endocrine Therapy on Survival in Men with Local or Regional Prostate Cancer—Feasibility Study	NCI Administrative Supplement	2001
HRT Initiation & Cessation After WHI Results (HRT Diffusion)	NCI Administrative Supplement	2002
Evaluation of Hospice Referral and Palliative Care for Ovarian Cancer in the Managed Care Environment	CDC Task Order	2002
Medication Use and Risk of Esophageal Adenocarcinoma & Barrett's Esophagus	NCI Contract	2002
Breast Cancer Treatment Effectiveness in Older Women (BOW)	NCI R01 Grant	2002
Clinical & Pathologic Predictors of Ductal Carcinoma *in Situ*	NCI CRN2 Project	2003
Making Effective Nutritional Choices (MENU)	NCI CRN2 Project	2003
Using Electronic Medical Records (EMRs) to Improve Adherence to Tobacco Control Guidelines (HIT 2)	NCI CRN2 Project	2003
Michigan Center for Health Communications Research (three projects)	NCI P50 Grant	2003
Optimizing Breast Cancer Outcomes: BMI, Tumor Markers, and Quality of Care	Training Grant	2003
Research Supplement for Underrepresented Minorities Program: Patterns of Preventive Services Utilization of Cancer Survivors	NCI Administrative Supplement	2003
HIT 2 Supplement	NCI Administrative Supplement	2003
Infrastructure: HMO Cancer Research Network	NCI CRN Infrastructure	2003
Medications and Colorectal Cancer Risk	AHRQ R03	2004

Project Title	Funding Source	Year Funded
Statins and Risk of Site-Specific Cancers	AHRQ R03	2004
Investigation of Age-specific Differences and Cancer of the Cecal Colon	NCI CRN Pilot Funds	2004
Do Acute and Chronic Illness Trump Preventive Care? A Case Study of Breast and Colon Cancer Screening	NCI CRN Pilot Funds	2004
Accuracy of Automated Data on Colorectal Cancer Screening	NCI CRN Pilot Funds	2004
African American Disparities in Lung Cancer Outcomes	NCI CRN Pilot Funds	2004
Multicenter Study of Pancreatic Cancer Etiology	NCI R01 Grant	2004
Anti-estrogen Therapies for Breast Cancer	Pilot Funds CRN Infrastructure	2005
Development of a Shareable Analytic Dataset for Studies of Racial Disparities	NCI Administrative Supplement	2005
Comparing Pancreatic Cancer Identification Using Health Plan Automated Data and SEER Cancer Registry	NCI Administrative Supplement	2005
Outcomes Of Genetic Counseling for Heritable Breast/Ovarian Cancer: Feasibility of Identifying Cohort Through EMR	NCI Administrative Supplement	2005
Development of a Method to Assess Obesity and Treatment via EMR	NCI Administrative Supplement	2005
Diffusion of Breast MRI Technology in Community Clinical Settings	NCI Administrative Supplement	2005
Virtual Data Warehouse (VDW) Enhancement	NCI Administrative Supplement	2005
4CQuality: Quality of Patient-centered Cancer Care, Communication, and Coordination	NCI Contract	2005
Use of an Interactive Voice Response System, with Physician Feedback, to Reduce Cancer Symptoms: A Pilot Study	NCI CRN Pilot Funds	2005
Informing an R01 Application: Interviewing Long-term Colorectal Cancer Survivors	NCI CRN Pilot Funds	2005
New Markers: Clinical & Pathologic Predictors of Ductal Carcinoma *in Situ*	NCI Administrative Supplement	2005
Systems Failures Contributing to Chemotherapy Error: A Project of the HMORN Center of Education in Research & Therapeutics	AHRQ Contract	2006
Descriptive Epidemiology and Clinical Course of Meyelodysplastic Syndromes (MDS) in an HMO	AMGEN Contract	2006
caBIG Population Sciences Special Interest Group	NCI caBIG Participant Contract	2006
Is Stroke a Late Effect of Chemotherapy?	NCI R01 Grant	2006
Ovarian Cancer Treatment Diffusion Study	NCI Administrative Supplement	2006
Multiplex Genetic Susceptibility Testing—An Interdisciplinary Collaboration	NHGRI Administrative Supplement to CRN	2006
Residential Segregation, Housing Status, and Prostate Cancer in African American and White Men	Training Grant	2006
DEcIDE Distributed-data Network: Comparative Effectiveness and Safety of Second-line Anti-hypertensive Agents	AHRQ Contract	2007
Impact of HIPAA Privacy Rule on Health Research	IOM Contract	2007
Economic Burden Pilot Study	NCI CRN3 Project	2007
Health Literacy and Cancer Prevention: Do People Understand What They Hear?	NCI CRN3 Project	2007
Cancer Prevention Index Pilot Study	NCI CRN3 Project	2007
Medical Care Burden of Cancer: System and Data Issues	NCI R01 Grant	2007
Increasing Patient Participation in Clinical Trials	NCI R01 Grant	2007
Colorectal Cancer Disparities	NIH Career Development Award	2007
Infrastructure: Cancer Research Network Across Health Care Systems	NCI CRN Infrastructure	2007
High Deductible Health Plans & Receipt of Cancer Prevention Services	ACS Research Scholar Grant	2008
Intestinal Ostomies and Informal Caregiving for Colorectal Cancer Survivors	NCI R21 Grant	2008

SCIENTIFIC STUDIES & SELECTED ACCOMPLISHMENTS

CRN 1 Scientific Accomplishments

Tobacco Control in Managed Care: HMOs Investigating Tobacco (HIT)

This CRN 1 study (Dr. Victor J. Stevens, KPNW, Principal Investigator) examined tobacco policies and delivery of cessation services in nine non-profit HMOs that collectively provide comprehensive medical care to more than eight million members. Three annual surveys with health plan managers showed that all of these organizations had written tobacco control guidelines that became more comprehensive over the span of the study. The project also surveyed a random sample of 4,207 current smokers who had attended a primary care visit in the past year (399 to 528 at each of nine health plans). Of these smokers, 71 percent reported receiving advice to quit, 56 percent were asked about their willingness to quit, 49 percent were provided some assistance in quitting (mostly self-help material or information about classes or counseling), and 9 percent were offered some kind of follow-up. Smokers receiving assistance in quitting reported higher satisfaction with their care. In general, health plans with the most comprehensive policies also showed higher rates of implementing tobacco treatment programs in primary care.

Toward Reducing Cervical and Late-stage Breast Cancer: Detecting Early Tumors Eases Cancer Therapy (DETECT)

This eight-site CRN 1 project (Dr. Stephen Taplin, formerly GHC, Principal Investigator) identified 1,347 women with late-stage breast cancer and 833 with invasive cervical cancer. The project estimated the proportion of each group attributable to potential problems in care delivery, absence of screening and detection, and deficiencies in follow-up. The project team created a model for considering quality issues in cancer care. They also profiled the screening practices, policies, and operational procedures in the eight HMOs and surveyed clinician attitudes about screening policies and practices. For both breast and cervical cancer, the absence of screening accounted for most of the late-stage cancers. The team also identified the characteristics of women among this insured population who were not screened or refused follow-up treatment. Older women were over-represented in both groups, and those refusing treatment tended to have more advanced cancer. Another analysis sought—and did not find—missed clinical opportunities for detection in women with advanced disease whose mammograms were normal. A methodologic comparison of patient self-report data with medical record data showed good congruence when patients reported receiving mammography, but lower congruence for receiving Pap tests. The team also published papers on methods to optimize implementation of physician surveys.

Effectiveness of Early Screening and Prophylactic Mastectomy in Women at Increased Risk for Breast Cancer: Program Testing Early Cancer Treatment and Screening (PROTECTS)

Project PROTECTS, a CRN 1 core project (Dr. Suzanne Fletcher, HPHC, Principal Investigator), evaluated the efficacy of bilateral prophylactic mastectomy (BPM) among women at high risk of developing breast cancer, and of contralateral prophylactic mastectomy (CPM) among women with unilateral cancer, in reducing subsequent breast cancer incidence and mortality. The 269 women who underwent BPM had a significant reduction in breast cancer risk, but approximately 2/3 experienced significant adverse effects. The retrospective cohort study of CPM, conducted in six CRN sites, identified 53,200 women age 18–80 years at diagnosis who developed unilateral breast cancer during 1979–1999. Of these, 1,074 women had CPM. Compared with a sample of 349 women without CPM, these women reduced their risk of contralateral breast cancer by 90 percent. After adjusting for breast cancer characteristics and

Managed care research networks have several potential advantages for studying questions about cancer care in older women. First, access to care is removed from the equation in survival outcomes. Second, they include large proportions of the population from almost all regions of the United States, providing an alternative universe for population-based studies. Third, the availability of computerized administrative databases linked to laboratory and pathology data and often electronic medical records allows careful delineation of disease and interventions and comprehensive, cost-efficient long-term follow-up. Thus, this network provides high-quality data for observational research and can fill critical gaps in our knowledge, especially in situations where large-scale clinical trials are not likely to be mounted.

Mandelblatt J. *To Screen or Not to Screen Older Women for Breast Cancer: A New Twist on an Old Question or Will We Ever Invest in Getting the Answers? J Clin Oncol* 2007; 25(21):2991-2.

treatment, the hazard ratios for the relationship of CPM to death from breast cancer, other causes, and all causes were 0.57, 0.78, and 0.60, respectively. The project also evaluated the efficacy of mammography and clinical breast exam in real-world settings. Among their methodologic contributions, this project team developed a computerized approach to medical record abstraction, which has been used in other CRN projects, and also examined the impact of multiple Institutional Review Board (IRB) reviews on the implementation of the study.

Patient-oriented Outcomes of Prophylactic Mastectomy

The Patient-oriented Outcomes of Prophylactic Mastectomy study led by Dr. Ann Geiger, formerly at KPSC and now at Wake Forest University, was funded as an R01 in January 2002. Using the extant prophylactic mastectomy efficacy study cohort of nearly 800 women at six CRN sites (GHC, HPHC, HPRF, KPNC, KPNW, and KPSC), the study gathered both quantitative and qualitative data from women who had undergone either contralateral prophylactic mastectomy (CPM) or bilateral prophylactic mastectomy (BPM), along with a comparison group of a random sample of women with breast cancer who had not undergone the procedure. A mailed survey ascertained: willingness to recommend prophylactic mastectomy; decision satisfaction; breast cancer risk-related stress; body image; and sexual activity. The majority of women undergoing prophylactic mastectomy were satisfied with their decision and reported contentment with their quality of life that was comparable to similarly at-risk women who had not had prophylactic mastectomy. Investigators also examined decision-making roles and what women wished they had known prior to the procedure. The study contributed methods papers on the validity of race prior to ethnicity data in medical records, and the impact of multiple IRB reviews on study operations and response rates. Collectively, these data provide a rich picture of women's medical and emotional needs as they undertake this profound decision.

Pilot Study of Organizational Barriers to Cancer Clinical Trial Participation by HMOs

This study, led by Dr. Carol Somkin (KPNC), used surveys and semi-structured interviews to investigate attitudinal and organizational barriers to clinical trial participation. A self-administered survey to oncologists at 10 CRN sites was fielded in 2001; 198 completed questionnaires were received, with a response rate of 90 percent. The team also conducted key informant interviews with health plan and oncology leaders at nine CRN sites to explore extant strategies and barriers to plan member participation in cancer trials.

The survey results revealed considerable enthusiasm for clinical trials, but also a critical need for infrastructure to support trials, especially additional support staff and research nurses. In addition, the need was expressed for better intra-organizational communication and consideration of the impact of trial design on internal health plan resources. This work led to a recent NCI R01 grant award for Dr. Somkin's team to evaluate the

effectiveness of increasing clinical trial participation using a tailored telephone counseling intervention for patients in addition to a system to notify oncologists about their potentially trial-eligible patients.

Pilot Study of Disenrollment among Cancer Patients in HMOs

The pilot study was conducted through an administrative supplement to assess turnover among HMO enrollees with cancer diagnoses—and how it may affect longitudinal cancer research. The Principal Investigator, Dr. Terry Field (MPCI), and colleagues studied the retention rates among survivors of the 132,580 patients diagnosed with cancer from January 1, 1993 through December 31, 1998 who were enrolled at five CRN HMOs. Enrollees were followed from cancer diagnosis through death, disenrollment, or the end of follow-up (December 31, 1999). The retention rate among survivors for all cancers combined at one and five years after cancer diagnosis was 96.0 percent and 83.9 percent, respectively. The proportion of enrollees diagnosed with cancer who remained enrolled and available for evaluation suggests that the CRN is well-suited for studies of the quality of care for cancer patients, survivorship, and long-term outcomes. This study led to the CRN Cancer Outcomes Cohort 1993–1998 Study that has published two manuscripts, both focused on racial disparities in cancer care and survival.

Breast Cancer Treatment Effectiveness in Older Women (BOW)

Dr. Rebecca Silliman at Boston University leads this large-scale cohort study of the care and outcomes of 1,859 older women with breast cancer at six CRN sites. By reviewing medical records and using administrative data, information was collected on initial surgery, adjuvant treatments, long-term surveillance, and recurrence and mortality outcomes. The study compared the effectiveness of different treatment and surveillance patterns, and identified the characteristics of providers, tumors, and patients associated with various treatment choices. Findings confirm that increasing age is associated with lower probability of receiving recommended therapy, and with worse survival.

CRN 2 Scientific Accomplishments

Making Effective Nutritional Choices for Cancer Prevention (MENU)

This CRN 2 core study, led by Dr. Christine Cole Johnson (HFHS), developed and evaluated an individually tailored, Web-based program to promote daily fruit and vegetable (F&V) consumption. Focus groups and a preliminary enrollment/retention study tested the feasibility of a Web-based dietary intervention program. The efficacy of the intervention was tested in a multi-site, randomized trial involving five CRN HMOs. The three strategies tested in the trial were: untailored Web program, tailored Web program, and tailored Web program plus email support. A diverse sample of adults enrolled (n=2,540), and the online intervention was shown to be effective. All three intervention arms showed early and sustained increase of more than two servings of F&V, on average. The untailored Web program arm was less effective than either the tailored arm or tailored plus email support arm. Across arms, those participating online at a higher rate had more gain in F&V servings, the retention rate was high (>80% at 12 months) and reported satisfaction with the online program was high. Further analyses will explore the effect of participants' demographic characteristics, family history of cancer, and stage of change on dietary behaviors at 3, 6, and 12 months.

Clinical and Pathologic Predictors for Recurrence after Ductal Carcinoma *in situ*

In this CRN 2 core project led by Dr. Laurel Habel (KPNC), investigators at three CRN sites (KPSC, HPHC, and KPNC) are studying clinical and pathologic factors that could be used to accurately identify DCIS patients at high and low risk of a recurrence. From medical records, investigators have identified DCIS patients (n=3,700) diagnosed between 1990 and 2001, treated with breast-conserving surgery (BCS) and followed for recurrence. Standardized reviews of diagnostic slides from the initial tumors of cases and controls have been completed by collaborating expert

pathologists at Beth Israel Deaconess Medical Center. Immunohistochemistry testing for several markers also has been completed. Initial results indicate that presence of flat epithelial atypia (FEA) is associated with several pathologic features in DCIS. Preliminary data indicate that rates of recurrence after BCS for DCIS have been declining as treatment with adjuvant radiotherapy and tamoxifen have increased; use of adjuvant treatment does not appear to differ markedly across racial/ethnic groups; and surveillance mammography after BCS for DCIS declines over time and becomes inadequate. This is the largest and most comprehensive study to date on prognostic factors for DCIS, and will improve our understanding of the natural history of DCIS and help in the development of individually tailored treatment strategies for patients with DCIS. This study also serves as a model of a CRN project that leverages the unique electronic and biologic data available in the CRN health plans.

Using Electronic Medical Records to Measure and Improve Adherence to Tobacco Treatment Guidelines in Primary Care (HIT2)

Electronic medical records (EMRs) offer an attractive method for evaluating guideline implementation and improving quality of care for entire patient populations. This CRN 2 study (HIT2), led by Dr. Victor Stevens of Kaiser Permanente Northwest, developed a method for coding tobacco-cessation activities (the "Five A's") in four HMOs using EMRs. In addition to data from coded fields (e.g., check boxes, standardized diagnosis and treatment codes, and prescriptions), information entered in free-text fields (e.g., progress notes) was coded using MediClass, a natural language processing program. The HIT2 investigator team evaluated the accuracy of MediClass in assessing whether clinicians adhered to the national tobacco treatment guidelines (the "Five A's") with patients. Specially trained medical records abstractors at each of the four participating HMOs manually coded 500 records according to whether or not each of the five guidelines for smoking cessation care were addressed during routine outpatient visits. For each patient's record, they compared the presence or absence of each of the guidelines as assessed by each human coder and by MediClass. MediClass performed as well as the human abstractors and was found to be a practical method for assessing adherence to the tobacco treatment guidelines in primary care.

Multicenter Study of Pancreatic Cancer Etiology

The Pancreatic Cancer Investigation: Finding Causes (PACIFIC) study is a large case-control study with recruitment based in two CRN HMOs (GHC and KPNC) with infrastructure to support ultra-rapid case identification as patients move through diagnostic evaluation. Led by Drs. Margaret Mandelson and John Potter of GHC and the Fred Hutchinson Cancer Research Center (FHCRC), and by Dr. Stephen Van Den Eeden of Kaiser Permanente Northern California, this study's methods allow researchers to enroll patients who represent the full spectrum of disease, including those typically omitted from prior epidemiologic research because of death shortly following diagnosis. Data collection consists of interview, biospecimen collection, and medical record review. With an anticipated recruitment of approximately 1,500 cases and controls, this is one of the largest and most comprehensive epidemiologic studies of pancreatic cancer undertaken to date.

Is Stroke a Late Effect of Chemotherapy?

This R01 grant, led by Dr. Ann Geiger of Wake Forest University, seeks to explore the hypothesis that chemotherapy may increase the risk of stroke for years after completion. The study team will estimate the relative risks of stroke due to chemotherapy among a group of over 30,000 ethnically diverse patients diagnosed from 1994 to 2003 with bladder, female breast, colorectal, Hodgkin's lymphoma, adult leukemia, multiple myeloma, non-Hodgkin's lymphoma, and ovarian cancers, adjusting for age, gender, race/ethnicity, anatomic cancer site, stage at diagnosis, year of diagnosis, receipt of radiation therapy, and dispensed medications for hypertension, diabetes, anti-coagulants, and tamoxifen (for breast cancer only).

NEW DIRECTIONS FOR CRN 3

CRN 3 priorities emphasize further development of the research infrastructure; increasing collaboration with external researchers, research institutions, and networks outside the CRN member organizations; increasing support for junior investigators; expanding research on the dissemination and impact of new cancer prevention and treatment modalities; and investigating strategies for increasing enrollment in clinical trials. In addition to comprehensive infrastructure enhancements, a significant proportion of CRN 3 funds in each year have been set aside to support pilot projects. The goal of the pilot program is to enable investigators in the CRN and collaborating institutions to produce information that will enhance innovative grant proposals.

Health Literacy and Cancer Prevention: Do People Understand What They Hear?

Principal Investigator:
Kathleen Mazor, Ed.D. (Meyers Primary Care Institute)

Participating sites: Meyers Primary Care Institute, Group Health, Kaiser Permanente Hawaii, Kaiser Permanente Georgia

This study proposes to develop a test to assess comprehension of oral (i.e., spoken) messages about cancer prevention and screening, to examine the relationship between health literacy and cancer prevention, and to test whether changing oral messages can improve comprehension. Findings will lay the foundation for future research into the prevalence of inadequate oral health literacy; identification of groups and individuals with inadequate comprehension skills; identification of risk factors and causes of limited comprehension; and development and evaluation of interventions to improve comprehension of orally transmitted messages. The study team will use both quantitative and qualitative methods to identify the factors that affect comprehensibility of oral messages about cancer prevention and screening. The project will develop recommendations for modifying oral messages so that they are easily comprehensible, and will test the impact of specific enhancements in a randomized experiment.

Economic Burden of Cancer

Principal Investigator: Mark Hornbrook, Ph.D. (Kaiser Permanente Northwest)

Participating sites: Group Health, Henry Ford Hospital and Health System, Kaiser Permanente Colorado, Kaiser Permanente Northwest

This two-year infrastructure pilot study will use data from four sites to estimate the cancer-related pharmacy costs among aged Medicare HMO beneficiaries who were omitted from SEER-Medicare data due to the exclusion of outpatient medication use/cost. The investigative team will test the hypothesis that SEER-Medicare data undercount the full economic burden of cancer care in the U.S., because of incomplete coverage of outpatient prescribed medications for aged Medicare beneficiaries. A byproduct of this research will be the development of a reusable infrastructure that will enhance the CRN VDW for other uses, including efforts focused on the dissemination of pharmacotherapy among cancer patients. This pilot study complements the R01 project, Medical Burden of Cancer: System and Data Issues.

Cancer Prevention Index: Using Electronic Records to Improve Cancer Prevention

Principal Investigator: Tom Vogt, M.D., M.P.H. (Kaiser Permanente Hawaii)

Participating sites: Kaiser Permanente Hawaii, Kaiser Permanente Northwest

This two-year pilot study will use the Prevention Index methodology and the CRN VDW to develop and apply a set of Cancer Prevention Index (CPI) metrics to assess the quality of primary and secondary preventive care for cancer. The study will identify retrospectively the variation in CPI scores across clinics and clinical practices, and determine the association of these variations to selected event rates several years later, to evaluate the association of clinician adherence to guidelines to subsequent events among their patients. The study will assess the CPI for secondary prevention (i.e., screening for breast, cervical, colorectal, and prostate cancers), and relate this index to stage at diagnosis, survival, and medical care utilization with 5- and 10-year follow-up for all persons by practice-level performance. The study will explore how variations across practices in intervals between testing and percent of eligible persons tested relate to these outcomes, and will conduct preliminary analyses on the CPI primary prevention measures and their relation to outcomes. The pilot study will inform the development of an R01 that will assess the CPI measures in multiple health systems to relate practice-level variations in the scores of morbidity, mortality, and cost outcomes. A complementary CPI study that incorporates preventive practices relevant to cardiovascular disease was recently funded as part of the newly initiated Cardiovascular Research Network, sponsored by the National Heart, Lung, and Blood Institute.

CRN DEVELOPMENTAL PILOT FUNDS

NCI awarded the CRN a developmental pilot fund program to be funded through April 2012. The program invites the submission of proposals for pilot activities that are consistent with the CRN's scientific priorities and leverage unique features of the CRN. The expectation is that the funds invested in this activity lead to a fundable proposal. Pilot activities involve at least one CRN site and have the potential to lead to research projects that involve two or more CRN sites. All investigators from within the 14 CRN sites are eligible to submit proposals. The CRN also welcomes new collaborations, including investigators who are not employed by a CRN site. There is a call for new pilot proposals each year.

THE CARDIOVASCULAR RESEARCH NETWORK

In December of 2006, the National Heart, Lung, and Blood Institute issued an RFA for a Cardiovascular Research Network (CVRN), with the goal of increasing scientific knowledge of cardiovascular diseases, including their epidemiology, risk and risk factors, prevention, detection and diagnosis, treatment, and prognosis, in the context of community-based health care delivery, the environment in which most clinical and preventive care is delivered. The RFA further stated that the research should be designed to take advantage of existing integrated data systems, and use complementary resources for collaborative activities relevant to the goal.

A cooperative agreement grant totaling $7.5 million was awarded to an HMO-based CVRN lead by Dr. Alan S. Go, of the Kaiser Permanente Division of Research in Oakland, California. In addition to the Kaiser Permanente Division of Research in Oakland, research collaborators span most of the CRN sites as well as other external organizations.

Initial CVRN research projects include:

- A study of hypertension recognition, treatment, and control
- A study of quality of care and outcomes of the blood thinner, warfarin, for atrial fibrillation and blood clots
- A study of the use, outcomes, and costs of implantable cardiac defibrillators for primary prevention of sudden death in heart failure.

Most collaborating research organizations in the HMO Research Network are participating in both the CRN and the CVRN. Through these common links, the CRN and the CVRN will have many opportunities to coordinate research activities of mutual interest, share complementary research infrastructure and expertise, and work to create creative synergy between the two networks.

To me, the CRN has provided unparalleled opportunities to test systems interventions on important cancer outcomes and cancer health disparities. I have had the opportunity to work and partner with investigators at various levels of experience, develop mentoring relationships with renowned investigators, and build collaborative relationships. The combination of data resources, systems to support the development of new investigators, and the academic partnerships has made it possible for me to train and grow as an investigator.

Chyke Doubeni, M.D., M.P.H.
University of Massachusetts Medical School, Meyers Primary Care Institute

PROGRAM FOR JUNIOR INVESTIGATORS

A research network should nurture and develop new talent. The CRN is currently extending its informal mentoring to include the systematic development of junior investigators, through a newly established CRN Investigator Development Core. This Core has two components: a one-on-one mentoring of 28 CRN Scholars (two groups of 14) over the five years of the grant cycle, and group sessions, including biweekly conference calls and in-person meetings at annual meetings of the CRN. An ultimate aim is to lead those investigators to develop successful grant applications and author papers published in peer-reviewed journals. The faculty leaders of the new CRN program for junior investigators are Drs. Suzanne and Robert Fletcher. Both are active in CRN, Suzanne as Site Principal Investigator of HPHC and Project Leader of the CRN 1 PROTECTS project, and Robert as Co-Principal Investigator of the CRN component of the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS) project. The Fletchers have extensive experience in research investigator development. Other senior CRN investigators participate in the program to expose participants to leaders in cancer research beyond those at their home institutions, and to increase the breadth and depth of expertise available to them.

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