Examples of Funded Grants in Healthcare Delivery Research

Overview
The National Cancer institute (NCI) frequently receives requests for samples of funded grant applications. Several investigators and their organizations agreed to let the Healthcare Delivery Research Program (HDRP) post excerpts of their healthcare delivery research grant applications online.

About
We are grateful too the investigators and their institutions for allowing us to provide this important resource to the community. We only include a copy of the SF 424 R&R Face Page, Project Summary/Abstract (Description), Project Narrative, Specific Aims, and Research Strategy; we do not include other SF 424 (R&R) forms or requisite information found in the full grant application (e.g., performance sites, key personnel, biographical sketches). To maintain confidentiality, we have redated some information from these documents (e.g., budgets, social security numbers, home address, introduction to revised application).

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424 R&R and PHS-398 Specific
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SF 424 R&R Face Page

PI: CARROLL, NIKKI

Grant Number: 1 R50 CA251966-01

Title: Natural History of Lung Cancer Diagnosed Within and Across Diverse Health Systems Implementing Lung Cancer Screening

FOA: PAR-19-290

FOA Title: NCI Research Specialist (Core-based Scientist) Award (R50 Clinical Trial Not Allowed)

Organization: KAISER FOUNDATION RESEARCH INSTITUTE

Senior/Key Personnel: Nikki Carroll MS

Organization: Kaiser Foundation Hospitals

Role Category: PD/PI

Project Summary/Abstract
The goal of this application is to support Nikki Carroll, MS, as a Research Specialist and Biostatistician at Kaiser Permanente Colorado Institute for Health Research. She supports the Cancer and Genomics Research Core under the direction of Debra Ritzwoller, PhD. The core of Ms. Carroll's productive and successful career as a Research Specialist and Biostatistician is in cancer-related treatment patterns and outcomes. This Research Specialist award would allow 5 years of funding to maintain protected time for Ms. Carroll to work exclusively on supporting and leading cancer research aimed at generating real-world evidence on cancer care that occurs outside of clinical trials. In particular, she will study the treatment patterns and risk of recurrence among those with screen detected lung cancer compared to lung cancers diagnosed outside of screening. These results could impact prognostic estimates, treatment choices, and future trials to develop tailored treatment and surveillance regimens for early-stage, screen-detected lung cancer patients and set the foundation for future studies of the natural history of lung cancer screening in community settings. Results will be broadly disseminated through local and national meetings as well as peer-reviewed journal manuscripts.

Project Narrative

Nikki Carroll, MS, supports the Cancer and Genomics Research Core at the Kaiser Permanente Colorado Institute for Health Research. Her work has made significant contributions to translational research in cancer treatment patterns and outcomes that occur in real world clinical settings (as opposed to clinical trial settings). Support from this award will allow her to continue her focus in cancer research with an emphasis on treatment and risk of recurrence in the context of screen-detected cancers.

Research Strategy

A. SIGNIFICANCE

A.1 Personal motivation and cancer research experience. My career began during graduate school when I worked in one of the top-rated Cystic Fibrosis clinics in the Rocky Mountain region. This is where I did my first outcomes analyses and statistics on health care data, and it cemented my passion for health services research that exists to this day. Soon after completing my Master's degree in Biometrics in 1994, I moved to Kaiser Permanente Colorado (KPCO). I started working in the Pharmacy Department as a pharmacy analyst and obtained a certificate in pharmaceutical economics. During this time, I learned the intricacies of pharmacy data and how different drugs are used to treat a variety of diseases. My work with pharmacy data developed my proficiency in large, complex databases as well as a love for the convolutions of pharmacy treatment data. This led to a first-author publication[1] as well as being the lead statistician for multiple projects.[2-7]

For the last 17 years, I have been a biostatistician in the Institute for Health Research (IHR) within KPCO. It was on a project in 2005 that I fell in love with cancer research. I was so excited by the challenge of correctly identifying patients diagnosed with cancer, learning how data were abstracted to populate the Tumor Registry, and linking these patients to their outcomes in different data sources including claims and electronic health (EHR) data. I participated in multiple studies in cancer health services and epidemiology research and developed my expertise in cancer tumor registry data and understanding treatment data.[8-12]

In 2012, the IHR created the Cancer and Genomics Research Core (C-Gen Core) with Dr. Debra P. Ritzwoller as a co-director. This research core serves to coordinate cancer and genomics research activities of both the IHR and the KPCO region. C-Gen is supported by a small amount of internal funds and multiple NCI-funded projects with the goal of advancing the field of cancer research conducted in real world clinical and community settings (described in detail in section C). I supported many of these NCI-funded grants as a biostatistician. My analytical expertise is in survival, logistic, Poisson analyses, and propensity score methods. However, it was the challenge of characterizing the systemic treatment history of patients diagnosed with cancer that attracted me to building logic and code-based algorithms. I created an algorithm (the Systemic Therapy Algorithm) that characterizes specific regimens in the course of treatment a patient receives for cancer.[13] This algorithm also includes cycles of each regimen and the total drug dose within each course of therapy (see section E.3.1).

The Systemic Therapy Algorithm was a pre-cursor to the collaborative work associated with the development of algorithms to detect recurrent cancers (i.e., metastatic cancer that develops after successful definitive therapy for earlier stage disease).[14-17] I contributed to the Recurrence Detection and Timing Algorithm (Recurrent Algorithm) by sharing my knowledge of cancer treatment data, along with ongoing work in algorithm development (see section E.3.2).

Over the last 5 years I have collaborated on studies where I developed an expertise in applying these 2 algorithms in large, complex multi-site databases.[18-25] This has helped me to understand how the algorithms and codes that support them work when applied to different cancer settings and databases. Research in cancer related treatment patterns and outcomes have become the core of my career as a biostatistician, and I look forward to taking that research to the next level.

A.2 Overarching significance of project goals. As detailed above, through my research support of the CGen core, I have made significant contributions to the field of cancer-related treatment patterns and outcomes, and with support from this award I propose to continue and expand my contributions, particularly in the field of lung cancer research. Lung cancer is an

urgent public health challenge, as noted by the Surgeon General.[26-28] It is potentially preventable, yet, it is the single largest cause of cancer death in the US and only 18% of patients survive >5 years after diagnosis.[27,29]

The National Lung Cancer Screening Trial (NLST) reported that screening with low-dose computed tomography (LDCT) reduced lung cancer mortality by 20% in people at increased risk.[30,31] In response the US Preventive Services Task Force recommended yearly screening LDCT for 55- to 80-year-old adults with 30+ pack per years of smoking who had not quit for more than 15 years.[32] Although health systems across the country have implemented Lung Cancer Screening (LCS), little is known about whether this may disrupt the natural history of lung cancer. Also unknown is how treatment patterns and risk of, and time to, recurrence may differ in those with screen-detected lung cancer compared to lung cancers detected outside of the screening setting. Based on studies of cancers from other organ sites, screen-detected cancers are also subject to overdiagnosis, lead time bias, and the detection of slow-growing, less aggressive tumors.[33-37] Therefore, uncertainty exists regarding the risk of patients diagnosed with early-stage screen detected cancers to develop a recurrent cancer, and very few community-based LCS programs have the ability to detect lung cancer recurrence and time to recurrence. Moreover, given the comorbidity profile of patients eligible for LCS, little is known regarding both treatment and survival patterns for patients diagnosed with screen detected lung cancer. Thus, ***the primary goal of this proposal is to understand treatment patterns and recurrence rates in screen-detected lung cancers***. To accomplish this goal, I propose the following objectives:

- Compare systemic therapy treatment patterns among patients diagnosed with screen-detected lung cancer to patients diagnosed outside of screening
- Examine the variation in recurrence and time to recurrence among patients diagnosed with screen-detected lung cancer compared to patients diagnosed outside of screening
- Among lung cancer patients with recurrence, compare the median time to recurrence, stage-distribution at initial diagnosis, and post-recurrence survival between patients whose original primary lung cancer was screen-detected to those diagnosed outside of screening

B. INNOVATION

I will complete these objectives through leveraging and extending the existing resources and data infrastructure of the C-Gen Core and the NCI-funded Population-based Research to Optimize the Screening Process (PROSPR) consortium. Specifically, I will work within the Lung PROSPR Research Center (PRC; U24CA171524: Principal Investigator Debra P Ritzwoller (MPI with Anil Vachani); http://www.optimizelungcancerscreening.org/) and use real-world data (as opposed to trials data) to address major gaps in knowledge about the treatment and recurrence of screen-detected lung cancer. The Lung PRC has pooled and harmonized data from 5 diverse health systems into a Common Data Model that contains data on over 1.8 million individuals age 35-89 receiving care at the five health systems, including 9,500 lung cancer patients diagnosed from 2014-2018. Four of the five health systems used the NCI- and CRN-supported Virtual Data Warehouse (VDW) to compile this data. The VDW contains data that links EHR, billing, and claims data for each health system's members. Specifically, it contains Tumor Registry data with extensive information on cancer diagnoses, and tumor characteristics; infusion data that contains specific drugs related to infused systemic therapy; and all outpatient pharmacy dispenses that captures oral therapies. The VDW also captures all procedures, diagnoses, and utilization for all members. These 5 health systems began to implement LCS programs during or before 2014 and have completed more than 10,300 baseline LCS LDTCTs. These longitudinal screening results can be linked to all data within the Common Data Model.

The results of the proposed research will inform future studies aimed at developing tailored treatment and surveillance regimens for screen-detected lung cancer and thereby have the potential to lead to significant improvements in the management of the growing numbers of patients diagnosed with screen-detected lung cancer.

My proposed work will extend the scope of, but not overlap with, the current aims and analyses proposed within the Lung PRC. *My proposed work will be the first to look at treatment and recurrence of lung cancers identified through LCS*. Using the Common Data Model will allow for an innovative and efficient application of both the Systemic Therapy and Recurrence Algorithms that will enhance my ability to successfully conduct the goals proposed under this award.

C. APPROACH

C.1 KPCO Cancer and Genomics Core (C-Gen Core). KPCO formed the C-Gen Core to develop strong expertise in cancer research, to enhance collaboration, and to promote translational cancer research. The CGen Core includes investigators, project managers, research assistants, programmers, and biostatisticians who all work towards advancing cancer prevention and treatment. The C-Gen Core has a long history of over 45 NCI-funded research projects and has made significant contributions through providing real-world evidence in cancer research. A subset of the key research projects related to this proposal are listed in Table 1. The CGen
Core continues to have a strong NCI-funded research portfolio and collaborates with a wide network of institutions that are recognized for their excellence in cancer research, including: The Cancer Research Network (CRN), University of Colorado Cancer Center, The Fred Hutchinson Cancer Research Center, Data Farber Cancer center, Abramson Cancer Center, the KP Center for Effectiveness and Safety Research (CESR), and NCI. See attached Letters of Support.

Since its inception, I have supported the C-Gen Core as a biostatistician and the NCI-funded grants noted in Table 1. My specific key accomplishments include, but are not limited to, the REACT project, where I implemented the Systemic Therapy Algorithm and assisted in the development of the Recurrence Algorithm. Under the Recurrence project, I updated the Recurrence Algorithm to be adapted to current ICD10 data coding During the last CRN funding cycle, I served as an analyst on the Lung Cancer Screening Pilot project and as a key contributor to the Infusion working group that led the implementation of the Infusion tables across all CRN health systems. As part of the validation work, I also disseminated the Systemic Therapy algorithm SAS-based code using the newly implemented Infusion tables to all CRN health systems to capture first line therapy for colorectal cancer. This last task demonstrated proof of concept that all CRN sites, including the 4 former CRN sites involved in the Lung PRC, could in fact, capture cancer related systemic therapy.

Table 1. Key C-Gen Core NCI-funded Research

Award Number	Principal Investigator(s)	Award Title	Start and End Dates
U24CA171524	Ritzwoller/Vachani	Center for Population-based Research to Optimize the Screening Process (PROSPR). Center for Research to Optimize Precision lung Cancer Screening in Diverse populations (**Lung PRC**)	05/01/2018 – 03/31/2023
R01CA218429-01	Rohan	Molecular Markers of Risk of Subsequent Breast Cancer in Women with Ductal Carcinoma in Situ	09/15/2017 – 07/31/2022
RSG-18-097-01-CPPB	Hassett	Disparitiies in Recurrence among Patients with Breast, Lung, and Colorectal Cancer (**Recurrence II**)	07/01/2018 – 06/30/2021
R01CA172143-01	Ritzwoller/Hassett	Cancer Recurrence: Detection in Administrative Data, Incidence, and Costs (**Recurrence**)	03/01/2013 – 02/28/2019
UG1CA189821	Fehrenbacher	Kaiser Permanente NCI National Community Oncology Research Program (NCORP)-Cancer Care Delivery Research program (**CCDR**)	08/01/2014 – 07/31/2019
U24CA171524	Kushi	Cancer Research Network: a Research Resource within Health Care Delivery System (**CRN4**)	09/25/2012 – 0831/2017
U54CA163262	Corely/Kushi	Lung Cancer Screening Data Resource Development: (**PROSPR/CRN Lung Cancer Screening Supplement**)	12/01/2014 – 05/31/2016
RC2 CA148185	Ritzwoller/Weeks	Building CER Capacity: Aligning CRN, CMS, and State Resrouces to Map Cancer care (**REACT**)	09/30/2009 – 08/30/2013

C.3 Current contributions and support to NCI-funded C-Gen Core projects. Below are the summaries of
the current support I provide to current NCI-funded C-Gen projects. Through this award, I will be able to
continue to provide support exclusively to cancer-related projects at KCPO and specifically to enhancing lung cancer research through the PROSPR Lung-PRC.

C.3.1 Center for Research to Optimize Precision Lung Cancer Screening in Diverse Populations
PROSPR II Lung [Lung PRC] (NIH/NCI: UM1 CA 221939; Ritzwoller/Vachani [MPI]). My current
contribution to the Lung PRC includes serving as the Data Acquisition Unit (DAU) Lead and DAU Analyst. The primary objective of the DAU is to support and enhance the data and technical resources of the Lung PRC, thereby facilitating the research goals of optimizing the delivery and effectiveness of LCS.

DAU Lead. Within the first 5 months of the Lung PRC, two key DAU programmers resigned from KPCO. Given my prior analytic work on the NCI/Cancer Research Network-funded LCS pilot along with my expertise in using key data sources, *I stepped up to fulfill the role of the DAU Lead to mentor new programmer staff and to keep the project moving forward*. This role included:

- providing oversight and leading programmers across the 5 Lung PRC health systems to efficiently and effectively capture, extract, pool, and harmonize all required multilevel data elements related to LCS processes and outcomes
- supporting the research projects by collecting the relevant data elements on patient, provider, facility, health care system characteristics and patient outcomes that are needed for each project, and working closely with the Lung PRC Biostatistics & Methods core to create and distribute analytic datasets
- developing the processes necessary for the Lung PRC health systems investigators to be able to request data from the Common Data Model to meet project needs (Data Request Process)
- developing and leading tasks for chart abstractors across the 5 health systems to obtain detailed Lung Cancer Screening data from the EHR that was not available via administrative data extracts

My FTE effort was increased to 0.75 (9 CMs) during the first 18 months of the grant to cover tasks previously assigned to former key programmers. The DAU Lead programmer position has now been filled *so I have returned to my original role as a biostatistician at an FTE of 0.50 (6 CMS)*.

DAU Analyst/Biostatistician. Responsibilities for this position include serving in a lead role for the DAU
Biostatistics Core, drafting analytic plans for projects (to include methods, statistical plan, and inclusion and exclusion criteria), pull and compile data from the Lung PRC Common Data Model, analyze data, and draft research manuscripts. If I receive this R50 award, I will specifically expand my contributions to support and lead Lung-PRC analyses and manuscripts related to understanding treatment patterns and recurrence risk of screen-detected lung cancers. Thus, I have provided additional details about the PROSPR Lung-PRC project rationale, aims and scope, below (section D.1).

C.3.2 Molecular Markers of Risk of Subsequent Breast Cancer in Women with Ductal Carcinoma in Situ (NIH/NCI: 1R01CA218429-01; Rohan/Loudig [MPI]). The aim of this study is to identify miRNA expression changes associated with risk of invasive breast cancer among a cohort of women initially diagnosed with Ductal Carcinoma in Situ (DCIS). This is a multi-site study led by Drs. Rohan and Loudig. My role on this project is as an analyst/SAS programmer. I significantly contributed to the definition of DCIS from the tumor registry and interpretation of data exported from the tumor registry. In addition, I saved hours of chart abstraction for additional clinical and demographic data with my expertise and deep knowledge of data within our electronic data systems by electronically pulling multiple variables from our electronic databases that then did not need to be chart reviewed.

C.3.3 Disparities in Recurrence among Patients with Breast, Lung and Colorectal Cancer (ACS: RSG-18-097-01-CPPB; Hassett [PI]). The goal of this project is to use the Recurrence Algorithm and the population-based SEER-Medicare dataset linked to the Rural-Urban Commuting Area code classification scheme to characterize rates of freedom-from-recurrence for three common and lethal cancers: breast, lung, and colorectal cancer. My role on this project is to assist in the implementation of the Recurrence Algorithm in non-VDW sites, using logic and code based on the ICD10 translated Recurrence Algorithm.

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