P10

Project Summary/Abstract:

Across the spectrum of cancer types, outcomes research has demonstrated that the quality of cancer care varies in the United States (US). Understanding this variation and, more importantly, *how to correct it* is the future direction for cancer health services research. This proposal seeks to understand and address the barriers to evidence-based cancer care while providing the career development candidate with a very rich research training and mentorship experience. The research proposal focuses specifically on the quality of surgical care for rectal cancer, which is diagnosed in more than 40,000 Americans each year. There is strong evidence linking the use of evidence-based surgical practices with improved outcomes for this disease. However, variation in the use of evidence-based practices and treatment outcomes for rectal cancer has been demonstrated, suggesting opportunities to improve the quality of care. The proposal's research aims include (1) assessing hospitals' compliance with evidence-based practices for rectal cancer, within the setting of an existing surgical quality-improvement organization; (2) qualitatively assessing barriers to uptake of evidence-based practices; and (3) designing and evaluating an intervention to increase use of evidence-based practices. This project, the multidisciplinary mentorship team, and the research environment are ideally suited to address the career goals and educational needs of the candidate, [redacted] is a board-certified colorectal surgeon with a clinical and research interest in colorectal neoplasms. Her prior research experience with measuring cancer outcomes and interventions to optimize cancer care has prepared her for this proposal. However, to achieve her career goal of improving colorectal cancer care through hospital-based quality-improvement programs, she will need additional training. Educational goals, including obtaining expertise in implementation science, advanced statistical methods for comparing hospital performance, and organization of collaborative programs, are feasible with the grant's educational plan and highly accomplished mentorship team. The educational program includes graduate-level courses in qualitative methods, hierarchical modeling, and health communications, as well as travel to centers of excellence and relevant national conferences. In summary, this research project, mentor team, and educational plan will lay the groundwork for [redacted] to perform ongoing, innovative, independent research to improve colorectal cancer treatment and outcomes.

Project Narrative

This proposal will measure variation in evidence-based practices for rectal cancer care, provide understanding of barriers to evidence-based practice via qualitative study of cancer surgeons, and implement an intervention to improve uptake of evidence-based practices through an existing healthcare quality organization. These results will have immediate impact on the understanding of best strategies for increasing implementation of evidence to decrease unwanted variation in cancer care.

	Reviewer 1	Reviewer 2	Reviewer 3
Candidate	3	1	2
Career Development	3	3	5
Research Plan	3	3	2
Mentors	3	3	1
Environment	3	1	1

1. INTRODUCTION TO THE REVISED PROPOSAL

Enclosed please find our revised proposal, "Improving Rectal Cancer Surgery Through Regional Collaboration." It was reviewed June 2011 and received an impact score of 35. Reviewers noted several strengths of the application including an "important and innovative" research proposal, an "outstanding" candidate, and environment. However, they identified several areas in which the grant could be improved. These critiques allowed us to strengthen this revised submission (changes highlighted with *italics* and a line in the right margin). Revisions included:

1. ***We have strengthened the career development plan.*** All reviewers indicated a need for additional details on the candidate's schedule and educational conferences, which have been provided in new tables. In response to comments from Reviewer 1, we have clarified the links between the candidate's prior research, career goals, and this proposal. Although Reviewer 3 correctly notes the unique challenges for surgeon-scientists, the [redacted] has an outstanding track-record in developing surgical health services researchers, by providing them with the support required. To ensure the success of this proposal, we worked with the Chief of General Surgery at the [redacted], to devise a plan for specific actions: (1) a decrease in clinical hours; (2) "coverage" of the candidate's patients/pager by other surgeons during critical academic activities; and (3) decreased teaching responsibilities (new letter enclosed).

2. ***The mentorship team has been streamlined.*** Although the Reviewers were generally complimentary regarding the mentors' skills, they noted potential downsides of coordinating a large mentorship team. In response, we have streamlined the team. Core mentorship will be provided by [redacted], the primary mentor, and co-mentors [redacted] and [redacted]. Co-mentors [redacted] will provide specific domain expertise in analytic methods and qualitative research. Mentors' roles and the planned schedule of meetings with the candidate have been clarified, including group meetings annually.

3. ***The candidate's leadership role in the MSQC organization has been made more explicit.*** Reviewers 1 and 2 expressed concern that the candidate may not have adequate authority within the MSQC organization to truly direct the proposed research. Since the original submission of this proposal, the MSQC organization has created a "cancer surgery initiative", of which the candidate has been promoted to Co-Director. As such, the candidate now has primary oversight in designing the data collection template for all colorectal cancer cases in the MSQC (organizational chart included in the Appendix). Letters from [redacted] reinforce that the proposed project has been designed (with mentorship) by the candidate, and will be executed by the candidate. In addition to having authority to conduct the research plan, we responded to Reviewer 3's question about adequacy of resources by confirming that the MSQC organization has funding for audit and feedback, electronic and written educational materials/videos, quarterly face-to-face meetings of surgeons, surveys, site visits, and visits by international experts to the MSQC meetings. As with other MSQC-led quality improvement initiatives, any other costs would be expected to be covered by participating hospitals.

4. ***Support for proposed quality measures has been provided, and research plans have been clarified.*** The reviewers commented that this proposal addresses an important issue in the quality of cancer care, is innovative and "exciting", and builds on existing resources. However, reviewers 1 and 2 requested additional details about several issues. Four of the five "evidence-based practices" that will be measured are accepted quality indicators (adjuvant therapy and the 12 lymph node standard are NQF measures; total mesorectal excision and margin negativity are NCCN clinical practice guidelines), while utilizing sphincter preservation whenever possible is generally accepted. The training of the data abstractors has been performed through regional and national training programs, and data quality is regularly audited [redacted]. Abstractors will be trained on new cancer-specific factors by MSQC staff under the direction of the candidate. Finally, it is clarified that *all* hospitals that perform rectal cancer surgery will be targeted for intervention in Aim 3, and the timeline and case numbers expected are spelled-out in a new table.

5. ***A model for barriers to evidence-based practice has been added to Aim 2.*** Reviewer 3 raised the important point that factors responsible for whether or not a hospital provides evidence-based care are complex. To prepare for this effort, we have conducted several exploratory interviews with surgeons and have produced a preliminary model of barriers to evidence-based practice that aligns with the work of [redacted] This framework will help to guide initial interviews and qualitative analysis (see new table).

2. CANDIDATE'S BACKGROUND

The goal of this grant application is to provide me with the knowledge, skills, and mentoring to become a leading researcher in the field of cancer surgery quality of care. My interest in this field developed over the last 9 years. I began medical training at [redacted] Medicine, and went on to an academic general surgery residency at the University of Pennsylvania. During my colorectal surgery fellowship at the [redacted] I developed an interest in clinical research under the mentorship of [redacted]. This led to publications in the field of quality of life and sexual functioning for rectal cancer patients.

My first faculty position was at the [redacted], where I was the first board-certified colorectal surgeon and served as acting chief of colorectal surgery. I quickly developed a busy clinical practice focused on colorectal neoplasms. I became a member of the Cancer Center, and was appointed to the multidisciplinary Cancer Committee, which focuses on quality of care. Subsequently I have been appointed to committees of the American Society of Colon and Rectal Surgeons focused on quality of care. These experiences gave clarity to my academic mission: *to improve the quality of care for colorectal cancer.* However, I quickly recognized the need for formal training in clinical research methodology. Thus I applied to the Masters' of Public Health program at the [redacted] completing the MPH degree in 2009. During this time, I was fortunate to begin a collaboration with health services researchers [redacted], [redacted] and became the Co-PI of a National Cancer Institute-funded randomized trial of patient navigation in cancer care. This multidisciplinary collaboration led to a number of publications on the topic of cancer health disparities. I later became co-investigator for a randomized intervention trial to improve cancer screening. These trials gave me a foundation in intervention studies.

In 2009, I was recruited by the department of surgery at the [redacted], a position which offered me the opportunity to develop my research career within the Center for Healthcare Outcomes and Policy (CHOP), led by [redacted]. A primary interest of CHOP is regional, collaborative quality improvement. In 2010, I became involved with the [redacted] Surgical Qualitative Collaborative, a 34-hospital quality improvement group. This inspired the current research proposal, in which the concept of regional collaboration for quality improvement will be adapted to cancer surgery. To date, my research with CHOP has consisted of studies assessing compliance with quality standards. *This proposal goes beyond performance measures to the next step---designing and implementing strategies for quality improvement.*

As summarized in Table 1, my prior research has focused on colorectal cancer, with specific projects assessing patient-centered outcomes, interventions for cancer health disparities, and the connections between evidence-based practices, surgical complications, and quality of care. These research projects show the important role cancer *surgeons* have in determining both short-term and long-term patient outcomes.

Table 1. Summary of Research Experience

Research Topic	Selected Publications
Patient-Centered Outcomes of Colorectal Cancer Surgery	• *Prevalence of male and female sexual dysfunction is high following surgery for rectal cancer. *Annals of Surgery* 2005 • The Impact of Surgery for Colorectal Cancer on Quality of life and Functional Status in the Elderly. *Diseases of the Colon and Rectum* 2006.
Cancer Health Disparities	• *A New Model of Patient Navigation to Reduce Cancer Health Disparities. *BMC Cancer 2010* • *Patients' Barriers to Receipt of Cancer Care, and Factors Associated with Needing More Assistance from a Patient Navigator. *JNMA in press* • Racial Disparity in Death from Colorectal Cancer: Dose Vitamin D Deficiency Contribute? *Cancer 2010* • Understanding the Processes of Patient Navigation to Reduce Disparities in Cancer Care: Perspectives of Trained Navigators from the Field. *J Cancer Educ.* 2010 Apr 21. • Get Screened: A Pragmatic Randomized Controlled Trial to Increase Mammography and Colorectal Cancer Screening in a Large, Safety Net Practice. *BMC Health Services Research 2010* • *Patient Navigation from the Paired Perspectives of Cancer Patients and Navigators: A Qualitative Analysis. Patient Educ Couns. 2011*
Adherence to Evidence-Based Care and Surgical Complications	• *Surgical Complications are Associated with Omission of Chemotherapy for Stage III Colorectal Cancer. *Diseases of the Colon and Rectum 2010* • *Prophylactic Antibiotic Practices for Colectomy in Michigan. *American Journal of Surgery 2011* • *Non-Fatal Adverse Events after Colorectal Operations. *Seminars in Colon and Rectal Surgery, in press* • *Early Discharge and hospital readmission after colectomy for cancer. Diseases of the Colon and Rectum 2011.*

*first-author publications

3. CAREER GOALS AND OBJECTIVES

A. Scientific Goals

At the [redacted], I have observed the potential benefits to both patients and practitioners of regional collaboration for healthcare quality improvement. As a result, my background in colorectal cancer outcomes research and intervention studies to improve cancer care has merged with a new interest in strategies for improving care across regional hospital groups. As such, my scientific goals include:

- Creating regional infrastructure for high-quality data collection for cancer quality improvement;
- Understanding barriers to evidence-based practice for colorectal cancer, including both practitioner and institutional factors;
- Informed design and testing of interventions to promote dissemination of high-quality cancer care.

These goals are reflected in the specific aims of this research proposal, which we have designed to serve as both a vehicle for skill development but also to create an infrastructure to support future research.

B. Career Goals

My career goal is to develop into an independent investigator with R01-level research grants, while maintaining a surgical practice caring for colorectal cancer patients. The [redacted] is an outstanding environment for surgeon-scientists with a track record of success and the educational and mentoring opportunities to help me achieve my scientific goals. This career development grant will allow me to take advantage of these opportunities with focused education and mentoring as outlined below. Ultimately I hope to use the scientific and leadership skills from this grant to become a national leader in cancer quality of care research and policy-making. As I progress academically, I also look forward to serving as a mentor to the next generation of clinician-scientists.

4. Career Development/Training Activities During Award Period

Overview: My career goal is to improve the quality of care for cancer patients through hospital-based interventions. In order to achieve this goal, I will need additional training in several specific areas. Most importantly, I will require training in the emerging field of implementation science, including qualitative methods, intervention strategies, organizational behavior, and evaluation. I also will require skills in hierarchical modeling, to account for clustering of patients within hospitals, since valid comparisons between hospitals are integral to this work. I also need mentorship in the organizational and team-building skills that are required for effective administration of collaborative projects. *A plan for career development is provided below.*

A. Mentorship Team

For this grant, we have assembled a highly multidisciplinary team of mentors, including experts in regional collaborative quality improvement, implementation science, and advanced statistical methods. The mentorship team also has extensive experience in research grants and high-impact publications.

Primary Mentor:

[redacted] Associate Professor of Surgery, [redacted] is an epidemiologist and a senior scientist in the University of Michigan's Center for Healthcare Outcomes and Policy (CHOP). [redacted] has published peer reviewed articles on the topics of surgical quality variation, regional collaborative groups as a mechanism for improving quality, and analytic methods for comparing hospitals' performance [1-12]. [redacted] current role as the director of the Michigan Bariatric Surgery Collaborative makes her particularly well-suited to mentor me on this proposal. [redacted] federal research funding includes a recently funded R01 entitled: "Return on Investment for Quality Improvement Collaboratives in Surgery" (AHRQ, PI role), reflecting her research focus on evaluating regional collaboration as a mechanism for effective healthcare quality improvement. Furthermore, [redacted] ongoing intervention study "Optimizing prophylaxis against venous thromboembolism in bariatric surgery" (AHRQ R01, PI role) uses a collaborative quality improvement approach to improve evidence-based practice, with direct applicability to mentoring the proposed study.

Co-Mentors:

[redacted] Professor of Surgery, [redacted] Director of the [redacted] Center for Healthcare Outcomes and Policy at the [redacted] He has a senior-scientist award and has mentored many K award recipients. [redacted] research funding and publications include work in cancer surgery outcomes, analytical methods for comparing hospitals' performance, and regional surgical quality improvement.[2, 4, 6, 13-45]

[redacted], Associate Professor of Internal Medicine, [redacted], and Research Scientist, [redacted] Center of Excellence in Health Services Research and Development: [redacted] is a research scientist whose training included a postdoctoral fellowship in cancer prevention and control at UT-MD Anderson Cancer Center. She conducted an NCI-funded project to evaluate preferences for colon cancer screening, and a subsequent randomized trial of a tailored intervention to improved cancer screening rates. Dr. Hawley has published on the following topics relevant to the current proposal: surgeons' influence on cancer care for breast cancer; factors associated with adherence to evidence-based cancer care practices; urban-rural differences in cancer care; and tumor registry-based research.[46-64]

[redacted] Research Professor of Biostatistics, [redacted] methodologic interests are in hierarchical and longitudinal modeling, survival analysis, and tree-structured regression methods. She has extensive experience collaborating with both junior and senior medicine faculty, including prior published research with me.[65] Relevant to this proposal, she has extensive experience with multilevel modeling in health services research, and teaches a graduate level statistics course on linear and generalized linear mixed models. She also has a special interest in statistical methods for analyzing cancer care and outcomes.[66-74]

[redacted], Professor of Public Health, [redacted] is an expert in qualitative methods, health communications, and behavior change and has extensive, funded research experience. He has published over 190 peer-reviewed articles and book chapters, has served on numerous advisory panels and review groups, and has mentored many young investigators. [redacted] will mentor me in designing the qualitative interviews/analysis and recruiting/training qualitative interviewer(s).

Collaborator:

[redacted] Professor of Surgery, [redacted]

[redacted] is the director of the [redacted], the research setting for this proposal.[75-82] A leader in regional and national surgical quality improvement, he has committed to providing infrastructure support, and to helping me develop leadership skills.

Schedule of Mentors' Meetings

As primary mentor, [redacted] will meet with me weekly for one hour to keep the entire research endeavor on track, including educational activities, the research plan and manuscript and grant preparation. She will also coordinate an annual meeting of the entire mentorship team. [redacted] and [redacted] will each meet with me monthly. As Director of the CHOP research center, [redacted] will ensure I have the resources to complete the research and will help me to plan for high-impact publications and future grants. [redacted] will share expertise on cancer research, implementation science and intervention studies, and will help me increase my involvement in the implementation science research group at the [redacted] and in the [redacted] research community. [redacted] will meet with me frequently during phases of the research that require analysis, and she will ensure I remain on track with developing analytic skills. [redacted] will meet with me at least monthly during the planning and conduct of Specific Aim 2, which involves his expertise in qualitative research. Finally, [redacted] will meet with me twice a month for regularly scheduled [redacted] leadership meetings. I will accompany him on hospital site visits, assist with planning the organization's quarterly meetings, and learn about the managerial and team-building skills required to lead a large organization.

B. Skill Development Plan

In order to achieve my goal of becoming an independent investigator designing and evaluating interventions to improve the quality of cancer care in hospitals, I will need additional training in 3 specific areas:

1. Develop expertise in implementation science and qualitative research methods.

My Masters in Public Health coursework did not include specific courses in implementation science. Fortunately, an educational program designed by [redacted] will correct this deficiency. During the first year of the grant, I will take a full-semester course in qualitative methods in the UM School of Public Health, "Qualitative Methods and Participatory Action Research" (HBEHED636). I will also attend a full-time, one month summer seminar series in the [redacted] Institute for Social Research (ISR Summer Institute) during the third summer of the funding period. Course content includes mixed-methods research, qualitative interviewing and analysis, survey methods, experimental and quasi-experimental study design, multi-level data analysis, and/or focus group techniques. I also plan to take a health communications course later in the funding period (SPH 661) to improve techniques for designing and conducting interviews and understanding clinician behavior change.

In addition, I have been invited to attend the monthly Implementation Science Investigative Team meetings held in the [redacted] school of nursing, which include investigators from across the University, including multiple experts in qualitative methods and organizational behavior. Additionally, the national VA has both in-person and cyber seminars on implementation science that I will participate in during the course of the award. [redacted] *will provide directed readings on implementation and dissemination research, qualitative methods and tailored intervention design.*

Travel to two national conferences is proposed for this part of the educational plan: (1) the National Institutes of Health Annual Conference on Implementation and Dissemination Research (March 2012); and (2) the NIH-sponsored Training Institute in Dissemination & Implementation Research in Healthcare. This 1 week program helps investigators develop R01 grants involving dissemination and implementation research.

2. Develop expertise in measuring and comparing healthcare quality, including hierarchical modeling.

This educational plan will improve my ability to analyze data for valid comparisons of hospitals' quality of care. The [redacted] School of Public Health (SPH) and the Institute for Social Research (ISR) both have relevant courses on healthcare quality, multilevel analysis, and causal inference. I propose to take "Quality of Care" (HMP 683), which focuses on quality of care assessment, control, and improvement in health care delivery settings. I also will take "An introduction to multilevel analysis in public health" (EPID 787), during the summer of the first year. Thereafter, I propose to take Biostat512 "Analyzing Clustered and Longitudinal Data Using Statistical Software". Also, the ISR holds 3-5 day seminars on statistical topics, and I propose to take "Causal Inference in the Social Sciences: Matching, Propensity Scores and Other Strategies".

3. Develop leadership skills necessary for management of regional quality-improvement initiatives.

The mentorship team assembled for this grant includes nationally-recognized leaders in surgical outcomes research and quality improvement. [redacted], are the directors of

regional hospital collaborative networks, with proven skills in engaging, motivating, and retaining hospitals and providers in these initiatives. They will provide me with mentorship in the leadership and organizational skills required to engage hospitals and providers. I will meet with [redacted] weekly and [redacted] monthly, to ensure progress in research and high-impact publication goals. I will also meet with [redacted] at least monthly, to ensure the success of the colorectal cancer project within the larger [redacted] organization. The mentors also plan to provide hands-on learning in the art and science of effective data presentation to motivate provider / hospital behavior change.

Finally, in order to become a true "expert" in surgery for rectal cancer, we have included a plan to observe surgical procedures and visit the pathology labs at centers of excellence for rectal cancer surgery. I have already been invited by the principal investigator of the current trial of open v. laparoscopic rectal cancer surgery (ACOSOG-Z6051), and by the department of surgery at [redacted]

C. Summary

As a result of this research and educational plan, at the end of the funding period I will have the skills to conduct independent research studies comparing the effectiveness of different strategies for hospital-based cancer quality improvement. The educational plan is summarized in Table 2.

Table 2. Timeline for Career Development Activities

<table>
<tr><th></th><th></th><th>Year 1</th><th>Year 2</th><th>Year 3</th><th>Year 4</th><th>Year 5</th></tr>
<tr><td rowspan="2">Skill Development 1: Implementation Science</td><td>Coursework</td><td>Qualitative Methods (HBHE 636)</td><td>Quality of Care (HMP 683)</td><td>ISR Summer Institute (4 weeks full time)</td><td></td><td>Health Communications (SPH 661)</td></tr>
<tr><td>Local and National Seminars</td><td>NIH Dissemination & Implementation Annual Conference (March 2012, Bethesda, MD)</td><td></td><td>Training Institute in Dissemination & Implementation Research in Healthcare (The Hill Group)</td><td></td><td></td></tr>
<tr><td colspan="6"></td><td>Monthly Implementation Science Investigator Team Meetings (UM)</td></tr>
<tr><td colspan="6"></td><td>VA HSR&D Implementation Science Cyber Seminar Series</td></tr>
<tr><td>Skill Development 2: Analytic Methods</td><td>Coursework</td><td></td><td>Multilevel analysis (EPID 787)</td><td>ISR Causal Inference Seminar (5 days)</td><td>Analyzing Clustered & Longitudinal Data (Biostat 512)</td><td></td></tr>
<tr><td></td><td>Local and National Seminars</td><td colspan="5">Statistical Methods Journal Clubs (CHOP)</td></tr>
<tr><td></td><td></td><td colspan="5">Weekly Research in Progress Seminars (CHOP)</td></tr>
<tr><td rowspan="3">Skill Development 3: Leadership Skills</td><td rowspan="3"></td><td colspan="5">Attend MSQC Site visits with Dr. Campbell</td></tr>
<tr><td colspan="5">Twice a month MSQC leadership meetings: planning and attending MSQC quarterly meetings</td></tr>
<tr><td colspan="5">Directed reading from Birkmeyer, Resnicow about effective data presentation</td></tr>
<tr><td>Research Ethics</td><td></td><td>PEERRS</td><td>PIBS 503</td><td></td><td>PEERRS</td><td></td></tr>
<tr><td rowspan="3">Mentored Research</td><td rowspan="3">Research Plan</td><td colspan="2">Aim 1: Retrospective Study of Rectal Cancer Quality of Care</td><td colspan="3"></td></tr>
<tr><td></td><td colspan="2">Aim 2: Qualitative Study</td><td colspan="2"></td></tr>
<tr><td colspan="2"></td><td colspan="3">Aim 3: Design and Implement Quality-Improvement Intervention (conduct intervention year 4, evaluate year 5)</td></tr>
<tr><td rowspan="2">Mentor Meetings</td><td colspan="5">Weekly mentor meetings with N Birkmeyer</td></tr>
<tr><td colspan="5">Monthly mentor meetings with J Birkmeyer, Hawley, Banerjee, Resnicow</td></tr>
<tr><td rowspan="4">Professional Development</td><td>Travel to Clinical Centers of Excellence</td><td>Washington University</td><td></td><td>MD Anderson Cancer Center</td><td></td><td></td></tr>
<tr><td>National</td><td colspan="5">ASCRS & ASCO Annual Meetings and Committee Positions</td></tr>
<tr><td>Local</td><td colspan="5">Tumor Board and other Cancer Center Meetings (UM)</td></tr>
<tr><td>Research Deliverables</td><td></td><td>Manuscripts related to Specific Aim 1</td><td></td><td>Manuscripts related to Specific Aim 2</td><td>Manuscripts related to Specific Aim 3</td></tr>
<tr><td colspan="3"></td><td colspan="3">Apply for Independent Funding (R01 or equivalent)</td></tr>
</table>

Abbreviations: HBHE-Health Behavior and Health Education division of the School of Public Health; HMP-Health Management and Policy division of the School of Public Health; ISR-Institute for Social Research of the University of Michigan; SPH-School of Public Health; NIH-National Institutes of Health; VA HSR&D-Department of Veterans' Affairs national Health Services Research and Development Service; UM-University of Michigan; EPID-Epidemiology division of the School of Public Health; Biostat-Department of Biostatistics; CHOP-Center for Healthcare Outcomes and Policy of the University of Michigan; MSQC-Michigan Surgical

5. TRAINING IN THE RESPONSIBLE CONDUCT OF RESEARCH

During my residency/fellowship, I completed educational programs on research ethics (1999, 2003). Upon becoming a faculty member (2005), I completed the Human Subjects Protection Certification, which required reading a textbook.[83] Thereafter, my Masters' in Public Health program included a 1 semester course entitled Ethics and Professional Integrity in Research—Clinical (IND 503, 2007). Topics included: human experimentation, conflict of interest, stem cell research, mentor-student relationship, plagiarism, scientific misconduct, publication, and copyright. The course included lectures and small discussion (led by ethics faculty). In 2009 I completed the on-line Program for Education and Evaluation of Research, Responsibility, and Scholarship (PEERRS). Specific topics included: Conflict of Interest, Foundations of Good Research Practice, Human Subjects, and Research Administration.

My primary mentor and I have determined that in addition to on-line training (PEERRS will be repeated in 2012), independent reading (*On Being a Scientist*[84]) and mentoring responsibilities (eg- for summer research students), I should take the course "Research Responsibility and Ethics" (PIBS 503) during the second year of the funding period. This course utilizes faculty-facilitated small-group discussion format, including case studies on: Fraud, Fabrication, and Plagiarism, Data Storage and Ownership, Peer Review, Animal Use and Care, Human Subjects Research, IRBs, Conflict of Interest, and Research in the Global Workplace (Cultural Issues, International collaboration, Women, Under-represented Minorities). [redacted] will also discuss research ethics topics with me weekly in mentorship meetings throughout the grant period.

8. DESCRIPTION OF INSTITUTIONAL ENVIRONMENT

[redacted]

The candidate is on the faculty of the [redacted], which ranks second in the United States in federal research and development funding, amongst all colleges and universities. Specifically, the Department of Surgery has a strong track record of commitment to protected research time for tenure-track faculty. The department has ranked in the top 5 for NIH funding for the last several years, currently ranked 2nd. These statistics reflect the institutional commitment to academic career development, including resources and protected time for research.

Center for Healthcare Outcomes & Policy

The majority of the proposed research will be conducted at the newly-established Center for Healthcare Outcomes & Policy (CHOP) at the [redacted]. CHOP is a large, multi-disciplinary consortium of 110 clinical and non-clinical faculty and staff sharing common interests in population-level health services research, including research based on clinical registries and large claims databases. Housed in a 20,000 square foot research building recently acquired by the University, CHOP has a well-organized administrative data management infrastructure, including programmers/analysts, secure computer systems, and a variety of clinical databases spanning many years. Members of CHOP include economists, epidemiologists, statisticians, and clinician-scientists, representing at least six major clinical departments from the School of Medicine. CHOP is directed by [redacted] of the Department of Surgery (co-mentor on this proposal), and the candidate's primary office is located at CHOP. As a member of the group, she will have access to the abundant resources available.

The Center is home to several statewide collaborative quality improvement programs, including [redacted], the research setting for this proposal. These programs collect detailed clinical data on more than 200,000 patients annually, provide regular feedback on performance to providers, and oversee quality improvement activities at more than 40 Michigan hospitals. Outcomes research and policy evaluation based on clinical registries comprise a large component of CHOP's research portfolio, including multiple R01 grants on topics related to collaborative quality improvement programs and the analytics of healthcare quality comparisons. CHOP investigators have mentored numerous junior faculty on K-awards and have a track record of candidates progressing to R01-funded independent research efforts.

Advantages of Research Environment for the Proposed Project

CHOP is an ideal setting for this project. The rich intellectual environment and regular seminars will provide the candidate ample opportunity to present her research and elicit feedback from a diverse group of scientists and clinicians. From a practical standpoint, the candidate's primary office at CHOP is just steps away from the offices of [redacted]. The physical co-location of the central offices of the MSQC in the CHOP facility will facilitate success of the collaboration.

10. SPECIFIC AIMS

Surgery is the primary treatment for rectal cancer, which is diagnosed in more than 40,000 Americans each year. There is broad consensus regarding optimal care for rectal cancer, including the total mesorectal excision surgical technique, adequate lymph node procurement, avoidance of colostomy when possible, and selective use of chemotherapy and radiation treatments. Strong evidence links the use of these practices with improvements in rates of local recurrence, survival and quality of life. Nonetheless, use of these evidence-based practices and outcomes for rectal cancer vary widely across US hospitals. These data suggest obvious opportunities for improving the quality of rectal cancer treatment.

However, little is known about the clinical and practical barriers to evidence-based practice by cancer surgeons. Although population-based methods for improving the quality of surgical care are not well-developed in the US, teaching and feedback programs for rectal cancer surgeons in Europe have resulted in significant reductions in local tumor recurrence rates, improved rates of sphincter-preserving surgery, and survival. These results provide empirical support for targeting surgeons for rectal cancer quality improvement. Because the US lacks a national healthcare system to mandate evidence-based practices, regional groups of practitioners have formed collaborative quality improvement programs. These regional programs have proven successful in decreasing surgical morbidity and mortality but have not targeted the longer-term patient outcomes of specific relevance to cancer surgery.

In this context, we propose to design, implement and rigorously evaluate a state-wide strategy for improving the quality of surgical management of rectal cancer that has potential implications for improving cancer surgery nationally. Specifically, we will study the barriers to evidence-based practice for rectal cancer, and then aim to improve the quality of rectal cancer treatment by introducing a targeted intervention into an existing collaborative quality improvement program in the state of Michigan. Our research proposal has three specific aims:

Specific Aim 1: To assess hospital compliance with evidence-based practices for rectal cancer care. We will study patients enrolled in the 34-hospital Michigan Surgical Quality Collaborative (MSQC) between 2006 and 2010 (n=1300), supplementing existing data with medical records and tumor registry data. The evidence-based practices that will be evaluated are: (1) adequacy of surgical resection (resection margins and lymph node procurement); (2) use of modern surgical techniques (total mesorectal excision and sphincter-preserving surgery); and (3) appropriate use of neoadjuvant treatment. We expect to find unwanted variation in these evidence-based practices across Michigan hospitals.

Specific Aim 2: To understand barriers to evidence-based practices. We will conduct semi-structured interviews with surgeons at low- and high-performing hospitals, then perform qualitative data analysis to identify key barriers to and facilitators of evidence-based practices. We hypothesize that reasons for non-adoption of evidence-based practices include lack of performance feedback, knowledge gaps, lack of multidisciplinary care, and poor documentation.

Specific Aim 3: To design and implement a collaborative quality improvement intervention, and determine if this results in an improvement in the time-trend for compliance with evidence-based practices for rectal cancer. Based upon the results from Aims 1 and 2, we will design a multi-modal quality improvement intervention based upon the established methods of the MSQC (audit and feedback, interactive group meetings, educational materials, site visits). Adherence to the quality measures above will be monitored over time to determine if improvement is achieved, while accounting for preexisting time-trends and hospital variation. In this aim we test our hypothesis that collaborative quality-improvement strategies previously used to decrease short-term surgical complications can be successfully applied to cancer care improvement.

Summary: This research program will have immediate impact on strategies for quality improvement in cancer surgery. It will also lay the groundwork for utilizing regional hospital collaboratives to improve the quality of cancer care. Furthermore, the project, multidisciplinary mentorship team, and educational plan will prepare the candidate to be an independent investigator.

11. RESEARCH STRATEGY

A. Significance

A1. The quality of rectal cancer surgery varies by surgeon and hospital.

Diagnosed in approximately 40,000 Americans each year,[85] rectal cancer is a common condition which is associated with high morbidity and mortality.[86] The core treatment for potentially-curable rectal cancer is surgical resection, and the surgeon usually coordinates care for this disease, including referral for radiation and chemotherapy treatments.[87] Compared to other solid tumors, the quality of surgery has a particularly strong influence on outcomes.[88-93] There is broad consensus regarding optimal surgical care, including the total mesorectal excision surgical technique,[89, 94] adequate lymph node procurement, avoidance of colostomy when possible, and appropriate referral of patients for adjuvant therapy.[95, 96] These practices have been clearly shown to decrease local recurrences and improve survival and quality of life.[88-93]

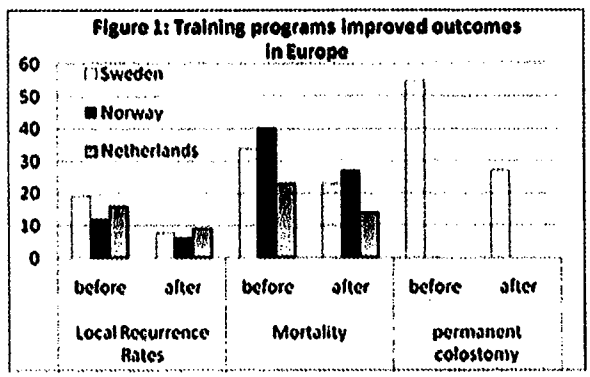
Unfortunately, variation in the quality of care for colorectal cancer has been demonstrated, even controlling for patient and tumor characteristics. Table 3 summarizes twenty years' data on variation in processes and outcomes. These dramatic data suggest opportunities to improve treatment quality.

Table 1: Quality Factors that Vary for Colorectal Cancer

Factor	Unit of Analysis	Selected Results of Studies
Lymph node (LN) procurement	Hospital[97-99] Pathologist[100]	• Survival increased with increased # of LN • Median LN # varied by hospital from 4-11 • Only 40% of hospitals met LN goal of median ≥12 LN
Negative circumferential margin	Surgeon[101]	• Rate of negative margin and quality of TME specimens directly assoc with LR rate • Positive margin 15-19% for specialists; 30% for other surgeons
Adjuvant Chemo-therapy	Hospital (colon)[102, 103], Surgeon (colon)[104]	• Large variation by hospital in chemo use, adjusting for tumor and patient factors • 20% of variation in seeing a medical oncologist attributable to the surgeon
Survival	Surgeon[105, 106] Hospital[91, 107]	• Survival varied by surgeon from 43-85% • Specialized hospitals' survival 62-75%; non-specialized hospital 42-44%
Local Recurrence (LR) rate	Surgeon[106], Hospital[93, 108]	• LR varied by surgeon from 0%-55% • Specialized hospitals' LR 4-9%; non-specialized hospital 32-35%
Sphincter preservation	Surgeon[109] Hospital[107, 109]	• Permanent colostomy rates varied by surgeon from 09-83% • High volume surgeons 5x more likely to perform sphincter preservation surgery

A2. International experience has shown that surgeons can be effectively targeted for rectal cancer quality improvement.

Surgeon training programs in Sweden, Norway, and the Netherlands have resulted in significant reductions in local tumor recurrence rates, improved rates of sphincter-preserving surgery, and survival (figure 1).[90, 110-116] Even low-volume practices can achieve excellent outcomes with training.[117, 118] These results provide empirical evidence to support the strategy of targeting surgeons for quality improvement. While the Scandinavian approach to high quality rectal cancer surgery has combined strict regionalization with training programs,[110] we hypothesize that it is possible to give the advantages of high-volume centers to surgeons operating in the community through regional collaboration.[119]



A3. In the United States, regional collaboration is effective in improving surgical safety.

Beginning in the late 1980's with the Northern New England Cardiovascular Disease Study Group, regional collaboratives demonstrated effectiveness in improving the safety of surgical care. The definition of *regional collaboration* is: "a voluntary... group of clinicians, hospital administrators, and health care research personnel who seek to improve continuously the quality, safety, effectiveness, and cost of medical interventions" (NNECDSG Mission Statement).[120] Early success was demonstrated with decreased mortality in cardiothoracic surgery (24% reduction in hospital mortality).[41] This led to successful efforts in other specialties, including general surgery.[121, 122] The precise activities of each regional collaborative vary, but core methods for quality improvement include (1) audit and feedback, (2) training programs and other tools such as standardized order sets, and (3) site visits to high and low-performing sites.

There is mounting evidence of the effectiveness of collaborative quality improvement (QI). Recent systematic reviews of QI collaboratives in medicine[123] and surgery[124] document positive improvements in 14 of 16 published studies. In the state of Michigan, short-term complication rates significantly decreased in the MSQC general and vascular surgery collaborative QI program, while the corresponding nationwide program (that feeds back data but does not utilize regional collaboration) did not show significant improvements.[82] Based on these results, we hypothesize that regional, collaborative QI initiatives are one of the most promising strategies for improving patient outcomes. However, this strategy has focused on reducing short-term complications of surgery, not the longer-term outcomes important for cancer surgery.

B. Innovation

This research program seeks to identify gaps in evidence-based practices for rectal cancer care, to study the barriers to implementation, and then to target hospitals with an intervention modeled on prior regional quality improvement initiatives. This proposal contains the following innovations:

(1)This project applies the *regional collaboration* concept, formerly used for improving short-term surgical safety, to cancer quality improvement.

(2)This project links detailed surgical and comorbidity information with tumor registry data to create a high-quality database that overcomes limitations of SEER-Medicare and NCDB data. One disadvantage of studies of cancer care is the use of administrative and registry data, with incomplete case-mix adjustment and lack of details about the surgical phase of care. This research study proposes to link an existing surgical audit and feedback system with tumor registry data to assess rectal cancer surgical care. This innovative approach provides an important bridge between existing data and infrastructure (tumor registry and surgical audit).

(3)This project targets the surgical operation itself for quality improvement. Surgical care has been a "black box" in the continuum of cancer care, seldom studied explicitly as a target for quality improvement.

(4)Finally, this study includes large and small hospitals across a region, rather than the selected subset of cancer centers in which most cancer studies take place. Furthermore, understanding the factors responsible for observed variation in evidence based processes---which may vary from hospital to hospital, making generalizability dependent on studying different types of hospitals---may ultimately translate into improvements in the quality of care for rectal cancer patients throughout the community. These results are therefore likely to have a significant impact for a group of traditionally understudied cancer patients.

C. Approach

C1. Overview of Research Plan

The long-term goal of this research is to improve the quality of care provided by rectal cancer surgeons, with downstream improvements in patients' local and systemic cancer control. The strategy for accomplishing this objective is to engage an existing regional collaborative group of Michigan hospitals in the goal of rectal cancer quality improvement. The research plan involves 4 steps: (1) creating a data platform and analyzing current adherence to evidence-based practices (Aim 1); (2) determining the barriers to implementation of evidence-based practices (Aim 2); (3) designing and implementing a quality improvement intervention (Aim 3); and (4) evaluating performance over time (Aim 3). These steps align with the following conceptual model.

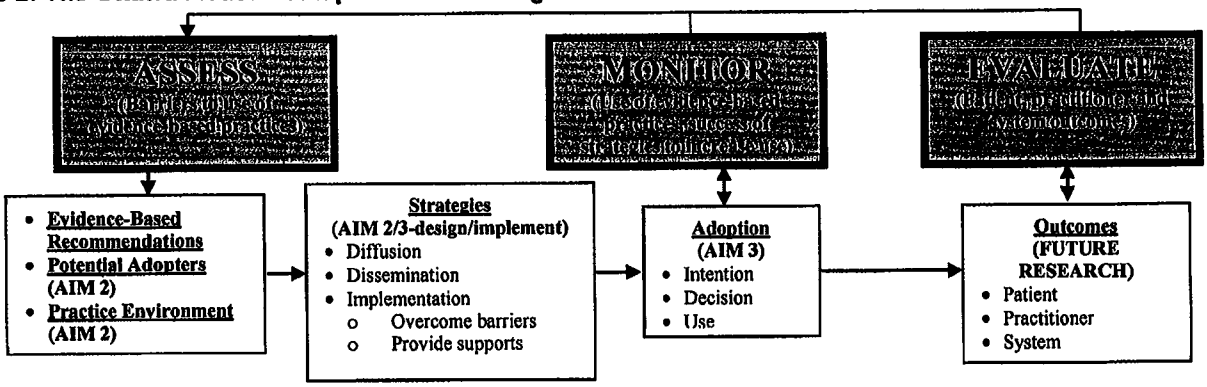
C2. Conceptual Model.

As in other areas of healthcare quality improvement, creating an effective intervention for rectal cancer surgery will rely on the principles of implementation science.[125] There are a variety of commonly-used strategies for translating evidence into practice, and most have mixed results[126]. As Grol and Grimshaw point out, barriers to implementation of evidence include organizational, social, and professional contextual barriers, and these barriers differ from place to place.[126] Therefore, assessing and reassessing barriers to implementation is an integral part of tailoring quality improvement efforts to their setting. Currently, the barriers to adoption of evidence-based practices for rectal cancer treatment are not known. As such, this proposal utilizes an action-based (planned change) model that provides a guide for iterative assessment, action and reassessment (The Ottawa Model of Health Care Research Use[125, 127]).

While there are a number of candidate models to describe the diffusion of healthcare innovations[128], we have chosen the Ottawa Model because it is a theory of planned change (rather than a static conceptual model). It begins with a goal of greater adoption of an evidence-based practice. As applied to this proposal, the evidence-based practices detailed in Aim 1 are the starting point. Potential adopters of the recommendations are surgeons, within the larger environment of their hospitals, and the barriers to adoption

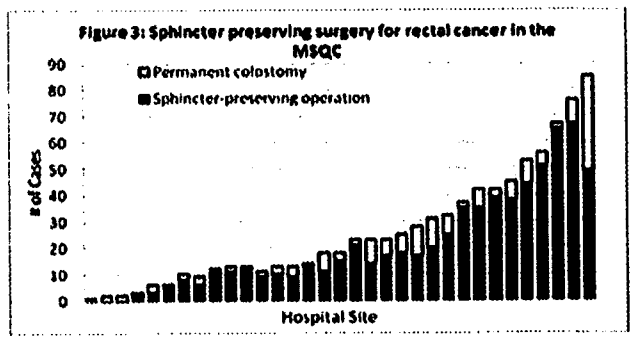
that will be studied in Aim 2 (such as knowledge, attitudes, skills/habits) will be assessed. Strategies that may be part of a multimodal intervention to promote adoption include Audit and Feedback, Academic Detailing, Influence of Leaders, Creating a Community of Practice[129], Regular Meetings, and Site Visits. Success will be measured as increased adoption of the monitored evidence-based processes. Finally, downstream outcomes of survival, local recurrence, and surgeon engagement/satisfaction will be the subject of future research.

Figure 2: The Ottawa Model[127] Adapted to Increasing Use of Evidence-Based Practices for Rectal Cancer



C3. Study Setting and Preliminary Data

The Michigan Surgical Quality Collaborative. The study setting is the Michigan Surgical Quality Collaborative (MSQC), a group of 34 Michigan hospitals participating in a quality improvement program for surgery. The MSQC uses an audit and feedback approach in which trained individuals in each hospital collect rigorously-defined patient and surgical data (including outcomes up to 30 days after surgery) as directed by the American College of Surgeons-National Surgical Quality Improvement Program. Other methods utilized by the group include site visits, face-to-face meetings, educational materials, and special projects which engage subgroups of hospitals and stakeholders (the current proposal would be one of these special projects). Financial support for hospitals' data collection is provided by Blue Cross and Blue Shield of Michigan, a private health insurer; however, the company does not limit or direct the activities of the collaborative. The hospital participants are predominantly community hospitals (62%) with some tertiary-care and/or academic sites.



Rectal Cancer Cases in the MSQC suggest variation in care. De-identified data on the number and types of rectal cancer surgical resections has been examined (Figure 3). These data suggest that there will be a sufficient number of patients in the database to permit a meaningful analysis of patterns of care in these hospitals. There are currently 921 rectal cancer surgery cases in the MSQC database, with data available through the first quarter of 2010. Furthermore, analysis of the operations performed in each hospital suggests the possibility of variation in rates of sphincter preservation, one of the quality measures in Aim 1. As shown in the figure, higher-volume hospitals range from 58% sphincter preserving surgery to 97%. While these results are not adjusted for differences in tumor location or stage, they raise the question of treatment variation.

C4. Aim 1: To assess hospital compliance with evidence-based practices for rectal cancer care.

C4.a. Study Sample

The patient sample relevant to this research is patients in the MSQC undergoing surgery for rectal cancer. This will be defined from existing MSQC data, which includes an ICD-9 diagnosis code (rectal cancer ICD-9=154x) and CPT codes for rectal cancer surgical procedures.

C4.b. Design for Aim 1

In Specific Aim 1 we will measure MSQC hospitals' current compliance with evidence-based practices including (1) adequacy of surgical resection (negative resection margins and lymph node procurement); (2) rates of use of modern surgical techniques (total mesorectal excision and sphincter-preserving surgery); and (3) appropriate use of neoadjuvant treatment. These practices were chosen because they are completely or in part under the control of the treating surgeon.

Existing cases from the MSQC database (2006-2010) will be studied. We anticipate 1300 cases (extrapolating 2009 case numbers to 2010 and subtracting 10% for anticipated missing data and miscategorized cases). MSQC data includes detailed comorbidity information, surgery information, and 30-day morbidity and mortality. However, the evidence-based processes of interest cannot be adequately evaluated from these data due to the need for additional information about tumor stage, location, pathology analysis, neoadjuvant treatment and surgical technique. These data will be abstracted from medical records and/or requested from the hospitals' tumor registrars by the *existing data abstractors employed in each hospital*, under the training and supervision of the candidate, her research assistant and other MSQC staff. These new data will then be de-identified and merged with MSQC data (Table 5). For the prospective phase of this research plan (Aim 3), similar data will be prospectively collected by existing hospital staff, as a routine addition to the core data collection.

Table 5. Variables and Data Sources	**Data Source (*=data already available)**
Hospital Factors	
Hospital Size/Volume	MSQC*
Hospital teaching status	MSQC*
Surgeon	MSQC*
Patient Factors	
Demographic factors (age, gender, race, insurance)	MSQC*
Surgery Type, date	MSQC*
Comorbidities (comprehensive, from ACS-NSQIP)	MSQC*
BMI	MSQC*
Tumor Factors	
Clinical Stage, staging modality	Operative and pathology reports
Pathologic Stage	Operative and pathology reports
Chemotherapy given, date	Tumor registry
Radiation therapy, date	Tumor registry
Location of tumor (eg: upper, middle, lower 1/3)	Operative and pathology reports
Gross margin status, perforation of specimen	Operative and pathology reports
Evidence-Based Practices	
Negative Resection Margins	Pathology report
≥12 Lymph nodes procured	Tumor registry
Total mesorectal excision performed	Operative, pathology reports
Sphincter-preserving surgery (if not contraindicated)	Operative, pathology reports
Neoadjuvant chemoRT given for stage II or III	Tumor registry, operative/path reprts
Outcomes	
30-day surgical morbidity (complications)	MSQC*
30-day surgical mortality	MSQC*
Annual recurrence status	Tumor registry
Annual vital status (dead/alive)	Tumor registry
Barriers to use of evidence-based practices	Qualitative Interviews (surgeons)
Elements of intervention with saliency to surgeons	Exit Interviews (surgeons)

C4.c. Analytic Plan for Aim 1

We will test the hypothesis that there is significant variation in use of evidence-based practices between hospitals in Michigan. To achieve this goal, each of the 5 evidence-based practices in Table 4 will be evaluated separately (binary outcomes: yes/no corresponding to adherence/non-adherence to evidence-based practices). The unit of analyses will be patients nested within hospitals. Specifically, we will use hierarchical logistic regression (a.k.a. generalized linear mixed model with logit link) to model adherence with evidence-based practices while accounting for the clustering of patients within hospitals. A hierarchical logistic regression model approach allows for the estimation and partitioning of variance in evidence-based practice use between the patient and hospital levels.

[redacted]r will supervise the analysis, which will be performed using the SAS version 9.2 software. To answer the first question (is there significant variation between hospitals in use of evidence-based practices), we will first fit an unconditional (null) model with hospital ID incorporated as a random effect in the model, and then a conditional (adjusted) model incorporating patient, tumor, and measured hospital factors (e.g. hospital size/volume, teaching status) as additional fixed effects covariates in the model. Estimates of the variance component associated with the hospital random effect will be obtained from both the unconditional and conditional models. As a measure of the importance of the hospital effect on patient-level use of evidence-based practice, we will estimate the percentage of the variance attributable to hospital, using the intraclass correlation coefficient (ICC). The ICC will be estimated based on the assumption of a threshold model that is appropriate for a binary outcome.[130] The analysis will be repeated for each of the 5 evidence-based practices. Note that the patient groups are smaller for the sphincter-preservation and adjuvant therapy practices, as these are not applicable to all patients. For these 2 measures, an algorithm will be developed to determine each subject's eligibility for the measure, based upon tumor and patient characteristics.

To determine whether each hospital is a high- or low-outlier for each quality measure, population-averaged and hospital-specific estimates of adherence rates will be obtained for each of the 5 evidence-based practices based on the corresponding hierarchical logistic regression model. We will then identify high- and

low- performing hospitals for each practice based on deviations from the mean (population-averaged) performance estimates. High- and low-performing hospitals for each practice will be identified and targeted for Specific Aim 2. Patterns of non-compliance will then be compared between hospitals, to determine if there are clusters of hospitals that perform well or poorly on multiple measures.

C5. Aim 2: To understand barriers to evidence-based practices.

C5.a. Study Sample

The subjects for qualitative analysis will be surgeons, chosen because they are hypothesized to be the most knowledgeable informants for these processes. Surgeons from high- and low-performing hospitals will be targeted for participation in this aim, with a goal of including at least 10 hospital sites. A purposive sampling approach will be used to ensure participation of surgeons from high-performing community and academic hospitals, as well as low-performing community and academic hospitals. We hypothesize that some hospitals will perform well on some evidence-based practices and poorly on others; as such the sampling strategy incorporates targeting the best and worst performing hospitals for each measure. Our goal is to continue interviewing surgeons until "saturation" or "convergence" is reached, which in qualitative research means there are no new themes/information being gained from each additional interview *(estimate 20-30 interviews).*

C5.b. Design for Aim 2

This aim will begin with a limited number (3-5) of unstructured interviews with surgeons, in order to identify the dominant themes that may explain non-adoption of evidence-based practices. *The framework of* [redacted]*, which details knowledge, attitude and behavioral barriers to physician use of practice guidelines, will form the basis for initial interviews (see table 6).*[131] Hypothesized themes include surgeon information gaps, unavailability of resources such as multidisciplinary cancer care, and poor documentation; these and other themes identified from exploratory interviews will then be used to construct the semi-structured interview template for use with other surgeons. [redacted] will assist with design of the semi-structured interviews. The interview template will be altered over time as themes emerge.

Table 6: Framework for Physicians' Barriers to Adhering to Evidence-Based Practice (based on Cabana *et al*)

Category of Barrier	Example
Lack of Awareness	Physician unaware of guideline
Lack of Familiarity	Physician not familiar with details of recommendation(s)
Lack of Agreement	Physician disagrees with guideline
Lack of Self-Efficacy	Physician doesn't believe he/she can do it
Lack of Outcome Expectancy	Physician doesn't believe it will have the desired effect
Inertia of Previous practice	Physician and practice accustomed to an alternative practice
External Barriers	Guideline is too cumbersome, patients may object, resources not available in facility

The interviewing will be performed by 2-3 trained interviewers, who will be trained in [redacted] *3-day interviewer training program in the UM Health Communications Laboratory, paid from the candidates start-up departmental research funding. This will also cover costs of transcriptions. Interviews will be conducted by the trained interviewer, audiorecorded, and transcribed, and analyses will be conducted concurrently with ongoing interviews, allowing themes identified from earlier interviews to inform subsequent interviews.* [redacted] *plans to recruit the interviewers from a pool of graduate students with interest in healthcare communications.* [redacted] *and the candidate will pause the interview process after the first 10 interviews, to map the main domains and determine a plan for the approximate number and content of further interviews.*

C5.c. Analytic Plan for Aim 2

The data analysis for this aim will consist of an iterative, qualitative research analysis. From the interviews, key barriers to implementation of the evidence-based rectal cancer practices will be identified. We will use the "Template Analysis Style" to code and analyze transcribed interview data, beginning with the themes identified in the exploratory surgeon interviews. The process of "coding" includes reading, discussing, and re-reading interview transcripts, with notation of each "theme" (concept) that emerges, supported by quotations that exemplify the theme. The research assistant and candidate will independently code interview transcripts, and will further refine the codes and their definitions (under supervision of mentorship faculty). Results will be compared until agreement is reached on code definitions and reliability of the coding process is established (>80% simple agreement). The entire data set will then be coded by the research assistant, with 5 transcripts coded by both candidate and research assistant and inter-coder reliability measured. Coding discrepancies will be discussed until agreement is reached. Once data are coded, we will use QSR NVivo® software to organize the data. Results from this analysis will inform the quality-improvement intervention in Aim 3, and will provide the data for a planned manuscript on this topic.

C6. Aim 3: To design and implement a collaborative quality improvement intervention, and determine if this results in an improvement in the time-trend for compliance with evidence-based practices for

rectal cancer.

C6.a. Study Sample

Participating MSQC hospitals will be the study setting for Specific Aim 3. Hospitals will be the target of the quality-improvement intervention, and the patient sample for ongoing evidence-based process compliance measurement will be all future cases meeting the inclusion criteria used to identify cases in Aim 1.

C6.b. Design for Aim 3

In Aim 3 we will test the hypothesis that collaborative quality-improvement strategies previously used to decrease short-term surgical complications can be successfully applied to cancer care improvement. First, based upon the results from Aims 1 and 2 we will design a tailored, multifaceted quality improvement intervention based upon the established methods of the MSQC. [redacted] *will guide intervention development and implementation, and* [redacted] *will help the candidate to tailor the intervention to each hospital. We anticipate developing the intervention during year 3 and implementing it during year 4 of the study period to all MSQC hospital sites. The intervention will then be evaluated in year 5.*

The intervention is planned to include (1)tailored audit and feedback to each hospital, (2)provision of concise evidence summaries to surgeons, to support use of practices each hospital does not use at targeted levels, and (3)site visits by the candidate, [redacted] and MSQC staff to high- and low-performing sites. Variation in these processes will also be regularly reviewed in the MSQC quarterly group meetings. *A checklist, weblog for surgeons, or other interventions may be included, depending on the results of Aim 2. A sample "tailored audit and feedback report" has been included in the Appendix.* The intervention can be tailored to each hospital in several different ways. For example, the audit/feedback, educational materials and use of surgeon leaders will be tailored to the quantitative and qualitative results. Also, new/innovative intervention components may be spurred by the results from the qualitative analysis. For example, it is hypothesized that sites with underuse of neoadjuvant therapy may have a lack of multidisciplinary care on-site. To address this we could create a statewide, electronic discussion forum for cases (eg weblog).

To evaluate the effect of the intervention, data on new rectal cancer cases will be prospectively collected throughout the study timeframe, and evidence-based processes will be monitored for changes over time. Our sample size calculation (below) is based upon a cross-sectional comparison of patients from years 1-3 with patients from year 5 (with year 4 excluded from analysis during the intervention). The table below specifies the expected sample sizes. However, additional analyses will also include time-trend analysis of adherence with each of the evidence based practices (utilizing all 5 years' data) to determine if the intervention alters the hospital-specific preexisting time trends of adherence improvement (see below). Finally, surgeons who participated in qualitative interviews will be surveyed at study conclusion regarding which elements of the intervention were most salient and/or motivating for them (to inform future research).

C6.c. Analytic Plan for Aim 3

Adherence to the quality measures above will be monitored over time to determine if improvements in evidence-based practice compliance occur, beyond what would be expected from pre-existing time-trends. The outcome variables in this aim are all binary, and each outcome variable will be modeled separately using generalized linear mixed model (GLIMMIX) to accommodate the hierarchical structure of the data. Let $Y_{ijk}=1$, if the *j*th patient in the *i*th hospital received adherent care in the *k*th time period (k=1,2,3 for the pre-, peri-, and post-intervention periods, respectively), and $Y_{ijk} = 0$ otherwise. The probability that the *j*th patient seen at the *i*th hospital received adherent care in the *k*th time period can be modeled as follows:

$$\text{logit}(P(Y_{ijk}=1)) = \beta_{00} + \beta_{0i} + \gamma_1 I_1 + \gamma_2 I_2 + X_{ijk}\theta$$

where β_{00} is the population-averaged log-odds of receiving adherent care, β_{0i} is the hospital-specific random effect (*i.e.* random departure for each hospital in the log-odds scale) assumed to follow a normal distribution with mean zero and variance $\sigma^2_{hospital}$, I_1 and I_2 are indicator/dummy variables corresponding to peri- and post-intervention time periods (i.e. I_1 =1 if k=2, and 0 otherwise; I_2 =1 if k=3, and 0 otherwise); X_{ijk} is a matrix of covariates (patient characteristics), γ_1, and γ_2 represent changes in the log-odds of receipt of adherent care due to intervention (baseline is pre-intervention period), and the parameter vector θ represent changes in the log-odds of receipt of adherent care corresponding to each unit change in the covariate values. Model estimates will be obtained using likelihood based approach (marginal or penalized quasi-likelihood). Alternatively, we will also employ a fully Bayesian approach using Markov Chain Monte Carlo (MCMC). Several software packages (SAS PROC GLIMMIX, R, WinBUGS) are available for fitting generalized linear mixed models through these approaches. This modeling approach will adjust for hospitals' individual pre-intervention adherence rates and time-trends of change in adherence, to permit a quasi-experimental test of the effectiveness of the intervention.

C7. Sample Size and Power

For the sample size calculation we focused on comparing the pre- versus post-intervention periods. The patient cohorts in the pre- and post-intervention periods are different, therefore assessment of the intervention effect is based on a cross-sectional comparison of the proportion of patients receiving care compliant with each evidence-based practice in the pre-intervention period v. the post-intervention period (see table), adjusted for clustering of patients within hospitals. Based on the literature, anticipated adherence rates to the five evidence-based practices range between 50-85% (pre-intervention period). *Based on 2010 case numbers, expected sample sizes are detailed in Table 7. We determined that with these sample sizes we will have at least 80% power to detect absolute improvements of 8-12% (best case scenario) and 11-20% (worst case scenario) in adherence rates from pre- to post-intervention using two-sided tests at α=0.05, assuming intra-cluster correlations ≤0.10.*

Table 7. Sample Sizes for Pre-Intervention v. Post-Intervention Analysis

	Pre-Intervention	Post-Intervention
Date Range	Years 1-3	Year 5
Total # of Patients	696	232
Patients per hospital (range)	6-54	2-18

C8. Limitations

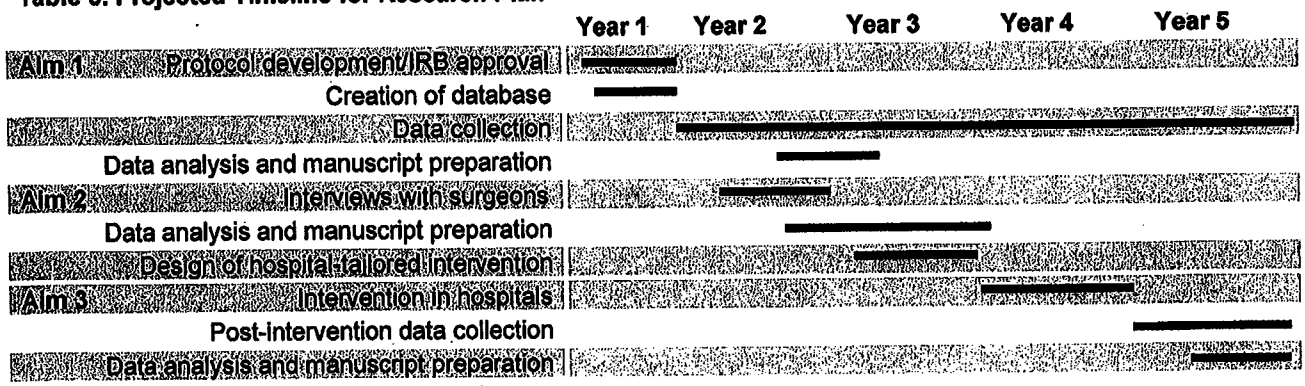
This proposal has several limitations. First, one may question the inclusion of neoadjuvant therapy as a quality measure for surgeons, given that the decision to give neoadjuvant therapy depends on appropriate staging, referral, medical and radiation oncologists, and patient preferences. However, appropriate staging and referral/encouragement by the surgeon to undergo multi-modal treatment are key steps in the process. Also, we may find that the evidence-based practice of total- or tumor-specific mesorectal excision may not be consistently documented in surgeons' operative reports. This will be further explored in the qualitative study for Aim 2. Documentation is a possible intervention target in Aim 3 (eg- through an operative report template).

Finally, the lack of a control group of hospitals limits our ability to demonstrate a causal effect of our intervention in Aim 3. To overcome this limitation, the generalized linear mixed model proposed in the analytic plan for Aim 3 adjusts for hospitals' starting rates of compliance and trends in uptake of practices.

C9. Timeline and Future Directions

Over 5 years, this research plan will lead to the development of a unique data infrastructure, a deeper understanding of barriers to evidence-based practices for cancer surgery, and provide empirical evidence to support strategies for cancer quality improvement in hospitals. We envision this grant to provide the basis for an R01-level grant to follow. Therein we propose to: (1) perform interviews and analysis of alternate informants such as pathologists and medical and radiation oncologists; (2) improve our intervention based upon results from the initial intervention and new informants; and (3) perform long-term follow-up (via hospitals' tumor registries) to test the effect of these strategies on cancer outcomes (survival and local recurrence rates). Other future research directions that will be feasible include: experimentally testing alternate intervention strategies (using cluster-randomization) for increasing use of evidence-bases cancer care practices, and disseminating successful strategies for nation-wide colorectal cancer quality of care improvement.

Table 6. Projected Timeline for Research Plan



14. Protection of Human Subjects

A. Risks to Human Subjects

There will be two types of human subjects in this study: (1) patients undergoing surgery in Michigan hospitals, and (2) physicians who will be interview and questionnaire subjects. For patients, there will be no direct contact or intervention, and risks to them consist only of data security risks. For the physicians, risks include data security and any discomfort or inconvenience associated with an interview.

Existing data use agreements between the Michigan Surgical Quality Collaborative (the data source for this study) and hospital sites allow for collection of data by trained personnel in each hospital for quality improvement. A limited data set is then sent to the Michigan Surgical Quality Collaborative, and this will be used for research study analysis. Existing data security measures will ensure that patient information remains completely secure. Patient information will remain in the MSQC database indefinitely (limited data set). For the patient study a waiver of informed consent is appropriate because:

1. The research involves no more than minimal risk;
2. The waiver will not adversely affect the rights and welfare of the subjects;
3. The research could not practicably be carried out without the waiver.

For physician interviews, digital audiorecordings will be saved on a secure server until study completion. Transcriptions of interviews will be stored on a secure server, with identifiers removed. Physician identifiers will be stored in a separate secure location. Verbal or written consent will be obtained from physicians who are interviewed for the study.

B. Adequacy of Protection Against Risks

There will be several types of data requiring security measures for this research study: (1) Michigan Surgical Quality Collaborative data (a limited data set, database already in existence); (2) digital audiorecordings; (3) transcriptions of audiorecordings; and 4) questionnaires.

The MSQC central database is stored on a server in the University of Michigan's Center for Healthcare Outcomes and Policy (CHOP). This existing database was created for quality improvement purposes and is IRB-exempt. The only protected health information included in the database are dates (eg: of surgery; it is a limited data set). Data can be linked to hospital sites' databases (which contain patient identifiers) via a common code number which is not the medical record number. Data security measures are maintained by the MSQC data manager.

All other data files including digital audiorecordings, questionnaire data, and analytic datasets, will be stored on a separate server at the University of Michigan's Center for Healthcare Outcomes and Policy (CHOP). The server has password protection and appropriate firewalls to ensure no outside access. Data will only be accessible for onsite users. Only the investigator and any data analyst or research assistant assigned to the project will have access to the data files. Furthermore, the computer facilities at the CHOP data center are behind locked doors when not in use. Project data with identifiers of any kind will not be transported or stored on a laptop computer or portable USB device. Identifiers will be destroyed/removed as soon as the research is inactive. Data with identifiers will not be disclosed/shared with any other groups or individuals.

C. Potential Benefits of the Proposed Research to Human Subjects and Others

The prospective subjects of this research study may gain an indirect benefit from the quality improvement initiative proposed, which is hypothesized to increase the use of evidence-based practices for rectal cancer care that have been linked to improved outcomes in prior research. Subjects in the retrospective phase of the study will not gain any benefit. Physicians may gain an educational or professional development benefit from participation in the collaborative quality improvement program. Prior participants in the Michigan Surgical Quality Collaborative have reported high levels of satisfaction from participation.

D. Importance of the Knowledge to be Gained

As outlined elsewhere in the proposal, approximately 40,000 Americans each year are diagnosed with rectal cancer, and inappropriate variation in the quality of care has been demonstrated. This proposal will substantially increase our understanding of barriers to use of evidence-based practices for rectal cancer care, and will test an intervention to improve care. This research study is a part of a larger quality improvement initiative, and has the potential to improve care and outcomes for cancer patients. A secondary goal is to

15. Inclusion of Women and Minorities

This project is based on patients treated in the hospitals of the Michigan Surgical Quality Collaborative (MSQC), which includes 34 community and academic hospitals. Thus, the gender and minority composition of our study population should mirror that of rectal cancer patients in Michigan generally. The table below shows the gender and race/ethnicity distribution of the entire general and vascular surgery population in the MSQC database (2005-2010). Rectal cancer patients will be a small subset of these patients [approximately 1300 (0.69%) of 187,819], expected to have similar gender and race/ethnicity distribution

Table 7. Gender and minority characteristics of MSQC patients (2005-2010)

	American Indian or Alaskan Native	Asian or Pacific Islander	Black, not of Hispanic Origin	Hispanic	White, not of Hispanic Origin	Other or Unknown	Total (%)
Female	178	741	15,537	1,208	73,532	16,912	108,274 (58)
Male	129	502	8,744	1,005	56,244	12,784	79,545 (42)
Total (%)	307 (<1)	1,243 (1)	24,281 (13)	2,213 (1)	129,776 (69)	29,696 (16)	187,819* (100)

*NOTE: Rectal cancer patients will be a small subset of these patients [approximately 1300 (0.69%) of 187,819], expected to have similar gender and race/ethnicity distribution

Targeted/Planned Enrollment Tables

This report format should NOT be used for data collection from study participants.

Study Title: [redacted]

Total Planned Enrollment: 1300 (208 with unknown race/ethnicity); see next page for Specific Aim 3

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	7	9	16
Not Hispanic or Latino	453	624	1077
Ethnic Category: Total of All Subjects *	460	633	1093
Racial Categories			
American Indian/Alaska Native	1	1	2
Asian	4	5	9
Native Hawaiian or Other Pacific Islander			
Black or African American	71	98	169
White	384	529	913
Racial Categories: Total of All Subjects *	460	633	1093

* The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

Study Title: [redacted]

Total Planned Enrollment: 1854 (297 with unknown race/ethnicity)

TARGETED/PLANNED ENROLLMENT: Number of Subjects			
Ethnic Category	**Sex/Gender**		
	Females	**Males**	**Total**
Hispanic or Latino	9	13	22
Not Hispanic or Latino	644	891	1535
Ethnic Category: Total of All Subjects *	653	904	1557
Racial Categories			
American Indian/Alaska Native	1	2	3
Asian	5	7	12
Native Hawaiian or Other Pacific Islander			
Black or African American	101	140	241
White	546	755	1301
Racial Categories: Total of All Subjects *	653	904	1557

* The "Ethnic Category: Total of All Subjects" must be equal to the "Racial Categories: Total of All Subjects."

NOTES: (1) gender and race/ethnicity distribution based on overall Michigan Surgical Quality Collaborative (MSQC) 2005 to 2010 patient characteristics, for which Asian and other Pacific Islander categories are combined; (2) case # for prospective study based on a 5 year study, with extrapolation of 2009 MSQC rectal cancer cases, minus 10%

17. INCLUSION OF CHILDREN

Not applicable.

Justification: The research topic to be studied is not relevant to children (rectal cancer). *Furthermore, the age range of eligible participants is ages 18 and older (patients under age 18 are excluded from case abstraction by the American College of Surgeons' National Surgical Quality Improvement Program, which is the core data collection platform for the Michigan Surgical Quality Collaborative, the research setting for this proposal).*