Expanding Comparative Effectiveness Research: Priority Areas in Oncology
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Expanding Comparative Effectiveness and Patient Centered Outcomes Research in the United States: Opportunities in Oncology

Background – Friends of Cancer Research and CER
For the last several years, Friends of Cancer Research (Friends) has been a thought leader in Comparative Effectiveness Research (CER) and its advancement in the cancer field. We convened a forum in June of 2010, for instance, after monumental health reform legislation had passed, and CER had received its most significant federal commitment ever through the formation of the Patient-Centered Outcomes Research Institute (PCORI)."

This meeting followed the 2009 Friends of Cancer Research forum in Washington, DC held in conjunction with the release of a white paper authored by an independent committee of 25 leading advocates, researchers and health practitioners, entitled: “Improving Medical Decisions Through Comparative Effectiveness Research: Cancer as a Case Study.” The report described the experiences of the clinical and research oncology communities with conducting comparative effectiveness research in the United States.

At that time, CER was a challenging and politically charged topic. Still today, as the U.S. expands the federal capacity for comparative effectiveness research and builds upon the $1.1 billion of funding from the American Recovery and Reinvestment Act (ARRA) designated for CER, debate continues over how to establish a robust CER program that can scientifically generate medical evidence and effectively implement findings into clinical practice.

The launch of the PCORI in September 2010 has created a new public-private entity that will help to drive CER in the United States. However, even if PCORI is fully funded (at an estimated $500 million or more), it will still be vital and necessary for all stakeholders—communities, advocates, federal agencies, academic research centers, and the private sector—to remain engaged and proactive in shaping the development of CER.

Forum for Public Discussion and Input
Building on our earlier events and momentum, Friends of Cancer Research held its latest forum on June 8, 2011 in Washington, DC. The conference, entitled "Expanding Comparative Effectiveness and Patient Centered Outcomes Research in the United States: Opportunities in Oncology" focused on Comparative Effectiveness Research (CER) hosted by Friends, brought together key members of government, industry, and advocacy to discuss current efforts and future priority areas relating to comparative effectiveness research (CER). Ellen Sigal, Chair of Friends and a member of the PCORI Board of Governors, and Brett Davis from Oracle Health Sciences made brief introductory statements emphasizing the role of the patient in CER, which was a common theme throughout the forum’s two panel discussions.

Government representatives, which included Dr. Francis Collins, Director of the National Institutes of Health (NIH), Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research, at the U.S. Food and Drug Administration (FDA) and Dr. Carolyn Clancy, Director of the Agency for Healthcare Research and Quality (AHRQ). They described examples of projects and any outcomes from the original ARRA funding for CER that their agencies received and how those initial research investments have bolstered their long-term vision for CER. The opening panel discussed CER
activities and plans within their agency, as well as collaborative research initiatives with other federal agencies and academic centers. The panelists elaborated on CER’s expanding role at their agencies. Dr. Collins and Dr. Clancy talked about how CER has been present in their agencies for many years, but enactment of the Patient Protection and Affordable Care Act formalized a relationship between AHRQ and the NIH that could give CER a much greater impact.

Looking to the patient perspective, Dr. Woodcock described how CER cannot be too broad and must have a sophisticated approach to answer the basic question every patient has: "Is this going to work for me?" All panelists agreed there will need to be significant coordination and cooperation among all stakeholders to see successful CER results.

Additionally, panelists discussed the PCORI and its role in disseminating CER information to the public. Panelists agreed greater communication directly from the agencies through medical journals, social media, and other communication mediums will be beneficial to helping the public understand the nuance of research data and help better inform patients.

Audience members asked questions throughout the panel, including how FDA data can be used to aid CER and how to get more patient involvement in CER.

A second moderated panel discussion featured oncology leaders, including: Dr. Amy Abernethy, Director, Duke Cancer Care Research Program; Dr. Jeff Allen, Executive Director, Friends of Cancer Research; Dr. Al Benson, Associate Director for Clinical Investigations, Lurie Comprehensive Cancer Center; Cindy Geoghegan, Chief Executive Officer, Y-ME National Breast Cancer Organization; and Dr. Sandra Wong, Assistant Professor, Division of Surgical Oncology, University of Michigan. Meeting attendees had the opportunity to react and discuss specific areas in oncology where additional research, particularly CER, could improve patient care. Attendees were asked to come prepared with topics and submit ideas in advance of the meeting so that the discussion could be moderated toward achieving succinct potential study areas for future uses.

This roundtable discussion continued to examine how to effectively disseminate information to patients and doctors and the further integration of research into the clinical setting. Advocates on the panel discussed the need to engage patients in a meaningful way by involving them throughout the research and treatment process, and in a way that they can fully understand the information being disseminated.

Further discussion focused on additional challenges that providers are facing with influxes of data and the need to integrate that information into the clinical environment. Dr. Amy Abernethy noted that studies that are released are new information for doctors as well and they are not always aware of the best way to communicate those results to the patient during a visit. "It can be very difficult when a patient has certain expectations and you don't have an answer for that particular patient," agreed Dr. Sandra Wong.
Potential Projects Submitted by the Cancer Community

Prior to the June 2011 conference, numerous advocacy organizations and professional societies were asked to work with their organizational advisory committees and invited to submit summary proposals for priority CER projects in oncology. As a result of this solicitation, over 40 different projects were identified and served as the discussion foundation for meeting participants. The panel then reviewed the proposed priority projects that aim to also accomplish a variety of methodological goals. Panelists came to consensus on the need for research to enhance how patients and clinicians make medical decisions.

Priority Projects in Oncology

This document is the outgrowth of the conference describing specific areas of CER that could improve the field of oncology. It contains 13 comparative effectiveness research priority studies in oncology that Friends of Cancer Research—guided by leaders of the cancer community, of our Comparative Effectiveness Research Advisory Committee, and the listed contributors to this document—recommend be addressed by public and private-sector funders of research. These entities include the publicly funded Patient-Centered Outcomes Research Institute, other government agencies, academic research institutions and the private sector.

Topic Identification Process

Based on the meeting feedback and their own assessment, the forum participants and the Friends of Cancer Research CER Advisory Committee narrowed the group down to the top 13.

This list was cross referenced to Clinicaltrials.gov to better understand if research is currently being conducted similar to, or even duplicative of, those proposed. The result of each search is listed following the project summary.

Finally, each potential study has been evaluated by the reviewers listed below and ranked in three categories:
1) Potential public health improvement
2) Feasibility to conduct the study
3) Unmet need for evidence that the study would address

Each study was given a cumulative score out of a possible 135 points. The composite score for each project is listed beneath the proposed study and its contributor.
Friends of Cancer Research Advisory Committee & Contributors

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Recommended Comparative Effectiveness Research (CER) Priority Project Areas in Oncology

A. Use of Proton Beam Therapy Compared to Intensity-Modulated Radiation Therapy (IMRT)

There has been increasing interest in the use of proton beam therapy for different cancer types because it allows for an increased targeted dose of radiation without increased side effects. However, its ability to impact overall mortality, as well as its cost, has been questioned.

A comparative study of proton beam therapy versus IMRT would help improve the decisions when examining treatment options. A study in primary lung cancer should be done in a shorter timeframe than frequently discussed studies in patients with localized prostate cancer. However, toxicities from treatments in lung cancer are greater than side effects experienced when treating prostate cancer. Therefore, symptom measures and quality-of-life metrics must be included to make the study most valuable.

Submitted by: Friends of Cancer Research

Currently Score: 96

Currently Funded Related Research:


NCT01326286: Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) for Localized Prostate Cancer. Vanderbilt University. Enrolling by invitation only.

NCT00388804: External Beam Radiation Therapy (EBRT) With or Without Hormonal Therapy in Prostate Cancer. MD Anderson Cancer Center. Terminated.

B. Use of Palliative Care with Standard Treatment to Improve Survival

In August 2010, Temel et al. published a study in the New England Journal of Medicine demonstrating that patients with metastatic non-small cell lung cancer who received early palliative care plus standard treatment as opposed to standard care alone experienced significant improvements in quality of life, chose the most appropriate treatments at end of life and experienced improved overall survival.

A similar comparative study should examine these findings in other forms of cancer, as well as whether they hold true in “real world” settings outside of academic research centers. Advantages to this type of study include relatively short duration and a current infrastructure of 11 existing National
Institutes of Health (NIH) sites that would be able to begin patient enrollment within a matter of months.

Submitted by: Friends of Cancer Research

Composite Score: 90

Currently Funded Related Research:

NCT00253383: Early Intervention Palliative Care or a Standard Palliative Care Program in Improving End-of-Life Care in Patients with Advanced Lung, Gastrointestinal, Genitourinary, or Breast Cancer. Norris Cotton Cancer Center. Status Unknown (2008 verified as Active, not Recruiting).


C. Metastatic Cancer Registry to Compare Duration of Chemotherapy Treatment

The duration of therapy in persons treated for metastatic cancer is perceived to be widely variable due to a lack of data on outcomes such as overall survival, treatment toxicity, and patient quality of life. Comparative effectiveness research through a prospective registry is needed to determine outcomes associated with differences in the number of lines of chemotherapy with respect to these outcomes. This research would provide critical guidance to clinicians and patients around cancer management towards the end of life. The registry may also allow comparison of outcomes for patients enrolled in phase I trials vs. those seeking 4th and 5th line, non-investigational therapy.

Submitted by: American Society of Clinical Oncology

Composite Score: 90

Currently Funded Related Research:


D. Imaging Surveillance Strategies (Frequency and/or Modality) for Cancer Survivors

Persons with common forms of cancer (e.g., breast, colon, lung, prostate, and pediatric cancers), are routinely followed after curative-intent therapy to detect recurrent disease. Current post-treatment follow-up (or surveillance) programs can include a range of laboratory tests, history and physical examination, and, more recently, diagnostic imaging studies such as MRI and CT and PET
scanning. Despite the prevalence of these cancers, it is thought that there is a wide variation in practice in the use of post treatment follow-up strategies. Studies comparing the comparative effectiveness of advanced imaging techniques versus non-imaging strategies to detect tumor recurrence could aid in the selection of post-treatment monitoring tools.

Submitted by: American Society of Clinical Oncology

Composite Score: 90

Currently Funded Related Research:

NCT00193752: Para-Aortic Lymph Nodal Staging and Evaluation of Treatment Outcome by 18F-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in Advanced Cancer of the Cervix. Tata Memorial Hospital. Unknown.

E. Effectiveness of Early Discussion of Advanced Directives and Resuscitation Choices on Quality of End-of-Life Care and Patient/Family Satisfaction

Substantial pain and distress, as well as false expectations, may be associated with discussions about inpatient resuscitation. Reduced comfort and dignity at the end of life may result from inadequate information provided to patients, families, and providers about this topic. This is an important issue that has come up in multiple prior discussions of stakeholders – particularly among patient advocates/representatives. Many practitioners do not have adequate information about the benefits and harms of aggressive resuscitation plans versus do not resuscitate (DNR), and how to provide evidence to patients to guide informed decisions. Systematic review will inform guideline developers and information disseminated by patient organizations. Patients without access to reliable healthcare information, or those with low education levels, different primary language spoken from their providers, or a different cultural orientation from their providers, may not understand the issues involved with this complex decision. Decision aids which are patient-centered are needed in this area.

Potential harms include: pain to the patient; psychological distress to the patient and family; false hope/expectations to the patient and family. Benefits and harms associated with cardiopulmonary resuscitation in patients with advanced cancers:

1) Likelihood of successful extubation/rehabilitation in patients undergoing resuscitation in the inpatient setting

2) Patient-level characteristics/variables associated with desirable and undesirable outcomes of resuscitation efforts in inpatients (i.e., can variables be identified for which resuscitation leads to greater harms than benefits)?

3) Survival rates for patients who undergo resuscitation compared to those who choose a DNR status

4) Review of various approaches to code status in inpatient settings and associated outcomes

Submitted by: American Society of Clinical Oncology

Composite Score: 85
Currently Funded Related Research:


F. Identifying Non-Responders to Approved Cancer Drugs by Using Data and Tools From the Human Genome Project

The genomic revolution has provided molecular insights into many diseases and in particular cancer, but our current standards of care do not reflect this new knowledge, as most first-line treatments are based on clinical trials in broad groups of patients that in some cases are decades old. As a result, only a small fraction of cancer patients (about 25 percent) currently benefit from approved standards of care. There is an unprecedented opportunity to create an effort to understand which cancer patients benefit from the treatments they are currently getting and which patients need to be treated (as soon as possible) with alternatives to standards of care being used today.

Billions of dollars are being spent in search of new drugs that target molecular changes in cancer, and these drugs are being tested in narrowly defined groups of patients. But there is a barrier to applying the information gained from the genomic revolution to how we treat patients with drugs that are already approved. Once an FDA-approved drug becomes standard of care, there is no incentive for the company developing and selling the drug to redefine (and likely narrow) the market for how that therapy is prescribed.

A focused effort to apply this information on patient outcomes from existing treatments would result in reducing healthcare costs and spare patients from unnecessary therapies that limit quantity and quality of life.

Submitted by: Y-Me, National Breast Cancer Organization

Composite Score: 85

Currently Funded Related Research:


NCT00550537: Proteomic Profiling in Predicting Response in Patients Receiving Erlotinib for Stage IIIB, Stage IV, or Recurrent Non-Small Cell Lung Cancer. Vanderbilt- Ingram Cancer Center. Active, not recruiting.

NCT00918385: Genomic Guided Therapy With Dasatinib or Nilutamide in Metastatic Castration-Resistant Prostate Cancer (ARS). Duke University. Terminated.
G. Development of Standards for the Use of Patient Reported Outcomes in CER

It is readily acknowledged, and required in the Patient Protection and Affordable Care Act, that patient reported outcomes (PROs) play a significant role in CER studies. The Patient Centered Outcomes Research Institute (PCORI) could commission work to establish standards for the use of PROs in CER studies. Currently there are two approaches being developed by the NIH: the Patient Reported Outcomes Measurement Information System (PROMIS), and the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). Both initiatives are intended to generate standards for the use of PROs in clinical studies. But the role of PROs in CER, and standards for evaluating PROs in real-world research contexts, remain relatively unexplored.

An initiative should be developed to establish PRO standards for use in CER that may have adjusted elements for optimal use in non-clinical trial settings. This could be done in collaboration with the FDA, which has recently developed guidelines for PRO use in clinical trials.

Submitted by: Friends of Cancer Research

Composite Score: 84

Currently Funded Related Research:


NCT00410579: Patient Reported Outcomes in Long-Term Survivors of Colon and Rectal Cancers. National Cancer Institute, University of California, Los Angeles. Completed.


H. Comparative Studies of the Effectiveness of Strategies for Surveillance of Treated Cancer Patients

Patients treated for cancer are typically followed with routine imaging post-therapy. The practice involves considerable healthcare utilization and cost. However, surveillance strategies have not been studied systematically for most cancers and limited information is available to guide choice of imaging modality, schedule of surveillance, and follow-up of findings. There is also limited information on the impact of imaging surveillance on patient outcomes.

A research program on post-therapy surveillance should combine several methodologic approaches,
including prospective clinical trials, patient registries and medical record data collection. Studies of surveillance would address a range of important questions, including the impact of imaging surveillance on care decisions; health outcomes and costs; the impact of early detection of recurrence of progression of the primary cancer on patient morbidity and mortality; the frequency and impact of the detection of secondary cancers; and the impact of incidental imaging findings.

Submitted by: Coalition of Cancer Cooperative Groups

Composite Score: 84

Currently Funded Related Research:

NCT00193752: Para-Aortic Lymph Nodal Staging and Evaluation of Treatment Outcome by 18F-Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in Advanced Cancer Cervix. Tata Memorial Hospital. Unknown.

NCT00767273: Investigate Role of Metabolic Imaging in Predicting Tumor Response/Outcome After Pancreatic Cancer Treatment. Stanford University. Completed.

I. Retrospective Analysis of Existing Trial Data to Determine How Health Outcome Trends Are Affected by Obesity

Most clinical trials are conducted in relatively homogenous patient populations that may not be reflective of the general population. This includes the presence of comorbidities. Recent research has shown that comorbid conditions such as obesity can result in worse prognosis, more rapid disease progression, and reduced response to treatment.

Retrospective analysis of existing trial data to evaluate the impact of factors such as BMI/obesity on outcomes would lead to improved understanding of the role comorbid conditions have on “real world” populations.

Submitted by: Friends of Cancer Research

Composite Score: 79

Currently Funded Related Research:

None Applicable.

J. Predicting and Preventing Thrombosis in Hematological Malignancies

The risk of thrombosis complications of cancer is greatly increased, including for patients with hematologic malignancies such as lymphoma. The mortality among cancer patients who develop thrombosis is high, with a rate of about 25 percent at 30 days after the thrombosis. In addition, complications and side effects of treatment are problematic for those patients who survive. Little is known about how best to predict—and how best to prevent—the development of thrombosis in cancer patients. Optimal treatment is cumbersome and requires injected anticoagulant medications.
An improved understanding of fundamental mechanisms and novel prevention and treatment strategies is urgently needed.

Submitted by: American Society of Hematology

Composite Score: 78

Currently Funded Related Research:

NCT00004875: Heparin or Enoxaparin in Patients With Cancer. Northwestern University. Completed.


NCT01094392: Hemostasis During Asparaginase Treatment in Acute Lymphoblastic Leukemia (ALL). Aarhus University Hospital. Recruiting.

K. Use of Extensive or Limited Lymph Node Dissection to Prevent Recurrence of Melanoma

Utilization of lymph node dissection should be examined in many types of cancer where there is currently a lack of evidence regarding recurrence rates and overall morbidity. The cost of this surgery is high and while there is positive evidence for its use in advanced bladder cancer compared to general chemotherapy, it is not well understood for use in other cancers, such as melanoma. A CER study comparing extensive node dissection versus limited dissection could be conducted fairly quickly, and expanded to explore lymph node dissection in other cancers.

Submitted by: Friends of Cancer Research

Composite Score: 74

Currently Funded Related Research:


L. Radiation Oncology Patient Registry

A central component of oncology comparative effectiveness research should include the creation and maintenance of a radiation oncology patient registry in order to aggregate the following data on a case-specific basis: (1) patient and disease characteristics; (2) technically detailed treatment planning and delivery information; (3) disease and toxicity outcomes reported by physician using common criteria; (4) quality of life (QoL) outcomes reported by patient using validated QoL instruments; and (5) other related therapeutic and diagnostic interventions. These data should be acquired electronically through the use of electronic health record systems that will interface with a data warehouse. The warehouse should then be queried to provide rapid reporting for the following key purposes: (1) to
compare effectiveness among different radiation modalities regarding outcomes, quality, safety, and
cost among different patient populations; (2) to identify gaps nationally regarding treatment quality
and outcomes; and (3) to provide benchmarking data and quality improvement reporting to
participating physicians.

Submitted by: Radiation Therapy Alliance

Composite Score: 70

Currently Funded Related Research:

NCT00742222: Electronic Xoft Intersociety Brachytherapy Trial: Electronic Brachytherapy (EBT)
For Treatment of Early Stage Breast Cancer (EXIBT). Xoft, Inc. Active, not recruiting.

NCT01226004: Multi-Institutional Registry for Prostate Cancer Radiosurgery (RPCR). Florida

NCT00992303: Collecting Tissue Samples From Patients With Cancer Undergoing Radiation
Therapy. Simmons Cancer Center. Not yet recruiting.

NCT01106521: A Registry Study of Permanent Breast Seed Implant. Sunnybrook Health
Sciences Centre. Recruiting.

NCT01080313: Head and Neck Cancer Registry (LORHAN). Eli Lilly and Company. Active, not
recruiting.

M. Comparison of Different Tumor Ablation Techniques and Devices

Studies should be conducted in different malignancies (e.g., liver metastases, breast, lung, kidney)
comparing various tumor ablation devices to each other. Additionally, studies should compare
systemic therapy with ablation versus without ablation.

Submitted by: American Society of Clinical Oncology

Composite Score: 68

Currently Funded Related Research:

NCT00510627: Study Comparing Radio Frequency Ablation Plus Chemotherapy and
Chemotherapy Alone in Patients With Secondary Liver Metastases (Prometheus). Boston
Scientific Corporation. Terminated.

NCT00922181: Single-probe Microwave Ablation (MWA) of Metastatic Liver Cancer
(LiverMWA1). University Hospital, Gasthuisberg. Completed.

NCT01032044: Confocal Laser Endomicroscopy for Assessment of Neoplasia After Mucosal
Ablation or Resection of Gastrointestinal Neoplasia (CLEAN-MARGIN). Mauna Kea
Technologies. Completed.
For more information please contact Friends of Cancer Research at: info@focr.org or 202.944.6700