Comparative Effectiveness Research in Cancer: Past, Present and Future

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Presentation Overview

• *Past*
  • Clinical trials system and population registries

• *Present*
  • Data linkage to enable large-scale CER

• *Future*
  • Personalized CER to establish clinical validity, utility and value
Existing NCI-Funded Infrastructure for Phase III Clinical Trials

• Cooperative group clinical trials system (est. 1955)
  – Over 3,100 institutions

• Community clinical oncology program (est. 1983)
  – Over 3,300 participating physicians, including primary care; also supports prevention studies
Reforming the System

- Improve operational efficiency
- Improve prioritization (fewer, better trials)
- Standardize and strengthen IT and reporting
- Increase role of non-NCI scientists and other stakeholders in governance
- Increase funding for complex trials
To Fully Leverage Clinical Trials for CER...

• Less restrictive enrollment criteria
• Cost-effectiveness analyses
• Enhanced patient-reported outcomes
• Longer post-treatment follow-up
NCI Emphases in CER

- Patient representativeness
- Highly diverse practice settings
- Practitioner and patient behavior outside of RCT setting
- Integration with molecular medicine and CaBIG initiative
- Role of incentives, systems and policies
- AHRQ, CDC, CMS and FDA collaboration
Patient-Reported Outcomes Measurement Information System (PROMIS™)

• Goal: Improve assessment of self-reported symptoms and other health-related quality of life domains across many chronic diseases.

• NIH Roadmap Initiative: Re-engineering the Clinical Research Enterprise
  – PROMIS I: 2004-2009 (7 Research Sites)
  – PROMIS II: 2009-2013 (15 Research Sites)
Integrating Patient Safety Monitoring to Improve Quality of Cancer Care Patient-Reported Outcomes version of the CTCAE

• More than one-third of adverse events in drug labels are symptoms (nausea, fatigue, sensory neuropathy, sleep disturbance)

• Traditionally in clinical trials, adverse symptom information is reported by research staff, not directly by patients

• Scientific evidence finds health professionals underestimate incidence and severity of symptoms compared to patients’ own accounts

• Staff-based adverse event reporting occurs at clinic visits, adverse events that occur between visits may be missed

• Increased regulatory focus on use of patient-reported outcomes (PROs) for reporting symptom outcomes in clinical research
Electronic Patient Reported Outcomes (ePRO)

Concept Title

Electronic Patient Reported Outcomes (ePRO)

View the Electronic Patient Reported Outcomes (ePRO) Project page.

Concept Initiator
Data Linkage Between and Across Levels:

Population
Clinical
Molecular
Linking Databases for Population Studies
SEER – Medicare Linkage

• SEER: population-level stage, demographic, survival, and cause of death data for over 6M persons with cancer

• Linkage of two population-based sources
  – cases from SEER and Medicare claims from CMS
  – Over 1.5 million persons with cancer
  – Can be used to examine health care before, during and after cancer diagnosis

• Details at: http://healthservices.cancer.gov/seermedicare/
Newly Linked Data: SEER-MHOS

- NCI - CMS research collaboration to link NCI’s SEER and the CMS’s Medicare Health Outcomes Survey (MHOS):
  - **MHOS:** Provides health-related quality of life outcomes data
    - Annual survey of Medicare Beneficiaries in CMS Managed Care plans. Includes 2-yr follow-up.
  - **SEER-MHOS:**
    - Currently includes 4 Cohorts from 1998-2003
    - Expanding data through 2008
    - Over 32,000 linked individuals with cancer or history of cancer
    - Over 163,000 non-cancer individuals living in SEER regions to use for case-controls studies

- **Goal:** Enable NCI and CMS to sponsor extramural research to monitor and improve the health-related quality of life (HRQOL) in cancer patients and survivors enrolled in Medicare (public access release planned Fall 2010).
Example of Research using the SEER-MHOS Database

Over 1,400 individuals were diagnosed with their first cancer between 2 MHOS surveys including: breast, colorectal, lung, prostate, kidney, NHL, endometrial, melanoma, and bladder.

Research Questions:
1. How does physical, mental, and social components of HRQOL change following cancer diagnosis and treatment?
2. How do the changes observed in cancer patients compare to individuals without cancer who are matched for age and comorbid conditions?

New NCI/AHRQ Population-based Surveillance Research Initiative – SEER/CAHPS

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<td>• Improve understanding of patient reported outcomes enrolled in Medicare as reported in the Consumer Assessment of Healthcare Providers and Systems (CAHPS) survey</td>
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<td>• SEER/CAHPS investigates patient experience in Medicare managed care and fee-for-service</td>
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<td>• CAHPS annually surveys patient reports and ratings of physician &amp; health plan communication, access to care, and practice style</td>
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<td>• Over 500,000 Americans complete a CAHPS survey each year</td>
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<td>• Estimate almost 80,000 Medicare beneficiaries diagnosed with cancer in SEER regions associated with the data set</td>
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New NCI/CMS Population-based Surveillance Research Initiative – SEER/CAHPS

**Potential research applications**

- Observational studies, e.g., influence of HRQOL & patient experience on health utilization and costs (CAHPS fee-for-service sample only)
- Program Surveillance, e.g., monitor plan performance across multiple tumor types, race and ethnicity
- Intervention research, e.g., health plan quality improvement studies on physician communication
- Policy research, e.g., assist beneficiaries concerned about cancer with plan/provider selection
Cancer Intervention and Surveillance Modeling Network (CISNET) Modeling to Guide Public Health Research & Priorities

- 5 cancer sites (lung, breast, colorectal, prostate, esophageal)
  - Multi-scale Modeling
  - Biomarkers
  - Health Disparities
  - Personalized prevention, screening, and treatment strategies
  - CER
Reconciling Trial Results of PSA Screening Efficacy

• Early results on the benefits of PSA screening from US and European trials differed (NEJM, March 26, 2009)
  – PLCO: no benefit
  – ERSPC: PSA screening reduced by 20% prostate cancer death rate

• CISNET, ERSPC and PLCO Collaboration
  – Published data from the trials will be used to inform the models, understand differences and clarify the message on screening efficacy from each trial in a controlled environment
Leveraging Clinical Data to Explain Variations in Care
Cancer Care Outcomes Research and Surveillance Consortium (CanCORS)

- Goal: Understand variation in care delivered to 5,000 patients with lung cancer and 5,000 with colorectal cancer
- Evaluates how characteristics of physicians, patients, caregivers, and delivery systems affect quality of care and outcomes during initial treatment and long-term survivorship
Physician Surveys: Examples

- Cancer Susceptibility Testing
- Colorectal Cancer Screening Policies & Practices
- Physician Attitudes Regarding the Care of Cancer Survivors
- Energy Balance-related Care among Primary Care Physicians
- Primary Care Physicians' Recommendations & Practice for Breast, Cervical, Colorectal, & Lung Cancer Screening
Integrating Molecular Tools and Data into CER
EGAPP: Knowledge Synthesis and Evidence Recommendations

- Evaluation of Genomic Applications in Practice and Prevention

- Non-regulatory
- Independent, non-federal, multidisciplinary Working Group
- Evidence-based, transparent, and publicly accountable
- 4 components: horizon scan; systematic reviews; appraisal and recommendations; evaluation of impact
EGAPP Findings
Gaps in Evidence

- Prevalence of polymorphisms and abnormalities in typical clinical populations
- Penetrance
- Clinical trials comparing testing and intervention strategies
- Assessment of all relevant outcomes
- Attention to benefits as well as harms
- Cost and feasibility

From Al Berg
NCI’s ARRA-Funded GO Grant Initiative

• 50M dollar investment in proof of principle and capacity development projects

• CER in Prevention, Screening and Treatment
• CER in Genomic and Personalized Medicine
Kaiser Permanente Northwest
Comparative Effectiveness in Genomic and Personalized Medicine for Colon Cancer

Objectives:
1- Evidence Synthesis of genetic testing in CRC
2- Cost-Effectiveness for Lynch Syndrome and KRAS testing
3- Utilization of KRAS testing in CRC
4- CER of KRAS testing before and after EGAPP recommendation

Partners:
Colorado DPH; Fallon Community Health Plan; Georgetown University; Harvard Pilgrim Health Care; Henry Ford Health System; HealthPartners; KPCO; KPG; KPH; KPNW; KPNC; KPSC; Lovelace Clinic; Marshfield Clinic; Ohio State University; Scott and White Heath System; University of Hawaii; University of Washington
Stakeholders

- Payers
- Clinicians
- Advocates and Consumer groups
- Researchers
- GPM test developers
- Pharmaceutical manufactures

External Stakeholder Advisory Group

- Comparative Effectiveness in Genomic and Personalized Medicine for Colon Cancer
  - Kaiser
- Center for Comparative Effectiveness Research in Cancer Genomics - CANCERGEN
  - Fred Hutchinson
- Developing Information Infrastructure Focused on Cancer Comparative Effectiveness
  - Moffitt Cancer Center
- Comparative Effectiveness in Genomic Medicine
  - University of Pennsylvania
- Clinical Validity and Utility of Genomic Targeted Chemoprevention of PCa
  - Wake Forest University
- Building a Genome Enabled Electronic Medical Record
  - University of Virginia
- Programs in Clinical Effectiveness of Cancer PGx
  - Duke University
Synergy of CER and Personalized Medicine

“Population-based evidence must be complemented by personalized evidence that accounts for how patients’ genomic and other personal traits affect their responses to health care. Considered alone, neither population-based evidence derived from CER nor personalized evidence derived from PGx and other research suffice. Research priorities, design and conduct of data collection, reporting of results, and translation of CER and PM into practice and policy should be fully integrated. This can achieve alignment, and even synergy, of CER and PM.”

Goodman, C. Comparative Effectiveness Research and Personalize Medicine: From Contradiction to Synergy. The Lewin Group, 2009