



A New Paradigm for Large, Simple Trials Based on Electronic Health Records

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Outline

Introduction

New Initiatives

UW-Madison Initiative

Discussion

Large, Simple Trials: NLM Defining Characteristics

- ▶ Randomized, controlled trials
- ▶ Large number of patients
- ▶ Broad patient inclusion criteria
- ▶ Minimum data requirements
- ▶ Electronic registries → **Electronic Health Record (EHR)**
- ▶ Small and moderate treatment effects
- ▶ Generate effectiveness data → **Comparative Effectiveness Research**
- ▶ External validity

Pragmatic vs Explanatory Trials

- ▶ Schwartz D, Lellouch J. J Chronic Dis 1967 Aug;20(8):637–48.
- ▶ Thorpe KE et al. J Clin Epidemiol 2009;62:464–75.

Pragmatic

Broad elig
 Flexible interventions
 General practitioners
 No follow-up visits
 Clinical outcomes
 Compliance as in usual care
 Intent-to-treat

Explanatory

Narrow elig
 Strict instructions
 Specialists
 Frequent f-u visits and labs
 Surrogate outcomes
 Close monitoring
 Per protocol

Comparative Effectiveness Research

- ▶ Per AHRQ, CER “is designed to inform health-care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options.”
- ▶ Per IOM, CER “is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.”
- ▶ Two ways that "evidence" is found:
 - ▶ Systemic review of completed clinical trials
 - ▶ Clinical studies that generate new evidence of (comparative) effectiveness
- ▶ A means for increasing quality while reducing costs

VA Point-of-Care Clinical Trials

- ▶ A CER pilot project of a clinical trial of two insulin regimens
- ▶ VA Electronic Record System
 - ▶ Computerized Patient Record System (CPRS)
 - ▶ Veterans health Information Systems and Technology Architecture (VISTA)
 - ▶ Support for enrollment, randomization and longitudinal data collection
- ▶ **Learning Health Care System**
 - ▶ Seamless and continuous development and application of evidence in the course of patient care
 - ▶ **Continual quality improvement** in patient care
 - ▶ Decision support
- ▶ “Much work is needed to understand better the optimal uses and designs for this new approach”

Electronic Health vs Medical Record

- ▶ Electronic Medical Record (EMR)
 - ▶ A computerized medical record created in a health care system such as a hospital or physician's office
 - ▶ A part of a local stand-alone health information system that allows storage, retrieval and modification of records
- ▶ Electronic Health Record (EHR)
 - ▶ An evolving concept defined as a systematic collection of electronic health information about individual patients or populations
 - ▶ A record in digital format that is theoretically **capable of being shared across different health care settings**
 - ▶ Usuable in pragmatic large, simple trials for CER
- ▶ Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009

HCS Research Collaboratory

- ▶ Funding Opportunity Announcement January 24, 2012
- ▶ Overall goal/aim
 - ▶ Strengthen the national capacity to implement cost-effective large-scale clinical studies that engage health care systems as research partners
 - ▶ Provide a framework of implementation methods and best practices enabling participation of health care systems in clinical research
- ▶ RFA-RM-11-021 for Coordinating Center (U54)
- ▶ RFA-RM-12-002 for Pragmatic Clinical Trials Demonstration Projects (UH2/UH3)
 - ▶ A one-year milestone-driven planning phase (UH2)
 - ▶ Rapid transition to the implementation phase (UH3)
- ▶ Efficient, large-scale pragmatic clinical trials



HCS Research Collaboratory

- ▶ Funding announcement September 25, 2012
- ▶ Coordinating Center at Duke (PI Califf)
- ▶ Seven pragmatic clinical trial demonstration projects
 - ▶ University of California, Irvine (PI Huang)
 - ▶ Kaiser Foundation Hospitals, Portland (PI Coronado)
 - ▶ Group Health Cooperative, Seattle (PI Simon)
 - ▶ University of Washington, Seattle (PI Jarvik)
 - ▶ University of Iowa, Iowa City (PI Rosenthal)
 - ▶ Kaiser Foundation Hospitals, Portland (PI DeBar)
 - ▶ University of Pennsylvania, Philadelphia (PI Dember)

HCS Research Collaboratory: Coordinating Center

- ▶ Marching orders
 - ▶ Provide national leadership and technical expertise in all aspects of HCS Research Collaboratory
 - ▶ Support design and rapid execution of demonstration projects
 - ▶ Make available data, tools and resources to facilitate a broad base of research partnerships with HCSs
- ▶ Key challenges
 - ▶ Regulatory
 - ▶ Integration of diverse EHR systems



Workshop

- ▶ Large Simple Trials and Knowledge Generation in a Learning Health System
- ▶ November 26 & 27, 2012
- ▶ Objectives
 - ▶ Explore accelerating the use of LSTs
 - ▶ Consider infrastructure needed to build LST capacity
 - ▶ Identify barriers hindering the development of an enhanced LST capacity
 - ▶ Suggest near-term strategies for accelerating LST uptake

National Patient-Centered Clinical Research Network

- ▶ Funding announcement April 23, 2013
- ▶ Improving Infrastructure for Conducting Patient-Centered Outcomes Research
- ▶ Goal: Improve the nation's capacity to conduct CER efficiently
 - ▶ Create a large, highly representative, patient-centered clinical research network for clinical outcomes research
 - ▶ A more comprehensive, complete, longitudinal data infrastructure
 - ▶ Broader participation of patients, clinicians, health care systems and payers in the research process
 - ▶ Improvements in analytic methods for both observational and experimental CER
 - ▶ Empower US to become a learning health care system

PCORI

- ▶ Clinical Data Research Networks (CDRNs)
 - ▶ System-based networks such as hospital systems
 - ▶ Have the potential to become an ideal electronic network, **without structural impediments**
- ▶ Patient Powered Research Networks (PPRNs)
 - ▶ Groups of patients interested in:
 - ▶ **Forming a research network**
 - ▶ Participating in research

A Pilot Hybrid Explanatory-Pragmatic Trial

- ▶ Resveratrol as a caloric restriction mimetic in patients with metabolic syndrome
- ▶ Concept of “metabolic reprogramming”
- ▶ At a single site UW Health West Clinic
- ▶ Explanatory
 - ▶ Small sample size: 100 patients
 - ▶ Insulin resistance as measured by HOMA-IR at baseline and 12 months
 - ▶ Other surrogates: metabolic parameters, gene expression
- ▶ Pragmatic
 - ▶ Broad entry criteria: Almost all obese clinic patients
 - ▶ Primary care provider
 - ▶ Diabetes medication, lipid, BP and weight via EHR

Building Infrastructure for Future EHR-based Pragmatic Trials

- ▶ CTSA and institutional funding
- ▶ Four Wisconsin Health Care Systems
 - ▶ UW Health
 - ▶ Marshfield Clinic
 - ▶ Aurora Health
 - ▶ Gunderson Health
- ▶ UW leads in building IT tools for longitudinal data extraction from EHR
- ▶ UW hosts central data repository for analysis

Challenges

- ▶ Clinical informatics prerequisites
 - ▶ Need to build health IT infrastructure
 - ▶ Integration of research and hospital databases into data warehouse
 - ▶ Expertise in natural language processing
 - ▶ Longitudinal data from EHR
- ▶ Costly
- ▶ Regulatory process streamlining
- ▶ Institutional buy-in
- ▶ Statisticians learn to work with clinical informaticians

Opportunities

- ▶ Pragmatic large, simple trials
- ▶ Point-of-care clinical trials
- ▶ Advance and promote CER
- ▶ Anxious to hear from the Health Care System Research Collaboratory
 - ▶ Duke about their experience in building central infrastructure and resources
 - ▶ UH2/UH3 recipients' experience in carrying out pragmatic LSTs using EHR
- ▶ Small steps at the UW-Madison to build capability may be more immediately relevant for most