Leveraging Electronic Health Data in a Multinational Clinical Trial: Early Learnings from the HARMONY-OUTCOMES EHR Ancillary Study

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July 14, 2017
Funding Sources

- GlaxoSmithKline
- United States Food and Drug Administration (FDA)
  - ROI: “Source Data Capture From Electronic Health Records: Using Standardized Clinical Research Data”
  - This funding will supplement the DataMart strategy (Objs. 2 & 3)
The EHR and clinical research

- Feasibility
- Cohort identification
- Recruitment
- Medical history
- Endpoint ascertainment
- And much more!
Are EHR data fit for research?

• Fragmentation of health care (and data)
• Completeness and accuracy of data
• Standardization of data across organizations
Why use EHR data for research?

- Reduce duplication of effort and inefficiency
  - implementation of findings into the real-world workflows of clinical care is very difficult
- Improve the quality and capture of data by repurposing it in visible ways
- Change the conduct of clinical trials – reduce the data work of the local site and enhance the ability to find potential patients
Evolving real-world landscape
Evolving real-world landscape

The 21st Century Cures Act of 2016 was signed into law on December 13, 2016, and is aimed at improving and accelerating the discovery, development, and delivery of new biomedical products.
Real World Evidence (Sec. 3022)
Requires FDA to establish a program to evaluate the potential use of real world evidence to:

- Help support the approval of new indications for an approved drug
- Help support or satisfy post approval study requirements

Cures definition of RWE: “Data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than clinical trials. May also include ongoing safety surveillance, observational studies, registries, claims data, and patient-centered outcomes research activities.”
Study Overview

• Albigrutide is an analogue of glucagon-like peptide-1 (GLP1), used to treat type 2 diabetes.

• Study tests whether albigrutide affects the occurrence of major cardiovascular events such as heart attacks or strokes in people with type 2 diabetes, when used alone or added to other diabetes treatments.

• 9,400 subjects; event-driven

• 27 countries; 633 study locations
Rationale for the HARMONY-Outcomes EHR Ancillary Study

• EHR is a rich source of clinical data, but designed to support reimbursement and clinical care.
• The assumption that EHR data are fit for use in high-quality clinical research has not been rigorously evaluated.
• An exploratory study embedded within a large pragmatic clinical trial at a select number of study sites will address this evidence gap.
Key questions

• How are EHR data used to facilitate trial recruitment?
• Are EHR data fit to use in populating the baseline characteristics?
• Are EHR data fit to use for clinical endpoints?
How are EHR data used to facilitate recruitment?

- Potential patients identified via EHR data
- What is the enrollment workflow at your site?
- How do you use EHR systems for screening/enrollment?
- How does your site use screening logs?
- What factors are important in prescreening?

Trial enrollment
How are EHR data used to facilitate recruitment?

**Step 1: Focus Groups**
- ~1.5 hours
- 15-20 site coordinators total (5-6 per group)
- Informal discussion about experiences as a study coordinator

**Step 2: Online Survey/Funnel Measure**
- Brief (10-15 minutes)
- N=400 Sites
- Questions about use of EHR for trial screening and recruitment
Key findings from the focus groups

• Medical chart review used with study-specific EHR queries to generate a list of potentially eligible patients identified as the highest yield method

• Lower yield methods of identification included:
  - Posting fliers in clinics or at local pharmacies
  - Building a community database of people interested in research participation
  - Advertising campaigns on local radio stations
  - Placing advertisements on online message boards
  - Informing patients in local diabetes patient education classes about upcoming trials
Methods for identifying potential participants

**Method 1**

1. Review upcoming clinic visit schedules
2. Cross-check list with EHR to identify any exclusion criteria
3. Flag potentially eligible patients for recruitment

**Method 2**

1. Input clinical trial criteria into EHR search
2. Compare list with medical records to identify exclusions
3. Flag potentially eligible patients with upcoming visits for recruitment
Perceived advantages of using the EHR vs. paper-only methods

- Ability for **more complex queries** and shorter turn-around time
- **More precise identification of potential participants**
- **Fewer screen failures**
- **Ability to send electronic messages** about the trial to non-study doctors
Institutional barriers to using EHR for recruitment

- Lack of availability of reporting or research modules in the EHR system
- Requirement to wait for patients to respond to a mailing before initiating contact
- Restrictions on accessing EHRs without patient consent
- Restrictions on contacting patients directly without consent
Survey: Funnel Measure

Response Options

- Patient is cared for by another provider
- Some trial criteria could not be queried or were not included in the EHR search and patient is ineligible
- Patient does not have an upcoming clinic visit
- Provider deems patient inappropriate for trial
- Patient Refusal
- Other (Describe)
Key questions

• How are EHR data used to facilitate trial recruitment?

• Are EHR data fit to use in populating the baseline characteristics?

• Are EHR data fit to use for clinical endpoints?
Are EHR data fit to use for baseline characteristics and clinical endpoints?

DataMart Strategy
~200 participants at 12 sites

National Strategy
~650 participants at 5 sites
The making of a datamart

1. Enter data into EHR during routine delivery of healthcare
2. Extract to internal data warehouse for internal research & quality reporting
3. Transform data into HARMONY Common Data Model format
4. Store in DataMart for responding to Ancillary Study queries
Compare EHR-based datamart with eCRF
What must a participating site have?

- A data warehouse based on EHR data
- Ability to organize EHR data into a common data format
  - Appropriate technical staff
  - Appropriate data
- An integrated clinical, operational, and technical team
Flow of data from the site to the DCRI

DCRI submits to sites for execution

Sites execute query against DataMart

EHR dataset used in comparison with Clinical Trial Dataset

Sites return datasets generated by query

Secure file sharing system
Key requirements for national partners

- Common person level ID
- Coverage of ~100% or defined population
- Available primary outcomes
- Academic partner with data experience
The work of the national partner

- Obtain regulatory and ethical approvals
- Prepare a ‘finder file’ of consented participants
  - Link study patients with national electronic data
  - Determine the variable definitions
- Create the de-identified patient-level dataset
  - Transfer data from NP to DCRI
Early lessons: General

• Data linkage is technically straightforward, but governance & process issues are not.

• The timing of AS team activities are mainly post-trial, so are at odds with busy times of overall trial (beginning and end of trial).

• Engagement from team members may ebb and flow with trial activities.
Early lessons learned

• There isn’t yet a natural bridge between the regulatory and “real” worlds.
• Access to EHR data for research uses varies widely across sites.
• Data linkage is technically straightforward, but governance & process issues are not.
• Data latency varies by site and country.
• Distributed research processes are new to some sites.
• When technical teams are available to support datamart work, these teams are different from the teams involved in the conduct of the HARMONY trial in general
• Local landscapes evolve rapidly.
# The HARMONY-Outcomes EHR Ancillary Study Team

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*PHSR – Pragmatic Health Systems Research*
Thank you!