Approaches to patient follow-up for clinical trials: What's the right choice for your study?

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Duke Clinical Research Institute | FROM THOUGHT LEADERSHIP TO CLINICAL PRACTICE

Scenario

- Planning a pragmatic clinical trial that leverages real-world data for some / all of the data collection
- Some of the sites are part of a distributed research network, but it necessary to include others
- What approaches do you take for the remaining sites? How do you make sure you are not paying for more data than you need?

Caveats

- Definition of “real-world data” here limited to events / outcomes found in electronic health records (EHRs) and / or claims
- Focusing on Medicare claims; private payers out of scope (for now)
- Privacy-preserving record linkage is out of scope – any linkage that might be needed can happen at the study coordinating center

Factors to consider

- What question(s) are you trying to answer with the data?

- How do you align questions to available data sources?

- What are the capabilities of potential sites?
  - Support for different data delivery methods (report, database, etc.)
  - “Sophistication” of implementation

- What is the per-site budget allocation?

Not all questions are created equal (in terms of data required)

- Hospitalizations
  - Was the participant hospitalized in the past year?
  - Was the most recent hospitalization the result of heart failure?
- Laboratory results
  - What was the participant’s most recent eGFR value?
  - What were the participant’s Hematocrit values 2 years prior to enrollment?
- Medication usage
  - How long was the participant on Xolair?
  - What medications were they taking on March 1, 2015?
  - Do their treatment patterns reflect standard of care?

Data sources & data delivery (primarily EHR)

- Can the source be used to answer the question?

- For a given source, there may be multiple ways of delivering the data
  - Some delivery methods may have pre-defined views or summarizations of the data
  - Do these views provide the right level of detail?

- Some delivery methods implicitly assume a certain level of data standardization
  - If you intend to take advantage of that standardization, have you made sure that the sites are compliant?

Data standardization in the EHR

- Most health systems still do not natively generate/capture data in standard terminologies (e.g., SNOMED, LOINC, RxNORM, etc.)
- If delivery method utilizes a standard, need to understand what progress sites have made, if any, before use
- Example – mapping lab tests to LOINC
  - All tests or just a subset?
  - All results or just from a specific point in time?
- Depending on mapping, how you ask the question will influence results
  - All Hemoglobin A1c results
  - All results for LOINC codes 4548-4, 41995-2, and 17855-8

Sources of Data & Modes of Delivery

Source

EHR

Sources of Data & Modes of Delivery

Source

EHR

Claims (CMS)

Sources of Data & Modes of Delivery

Source

EHR

Claims (CMS)

Participant

Sources of Data & Modes of Delivery

Source Who procures the data?	EHR	Claims (CMS)	Participant

Sources of Data & Modes of Delivery

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Patient			

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Clinician / Staff			

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Modes of Delivery – EHRs

Blue Button / Direct

- Patient can request a structured (XML) Summary of Care document with information about most recent visit & some longitudinal values.
- Pros:
  - All patients can obtain from their EHR
- Cons:
  - Completeness of implementation varies by site/EHR
  - Text-based document
  - Typically needs to be brokered through an app (e.g., Hugo)
  - If care is received from multiple systems, need to request multiple documents

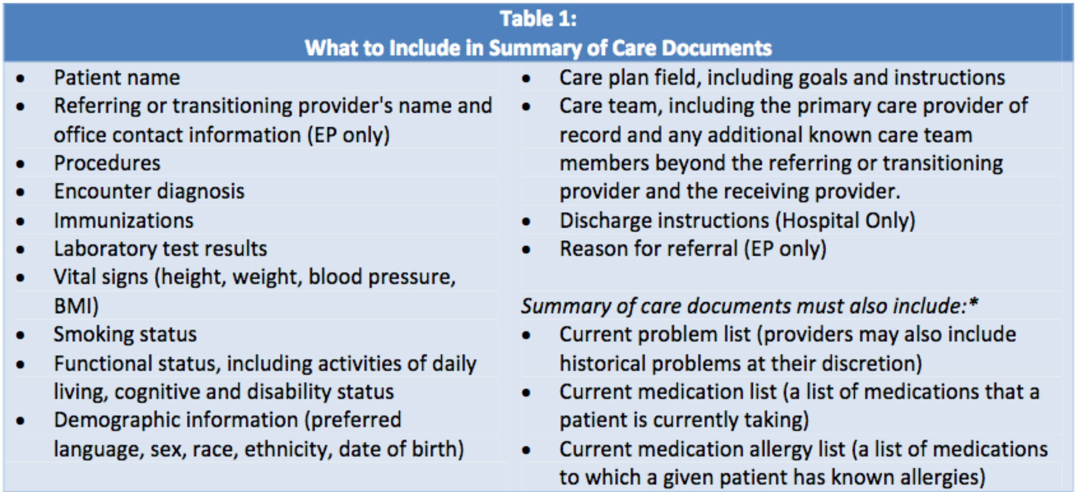

Table 1:
What to Include in Summary of Care Documents

- Patient name
- Referring or transitioning provider's name and office contact information (EP only)
- Procedures
- Encounter diagnosis
- Immunizations
- Laboratory test results
- Vital signs (height, weight, blood pressure, BMI)
- Smoking status
- Functional status, including activities of daily living, cognitive and disability status
- Demographic information (preferred language, sex, race, ethnicity, date of birth)
- Care plan field, including goals and instructions
- Care team, including the primary care provider of record and any additional known care team members beyond the referring or transitioning provider and the receiving provider.
- Discharge instructions (Hospital Only)
- Reason for referral (EP only)

*Summary of care documents must also include:**

- Current problem list (providers may also include historical problems at their discretion)
- Current medication list (a list of medications that a patient is currently taking)
- Current medication allergy list (a list of medications to which a given patient has known allergies)

Image source: https://www.cms.gov/Regulations-and-Guidance/Legislation/EHRIncentivePrograms/Downloads/2014_HealthInformationExchange.pdf

Apple Health Records

- iPhone users have the ability to download records from their EHR(s) into their Health app
- More computable than Summary of Care document – discrete data, not just XML
- Pros:
  - Health app already installed (need secondary app for data sharing)
  - Process to share results with other apps is easy
  - Supported by ~210 health systems (and growing)
- Cons:
  - Leverages Fast Healthcare Interoperability Resources (FHIR) as a backend (not a bad thing)
    - However – need to understand the quality of the FHIR implementation – what's available vs. the rest of the EHR
  - Permissions allow patients to share all records, or "ask when updates available" – may result in loss over time
  - Participants need to make a new connection for every health system in which they receive care
  - App is in beta & no Android equivalent (for now)

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‹ Health Data

Health Records

All Records	50 ›
Allergies	2 ›
Clinical Vitals	10 ›
Conditions	4 ›
Immunizations	3 ›
Lab Results	25 ›
Medications	4 ›
Procedures	2 ›

ACCOUNTS

Image source: https://www.apple.com/healthcare/health-record

Clinician-generated reports

- Most EHRs provide functionality that allows clinicians to generate on-demand reports geared towards answering care management-type questions (e.g., who received flu shot in last 30 days, who was in the ED last night, etc.)
- Pros:
  - Low-cost; can be generated in seconds
  - Real-time results
- Cons:
  - Limited ability to pull longitudinal results; geared towards "most recent" values – most recent lab result, date of last test
  - Clinicians may not know that they have the ability to do this – training & support varies by health system

Analyst-generated report / Database extract

- Work through local / vendor-based IT resources to generate a query from the site’s reporting database and/or data warehouse
- Pros:
  - “Lowest common denominator” approach for obtaining large-scale extracts
  - If pulling all/subsets of a database table or a standard format (e.g., Summary of Care), can often reuse the same query across vendors
  - Once implemented, sites can typically automate production & delivery
- Cons:
  - Approach may not be feasible for smaller sites or sites without local IT support
  - Complex queries rely on skillset/knowledge of local analyst – quality will vary across sites
  - Timeline / cost is variable

Common Data Model (CDM)

- Sites that participate in distributed research networks may have their data loaded into a CDM (e.g., PCORnet, Sentinel, OMOP/OHDSI, VDW, etc.)

- Pros:
  - Process to develop/distribute query is relatively straightforward
  - Can submit one query and get back results from the whole network
  - Most networks perform some level of data curation, though curation varies

- Cons:
  - Data elements of interest may not be in the CDM (not place in CDM and/or site has not loaded them)
  - Large studies will likely need to go beyond a single network

Application programming interface (e.g., FHIR)

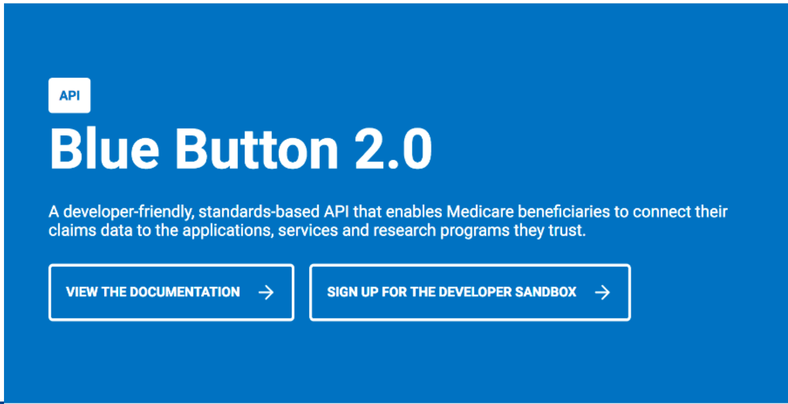
- Standardized interface that allows data to be requested via discrete function calls
- Pros:
  - Allows for easier integration into apps or other programs
  - Can be used to pre-populate case report forms
  - If all sites have the same set of APIs, the “query” can be reused
  - Office of the National Coordinating for Health Information Technology (ONC) recently proposed a rule requiring all EHRs to support FHIR APIs as mechanism of data exchange
- Cons:
  - Potential for data mapping issues
  - A traditional query may translate into dozens/hundreds of API calls
  - Most sites have limited experience in delivering data this way
  - Skillset required to maintain/administer APIs is highly-specialized (i.e., sites have few of these people & they are very in-demand)

ONC NPRM: https://www.healthit.gov/topic/laws-regulation-and-policy/notice-proposed-rulemaking-improve-interoperability-health

Modes of Delivery – CMS Claims

CMS Blue Button 2.0

- Contains four years of Medicare Part A, B and D data for 53 million Medicare beneficiaries in a discrete format (requested via FHIR API)
- Pros:
  - Can obtain data directly from the participant – avoid CMS file charges
  - Data should update as they are made available by CMS
  - CMS has recently proposed that all Medicare Advantage organizations, Medicaid managed care plans, CHIP managed care entities and Qualified Health Plan issuers in the Federally-Funded Exchanges support similar APIs
- Cons:
  - Need to go through a secondary app (i.e., cannot download to Apple Health)
  - Not all participants may follow through / continue to allow access for life of the study



API

Blue Button 2.0

A developer-friendly, standards-based API that enables Medicare beneficiaries to connect their claims data to the applications, services and research programs they trust.

CMS NPRM: https://www.cms.gov/newsroom/fact-sheets/cms-advances-interoperability-patient-access-health-data-through-new-proposals

Image source: https://bluebutton.cms.gov/

CMS Research Identifiable Files

- Traditional process of requesting CMS data through ResDAC
- Pros:
  - Data are well-curated
  - Complete data for all patients in Finder File
- Cons:
  - Need to go through CMS request process
  - Can be expensive
  - Latency may be a factor for some studies

Modes of Delivery – Participant-as-Source

Portal / Mobile app

- Participants self-report events / outcomes via a web portal or mobile app
- Pros:
  - Relatively low cost
  - Single solution for all sites
  - Increased participant engagement
- Cons:
  - Potential for recall bias for some events
  - May lose participants for longer studies
  - Some participants may not be comfortable/capable of using portal/app

Call center

- Staff can reach out to participants via phone (or text / messaging) to follow-up if portal/app assessments are not completed
- Pros:
  - Can mitigate some loss-to-follow-up
  - Some participants may prefer to interact with call center
- Cons:
  - Staffing costs are non-trivial
  - Certain demographics may be less interested in answering the phone (i.e., millennials)

Summary

- Trials with many sites will require a “patchwork quilt” of approaches (for now)
  - Quilt will look different depending on the needs of the trial
- Clinician-generated reports are an often-overlooked option
- Direct-from-patient solutions (i.e., Blue Button / Health Records) offer a relatively low-cost way of obtaining data on trial participants
  - Unlikely to obtain *all* data from *all* patients in this way
  - For some trials, that may not be a problem
  - If it is, need to consider site-based solution – otherwise, just wasting effort
- Regulations are moving industry towards more standardized methods of data exchange via APIs
  - Solves the data model problem (hooray!)
  - Until data are collected/generated using same standards/formats as the API, still need to understand the EHR-to-interface mapping
  - In particular, what is NOT available via the API