HDR UK London

The use of electronic health records (EHR) to support clinical trials

James Carpenter

MRC Clinical Trials Unit at UCL

25 September 2018

Overview

- HDR UK

- London Substantive Site

- Three proposed implementation projects
  - PACESETTING
  - Developing routine clinical data sources to support faster, cheaper, more generalizable clinical trials
  - Transforming primary care clinical trials

- Discussion

HDR UK Sites

1. Wales and Northern Ireland (Swansea and Queen's University Belfast)

2. Midlands (Birmingham, Leicester, Nottingham, Warwick)

3. Scotland (Glasgow, Edinburgh, Dundee, Aberdeen, Strathclyde, St Andrews)

4. London (Imperial, Kings, LSHTM, Queen Mary, UCL)

5. Oxford

6. Cambridge (EBI, Sanger, Cambridge University)

Note: London and Oxford hubs are directly involved in their local substantive sites

HDR UK Phase 1– Core Research Priorities

Actionable Health Data Analytics:

- Structured & unstructured (eg imaging, text) data for derivation of new or deep phenotypes.

- …

Precision Medicine:

- Development of "eCohorts" & tissue based phenotyping

- …

21st Century Trial Design:

- Transform Phase II – Phase IV clinical trials including 'real world evidence' studies

- Remote phenotyping; self phenotyping; integrated phenotyping

Modernising Public Health: towards prevention and early intervention:

- Systematic linkage to administrative data and primary and secondary care EHRs enabling look-forward and -back, recreating the life course of NHS interactions.

- New technologies, from sensors to wearable devices to artificial intelligence

- …

HDR UK London

Research initiatives

- **RI-1 Actionable analytics:** Unlocking the longitudinal clinical phenome
- **RI-2 Precision medicine:** Connecting omic data to the clinical phenome
- **RI-3 Clinical trials:** Unlocking the potential of EHRs to deliver better, cheaper, quicker trials
- **RI-4 Public health:** Connecting the exposome to the clinical phenome

Imperial College London

UCL

KING'S College LONDON

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Queen Mary University of London

Four objectives

1. Path-finder projects
- Using EHR systems to flag eligible patients for recruitment to trials
- Understand how EHR can be used to collect short and long-term safety and effectiveness outcomes
- Understand how data quality issues (e.g. missing data) can be addressed in a standardised and scalable manner

2. Scalable EHR-based trials informatics infrastructure
- Build a scalable standards-based informatics infrastructure for clinical trials (building on TRANSFoRm)
- Identify how different data types (structured, unstructured personal device) can be used for recruitment and follow-up

3. Drug repurposing and license extension
- Use EHR to support extension of existing trial datasets to support regulatory applications

4. Statistical innovation
- Statistical methodology for wearables

Proposed Implementation Projects

1. PACESETTING: Prospective and coordinated evidence synthesis of using EHR in clinical trials: evaluating resources and supporting trials
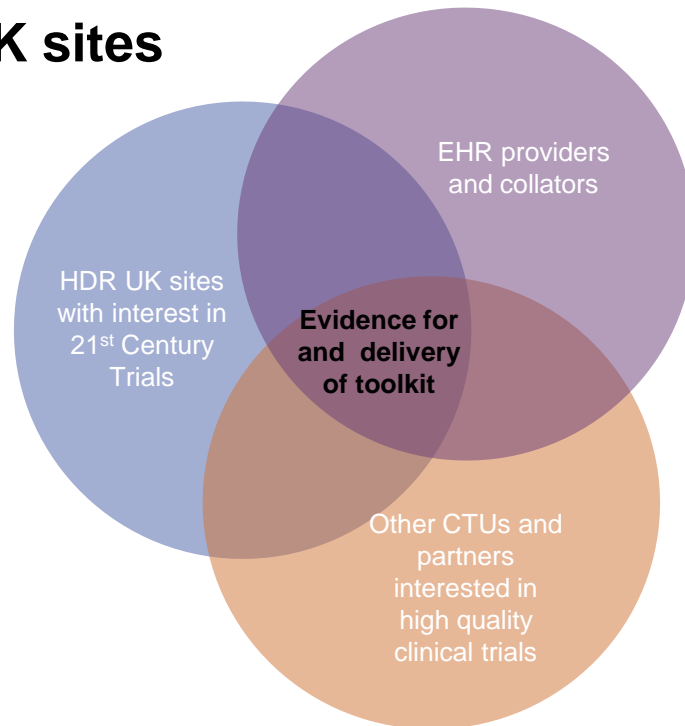
(Project lead: Matt Sydes)

Research Question(s)

When and how can routinely-collected EHR data help to improve the design and conduct of clinical trials?

- How can they be obtained quickly enough for the purpose? And retained?
- When and where are these data available?
- What, if any, are they cost savings?
- Do the data available avoid ascertainment bias?
- What are the gaps from different national sources?
- Trial-specific issues around choice of efficacy outcome measures, safety measurements, treatment compliance, non-trial treatments

Timelines	High-level delivery plans
Q4-2018	**Initiate comprehensive survey of:** 1. Trials (primary and secondary care) that have gained access to and used EHR data 2. Completed, ongoing and planned comparisons that assess routinely-collected EHR to specifically-collected trial data
Q1-2019 - onwards	Initiate and maintain national picture of experiences, including which trials have successfully used EHR
Q2-2019	**National meeting to:** 1. Review and reflect on these case studies 2. Prioritise potential SWATs to address key evidence gaps
Q2-2019	Initiate up to 4 SWATs across many UK-wide clinical trials Priorities for evidence games in Research Qs
Q3-2021	Collate and review SWAT findings – report and national meeting
Q1-2022	"Evidence-based toolkit" delivery for researchers running clinical trials → Draw parallels to NIHR Toolkit for Clinical Trials

PACESETTING – Be broad and inclusive !

All HDR UK sites

EHR providers and collators

HDR UK sites with interest in 21st Century Trials

Evidence for and delivery of toolkit

Other CTUs and partners interested in high quality clinical trials

EHR sites
- **NHS Digital**
- **Public Health England**
- **National Cancer Research and Analysis Service**
- **Others…**

Non-HDR UK sites
- **Partnership for Trials Methodology Research**
- **Registered CTUs**
- **Trial Forge**
- **MHRA**
- **Health Research Authority**
- **Others…**

2. The feasibility of developing routine clinical data sources to support novel methodologies for faster, cheaper, more generalizable clinical trials

(Project leads: Clare Relton, Sandra Eldridge)

Vision

Combine a **staged approach to consent** with **routinely collected health data to measure outcomes**

- Consent to take part in future trials/for use of routine data
- For a given future trial: consent sought to receive the intervention only from participants randomised to the intervention arm.
- Outcomes are measured on all randomised participants.

This allows the integration of intervention trials within the patient's routine healthcare pathway and the efficient use of routine data.

Objectives

1. Assess public willingness to integrate pragmatic randomised trials within their routine healthcare including use of their routine NHS health data for future health research.
2. Review potential interventions for two exemplar conditions (asthma, diabetes) and two health-related behaviours (fresh fruit & veg consumption, breastfeeding up to 6 months).
3. Create a preliminary public consensus on integrating a staged approach to consent in routine NHS healthcare.
4. Evaluate the feasibility of several intervention trials at scale using the novel trial methodologies for the exemplar conditions.

Data

- **Clinical Effectiveness Group (CEG) [London, QMUL]**

  o   Primary care data in population of about 2 million (7 Clinical Commissioning Groups).

  o   CEG funded by CCGs, GP Confederations, Public Health and research grants.

  o   Partner in: the Discovery Project (integrating hospital, GP, local authority records), the pan-London MRC Health Data Science UK, and the pan-London Local Integrated Health Record Exemplar.

- **Yorkshire Health Study [Sheffield, ScHARR]**

  o   Live, regional Public Health Cohort with self-reported health & health behaviour data on 69,000+ adults.

  Funded by NIHR CLAHRC Yorkshire; permission to link to hospital and GP records and all local authorities.

Delivery plans

1. **Conduct surveys** of public willingness to integrate randomised trials within their routine healthcare. These surveys will ascertain public willingness to consent for: *ongoing use of their routine NHS health data for future health research, future contact for research, and if eligible - random allocation to usual care or intervention.*

2. **Conduct reviews of possible interventions** for asthma and diabetes, and two health-related behaviours (fresh fruit & veg consumption and breastfeeding to 6 months).

3. **Facilitate one Citizens Jury** to create preliminary public consensus on integrating a staged approach to consent in routine NHS healthcare & **hold a workshop for key stakeholders** to disseminate knowledge gained, assess acceptance, & make recommendations for future research.

4. **Explore feasibility of extracting required data** from routine sources for several trials at scale for the exemplar conditions and health behaviour, **develop at least 2 protocols for actual trials**.

3. Transforming Primary Care Clinical Trials

Overview

- The TRANSFoRm project developed and validated a standard-based eSource RCT system across 5 EHR systems in 4 countries.

- We now seek to establish a UK partnership for the optimal use of standards-based, open source e-health systems in primary care based trials.

Some details

- GCP requires resource intensive 'source verification' **:** TRANSFoRm collects provenance in real-time. This can be used to establish validity.

- TRANSFoRm allows clinical trial data and workflow to be expressed in a standard fashion using the Clinical Data Interchange Standards Consortium (CDISC) model.

- Databases can be pre-populated from data extracted from EHR systems in real time; eligible subjects and study-follow up can be alerted in real time, and data collected across a range of smartphones and the web.

- To scale up TRANSForM, a variety of tools need to be deployed in a secure environment to enable the creation, curation and deployment of files.

Objectives:

1. To develop a UK primary care partnership in eSource
2. To manage a staged implementation of e-Source for clinical trials
3. To utilise international data standards (*CDISC)* and develop the NHS as an international exemplar
4. To evaluate a series of digital enhancements to trials (design, recruitment, event-based follow up, digital PROMs, SAE monitoring)

Delivery plans:

1. Creation of a consortium: HDR partner sites, NIHR CRN, RCGP and RCGP RSC, NHS Digital, EHR vendors, other commercial organisations with access to patient data and the Public
2. Recruit a pipeline of suitable NIHR studies for development and evaluation.
3. Scaling up, and integrating, the TRANSFoRm infrastructure
4. Identification of specific interventions for evaluation and to enhance study design, and demonstrate the feasibility of recruitment and follow up.
5. Transition to a sustainable business model
6. Disseminate internationally

Experiences of MRC CTU at UCL with EHR

This work builds on previous/ongoing work in the London Hub, e.g.

- N-ALIVE

- SELPHI

- PATCH

- STAMPEDE

Discussion

- HDR UK presents an exciting opportunity to address the outstanding challenges in releasing the potential of EHR.

- It provides a welcome platform for partnership between institutions.

- We are keen to connect will all those interested.