Dealing with real world data in clinical trials

Catriona Keerie

Christopher Tuck, Ronald Harkess, Fiona Strachan
Outline

- Background
- A real world example
- Data Challenges
- What have we learnt?
Background – who are we?

ECTU
Edinburgh Clinical Trials Unit

NINE Bioquarter

Founded in 2006

60 staff, multi-disciplinary

• Trial managers
• Database programmers
• Statisticians
• Health Economists

• Over 40 studies ongoing
• Drugs, devices, complex interventions
• A range of study designs
• Publicly funded and/or commercial
Data today

Data sits in the cloud

No shortage of data!

Storage is cheap
Data in the real world

BUT... people still get sick

We still need real world healthcare research

Personal data is important
Using our data better

‘Classic’ clinical trials retain their place in medical research

HOWEVER...

There is a wealth of routinely collected NHS data
Potentially large patient populations

BUT...

We need to be cautious
Rigorous data governance needed
Patient privacy must be ensured
Today’s talk

Large multi-site clinical trial
- Final reporting in 2018
- Published in The Lancet, Aug 2018

Challenging on many fronts!
- Data extraction and linkage
- Governance requirements

Fits well with ‘Dealing with Data’ conference themes
- Balancing Demands
- New Tools
- the right to privacy of research participants
- access to routine electronic healthcare data
High-Sensitivity Troponin in the Evaluation of patients with Acute Coronary Syndrome

A stepped wedge, cluster-randomised trial

Professor Nicholas Mills
British Heart Foundation Centre for Cardiovascular Science

https://doi.org/10.1016/S0140-6736(18)31923-8
Study rationale

Research question

Can a high-sensitivity cardiac troponin assay improve outcomes in patients presenting with heart attack symptoms?

Heart attack

- most common reason for emergency admission to hospital
- Improving outcomes would be a major benefit to the NHS

Troponin

- a protein released when the heart muscle has been damaged i.e. a heart attack
- greater damage to the heart, the greater the amount of troponin there will be in the blood
Study sites

Approx. 48,000 patients
June 2013 to March 2016
Data features

Use of routine electronic healthcare data
   Linked and de-identified within the NHS Safe Haven
   Stored securely, restricted access

Unconsented patients
   Individual patient consent not needed
   Randomisation performed at the hospital (site) level

Two health boards
   NHS Greater Glasgow and Clyde
   NHS Lothian

Site closures and mergers
   Governance approvals needed
Data sources

12 distinct data sources – separately for each health board

Patient CHI number critical for linkage

CHI = community health index
Data linkage

Safe Haven

Data Sources (TRAK, SMR01 etc.) → SQL tables → Analysis datasets → Index adjudication

Analysis datasets

National Safe Haven

COMBINED analysis datasets → Statistical analyses

Safe Haven

Data Sources (TRAK, SMR01 etc.) → SQL tables → Index adjudication

Index adjudication → Analysis datasets → Outcome adjudication

Results released and published
Data challenges

Extracting the right data

- Distinct IT teams at each health board
- Time-consuming – identifying the correct data sources and fields over specific time periods
- No economies of scale - tasks performed separately for each health board

Identifying unique patients

- Patients could be seen at different times in both health boards
- De-duplication required – secure encryption process
- Avoidance of double-counting
More data challenges!

**Data formats – local data**

- Inconsistent data formats between health boards
- Discharge dates and assay times captured incorrectly at times

**Data integrity**

- Difficult to create a set of validation checks to identify all issues
- Publication timescales + data transfer delays = little time for data validation

**Data Transfer/Release**

- Turnaround time was undefined for data in and out of the secure platform areas
Governance challenges

**General**

Ethics approval from Scotland A REC (REC 12/SS/0115)

Co-sponsorship agreement

Privacy Advisory Committee (PAC) – use of patient data without consent

Public Benefit and Privacy Panel (PBPP) - Health and Social Care approval

**Lothian and GG&C**

R&D approval

Site agreements

Board approval – changes to patient care pathway

Caldicott Guardian approval – patient data in Safe Haven

**Data suppliers**

FARR Institute agreement

**Abbott**

**TRAKCare**

TRAKCare

Farr
What can we do better?

1. Data validation is crucial
2. Involve the clinical team early in the process of validation
3. Working within a secure platform creates time-lags on either side of the process – incorporate this into timelines
What have we learned?

High STEACS

One of the first trials of its kind to include a large number of patients via routinely collected healthcare data

**Strengths**

- Less expensive and resource intensive
- Large representative patient population, not pre-selected
- Complex data linkage in a secure environment
- Restricted user access

**Limitations**

- Data quality less accurate
- Variation in datasets across health boards
- Transfer of data and results inefficient
- Governance complex and changing
High-sensitivity troponin in the evaluation of patients with suspected acute coronary syndrome: a stepped-wedge, cluster-randomised controlled trial


Summary

**Background** High-sensitivity cardiac troponin assays permit use of lower thresholds for the diagnosis of myocardial infarction, but whether this improves clinical outcomes is unknown. We aimed to determine whether the introduction of a high-sensitivity cardiac troponin I (hs-cTnI) assay with a sex-specific 99th centile diagnostic threshold would reduce subsequent myocardial infarction or cardiovascular death in patients with suspected acute coronary syndrome.

**Methods** In this stepped-wedge, cluster-randomised controlled trial across ten secondary or tertiary care hospitals in Scotland, we evaluated the implementation of a hs-cTnI assay in consecutive patients who had been admitted to the hospitals’ emergency departments with suspected acute coronary syndrome. Patients were eligible for inclusion if they presented with suspected acute coronary syndrome and had paired cardiac troponin measurements from the standard care and trial assays. During a validation phase of 6–12 months, results from the hs-cTnI assay were concealed from the attending clinician, and a contemporary cardiac troponin I (cTnI) assay was used to guide care.