Can electronic health records improve the efficiency of large clinical trials?

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Background

Clinical outcomes mega-trials are often required to provide robust assessment of the risks and benefits of treatment. A typical mega-trial is initiated outside routine health care in selected cohorts and requires an extensive and expensive trial machinery to provide multicentre scientific, ethical, and regulatory oversight. To limit costs, the trials are large but with short durations of follow-up, measure surrogate or limited outcomes, and often leave important long-term risk-benefit balance questions unanswered. For change to be possible, more efficient trial methodologies are necessary.

The use of "real world evidence" (RWE) has been proposed as a solution. Typically, RWE is obtained via retrospective or observational analyses of routinely collected data in electronic health records (EHR), which is hampered by measured and unmeasured confounders that influence outcomes. But, when EHR are used in conjunction with the principles of randomization or in conjunction with ongoing randomized clinical trials, routine data sources can be powerful tools to increase efficiency and reduce trial cost. Advantages include capacity for long-term multidimensional follow-up of disparate outcomes (e.g. cancer, fracture) and, when process data is available (e.g vital signs, laboratory values), could obviate the need for clinical trial visits. However, use of EHR to replace established patient follow-up practices requires validation. It is possible not all event types (e.g. cardiovascular events versus safety events) are equally ascertained. Furthermore, specialized expertise is required to understand diagnostic coding, manage and analyse large datasets and interpret outcomes.

Hypothesis

Routinely collected data in EHR can reliably identify important 1) cardiovascular outcomes, 2) diabetes-related outcomes and 3) safety outcomes.

Aims

Event ascertainment from completed clinical trials, including but not limited to the United Kingdom Prospective Diabetes Study (UKPDS), the UKPDS post trial monitoring study (UKPDS-PTM), and the Anglo-Danish-Dutch Study of Intensive Treatment In People with Screen Detected Diabetes in Primary Care in the UK (ADDITION-UK), will be compared with events ascertained from UK Health Episode Statistics (HES).

Description of Work

1. *Training:* Coursework focused on using HES data for research. Topics are data coding, preparing the data for analysis, handling of missing data and duplicates, and cost analyses.
2. *Obtain relevant HES data and prepare it for research use.* Complete HES application and relevant regulatory processes that support its use.
3. *Evaluate EHR for event ascertainment.* Compare trial-Identified events with HES-identified events. Benchmarks for comparison will include: ascertainment, concordance with investigator reported events, cost of ascertainment, and adjudication, where relevant. Validation in multiple datasets will allow comparisons of EHR to trial data obtained via clinic visits and/or questionnaire follow up protocols.
4. *Evaluate HER event ascertainment in real time.* In event-driven trials, event ascertainment must be timely as it affects trial duration. If robust event ascertainment is possible with EHR, it will be applied within an ongoing outcomes trial to determine it is also timely. Time lags between event occurrence and investigator reporting versus EHR ascertainment will be compared to determine if delays or efficiencies are introduced. The cost of using EHR for real time event identification (e.g. requiring monthly data downloads) will also be evaluated.

Supervisor's recent relevant publications

1. Holman RR, Sanjoy KP, Bethel MA, et al. 10-Year Follow-up of Intensive Glucose Control in Type 2 Diabetes. *N Eng J Med* 2008;359:1577-89

2. Griffin SJ, Borch-Johnsen K, Davies MJ, et al. Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION-Europe): a cluster-randomised trial. *Lancet* 2011;378:156‑67

3. Bulbulia R, Bowman L, Wallendszus K, Parish S, et al. Effects on 11 year mortality and morbidity of lowering LDL cholesterol with simvastatin for about 5 years in 20,536 high-risk individuals: a randomised controlled trial. *Lancet* 2011;378:2013-2020.

4. Aung T, Cowan H, Haynes R, Bowman L, Armitage J. Recruiting patients cost-effectively by mail. *Trials* 2011;12(Suppl 1):A117