Research letter: E-health data to support and enhance randomised controlled trials in the UK

Running head: E-health data and trials

Words: 1058

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Recent years have seen expanding opportunities to use electronic health and administrative data for efficient, real world studies to inform planning and innovations in clinical practice. Attracting inward investment is a further goal behind the UK government's *Strategy for UK Life Sciences,* which has sanctioned huge investment in e-health and administrative data, including the Clinical Practice Research Datalink (£60m), the ESRC investment in Big Data (£64m), the creation of four UK e-health research centres (£39m), and a new Office for Life Sciences. This investment is also reflected within the EU more broadly (www.ehr4cr.eu)[1].

While opportunities for more efficient recruitment and follow-up in randomised controlled trials (RCTs) have been key drivers for greater use of e-health data, there is scope to add further value from combining trials with e-health data[2, 3]. We propose that e-health data has the potential to support and enhance RCTs in four main areas.

Firstly, pre-trial study design and recruitment. The national coverage of e-health data can be exploited to identify potential patient cohorts, including those who are typically difficult to recruit into trials[4]. This could allow identification of complete populations of cases either through linkage with disease-specific registries (such as the UK Cystic Fibrosis Registry) or by capturing populations with rare conditions within e-health data, that it might otherwise be difficult to identify and recruit. These data sources could also be used to identify sub-populations who are most at risk and who could benefit most from evidence on potential new interventions, to aid site selection, and to establish potential study samples that reflect the mix of patients seen in practice. E-health data can also support robust, cost-effective and efficient feasibility studies, the importance of which is increasingly being recognised by funders[5]. Determining event rates and parameters to support sample size calculations, and identifying variation in care across services, will lead to more well-designed trials that are likely to succeed.

Secondly, outcomes and comparative effectiveness. E-health data may help to augment primary data collection by capturing information on clinical events, thereby preventing replication of labour-intensive data collection and greatly reducing the burden on research nurses. E-health data could completely replace outcome measurement in specific situations (but may not be approved in others e.g. clinical trials of investigational medicinal products)[6]. Linkage of longitudinal records belonging to the same individual allows different episodes and mortality records to be complied, providing comprehensive information on patient

characteristics and previous medical history. This is particularly relevant for capturing long-term outcomes and safety measures that could not be collected during the trial (e.g. deaths, cancer outcomes, or educational outcomes)[7]. Additionally, e-health data could contribute to assembling core outcome sets (e.g. www.comet-initiative.org).

Thirdly, assessment of generalisability. The extent to which the results of a trial are relevant to a definable group of patients in a particular clinical setting can be determined through the use of e-health data. E-health data can be used to assess how trial results generalise to wider populations and to contextualise results by measuring changes over time in event rates in patients not in the trial. In addition, e-health data can be used to identify variation in care and outcomes across units, allowing targeted improvement and more rapid adoption of interventions for populations most likely to benefit (e.g. targeting infection prevention strategies at patient groups at high risk of infection). Exploiting e-health data supports the efficient translation of evidence of effectiveness into practice.

Fouthly, post-trial monitoring. E-health data can be used to monitor the scaling-up of interventions found to be effective in trial settings and to detect variation in the adoption of interventions. This would provide a cost-effective approach for continued study of safety and efficacy of new medicines and devices after approval and also for monitoring shifts in practice for off-label treatments that are already in widespread use[8].

There are now some examples of e-health data being successfully used within or alongside RCTs. The CATCH trial (CATheters infections in CHildren) is using routinely-collected hospitalisations data (hospital episode statistics) for 6-month follow-up, and linkage between the national laboratory surveillance system and the Paediatric Intensive Care Audit Network (PICANet) for a generalisability study.

However, challenges to realising the full potential for integrating e-health data into RCTs remain. There are concerns about the quality of data that has not been collected primarily for research, specifically relating to the completeness and accuracy with which particular conditions and interventions are coded, the types of outcomes that need to be recorded, and the representativeness of identified cohorts and events rates . Improving data quality may pose significant administrative burden. Regulatory compliance, including management of data queries, audit trails and adverse event reporting, can also be an issue. There are ethical considerations in accessing anonymised patient data for the purposes of trial design (e.g. for determining

event rates and selecting sites) and contacting potential participants identified through e-health data. Recent investments are helping to address some of these issues through development of robust safeguards for confidential information, including data 'Safe Havens'. The appropriateness of each of the four facets of e-health infrastructure should therefore be considered on an individual study basis.

Evidence shows that patients are supportive of the use of e-health data for health research, but appropriately simple consent models for the use of e-health data for these purposes still need to be developed[9,10]. This approach may be particularly useful where consent to the trial can be integrated into routine care, for example surgical procedures or insertion of catheters, as in the CATCH trial. The use of e-health data for RCTs could be further streamlined if research participation could be routinely recorded in administrative data. Such recording could be used to identify under- and over-investigated patient groups and allow monitoring of safety and hospitals that do not participate in research[11].

Using e-health data to support RCTs provides an opportunity to efficiently investigate short- and long-term effectiveness of medical interventions in real healthcare settings, and to assess the broader impact of treatments across entire health systems[12]. Ultimately, this has the potential to improve quality and decrease the burden and cost of RCTs, and provide evidence on interventions to help policy makers and practitioners implement improved healthcare treatments quickly for those who would benefit most. In order to unlock this potential in all countries where e-data is available, further research on the challenges and benefits of using e-health data for supporting RCTs should be a priority.

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Funding

This project was funded by the National Institute for Health Research Health Technology Assessment (NIHR HTA) programme (project number 08/13/47). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health.