

Clinical trials data sharing: science, privacy and ethics

Note of the dinner discussion, 28 November 2013

Background

Greater access to clinical trial data offers opportunities to conduct further research to advance science and improve patient care. These benefits include the ability to identify new trends and associations that were not the focus of the original study, validate results and ensure that data provided by research participants are used to maximum effect in the creation of new knowledge. However, there are important scientific and ethical questions around what constitutes responsible use of these data.

The Academy of Medical Sciences brought together experts in clinical trials, ethics and data privacy, as well as patient representatives, for a dinner discussion on 28 November 2013 to consider what constitutes appropriate access to clinical trial data with a focus on patient level data. The dinner provided an opportunity to consider different perspectives relating to data sharing and privacy, in order to inform the many discussions and initiatives currently underway to improve access to clinical trial data. Attendees are listed in the Annex. The dinner was chaired by Professor Robert Souhami CBE FMedSci, the Academy's Foreign Secretary, and was supported by GlaxoSmithKline.

Key issues raised

A range of issues were discussed which can broadly be grouped into the following areas: purpose of sharing clinical trial data; open vs. controlled access; different models of controlled access; patient/participant perspectives; and consent.

Purpose of sharing clinical trial data

The importance of articulating the purpose of sharing clinical trial data - the effective and productive use of data to create a sound basis for science, ultimately for population gain - was acknowledged. The benefits that arise for researchers and participants include the: identification of matters that require further investigation; generation of new hypotheses; development of better study designs; and avoidance of participant involvement in unnecessary future studies.

The benefits and possible risks involved in sharing and not sharing clinical trial data need to be widely understood, as well as who makes the ultimate decisions about sharing. More fundamentally, there needs to be clarification of what imprecise terms such as 'transparency' and 'sharing' might imply, since a cautionary stance could be perceived as favouring concealment. The term 'sharing' can also be taken to mean giving to someone else, but many of the systems that enable access to data do not involve this: rather, data is accessed in strictly controlled environments. It is therefore more accurate to talk about

access and usage of data rather than sharing, which implies the person who gets the data receives it with the same freedom as the sharer.

Given the large number of stakeholders involved a consensus concerning the principles and processes for accessing clinical trial data needs to be developed, preferably with international agreement, to reflect the global nature of conducting trials and to ensure that moves to open up access do not exclude trials in low and middle income countries. Such principles may sometimes apply to the secondary uses of patient and population data more widely, for example from population cohorts, case-control studies and other epidemiological investigations.

Open vs. controlled access to data

There was agreement that a model of open access to individual level clinical trial data raises concerns about privacy risks and the quality and appropriateness of secondary analyses conducted with the data, either by researchers or citizen scientists. Reputational risk to the data holder was another issue that was highlighted, including potentially adverse public responses to industry having access to data generated through government and charitable funding. Several participants favoured the development of a system governed by an independent third party. A number of companies have come together to adopt a model where an independent panel currently reviews requests for access to anonymised patient level trial data, with a vision to ultimately transition to a fully independent system with data from multiple companies and non-industry organisations over time¹.

Several issues were identified in discussion:

- There are resource implications with controlled access models (e.g. review and monitoring of requests, provision of statistical support, maintenance). For both open and controlled access models there are also resource implications of data preparation. However, there may be benefits for organisations wanting to provide access to data by joining up with existing systems and established environments to provide secure access to data.
- Good data management practices and standardisation are vital for both open and controlled access models - again with resource implications - so that data can be analysed. In particular, data fields and attributes need to be subject to standardisation for meaningful data sharing to occur. There are frequently difficulties around retrospective comparison of data, due to different standards having been employed in collecting them.
- Technological developments are increasingly facilitating universal access to a variety of data and this trend will continue. Splunk, for instance, enables access to machine data generated by websites, applications, servers, networks and mobile devices. As noted already, however, without appropriate management and standardisation there is likely to be difficulty concerning the utility of these data and the validity of secondary analysis.

Different models of data access

The importance of having a broadly common approach to data access was emphasised as otherwise there will potentially be different standards for accessing the same set of trial data held in different systems. Lack of a uniform approach may also lead to

¹ <https://clinicalstudydatarequest.com/>

fragmentation and reduction in the data utility, with researchers having to go to different places to access, and possibly not being able to combine, different data sets. Operational aspects of a number of existing and proposed systems were discussed.

Review mechanisms

Under the system established by a number of pharmaceutical companies noted above, an independent panel reviews the protocol and details of the data requester. The model proposed under the European Medicine Agency's draft policy on publication and access to clinical trial data², on the other hand, would enable access to 'raw clinical trial data' without any independent review. The Scottish Health Informatics Programme (SHIP)³ has developed a template to facilitate the concept of 'safe people, safe data and safe environment': if the data requester can demonstrate all three components, the proposals can be triaged for faster access. It was acknowledged that there is a range of motivation for data access - including replication or verification of findings, seeking opportunities for collaboration, and new hypothesis generation – and further discussions and broad agreement are required on what are considered as acceptable reasons.

Post analysis-sharing

Participants considered that, if new findings are made through secondary analysis, there should be a commitment by the data requester to publish the results and share the new data generated. There is also the aspect of new intellectual property derived from secondary research. For example, where access is granted to GSK trials, the external researcher will have the rights to any new intellectual property derived from their research, but the company is allowed non-exclusive rights to use any such IP that would impact on their ability to continue to provide access to, and commercialise, the original medicine and other GSK products.

Feeding back the findings from secondary analysis to trial participants, where this is feasible, was considered to be good practice. A note of caution was raised, however, that not all participants wish to receive such information. Use of platforms such as the EU register for clinical trials to display information such as who accessed the data for what purpose, and the results and any publications, was also raised as an alternative to providing individual feedback.

Data security

For highly aggregated data, the risk of identification is very low. Data security issues are therefore focused more around privacy protection of individual level data. Anonymisation is frequently used as a means of privacy protection although this in itself is not a fully secure mechanism in all situations. It was noted that inferential disclosure has always gone on and advances in technology – such as genomics and stratified medicine – coupled with a wider range of open access data sources mean that it will not be possible to guarantee absolute anonymisation in all situations. Some participants considered that the more stringent the anonymisation the greater the loss of useful data for secondary analyses.

The solution to ensuring privacy protection may therefore be through controlled access to data in safe havens employing both technical and contractual safeguards. Further

² http://www.ema.europa.eu/docs/en_GB/document_library/Other/2013/06/WC500144730.pdf

³ <http://www.scot-ship.ac.uk/>

security could also be provided through a layered approach to data provision: different types of access for different types of data. The Department of Health in England is currently considering the technical standards that should be applied for data safe havens, in response to the Information Governance Review led by Dame Fiona Caldicott⁴. There was agreement that clarity is needed on what different organisations mean by data safe havens.

Patient/participant perspective

It was noted that discussions on clinical trial data sharing often do not take account of the interests or wishes of participants. There have to be more discussions with patients, patient organisations and the general public to find out what is acceptable, in addition to providing accurate information about how data is being accessed and the benefits and possible risks of secondary analysis. In rare diseases there are already good links between research, clinical practice and patient support. In this setting, concern about privacy risk, which may be greater due to the smaller size of the cohort, is often not considered by patient groups to be as important as the need for progress in understanding and management. Some thought that in many countries, there has been general acceptance of researchers accessing data on patients with rare diseases. It was also thought that, in general, patients wish their personal data to be used for reliable research. This raises the question of the competence of those accessing and analysing participant level trial data.

Consent

Participants acknowledged that there is a spectrum of opinion on what 'consent' means in the context of secondary analyses. The common conception is that re-use of personal data should be aligned with the terms of the original consent. One alternative that may facilitate data sharing from future and historical studies is to anonymise data so they can be used without needing to retrieve and compare historical consent forms. As noted before, however, absolute anonymisation is difficult to achieve.

Some argued that the Regulation which is currently being considered by the EU to replace the Data Protection Directive may require more explicit and specific consent for any reuse of lawfully held personal data.

There are evident limits to what is meant by informed consent when research participants are asked for consent for reuse of their data in various, still-to-be defined future studies. In these circumstances informed and specific consent cannot be said to have been obtained. A return to research participants for specific re-consent for a proposed future study may not be practical or possible, and repeated requests may not be welcomed by participants.

A more exacting standard of consent, therefore, should not be considered as a more ethically sound mechanism or means to strengthen data protection. Instead, greater consideration should be placed on controlled access to data in safe havens with good governance and data security measures, and appropriate sanctions in cases of data breach.

⁴ <https://www.gov.uk/government/publications/caldicott-information-governance-review-department-of-health-response>

This document reflects the views of the attendees expressed at the dinner and does not necessarily represent the views of all participants, their organisations, the Academy of Medical Sciences or GlaxoSmithKline who supported the dinner. For further information, please contact Dr Naho Yamazaki, Head of Policy (naho.yamazaki@acmedsci.ac.uk, (0)20 3176 2168)

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Annex: Attendees at the dinner

- **Professor Robert Souhami** CBE FMedSci, Foreign Secretary, Academy of Medical Sciences and Emeritus Professor of Medicine, University College London (Meeting Chair)
- **Professor Douglas Altman**, Director, Centre for Statistics in Medicine and CRUK Medical Statistics Group, University of Oxford.
- **Mr Russell Brooks**, Vice President, II-ID & Biopharm Lead, Pharma R&D & Global Commercial Legal Operations, GSK
- **Sir Iain Chalmers** FMedSci, Co-ordinator, James Lind Initiative
- **Sir Gordon Duff** FMedSci, Chairman, Medicines and Healthcare Products Regulatory Agency
- **Dr Robert Frost**, Policy Director, Medical Policy, GlaxoSmithKline
- **Mr François Houyez**, Treatment Information and Access Director, EURODIS.
- **Mr Per Johansson**, Legal Officer, European Data Protection Supervisor.
- **Dr Trudie Lang**, Nuffield Department of Medicine, University of Oxford and Committee Member, Institute of Medicine consensus study on 'Strategies for Responsible Sharing of Clinical Trial Data'.
- **Dr Kate Law**, Director of Clinical and Population Research, Cancer Research UK
- **Professor Graeme Laurie** FRSE FMedSci, Chair of Medical Jurisprudence, School of Law, University of Edinburgh.
- **Professor Jonathan Montgomery**, Professor in Healthcare Law, University of Southampton, Chair, Nuffield Council on Bioethics, and Chair, Health Research Authority.
- **Baroness Onora O'Neill**, CBE HonFRS FBA FMedSci.
- **Dr Nicola Perrin**, Head of Policy, Wellcome Trust
- **Dr Francesco Pignatti**, Head of Oncology, Haematology and Diagnostics, Scientific and Regulatory Management Department, Human Medicines Evaluation Division, European Medicines Agency
- **Professor Martin Richards**, Emeritus Professor of Family Research at the University of Cambridge and Chair, Nuffield Council on Bioethics Working Party on 'Biological and Health Data'.
- **Dr James Shannon**, Chief Medical Officer, GlaxoSmithKline.
- **Mr Derek Stewart**, Associate Director, National Institute for Health Research Clinical Research Networks (NIHR CRN)
- **Ms Caroline Stockwell**, Assistant General Counsel, Pfizer
- **Dr Matt Sydes**, Senior Scientist and Senior Medical Statistician, MRC Clinical Trials Unit
- **Dr Naho Yamazaki**, Head of Policy, Academy of Medical Sciences