



Review

To share or not to share is the question



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ARTICLE INFO

Keywords:

Data sharing
Personalised medicine
Privacy

ABSTRACT

Data sharing is increasingly becoming an essential component of clinical practice and biomedical research. The debate has shifted from whether or not to exchange data to how best to achieve optimal sharing. This raises new ethical and legal challenges, particularly with regard to consent and privacy. This article discusses recent developments in the formulation of best practice guidelines for data sharing. Particular attention is focused on the Global Alliance for Genomics and Health (GA4GH) draft Framework of Conduct for Data Sharing.

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1. Introduction

As the power of integrating multiple sources of data to progress understanding of human health is becoming increasingly understood, there is a general recognition that the next phase of personalised medicine will see acceleration in data sharing to link genome scans to clinical data.¹ In the clinical context, the move to electronic health records and electronically stored data provides opportunities to use and share data to better understand disease and illness, inform treatment choices and patient care and improve health outcomes.² In the research context, organisations such as the International Cancer Genome Consortium (ICGC)³ and, more recently, the Global Alliance for Genomics and Health (GA4GH)⁴ have embraced policies and plans to proselytise and promote the exchange of clinical data not only amongst Consortium and Alliance

members but also more widely in research and clinical care. The overarching aim is to drive the research into the translation phase where the clinical data will be matched with genomic data to inform the development of treatments and medications.

'Data sharing' can take many different forms; e.g. patients agreeing to share their genomic and/or clinical data with researchers; researchers sharing their preliminary data with other researchers; biobanks and other holders of specimens and data sharing their resources with researchers in other countries. This paper encompasses all such forms of data sharing, but is particularly focused on larger scale data sharing involving multiple players, across jurisdictions.

The importance of data sharing has become something of a 'mantra'⁵ amongst medical and health researchers. This mantra has been fashioned by government initiatives to promote the new knowledge economy.⁶ As an example in the clinical context, the Strategy for UK Life Sciences states:

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¹ Knoppers BM et al (2011). 'Towards a Data Sharing Code of Conduct for International Genomic Research', *Genome Medicine* 3:46–49; Kaye J et al (2009) 'Data Sharing in Genomics – Re-shaping Scientific Practice', *Nature Genetics* 10(5):331–335.

² Schneeweiss, S (2014). 'Learning from Big Health Care', *New England Journal of Medicine* 370(23):2161–2163; Olver I, (2014) 'Linking Data to Improve Health Outcomes' 200 *Medical Journal of Australia* 368.

³ <http://icgc.org>.

⁴ <http://genomicsandhealth.org/>.

⁵ Jasny B (2013). 'Realities of Data Sharing Using the Genome Wars as a Case Study – an Historical Perspective and Commentary', *EPJ Data Science* 2:1 doi:10.1140/epjds13.

⁶ Academy of Medical Sciences UK (2010), *Review of the Regulation and Governance of Medical Research*, <http://www.acmedsci.ac.uk/>.

The UK can do much more to harness the opportunity that exists in the NHS. There is huge potential to better support the adoption and diffusion of innovation, to access patient data to inform the developmental phase, and to involve patients in trials and early access schemes for the treatment of chronic diseases, such as cancer.⁷

The sheer volumes of data are creating mountainous storage and download exchange challenges.⁸ The debate has shifted from whether or not to share data for research, together with the accompanying technical challenges, to how data exchange should be done in order to add value to the research endeavour whilst protecting research participants.⁹ However, like genomic science itself, data sharing in this arena has not proven to be easy and a long road lies ahead. There is recognition of the need for a risk/benefit analysis; whilst data sharing is seen as essential to promote the goals of the genome era, care must be taken to minimise the risk of harm from such data sharing. Of its nature, genetic data has some particular characteristics: genetic information is ubiquitous, permanent and unalterable. Even when de-identified, genetic data is always inherently identifiable, and this applies also to person's whole genome sequence, so special protections are required if such data is to be linked to other sensitive information.¹⁰ As mechanisms for data protection become increasingly sophisticated, risk arises from new strategies to out-flank protections.¹¹ Once data is released into the public domain, neither participants nor researchers can control its use, or the possibility of that data being linked to other data sets.¹² The pitfalls for data sharing are many, with privacy, industry–academia divides, distinction between first and third world technological capacities, and diverse researcher, clinical and institutional practices amongst the regulatory hurdles across national borders.¹³ Other challenges include workforce and infrastructure limitations but one of the greatest challenges is overcoming policy issues.¹⁴ Kaye has identified four particular areas for attention:

The difficulties of acknowledging individual contributions to the generation of data; the way that these policies change the responsibilities towards participants; the implications that this has for maintaining public trust; and the new mechanisms that have been developed for oversight of access to data.¹⁵

A key issue in this context is the level of informed consent for data sharing. Potentially there are a range of models – at one extreme – no consent or notice, or notice only, or 'opt-out' rights or 'opt in' rights or other forms of express consent. Because of the scale of genomic data and very nature of biobanks as platforms for research undertaken over a period of time, there has been considerable support for a 'broad consent' model whereby participants give agreement to the use of their samples and information, in a de-identified form, for future as yet unspecified research, subject to normal ethics committee review and this approach is endorsed in a number of jurisdictions.¹⁶ There are

some commentators, however, who contest that this can ever be an effective consent.¹⁷

Kaye has promoted technologically aided 'dynamic consent' as part of a more sophisticated genomic data management system: i.e. 'a personalised, digital interface that connects researchers and participants,' facilitating 'two-way communication to stimulate a more engaged and informed.. participant population where individuals can tailor and manage their own consent and preference.'¹⁸ There is continuing debate about optimal consent models for biobanks and large data sharing platforms¹⁹; for the purposes of this paper, as a minimum, broad consent should be obtained from participants to future genomic research and for data sharing, as a precondition for data sharing.

The development of data sharing policies and practices will require the development of standards.²⁰ This article examines how far an international code or framework of ethics may contribute to changing attitudes and practices towards more responsible and secure sharing of research and clinical data.

2. Background to data sharing

There has been major expansion of globalisation of research in the 'Genome Era'. This has prompted a range of international organisations to enter the arena of international ethics standard setting. Examples are UNESCO (and their trilogy of Declarations on the Human Genome and Human Rights, 1997; Human Genetic Data 2005; and Bioethics and Human Rights 2005) and the OECD (particularly their Report on *Creation and Governance of Human Genetic Research Databases*, in 2007 and their *Guidelines on Human Biobanks and Genetic Research Databases* 2009). Similarly, there has been a great deal of progress by national organisations in the development of governance frameworks for biorepositories, which are seen as essential resources for global genomic research. As examples, the National Cancer Institute of the National Institutes of Health provided guidance on biobanks in 2006,²¹ as did the international Human Genome Organisation in their Human Genomic Databases Report in 2002. In Australia, the National Health and Medical Research Council commissioned a Biobanks Information Paper in 2010.

From the 1996 Human Genome Project Bermuda Declaration onwards, researchers themselves have also embraced the data sharing movement.²² There is a realisation by researchers of the power of shared data.²³ This can, however, represent a tension with university policies focusing on protection of intellectual property rights, engagement with industry and formalisation of exchanges of materials.²⁴ Despite this, it is widely understood that genomic research is a

⁷ Academy of Medical Sciences UK (2010), *Review of the Regulation and Governance of Medical Research*, <http://www.acmedsci.ac.uk/>.

⁸ Google, Amazon and Microsoft are active in this new cloud commercial environment.

⁹ Ohno-Machado, L (2012) 'To Share or not to Share: That is Not the Question' *Science Translation Medicine* 4:1–4.

¹⁰ Ohno-Machado, L (2012) 'To Share or not to Share: That is Not the Question' *Science Translation Medicine* 4:1–4.

¹¹ Erlich Y and Narayanan A, (2014) 'Routes for Breaching and Protecting Genetic Privacy' *Nature Review Genetics* 15:409.

¹² Kaye J et al (2009). 'Data Sharing in Genomics – Re-shaping Scientific Practice', *Nature Genetics* 10(5):331–335.

¹³ Jasny B (2013). 'Realities of Data Sharing Using the Genome Wars as a Case Study – an Historical Perspective and Commentary', *EPJ Data Science* 2:1 doi:10.1140/epjds13.

¹⁴ Ohno-Machado, L (2012) 'To Share or not to Share: That is Not the Question' *Science Translation Medicine* 4:1–4.

¹⁵ Kaye J et al (2009). 'Data Sharing in Genomics – Re-shaping Scientific Practice', *Nature Genetics* 10(5):331–335.

¹⁶ Otlowski, M (2012). 'Tackling Legal Challenges Posed by Population Biobanks: Reconceptualising Consent Requirements' *Medical Law Review* 20, 191–226.

¹⁷ Allen, C Joly, Y and Grandos Morena, P (2013). 'Data Sharing, Biobanks and Informed Consent: A Research Paradox?' *McGill Journal of Law Health* 7, 85–120.

¹⁸ Kaye J et al 'Dynamic consent: a patient interface for twenty-first century research networks' *European Journal of Human Genetics* (2014) advance online publication 7 May 2014; doi: 10.1038/ejhg.2014.71 <http://www.nature.com/ejhg/journal/vaop/ncurrent/full/ejhg201471a.html>.

¹⁹ Stein, D (2013) 'Reforming Biobank Consent Policy: A Necessary Move Away from Broad Consent Toward Dynamic Consent' *Genetic Testing and Molecular Biomarkers* 17 (12) 855–856; Steinbekk, K Myskja B and Solberg B (2013). 'Broad Consent versus Dynamic Consent in Biobanks Research: Is Passive Participation an Ethical Problem?' *European Journal of Human Genetics* 21, 897–902.

²⁰ Kush R and Goldman M (2014). 'Fostering Responsible Data Sharing through Standards', *New England Journal of Medicine* 370(23):2163–2165.

²¹ National Cancer Institute, National Institutes of Health, US Department of Health and Human Services (2006). *First-Generation Guidelines for NCI-Supported BioRepositories*, <http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf>.

²² Sulston J and Ferry G (2003). *The Common Thread*, Corgi Books 165-9 and *passim*.

²³ Joly Y, Dove ES, Knoppers BM, Bobrow M & Chalmers D (2012). 'Data Sharing in the Post-genomic World: the Experience of the International Cancer Genome Consortium (ICGC) Data Access Compliance Office (DACO)', *PLoS Computer Biology* 8(7): e1002549. doi:10.1371/journal.pcbi.1002549.

²⁴ Caulfield T, Harmon SHE and Joly Y (2012). 'Open Science Versus Commercialization: a Modern Research Conflict', *Genome Medicine* 4:1.

worldwide endeavour that requires the cooperation of researchers working together between nations. However, the laws and guidelines that govern such exchanges, including any subsequent use, differ between countries, reflecting the cultural diversity that exists between them. This presents a challenge, as there is no current international agreement between nations at a high level that governs such exchange, and national ethical guidelines are often developed without considering the need for international harmonisation (with the exception of EU member states).

The exchange of biological materials provides a useful reference point. One of the features of the early stages of this biotechnology revolution in the 1980s and 1990s was an increase in collaborations between academia and industry, usually accompanied by transfer of intellectual property rights and essential biological research materials. Traditionally, these were freely shared and exchanged between researchers, frequently without any type of legal documentation.²⁵ The 1980s saw increasing engagement of universities with industry and the development of national biotechnology strategies aimed at commercialising research, coinciding with a move away from this scientific norm of free and open sharing. University policies for engagement with industry began to be directed towards protection of intellectual property rights and their transfer to industry through assignment, licensing and the creation of spin out companies. This university and industry engagement saw the emergence of specialist technology transfer offices.²⁶

There are great expectations that research in the 'Genome Era'²⁷ will lead to the development of innovative products and processes in human healthcare, agriculture, the environment and industry. Government policy in many developed nations, expressly supports this research direction. Although the impetus to secure intellectual property rights remains strong, raw research data are increasingly shared amongst researchers and uploaded on open access sites to maximise their availability to other interested research groups.²⁸ Leading research funders, such as the United States National Institutes of Health (NIH) *Policy for Sharing of Data Obtained in NIH Supported or Conducted Genome-Wide Association Studies* have led initiatives to promote the sharing of data by requiring that datasets remain available to all investigators, unencumbered by intellectual property claims.²⁹ Similarly, many public foundations such as the Wellcome Trust and other signatories to the Full Joint Statement by Funders of Health Research,³⁰ have joined these initiatives to promote the sharing of data generated in research activities by publication of open access sites.

This modern open access culture, often referred to as the 'research commons' aims to increase the volume and quality of research using existing and new datasets.³¹

²⁵ Bennett A, Streitz W and Gaecel R (2007). 'Specific Issues with Material Transfer Agreements', in Krattiger A, Mahoney R, Nelsen, L et al (eds) *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices*. MIHR: Oxford; UK and PIPRA: Davis, USA. Chapter 7.3: 697–706.

²⁶ Rodriguez, V. (2007) Merton and Ziman's mode of science: the case of biological and similar material transfer agreements. *Science and Public Policy* 34: 355–363 There was also a formalisation of exchanges of biological materials, through material transfer agreements.

²⁷ Collins F (2010) *The Language of Life: DNA and the Revolution in Personalized Medicine*, Harper Collins Publishers *passim*.

²⁸ Toronto International Data Release Workshop Authors (2009). 'Prepublication Data Sharing', *Nature* 461:168–170.

²⁹ National Institutes of Health (NIH), *Final NIH Statement on Sharing Research Data* (26 February 2003), <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>. See also Glitter DM, 'The Challenges of Achieving Open Source Sharing of Biobank Data' (2010) 29(6) *Biotechnology Law Report* 623 at 627–628.

³⁰ Karunakara U (2013). 'Data Sharing in a Humanitarian Organization: The Experience of Medecins Sans Frontieres', *PLoS Medicine* 10(12):e1001562.

³¹ Bubela T, Schofield PN, Ryan CD, Adams A and Einhorn D (2012). 'Managing Intellectual Property to Promote Pre-Competitive Research: the Mouse as a Model for Constructing a Robust Research Commons', *Journal of Law, Information and Science* 22:98–121.

3. How to regulate sharing?

If the question on sharing data is more and more receiving an affirmative answer, because it is seen as an ethical and scientific imperative, regulation will need to be reviewed and tested for ethical and legal 'fitness-for-purpose'. In addition, the amount of data and the frequency of access will expand exponentially, making this testing for ethical and legal 'fitness-for-purpose' essential. In this regard, three organisations have taken leadership in promoting and developing data sharing principles in the specific context of collaborative international genomics research.³² These organisations, together with the Global Alliance for Genomics and Health (GA4GH) have prepared a set of guiding principles in a preliminary international data sharing Framework of Conduct for Data Sharing. The Framework is a preliminary set of standards for ethical and legal 'fitness-for-purpose' in data sharing and a focus to promote and maintain ongoing international discussion.³³

The challenges of responsible ethical and legal data exchange have clear parallels with the development of regulatory frameworks for biobanks. Challenges to traditional notions of individual consent, privacy and public trust were acknowledged,³⁴ and were particularly pertinent to large-scale population biobanks involving long-term tissue and data storage; multiple research projects, often involving different research teams in different countries; and research projects which were not clearly defined when the biobank was created. The establishment of these large-scale biobanks around the world led to the development of policy statements by the OECD,³⁵ practical guidelines from funders, such as the US NCI³⁶ and professional societies, such as ISBER³⁷ and much academic commentary debating the nature, form and content of the instruments needed to regulate this activity. In addition, some biobanks, like the UK Biobank, developed their own ethics and governance frameworks.³⁸ Large-scale data sharing initiatives and related issues of 'big data' can be seen from this perspective. The effort of the GA4GH in its preliminary international Framework of Conduct for Data Sharing is a major direction-setting initiative towards the development of responsible ethical and legal standards by the research community. The Framework incorporates four *Foundational Principles for Responsible Data Sharing* {Respect Individuals, Families and Communities; Advance Research and Scientific Knowledge; Promote Health, Wellbeing and the Fair Distribution of Benefits; and, Foster Trust, Integrity and Reciprocity} and ten *Core Elements for Responsible Data Sharing* (Transparency; Accountability; Engagement; Data Security and Quality; Privacy, Data Protection and Confidentiality; Risk–Benefit Analysis; Recognition and Attribution; Sustainability; Education and Training; and, Accessibility and Dissemination). These are standards and do not provide a single

³² The international Public Population Project in Genomics (P³G), an international consortium of large-scale genetic epidemiological studies and biobanks; the European Network for Genetic and Genomic Epidemiology (ENGAGE), a research project to translate data from large-scale epidemiological research initiatives into relevant clinical information; and the Centre for Health, Law and Emerging Technologies (HeLEX).

³³ This idea was promoted and adopted by the GA4GH from the article by Knoppers BM et al (2011). 'Towards a Data Sharing Code of Conduct for International Genomic Research', *Genome Medicine* 3:46–49. The "Code" was replaced in version 7 with "Framework".

³⁴ Knoppers BM and Chadwick R (2006). 'Human Genetic Research: Emerging Trends in Ethics', *Nature Reviews Genetics* 6:75–79.

³⁵ Organisation for Economic Cooperation and Development, *Guidelines on Human Biobanks and Genetic Research Databases* (OECD, 2009), www.oecd.org/dataoecd/41/47/44054609.pdf.

³⁶ See, for example, *First-Generation Guidelines for NCI-Supported Biorepositories* April 2006, National Cancer Institute, National Institutes of Health, U.S. Department of Health and Human Services <http://biospecimens.cancer.gov/biorepositories/First%20Generation%20Guidelines%20042006.pdf>.

³⁷ International Society for Biological and Environmental Repositories (ISBER). "Best Practices for Repositories I: Collection, Storage, and Retrieval of Human Biological Materials for Research" (2005) 3 *Cell Preservation Technology* 1, 5–48.

³⁸ UK Biobank, Ethics and Governance Framework, Version 3.0 2007 <http://www.ukbiobank.ac.uk/wp-content/uploads/2011/05/EGF20082.pdf?phpMyAdmin=trmkQIYdjjnQIqj%2CfAzikMhEnx6>.

one-size-fits-all model, but must recognise research, cultural, regulatory, and healthcare differences between countries.

4. Conclusions

If data sharing is no longer a question but a goal to be facilitated, without compromising proper ethical standards, there is a need to review the current data sharing practices to see whether any of the pitfalls identified in the literature are in fact blocking sharing. As noted, the potential pitfalls to data sharing are many and include differences in more protective cultural approaches to clinical care records and data. The GA4GH Framework of Conduct for Data Sharing will, hopefully be a touchstone for developing and accelerating responsible data sharing. Before increased regulation is proposed a study of the actual legal blockages should be undertaken. There is a possibility, if not likelihood, that blockages are, in many instances, more of a practical and cultural nature. On a practical level, ethical approval of research should probably now include a standard reference to data sharing, with institutions endorsing the GA4GH Framework of Conduct for Data Sharing. In

the genome age of globalised research and electronic data linkage, consent remains important but there must be a focus on the 'governance' approaches to the administration, management, custodianship, access to data and monitoring of research, particularly large-scale multi-centre international projects. The ethical 'health' of data sharing practices and systems is highly dependent on researchers' primary responsibilities under the national codes of research practice, the second tier of review of research projects system and also, importantly, on the integrity of the researchers themselves.³⁹ Success can only be achieved through the power of collaborative action with a shared mission. The GA4GH Framework for Conduct for data sharing potentially has an important role to play in galvanising this effort.

Acknowledgments

This research was supported by the Australian Research Council Discovery Project DP11010069.

³⁹ See Chalmers D and Pettit P (1998). 'Towards a Consensual Culture in the Ethical Review of Research', *Medical Journal of Australia* 168:79–82.