Biobanking, networks and the challenge of globalisation

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Declarations

• Haematologist/BMT Physician RNSH
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• Director (Sydney Uni) of *Praxis Australia*
• Chair RACP Ethics Committee
• Chair ABMDR REC 2006-2016
• Investigator on Phase 1-3 Clinical Trials in BMT, Haematological malignancies and ethics
• Recruit to industry-sponsored clinical trials
• No other research, education or consultancy-relationship with Pharmaceutical, Pathology or Biotech industry.
Outline

1. The emergence of Biobank Networks

2. Globalisation and the ethics of networking
   Ethical issues raised by biobank networks and “global” biobanking
   Insights from empirical research

3. Broad and Dynamic Consent
Networking and globalisation

• Increasingly clear that single project, single institution biobanks have limited utility and are often unsustainable

• Biobanks becoming larger and more often defined by informatics platforms that open them up to researchers.

• Biobanks increasingly ‘networked’ to maximise their power
Bionetworks

• Networks can be domestic or global
• Many benefits:
  – Expertise sharing (international consortia)
  – Necessity for large integrated collections
    • Deals with population heterogeneity
    • Molecular epidemiology to isolate biomarkers
    • Longitudinal analysis to understand rare and complex diseases
    • Necessary for constructing predictive analytics
  – Sustainability of single disease specific tissue banks
  – Regulatory requirements for clinical trials to include ethnically diverse populations
  – Standardisation of operations and governance internationally (ICH /GCRP)
The networking and globalisation of biobanks

1. Pooling and/or centralising resources
   - Samples
   - Associated data
   - Analytic facilities/expertise
   - Includes
     • Physical joining → larger collections/resources
     • Virtual networking to facilitate access

2. Distribution and compartmentalisation
   - Different locations for e.g. financing, collection, storage, research, etc

3. Single organisation operating globally
Example 1: Pooling and/or centralising resources

Latin American and Caribbean Network of Tumour Banks

- Red de Bancos de Tumores de la América Latina y Caribe (ReBT-LAC) Created in 2007

- Linked to Network of National Cancer Institutes

- As of 2015, 19 banks in 9 countries

- Activities
  - Technical support for the standardization of existing tumour banks.
  - Implementation of new tumour banks.
  - Creation of regional training and technical capacity building centres
Example: Pooling and/or centralising resources

EuroBioBank

- Network of DNA, cell and tissue samples for rare diseases
- Europe, Israel, UK, Canada
- Funded by Fondazione Telethon
- Virtual network (central online catalogue)
- Offers ethics documents and standard operating procedures
- Over 440,000 samples across the network
  - 13,000 collected each year
  - 7,000 distributed
Variations of Pooling/Centralising resources

- **Storage Networks**: Shared facilities to reduce costs
- ‘**Bring and Share’ Networks**: Lower fee structures and resource sharing for researchers [eg. Genetic Repositories Australia]
- **Catalogue Networks**: Maintain database searchable by external researchers
- **Partnership Networks**: Share costs in recruitment
- **Contributor Networks**: Individuals donate directly [eg. ALLG Tissue Bank]
- **Expertise Networks**: Shared expertise in ethics and governance procedures [eg ABNA Network]

[Shickle et al., 2010]
Example 2: Distribution and compartmentalisation

China Kadoorie Biobank

- Prospective cohort focused on common chronic diseases in the Chinese population
- During 2004-8, over 510,000 adults recruited from 10 geographically defined regions → ongoing follow up
- Funded by
  - Wellcome Trust, UK Medical Research Council (MRC), British Heart Foundation (BHF) and Cancer Research UK (CRUK)
  - Chinese Natural Science Foundation and Chinese Ministry of Science and Technology
China Kadoorie Biobank

- Conducted jointly by
  - University of Oxford’s Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU)
  - Chinese Academy of Medical Sciences (CAMS), China CDC
- Led by a Steering Committee Study with coordinating centres in Oxford, Beijing and each of the 10 study areas in China.
- International Scientific Advisory Committee
- Complex array of different stakeholders with varying interests.
Example 3: Single organisation operating globally

23andMe

• For-profit incorporated company offering direct-to-consumer DNA analysis

• Retains saliva samples and/or genetic data from its customers

• Boasts 1 million customers globally

• Actively seeking to expand globally
The networking and globalisation of biobanks

• All have in common
  – Increased size
  – Increased heterogeneity
  – Interactions and movements across jurisdictions

• What ethical issues does this raise?
Ethics and biobanking research: The ‘old ones’

- Confidentiality
- Ownership
- Benefit sharing (especially if commercial)
- Respect for tissue (disposal)
- Consent
Ethics of biobank networks

All the issues of "local" biobanks, but more complex

Consent

• Specific or broad?
• OK if person knowingly donates to a formal network
• BUT what if Researcher A is given access to tissue from a Biobank A,
  ... And wants to collaborate with, and send tissue to Researcher B
  ...Who wants to collaborate with, and send tissue to Researcher C etc etc etc.
  – What consent is appropriate?
  – Can Institution A relinquish custodianship?
  – Case example: ABMDR Board consideration of Networks and Sharing and the meaning of Custodianship
Ethics of biobank networks

Privacy

• Does privacy exist? (data insecurity increasingly obvious)
• How can we accommodate different privacy regulations across different jurisdictions
• How can we avoid data breaches when more and more samples and information are being virtually linked and/or physically transported?

Communication with donors
Ownership

• Cultural significance of biomaterials
• Ongoing questions regarding who owns the data and tissue in biobank networks?
  – The people who originally collected it?
  – The people who now have it?
  – The people who “do something” with it?

Benefit sharing/justice

• How can we ensure that people who donate tissue to large networks share in benefits if results are commercialised and products result?
  – E.g. access to “precision medicine” in LMIC
Ethics of biobank networks

Additional issues

- Cross-jurisdiction regulatory and governance issues
- Replicative review
- Reciprocity and delegation (accepting other reviews and oversight)
- Federation (joining together review and oversight)
- Lack of regulatory harmonisation
- Issues of scale (getting into “big data”)
  - Research funding – esp of consortia (scale)
  - Data quality and governance
  - Curation (Storage, annotation)
  - Cost-sharing
  - Linkage ability; comparability across sites and times
  - Complexity of analysis/interpretation (signal vs. noise; confounders)
  - Translation to local contexts
Ethics of biobank networks

As biobanking becomes more complex, the sub-components will become more specialised and position themselves in the most favourable national contexts. By exploiting the most favourable country-specific benefits for their subcomponents, will biobanks escape national oversight and governance from any single jurisdiction? What might be the unintended consequences of this?
Biobank networks and globalisation: Emerging research insights

- CATI public survey
- ATSI community engagement
- Interviews
- Stakeholder survey
- Legal audit

Trust high but not absolute
Distrust of commercial interests
Cultural control
Nationalism (trust)
National interests more important than global benefit
CONSENT – ENDURING CHALLENGES
Challenge of Consent

• Requirement for consent is a fundamental principle of research.
• Enshrined in Declaration of Helsinki and all subsequent legal instruments (although some exemptions for medical/public health research)
• Manifestation of respect for persons/human dignity and autonomy
• Formalisation of social contract
• Basis for data protection and privacy legislation
Consent in context of Biobanking

- Multiple researchers
- Multiple projects
- Emergent science and necessity for re-analysis
- Re-consenting costly, time-consuming and leads to high drop-out rates.

**Solution:**
- *Stakeholder engagement*
- *Broad consent (Practical and simple)*
- *Broad consent + Regular Updates on bank/projects*:
  - UK Biobank, Norwegian Mother-Child Cohort Study etc
Problems of Broad Consent

- **Still static** – little difference with project-specific paper-based consent
- **Communication/contact generally an ‘extra’** with limited meaningful dialogue between researchers and participants.
- **Consent not meaningful** – does not genuinely enable participant to consider risks/benefits of projects – including risks to privacy.
- **Does not accommodate changing views/interests of participant.**
- **May mandate other (associated) conditions** eg return of incidental findings
- **May not promote active on-going engagement and/or recontact.**
- **May not satisfy change legal requirements** that privilege explicit consent (eg European Data Protection Regulations).
- **May be insufficient protection against loss of privacy** (analogy medical cases, case reports) – increasingly possible with advances in IT – which are making anonymisation, coding etc ineffectual – and suggest that participants need to explicitly agree to identification or the possibility of identification.
DYNAMIC CONSENT
Dynamic Consent

• Personalised, interactive IT interface for ongoing research participant engagement.
• **Dynamic because it enables ongoing interaction with new and continuing consent and tailored communication. Not locked in time.**
• Facilitates different consent for different projects – not just project specific OR broad.
• Enable change of contact details/circumstances
• Recognises move from third party consent – assent – consent with age/maturation.
• Enables participate to set and alter contact preferences and even track their research/sample
• Enables tailoring of preferences for research; all, some, none etc
• New encryption techniques enable consent/communication preferences to ‘wrapped’ around donors data and sample so that it travels with it.
• Customised to needs/capabilities of biobank/research facility
Proposed advantages of Dynamic Consent

• Philosophical: Provides more meaningful consent (than broad consent)
• Builds trust
• Streamlines recruitment (participant selection, IT-approach)
• Enables efficient and cost-effective recontact
• Participant can adjust privacy settings
• Conforms to highest legal standards with regards to consent, recontact etc
• Enables differential consent – opt-in and opt-out
• Enables nuanced withdrawal (as opposed to all-or-nothing)
• Facilitates communication: not just initial PIF but - lay summaries, simple ‘thank-you’ notes, general or specific research results, biobank or trial updates, academic publications, links to materials in other languages, summaries etc.
• Overcomes digital divide as it can tailored to web, tablets, mobile phones etc (and so may be more accessible to elderly etc)
• Improves scientific literacy
• Improves transparency and risk management (through ongoing identification of samples/data through ‘wrapped information’ and capturing of complete audit trail.)
Emergence of Dynamic Consent

• Initial work done in *EnCoRe* (Ensuring Consent and Revocation) project (combining Oxford Radcliffe Biobank, Oxford Musculoskeletal Biobank and the Oxford Biobank). Kaye and colleagues.

• Reg4All [https://www.reg4all.org/](https://www.reg4all.org/)

• Michigan’s *Biotrust for Health* (newborn Screening Biorepository) [http://www.michigan.gov/mdhhs/0,5885,7-339-73971_4911_4916-209738--,00.html](http://www.michigan.gov/mdhhs/0,5885,7-339-73971_4911_4916-209738--,00.html)
Next, you can choose to share...

everything with everyone,
some things with some people,
nothing with no one,

Reg4All puts you in control and reflects your sharing preferences, however simple or complicated they may be.

<table>
<thead>
<tr>
<th>Your Sharing Preferences</th>
<th>Discover Me</th>
<th>Contact Me</th>
<th>Use My Data</th>
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<td>![Allow]</td>
<td>![Allow]</td>
</tr>
<tr>
<td>Trusted researchers working on my condition</td>
<td>![Allow]</td>
<td>![Ask Me]</td>
<td>![Ask Me]</td>
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<tr>
<td>Researchers not working on my condition</td>
<td>![Deny]</td>
<td>![Deny]</td>
<td>![Deny]</td>
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</table>
Challenges

- **Requires cultural change** (for HCPs, researchers and patients/public).
- **Claims** of increased efficacy, participation, recruitment and scientific literacy **unproven**.
- **IT infrastructure/technical capacity needs substantial** (high up-front cost)
- **Sustainability**
- **Access and equity** problems remain
- **Variable uptake** (less by lower socioeconomic groups and less well-educated)
- **Consent/contact fatigue**
- **Overstated interest** (no-one cares!)
- **Does not really overcome digital divide** (either for individuals or for countries/populations)
- **Does not address other ethical issues raised by creation of biobank networks**
The enduring challenges of dynamic consent

Appealing alternative to simply going with Broad Consent – dynamic and more legally/ethically coherent, BUT

– Requires technological capacity
– Requires a profound cultural re-imagining of researcher-research participant relationship
– Will only work with resources, commitment and trust
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