International Lessons: Biobanks

Clémentine Sallée, Research Associate

Genetic and Society Project, C.R.D.P.

Université de Montréal

Professor Bartha Maria Knoppers,

Canada Research Chair in Law and Medicine

Université de Montréal

OUTLINE

I. Human Genetic Research Databases (HGRDs): In Search of an Adequate Legal and Ethical Framework

II. Population HGRDs: A Selection of Existing Projects

III. Population HGRDs: A Typology of Challenges and Issues

Introduction

→Advances in Genetics and Genomics, Biotechnology and Bioinformatics: Implications for Research

- From rare single gene disorders (candidate genes/linkage studies) to common complex diseases (association studies)
- From national research to regional and international collaboration
- From traditional research biobanking to studies relying on human genetic research databases (HGRDs)
- From reification (waste) ⟶ sacralization (samples = persons)
  ⟶ byzantine bureaucratization of ethics review
  ⟶ internationalization?

→ Human Genetic Research Databases: Definition and Context

- A collection of information organized in a systematic way for research purposes and from which genetic material and related data can be derived
- Terminology used: biobanks, collections, cohorts, gene banks, population studies, genome databases
- Existing databases: a diverse typology
- The new reality of HGRDs: the birth of large-scale populations HGRDs (min: 10 000 individual participants)

I. HGRDs: In Search of an Adequate Legal and Ethical Framework

- Trend: proliferation and specialization of national and international policies : (from principles governing research involving human subjects to genetic or genomic database management)
- Demonstrate the Need for Harmonization of Principles and Terminology

A. Proliferation and Specialization of Laws and Policies

1) International and Regional Jurisdictions

2) National Jurisdictions: An Uneven Playing Field

B. The Challenge of Harmonization

1) Internationally: Increasing Need for Harmonization

2) Nationally: Moving towards the Harmonization Approaches

3) Emerging Consensus on Some Ethical Principles

4) Some Controversial Issues

A. Proliferation and Specialization of Laws and Policies:

(1) International and Regional Jurisdictions

- Council for International Organizations of Medical Sciences (CIOMS), *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (2002)
- World Medical Association (WMA), *Declaration on Ethical Considerations regarding Health Databases* (October 2002)
- Human Genome Organization (HUGO), *Statement on Human Genomic Databases* (December 2002)
- UNESCO – General Conference, *International Declaration on Human Genetic Data*, Geneva (2003)
- World Health Organization (WHO), *Genetic Databases – Assessing the Benefits and the Impact on Human Rights and Patient Rights* (2003)
- European Commission, *The 25 Recommendations on the Ethical, Legal and Social Implications of Genetic Testing* (2004)

2) National Jurisdictions: An Uneven Playing Field

i. Disparity between jurisdictions

- A few countries have implemented legislation that specifically regulates HGRDs (establishment, governance structure, collection, processing and storage mechanisms, etc.):

* *Human Genes Research Act*, December 13, 2000 (Estonia)
* *Biobanks [Health Care] Act* (2002:297), May 23, 2002 (Sweden)
* *Act on Biobanks no. 1102000*, May 13, 2000 (Iceland)
* *Act on Biobanks No 12*, February 21, 2003 (Norway)
* *Danish Law on Biobanks*, May 5, 2004 (Denmark)

- In other jurisdictions, application of existing legislative schemes pertaining to traditional research, data protection, public health issues …

  → confusion, overlap, conflicts, or areas left unregulated

  → "…several systems co-exist so that the problems are approached from different angles which ignore each other" (France, CCNE, Opinion 77, 2003)

ii. However, increasing interest and debate surrounding HGRDs at a national level

Examples of reports/opinion/ by National Ethics/ Advisory Committees or Law Reform Commissions

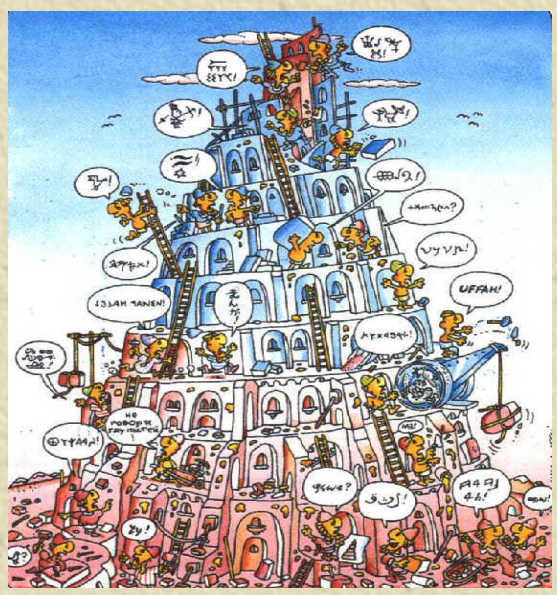
- Israel's Bioethics Advisory Committee, *Population-Based Large-Scale Collections of DNA Samples and Databases of Genetic Information* (2002)
- Australia Law Reform Commission, *Essentially Yours*, Part E: Human Genetic Databases (2003)
- France – CCNE Opinion 77, *Ethical Issues Raised by Collections of Biological Material and Associated Information Data: "Biobanks", "Biolibraries"* (2003)
- German National Ethics Council, *Biobanks for Research* (2004)
- Canadian Biotechnology Advisory Committee, *Genetic Research and Privacy* (on genetic biobanks) (2004)

B. The Challenge of Harmonization

1) **Internationally: Increasing need for harmonization**

- Lack of internationally agreed upon rules and common taxonomy detrimental to research collaboration, databases compatibility, exchange and transfer of information and researchers
- The acknowledged need for harmonization of nomenclature and principles: e.g. International projects to further harmonization: ex WHO project; « Human Genetic Databases: Towards a Global Ethical Framework » (Empirical study of existing HGRDs and policy frameworks to design global HGRDs policies)

- « [d]espite the existence of numerous declarations, guiding principles and codes dealing with the issue of genetic data, the changing conditions of genetic research call for the establishment of an international instrument that would enable State to agree on ethical principles, which they would then have to transpose into their legislation » Secretary-General UN- Economic and Social Council (2003)



2) Nationally: Harmonizing Approaches

- The specificity of HGRDs acknowledged (long-term storage, consent, structure…)
- The limits of traditional consent and personal data/privacy legislation
- A call for the implementation of a coherent and comprehensive regulatory framework that would address the issues of banking and population-based HGRDs: avoiding strict regulatory mechanisms while adequately protecting participants and structuring the conduct of research

  "the magnitude of the operation together with the specific ethical issues mentioned above – particularly regarding commercial initiatives- underscore the need for national guidance" (Israel Bioethics Advisory Committee (2002))

3) Emerging consensus on some ethical principles

- Tailoring of traditional consent mechanisms to the specificity of databases
- Correlation between the degree of data identifiability, need to re-contact, withdrawal of consent, return of results, access
- The need for adequate ethical oversight from the inception of a database as well as monitoring mechanisms
- Initiating, promoting and strengthening the professional/public dialogue: the public as active participants:
  - In the elaboration of the legal and ethical framework and;
  - In the establishment of any new population-based HGRD (strengthening the professional/public dialogue) :

  "a public education and consultation strategy must precede the establishment of any large-scale population genetic research initiative" (Canadian Technology Advisory Committee – 2004)
- The need to develop a benefit-sharing policy: giving back to the community /population opening the door to the possibility of commercialization

4) Some controversial issues

- Funding (private Vs public or semi-public endeavours)
  - Analysing differences, advantages/disadvantages: (Israel Bioethics Advisory Committee – 2002)
- Original informed consent and secondary uses of samples and data (from specific, to broad or even blanket consent, authorization model)
- Protecting privacy (choice of words and adequate mechanisms: anonymization Vs coding)
- Personal feedback: right to know in a large-scale setting (clinical relevance of results, genetic counseling, interpretation of results)
- Status of genetic material (ownership/remuneration/financial gains)
- Governance structure (check and balances)
- Ethical review for multi-centered projects
- On-going monitoring
- Involvement of industry

II. HGRDs: A Typology of Populations

- 9 HGRDs selected and classified according to sample size :

A. Regional or Provincial HGRDs
B. National Population HGRDs
C. Ethnic-based HGRDs
D. International Endeavours

A. Regional or Provincial HGRDs

i. **The Personalized Medicine Research Project (PMRP) (Wisconsin):** a community public/private effort to personalize medicine

ii. **CARTaGENE (Québec)**: analysing genetic variation in a modern, heterogeneous population

B. National Population HGRDs

- **Iceland DeCode BioBank:** Commercializing DNA and genetic research
- **The Estonian Genome Project:** A ‘medical care’ model
- **The UK Biobank**: Genetic epidemiology for public health purposes

C. Ethnic-based Population HGRD

i. **Genomic Research in the African Diaspora (GRAD):** The challenge of studying the genetic variation of a particularly underrepresented ethnic group

D. International Population HGRDs

i. **GenomEUtwin:** building on collaboration of existing twin cohort studies to analyse **g**enetic and lifestyle risks of common diseases

ii. **HapMap:** Haplotype map ("ancestral" blocks of SNP's) to be freely available in the public domain

E. Regional/International Endeavours

i. **Public Population Project in Genomics (P3G):** Harmonization of national biobanks for international collaboration: a common, open data knowledgebase – the challenge of international collaboration and sharing of data

III. Population HGRDs: From Principles to Practice: A Typology of Challenges and Issues

A. Establishing HGRDs: Ensuring Legitimacy
B. Building HGRDs: Ensuring Adequate Protection, Building Trust
C. Governing HGRDs: Ensuring the Existence of Adequate Checks and Balances

A. Establishing HGRDs: Ensuring Legitimacy

i. Justifying: key to funding and support from research community

- No or little immediate personal benefit
- Disproportionate expenses? Long-term benefits?
- Futility or ineffectiveness?

"although many geneticists agree that these databases will yield a plethora of useful information, it is not clear that they will deliver on their most ambitious promises"(Kaiser J., Science (2002))

→ Necessary insistence on societal benefits; scientific transparency, public engagement, inform media and involve stakeholders.

ii. Establishing the research infrastructure: ensuring democratic legitimacy

- **The legislative path (Estonia/Iceland): is Parliament the most democratic forum?**
  - Absence of prior public communication or engagement process ?
  - Iceland: absence of public involvement, the establishment of the biobank shadowed by the passing of the *Health Sector Database Act*
  - Estonia- passing of the Act caught the media's attention – though absence of prior debate, Estonian Genome Project has promoted public communication ever since
  - Norway Biobanks Act (2003) and existing databanks: legislation preventing the functioning of existing HGRDs
  - ➢ Legislation, if implemented, should be preceded by a debate involving the community at large (from scientists to representatives of the public and legal experts)

iii. Self-regulation: The public (designer of its own involvement) (Cart@Gene, UK Biobank, HapMap, Marshfield Clinic, GRAD)

- Initiation of the projects by scientists themselves
- Adapting science to communities' or populations' desires, preferences, trust, traditions

(examples)

- HapMap: Community engagement and public consultation in each community, the creation of a Community Advisory Board in accordance with Coriell policy
- UK Biobank protocol elaboration and framework design involving professionals and the community
- GRAD: the GenEthics Core involvement: Building bridges between scientists and the community
- Cart@Gene , RMGA Statement (2003) "A guiding mechanism for population genetic research is prior and on-going public consultation"

➢ Self-regulation – lack of a uniform national standard.

➢ Solution? the public as participants in the elaboration of national regulatory frameworks

▪ Trans-national enterprises: the dilemma of harmonization (GenomEUtwin, P3G, HapMap)

- Projects based on trans-national/international collaboration: the necessity of a minimal threshold of harmonization if not standardization
  - Of scientific approaches, technologies, standards and measurements
  - Of ethical issues/governance structure: finding a framework that is both adapted to the trans-national or international nature of the project while taking into consideration the specificity of the projects
    - → P3G international working groups and knowledgebase
    - → GenomeEUtwin Cores
    - → HapMap research groups/ethics committee
    - ➢ Success dependent on trust and communication between members, and based on a common understanding of the issues involved, agreement on the scientific, ethical, legal, governance aspects of the project and common philosophy

B. Building HGRDs: ensuring adequate protection, building trust

i. Ensuring representation: the selection process

- Ideal: inclusion of all groups represented in the sampled population
- Reality: financial constraints, careful selection process critical (ex: HapMap selection of 270 representative samples from four different regions in the world and parallel study to verify this postulate**)**

ii. Building public trust:

- Adapting communication strategies
- Taking into account the media, community-based and advocacy groups
- Creating incentives for participation: reassuring the public in terms of benefits, confidentiality, privacy and commercialization of samples
- Remuneration/ benefit-sharing policy

iii. Ensuring data collectors' participation and expertise:

- The controversial issue of the remuneration of data collectors ; the EGP and Marshfield Clinic's choice to remunerate GPs

- Training data collectors: Designed for health care professional not familiar with genetic research and bio-informatics: e.g. the EGP training program

- Training researchers: further collaboration and exchange; education of the next generation of scientists: e.g. the GenomEUtwin or P3G training programs

iv. Privacy/consent issues

- Choosing the appropriate consent process: broad consent procedures? (exception: Iceland); however under discussion (i.e. UK Biobank Draft Framework)

- Nature and information for prospective participants: when transparency leads to skepticism (HapMap experience)

- Identifiability of samples and data: unidirectional encryption (Iceland), complete anonymization (HapMap) or single/double coding (other projects). CART@GENE's from anonymization to double-coding

v. Individual feedback and general results

- Estonia: participants' right to know
- CARTaGENE respect for individuals' right to know before anonymization
- Other projects: no individual research results (medical examination results excepted)

➢ Is individual feedback possible in such large-scale projects?

(low clinical relevance, absence of funds for genetic counseling, misinterpretation of results and possible discrimination)

vi. Determinism/stigmatization/discrimination

- HapMap desire to be distinguished from the Human Genetic Diversity project

- The GRAD project: juggling between ethnic discrimination and under-representation

vii. Commercial aspects:

- Commercialization and free, public access … data as a common public good (e.g. HapMap click-wrap license)

- Industry involvement (a crucial financial partner?); keeping public trust: market Vs values of prospective participants

C. Governing HGRDs: ensuring the existence of adequate checks and balances

i. Project framework and protocol assessment

- "Stamp of approval" of authorities
- The public as a true partner
- Need for built-in mechanisms and review procedures

ii. Research Project review and monitoring

- On-going monitoring of research projects
- Necessary adjustments of protocol over time
- Projects' choice of an independent scientific/ethical monitoring (membership on committees, projects' selection process)

iii. Management structure

- Complexity in light of the long-term existence of the projects, and multiplicity of partners (interests)

- Accountability mechanisms: a difficult challenge: e.g. the UK Biobank ethics and Governance Council and control resting on honest communication between the Council and UK Biobank team

- Accountability (*ibid*): the impact of private or private public partnerships: accountability to both stakeholders (meeting commercial objectives) and the public

- The need for projects to clarify their policies regarding management of commercial aspects

- Ensuring transparency, independence, integrity

iv. Monitoring data protection and security mechanisms

- National projects have established national protection authorities or bodies specifically for this purpose
- Expectation: that these independent bodies act as impartial judges protecting participants and verifying the compliance of the projects with established standards and rules
- The questionable powers of sanction to be conferred to these entities for effectiveness

Conclusion

- Research community designing unique infrastructures with the potential to benefit the community as a whole serving generations to come
- Need for national, regional and international jurisdictions to be careful watchdogs, prudent and vigilant both in the elaboration of guiding principles and in the implementation of adequate enforcement and monitoring mechanisms
- Longitudinal studies and genomic databases have yet to pass the test of time
- Important to distinguish disease cohorts (hypothesis-driven) from HGRDs (research tools/infrastructure)

"Are these just guidelines, or are they actual new policies?"