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REGULATION OF INTERNATIONAL DIRECT-TO-PARTICIPANT RESEARCH

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Some Modern Challenges to Research Ethics

- Biobanking
- International research
- Direct-to-participant research

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HARMONIZING

Privacy Laws to Enable International Biobank Research

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Biobanking and International Collaboration: ELSI Issues

Future uses of post-genomic biobanks are indeterminate

Different types of laws apply across countries

International research consortia w/biobanks have their own contracts, guidelines, or ethics policies

Enforceability of laws or agreements to sample/data use transferred across borders unclear

Research materials and methods change rapidly, laws do not

Benefits of International Data Sharing

"...increased statistical power through data aggregation and linkage; reduced costs through reduction in duplicative research; optimal utilization and effective validation, comparison, replication, and refinement; compliance with data sharing requirements by many funding organizations; and transparency obligations imposed in many guidelines and regulations."

Edward Dove, Biobanks, Data Sharing, and the Drive for a Global Privacy Framework, (LME (2016).

Diversity:

Public | Private | Non Profit

Population | Disease Specific | Clinical Trial | Residual Tissue

Governance:

National and International

Laws: biobank-specific, genetic (e.g. non-discrimination), human subjects, human samples, health privacy, data security

Ethics guidelines and approvals

Contracts

Author Template

Legend

Activity

- National Biobank

Governance Framework

- Specific Law or Articles
- Data protection law
- Specific Guidelines
- Genetic-specific restrictions
- Government approval/license required

Consent, Privacy and Security Issues

- Broad consent
- Int'l sharing
- De-identification preferred or required
- Specific security req'ts*
- Prohibited

Access Restrictions

- Ethics approval for access required

* No symbol = no data available

International / Regional Guidance

OECD	OECD	WMA	GA4GH	EU
OECD Guidelines for the Protection of Privacy and Transborder Flows of Personal Data (1980/2013)	OECD Recommendation on Human Biobanks and Genetic Research Databases (2009)	WMA Declaration of Helsinki (2013)	Framework for Responsible Sharing of Genomic and Health-Related Data (2014)	EU Data Protection Directive

Source
To be published as two special issues in Journal of Law, Medicine & Ethics (2016).
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McGill

CGP Centre of Genomics and Policy / Centre de génomique et politique

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Law, Medicine & Ethics

AUSTRALIA

BRAZIL

CANADA
* Federated

CHINA

DENMARK

FINLAND

FRANCE

GERMANY

INDIA

ISRAEL

MEXICO

USA
New rules proposed

UK

TAIWAN

SPAIN

SOUTH AFRICA
* Permit needed

NIGERIA

NETHERLANDS
* Federated

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Research Strategy

1. Laws in some countries impede the international sharing of specimens and data for biobank research.
2. It should be possible both to protect individual privacy interests and promote international biobank research.
3. The starting point should be an in-depth analysis of the laws in the countries most active in genomic and biobank research.

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Other Articles

Introduction	Mark A. Rothstein Bartha M. Knoppers
Need for Harmonization	Edward S. Dove
International Norms	Ma'n H. Zawati Adrian M. Thorogood
International Sharing	Jennifer Stoddart Benny Chan Yann Joly
Security and Technology	Raymond Heatherly
Comparative Approaches to Biobanks and Privacy	Mark A. Rothstein Bartha M. Knoppers Heather L. Harrell

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Legislative Coverage of Biobanks

1. Biobank statutes
   - China
   - Estonia
   - Finland
   - Taiwan
2. Biobank provisions
   - Brazil
   - France
   - South Korea
   - Spain

3. General health research laws; privacy/data protection laws

Australia
Canada
Denmark
Germany
India
Israel
Mexico
The Netherlands
South Africa
Uganda
United Kingdom
United States

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A Sample of Key Provisions

- Taiwan prohibits sending samples to other countries.
- Some countries require a "permit" before samples and data can be sent to other countries (e.g., Estonia, Mexico, Nigeria, South Africa).
- Some countries prohibit the use of broad consent (e.g., Germany, South Africa).

- Laws generally deal only with export of samples and data (but Spain also deals with import).
- Some countries require the participation of a local researcher before samples can be exported (e.g., China, Uganda).

- Some countries have different rules for specimens and data (e.g., China).
- Some countries prohibit anonymization unless specifically authorized (e.g., Brazil, Germany).

- Some countries require destruction or anonymization when research use is completed (e.g., Denmark, South Korea).

- All countries require IRB or comparable review before researchers may access biobanks, but some countries require a higher level of approval for access to genetic data (e.g., Brazil, France, Israel).

- Some key terms often have different meanings in different countries.
- An example is “consent.”

MODELS OF BIOBANK CONSENT	
Blanket consent	One-time consent in which participants agree to all subsequent research uses of their specimens and data
Broad consent	One-time consent by participants, but each research use of their specimens and data must receive prior approval from an IRB or comparable body
Dynamic consent	Initial consent by participants is followed up by electronic notification of each proposed use of their specimens and data, and participants can opt out of any specific research use

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MODELS OF BIOBANK CONSENT	
Open consent	Data, typically anonymized, are posted on the internet and available to anyone in the world
Specific consent	Separate consent is required for each new research use of the participant's specimen and data
Tiered consent	During the consent process participants are given a menu of different types of research (e.g., cancer, heart disease) and they can elect for which research they consent to having their specimens and data used
Registered access	One-time consent to permit registered researchers to access specimens and data without review of each protocol

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Why are some countries reluctant to share specimens and data?

1. Residual effects of colonialism and imperialism

2. Potential economic value

3. Genetic legacy of the people

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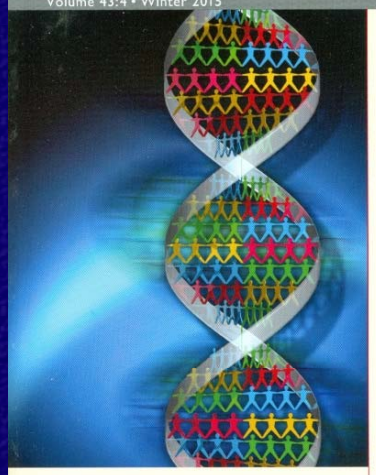

INDEPENDENT ARTICLES

Automatic Placement of Genomic Research Results in Medical Records: Do Researchers Have a Duty? Should Participants Have a Choice?
Anya E.R. Prince, John M. Conley, Arlene M. Davis, Gabriel Lázaro-Muñoz, and R. Jean Cadigan

Conflict Resolution in the Clinical Setting: A Story Beyond Bioethics Mediation
Haavi Morreim

An Ethical and Legal Framework for Physicians as Surrogate Decision-Makers for Their Patients
Philip M. Rosoff and Kelly M. Leong

Regulating Tobacco Product Advertising and Promotions in the Retail Environment: A Roadmap for States and Localities
Tamara Lange, Michael Hoefges, and Kurt M. Ribisl

SYMPOSIUM

Harmonizing Privacy Laws to Enable International Biobank Research: Part I

GUEST EDITED BY Mark A. Rothstein and Bartha Maria Knoppers

Plus more inside...

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The Forced Marriage of Minors: A Neglected Form of Child Abuse
Loretta M. Kopelman

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Joseph J. Fins, Megan S. Wright, Claudia Kraft, Alix Rogers, Marina B. Romani, Samantha Godwin, and Michael R. Ulrich

Contrasting Medical and Legal Standards of Evidence: A Precision Medicine Case Study
Gary E. Marchant, Kathryn Scheckel, and Doug Campos-Outcalt

Genomic Test Results and the Courtroom: The Roles of Experts and Expert Testimony
Edward Ramos, Shaweneequa L. Callier, Peter B. Swann, and Hosea H. Harvey

SYMPOSIUM

Part II: Harmonizing Privacy Laws to Enable International Biobank Research

GUEST EDITED BY Mark A. Rothstein and Bartha Maria Knoppers

Plus more inside...

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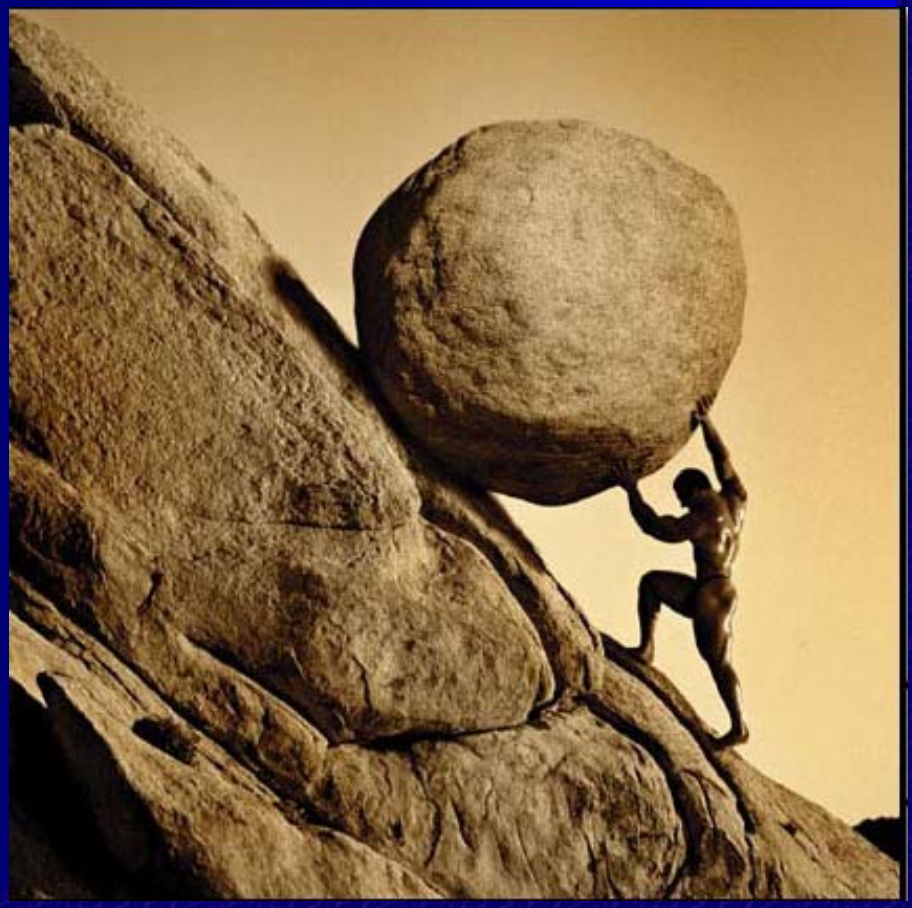
Do I want to do this again?

What are the issues?



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Will online DTP research increase or decrease diversity?

- 81% of subjects in GWAS studies are people of European descent.
- In 2017, 40% of people worldwide have internet access.
- By 2020, 70% of people worldwide will have smartphones.

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Council for International Organizations of Medical Societies (CIOMS)

International Ethical Guidelines for Health-Related Research Involving Humans (2016)

Guideline 11

"Biological materials and related data should only be collected and stored in collaboration with local health authorities. The governance structure of such collection should have representation of the original setting. If the specimens and data are stored outside the original setting, there should be provisions to return all materials to that setting and share possible results and benefits."

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International legal obstacles

- Genetic privacy laws
- Data protection laws
- Biomedical import/export laws
- Consumer protection laws

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Is local IRB approval necessary or desirable?

- The same issue is being debated about multi-center studies in the US.
- Local IRBs ensure that the special circumstances of local populations are considered by the researchers.
- Do the potential gains of local review outweigh the potential harms of, in effect, excluding certain populations from participating in research?

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The problem of trust in international DTP research

- People are often suspicious of outsiders.
- International research has had incidents of exploitation.
- The lack of face-to-face contact makes it difficult to build trust.

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How comfortable are you with your health information being accessed for the following purposes?

	Comfort level (n=1319)	
Purpose, N (%)	Comfortable	Not comfortable
Your clinical care/treatment	1195 (91)	124 (9)
Healthcare operations (e.g. quality of improvement of hospital care)	987 (75)	332 (25)
Payment for care by health insurance	916 (69)	403 (31)
Public health (e.g. tracking spread of disease)	712 (54)	607 (46)
U.S. academic researchers	**641 (49)**	**678 (51)**
Non-U.S. academic researchers	**385 (29)**	**934 (71)**
National security (e.g. counter-terrorism)	371 (28)	948 (72)
Law enforcement (e.g. use of DNA in crime investigation)	349 (27)	970 (74)
Commercialization (e.g. develop commercial products)	173 (13)	1149 (87)
Marketing/promotions (e.g. advertisements targeted to you.)	157 (12)	1162 (88)

4-point scale: Not at all comfortable, Not very comfortable, Somewhat comfortable, Very comfortable: Dichotomized to Comfortable, Not comfortable

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The 2017 revision of the Common Rule adopts "broad consent" for research with biospecimens and data. Among the required elements of broad consent is the following:

> Broad consent must contain . . . a description of the specimens or data that might be used in the research, whether sharing might occur, **and the types of institutions that might conduct the research** . . . .

45 C.F.R. § 46.116.

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Verifying the credentials of researchers

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Informed consent

What is the most feasible and effective way of obtaining meaningful, informed consent online?

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Parkinson's Disease mPower Study

- Sage Bionetworks with Parkinson's Disease researchers and advocacy groups.
- Uses Apple ResearchKit and software for iPhones.
- Uses microphone, accelerometer, touchscreen, and other sensors.

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- Online consent toolkit, including e-consent and quiz.
- Study was approved by Western IRB.
- 17,000 participants enrolled in 6 months.

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Why researchers do not like to return results

- It is burdensome
- It is usually not funded
- Researchers are not clinicians
- It is not clear when RoR is required or permitted
- The obligation can be open-ended
- Concern about legal liability

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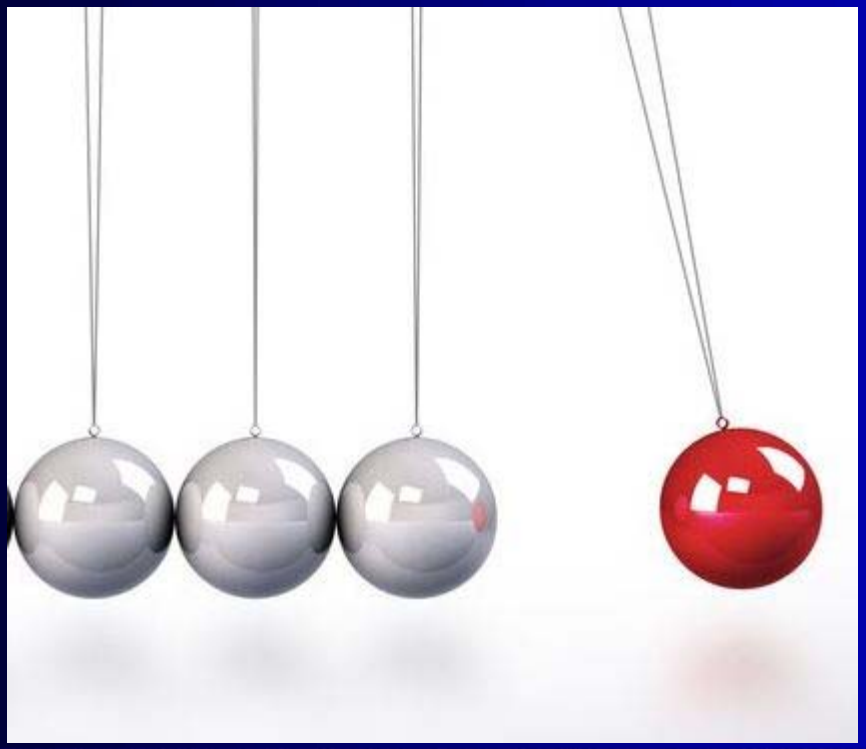
Return of results:

Has the pendulum swung too far?



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Treatment vs. Research

Purpose	Individual care	Generalizable knowledge
External approval	Not required	IRB
Consent	Informal, oral	Detailed, written, informed
HIPAA-compliant authorization	Not required	Required
Info. sharing with individual and others	Professional standards	Research protocol
CLIA-certified lab	Required	Not required
Professional training	M.D.	Ph.D., M.D.
Who regulates?	State Med. Bds., local institutions, payers	IRBs, OHRP
Legal relationship	Fiduciary	Non-fiduciary

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An ethical duty to engage in benefit sharing?

Patients with Laron-type dwarfism, mainly in rural Ecuador, supplied samples that helped drug companies discover and produce insulin-like growth factor (IGF-1).

Many of these individuals have children that need to start taking the drug before puberty, but they cannot afford the drug, and the drug companies will not provide the drug.

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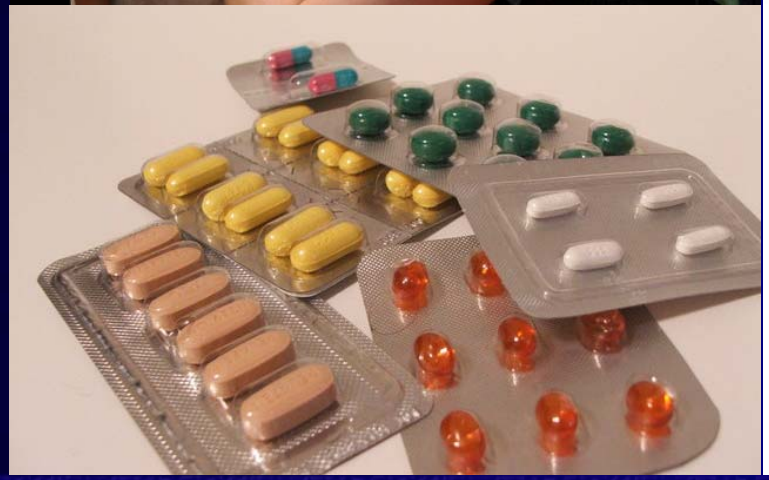

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My Conclusion . . .

- It's important
- It's interesting
- We ought to try to do it!

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My absolutely, positively last international grant proposal . . . (of 2017)

University of Louisville	Mark A. Rothstein
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Duke University	Laura M. Beskow
Broad Institute	Daniel MacArthur

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- Leading biotech companies
- Leading pharmaceutical companies
- Leading clinical genetic testing company
- Leading DTC genomics company
- Independent researchers
- Patient advocacy groups
- Academic, private, and foreign IRBs
- Professional societies

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32 Countries

Australia
Brazil
Canada
China
Denmark
Egypt
Estonia
Finland
France
Germany
Greece
India
Israel
Italy
Japan
Mexico
Netherlands
Nigeria
Peru
Poland
Qatar
Singapore
South Africa
South Korea
Spain
Sweden
Switzerland
Taiwan
Uganda
United Kingdom
United States
Vietnam

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- Common Rule Amendments published January 19, 2017.
- Broad consent for specimens and data to be used for secondary research.

  Broad consent means one-time consent from a participant with "limited IRB review" to determine the appropriateness of each new research use.
- Regs do not say what "limited IRB review" means, but guidance will be developed by HHS and published in the next year.

- How can you determine what type of "limited IRB review" is easiest to understand, most effective, least intrusive, etc.?
- What about looking to other countries already using external review of broad consent?
- What countries? Some examples: Australia, Brazil, Canada, Denmark, Estonia, Finland, India, Israel, Nigeria, Spain, Taiwan, Uganda, UK.
- Who has expert contacts in these countries and can find out what works best?

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