Ethics and Governance Issues: Patient Registries for Rare Diseases

Simon Woods: Policy Ethics and Life Sciences Research Centre (PEALS), Newcastle University
Ethics and Governance: Outline

1. Introduction to TREAT-NMD
2. The ethical challenges for RD registries
3. TREAT-NMD National and Global Data-base
4. Questions and discussion
TREAT-NMD

- Translational Research in Europe - Assessment and Treatment of Neuromuscular Diseases
- Five years, FP6, network of excellence
- Researchers, clinicians, industry and patient groups
- Collaborate to resolve bottlenecks and accelerate treatments
- TREAT-NMD Coordination Centre based at Newcastle University
TREAT-NMD Progress

- Publish harmonised standards of care
- Registry of outcome measures for clinical trials and act as an advisory body for industry and regulatory authorities
- Establish and assist in national registries
- Establish and run a global patient registry – speed up trial recruitment process
- Establish a clinical trials co-ordination centre
Ethical & social concerns: patient registries

- Problem of definition
  - Data-base
  - Biobank
  - Register

- Common ethical concerns
- UK Biobank, DeCode etc.
Comparison of public vs rare disease databases: values and expectations

- Established by “external agents” (top down)
- Broad in purpose
- Apolitical in nature
- Altruistic volunteers from the “public”
- Feed-back unlikely
- Control not expected
- Benefit sharing – “public good”

- Established by “interested agents”
- “political” in nature
- Specific in purpose
- Self-interested volunteers (or restricted altruists)
- Feed-back expected
- Control expected
- Benefit sharing – expected within the RD community
Ethical & social concerns: RD registries

- “Ownership”
- Custodianship
- Conflicts of interest
- Consent
- Privacy and confidentiality
- Disseminating best practice
- Maximising benefit
Key Consideration for RD data-base

• What will enable *this* collation of information to do the most possible good for *this* community of interest?

• At the same time protecting the rights and interests of that community
Design and management

• Type of registry – fit for purpose
  ▪ Medical records
  ▪ Ad hoc surveys
  ▪ Be-spoke data-base

• Sustainability
  ▪ Longevity
  ▪ Financially viable
  ▪ Control and governance
Consent

• Nuremberg to Helsinki to Oviedo
• Free and informed consent of “research” participants is an essential and necessary pre-requisite

BUT

• What information?
  ▪ Transparency (conflicts of interest)
  ▪ Potential benefits
  ▪ Scientific design and goals (peer review)
  ▪ Ethics approval (IRB/ Ethics Committee)
  ▪ Liability
Consent

• Forms of consent
  ▪ None! (completely anonymised data)
  ▪ Broad/specific consent
  ▪ Does open-ended consent leave the door too open? (Deschenes et al 2001)

• Duration - Time limitations
  ▪ Time limited consent/ “sell-by date”

• Who gives consent?
  ▪ Parent/child
Confidentiality

Common approach in European law

- Protecting interests
- ECHR – right to private and family life
- Protection from exploitation
- Protection from detrimental use

Consent (again)

- Levels of confidentiality/anonymity
- Who is
  - Data manager?
  - Who will have/what sort of access?
“Ownership”

- Information cannot be owned! – therefore legal protection of interests lies with the protection of privacy
- Approach taken in UK – information cannot be owned but “records” can – so NHS own medical records but not the information in those records (although see US for contrary legal position)
- Ownership questions do arise with intellectual property rights or “private” data bases e.g. Created by pharma in drug trial
Ownership: information and tissue

- “No property rights in the body” – but tissue increasingly treated as property
- Tissue can be “gifted” – can information?
- DNA – blurs the tissue/information.
- Information can be given more than once

Should information be treated as property?
Ownership: common concerns

- Fear of exploitation
- Losing control
- Loss of momentum
- Failure to maximise benefits
- Prioritising of other interests
- Disrespect for those who contributed...

Will settling the ownership question satisfy these concerns?
Custodianship/ stewardship

• Mindful of raison d'être (and acknowledgement of the range of interests)
• Terms of reference and explicit ethical principles of management
• Efficient and professional management incorporating best practices
• Transparency in all aspects of management (consistent with other responsibilities)
• “representation” in oversight and communication with widest possible community of interest
• Review and revision of management and governance
Governance: recommendations

Ségolène Aymé Orphanet / INSERM, (EPPOSI)

Ownership

• Agreements about ownership should be determined by multi-party contracts
• The subject is the primary controller of his/her own data
• The funder is the owner of the database
• The institution of the researcher at the origin of the data is the owner of the aggregated data
• When processed, the data becomes research data
Ownership (2)

• The principal investigator is the custodian of the data
  ▪ Has to take all appropriate steps to protect the data, its storage, use and access

• Intellectual property to the researcher with due consideration for benefit sharing

• Use by third parties but no transfer of ownership
TREAT-NMD Case study
TREAT-NMD Project Ethics Council

Internal mechanism for scrutiny from “stakeholders” and “critical friends”

• Membership: Lay, expert, patient representatives
• Access to wide constituency
• Reports to and makes recommendations to TREAT-NMD Governing Board
• Public Minutes
Issues raised by PEC

- Should be an OC to protect patients’ interests
- Should aim to make best use of database and be in the patients’ interests
- Should not enter into exclusive contracts with industry
- Should manage conflicts of interest e.g. contemporaneous clinical trials
- Management of information about trials and studies – endorsing/ informing
- Managing feedback and information flow to patients
National TREAT-NMD registries – leaflets

German SMA registry

UK SMA registry

Hungarian SMA registry
Benefits

• Many benefits to registered patients
  ▪ Feedback on standards of care and new research developments
  ▪ Feeling a sense of “belonging” to a broader community
  ▪ Not being left behind as clinical trials develop
  ▪ A link to the research community

• Many benefits to industry
  ▪ Easy access to patient community
  ▪ Clear concept of target market
  ▪ Feasibility and planning of clinical trials
  ▪ Recruitment of patients into clinical trials
Patient registries: national curators

• Collect the data in each country
  - from the professionals (geneticists, physicians)
  - from the patients (self-report)

• Genetics: mutations of SMN1 gene & copy number of SMN2 gene
  (use the international mutation nomenclature: standardisation)

• Validate the genetic & clinical data in order to maintain high-quality / accurate data

• Feed the medical data into the national and global databases
TREAT-NMD

global database

Patient report
(self-report)

Professional report
(geneticist, physician)

Curator

National database/registry
Mandatory items

Highly encouraged items

TREAT-NMD
global database

Pseudonymised (encrypted) data

EURORDIS
Athens 7-9 May 2009
Ethics and governance within TREAT-NMD
TREAT-NMD SMA patient registry
Institute of Human Genetics
Newcastle University
International Centre for Life
Newcastle upon Tyne
NE1 3BZ
United Kingdom

Bloggs, Fred *19/6/1998
ID: 23
2008-06-30T16:45:14+02:00

Patient Information and Informed Consent

Please print this document, read it carefully, sign it and send it to us. You can either send it by post to the address above or by fax to the following number:
+44 (0) 191 241 8770

If you send this form by post, please don’t forget to note your return address. Please also keep a copy of this form with your documents.

Father: Joe Bloggs, *19/3/1967
Project: Jennifer Trust/TREAT-NMD Patient Registry for Spinal Muscular Atrophy
Chart for TREAT-NMD Patient Database

CHARTER FOR TREAT-NMD PATIENT DATABASE/REGISTRY

Revision History

Preamble
Inherited neuromuscular diseases (NMD) form a large group of diseases, each of which is individually rare (prevalence < 1/50,000). They are present in all populations and affect both children and adults. Most NMDs result in chronic long-term disability that poses a significant healthcare burden for society. Death may result from cardiac and respiratory muscle involvement. The goal of existing management is to minimise the impact of complications such as contracture or spinal deformity and improve cardiac and respiratory function as there are currently no curative treatments for any NMD.

Scientific advancement recently has lead to substantial changes on how to approach the treatment of NMD. New therapeutic strategies are being developed, and for some of these treatments, there are plans for large, multi-centre studies already in place. Several new therapeutic strategies for NMD aim to target specific genetic defects. Once planning for a clinical trial starts, it is very important that patients are identified and contacted within a short period of time. In national and pan-European databases registries initiated by TREAT-NMD for Duchenne Muscular Dystrophy, Spinal Muscular Atrophy and other muscular dystrophies, patients will be registered with their genetic defects and clinical status and can be contacted if their profile fits the inclusion criteria of a clinical trial. Moreover, the patient registries will help to answer research questions such as the prevalence of neuromuscular disorders in Europe and support other activities such as assessing standards of diagnosis and care. The main objective of the TREAT-NMD patient registries/databases for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy is to assess the feasibility of clinical trials, to facilitate the planning of appropriate clinical trials and to support the enrolment of patients in clinical trials, in compliance with Ethical guidelines for research involving human subjects.
5) TREAT-NMD Global Database Oversight Committee

- The TREAT-NMD Global Database Oversight Committee (GDOC) is the governing structure of the TREAT-NMD global database on behalf of TREAT-NMD and national registries.

- The TREAT-NMD GDOC is composed by representatives of the TREAT-NMD network (Leader of the work package on patient registries; Clinical Trial Coordination Centre; Ethics Council; and partner organizations), patient organizations, and national registries. It is chaired by the TREAT-NMD activity leader on databases. Industry partners of TREAT-NMD shall not be represented in the committee.

- All members of the TREAT-NMD GDOC must disclose financial interests and update the disclosure statements on an annual basis. All members of the TREAT-NMD GDOC will be required to sign confidentiality agreements if a third party requests them prior to having access to the inquiry of the third party.

- The TREAT-NMD GDOC will meet in person, by teleconference or by e-communication at least once per year, and upon request.

- The TREAT-NMD GDOC will report to the TREAT-NMD Governing Board and to the national registries annually.

- The TREAT-NMD GDOC reviews inquiries of third parties into the TREAT-NMD global database. The committee will come to a decision within 14 calendar days upon receipt of the inquiry and will report the decision in writing to the third party, the owner of the global database and the TREAT-NMD Governing Board as per the approval process agreed by the GDOC. If a decision cannot be reached, the inquiry shall be rejected. In the case of a rejection, the GDOC may report the reason for rejection to the third party and set a time frame for reconsideration.

- Until TREAT-NMD will be established as a legal entity, the TREAT-NMD GDOC shall report to the owner of the global database the decision to give access to the global database. A contract will be signed, as mentioned supra (3) between the owner of the global database and the third party.
• Declaration of interests (annual)
• Process of review and decision-making of applications
• Membership of OSC open to revision
• Transparency at every stage
• Committed to benefit sharing
Summary

• TREAT-NMD Governance model
• Ownership (again) but with principles of custodianship
• Dissemination of good practice
  ▪ Registries toolkit
• Changing landscape – so need for vigilance and reflection on practices

Schroeder JME (2009)
www.mrc.ac.uk/research_collection_access
For more information…

www.treat-nmd.eu
Hanns.Lochmuller@ncl.ac.uk
Simon.woods@ncl.ac.uk