

Opportunities and challenges of registries and repositories

December 13th -14th, 2010

Richard T. Moxley, III, MD

NIH Senator Paul D. Wellstone Muscular Dystrophy
Cooperative Research Center (MDCRC)



Acknowledgements - Registry

University of Rochester Medical Center

Principal Investigator: Richard T. Moxley, III, MD

Co-Investigators: Michael McDermott, PhD
Rabi Tawil, MD
Charles Thornton, MD

Coordinators: James Hilbert, MS
Liz Luebbe

Data Management: Bill Martens
Eileen Eastwood

National Institute of Health Project Officers

NIAMS: Glen Nuckolls, PhD

NINDS: John Porter, PhD



dystrophyregistry.org

Registry

Registry Scientific Advisory (SAC) Committee Members:

Tetsuo Ashizawa, MD	University of Florida
Richard Barohn, MD	University of Kansas
Paula Clemens, MD	University of Pittsburgh
Michael Conneally, PhD	Indiana University
John Day, MD	University of Minnesota
Denise A. Figlewicz, PhD	ALS Society of Canada
Jacqueline M. Jackson	Indiana University
John Kissel, MD	The Ohio State University
Shannon Lord	Patient advocate
Katherine Mathews, MD	University of Iowa
Don Sanders, MD	Duke University
Stephen Tapscott, MD, PhD	University of Washington

Various registries and goals

- Goals may be to facilitate recruitment into clinical trials, collect and analyze clinical data, or mixed goals.
- Specific aims of registries can be to study:
 - Genotype-phenotype correlations
 - Health-related quality of life
 - Prevalence and risk factors of diseases
 - Natural history
 - Standards of care and healthcare policies
- Data collection can be from:
 - Medical literature
 - Patient reported outcomes
 - Clinical exams
 - Governmental or healthcare records



Many sub-categories; example, “genotyping”

Challenges and opportunities of registries

- ORDR has as their goal to create a global patient registry using standardized data elements and linking the registry to bio-repositories for rare diseases;
- Challenges in using standardized data elements:
 - Example: “*278 ways to describe fever for 465 patients in a one day record from Children’s Hospital in Philadelphia.*” *

* Reference:

- *Creating a global rare disease patient registry linked to a rare diseases biorepository database: Rare Disease-HUB (RD-HUB). *Contemp Clin Trials*. 2010 Sep;31(5):394-404. Epub 2010 Jul 8
- www.rarediseases.info.nih.gov/PATIENT_REGISTRIES_WORKSHOP/

Challenges to link registries with bio-repositories

- Develop guidelines to counsel patients:
 - Who takes responsibility for patients whose expectations about care will be influenced by how well they understand the role of a registry-based tissue repository or DNA gene testing?
- Develop standardized methods to collect, store, and analyze tissue samples;
- Assure the privacy and de-identification of data;
- Link to clinically meaningful outcomes:
 - “*greater the utility of the clinical data...the greater the risk of re-identification....*” (letter to FDA by Sharon Terry of Genetic Alliance);
- Develop and assure standardized clinical exams.

National Registry of DM and FSHD Patients and Family Members

- NIH Contract (2000-2010)
 - Funded by NIAMS (National Institute of Arthritis and Musculoskeletal and Skin Diseases) and NINDS (National Institute of Neurological Disorders and Stroke)
- NIH Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers (MDCRC); (2010-2013)
 - Transitioned funding of Registry in Sept 2010 to our NIH Cooperative Specialized Research Center (U54) Grant; (NINDS; 2003-2013)

Rochester Wellstone MDCRC Scientific Core

- Repository and National Registry of DM and FSHD Patients and Family Members.
- Repository goals are to:
 - Collect and distribute FSHD muscle and nerve tissues;
 - Collect and distribute biological materials necessary for DM research;
 - especially mouse models of DM and other tissues samples.

Goals of National Registry

- Data: to develop an extensive repository of de-identified patient information on pathophysiology and clinical spectrum of disease manifestations in DM and FSHD
 - With longitudinal follow-up to track disease progression
- Recruitment: to assist researchers in the recruitment of well-classified subjects into clinical studies, especially treatment trials
- Education: to disseminate information about advances in DM and FSHD research and clinical care amongst physicians, researchers, patients, and family members.
 - *Aspire to develop standards of care and develop outcome measures to assess burden of disease*

Application Materials

- Application packets consist of:
 - Cover Letter
 - **Informed Consent Form (2 copies)***
 - Patient Information Form
 - **Medical Release Form**
 - Email Consent Form (2 copies)
 - Business Reply Envelope
- ***Informed Consent Forms**
 - Affected:
 - Consent Form (adult)
 - Assent Form (children 12-17)
 - Permission Form (children)
 - Unaffected:
 - Consent Form (adult)
 - Assent Form (children 12-17)
 - Permission Form (children)

**National Registry of Myotonic Dystrophy and Facioscapulohumeral
Muscular Dystrophy Patients and Family Members**



**National Registry for Myotonic Dystrophy and Facioscapulohumeral Muscular
Dystrophy Patients and Family Members**

Consent Form – Affected Adult

Principal Investigator: Richard T. Moxley, III, M.D.
Study Coordinator: James Hilbert, MS
Study Coordinator: Elizabeth Luebbe

INTRODUCTION

You are being asked to participate in a National Registry for research in myotonic dystrophy (DM) and facioscapulohumeral muscular dystrophy (FSHD) and related diseases (whose symptoms are identical to those of DM or FSHD) because you are affected with either myotonic dystrophy or FSHD. The Registry has been established at the University of Rochester with the support of The National Institutes of Health (NIH). Please read this consent form carefully and ask any questions you may have before making a decision whether or not to participate. This form contains important information that might be helpful in the future.

PURPOSE

The purpose of the Registry is to:

- Encourage more research on these diseases.
- Facilitate research by collecting names of individuals who are either affected or related to affected individuals.
- Use the information provided by participants to understand how these diseases can affect people.
- Establish contact between researchers and Registry participants.

IMPORTANT FACTS ABOUT THE REGISTRY

- Participation is totally voluntary.
- You may ask that your name be removed at any time.
- No personally identifiable information about you will be given to anyone.
- No one, including your own family members, can find out if you are listed in the Registry.

Ver 5: 09/30/2010 Address: 601 Elmwood Ave, Rochester, NY 14642 RSRB# 12163
Phone: Toll-free 1-888-925-4302 Local 585-276-0004 Fax 585-273-1255
E-mail Dystrophy_registry@umc.rochester.edu
Web www.dystrophyregistry.org
Expires September 26, 2011
- of 147216 -

Consent process

- Enrollment into Registry – open consent process:
 - Members provide consent for the analysis and reporting of anonymous data in unknown future studies.
- Recruitment for clinical studies – restricted consent process:
 - Members are sent descriptions about research studies from investigators approved to use the Registry;
 - Members contact investigators if interested;
 - Members provide consent to investigators:
 - *Protection of subjects is best suited to investigators who are most knowledgeable regarding their protocol, etc.*

Consent Process

- Registry has minimal risk to subjects and its IRB does not require consent to be received in person:
 - Advantages
 - It is more feasible and less costly to enroll patients throughout the US;
 - Likely to enroll a more diverse group of patients;
 - Can provide application forms online.
 - Challenges
 - Potential confusion of risks/benefits;
 - Potential to receive applications with missing, incomplete, incorrect, or expired consent forms;
 - Receive materials from vulnerable populations (ex: prisoners);
 - Receive materials from ineligible patients (ex: those outside the US or those with an alternative diagnosis).

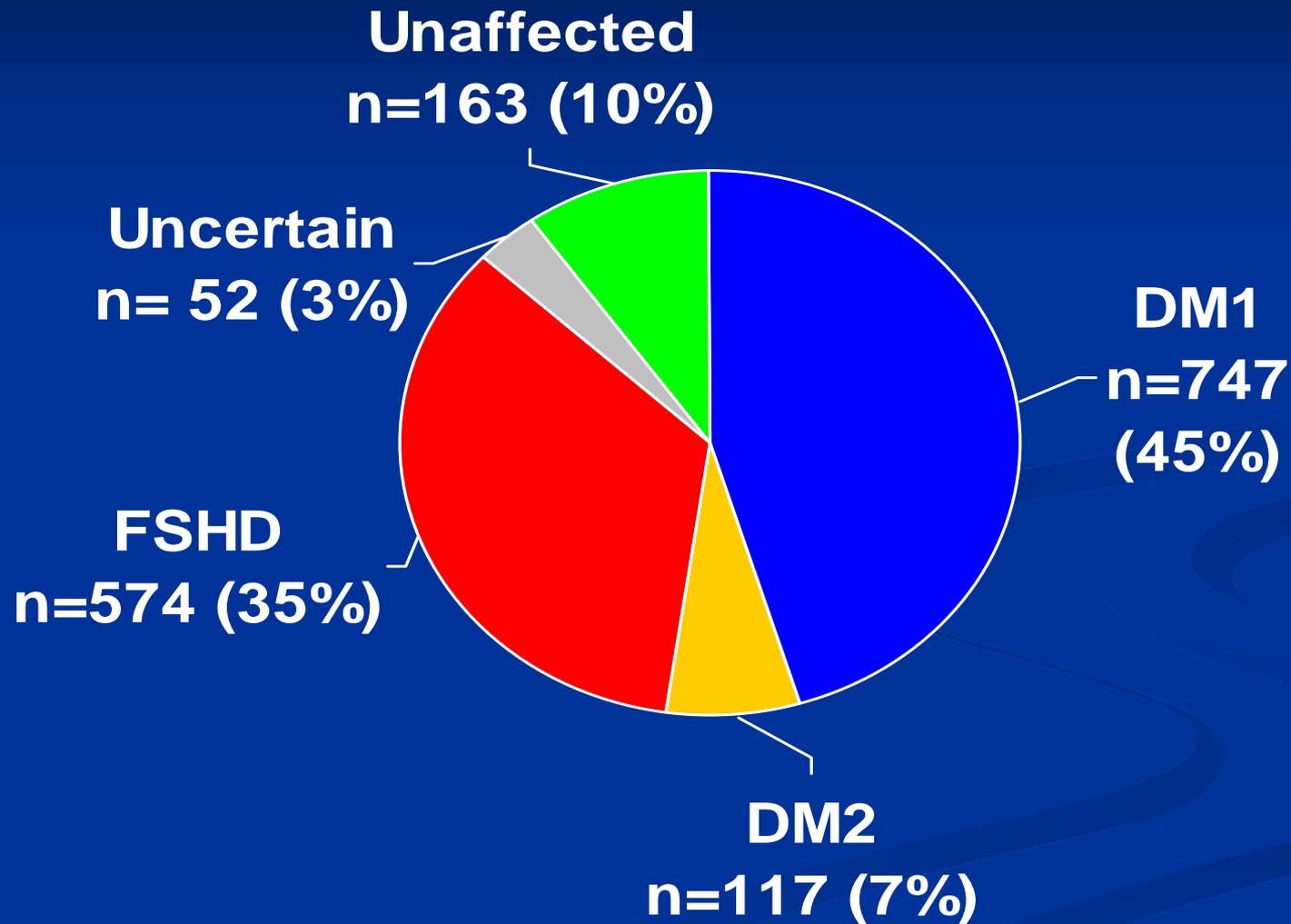
Protection of Human Subjects

- Institutional Review Board (IRB)
 - Annual review;
 - Approval of any changes to enrollment forms, recruitment tools, protocol, and operations;
 - Review of unintentional breaches of confidentiality.
- Certificate of Confidentiality:
 - Added protection due to the collection of sensitive personal and genetic information;
 - Helps Registry staff avoid involuntary disclosures (e.g. audits) which could expose subjects and their families to adverse economic, legal, psychological, and/or social consequences.

Quality Control

- Stringent review of medical records to assure “accuracy” of diagnoses.
- Standard operating procedures to enter and verify data.
- Standard operating procedures to re-contact patients through annually updated forms, recruitment letters, and newsletters.

1,654 members

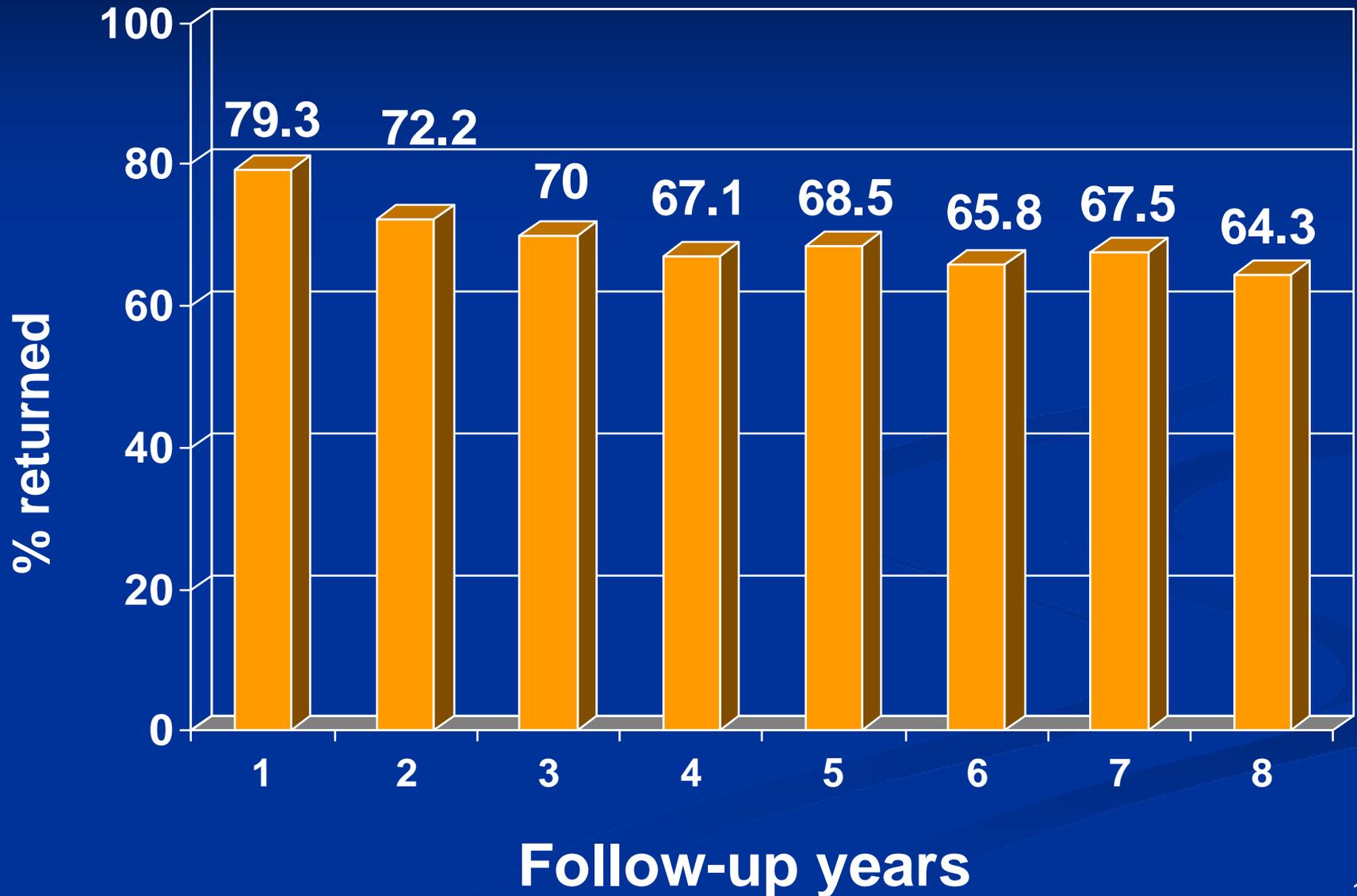


Characteristics

Characteristic	DM1 (n=622); excluding congenital DM	DM2 (n=117)	FSHD (n=574)
Sex (% Female)	51.1	66.7	52.3
Age (mean (SD) yrs)	43.5 (12.1)	54.3 (12.4)	46.1 (15.9)
DNA confirmed (% (n))	51.4% (320)	58.1% (68)	59.1% (339)
Genetic data* (mean (SD))	419.0 (305.0)	12,292.2 (4,406.2)	26.7 (7.2)

* Reported as repeat size for DM1, base pairs for DM2, 4q35 small allele size (kb) for FSHD.

% of Annual updates returned



Methods for Investigator Applications

Investigator Applications and Use of Registry

Application submitted to Registry



Application reviewed by NIH and SAC
(Proper human subjects review, feasibility,
safety, scientific merit)



Determination of eligible Registry members by staff



Registry staff send
description of study
and contact information to
Registry participants



Registry staff
supply
anonymous data
to investigator

Partnership to link Registry and an independent repository

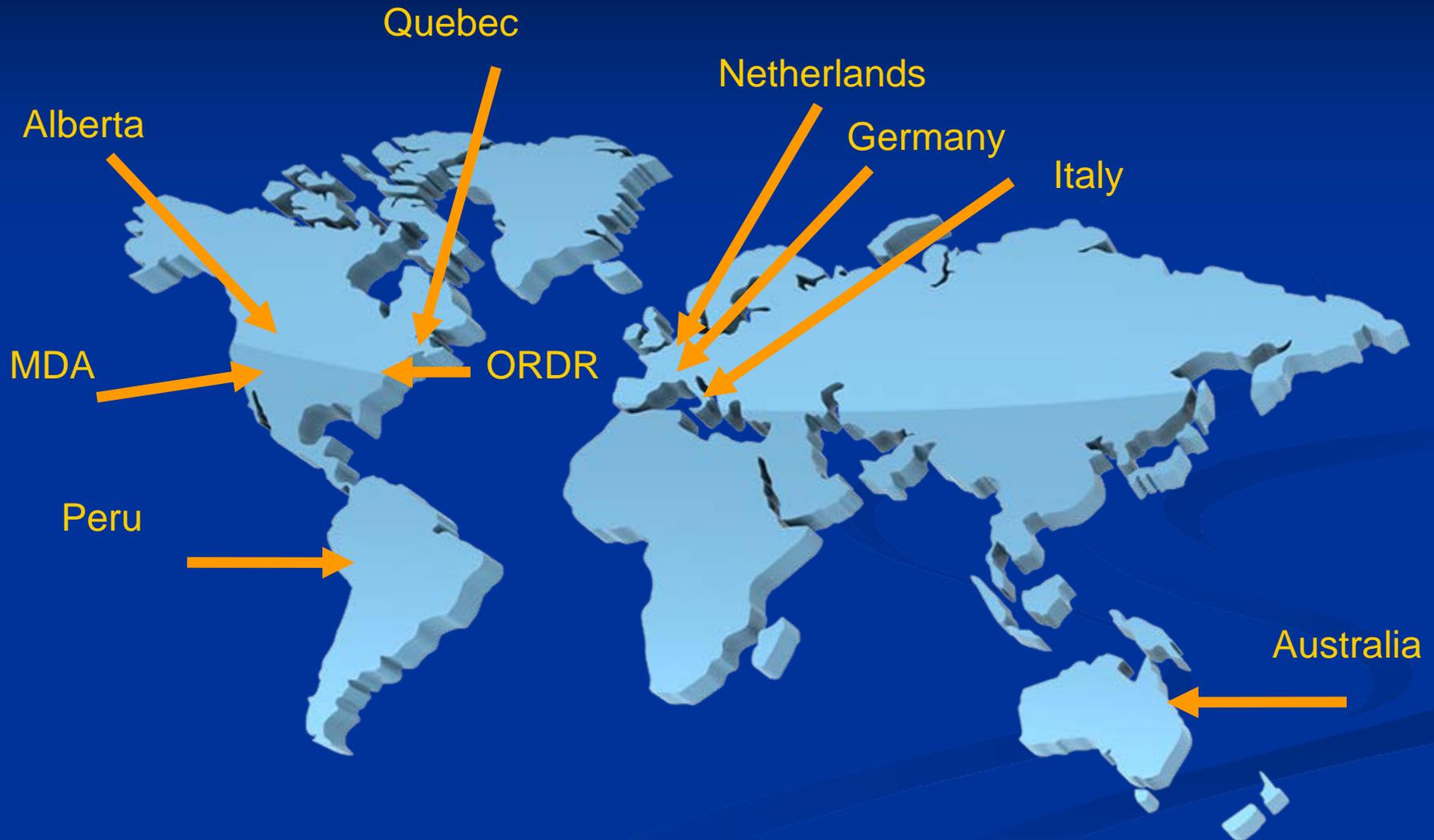
- Collaboration amongst CDC, Coriell Cell Repository, National Registry, & University of Rochester:
 - **Goal:** to increase the public availability of well-documented, well-characterized, renewable cell lines and genomic DNA for research and improved genetic testing.
- **Methods:**
 - Collect blood samples from affected patients and family members to establish cell cultures in the NIH Coriell Cell Repository;
 - Open consent obtained for unknown future studies.

Patient Education and Collaboration with investigators

Examples of outreach

- Regular updates to Registry website (dystrophyregistry.org), which includes:
 - Relevant research information
 - Information on DM and FSHD genetics, testing, and counseling
 - Columns about “aging well with muscular dystrophy”
- Annual newsletter mailings to members.
 - Newsletter includes educational information and research updates in DM and FSHD.

Consultations in Registry Development



Opportunities and challenges of registries

Challenges

- Assure privacy of protected health information
 - Loss of confidentiality – risk of participation stated in consent
 - Process thousands of letters each year
 - Inadvertent disclosure of protected health information (PHI)
- Collect sufficient medical records of enrollees to verify diagnosis.
- Assess potential language and socio-economic barriers.

Opportunities

- Develop questionnaires or additions to Registry to assess burdens of disease and standards of care.
- Use Registry to recruit subjects into therapeutic trials.
 - Target recruitment (examples: DNA confirmation, age, gender, location, etc).
 - Collaborate and cost-share with pharmaceutical companies.
- Enhance teamwork approach to patient, investigator, and clinician education and outreach.

Discussion items

- How to balance privacy risks versus collecting sufficient clinical and molecular data?
- How can we collaborate and share data?
 - What is the purpose to compare data across disease groups?
 - Who has access to data?
 - Will there be “competition” amongst industry and academia?
 - How do we develop and implement common data items?
- How can registries influence standards of care?
- What matters most to patients?

Thank you

Welcome recommendations and questions.



UNIVERSITY *of*
ROCHESTER
MEDICAL CENTER