

Uniting rare diseases

Vanessa Rangel Miller

- 1) Importance of establishing a rare disease registry
 - a. Accelerate research & clinical trials
 1. Perspective changes - patients can proactively accelerate research advances (proactive vs reactive)
 2. Develop a longitudinal portrait of the community – where; how many; disease severity; clinical status; registries enable determination of a target sub-population
 3. Facilitate information sharing between interested patients and interested investigators – provide information needed in planning stages of clinical trials & research studies and reduce the time for enrollment
 - b. Registry collaboration and unity
 1. Partnership with existing & future registries – a common rare disease registry would complement not replace existing/future registries
 2. Facilitate information sharing and collaboration
 3. Necessity for common elements
 - c. Unite the community – Demonstrates unified effort; calls attention to community needs; increases value as research target – either alone or in combination with multiple diseases
- 2) How do stakeholders maintain their identity (branding)?
 - a. Reduce fragmentation of patients across multiple registries
- 3) Stakeholders – Partnerships & Benefits
 - a. Examples of varying needs, wants, contribution areas for differing stakeholders – Patients, Research/clinical investigators, Advocacy/Foundations, Medical Care community
 - b. Examples of successful and unique features from existing registries to date
 - c. Preserve reciprocity and trust in information-sharing
- 4) Learn from related and unrelated diseases
 - a. Establish registries for comparison; recognize diversity in data collection practices
 - b. Importance of registry data curation/verification
 - c. Global characterization and access



Uniting Rare Diseases

*Advancing Rare Disease Research:
The Intersection of Patient Registries, Biospecimen Repositories
and Clinical Data*

Plenary Session A

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DuchenneConnect Registry
Emory University*

DuchenneConnect

The Duchenne/Becker testing + treatment resource community for families, healthcare professionals, researchers, industry + policy makers

Overview

- The DuchenneConnect registry
- Why a rare disease(s) registry?
- Fitting the pieces together
- Data collection, verification and access

The DuchenneConnect Registry

History

- DuchenneConnect registry founded in 2007 as a collaboration between Parent Project Muscular Dystrophy, Emory, CDC, CETT program and ORD
- Focused on signing up new participants, development of educational materials, and access to research

Participants

- ~1700 patients and 275 medical professionals registered in first two years
- Registrants live in 67 countries – without dedicated international efforts

Participant involvement

- Participants are involved in:
 - Feasibility assessments and clinical trial planning
 - Clinical trial, research study, and biorepository announcements

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Why a Rare Disease(s) Registry?

- Several trends exist that are driving creation and growth of disease registries
 - Growing awareness and focus on rare diseases
 - Advances in rare disease testing and treatment
 - Patient organizations becoming proactive participants in research generation
 - Increasing use of Internet and social networking to connect patient groups globally
 - Virtuous circle > Increased registry participation strengthens value of the data collected and the registry's profile, which draws additional participation and so on

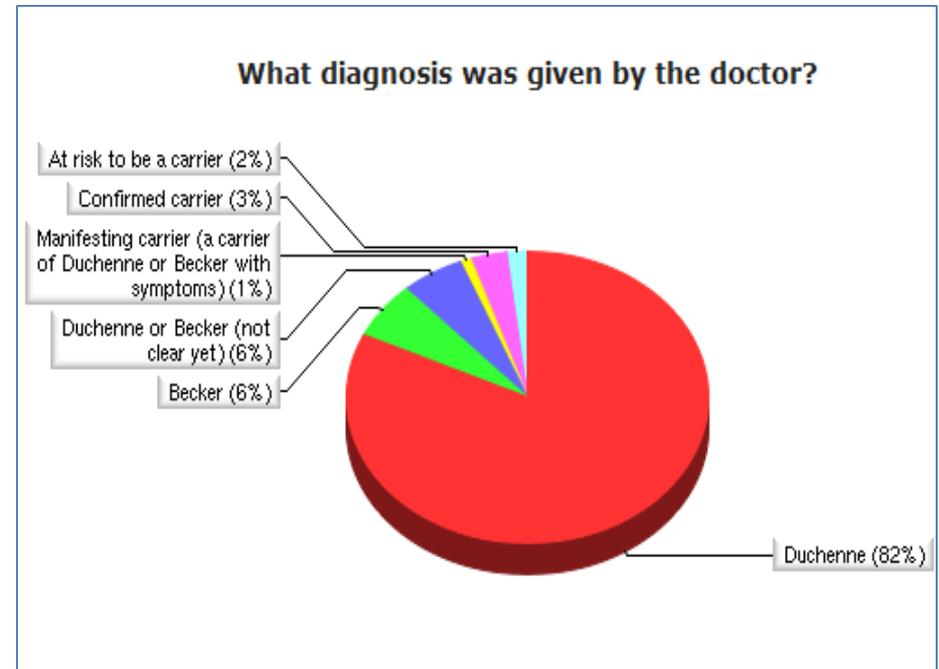
Why a Rare Disease(s) Registry?

Key benefits include:

- A Sharing of key resources across multiple registries provides economies of scale
- B Enhanced learning systems
- C Facilitate clinical trials & research studies

- Technology and infrastructure
- Human subjects
- Research time, effort, and attention
- Administrative and operational resources

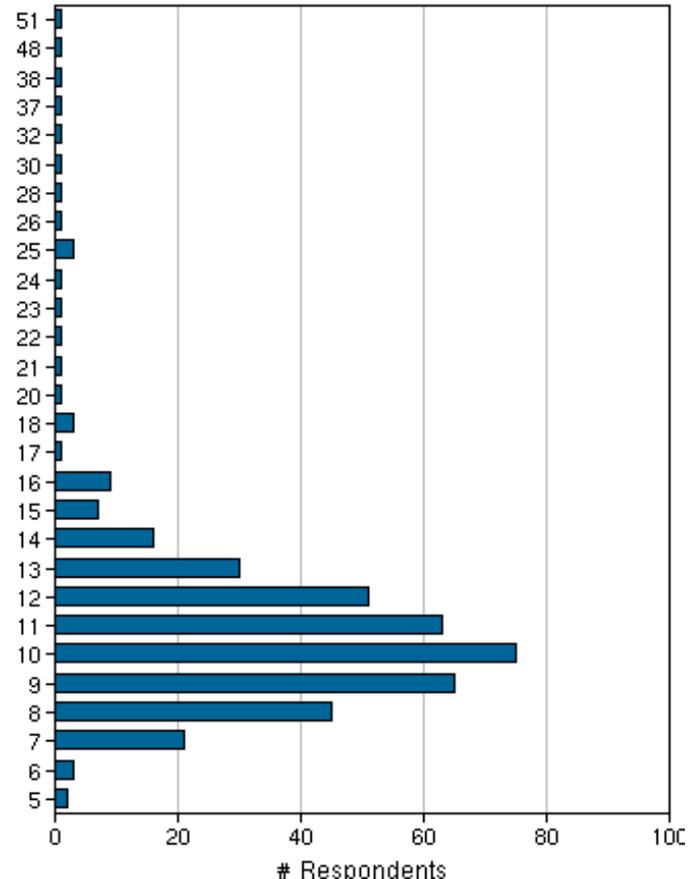
- **Characterize the community – DuchenneConnect helps characterize today's Duchenne/Becker population**
- Longitudinal data collection
- Information sharing and collaboration across related and unrelated diseases
- Accelerate hypothesis generation, hypothesis testing, clinical trials, research studies, recruitment, patient stratification, etc.



Enhanced learning systems

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- **Longitudinal data collection**
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If a wheelchair is used all the time to move around, at what age did this become necessary?

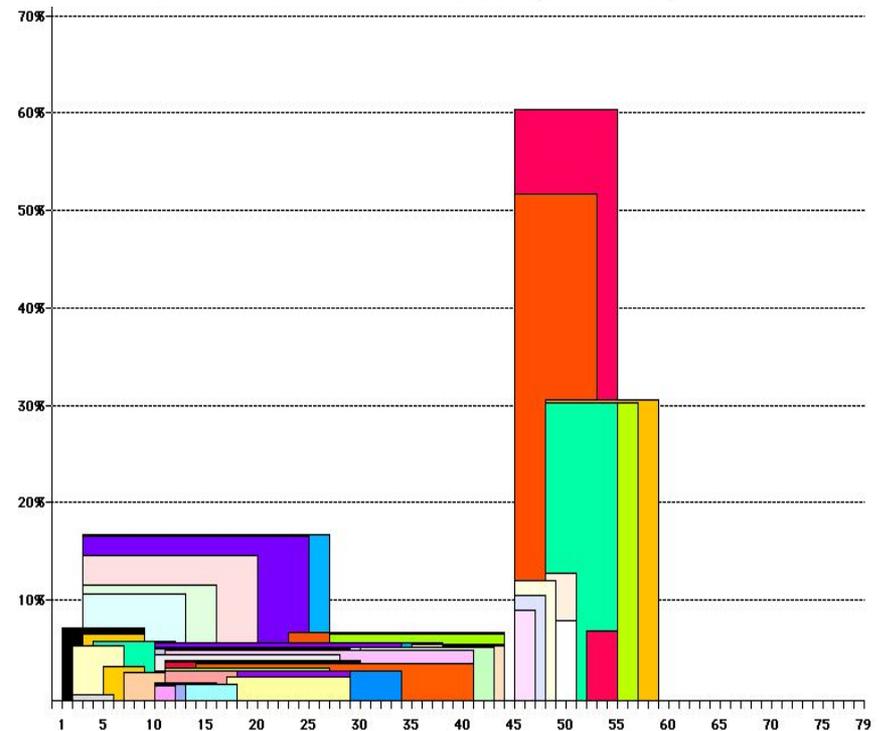


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French UMD-DMD mutations database
Hypothesis generation from registry data translated into laboratory testing of hypothesis

A map of Multi-exon skipping leading to BMD



C Facilitate clinical trials & research studies

- Registry data contributes to development, feasibility assessment and study planning
- Through TREAT-NMD, DuchenneConnect has participated in 5 feasibility assessments and study planning inquiries
 - June 2008: Identified cohorts sized 6-182
 - Feb 2009: Identified 182 potential subjects
 - April 2009: Identified 27 potential subjects
 - July 2009: Identified cohort sized 34
 - Dec 2009: Feasibility inquiry – in process

c Facilitate clinical trials & research studies

- Registry provides a conduit for communication between researchers/investigators and prospective participants
 - Complement the pre-screening process
 - Disseminate study findings
 - Reduce enrollment lag – Friedreich Ataxia Registry (FARA)
 - Study recruitment announcements
- DuchenneConnect has distributed study enrollment information regarding 2 clinical trials:
 - April 2008 - phase 2b recruitment announcement, 35 participants targeted, over 900 participants informed
 - Oct 2009 – interview study opportunity announcement, ~1200 informed, over 40 enrolled

Patient Registry- Clinical Studies & Trial Recruitment

Clinical Studies

- Retrospective data- Cardiac Abnormalities in FA
- Blood studies- Repligen w/ Development of HDAC inhibitors
- Newborn screening assay

Clinical Trial Recruitment

- First Recruitment- Idebenone
 - Pediatric patients
 - Drug available off label
 - Modest effect

***Wait list at one center within two weeks (Total enrollment 70 pts)**

We here at Santhera know very well that our ambitious target of 70 patients into the US Phase III study with idebenone (IONIA trial) would have never been accomplished without the active and continuous support by FARA's Patient Registry and FAPG.
Thomas Meier

- Third recruitment- Varenicline
 - Ambulatory & non-ambulatory adults
 - Drug available off label

***Wait list at one center within 1 week (Total enrollment 32 pts)**



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Fitting the pieces together

- Assumptions of a rare disease(s) registry
 - Existence of advocacy groups/foundations that seek to establish registries
 - Inclusion of diseases without established organizations
- Aspects of coordination
 - Existing registries – collaboration & partnership
 - Complement not replace
 - Manage the brand of each organization
 - Two US TREAT-NMD affiliated Duchenne/Becker registries, DuchenneConnect and United Dystrophinopathies Project
 - Balance the goals of the organization with the goals of the registry
- Data selection across registries
 - Single disease; multiple diseases (related and unrelated)
 - Core datasets vs registry-specific datasets



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DuchenneConnect



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Data collection, verification and access

Data Collection

- Logistics of collection and structure of data input
- Various mechanisms for data entry exist with various tradeoffs (e.g. accuracy, cost, level of detail)
 - Clinician entered, patient entered, medical record abstraction
 - Web-based, form-based, interview

Data Verification

- Think global and act local
 - Establish common practices to ensure consistency across registries
 - Registry curators: CMDIR & DuchenneConnect have trained curators to verify data, in coordination with global registry

Data Access

- Models: restricted vs. approved vs. global access
- Using an aggregate de-identified approach
- Patient preference for open access to data

Summary



A united rare disease(s) registry complements existing programs and facilitates new opportunities

Acknowledgements

- DuchenneConnect participants & families
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- TREAT-NMD Neuromuscular Network