NORD, OAA, AND A REGISTRY

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Disclosures

- No Conflicts to disclose
- Children's and HemoShear Therapeutics are collaborators
- NIH: K08DK105233

Learning objectives

- Registries: What are they?
- Registries: Why are they important?
- Registries: How can I help?

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National Organization for Rare Disorders

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Registries: What are they?

- Databases which hold information about something
- The content is often determined by the creator

- Several:
  - Urea cycle disorder consortium longitudinal (UCDC)
  - European registry and network for Intoxication type disorder (E-IMD)
  - European network and registry for homocystinurias and methylation defects (E-HOD)
  - Inborn Errors of Metabolism Collaborative (IBEM-IS)

What has E-IMD been able to show from their registry?

J Inherit Metab Dis (2016) 39:341–353
DOI 10.1007/s10545-015-9907-8

ORIGINAL ARTICLE

Impact of age at in organic acidur

Jana Heringer[1] · Vassili Valay
Peter Freisinger[5] · Ivo Barić[9]

J Inherit Metab Dis (2015) 38:1041–1057
DOI 10.1007/s10545-015-9839-3

ORIGINAL ARTICLE

The phenotypic spectrun disorders. Part 1: the init

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Chris Mühlhausen · Hélène Ogier de Baulny · Carlos Ortez · Luis Peña-Quintana ·
Danijela Petković Ramadža · Esmeralda Rodrigues · Sabine Scholl-Bürgi · Etienne Sokal ·

J Inherit Metab Dis (2015) 38:1059–1074
DOI 10.1007/s10545-015-9840-x

ORIGINAL ARTICLE

The phenotypic spectrum of organic acidurias and urea cycle disorders. Part 2: the evolving clinical phenotype

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Diego Martinelli · Shirou Matsumoto · Chris Mühlhausen · Elaine Murphy ·
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Luis Pena-Quintana · Danijela Petković Ramadža · Esmeralda Rodrigues ·
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The impact of rare diseases

- 34% of children admitted to the hospital have a clear genetic condition (i.e. rare disease)
- 50% of all hospital bills
- 81% of hospital bills with at least a genetic determinant

The Burden of Genetic Disease on Inpatient Care in a Children's Hospital, McCandless et al 2004, AJHG

Importance of registries

- Rare Diseases are by their very nature……rare
- Few numbers at any one site. De-identification is difficult at best.
- Most expertise is in an academic medical setting usually amongst a handful of physicians, so the researchers are also often the clinicians.
- Large sets of natural history information typically don't exist.
- To collect data you have to go multi-center or multi-year. Preferably both. This is complex from a consent status. Many patients cross over to adulthood during the study.

You have a registry

- Leadership has received a grant to fund a registry in conjunction with NORD (which is funded by the FDA)
- We have commitment from HemoShear Therapeutics to assist in funding as well
- Data entry planned to start in October 2016

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What can a registry do for us?

- Can determine
  - Frequency
  - Variability
- Co-morbid conditions
- Pre-condense
  - Expertise
  - Patients
  - Care givers

How do we use a registry?

- Registry in this context allows us to:
  - Identify complications which are seen
  - Identify medications that are used
  - Dietary history
- Registry may allow us to:
  - Natural History
  - Frequency of disease
  - Timing of complications
  - Genotype/phenotype correlations

What is going to be in our registry?

- Demographic data
- Presentation history and admissions
- Growth data
- Developmental data (once/year)
- Immunization data
- Medication data
- Interim health history
- Dietary data
- Physical examination data at each visit (min. 6 months)
- Review of systems at each visit (6 months)

NORD Project

- Joint project with FDA and NIH
- Data housed at NORD (Switzerland)
- Common data elements for natural history and specific disease elements
- Entry by Patient/Families and Med Profs. Via web
- Data ownership by disease organization but can partner and also legacy option if organization fails etc.
- Common IRB nationally
- In Pilot phase with 5 rare disease groups
- Cost is a fraction of RDCRN registry $10-25,000/year compared to > $1,000,000/year for RDCRN model.

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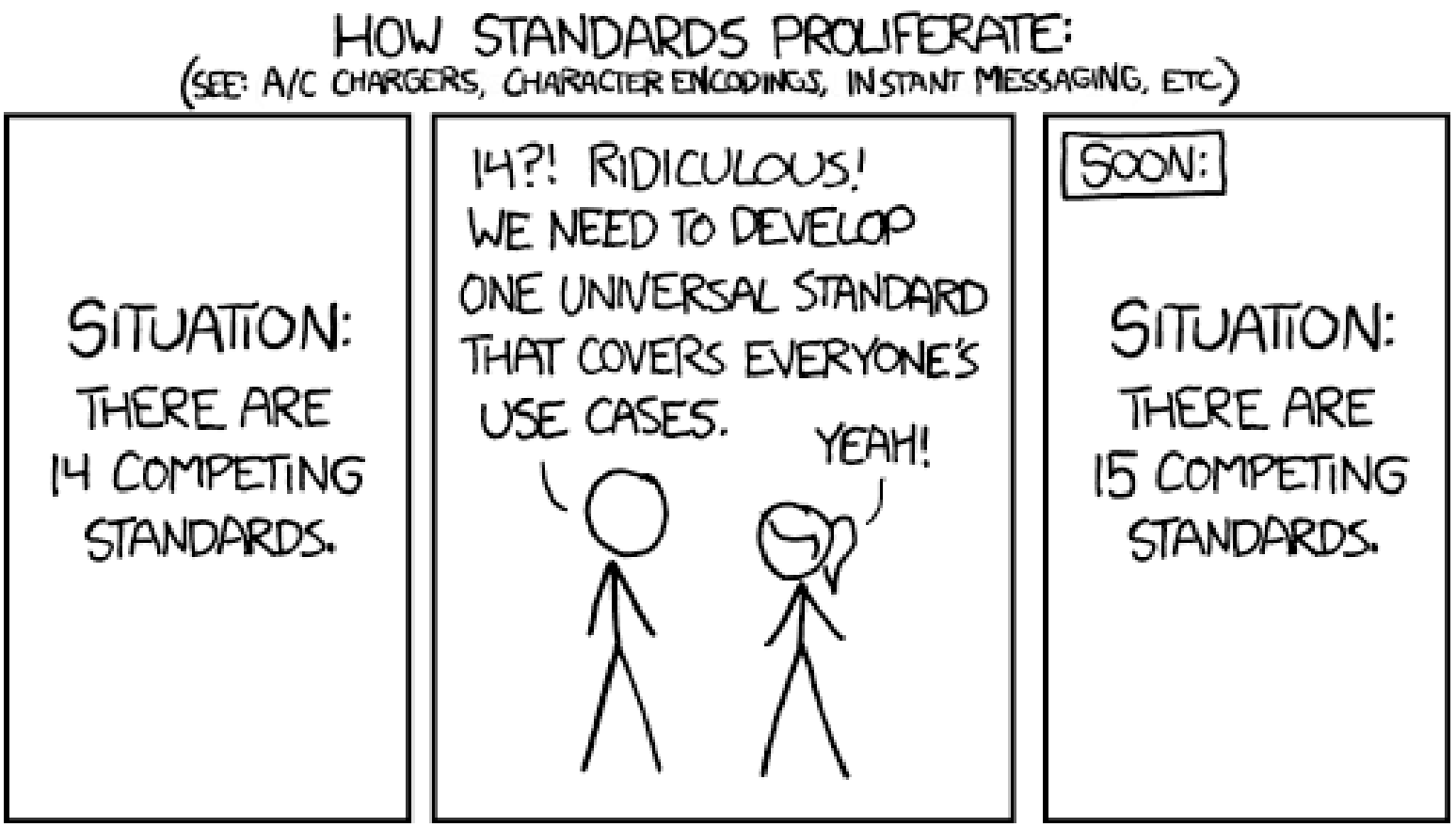

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How to I help with making this work?

- Enter data
- Let me and Sam know what you would like to include
- Volunteer to help with the registry- Sign up sheet at OAA desk

SAM

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What else can a registry do?

- It can enhance research
- Our registry will give you the option to be contacted for research
- Natural history from a good registry can be used by the FDA as a control for intervention trials

Registries and research

- Natural History needs multiple entries

- Recruitment can sometimes be difficult (identification of patients and awareness of study)
  - E.g. Short term outcomes of NCG in hyperammonemia (including OA); PI: Mendel Tuchman
    - Acute study (9 sites, consented ~30s OAA, studied ~15 patients)
    - Nearly 70 episodes, interim review and green light to continue
    - Ongoing since December 2012

Sometimes finding the patient means you can learn basic things about the disease

- The registry can help identify someone who has something rare or is having something done
- E.g. Organ procurement project
- Liver transplants, saving explants and OAA biology

Acknowledgements:

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Division of Genetics and Metabolism
Our Laboratory