

Day one-presentation-session II

Rare Disease Biorepositories and Registries: The Need for Collaborative and Novel Approaches

Benjamin M. Greenberg, MD, MHS

- *We will discuss different types of data that need tracking (patient derived data, clinician derived data, laboratory derived data, radiology derived data)
- *Longitudinal clinical data is critical for adding value to specimens that are gathered
- *Making clinical visits research visits – the need for a change in culture and technology
- *Data and specimen acquisition before diagnosis
- *Collaboration between rare disease communities and common disease categories (using neuroimmunology as a model)
- *Moving away from the investigator/university driven model of repositories. Using Transverse Myelitis and Neuromyelitis as a model.



Uniting Rare Diseases

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

*Session II
Biospecimens/Biorepositories*

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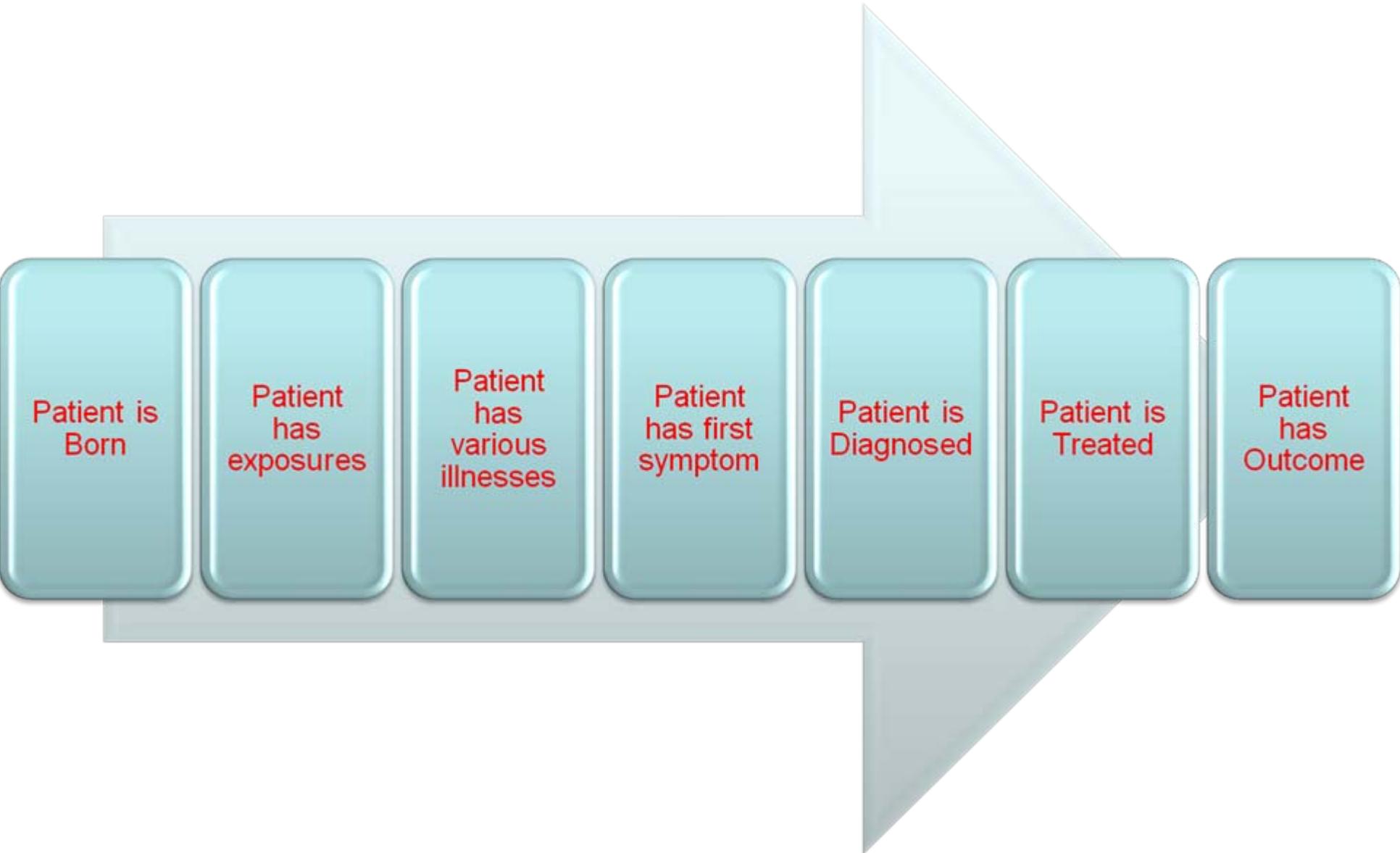
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***Rare Disease Biorepositories and registries: The Need
for Collaborative and Novel Approaches***

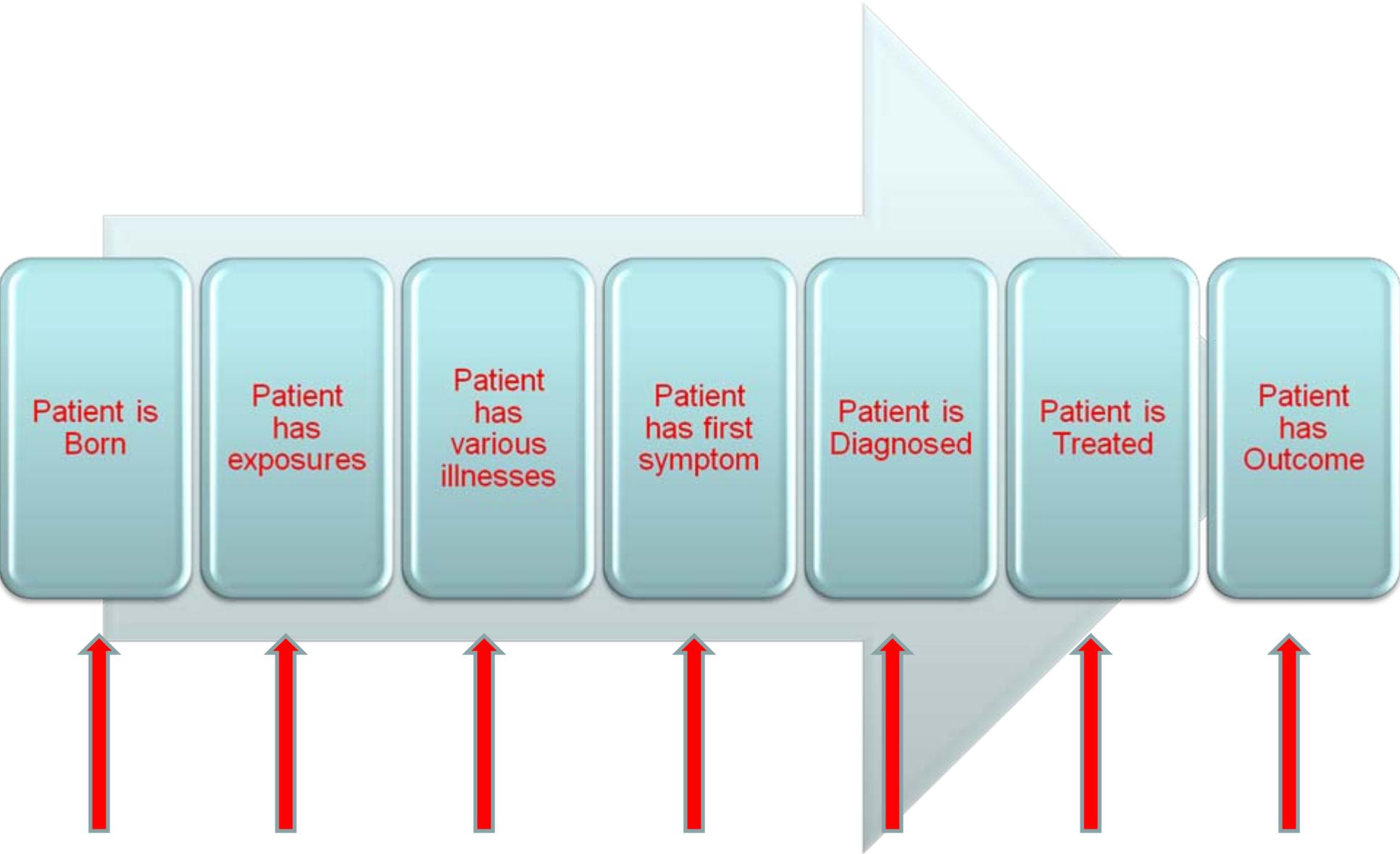
The Alchemy of Biorepositories: Turning Samples into Gold

- A sample's value is based on several factors
 - When was the sample obtained
 - How was the sample obtained
 - How was the sample processed
 - How was the sample stored
 - What prospective data is subsequently gathered about the patient.

Example Patient



The Ideal Biorepository



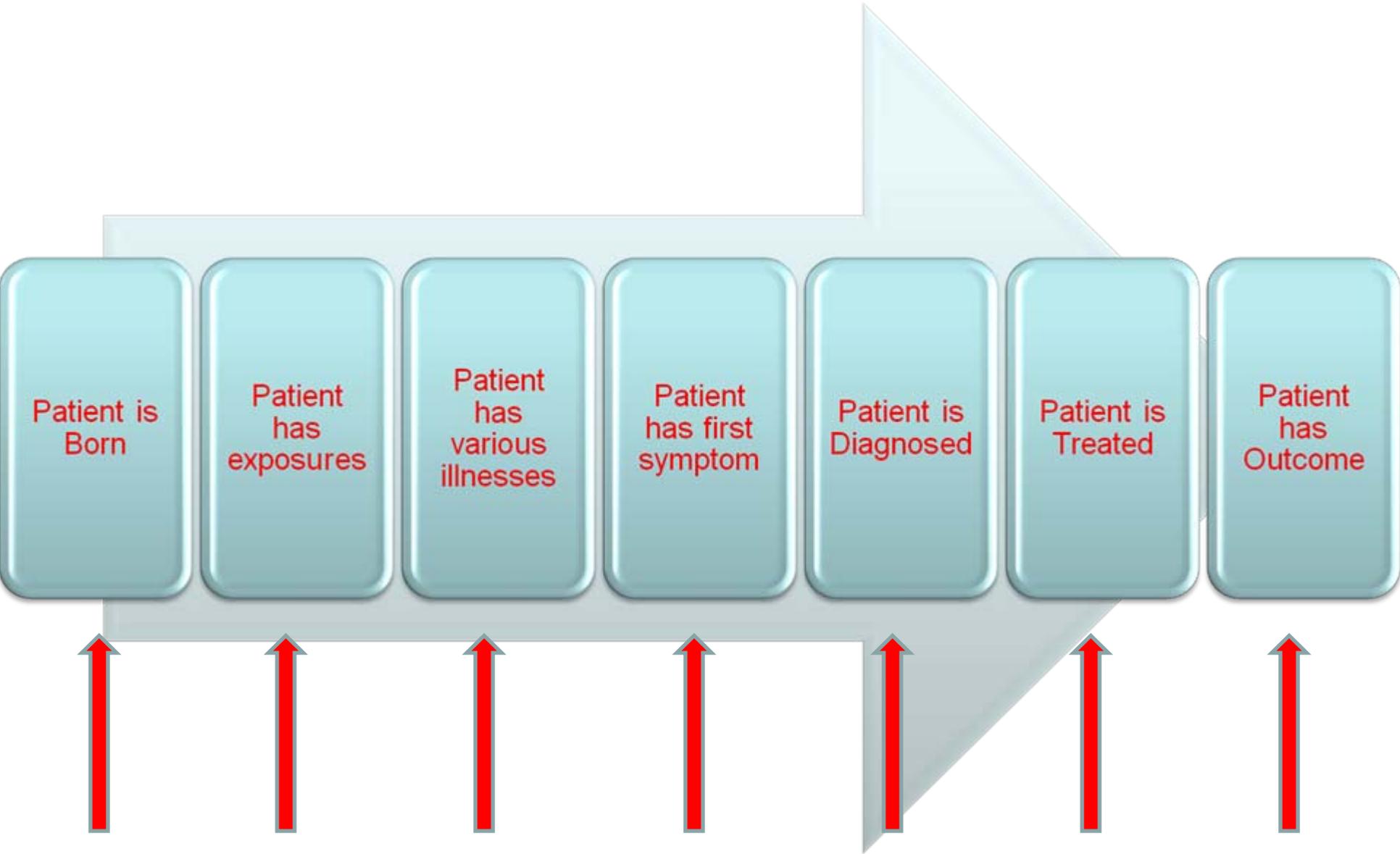
Reality

Patient is
Diagnosed

Patient is
Treated

Patient
has
Outcome

The Ideal Biorepository



The Donald Rumsfield Analysis of Biorepositories for Rare Diseases

“ Reports that say that something hasn’t happened are always interesting to me, because as we know, there are *known knowns*, there are things we know we know. We also know there are *known unknowns*, that is to say, we know there are some things we do not know. But there are also *unknown unknowns* – the ones we don’t know we don’t know.”

-Donald Rumsfeld, Frmr. Secretary of Defense

February 12, 2002

Translation: We Don't Know The Questions That Are Going to Be Asked Tomorrow

Everything can't be designed
around hypothesis driven
research

Remodeling Repositories

- Historically, repositories have been created for genetics research
 - Simple sample acquisition and storage
 - Easy hypothesis testing
- BUT, Most diseases are the result of the following formula:

Disease = Genetics + Environment + Timing

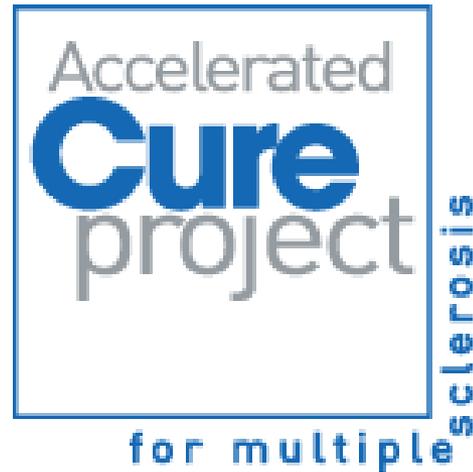
Examples of Discoveries Since 2000

- siRNA
- miRNA
- *Granulobacter bethesdensis* in patients with CGD
- Metapneumovirus in children with hospitalizations for respiratory infections.
- Th17 immune cells
 - 3 articles in 2003
 - Over 700 in 2009

The Broken Repository Model

- The silo approach has failed
 - Every institution has their own program.
 - Individual studies on small numbers
- Hypothesis driven research is the only way to get funding
- Academia is not inherently collaborative
- Intellectual Property issues create obstacles.
- Charts are awful places to get data

Designing Repositories in an Ever Changing World



The Accelerated Cure Project Model for Overcoming These Issues

T H E R E P O S I T O R Y

TWO REQUIREMENTS FOR SOLVING THIS COMPLEX MEDICAL MYSTERY

1. MS is a complex (multifactorial) disease — therefore we need to aggregate data across causes



2. MS may even be a group of diseases — therefore we need to collect and analyze information on large numbers of subjects

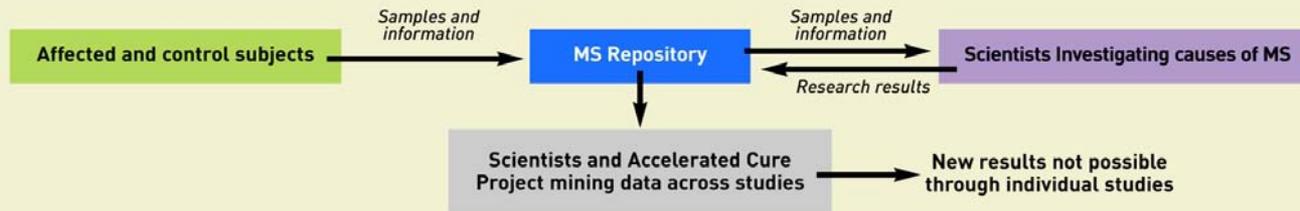
THE ACCELERATED CURE PROJECT MS REPOSITORY ADDRESSES BOTH REQUIREMENTS

Scientists working in different areas can pool their results to find important patterns and correlations if they study the same population.



Results and data are maintained on sufficient numbers of subjects to permit finding meaningful similarities

OPERATION OF THE ACCELERATED CURE PROJECT MS REPOSITORY



This Model Is Impractical For Stand Alone Rare Disease Repositories

- Too few numbers
- Too few points of entry into study
- Too little infrastructure for longitudinal expenses.

- Solution: Combining repositories with registries and partnering up with common conditions.....

The Challenges for Transverse Myelitis and Neuromyelitis Optica Programs

- Rare (less funding, fewer patients, very difficult to get pre-treatment samples)
- Public perception eclipsed by multiple sclerosis
 - Patient advocacy groups appropriately want to maintain distinct identity due to distinct needs.
- Difficult semantics/misdiagnosis

Finding Common Ground

- Much can be learned by studying outliers.
 - Comparing related, albeit distinct diseases allows for new discovery
 - Neuromyelitis Optica versus Multiple Sclerosis versus Myasthenia Gravis
- The notion of “controls”
 - Allows for collaborations between “common” and “rare” disease groups.

Connecting Registries to Repositories

- Patient Referral
- Education of patients, families and physicians
- Longitudinal follow up structure

Collaborative Solutions



Status

- 9 enrolling sites
- Over 1400 cases
 - 880 MS
 - 80 NMO
 - 125 TM
- Over 400 controls

***Overrepresentation of the rare diseases!!!!**

Conclusions

- Link to registries
- Link to common diseases
- Remove structure from universities
- Data sharing plan
- Broad sample procurement

- Public policy: rare disease community coming together

every visit is a research visit.....

The Ideal Biorepository

