The Pillars

*Defining the scientific aims*

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Presentation agenda

1. What are the PILLARS?
2. Role of scientific observation and aims of a registry (Huntington disease)
3. Clear aims have impact – the registry’s purpose
4. Registry adaptability
Registries defined

- “a file of documents containing uniform information about individual persons, collected in a systematic and comprehensive way, in order to serve a predetermined purpose.”

- “an organized system for the collection, storage, retrieval, analysis, and dissemination of information on individual persons who have either a particular disease, a condition (e.g., a risk factor) that predisposes [them] to the occurrence of a health-related event, or prior exposure to substances (or circumstances) known or suspected to cause adverse health effects.”


The Pillars of a successful registry

Aims

Patients
Families, Carers

Investigators/HCPs
Academia, Hospitals, Community

Researchers
Basic, Translational, Public Health

Government
Public Health, Payers, Regulators

Industry
Pharma/Biotech, CROs

Sustainability

Governance
Aims
The overall purpose of the registry, clearly defined, aligned with important questions and other objectives stakeholders want to achieve

Sustainability
The continuation of a registry’s efforts to meet current needs and deliver its desired outcomes to the community of stakeholders.

Governance
The processes of governing: Policies, monitoring progress, scientific integrity, ethical oversight
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Always begin with observation
The original observations of George Huntington

The hereditary chorea, as I shall call it, is confined to certain and fortunately a few families, and has been transmitted to them... hardly ever manifesting itself until adult or middle life, and then coming on gradually but surely, increasing by degrees, and often occupying years in its development, until the hapless sufferer is but a quivering wreck of his former self.

There are three marked peculiarities in this disease:
1. Its hereditary nature.
2. A tendency to insanity and suicide.
3. Its manifesting itself as a grave disease only in adult life.

Scientific aims

• Understand the phenotype as it evolves over time
• Differences between prodromal and manifest disease
• Patterns of symptom onset: age, family history, gender
• Treatment effects on different symptoms
• Prevalence and risk factors for suicide
The HD mutation

CAG CAG CAG CAG+n

> ~70 juvenile onset HD
> 40 adult onset HD
36-39 incomplete penetrance
6-35 unaffected

≤ 35 CAG - unaffected
36 - 39 CAG – increased likelihood of developing HD
≥ 40 CAG – causes disease within normal lifespan
≥ 70 CAG – causes childhood onset

Organised by Istituto Superiore di Sanità
Rome (Italy), September 26-28, 2016
A single mutation with an expanded tri-nucleotide repeat

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HD Degeneration

Normal

Striatum

HD

Caudate

Putamen

Ventricular Enlargement

Basal Ganglia Degeneration

Cortical Thinning

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Scientific Aims

• Neuronal/structural correlates of disease symptoms
• CAG-length relationship to structural changes and neuronal dysfunction
• Genetic modifiers of disease onset – GWAS
The three main aims for Enroll-HD

Enable clinical research
- Sub-studies (e.g. rating scale validation)
- Experimental medicine studies
- Accelerating clinical trial recruitment

Understand HD
- Longitudinal observational study
- Standardize core data collection
- Bio-samples

Improve clinical care
- Facilitate quality care improvement
- Conduct outcomes research
- Promote standards of care

Registry scope

• What data will be collected?
  – Characterization of the phenotype
  – Natural history, symptom progression
  – Disease sub-types

• Sample collections?
  – DNA
  – Plasma, lymphocytes

• Tissue donations?
  – Biopsies
  – Target organs
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"It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is most adaptable to change".

Charles Darwin
Why do registries need to be adaptable?

Adaptability – able to adjust the registry readily to changing conditions

- Changes in science and medicine (new observations)
- Changes in personnel and leadership
- Patient reported outcomes (PRO): testing, validating and adopting
  - Include new measures to replace old
- Important for sustainability
- Align technology for adaptability
- Align governance for adaptability