More and Better Data: Partnering to Improve Clinical Outcomes

Improving Multiple Sclerosis Care through a Learning Health System
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Celeste Adams is an employee of Wolters Kluwer Health Language
MS PATHS: a demonstration project of Learning Health System in Multiple Sclerosis

- LHS Design
- Point of View: Data Models and Real World Evidence Utility
- Initial Insights
- Lessons Learned
Multiple Sclerosis is an immune-mediated condition characterized by inflammation, demyelination, and axonal loss.

Immunopathology of MS

1. Circulation
   - BBB
     - 1. White blood cells cross the BBB...
     - 2. ...and attack the myelin in the CNS

2. CNS
   - 3. Resulting in demyelination, nerve dysfunction, and axonal loss

Inflammation, Demyelination and Axonal Loss

- T1-hypointense lesion (black hole)
- T2-hyperintense lesion (partial remyelination)
- Gd+ lesion (inflammation)

BBB=blood-brain barrier; CNS=central nervous system; Gd+=gadolinium-enhancing.

Real World Data Challenges in MS

- Prospective clinical research, where assessments may be quantitative and standardized, is expensive and has low participation rates

- Administrative and EMR data
  - Often lack outcomes measured in MS clinical trials
  - Disease progresses over decades
    - Patient’s experience spans over time
    - Care experience changes over time (e.g., insurers, health providers)

- Clinical Practice
  - Standardized clinical assessments tools and documentation often not used
  - Clinical assessments are often subjective and qualitative
Creating One, Highly Interactive Universe

Merge research with healthcare enterprise to capture standardized data during routine care to enable:

1. Comparative effectiveness research, translational medicine
2. Value-based reimbursement
3. Regulated drug development
“Clinical research has proven to be slow, difficult, and increasingly expensive—and even so, it often fails to yield the information needed... But these problems can be overcome by integrating research with clinical practice, a concept known as the “learning health system....”

Rob Califf, MD
Immediate Past Commissioner, FDA
What is MS PATHS?

• Multiple Sclerosis Partners Advancing Technology and Health Solutions

• Demonstration project sponsored by Biogen in collaboration with 10 healthcare institutions in the US and EU

• Uses innovative healthcare technology to capture standardized, quantitative clinical, Quality of Life (QoL), neuro-performance and imaging data during routine clinical practice and aggregates the data for research

• As of December 1, 2018
  — more than 14,000 patients have agreed to share their healthcare data
  — 40% have longitudinal data
# MS PATHS Network

<table>
<thead>
<tr>
<th>Healthcare Institution</th>
<th>United States</th>
<th>Europe</th>
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<tbody>
<tr>
<td>Cleveland Clinic</td>
<td>Johns Hopkins</td>
<td>UKGM</td>
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<td>Brain Health</td>
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<td>Las Vegas, NV</td>
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MS PATHS Learning Health System

1. Standardized data collection during routine care
   - Clinical, QoL & Neuroperformance data
   - MRI data
   - Biologic data

2. Data aggregation across healthcare institutions
   - Store, analyze, visualize data

3. Insights
   - Research
   - Point of care
Multiple Sclerosis Performance Test (MSPT)

- iPad-based assessment tool
- Designed to objectively quantify the major motor, visual, and cognitive symptoms and quality of life outcomes associated with MS
- Comprises:
  - Structured patient history (MyHealth)
  - The Neurological Quality of Life (Neuro-QoL) assessment
  - An electronic adaptation of the MS functional composite (MSFC)
- Is not intended to provide recommendations or conclusions related to diagnosis or treatment and should be used in a manner consistent with good clinical judgment

*Concept and prototype developed by Cleveland Clinic Neurological Institute, licensed by Biogen.*
MS PATHS institutions have standardized key aspects of MS MR-imaging

Highly standardized 3-dimensional magnetization-prepared rapid gradient-echo imaging [3D MP RAGE] and 3-dimensional fluid-attenuated inversion recovery [3D FLAIR] incorporated into routine MS imaging protocol

Product sequences; in line with Consortium of Multiple Sclerosis Centers imaging guidelines

Images acquired on Siemens 3T MRI scanners
Quantitative MRI Measures

In collaboration with Siemens Healthineers working to develop image analysis software to calculate quantitative imaging metrics at the point of care

- Automated measurements of T2 lesions and brain volume

MS PATHS aims to develop a biobank of samples from MS patients to enable development of biomarkers for prognosis and treatment response.

Sample collection will include 42 mL* of whole blood, drawn for the biobank as:

<table>
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<th>Component</th>
<th>Description</th>
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<tr>
<td><strong>DNA</strong></td>
<td>15 mL whole blood into one 10 mL and one 6 mL K2 EDTA tubes</td>
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<tr>
<td><strong>RNA</strong></td>
<td>10 mL whole blood into 4 PAXgene RNA tubes (4 x 2.5 mL)</td>
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<tr>
<td><strong>Serum</strong></td>
<td>17 mL blood (2 x 8.5 mL)</td>
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*Volumes may vary slightly based on tubes available in different countries.
## MS PATHS At-a-Glance

**Unique consented patients:** 14823

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<thead>
<tr>
<th>Category</th>
<th>Unique</th>
<th>Total</th>
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<td>MSPT assessments</td>
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<td>32471</td>
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<tr>
<td>Imaging studies</td>
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<td>9835</td>
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<tr>
<td>EMRs</td>
<td>14139</td>
<td>91901</td>
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<tr>
<td>Biobanking samples</td>
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<td>6913</td>
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**Patients with >1 MSPT Assessment**

<table>
<thead>
<tr>
<th># MSPT Assessments</th>
<th># Patients</th>
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<tr>
<td>2</td>
<td>3892</td>
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<tr>
<td>3</td>
<td>2506</td>
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<tr>
<td>≥ 4</td>
<td>2550</td>
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Current as of 10.16.2017 and 01.02.2019
# MS PATHS Core Data Elements

## MyHealth
### Demographics & Socioeconomics
- Gender
- Age
- Marital Status
- Race and Ethnicity
- Education
- Handedness
- Employment Status
- Insurance
- Living Situation

### MS
- Age of MS SX onset
- Age MS DX
- MS Subtype
- Relapse(s) in past 12 months
- Last steroid use
- Current DMT and date
- Previous DMT and date
- Patient-Determined Disease Steps (PDDS)
- Mobility Aid

## Neuro-QoL
### Mental
- Emotional Health (e.g., anxiety, depression, stigma)
- Cognitive Health (e.g., applied cognition - general concerns and executive function)

### Physical
- Function/Health (e.g., upper and lower extremity function)
- Symptoms (e.g., fatigue and sleep disturbance)

### Social
- Ability to Participate in Social Roles
- Satisfaction with Social Roles

## EMR Data Elements
### Medication
- Full medication list
- MS Disease Modifying Therapy (DMT) and other therapeutic group list

### Labs
- JCV antibody status
- Vitamin D levels
- Panel: CBC, CMP, Lipid, LFT, RFT, Thyroid
- Other: Glucose, HbA1c, Homocysteine, CRP, ESR, ANA, IgG, Oligoclonal banding

### Observations
- Smoking history
- Vital signs

## Neurological Function Elements
- Contrast Sensitivity Test
- Manual Dexterity Test
- Processing Speed Test
- Walking Speed Test

## Biobanking
- Sample: DNA, RNA, Serum, EDTA whole blood
- Time of last meal
- Smoking status
- Sample collection date

## MRI
- Semi-Quantitative Assessment (Radiology Report)
  - New or enlarging T2 lesion count (0, 1, 2 or ≥ 3)
  - Gadolinium-enhancing lesion count (0, 1, 2, or ≥ 3)

- Quantitative Assessment (Image Analysis Software)
  - New or enlarging T2 lesion count
  - Brain volume & brain volume change

- 3D MPRAGE & 3D FLAIR Images, 3T Scanner
LHS – Harmonization Engine

LHS uses third-party services engine for harmonization
- Library of clinical terminology dictionaries that are updated and current with industry
- Back-end API web services
- Front-end UI for manual data curation

Option for Biogen-curated content when needed
- Derived medication table
- Non Meaningful Use-compliant EMR data

LHS designed to allow for re-harmonization of data at any point in time along with audit trail of all actions
LHS – Data Sets

Data Cut #7 (published 12/18/18)

**MSPT:** reported by 13,559 patients

**EMR:** reported by 11,658 patients
- 287,849 medication records (based on RxNorm)
  - 30,559 DMT derived med records
  - 20,344 anti-depressant derived med records
  - 11,763 anti-hypertensive derived med records
  - 3,333 anti-diabetic derived med records
- 217,861 lab results (based on LOINC)

**Biobanking:** 6,068 samples (4,571 patients)
- 2,503 serum neurofilament results (2,192 patients)

**RIS:** reported for 7,973 patients

**DICOM:** ~10,000 standardized MRI studies (7,724 patients)
- 864 MRI studies tagged with quantitative metrics (513 patients)
MS PATHS Data Curation Policy

Why do standards matter?

- To ensure uniform and consistent meaning for clinical data elements
- To promote system-agnostic and site-agnostic curation method that relies on common terminology and semantics
- To ensure that harmonization is not reliant on any one form of data transmission or data storage

Our position: To harmonize clinical data by using industry-accepted clinical terminology standard libraries/data sets

- SNOMED CT®: smoking status, social history, problems
- LOINC®: lab orders, lab results, vital signs
- RxNorm and NDC: medications
- HCPCS: DMEs
What we have learned so far

IT IS POSSIBLE TO...

Create a collaboration between industry and multiple stakeholders within healthcare institutions. However, a program like this is built on shared goals, trust, and respect.

Introduce new approaches and technology into the current healthcare system

Align diverse stakeholders to drive standardization

Implement an infrastructure that allows for real-time access to data from health IT systems

Deliver highly curated, interoperable data sets for real world evidence