National
Multiple Sclerosis
Society

MS Outcomes Assessment Consortium Overview

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Clinical Outcome Measures for Multiple Sclerosis
Why do we struggle with this?

"Precise measure of the clinical manifestations of MS is difficult because neurological impairment and disability vary in different patients and over time, and neurological function is inherently difficulty to quantify."

Rudick, Antel, Confavreux, et al. *Annals of Neurology,* 1997

Disability outcome measures in multiple sclerosis clinical trials: current status and future prospects

Jeffrey A Cohen, Stephen C Reingold, Chris H Polman, Jerry S Wolinsky, for the International Advisory Committee on Clinical Trials in Multiple Sclerosis

Lancet Neurology, 2012

"For the study of MS to advance, more informative disability measures are needed."

"To attain these goals will require a collaborative approach that involves academic experts, regulators, industry representatives, and funding agencies."

Attributes of a new MS COA

- Measures the impact of an intervention on the disability due to MS and is qualified for use in registration trials

- Acceptable to patient, and be:
  - Multidimensional to reflect the principal ways that MS affects an individual
  - Highly reliable and valid - including meaningful to the patient
  - Sensitive to change over time to permit demonstration of a therapeutic effect
  - Practical and cost-effective

Goals of the MSOAC Consortium

- Create MS therapeutic area data standards, leveraging efforts already underway
- Remap legacy MS clinical trial data into common MS therapeutic area data standards.
- Create an online MS database of aggregated, standardized clinical data, and make this resource publicly available to qualified researchers
- Create scientific consensus on the optimal components for inclusion in a modified MS Functional Composite (MSFC)
- Advance a new clinical outcome assessment drug development tool based on the MSFC to the FDA and EMA for regulatory qualification

Deliverables

- A CDISC data standard for MS
  - CDISC is a standards setting organization that has established standards to support the acquisition, exchange, submission and archive of clinical research data and metadata
- A database of pooled, de-identified clinical trial data mapped to the CDISC standard
- A new methodology to measure performance as a primary or secondary endpoint in MS clinical trials. The composite measure will be submitted for qualification by the EMA and FDA

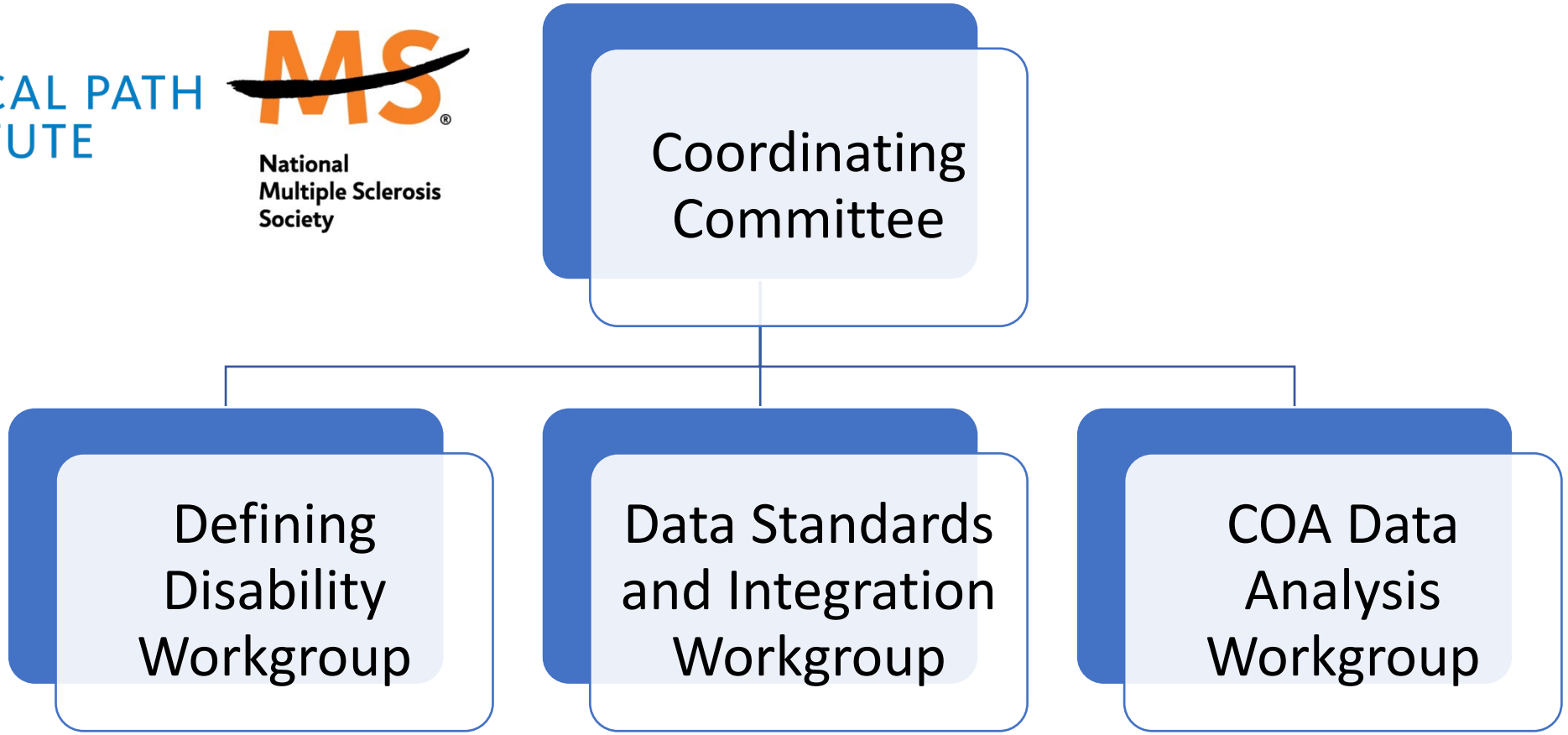
MSOAC Engages all Stakeholders

- **MSOAC Leadership**
  - Lynn Hudson (C-Path), Nicholas LaRocca (NMSS), Richard Rudick (Cleveland Clinic)
- **10 pharmaceutical companies**
  - Abbvie, Acorda, Biogen Idec, Bristol-Myers Squibb, Glaxo Smith Kline, EMD Serono, Novartis, Genzyme/Sanofi, Roche, Teva
- **Patient Advocacy Organizations**
  - NMSS, AISM, MS Society of UK, MS Society of Canada, Alberta MS Research Foundation, CMSC
- **Regulators and Government Funding Agencies**
- **30 Academic Investigators**

MSOAC Structure

CRITICAL PATH INSTITUTE

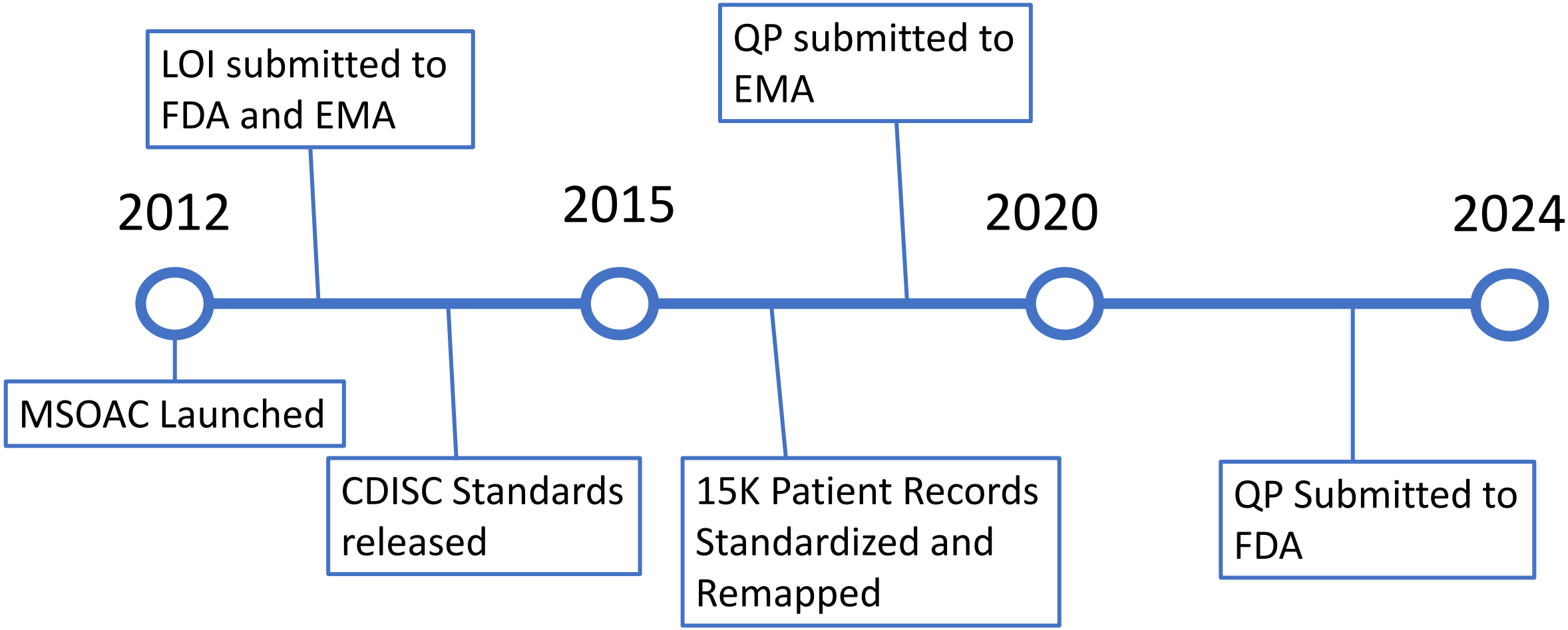
National Multiple Sclerosis Society



Data Sets Collected

Study	CT.gov #	n	Type	EDSS	FSS	T25FW	9HPT	PASAT	SDMT	LCVA	SF-36	BDI-II
ADVANCE	NCT00906399	1512	RRMS	√	√	√	√	√	√	√	SF-12	√
AFFIRM	NCT00027300	939	RRMS	√	√	√	√	√	No	√	√	No
CARE-MS 1	NCT00530348	563	RRMS	√	√	√	√	√	No	√	√	No
CARE-MS 2	NCT00548405	798	RRMS	√	√	√	√	√	No	√	√	No
CombiRx	NCT00211887	1008	RRMS	√	√	√	√	√	No	√	√	No
FREEDOMS	NCT00289978	1272	RRMS	√	√	√	√	√	No	No	No	No
FREEDOMS II	NCT00355134	1083	RRMS	√	√	√	√	√	No	√	No	No
IMPACT	N/A	434	SPMS	√	√	√	√	√	No	No	√	√
MAESTRO	NCT00869726	610	SPMS	√	√	√	√	√	No	No	√	No
PROMISE	N/A	943	PPMS	√	√	√	√	√	No	No	√	No
SENTINEL	NCT00030966	1196	RRMS	√	√	√	√	√	No	√	√	√
STRATA	NCT00297232	1094	RRMS	√	√	No	No	No	√	No	No	BDI-FS
TEMSO	NCT00134563	1086	RRMS	√	√	√	√	√	No	No	√	No
TRANSFORMS	NCT00340834	1292	RRMS	√	√	√	√	√	No	√	No	No

Timeline


LOI submitted to FDA and EMA
QP submitted to EMA
2012
2015
2020
2024
MSOAC Launched
CDISC Standards released
15K Patient Records Standardized and Remapped
QP Submitted to FDA

Outcomes

- **International collaborative effort that elevated importance of new MS outcomes**
- **CDISC standards for MS**
- **Pooled clinical trial data available to the MS community**
- **Qualification package of MS COA submitted to EMA**
  - Agency declined to qualify as stand-alone measure. Ok when used with EDSS
- **Qualification package to FDA for SDMT**
  - Anticipate decision in 2024

Considerations

- **Clear rationale**
- **Investment (Society funding ~$3 million plus in kind from data contributors)**
- **Partner with regulatory expertise and connection to FDA/EMA**
- **Patience**
- **Adaptability**