Improving Performance of Algorithms to Power Unmet Need and Effectiveness in Health Economics and Outcomes Research Using Electronic Health Records and Healthcare Claims Data Sources

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Workshop Overview

Optimized Patient Access Requires Life Cycle Evidence Generation

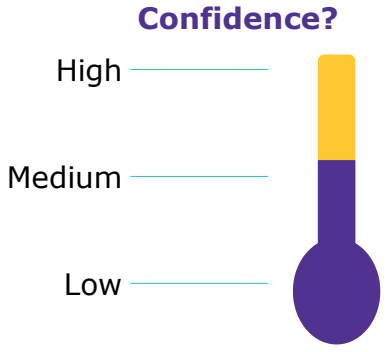
Real-World Evidence

1. **Inform and enhance clinical development and regulatory decision-making; characterize unmet need, support product differentiation; demonstrate effectiveness and safety**
2. **Inform options for innovative pricing; access agreements with payers; pay-for-performance**
3. **Fulfill post-marketing commitments**
4. **Healthcare quality metrics**

Accurate Case Ascertainment and Health Outcomes Identification is Critical

Misclassification is a Risk to Sound Inferences & Healthcare Decision Making

- Commonly use algorithms
  - Ad-hoc
  - Inconsistent
  - May not be fit-for-purpose
  - May not be apt for the data source
- Validity non-commonly assessed



Health Outcome Example: Multiple Sclerosis (MS) Relapse Episodes

Option 1: Occurrence

Option 2: Severity
- Mild
- Moderate
- Severe

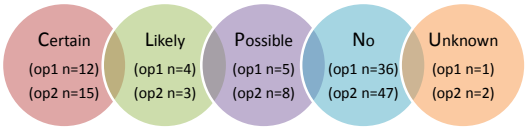
EHR clinical notes-based algorithm
- Natural language processing (NLP)

Claims-based algorithm

Positive predictive value (PPV) calculations for validation

Health Outcome Example: MS Relapse Episodes

EHR Clinical Notes-Based Algorithm
(NLP-type validation)

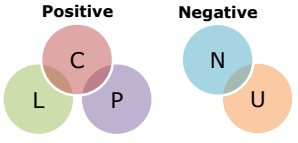


PPV (calculation 1)

Option 1 PPV=25.0%
(95% CI: 14.1-39.9%)

Option 2 PPV=24.2%
(95% CI: 14.6-37.0%)

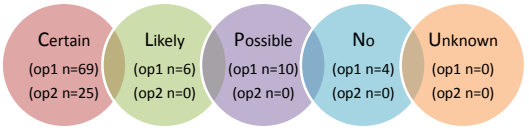
PPV (calculation 2)



Option 1 PPV=36.2%
(95% CI: 24.3-49.9%)

Option 2 PPV=34.7%
(95% CI: 24.3-46.6%)

Claims-Based Algorithm
(Validation via Comprehensive Patient Profiles)



Option 1 PPV=94.5%
(95% CI: 86.3-98.3%)

Option 2 PPV=100%
(95% CI: 86.3-100.0%)

Option 1 PPV=95.5%
(95% CI: 88.9-98.8%)

Health Outcome Example: MS Relapse Episodes Key Findings

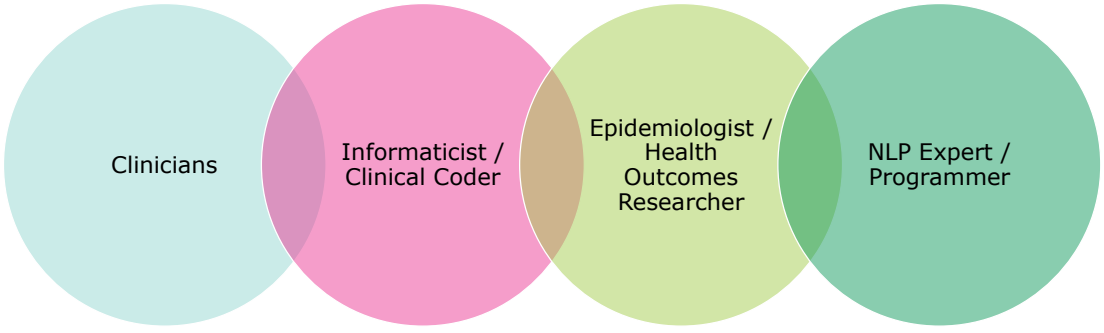
EHR Clinical Notes-Based Algorithm

- Relapses were not explicitly recorded within the clinical notes
- Search terms were too general, not limited to MS and/or relapse, and therefore returned false positives

Claims-Based Algorithm

- Option 1 identified more than three times as many relapse episodes and about 50% more patients (n=11,362 relapses), than Option 2, designed to categorize severity among relapses (n=3,444 relapses)

Algorithm Development Starts With a Team



NLP = Natural language processing

Consider Your Data Source

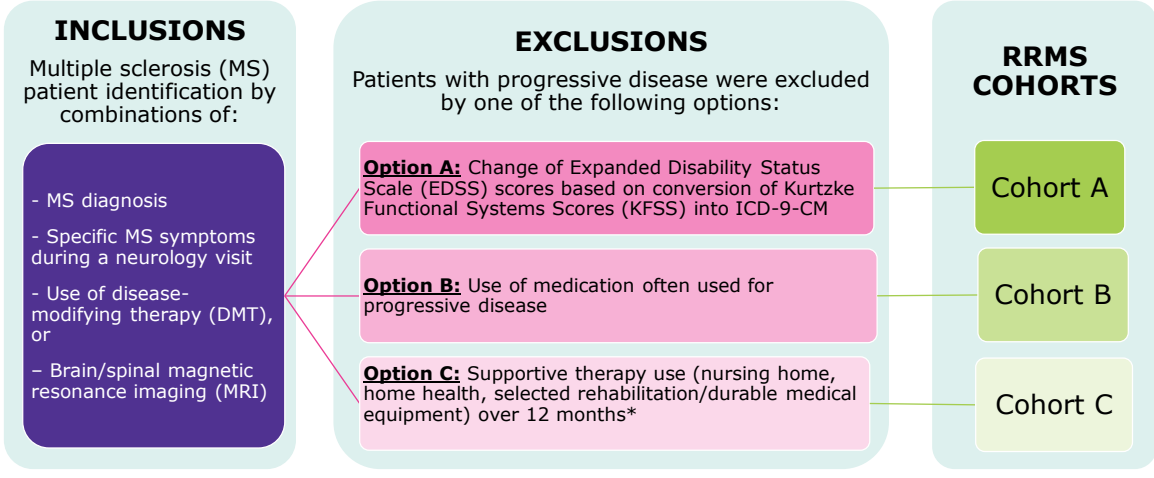
- Structured or Unstructured data
- Population captured
- Single or multiple source
- What data will not be captured?
- Where is data captured?
- Follow-up & look-back periods
- Validation

Validation Measures

- Sensitivity
- Specificity
- Positive predictive value (PPV)
- Negative predictive value (NPV)
- Area under curve
- Likelihood ratio
- Youden's index
- Diagnostic odds ratio (DOR)

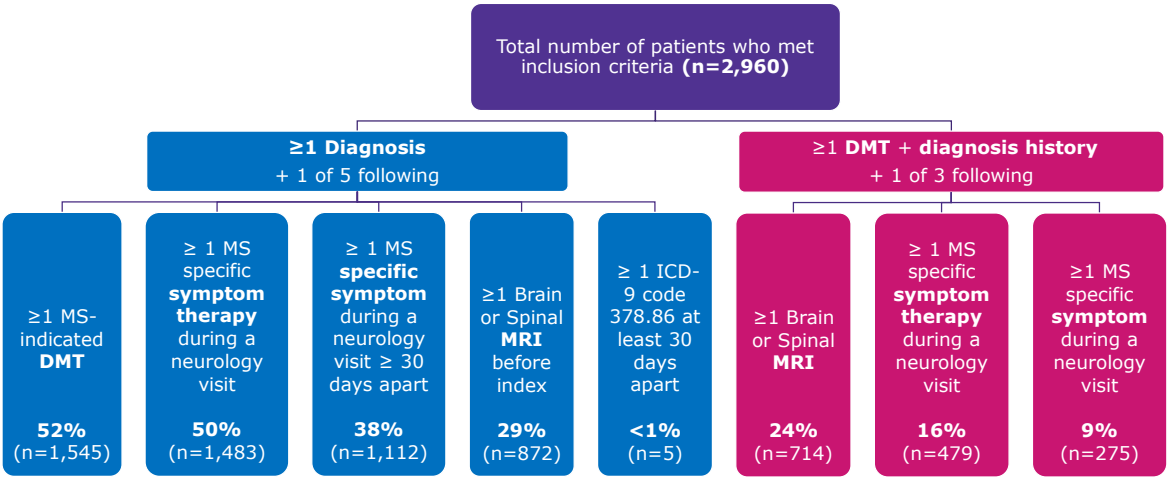
Case Ascertainment Algorithm Example: Subtype Identification

Inclusion And Exclusion Criteria



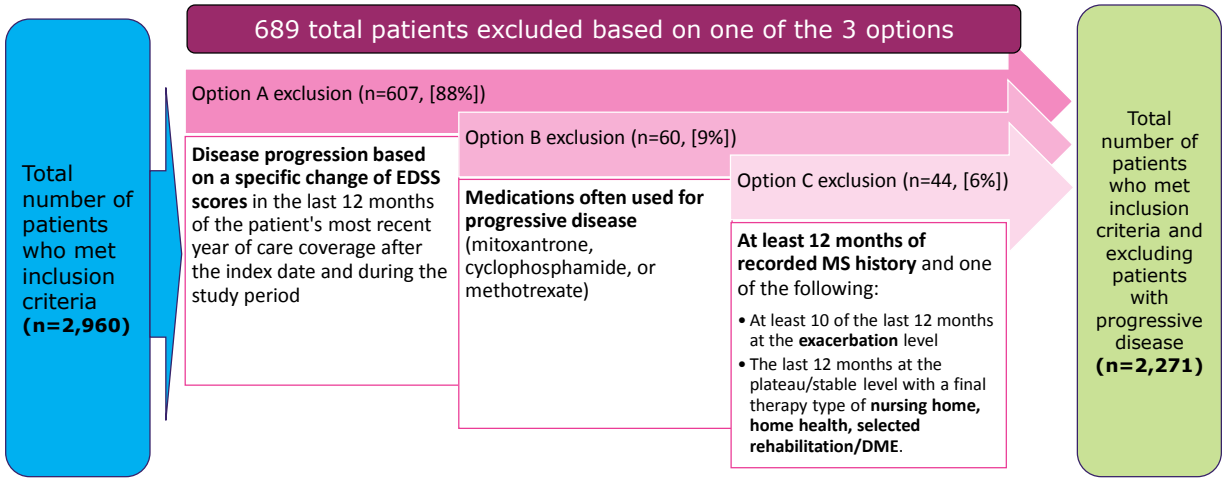
** Adapted from Gilden et al. 2011*
RRMS = Relapsing-remitting multiple sclerosis

Criteria Contributions



ICD-9 378.86: Internuclear ophthalmoplegia

Progressive MS Identification



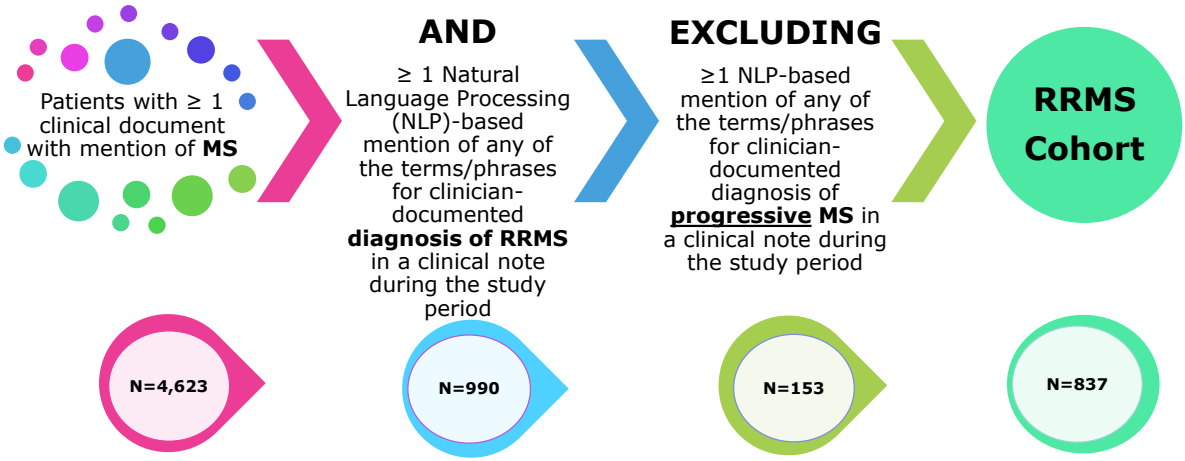
EHR Clinical Notes-based Case Ascertainment Algorithm Example: Subtype Identification

Natural Language Processing Search

Search terms and % hit of 62,909 documents

multiple'	97%
sclerosis'	96%
relapsing'	4.7%
remitting'	4.2%
progressive'	5.6%
subtype'	0.055%
RRMS'	0.098%
multiple sclerosis'	94.8%
relapsing remitting'	2.79%
NEAR((multiple, sclerosis) , 3, TRUE) '	95.2%
NEAR((relapsing, remitting) , 4, FALSE) '	4%
NEAR((relapsing, remitting, multiple, sclerosis) , 12 , FALSE) '	2.8%
NEAR((multiple, sclerosis, relapsing, remitting, subtype) , 12, FALSE) '	0.023%
NEAR((remittent, progressive , multiple, sclerosis) , 12, FALSE) '	0.003%
NEAR((multiple, sclerosis, relapsing, remitting, type) , 12, FALSE) '	0.063%
NEAR(({not}, multiple, sclerosis) , 20, FALSE) '	0.95%
NEAR((unlikely, multiple, sclerosis) , 15, FALSE) '	0.12%

Inclusion and Exclusion Criteria



Challenges & Considerations

- Case definitions and data capture
- Availability of data recorded in clinician's documentation
  - Explicit documentation
  - Detail on image report vs clinical notes
- Measure(s) for validation and data availability

Audience Participation

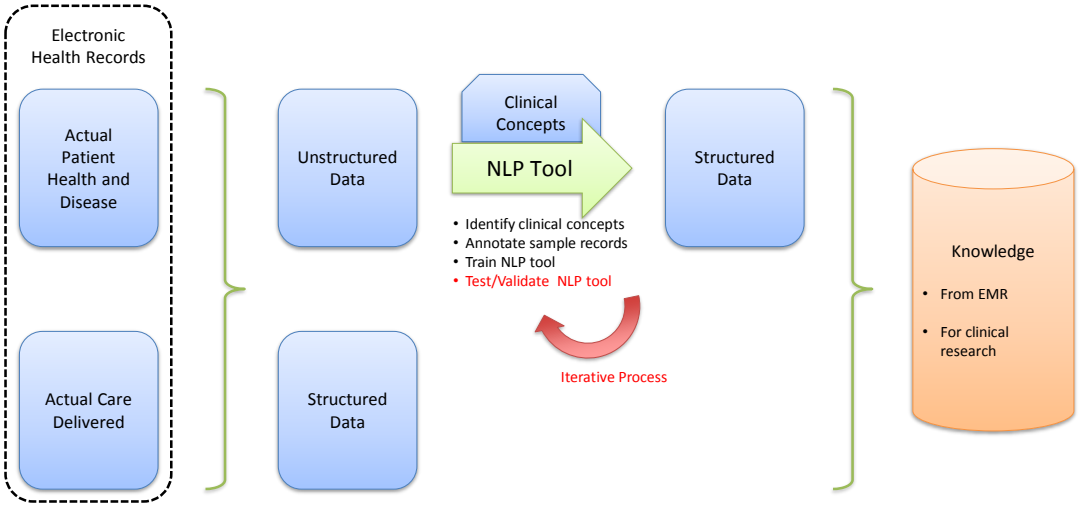
- What has been your experience with developing algorithms?
  - Intended purpose of the algorithm
  - Challenges encountered
  - Lessons learned
  - Impact

Healthcare Data

- Diagnoses, medications/prescriptions, procedures
- Observations (including vital signs)
- Problem lists with symptoms
- Laboratory and microbiology/pathology results
- Imaging studies (PACS images & radiologist notes)
- **Clinical documents**
  - **Clinician notes, radiology reports, microbiology/pathology reports**
  - **Medical test results, symptoms, disease characteristics/qualities**

- Advanced state-of-the-art **Natural Language Processing (NLP)** methods extract meaningful information from text notes

Natural Language Processing (NLP)



NLP Example: Relapsing Multiple Sclerosis

Evidence of RRMS

RRMS Terms	# of Unique Patients
relapsing remitting	839
relapsing	970
remitting	862

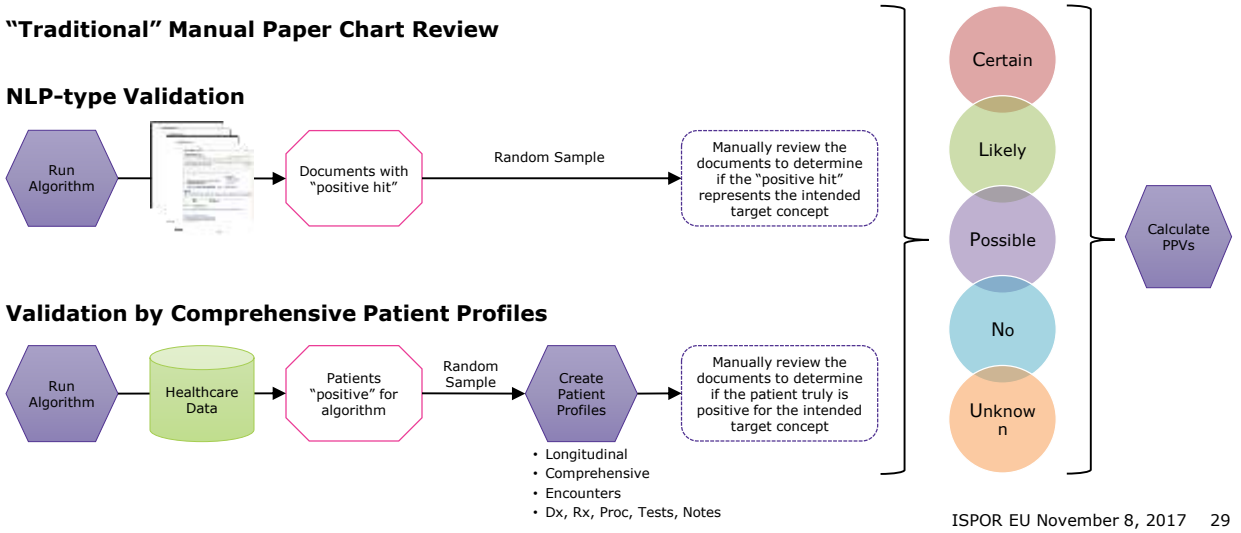
Evidence of Progressive MS

Progressive MS Terms	# of Unique Patients
contains(document_text,' NEAR((progressive, multiple, sclerosis) , 6, FALSE) ' ,18)> 0	153
~~contains(document_text,'progressive', 5)>0~~ *Not used: proved too broad, resulting in false positives*	522

Why Validate Algorithms?

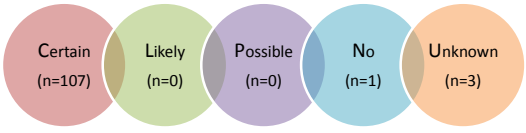
- Determine measurement characteristics (accuracy) of the algorithm
- Provides baseline understanding to support interpretation of results
- Support improvement of the algorithm for case ascertainment or study measures
- Higher accuracy → step toward standardization of case ascertainment or study measures

Some Types of Validation

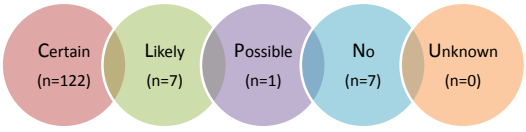


Case Ascertainment Algorithm Example: Multiple Sclerosis Subtype RRMS

EHR Clinical Notes-Based Algorithm
(NLP-type validation)



Claims-Based Algorithm
(Validation via Comprehensive Patient Profiles)

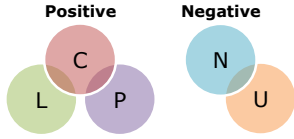


PPV (calculation 1)

PPV=99.1%
(95% CI: 94.2-100%)

PPV=94.6%
(95% CI: 89.0-97.5%)

PPV (calculation 2)



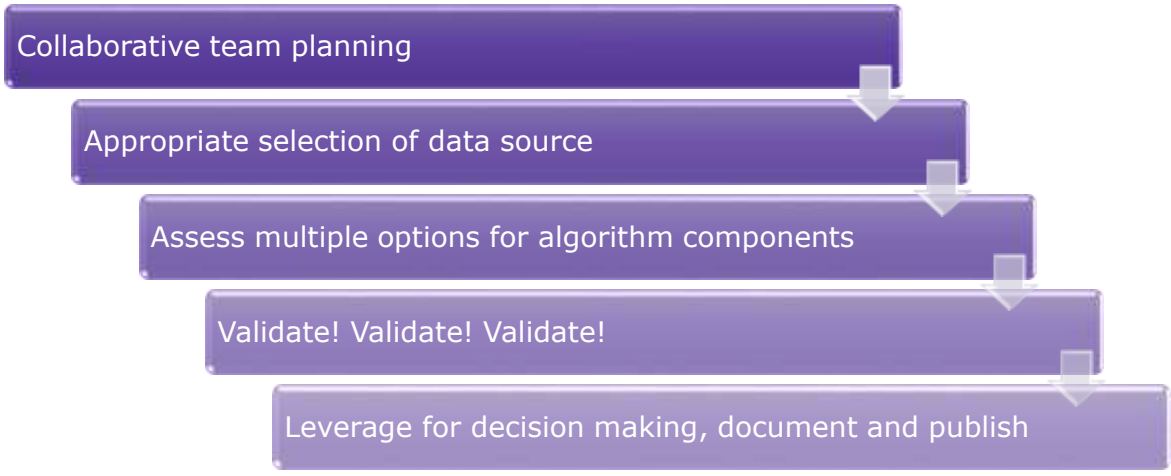
PPV=96.4%
(95% CI: 90.5-98.8%)

PPV=94.9%
(95% CI: 89.6-97.7%)

Audience Participation

- What is your perspective on algorithm validation as represented in the literature?
  - Quality of the evidence?
  - Quality of the described methods?
- Experience with algorithm validation
  - Methods used
  - Challenges encountered
  - Lessons learned
  - Impact
- Any experience using NLP or another advanced methodology?
- Other thoughts?

Concluding Power Points for Algorithms



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Questions?

Thank you!

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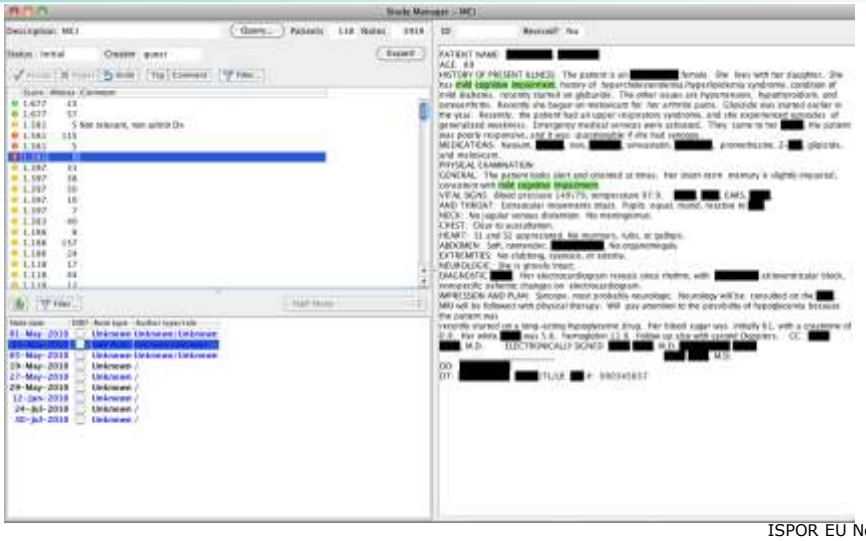
Back-up slides

Claims and EHR clinical note-based algorithms to support Multiple Sclerosis research

Title	Conference	Date
Lessons Learned in Identifying Relapsing-Remitting Multiple Sclerosis (RRMS) in United States Integrated Delivery Network Healthcare Claims and Electronic Health Record (EHR) Data	ISPOR 2017 (Podium Presentation)	May 2017
Preliminary performance of EHR-based algorithm to identify relapsing-remitting multiple sclerosis (RRMS) in United States integrated delivery network electronic health record data	ICPE 2017 (Podium Presentation)	August 2017
Identifying Relapsing-Remitting Multiple Sclerosis (RRMS) in United States Integrated Delivery Network Healthcare Claims Data	ICPE 2017 (Poster)	August 2017
Creating a Claims-Based Adaptation of Kurtzke Functional Systems Scores for MS Severity/Progression	ECTRIMS/ACTRIMS (ePoster)	October 2017
Using algorithms to identify High Disease Activity Relapse-Remitting Multiple Sclerosis patients using electronic health record data with natural language processing	ECTRIMS/ACTRIMS (Poster)	October 2017
Lessons Learned Using United States Integrated Delivery Network (IDN) Claims-Based Algorithms to identify relapses in Relapse-Remitting Multiple Sclerosis (RRMS) Patients	ECTRIMS/ACTRIMS (Poster)	October 2017
Identifying Relapses in Relapsing-Remitting Multiple Sclerosis Patients in United States Integrated Delivery Network Healthcare Electronic Health Record Data	ECTRIMS/ACTRIMS (Poster)	October 2017
Considerations in the use of EHR- and Claims-based Algorithms to Identify RRMS and Relapse in an US IDN database	AMIA (Podium Presentation)	November 2017

NLP Example: Mild Cognitive Impairment



NLP Example: Prostate Cancer