ISPOR 2026 · Pennsylvania Convention Center, Philadelphia · May 18–20, 2026

Shifting the Curve: Valuing Healthcare Utilization across Preclinical and Symptomatic Alzheimer's Disease

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SUPPLEMENTAL MATERIALS · Poster EE454

Content

About SiteRx

SiteRx operates a longitudinal, community-based de-identified EHR data platform spanning primary care and neurology practices across 4,000+ providers in 36 states. Unlike claims databases or academic medical center cohorts, the SiteRx network captures the full spectrum of community-based outpatient care -- the setting where preclinical AD signals first surface in routine clinical language, years before a formal diagnosis. The platform is purpose-built for real-world evidence generation: de-identified, longitudinally linked records with rich clinical note content, enabling NLP-based phenotyping at a scale and care-setting diversity that structured data sources cannot replicate.

SiteRx's core services include NLP-enabled cohort identification, multi-site clinical study design and recruitment support, and health economics and outcomes research (HEOR) partnerships with life science sponsors, payers, and biomarker platforms. This analysis represents SiteRx's applied research capability: converting network-scale EHR data into actionable economic evidence for real-world treatment decisions.

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Extended Methods

NLP Pipeline Design

The classifier is a 7-bucket regex system with 93 curated patterns applied to de-identified clinical notes via Apache OpenSearch. Buckets map to distinct symptom domains associated with the SCI stage of Alzheimer's disease:

Memory complaints: Self-reported forgetfulness, difficulty recalling recent events, subjective memory decline.

Word-finding difficulty: Pauses in speech, tip-of-tongue phenomena, circumlocution noted in clinical language.

Functional changes: Changes in complex instrumental activities attributed by clinician or patient to cognition.

Mood and sleep changes: Anxiety, depression, or sleep disturbance noted in association with cognitive concerns.

Caregiver concern: Family or caregiver-reported observations of behavioral or cognitive change.

Misplacing items: Repetitive misplacement of objects noted as a new or progressive symptom.

New-onset anosmia: Loss of smell flagged as a potential early neurodegenerative marker.

A patient is classified as NLP-positive if any fragment matching the SCI bucket is detected within a 5-year lookback window ending 90 days before the index MCI diagnosis code (ICD-10 G31.84). The 90-day pre-index buffer is designed to exclude notes written in close proximity to diagnosis, where SCI-stage language may reflect imminent MCI rather than true preclinical detection.

Negation and Uncertainty Filtering

The ConText algorithm (Harkema et al. 2009) was applied to all fragment candidates to exclude negated, uncertain, or hypothetical mentions. This step is critical for NLP classifiers operating on clinical notes, which frequently contain language such as "denies memory problems," "no evidence of cognitive decline," or "if patient develops word-finding difficulty" — all of which would generate false positives without contextual filtering. Post-ConText sensitivity reflects the classifier's real-world deployable performance rather than raw pattern match rates.

Cohort Construction

Cases: 79,863 patients with ≥1 ICD-10 G31.84 (Mild Cognitive Impairment) code and ≥1 clinical note in the 5-year lookback window. Cohort drawn from the SiteRx EHR network.

Controls: 157,512 patients matched 2:1 on age (±2 years) and biological sex, with no MCI or dementia diagnosis code at any point in the record, drawn from the same provider network.

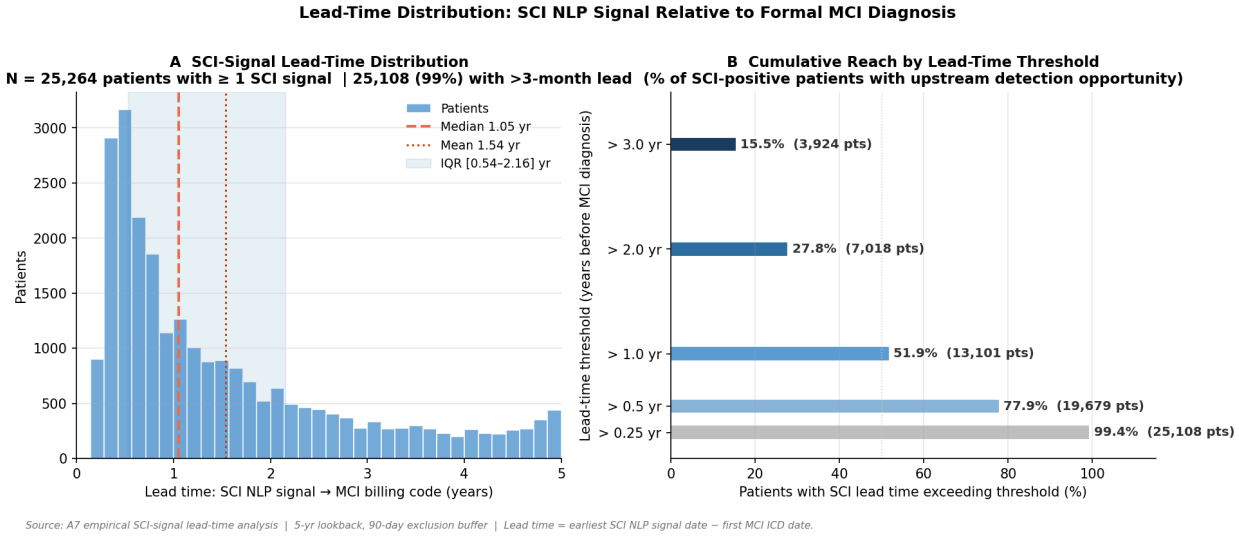
Index date: First occurrence of the MCI diagnosis code in the case record.

Lookback window: 5 years prior to index date, with a 90-day exclusion buffer immediately pre-index.

Bootstrap validation: N=10,000 resamples of the full 237,375-patient cohort; confidence intervals reflect classifier stability across the cohort, not deployment uncertainty.

Supplemental Figures and Table

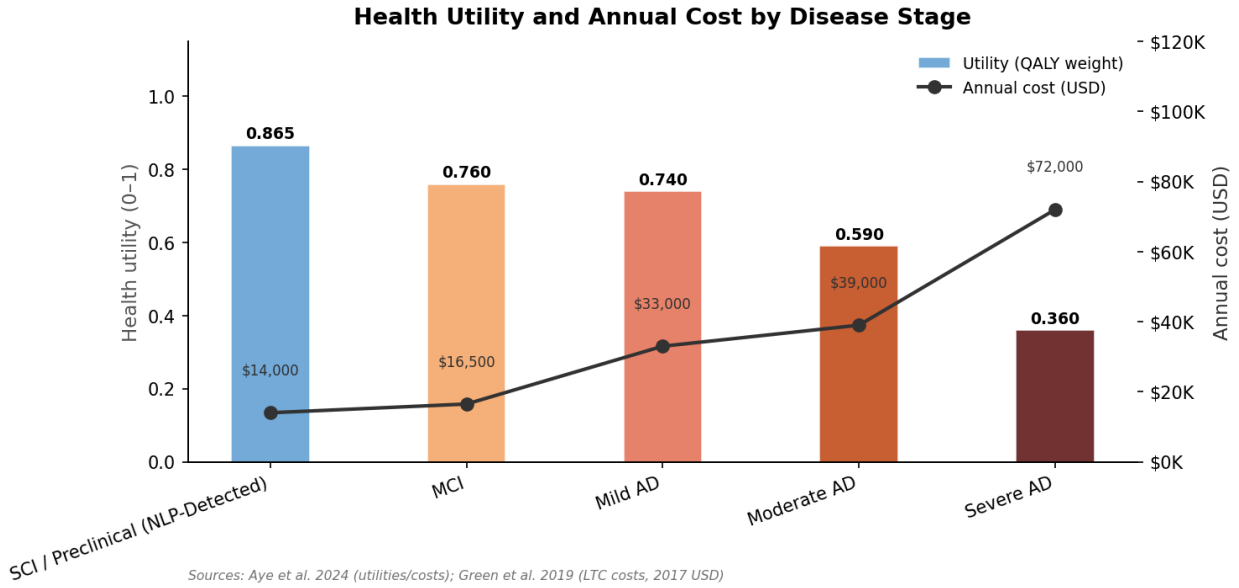
Supplemental Figure 2. Lead-Time Distribution



Source: A7 empirical SCI-signal lead-time analysis | 5-yr lookback, 90-day exclusion buffer | Lead time = earliest SCI NLP signal date − first MCI ICD date.

Supplemental Figure 2. Lead-Time Distribution (N=25,264 detected patients). Days between earliest SCI-bucket fragment and MCI billing code. Median 1.05 yr (384 d); IQR 0.54–2.16 yr. 99.3% of detected patients had signal >90 days prior to diagnosis.

Supplemental Figure 3. Time in State by Scenario



Sources: Aye et al. 2024 (utilities/costs); Green et al. 2019 (LTC costs, 2017 USD)

Supplemental Figure 3. Time in State by Scenario. Stacked bars (years) segmented by health state. NLP+DMT arm shows upstream SCI time (1.05 yr) and compressed late-stage disease relative to both comparators.

Supplemental Table S4. Tornado Summary (Base ICER $262,234/QALY · WTP $150,000/QALY)

Parameter	Low	ICER @Low	High	ICER @High	Range
NLP lead time	0.5 yr	$375K	2.0 yr	$176K	$199K ✓
DMT annual cost	$18,000	$173K	$36,000	$362K	$189K ✓
NLP sensitivity	20%	$336K	55%	$207K	$129K
DMT effectiveness (RR)	0.59	$222K	0.81	$334K	$112K
Discount rate	0%	$232K	5%	$285K	$53K
Downstream compression	6%	$254K	20%	$276K	$22K

✓ Nearest to $150K WTP threshold (does not cross within tested range). ICER = Incremental Cost-Effectiveness Ratio. WTP = Willingness-to-Pay threshold.

SiteRx Research Infrastructure

SiteRx

SiteRx Research Infrastructure

LARGEST EMBEDDED NEURO DISTRIBUTION FOR DECENTRALIZED STUDIES

Purpose-built for today's evolving neuroscience landscape

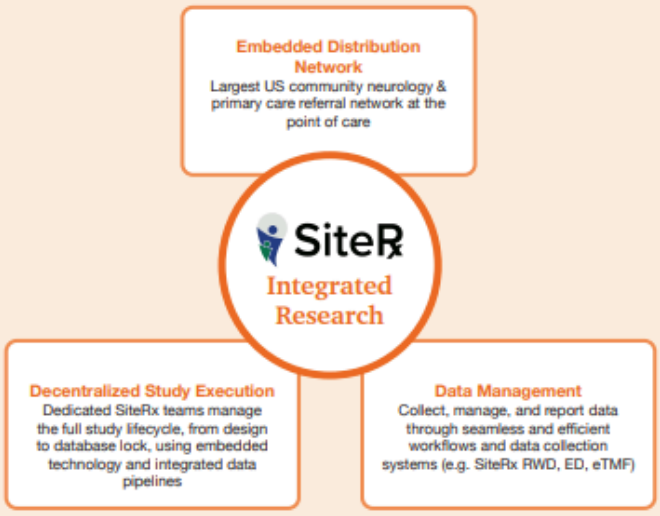
SiteRx Research Infrastructure is designed to meet the demands of modern research by embedding clinical trials directly into real-world care. We activate studies through the largest community-based network of neurologists and primary care providers in the US, powered by a real world database of millions of patients and turnkey end-to-end trial delivery.

Unlocking insights at the point of care

We don't layer research on top of care, we embed and route it into care pathways. SiteRx identifies patients in real time and manages the full trial delivery and lifecycle with speed, consistency, and oversight through a single virtual, decentralized site model.

Answering your emerging questions

SiteRx Research Infrastructure supports decentralized, hybrid and RWE studies with retrospective and prospective designs. This allows our partners to optimize patient access, execution and observation of real world care dynamics to answer critical questions faster and more efficiently.



Virtual Site Model

Single Virtual Site
SiteRx operates a single virtual site with access to SiteRx nationwide RWD, eliminating the need for multiple CTAs, IRBs and vendors.

Streamlined Start-Up & Oversight
Site start-up is immediate with a single site IRB submission, no CTA, and no lengthy budget negotiations. Monitoring is centralized and risk-based, reducing time and complexity.

Fully Managed Execution
SiteRx can manage the entire research cycle from activation to closeout with unified systems and purpose built teams.

Vendor Consolidation & Cost Control
SiteRx can manage the end-to-end trial process, replacing the need for multiple point solutions and up to 70% cost savings.

Our Partners

SiteRx is designed to meet the dynamic needs of the Neuroscience space. We are proud to partner with key stakeholders across the industry looking to answer complex questions quickly and rooted in real-world clinical practice:

- Clinical Operations and Design
- Diagnostics
- Medical Science Liaisons (MSL)
- Health Economics and Outcomes Research (HEOR)
- Human Factors Research
- And more!

ALZHEIMER'S DISEASE - LIFE SCIENCES PARTNER

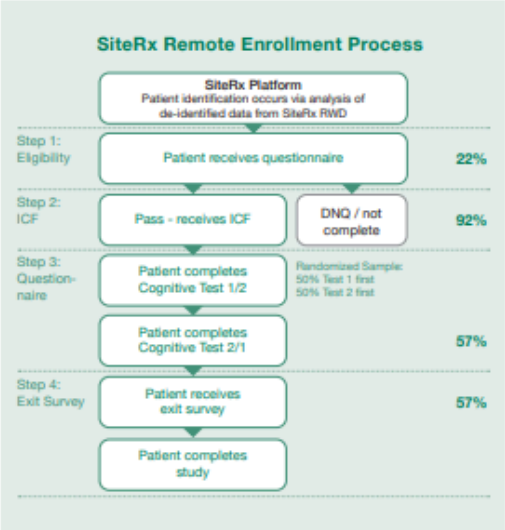
Remote Digital Cognitive Tests
SiteRx fully enrolled Non-Interventional, Remote, Observational Research Candidates

Planning, Implementation and Management
Designed & Implemented all research aspects
- Study materials: protocol & questionnaires
- Trained central PI & research staff
- Configured EDC system
- Managed compliance / data quality

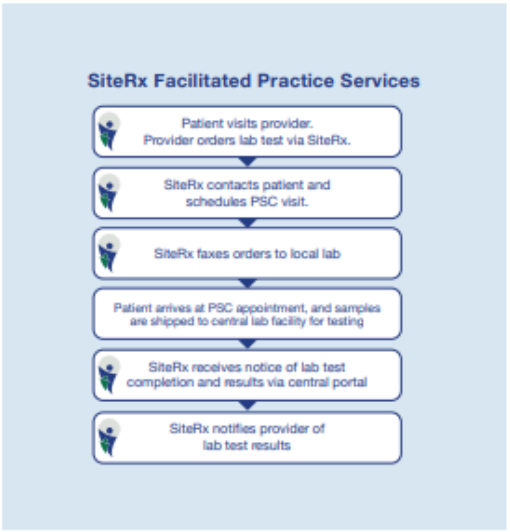
Targeted Outreach & High Qualification Rate
- SiteRx identified potential candidates via pre-defined ICD10 codes & segmented enrollment to meet endpoints
- >90% of identified candidates qualified that completed the questionnaire

Diverse & Representative Enrollment
SiteRx conducted fully remote research that enrolled 60 diverse AD patients & their caregivers

SiteRx can conduct fully decentralized research and capture research data through digital clinical screening tools and health record access.



SiteRx Research Infrastructure



ALZHEIMER'S DISEASE - DIAGNOSTICS PARTNER

Blood Based Biomarkers
SiteRx and 3rd party lab vendor stocked BBBM kits at local Patient Service Centers.

Aligned Labs Dispersion & SiteRx RWD
SiteRx and the third-party BBBM vendor aligned on 10 geographies to stock BBBM kits. After testing, samples were sent to the vendor's central lab, and results were returned to SiteRx through a central portal. SiteRx then shared the results with the ordering provider.

Simplified Workflow for SiteRx Practices
SiteRx designed 3 sets of materials to offer BBBM to practices that allowed for:
- **Authorization for Testing** - shared 3rd party vendor white papers & authorization form to allow for identification of candidates for testing
- **Requisition Form** - SiteRx facilitated individual forms per patient for testing at facilities
- **Lab Form** - SiteRx eFaxed completed forms to local labs to allow for blood draw and receipt of results

High Rate of Positive Tests
Through targeted identification, **SiteRx helped practices identify over 70% of MCI / Early AD patients that presented positive** on AD BBBM tests performed at local facilities.

Through SiteRx's national provider network, SiteRx can coordinate decentralized research activities as part of providers routine care in the community.

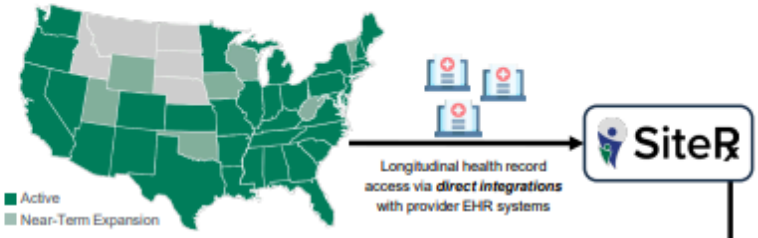
SiteRx RWE

Alzheimer's Real-World Evidence

Via the SiteRx Real-World Data Platform

SiteRx maintains the **largest neurology-focused, real-world database in the U.S.**, with a focus on Alzheimer's disease. We unlock clinical care data directly from patient health records at the provider point of care and transform it into immediately accessible, research-grade evidence that accurately reflects real-world health outcomes across the spectrum of primary through specialized care.

The SiteRx Real-World Data Platform



>9M patients | **>4,000** providers | **38** active states

SiteRx Data is Essential for AD Real-World Evidence

The SiteRx Data Difference	Dimension	Claims Data
Direct EHR integrations with full clinical documentation	**Source of Truth**	Generated **only** for billing
Comprehensive Data: ICDs, meds, labs, imaging, biomarkers, cognitive scores, notes	**Depth of Insight**	**Codes only:** diagnoses + procedures
Encounter-level detail + clinician narratives	**Granularity**	**Claim-line structured fields only**
Real-time access from provider EHRs	**Timeliness**	**30–90 day lag**
Longitudinal view across all encounters within the network	**Continuity**	**Fragmented** by payer or provider
Shows the "how" and "why" behind decisions	**Context**	Shows **only the "what"** happened
Rich phenotyping (symptoms, severity, comorbidities)	**Clinical Completeness**	**Missing** labs, vitals, imaging, notes
Maps comprehensive patient journeys and care pathways	**Pathway Insight**	Cannot reconstruct clinical pathways
Supports advanced modeling using labs, notes, biomarkers	**Analytic Power**	Limited to **utilization + cost** patterns

How SiteRx Structures AD Diagnostics Data

Providing Full Visibility into Emerging Diagnostics Use in the Real-World Setting

Test Type	Lab Name	Result Value
Biomarker Type	Assay Name	Diagnosis Outcome

1. Unstructured Data: Health Record Text
Clinical notes via EHR detailing diagnostics

2. EHR Text Processing: Parsing and Linking
Semantic parsing to identify, extract, and link key text

3. Structured Data: Normalizing and Filling
Structured data tables across data elements

Our Approach

SiteRx was built to reflect the real-world needs of treating physicians, sponsors & investigators. SiteRx CMO Dr. Ira Goodman brings decades of experience as a practicing neurologist and principal investigator, shaping the approach through firsthand experience.

SiteRx is transforming real-world evidence generation in Alzheimer's Disease by unlocking the full depth of clinical data directly through the community provider point of care. Through the largest neurology-focused provider network in the U.S., SiteRx's RWD platform provides real-time access to longitudinal, encounter-level patient records across diverse community settings.

The SiteRx RWD platform is uniquely enabled by four core elements:

1. **Real-Time Access** to longitudinal, encounter-level data primary-sourced through direct integrations with provider EHR systems.
2. **Clinical Data Intelligence** via AI-enabled data harmonization and clinician-validated curation across all structured and unstructured data domains within each record.
3. **Patient Journey Intelligence** via longitudinal visibility- both retrospective and prospective- across all care events spanning the patient's full health history.
4. **Analysis and Research-Ready** datasets via harmonized datasets that are purpose-built to accelerate decision-making and real-world impact through evidence generation.

For more information:
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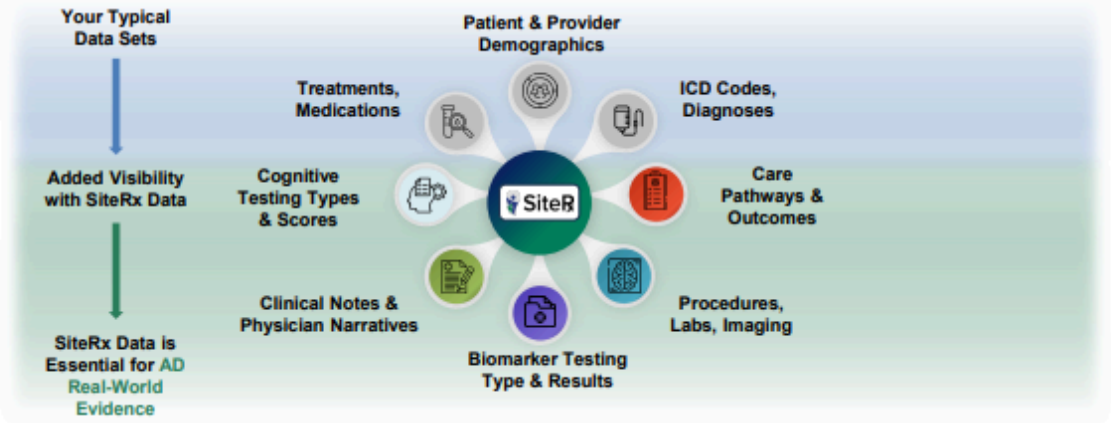
SiteRx Real-World Data:
The Complete Clinical View of the Alzheimer's Disease Patient Journey



SiteRx Real-World Alzheimer's Disease Data
Purpose-Built to Advance Research and Health Outcomes

Example Use-Cases / Key Areas of SiteRx Support:

Real-World Diagnostic and Treatment Pathways
Map how patients move from first cognitive concerns to confirmed AD, revealing real-world delays, referral patterns, and variation in testing across primary and specialty care.

Biomarker Adoption and Testing Behaviors
Understand real-world use of amyloid PET, CSF, and blood-based biomarkers- where testing occurs, why it's ordered, and the drivers vs. barriers shaping provider/patient adoption and outcomes.

Real-World Utilization of Amyloid-Targeting Therapies (ATT)
Evaluate how and why patients advance toward ATT initiation, including real-world access barriers, persistence vs. discontinuation, and clinician decision-making.

Treatment Safety Monitoring and Care Management
Assess how providers monitor safety, manage adverse events, and adjust therapy in everyday practice across emerging AD diagnostics and therapeutics.

Longitudinal Disease Progression and Outcomes
Track multi-year cognitive, functional, imaging, and clinical trajectories to characterize real-world AD progression in diverse, community-treated populations.

Caregiver Burden and Social Determinants of Care
Reveal how caregiver support, socioeconomic factors, and logistical barriers influence screening, diagnosis, treatment adherence, and real-world outcomes.

Symptomatic Treatment Patterns and Behavior
Characterize real-world prescribing patterns - initiation, switching, and discontinuation- across AD supportive therapies and their impact on care management.

Healthcare Utilization and System Burden
Quantify hospital, emergency, imaging, and infusion center use to uncover the operational and resource demands of real-world AD care management across all events.

Disclosures: Dooley J and Gautieri D are employees of SiteRx. No external funding declared. This document is intended as supplemental conference material for ISPOR 2026 poster EE454.