Tables & Figures

High-quality figures for download available by request or via Sharepoint and GitHub (https://github.com/xialab2016/BCD_NTZ_SemiSupervisedCausal).

Main

Figure 1 - Study Design

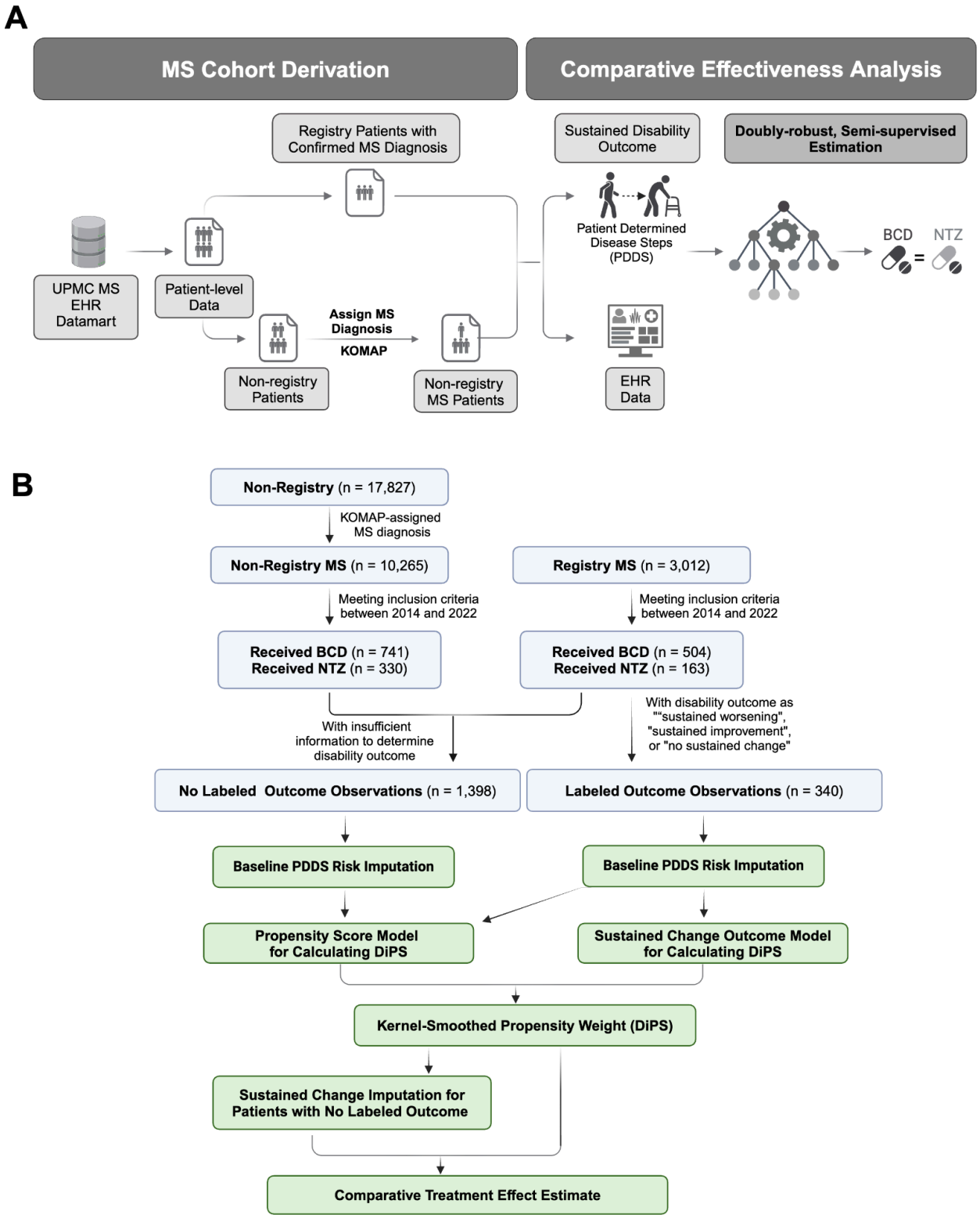


Figure 1. Study design. (A) Schematic overview. (B) Flowchart of cohort derivation steps (boxes with blue outline) and the modeling steps in the causal analysis (green boxes). The “Non-Registry - MS” panel represents patients with a KOMAP algorithm-phenotyped MS diagnosis who were not enrolled in the clinic-based MS registry. The “Registry - MS” panel represents patients with neurologist-confirmed MS diagnosis who were enrolled in the clinic-based MS registry (with linked EHR data). Sample sizes for the “Received” DMT categories correspond to patients with a first record of BCD or NTZ between January 1, 2014 and December 31, 2022. See Methods for details on the cohort derivation. “Labeled outcome observations” correspond to patients with “sustained worsening”, “sustained improvement”, or “no sustained change” in PDDS score, while “no labeled outcome observations” correspond to patients with “insufficient information” for assessing sustained changes.

Abbreviations: BCD, B-Cell Depletion therapy. DMT, Disease Modifying Therapy. EHR, Electronic Health Record. NTZ, natalizumab. PDDS, Patient Determined Disease Steps.

Table 1 - Cohort Characteristics

Clinical or Demographic Variable	Overall (n=1,738)	Registry (n=667)	Non-Registry (n=1,071)	P-Value
Age at target treatment initiation, years, mean (SD)	45.98 (13.02)	44.51 (12.77)	46.89 (13.10)	<0.001
Self-reported gender: n (%)				0.678
Men	488 (28.08%)	183 (27.44%)	305 (28.48%)	
Women	1,250 (71.92%)	484 (72.56%)	766 (71.52%)	
Race and ethnicity: n (%)				0.982
White, Non-Hispanic	1,507 (86.71%)	579 (86.81%)	928 (86.65%)	
Other race and ethnic groups	231 (13.29%)	88 (13.19%)	143 (13.35%)	
Disease duration: years, mean (SD)	5.26 (4.77)	5.17 (5.00)	5.31 (4.62)	0.063
Follow-up duration: years, mean (SD)	9.32 (4.99)	9.85 (4.91)	8.98 (5.01)	<0.001
Target treatment class*: n (%)				<0.001
BCD	1,245 (71.63%)	504 (75.56%)	741 (69.19%)	
Ocrelizumab	799 (45.97%)	263 (39.43%)	536 (50.05%)	
Ofatumumab	38 (2.19%)	1 (0.15%)	37 (3.45%)	
Rituximab	408 (23.48%)	240 (35.98%)	168 (15.69%)	
NTZ	493 (28.37%)	163 (24.44%)	330 (30.81%)	
Baseline total healthcare utilization: number of codes and CUIs, mean (SD)	1374.14 (1504.90)	1474.55 (1529.81)	1311.60 (1486.47)	<0.001
Baseline PDDS risk: mean (SD)	2.06 (0.71)	2.07 (0.73)	2.05 (0.70)	0.571
Year-1 PDDS risk: mean (SD)	2.10 (0.91)	2.04 (0.87)	2.13 (0.92)	*0.008*
Post-treatment disability outcome, n (%)				*<0.001*
No sustained change	130 (7.48%)	130 (19.49%)	0 (0.00%)	
Sustained improvement	92 (5.29%)	92 (13.79%)	0 (0.00%)	
Sustained worsening	118 (6.79%)	118 (17.69%)	0 (0.00%)	
No Labeled Outcome	1,398 (80.44%)	327 (49.03%)	1,071 (100.00%)	

Table 1. **Cohort characteristics.**

Note: We presented mean (standard deviation) for continuous variables and count (percentage) presented for categorical variables. Baseline total healthcare utilization was the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS score at the time of target treatment initiation, using independently fitted PDDS imputation models. Year-1 PDDS risk was calculated as the average of observed PDDS scores within 1 year post-treatment initiation for patients with any available PDDS data and otherwise imputed by the same, independent PDDS imputation models using additional covariate information through 1 year post-treatment initiation. P-values were reported from chi-square tests for categorical variables (race-ethnicity, gender, target treatment category, and disability outcome) and Mann-Whitney U-tests for the remaining, continuous variables, comparing Registry and Non-Registry observations. (*) We reported the sample size (and the percentage within the BCD mechanistic class) of each specific BCD DMT agent.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Figure 2 - Cohort Characteristics by Treatment Class and Outcome Category

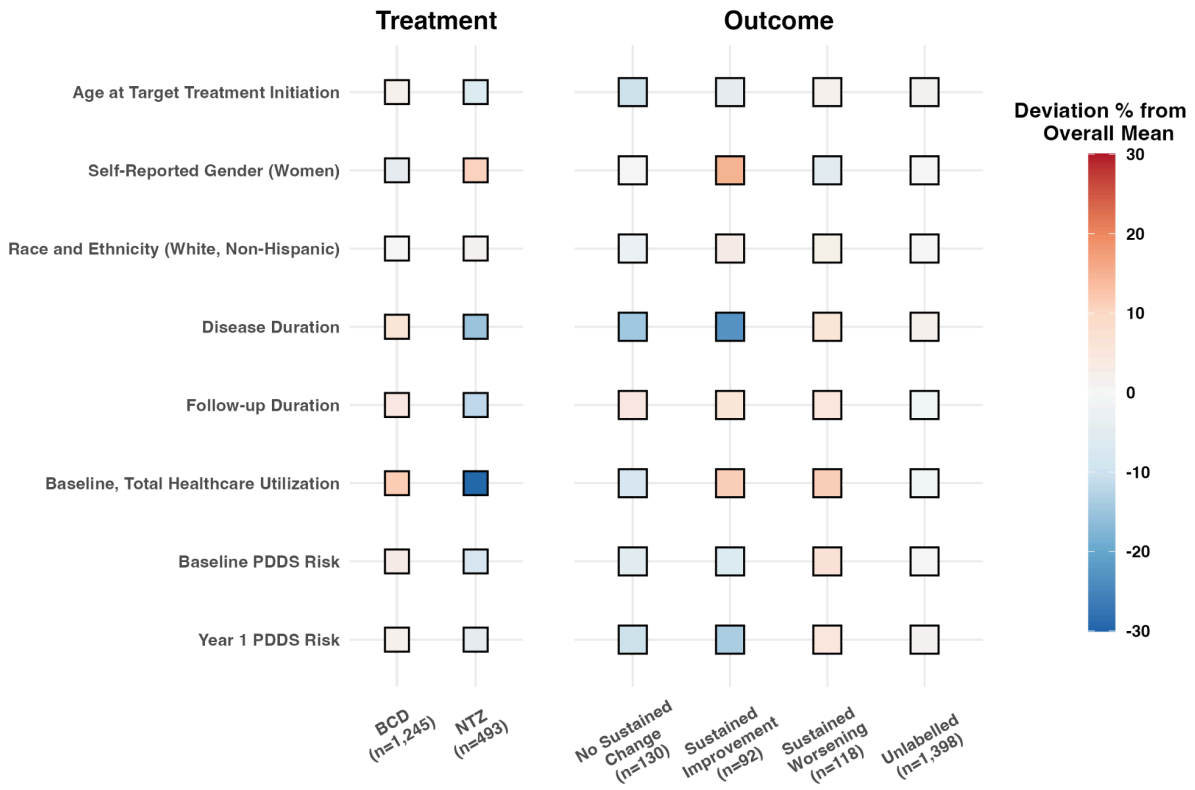


Figure 2. **Cohort characteristics by treatment class and outcome category.**
Each square reports the difference between the column-wise subgroup mean and the overall cohort mean for the variable listed in each row. Red squares indicate values for a sub-group being greater than the overall mean, while blue squares indicate values being less than the overall mean. The left panel summarizes differences across treatment assignments. The right panel summarizes differences across the four sustained change categories. For categorical variables (Women, White, Non-Hispanic race/ethnicity), the mean corresponds to the percentage of the category.
Abbreviations: BCD, B-Cell Depleting drugs. NTZ, Natalizumab. PDDS, Patient Determined Disease Steps.

Table 2 - Treatment Effect Estimates

Outcome	ATE	Std. Err	95% CI	P-Value
Sustained Worsening	-0.020	0.058	(-0.149, 0.076)	0.755
Sustained Improvement	-0.073	0.052	(-0.187, 0.009)	0.114

Table 2. Comparative treatment effect with NTZ as the reference treatment class.
Note: Visualization of the results is presented in **Supplementary Figure 2**.
Abbreviations: ATE, Average Treatment Effect; CI, Confidence Interval. Std. Err, Standard Error.

Figure 3 - Coefficients in Treatment and Outcome Models for DiPS Calculation

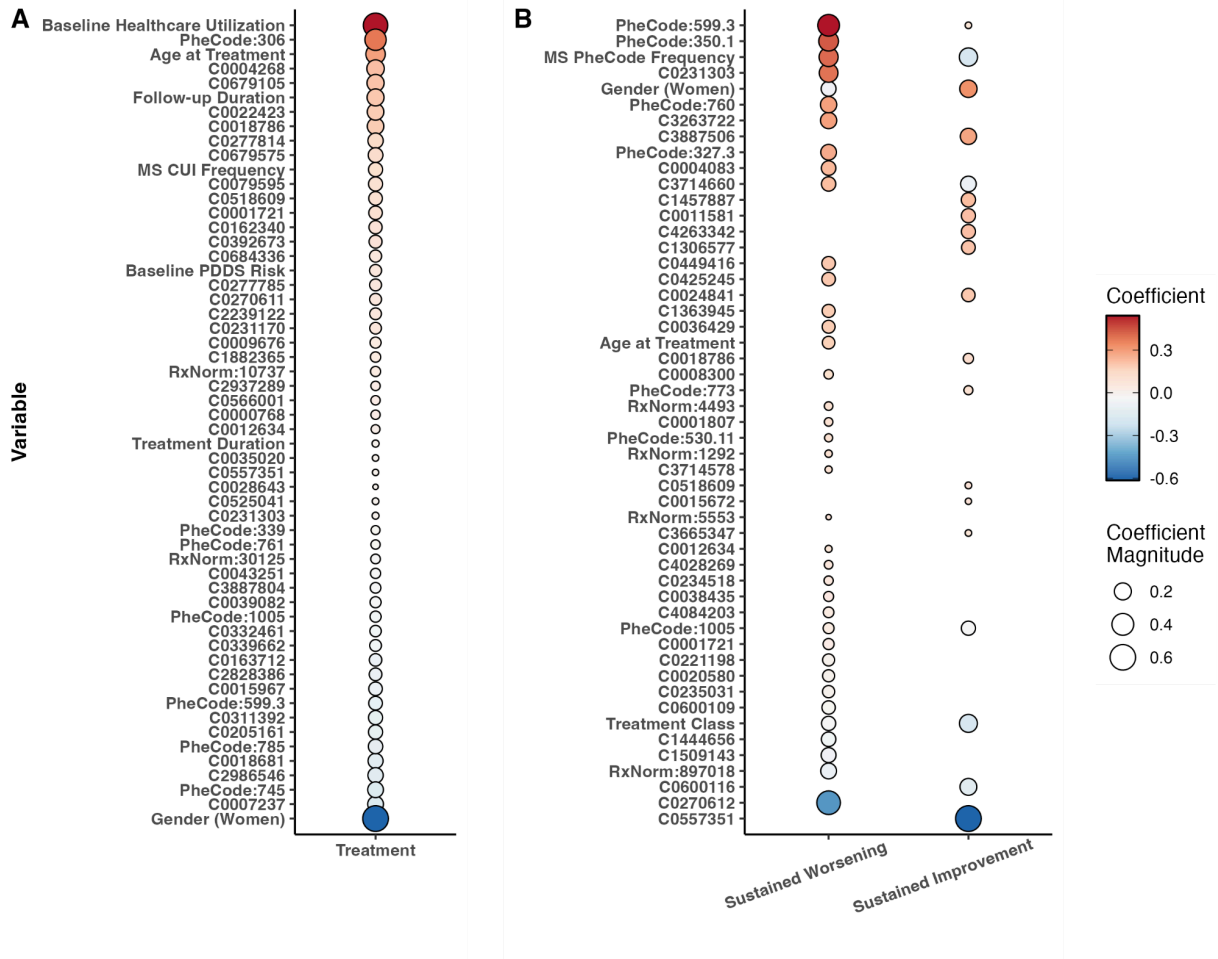
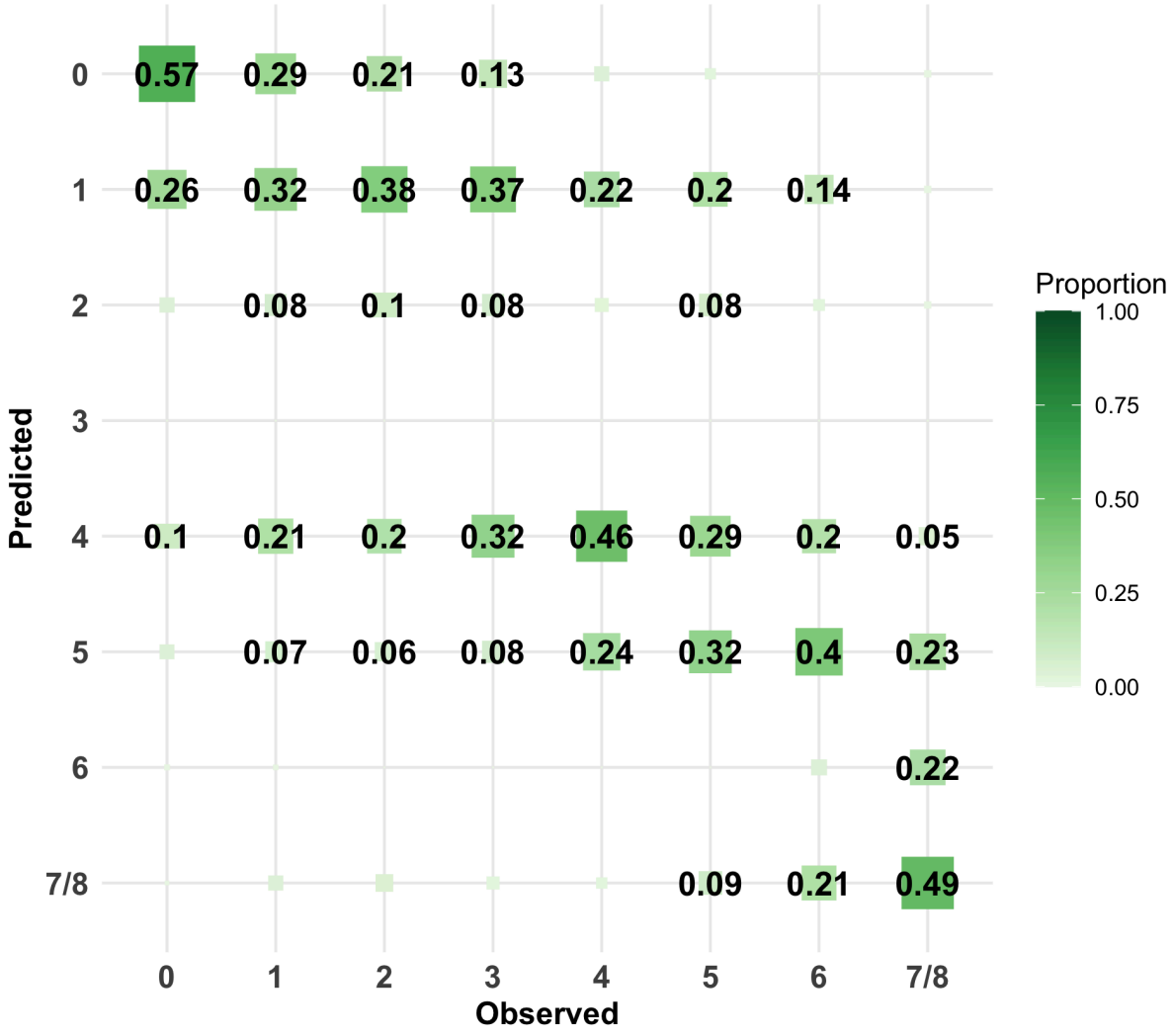


Figure 3. **Coefficients in the treatment and outcome models.**
Coefficients in the initial propensity score model (**A**) and two initial outcome models (**B**) were fitted to inform the kernel-smoothed propensity score estimator. The same treatment model was used for the final causal analysis of each outcome. These models collectively informed the final inverse probability weight that was used to weight/balance for the final ATE calculation, but no balancing/weighting was used to calculate the coefficients shown here. Only variables with non-zero coefficients were shown in each panel. Dot size represents the magnitude of the coefficient, while color corresponds to both effect size and direction. In Panel A, covariates with larger (positive) coefficients are associated with greater probability of receiving BCD than NTZ while the inverse is for smaller coefficients. Detailed descriptions of CUI, PheCode, and RxNorm codes were included in **Supplementary Tables 3a-d**. All covariates were standardized (to mean 0, unit variance) prior to model fitting.
Abbreviations: CUI, Concept Unique Identifier.

Supplement

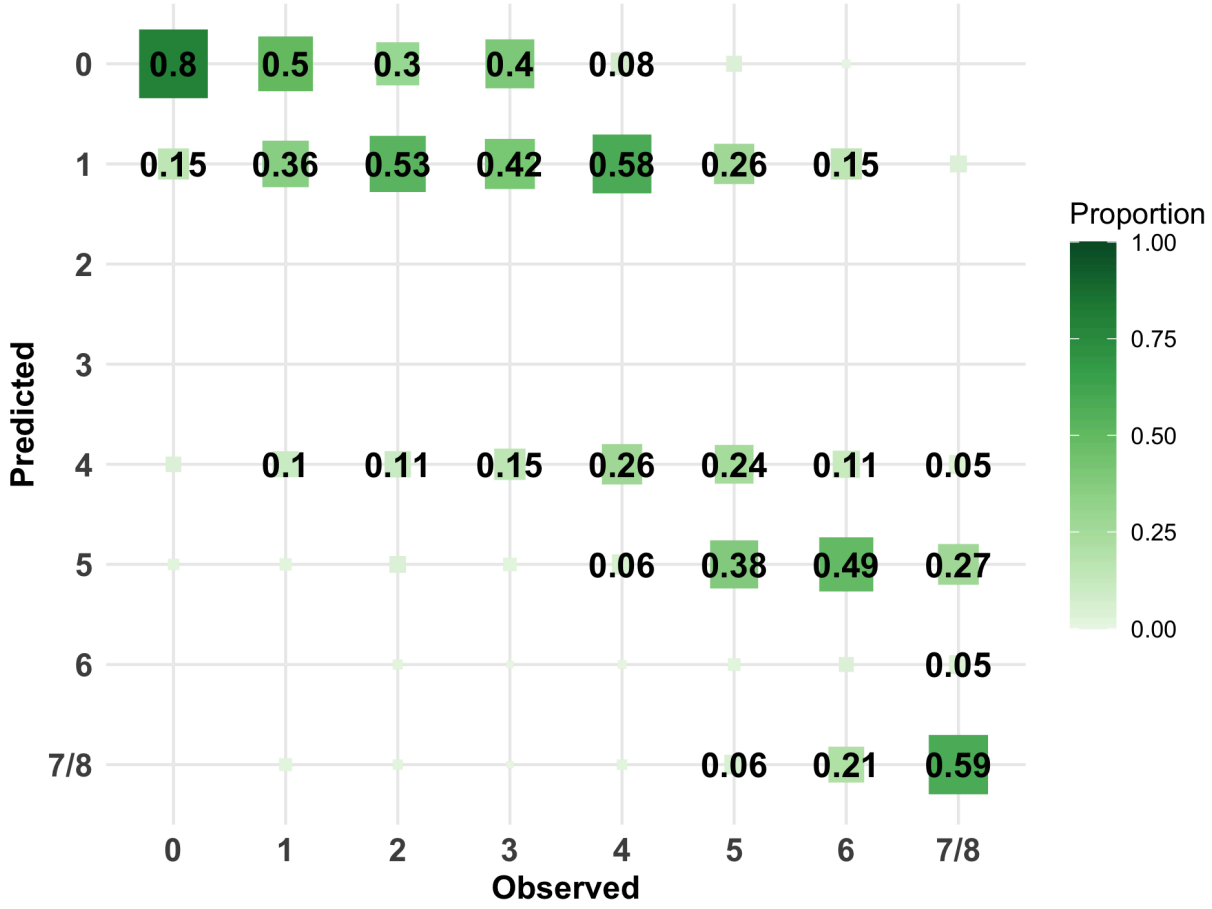
Supplementary Figure 1a. Calibration of a PDDS Imputation Model with an All-Lookback Period and All Available EHR Features



Numbers correspond to the column proportion of observations in each cell. For example, 0.57 in the top left indicates that among all observations where the true PDDS score was 0, we

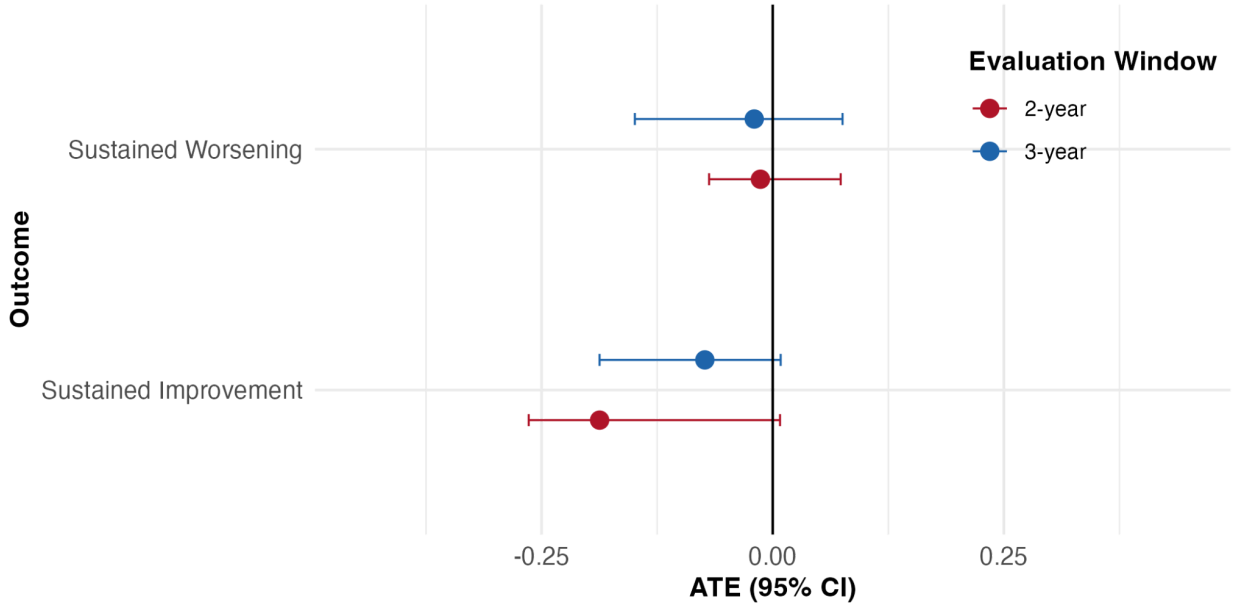
predicted 0 in 0.57 (or 57%) of the observations. Only values >0.05 (5%) reported. A perfect model would demonstrate values of 1 across the top-left to bottom-right diagonal.

Supplementary Figure 1b. Calibration of a PDDS imputation Model with a 12-Month Lookback Period and All Available EHR Features



Numbers correspond to the column proportion of observations in each cell. For example, 0.8 in the top left indicates that among all observations whose true PDDS score was 0, we predicted 0 in 0.8 (or 80%) of observations. Only values >0.05 (5%) reported. A perfect model would demonstrate values of 1 across the top-left to bottom-right diagonal.

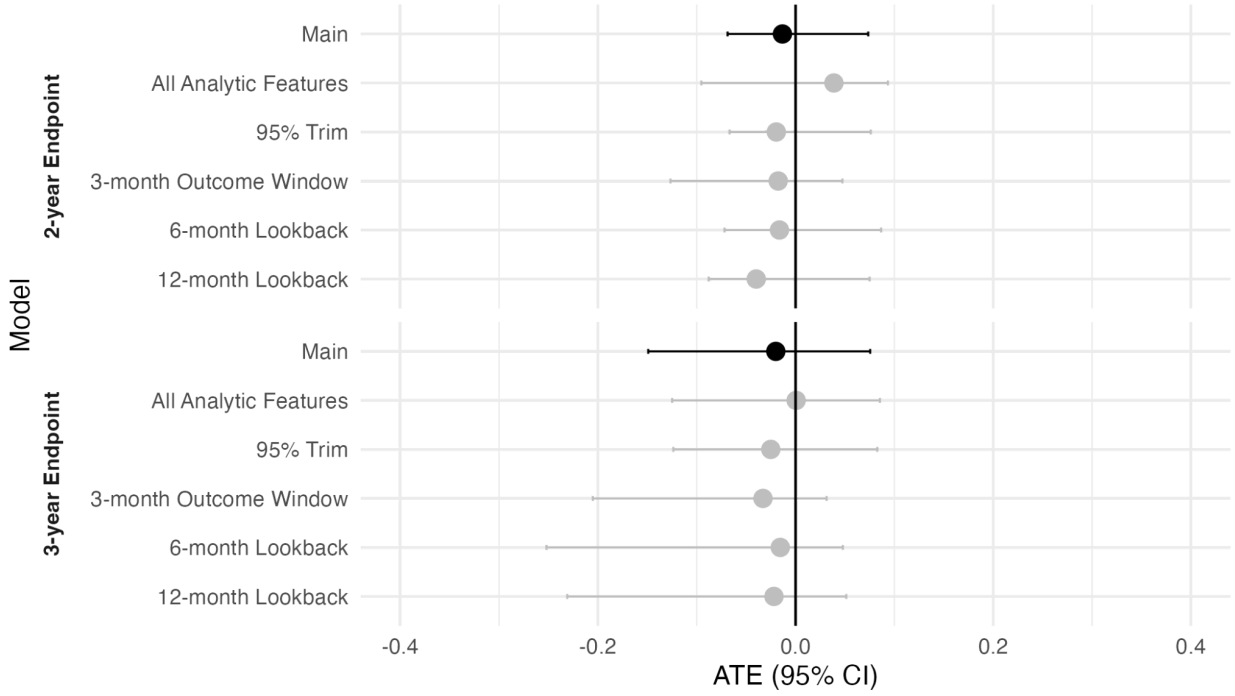
Supplementary Figure 2. Average Treatment Effects for 2- and 3-year Evaluation Windows



Points correspond to estimates of average treatment effect (ATE). Lines correspond to 95% confidence intervals estimated by perturbation analysis. With NTZ as the reference treatment class, a positive ATE for the sustained worsening outcome would indicate BCD as *less* effective than NTZ in reducing patient-reported disability worsening. Conversely, a positive ATE for the sustained improvement outcome would indicate BCD as *more* effective than NTZ in promoting patient-reported disability improvement.

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval.

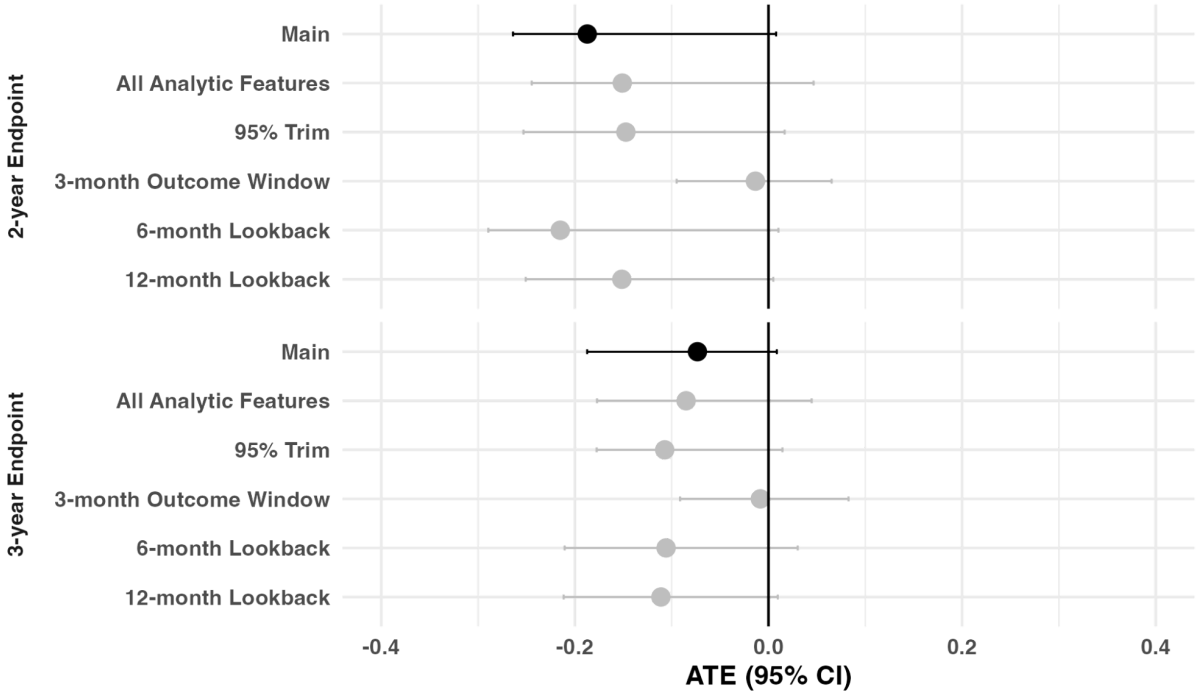
Supplementary Figure 3a. Sensitivity Results for Sustained Worsening Models



Points correspond to estimates of average treatment effect (ATE). Lines correspond to 95% confidence intervals estimated by perturbation analysis. Results are grouped by end point (2- or 3-years after treatment initiation). Each row corresponds to the result of a respective sensitivity analysis for the sustained worsening outcome. With NTZ as the reference treatment class, a positive ATE for the sustained worsening outcome would indicate BCD as *less* effective than NTZ in reducing patient-reported disability worsening.

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval.

Supplementary Figure 3b. Sensitivity Results for Sustained Improvement Models



Points correspond to estimates of average treatment effect (ATE). Lines correspond to 95% confidence intervals estimated by perturbation analysis. Results are grouped by end point (2- or 3-years after treatment initiation). Each row corresponds to the result of a respective sensitivity analysis for the sustained improvement outcome. A positive ATE for the sustained improvement outcome would indicate BCD as *more* effective than NTZ in promoting patient-reported disability improvement.

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval.

Supplementary Table 1a. Cohort derivation for All-Lookback Cohorts in PDDS Imputation Modeling

Step	Patients (N)	PDDS Observations (n)
(0) Observations of any PDDS Score	1,985	17,626
(1) PDDS Scores Occurring 1+ Months Apart	1,985	14,294
(2) Patients with Complete Demographic and Clinical Covariates	1,680	13,258
(4) Observations Unused in Causal Analysis to Categorize Post-treatment Sustained-Change Outcome	1,596	10,658

Supplementary Table 1b. Cohort Derivation for 12-month Lookback Cohorts in PDDS Imputation Modeling

Step	Patients (N)	PDDS Observations (n)
(0) Observations of any PDDS Score	1,985	17,626
(1) PDDS Scores Occurring 1+ Months Apart	1,985	14,294
(2) Patients with Complete Demographic & Clinical Covariates	1,676	13,164
(4) Observations Unused in Causal Analysis to Categorize Post-treatment Sustained-Change Outcome	1,592	10,572

Supplementary Table 1c. Cohort Derivation for 6-month Lookback Cohorts in PDDS Imputation Modeling

Step	Patients (N)	PDDS Observations (n)
(0) Observations of any PDDS Score	1,985	17,626
(1) PDDS Scores Occurring 1+ Months Apart	1,985	14,294
(2) Patients with Complete Demographic & Clinical Covariates	1,669	13,027
(4) Observations Unused in Causal Analysis to Categorize Post-treatment Sustained-Change Outcome	1,585	10,456

Supplementary Table 2. Summary of PDDS Imputation Model Performance by Penalty, Covariate Set, and Lookback Window

Lookback	Penalty	Covariates	Used in Causal Analysis	Concordance (PDDS Category)	Concordance (Mean PDDS)
Inf months	**ridge**	**All Available Features**	**Yes**	**0.783**	**0.807**
12 months	ridge	All Available Features	No	0.770	0.804
Inf months	ridge	Knowledge Graph Derived	No	0.764	0.803
6 months	ridge	All Available Features	No	0.754	0.800
12 months	ridge	Knowledge Graph Derived	No	0.725	0.799
Inf months	lasso	Knowledge Graph Derived	No	0.768	0.799
12 months	lasso	Knowledge Graph Derived	No	0.763	0.798
12 months	lasso	All Available Features	No	0.758	0.789
6 months	lasso	All Available Features	No	0.764	0.786
6 months	ridge	Knowledge Graph Derived	No	0.717	0.782
Inf months	lasso	All Available Features	No	0.767	0.781
6 months	lasso	Knowledge Graph Derived	No	0.744	0.778

“All available features” correspond to inclusion of any available EHR feature (PheCode, CCS, RxNorm, LOINC) observed in at least 10% of patients (and included after applying the PheCode roll-up procedure). Concordance was calculated using the predicted PDDS risk, assigned as the PDDS category with highest probability of membership. Categories 7 & 8 (represented highest level of disability) were combined due to sparsity of membership in category 8 (<1% of observations).

Supplementary Table 3a. Knowledge Graph-Derived, Codified EHR Features Related to Multiple Sclerosis

Variable	Description
RXNORM:897018	dalfampridine
PheCode:596.5	functional disorders of bladder
PheCode:341	other demyelinating diseases of central nervous system
RXNORM:30125	modafinil
PheCode:296	mood disorders
PheCode:300	anxiety disorders
RXNORM:1292	baclofen
PheCode:296.2	depression
PheCode:377.3	optic neuritis/neuropathy
PheCode:334	degenerative disease of the spinal cord
PheCode:350.1	abnormal involuntary movements
PheCode:296.22	major depressive disorder
PheCode:377.1	optic atrophy
PheCode:323.2	acute (transverse) myelitis
PheCode:707.1	decubitus ulcer
PheCode:596	other disorders of bladder
PheCode:709.3	systemic sclerosis
RXNORM:6832	methenamine
PheCode:300.9	posttraumatic stress disorder
PheCode:290.16	vascular dementia
PheCode:300.1	anxiety disorder
PheCode:798	malaise and fatigue

Supplementary Table 3b. Knowledge Graph-Derived, Narrative EHR Features Related to Multiple Sclerosis

CUI	Variable
C0026769	Multiple Sclerosis
C0751967	Multiple Sclerosis, Relapsing-Remitting
C0011304	Demyelination
C0029134	Optic Neuritis
C0011303	Demyelinating Diseases
C0011570	Mental Depression
C0231170	Disability
C0069426	Oligoclonal Bands (protein)
C2752009	White matter lesion
C1579931	Depressed - symptom
C0035020	Relapse
C0026838	Muscle Spasticity
C0011581	Depressive disorder
C0004093	Asthenia
C0682148	Disability status
C0087136	Unmarried
C0423551	Sensory symptoms
C3540014	CENTRAL NERVOUS SYSTEM DIAGNOSTIC RADIOPHARMACEUTICALS
C0163712	Relate - vinyl resin
C0202205	Oligoclonal protein measurement
C0004268	Attention
C0066677	modafinil
C0344315	Depressed mood
C5203119	Intensity and Distress 5
C0010957	Tissue damage
C1558916	Adverse Event Associated with Syndromes
C0878575	Peripheral demyelination
C1457887	Symptoms
C5202921	RECIL PD
C0241224	Spinal cord lesion
C5202991	IMWG Progressive Disease
C0017639	Gliosis
C0015672	Fatigue

C3539781	Progressive cGVHD
C2004461	Bowel dysfunction
C3714552	Weakness
C4551520	Intention tremor
C0338656	Impaired cognition
C1963758	Immunomodulation
C0339662	Afferent Pupillary Defect
C4050309	Central Nervous System Involvement
C0040997	Trigeminal Neuralgia
C0036429	Sclerosis
C0235946	Cerebral atrophy
C0024485	Magnetic Resonance Imaging
C3665386	Abnormal vision
C0237607	Practice Experience
C4723839	irPD (Immune-Related Response Criteria)
C0004609	Baclofen
C5202924	Global Progressive Disease in Skin
C0741548	bladder symptoms
C0037763	Spasm
C0221423	Illness (finding)
C1522240	Process
C0221198	Lesion
C4084203	Improved - answer to question
C3887651	Palsy
C0039082	Syndrome
C0004134	Ataxia
C1561270	Adverse Event Associated with Neurology
C0436596	On examination - apathetic
C1299586	Has difficulty doing (qualifier value)
C0043143	wheelchair
C0443306	Spastic
C0027627	Neoplasm Metastasis
C0025260	Memory
C0525041	Neurobehavioral Manifestations
C4263551	Multisection for pediatrics
C1269683	Major Depressive Disorder
C4721418	Legally Separated
C0232841	Bladder dysfunction

C0012569	Diplopia
C0242656	Disease Progression
C3263723	Traumatic injury
C4042908	Seroconversion
C0042024	Urinary Incontinence
C0849867	Generalized illness
C0004364	Autoimmune Diseases
C2239268	magnets - physical therapy modality
C0013362	Dysarthria
C0002403	Amantadine
C0422943	Visual symptoms
C5202689	HIV Seroconversion
C0021368	Inflammation
C0235146	Euphoric mood
C4551583	Cerebral cortical atrophy
C0003469	Anxiety Disorders
C0037928	Spinal Cord Diseases
C5401372	CTRP Disease Finding
C1291764	Immune System Finding
C0025815	Methylprednisolone
C0007758	Cerebellar Ataxia
C0579152	Bladder problem
C3665346	Unspecified visual loss
C0012634	Disease
C0018681	Headache
C0041696	Unipolar Depression
C3539106	Sufficiently defined concept definition status (core metadata concept)
C0700327	Memory observations
C0684336	Impaired health
C0234518	Slurred speech
C0004083	Mental association
C0005956	Bone Marrow Diseases
C0271051	Macular retinal edema
C0036454	Scotoma
C0086045	Mental concentration
C0025611	Methamphetamine
C1556682	Adverse Event Associated with Infection
C1363945	Therapy Object (animal model)

C0596545	Experience
C0270612	Leukoencephalopathy
C3263722	Traumatic AND/OR non-traumatic injury
C0003537	Aphasia
C0525045	Mood Disorders
C0042571	Vertigo
C0019202	Hepatolenticular Degeneration
C0231217	Multiple symptoms
C0544452	Disease remission
C0038435	Stress
C0439044	Living Alone
C0028643	Numbness
C0003467	Anxiety
C0235031	Neurologic Symptoms
C0009450	Communicable Diseases
C0036572	Seizures
C0332461	Plaque (lesion)
C0009024	Clonus
C0022423	Judgment
C3839460	Nonprogressive
C0549622	Sexual Dysfunction
C5142828	Full recovery
C0040822	Tremor
C0543488	Interested
C0085633	Mood swings
C0021345	Infectious Mononucleosis
C0030554	Paresthesia
C0000768	Congenital Abnormality
C0004368	Autoimmune state
C0679575	Neuroimaging
C4028269	Nuclear magnetic resonance imaging brain
C1306577	Death (finding)
C1509143	Physical assessment findings
C0005525	Biological Response Modifiers
C0522224	Paralysed
C2936842	Vitamin D [EPC]
C1964257	Observation - diagnostic procedure
C0687702	Cancer Remission

C1838681	Rapidly progressive
C0014544	Epilepsy
C0020580	Hypesthesia
C0860603	Anxiety symptoms
C0027404	Narcolepsy
C0079595	Imaging Techniques
C0456909	Blindness
C3887506	Hyperkinesia
C0558058	Reflecting
C0229992	Psyche structure
C0013781	Shock from electric current
C0015967	Fever
C4551761	Excessive daytime sleepiness
C0277785	Functional disorder
C0032989	Multiple Pregnancy
C0005586	Bipolar Disorder
C0008300	Choice Behavior
C0009806	Constipation
C0080274	Urinary Retention
C0919758	Vitamin D measurement
C0233496	Aversion (finding)
C0042866	Vitamin D

Supplementary Table 3c. Knowledge Graph-Derived, Codified EHR Features Related to Disability

Variable	Description
PheCode:296.2	depression
PheCode:296.22	major depressive disorder
PheCode:296	mood disorders
PheCode:300.1	anxiety disorder
PheCode:300	anxiety disorders
CCS:218	psychological and psychiatric evaluation and therapy
PheCode:300.4	dysthymic disorder
PheCode:300.9	posttraumatic stress disorder
PheCode:317.1	alcoholism
PheCode:301	personality disorders
PheCode:297.1	suicidal ideation
PheCode:317	alcohol-related disorders
PheCode:300.11	generalized anxiety disorder
PheCode:316	substance addiction and disorders
PheCode:300.13	phobia
PheCode:304	adjustment reaction
PheCode:295.3	psychosis
PheCode:327.4	insomnia
PheCode:295	schizophrenia and other psychotic disorders
PheCode:300.12	agorophobia, social phobia, and panic disorder
PheCode:315.3	mental retardation
PheCode:969	poisoning by psychotropic agents
PheCode:301.2	antisocial/borderline personality disorder
PheCode:300.8	acute reaction to stress
PheCode:312	conduct disorders
PheCode:338	pain
PheCode:760	back pain
PheCode:313.3	autism
PheCode:318	tobacco use disorder
PheCode:340	migraine
PheCode:295.2	paranoid disorders
PheCode:296.1	bipolar
PheCode:295.1	schizophrenia
PheCode:305.21	anorexia nervosa

PheCode:313.1	attention deficit hyperactivity disorder
PheCode:773	pain in limb
LOINC:3349-8	loinc:amphetamines
LOINC:3397-7	loinc:cocaine
PheCode:303.1	dissociative disorder
PheCode:745	pain in joint
PheCode:327	sleep disorders
CCS:237	ancillary services
PheCode:303.3	psychogenic disorder
LOINC:3879-4	loinc:opiates
LOINC:18282-4	loinc:cannabinoids
PheCode:300.3	obsessive-compulsive disorders
LOINC:3390-2	loinc:benzodiazepines
PheCode:305.2	eating disorder
PheCode:297.2	suicide or self-inflicted injury
PheCode:963	poisoning by primarily systemic agents
PheCode:338.2	chronic pain
PheCode:789	nausea and vomiting
LOINC:14314-9	cocaine, urine (group:urcoca)
LOINC:17384-9	opiates, urine (group:uopi)
PheCode:292.6	hallucinations
PheCode:278.1	obesity
LOINC:16369-1	amphetamine(s), urine (group:uamph)
PheCode:761	cervicalgia
RXNORM:42347	bupropion
PheCode:290.13	senile dementia
PheCode:306	other mental disorder
PheCode:292.3	memory loss
PheCode:530.11	gerd
LOINC:14316-4	benzodiazepines, urine (group:ubenz)
PheCode:306.9	tension headache
PheCode:704.1	alopecia
PheCode:737.2	lordosis (acquired)
LOINC:3773-9	loinc:methadone
PheCode:313	pervasive developmental disorders
PheCode:315.1	learning disorder
PheCode:563	constipation
PheCode:290.1	dementias

PheCode:260.6	anorexia
PheCode:312.3	impulse control disorder
PheCode:303.4	somatoform disorder
LOINC:16254-5	phencyclidine, urine (group:urpcp)
LOINC:14624-1	barbiturates, urine (group:ubarb)
PheCode:704.2	hirsutism
PheCode:599.4	urinary incontinence
LOINC:X7003-7	ethanol (tox panel) (group:tox1)
PheCode:798	malaise and fatigue
PheCode:244	hypothyroidism
PheCode:293	symptoms involving head and neck
PheCode:264	lack of normal physiological development
PheCode:355.1	chronic pain syndrome
LOINC:14313-1	thc/cannabinoids, urine (group:uthc)
PheCode:389.4	tinnitus
PheCode:303	psychogenic and somatoform disorders
LOINC:5643-2	loinc:ethanol
PheCode:327.3	sleep apnea
LOINC:35635-2	trazodone (group:trazo)
PheCode:799	debility unspecified
PheCode:605	erectile dysfunction [ed]
RXNORM:1547099	suvorexant
RXNORM:3554	disulfiram
LOINC:X7011-0	other findings (tox) (group:otfi)
LOINC:3494-2	clonazepam (group:clonaz)
PheCode:339	other headache syndromes
LOINC:10998-3	loinc:oxycodone
PheCode:278.4	abnormal weight gain
PheCode:536.3	gastroparesis
RXNORM:72625	duloxetine
PheCode:389	hearing loss
PheCode:342	hemiplegia
RXNORM:4493	fluoxetine
PheCode:301.1	schizoid personality disorder
PheCode:785	abdominal pain
PheCode:755.4	congenital anomalies of upper limb, including shoulder girdle
PheCode:292.4	altered mental status

RXNORM:5553	hydroxyzine
LOINC:13572-3	nordiazepam (group:ddiaz)
PheCode:1005	other symptoms
LOINC:5644-0	loinc:ethanol
RXNORM:10737	trazodone
PheCode:975	poisoning by agents primarily acting on the smooth and skeletal muscles and respiratory system
PheCode:367.1	myopia
PheCode:625.1	dyspareunia
PheCode:261.1	vitamin a deficiency
PheCode:966	poisoning by anticonvulsants and anti-parkinsonism drugs
PheCode:292.12	symbolic dysfunction
RXNORM:3638	doxepin
LOINC:X7004-5	ats (tox panel) (group:tox2)
PheCode:350.3	lack of coordination
PheCode:599.3	dysuria
PheCode:1010.7	persons with potential health hazards related to socioeconomic, psychosocial, and other circumstances
RXNORM:1455099	vortioxetine
LOINC:X7005-2	barbiturates (tox panel) (group:tox3)
CCS:219	alcohol and drug rehabilitation/detoxification
PheCode:626.2	dysmenorrhea
LOINC:2106-3	loinc:choriogonadotropin (pregnancy test)
PheCode:710.2	periostitis

Supplementary Table 3d. Knowledge Graph-Derived, Narrative EHR Features Related to Disability

CUI	Variable
C0231170	Disability
C3714756	Intellectual Disability
C0684336	Impaired health
C5203119	Intensity and Distress 5
C0008073	Developmental Disabilities
C4084203	Improved - answer to question
C0595998	Household composition
C0751265	Learning Disabilities
C0004936	Mental disorders
C1299586	Has difficulty doing (qualifier value)
C0163712	Relate - vinyl resin
C0229992	Psyche structure
C0596545	Experience
C1509143	Physical assessment findings
C0087136	Unmarried
C0004268	Attention
C0237607	Practice Experience
C0004271	Attitude
C3665347	Visual Impairment
C0004083	Mental association
C0231172	handicapping condition
C0700327	Memory observations
C0025260	Memory
C0543488	Interested
C0221423	Illness (finding)
C0004448	Awareness
C0557351	Employed
C0041674	Unemployment
C0678856	skill
C0011570	Mental Depression
C2239122	Social history of activities
C0023185	Learning
C0162429	Malnutrition
C0597198	Performance

C0025362	Mental Retardation
C0013658	Educational Status
C0455498	History of - psychiatric disorder
C0456909	Blindness
C1306597	Psychiatric problem
C1522240	Process
C1579931	Depressed - symptom
C0030971	Perception
C0476254	Dyslexia
C3263723	Traumatic injury
C0010957	Tissue damage
C0025611	Methamphetamine
C0542559	contextual factors
C0001721	Affect (mental function)
C0424605	Developmental delay (disorder)
C0034991	Rehabilitation therapy
C3495449	Mobility aid
C0043143	wheelchair
C1384666	hearing impairment
C0002957	Anger
C0007237	Encounter due to care involving use of rehabilitation procedures
C0011581	Depressive disorder
C0311392	Physical findings
C1457887	Symptoms
C0018772	Hearing Loss, Partial
C0205082	Severe (severity modifier)
C0004352	Autistic Disorder
C0558058	Reflecting
C0038272	Stereotyping
C5399832	Inclusion Body (finding)
C1550518	incapable
C0007952	Personality Character
C4551887	birth (history)
C1444648	Offered
C1171285	Enabling
C0332218	Difficult (qualifier value)
C0277787	Social stigmata
C0344315	Depressed mood

C0680095	Personal failure
C0033975	Psychotic Disorders
C0441722	Force
C0012634	Disease
C4745084	Medical Condition
C0876926	Traumatic Brain Injury
C0233820	Insight
C5201148	Moderate
C3263722	Traumatic AND/OR non-traumatic injury
C0185117	Expression procedure
C0023186	Academic skill disorder
C1548428	Referral type - Psychiatric
C0184511	Improved
C0349588	Short stature
C0425245	Mobility as a finding
C0557874	Global developmental delay
C0162340	Comprehension
C0557061	Discussion (procedure)
C0600138	Does play
C0026769	Multiple Sclerosis
C0332840	Amputated structure (morphologic abnormality)
C0178499	Base
C0022423	Judgment
C0439044	Living Alone
C0013987	Emotions
C1306577	Death (finding)
C0765629	President brand of dental material
C0424939	Learning difficulties
C2733607	Developmentally disabled (finding)
C1527305	Feelings
C0013146	Drug abuse
C0036341	Schizophrenia
C0013336	Dwarfism
C0011053	Deafness
C3526598	Psychiatric service
C0005586	Bipolar Disorder
C0038436	Post-Traumatic Stress Disorder
C0562342	Empowered

C1559081	Adverse Event Associated with Death
C0522224	Paralysed
C0338656	Impaired cognition
C0000768	Congenital Abnormality
C0001807	Aggressive behavior
C0013080	Down Syndrome
C0848067	Mental problem
C0036597	Self Esteem
C2237041	SHOX gene with short stature
C0036605	Self-Help Devices
C0162425	Intention - mental process
C0009671	Conflict (Psychology)
C3714660	Trauma
C1273518	Responsible to
C5441521	Complaint (finding)
C0024841	Marriage, life event
C0231303	Distress
C2347509	Physical Shift
C3887873	Hearing Loss
C0600116	Does speak
C1263846	Attention deficit hyperactivity disorder
C3539106	Sufficiently defined concept definition status (core metadata concept)
C4759845	CTCAE v4 Grade 2
C0000924	Accidents
C2029884	hearing loss by exam
C1457898	Growth & development aspects
C3844700	Two or more
C0037420	Social Interaction
C0424215	Sense of identity (observable entity)
C0042798	Low Vision
C0683525	treatment options
C0018674	Craniocerebral Trauma
C0018786	Hearing Tests
C0009241	Cognition Disorders
C1269683	Major Depressive Disorder
C1704241	complex (molecular entity)
C0233514	Abnormal behavior
C0566001	Does communicate

C0014544	Epilepsy
C0678341	Responsibility
C5452990	Helped
C2937289	Adapt (substance)
C0459920	Abstract thinking ability
C0424595	Undifferentiated illness
C0003469	Anxiety Disorders
C0392673	Adaptation
C0679199	Strategy
C0425382	Personal status - Adopted
C0041696	Unipolar Depression
C3714578	Fix
C0681405	Preschool Completion
C1821973	Vulnerability
C0237529	Self Confidence
C4316940	Joy
C2220266	exposure history
C0424589	Vitality
C0025353	mental health
C1444656	Indicated
C3275042	Abandoned Lead
C0039082	Syndrome
C2745965	Emergencies [Disease/Finding]
C2242890	History of deprivation
C3540014	CENTRAL NERVOUS SYSTEM DIAGNOSTIC RADIOPHARMACEUTICALS
C0015726	Fear (Mental Process)
C0027627	Neoplasm Metastasis
C3714552	Weakness
C1171947	Commit Lozenge
C0441516	Demand (clinical)
C2242855	personal hygiene (history)
C0013956	Emergency Situation
C0234856	Speaking (activity)
C0740858	Substance abuse problem
C0871633	desire
C5234924	Positive Attitude
C0332447	Morphologically abnormal structure (morphologic abnormality)
C0449416	Source

C0043251	Wounds and Injuries
C0033211	Problem Solving (mental process)
C1458132	Treatment/Psychosocial Effects
C3887651	Palsy
C0525045	Mood Disorders
C0018379	Guilt
C0278061	Abnormal mental state
C0518609	Consideration
C0270611	Brain Injuries
C1559524	Adverse Event Associated with Growth And Development
C0002688	Amputation
C0871215	Reading Disabilities
C0277814	Sitting position
C1821293	Worthlessness
C0020039	Hostility
C0150055	Chronic pain
C0425229	Overcrowded in house
C0521874	Victim of neglect (finding)
C1363945	Therapy Object (animal model)
C0358514	Diagnostic agents
C0039869	Thinking, function
C0013126	Intrinsic drive
C2169640	recently raped (history)
C0022107	Irritable Mood
C0028768	Obsessive-Compulsive Disorder
C0274281	Injury due to exposure to external cause
C1882365	Phenomenon
C3887804	Feeling upset
C2986546	Target Lesion Identification
C0683323	physical illness
C4738113	Fatalities
C0026838	Muscle Spasticity
C0679105	pleasurable emotion
C0037937	Spinal Injuries
C4263342	Multisection metabolic
C0442797	Decreasing
C4760315	Obsessive compulsive disorder drugs
C2828386	Pass (indicator)

C0424318	Bullying
C0038435	Stress
C0282350	Sexual abuse
C0231173	Invalidism
C0003467	Anxiety
C0004930	Behavior Disorders
C0018524	Hallucinations
C0008679	Chronic disease
C0231441	Immobile
C0004044	Asphyxia
C0860603	Anxiety symptoms
C0020580	Hypesthesia
C0035345	Retirement
C0679006	Decision
C5236074	Identified By
C0009676	Confusion
C0205161	Abnormal
C4263551	Multisection for pediatrics
C2700617	Irritation - emotion
C0002658	Amphetamine
C2186378	Reported history of chronic illness
C0600109	Willing
C0231337	Senility
C0497327	Dementia

Supplementary Table 4a. Cohort Characteristics (by 2-Year Evaluation Window)

Variable	No Sustained Change (n=114)	Sustained Improvement (n=44)	Sustained Worsening (n=59)	Unlabeled (n=1521)
Age at Target Treatment Initiation: years, mean (SD)	41.51 (12.16)	42.41 (10.56)	46.36 (13.25)	46.40 (13.07)
Self-Reported Gender: n (%)				
Men	31 (27.19%)	6 (13.64%)	22 (37.29%)	429 (28.21%)
Women	83 (72.81%)	38 (86.36%)	37 (62.71%)	1,092 (71.79%)
Race and ethnicity: n (%)				
White, Non-Hispanic	97 (85.09%)	40 (90.91%)	55 (93.22%)	1,315 (86.46%)
Other race and ethnic groups	17 (14.91%)	4 (9.09%)	4 (6.78%)	206 (13.54%)
Disease Duration: years, mean (SD)	4.23 (5.16)	3.76 (4.46)	5.03 (5.31)	5.39 (4.71)
Follow-up Duration: years, mean (SD)	9.77 (5.13)	10.12 (4.47)	9.60 (4.99)	9.25 (4.99)
Target Treatment Class: n (%)				
BCD	92 (80.70%)	29 (65.91%)	46 (77.97%)	1,078 (70.87%)
NTZ	22 (19.30%)	15 (34.09%)	13 (22.03%)	443 (29.13%)
Baseline Total Healthcare Utilization: number of codes and CUIs, mean (SD)	1403.82 (1572.31)	1584.34 (1280.30)	1548.83 (1315.00)	1359.05 (1512.99)
Baseline PDDS Risk: mean (SD)	1.83 (0.65)	1.83 (0.53)	2.23 (0.81)	2.07 (0.71)
Year 1 PDDS Risk: mean (SD)	1.73 (0.77)	1.64 (0.53)	2.29 (1.05)	2.13 (0.91)

Cohort characteristics with mean (standard deviation) were presented for continuous variables and count (percentage) were presented for categorical variables. Baseline total healthcare utilization corresponds to the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS as time of target treatment initiation, using independently fitted PDDS imputation models. Year 1 PDDS risk was calculated as the average of observed PDDS scores within one year of target treatment initiation for observations with available PDDS data and otherwise imputed by the same, independent PDDS imputation

models using additional covariate information through one-year following target treatment initiation.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Supplementary Table 4b. Cohort Characteristics (by 3-Year Evaluation Window)

Variable	No Sustained Change (n=130)	Sustained Improvement (n=92)	Sustained Worsening (n=118)	Unlabeled (n=1398)
Age at Target Treatment Initiation: years, mean (SD)	41.30 (13.43)	44.04 (11.85)	47.16 (12.61)	46.44 (13.01)
Self-Reported Gender: n (%)				
Men	37 (28.46%)	16 (17.39%)	38 (32.20%)	397 (28.40%)
Women	93 (71.54%)	76 (82.61%)	80 (67.80%)	1,001 (71.60%)
Race and ethnicity: n (%)				
White, Non-Hispanic	110 (84.62%)	82 (89.13%)	105 (88.98%)	1,210 (86.55%)
Other race and ethnic groups	20 (15.38%)	10 (10.87%)	13 (11.02%)	188 (13.45%)
Disease Duration: years, mean (SD)	4.49 (4.91)	4.05 (4.46)	5.58 (5.51)	5.38 (4.69)
Follow-up Duration: years, mean (SD)	9.75 (4.88)	9.85 (4.65)	9.79 (4.82)	9.20 (5.03)
Target Treatment Class: n (%)				
BCD	105 (80.77%)	64 (69.57%)	88 (74.58%)	988 (70.67%)
NTZ	25 (19.23%)	28 (30.43%)	30 (25.42%)	410 (29.33%)
Baseline Total Healthcare Utilization: number of codes and CUIs, mean (SD)	1264.22 (1182.96)	1529.38 (1277.17)	1528.79 (1581.96)	1361.09 (1538.16)
Baseline PDDS Risk: mean (SD)	1.94 (0.74)	1.93 (0.62)	2.19 (0.72)	2.07 (0.71)
Year 1 PDDS Risk: mean (SD)	1.88 (0.95)	1.81 (0.70)	2.21 (0.93)	2.13 (0.91)

Cohort characteristics with mean (standard deviation) were presented for continuous variables and count (percentage) were presented for categorical variables. Baseline total healthcare utilization corresponds to the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS as time of target treatment initiation, using independently fitted PDDS imputation models. Year 1 PDDS risk was calculated as the average of observed PDDS scores within one year of target treatment initiation for observations with available PDDS data and otherwise imputed by the same, independent PDDS imputation

models using additional covariate information through one-year following target treatment initiation.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Supplementary Table 4c. Cohort Characteristics (by Target Treatment Group)

Variable	BCD (n=1245)	NTZ (n=493)
Age at Target Treatment Initiation: years, mean (SD)	47.33 (13.39)	42.56 (11.37)
Self-Reported Gender: n (%)		
Men	394 (31.65%)	94 (19.07%)
Women	851 (68.35%)	399 (80.93%)
Race and ethnicity: n (%)		
White, Non-Hispanic	1,073 (86.18%)	434 (88.03%)
Other race and ethnic groups	172 (13.82%)	59 (11.97%)
Disease Duration: years, mean (SD)	5.62 (4.84)	4.33 (4.43)
Follow-up Duration: years, mean (SD)	9.82 (4.95)	8.05 (4.86)
Baseline Total Healthcare Utilization: number of EHR codes and CUIs, mean (SD)	1561.60 (1606.35)	900.72 (1076.00)
Baseline PDDS Risk: mean (SD)	2.13 (0.72)	1.88 (0.66)
Year 1 PDDS Risk: mean (SD)	2.14 (0.87)	2.00 (0.98)
Post-Treatment Disability Outcome, n (%)		
No Sustained Change	105 (8.43%)	25 (5.07%)
Sustained Improvement	64 (5.14%)	28 (5.68%)
Sustained Worsening	88 (7.07%)	30 (6.09%)
No Labeled Outcome	988 (79.36%)	410 (83.16%)

Cohort characteristics with mean (standard deviation) were presented for continuous variables and count (percentage) were presented for categorical variables. Baseline total healthcare utilization corresponds to the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS as time of target treatment initiation, using independently fitted PDDS imputation models. Year 1 PDDS risk was calculated as the average of observed PDDS scores within one year of target treatment initiation for observations with available PDDS data and otherwise imputed by the same, independent PDDS imputation models using additional covariate information through one-year following target treatment initiation.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Supplementary Table 5a. Cohort Characteristics by Target Treatment Group: Comparing Observed and DiPS-Balanced Statistics (Sustained Improvement Outcome)

Variable	BCD (n=1245)	NTZ (n=493)	P-Value	BCD (n=1245)	NTZ (n=493)	P-Value
	Observed, Unbalanced			Balanced by DiPS (Sustained Improvement-Informed)		
Age at Target Treatment Initiation: years, mean (SD)	47.33 (13.39)	42.56 (11.37)	<0.001	46.03 (13.51)	44.59 (11.84)	0.092
Self-Reported Gender: n (%)						
Men	394 (31.65%)	94 (19.07%)	<0.001	470 (27.85%)	343 (23.22%)	0.028
Women	851 (68.35%)	399 (80.93%)		1,217 (72.15%)	1,133 (76.78%)	
Race and ethnicity: n (%)						
White, Non-Hispanic	1,073 (86.18%)	434 (88.03%)	0.345	1,461 (86.65%)	1,315 (89.12%)	0.118
Other race and ethnic groups	172 (13.82%)	59 (11.97%)		225 (13.35%)	161 (10.88%)	
Disease Duration: years, mean (SD)	5.62 (4.84)	4.33 (4.43)	<0.001	5.19 (4.74)	5.08 (4.68)	0.745
Follow-up Duration: years, mean (SD)	9.82 (4.95)	8.05 (4.86)	<0.001	9.34 (5.09)	9.23 (5.00)	0.601
Baseline Total Healthcare Utilization: number of codes, mean (SD)	1561.60 (1606.35)	900.72 (1076.00)	<0.001	1392.18 (1479.45)	1327.13 (1513.32)	0.054
Baseline PDDS Risk: mean (SD)	2.13 (0.72)	1.88 (0.66)	<0.001	2.06 (0.71)	2.00 (0.68)	0.316

Cohort characteristics with mean (standard deviation) were presented for continuous variables and count (percentage) were presented for categorical variables. P-values for results after balancing were reported from weighted chi-square tests for categorical variables (race-ethnicity and gender) and weighted Mann-Whitney U-tests for the remaining, continuous variables. P-values for observed (*i.e.,* unbalanced) characteristics were calculated using unweighted versions of the same tests. The subset of variables from **Table 1** defined only by pre-target treatment initiation were included. Only the difference in self-reported gender remains statistically significant, but the observed difference between treatment groups was modest (4.6 percentage points) and showed largely improved covariate balance to the observed proportions.

Baseline total healthcare utilization corresponded to the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS as time of target treatment initiation, using independently fitted PDDS imputation models. Year 1 PDDS risk was calculated as the average of observed PDDS scores within one year of target treatment initiation for observations with available PDDS data and otherwise imputed by the same, independent PDDS imputation models using additional covariate information through one-year following target treatment initiation.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Supplementary Table 5b. Cohort Characteristics by Target Treatment Group: Comparing Observed and DiPS-Balanced Statistics (Sustained Worsening Outcome)

Variable	BCD (n=1245)	NTZ (n=493)	P-Value	BCD (n=1245)	NTZ (n=493)	P-Value
	Observed, Unbalanced			Balanced by DiPS (Sustained Worsening-Informed)		
Age at Target Treatment Initiation: years, mean (SD)	47.33 (13.39)	42.56 (11.37)	<0.001	45.93 (13.54)	45.08 (12.49)	0.325
Self-Reported Gender: n (%)			<0.001			
Men	394 (31.65%)	94 (19.07%)		474 (28.05%)	350 (22.59%)	0.009
Women	851 (68.35%)	399 (80.93%)		1,217 (71.95%)	1,198 (77.41%)	
Race and ethnicity: n (%)			0.345			
White, Non-Hispanic	1,073 (86.18%)	434 (88.03%)		1,465 (86.64%)	1,373 (88.67%)	0.198
Other race and ethnic groups	172 (13.82%)	59 (11.97%)		226 (13.36%)	175 (11.33%)	
Disease Duration: years, mean (SD)	5.62 (4.84)	4.33 (4.43)	<0.001	5.18 (4.74)	5.38 (5.02)	0.797
Follow-up Duration: years, mean (SD)	9.82 (4.95)	8.05 (4.86)	<0.001	9.29 (5.11)	9.34 (5.05)	0.970
Baseline Total Healthcare Utilization: number of codes, mean (SD)	1561.60 (1606.35)	900.72 (1076.00)	<0.001	1389.27 (1486.29)	1409.20 (1544.53)	0.345
Baseline PDDS Risk: mean (SD)	2.13 (0.72)	1.88 (0.66)	<0.001	2.06 (0.71)	2.05 (0.71)	0.944

Cohort characteristics with mean (standard deviation) were presented for continuous variables and count (percentage) were presented for categorical variables. P-values were reported from weighted chi-square tests for categorical variables (race-ethnicity and gender) and weighted Mann-Whitney U-tests for the remaining, continuous variables. P-values for observed (i.e. unbalanced) characteristics were calculated using unweighted versions of the same tests. The subset of variables from **Table 1** defined only by pre-target treatment initiation were included. As in **Supplemental Table 5A,** the difference in self-reported gender remained statistically significant, but the observed difference between treatment groups was similarly small (5.5 percentage points) and improved over the unbalanced proportions.

Baseline total healthcare utilization corresponded to the count of all codified EHR features and narrative CUI features observed during distinct clinical encounters occurring prior to target treatment initiation. Baseline PDDS risk was derived as the predicted mean PDDS as time of target treatment initiation, using independently fitted PDDS imputation models. Year 1 PDDS risk was calculated as the average of observed PDDS scores within one year of target treatment initiation for observations with available PDDS data and otherwise imputed by the same, independent PDDS imputation models using additional covariate information through one-year following target treatment initiation.

Abbreviations: BCD, B-cell depletion. PDDS, Patient Determined Disease Steps.

Supplementary Table 6a. Sensitivity Analysis Results for Sustained Worsening Models

Endpoint	Model	ATE	Std. Err	95% CI
2-year	**Main Analysis**	-0.013	0.037	(-0.069, 0.074)
	All Analytic Features	0.039	0.048	(-0.095, 0.093)
	95% Trim	-0.02	0.036	(-0.067, 0.076)
	3-month Sustainment Window	-0.018	0.043	(-0.127, 0.047)
	6-month Lookback	-0.016	0.039	(-0.072, 0.087)
	12-month Lookback	-0.04	0.041	(-0.088, 0.075)
3-year	**Main Analysis**	-0.020	0.058	(-0.149, 0.076)
	All Analytic Features	0.001	0.052	(-0.125, 0.085)
	95% Trim	-0.025	0.049	(-0.124, 0.083)
	3-month Sustainment Window	-0.033	0.060	(-0.205, 0.031)
	6-month Lookback	-0.016	0.078	(-0.252, 0.048)
	12-month Lookback	-0.022	0.073	(-0.231, 0.051)

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval. Std. Err, Standard Error.

Supplementary Table 6b. Sensitivity Analysis Results for Sustained Improvement Models

Endpoint	Sensitivity Model	ATE	Std. Err	95% CI
2-year	**Main**	-0.187	0.072	(-0.264, 0.008)
	All Analytic Features	-0.151	0.076	(-0.245, 0.047)
	95% Trim	-0.147	0.071	(-0.253, 0.017)
	3-month Sustainment Window	-0.014	0.040	(-0.095, 0.065)
	6-month Lookback	-0.215	0.086	(-0.289, 0.01)
	12-month Lookback	-0.152	0.07	(-0.251, 0.005)
3-year	**Main**	-0.073	0.052	(-0.187, 0.009)
	All Analytic Features	-0.085	0.055	(-0.177, 0.045)
	95% Trim	-0.107	0.048	(-0.178, 0.014)
	3-month Sustainment Window	-0.008	0.044	(-0.091, 0.083)
	6-month Lookback	-0.106	0.065	(-0.211, 0.03)
	12-month Lookback	-0.111	0.056	(-0.212, 0.01)

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval. Std. Err, Standard Error.

Supplementary Table 7. Summary of Treatment Effect Estimates

Evaluation Window	Outcome	ATE	Std. Err	95% CI	P-Value
3-years	Sustained Worsening	-0.020	0.058	(-0.149, 0.076)	0.755
	Sustained Improvement	-0.073	0.052	(-0.187, 0.009)	0.114
2-years	Sustained Worsening	-0.013	0.037	(-0.069, 0.074)	0.819
	Sustained Improvement	-0.187	0.072	(-0.264, 0.008)	0.135

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval.

Supplementary Table 8a. Power Analysis of 3-year Evaluation Window Analyses

Outcome	Model	ATE	95% CI	Std. Err	MDE
Sustained Improvement	Labelled Data Only	-0.184	(-0.229, 0.009)	0.060	0.132
	Semi-Supervised (3-month PDDS separation)	-0.008	(-0.091, 0.083)	0.044	0.096
	Semi-Supervised (6-month PDDS separation)	-0.073	(-0.187, 0.009)	0.052	0.114
Sustained Worsening	Labelled Data Only	0.012	(-0.129, 0.079)	0.055	0.122
	Semi-Supervised (3-month PDDS separation)	-0.033	(-0.205, 0.031)	0.060	0.133
	Semi-Supervised (6-month PDDS separation)	-0.02	(-0.149, 0.076)	0.058	0.127

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval. Std. Err, Standard Error. MDE, Minimum Detectable Effect.

Supplementary Table 8b. Power Analysis of 2-year Evaluation Window Analyses

Outcome	Model	ATE	95% CI	Std. Err	MDE
Sustained Improvement	Labelled Data Only	-0.132	(-0.288, -0.010)	0.070	0.157
	Semi-Supervised (3-month PDDS separation)	-0.014	(-0.095, 0.065)	0.040	0.087
	Semi-Supervised (6-month PDDS separation)	-0.187	(-0.264, 0.008)	0.072	0.165
Sustained Worsening	Labelled Data Only	0.027	(-0.099, 0.136)	0.061	0.134
	Semi-Supervised (3-month PDDS separation)	-0.018	(-0.127, 0.047)	0.043	0.089
	Semi-Supervised (6-month PDDS separation)	-0.013	(-0.069, 0.074)	0.037	0.079

Abbreviations: ATE, Average Treatment Effect. CI, Confidence Interval. Std. Err, Standard Error. MDE, Minimum Detectable Effect