**Patient-Level Prediction: *External Validation of Model Predicting Bipolar Misdiagnosed as MDD***

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# List of Abbreviations

| Abbreviation | Phrase |
| --- | --- |
| AUC | Area Under the Receiver Operating Characteristic Curve |
| CDM | Common Data Model |
| O | Outcome Cohort |
| OHDSI | Observational Health Data Sciences & Informatics |
| OMOP | Observational Medical Outcomes Partnership |
| T | Target Cohort |
| TAR | Time at Risk |

# Responsible Parties

Author: Jenna Reps

Investigators: Jenna Reps, Christophe Lambert, [add others]

Reviewers:

# Executive Summary

Patients with bipolar are often misdiagnosed as having major depression disorder (MDD). We have developed a simple score based risk prediction model that can predict the risk that a patient who is newly diagnosed with MDD will be diagnosed with bipolar within 3 years. We now aim to externally validate this model across the OHDSI network.

The objective of this study is to validate a patient-level prediction models for patients in 1 target cohort(s) ([PLP tutorial 2018] first MDD aged 10 or older) to predict 1 outcome(s) ([OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder) for 1 time at risk(s) ([Time at Risk Settings #1] Risk Window Start: 1, Add Exposure Days to Start: FALSE, Risk Window End: 365, Add Exposure Days to End: FALSE).

# Rational & Background

Patients with bipolar are often misdiagnosed as having major depression disorder (MDD). It can take many years before the correct bipolar diagnosis is made. During this misdiagnosis period patients will not be getting correct treatment for their condition. We developed a model that can be implemented when a patient is first diagnosed with MDD to highlight patients who may actually have bipolar. If this model works then it may help patients with bipolar get diagnosed years earlier. The access the performance of our model, we now wish to externally validate it across the OHDSI network.

# Objective

The objective is to validate our simple score patient-level prediction model for the following prediction problems:

| Target Cohorts | Outcome Cohorts | Time at Risk |
| --- | --- | --- |
| [PLP tutorial 2018] first MDD aged 10 or older | [OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder | [Time at Risk Settings #1] Risk Window Start: 1, Add Exposure Days to Start: FALSE, Risk Window End: 365, Add Exposure Days to End: FALSE |

# Methods

## Study Design

This study will follow a retrospective, observational, patient-level prediction design. We define 'retrospective' to mean the study will be conducted using data already collected prior to the start of the study. We define 'observational' to mean there is no intervention or treatment assignment imposed by the study. We define 'patient-level prediction' as a modeling process wherein an outcome is predicted within a time at risk relative to the target cohort start and/or end date. Prediction is performed using a set of covariates derived using data prior to the start of the target cohort.

Figure 1, illustrates the prediction problem we will address. Among a population at risk, we aim to predict which patients at a defined moment in time (t = 0) will experience some outcome during a time-at-risk. Prediction is done using only information about the patients in an observation window prior to that moment in time.

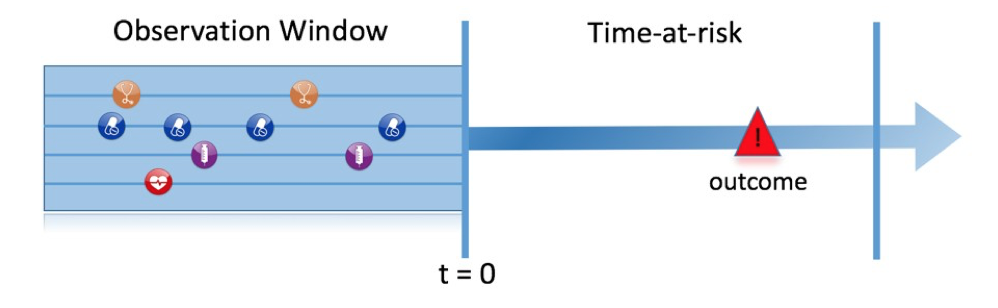


Figure 1: The prediction problem

*Citation:*

We follow the PROGRESS best practice recommendations for model development and the TRIPOD guidance for transparent reporting of the model results.

*Citation: Steyerberg EW, Moons KG, van der Windt DA, Hayden JA, Perel P, Schroter S, Riley RD, Hemingway H, Altman DG; PROGRESS Group. Prognosis Research Strategy (PROGRESS) 3: prognostic model research. PLoS Med. 2013;10(2):e1001381. doi: 10.1371/journal.pmed.1001381. Epub 2013 Feb 5. Review. PubMed PMID: 23393430; PubMed Central PMCID: PMC3564751.*

*Citation: Collins, G., et al. (2017.02.01). 'Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement.' from https://www.equator-network.org/reporting-guidelines/tripod-statement/*

## Data Source(s)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Database Name | Version | Start date | End date | Description |
| CCAE |  |  |  |  |
| MDCD |  |  |  |  |
| Optum claims |  |  |  |  |
| Optum EHR |  |  |  |  |
|  |  |  |  |  |
|  |  |  |  |  |

## Study Populations

### Target Cohort(s) [T]

| Cohort ID | Cohort Name | Description |
| --- | --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older | TBD |

[PLP tutorial 2018] first MDD aged 10 or older

Initial Event Cohort

People having any of the following:

* a condition occurrence of Major depressive disorder3
* for the first time in the person's history
* with age >= 10
* with continuous observation of at least 365 days prior and 0 days after event index date, and limit initial events to: earliest event per person.

Inclusion Rules

Inclusion Criteria #1: no prior major mental health illness

Having all of the following criteria:

exactly 0 occurrences of a condition occurrence of Depressive disorder2

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a condition occurrence of Major mental illness4

where event starts between all days Before and 0 days Before index start date

Inclusion Criteria #2: No prior antidepressants

Having all of the following criteria:

exactly 0 occurrences of a drug exposure of [plp tutorial 2018] antidepressants drug/measurement5

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a measurement of [plp tutorial 2018] antidepressants drug/measurement5

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of an observation of [plp tutorial 2018] antidepressants procedures/observations6

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a procedure of [plp tutorial 2018] antidepressants procedures/observations6

where event starts between all days Before and 1 days Before index start date

Inclusion Criteria #3: no prior antipsychotic use

Having all of the following criteria:

exactly 0 occurrences of a drug exposure of Antipsychotics1

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a drug exposure of [plp tutorial 2018] antipsychotic drug/measurement/observation/procedure7

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a measurement of [plp tutorial 2018] antipsychotic drug/measurement/observation/procedure7

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of a procedure of [plp tutorial 2018] antipsychotic drug/measurement/observation/procedure7

where event starts between all days Before and 1 days Before index start date

and exactly 0 occurrences of an observation of [plp tutorial 2018] antipsychotic drug/measurement/observation/procedure7

where event starts between all days Before and 1 days Before index start date

Inclusion Criteria #4: No prior lithium

Having all of the following criteria:

exactly 0 occurrences of a drug exposure of [plp tutorial 2018] lithium drug/procedure/measurement8

where event starts between all days Before and 0 days Before index start date

and exactly 0 occurrences of a measurement of [plp tutorial 2018] lithium drug/procedure/measurement8

where event starts between all days Before and 0 days Before index start date

and exactly 0 occurrences of a procedure of [plp tutorial 2018] lithium drug/procedure/measurement8

where event starts between all days Before and 0 days Before index start date

Inclusion Criteria #5: No prior mood stabilizer

Having all of the following criteria:

exactly 0 occurrences of a drug era of [plp tutorial 2018] mood stabilizers drug/measurement9

where event starts between all days Before and 0 days Before index start date

and exactly 0 occurrences of a measurement of [plp tutorial 2018] mood stabilizers drug/measurement9

where event starts between all days Before and 0 days Before index start date

Limit qualifying cohort to: earliest event per person.

### Outcome Cohorts(s) [O]

| Cohort ID | Cohort Name | Description |
| --- | --- | --- |
| 7746 | [OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder | TBD |

[OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder

Initial Event Cohort

People having any of the following:

* a condition occurrence of Bipolar disorder1 for the first time in the person's history with continuous observation of at least 0 days prior and 0 days after event index date.

.

### Time at Risk

| Time at Risk |
| --- |
| [Time at Risk Settings #1] Risk Window Start: 1, Add Exposure Days to Start: FALSE, Risk Window End: 365, Add Exposure Days to End: FALSE |

### Additional Population Settings

***Population Settings #1***

| Item | Settings |
| --- | --- |
| minTimeAtRisk | 364 |
| requireTimeAtRisk | TRUE |
| addExposureDaysToStart | FALSE |
| riskWindowStart | 1 |
| washoutPeriod | 365 |
| addExposureDaysToEnd | FALSE |
| includeAllOutcomes | FALSE |
| priorOutcomeLookback | 99999 |
| binary | TRUE |
| removeSubjectsWithPriorOutcome | TRUE |
| riskWindowEnd | 365 |
| firstExposureOnly | TRUE |

## Statistical Analysis Method(s)

### Algorithms

| Algorithm | Description |
| --- | --- |
| Simple Score Model | Each predictor is assigned a number of points and the patients total score is calculated as the sum of the predictor points they have. |

### Model Evaluation

The following evaluations will be performed on the model:

| Evaluation | Description |
| --- | --- |
| Box Plots | The prediction distribution boxplots are box plots for the predicted risks of the people in the test set with the outcome (class 1: blue) and without the outcome (class 0: red). |
| Calibration Plot | The calibration plot shows how close the predicted risk is to the observed risk. The diagonal dashed line thus indicates a perfectly calibrated model. The ten (or fewer) dots represent the mean predicted values for each quantile plotted against the observed fraction of people in that quantile who had the outcome (observed fraction). The straight black line is the linear regression using these 10 plotted quantile mean predicted vs observed fraction points. The two blue straight lines represented the 95% lower and upper confidence intervals of the slope of the fitted line. |
| Demographic Summary Plot | This plot shows for females and males the expected and observed risk in different age groups together with a confidence area. |
| Precision Recall Plot | The precision-recall curve is valuable for dataset with a high imbalance between the size of the positive and negative class. It shows the tradeoff between precision and recall for different threshold. High precision relates to a low false positive rate, and high recall relates to a low false negative rate. High scores for both show that the classifier is returning accurate results (high precision), as well as returning a majority of all positive results (high recall). A high area under the curve represents both high recall and high precision. |
| Prediction Distribution Plots | The preference distribution plots are the preference score distributions corresponding to i) people in the test set with the outcome (red) and ii) people in the test set without the outcome (blue). |
| ROC Plot | The ROC plot plots the sensitivity against 1-specificity on the test set. The plot shows how well the model is able to discriminate between the people with the outcome and those without. The dashed diagonal line is the performance of a model that randomly assigns predictions. The higher the area under the ROC plot the better the discrimination of the model. |
| Smooth Calibration Plot | Similar to the traditional calibration shown above the Smooth Calibration plot shows the relationship between predicted and observed risk. the major difference is that the smooth fit allows for a more fine grained examination of this. Whereas the traditional plot will be heavily influenced by the areas with the highest density of data the smooth plot will provide the same information for this region as well as a more accurate interpretation of areas with lower density. the plot also contains information on the distribution of the outcomes relative to predicted risk. However the increased information game comes at a computational cost. It is recommended to use the traditional plot for examination and then to produce the smooth plot for final versions. |
| Test-Train Similarity Plot | The test-train similarity is presented by plotting the mean covariate values in the train set against those in the test set for people with and without the outcome. |
| Variable Scatter Plot | The variable scatter plot shows the mean covariate value for the people with the outcome against the mean covariate value for the people without the outcome. The size and color of the dots correspond to the importance of the covariates in the trained model (size of beta) and its direction (sign of beta with green meaning positive and red meaning negative), respectively. |

## Quality Control

The PatientLevelPrediction package itself, as well as other OHDSI packages on which PatientLevelPrediction depends, use unit tests for validation.

*Citation:*

## Tools

This study will be designed using OHDSI tools and run with R.

*Citation: R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.*

More information about the tools can be found in the Appendix 'Study Generation Version Information'.

# Diagnostics

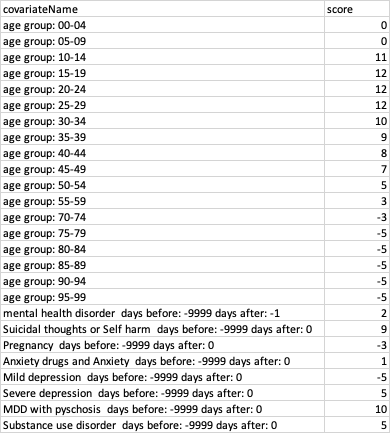
Reviewing the incidence rates of the outcomes in the target population prior to performing the analysis will allow us to assess its feasibility. The full table can be found in the 'Table and Figures' section under 'Incidence Rate of Target & Outcome'.

Additionally, reviewing the characteristics of the cohorts provides insight into the cohorts being reviewed. The full table can be found below in the 'Table and Figures' section under 'Characterization'.

# Data Analysis Plan

## Algorithm Settings

***Model***



## Model Evaluation

We will use the area under the receiver operating characteristic curve (AUC) to evaluate the discriminative performance of the models and plot the predicted risk against the observed fraction to visualize the calibration. See 'Model Evaluation' section for more detailed information about additional model evaluation metrics.

## Analysis Execution Settings

There are 1 target cohorts evaluated for 1 outcomes over 1 models over 1 covariates settings and over 1 population settings. In total there are 1 analysis performed. For a full list refer to appendix 'Complete Analysis List'.

# Strengths & Limitations

* The model is simple to implement
* We are validating the models across a diverse set of patients
* Model validation is possible due to the OHDSI standardizations
* Not all medical events are recorded into the observational datasets and some recordings can be incorrect. This could potentially lead to outcome misclassification.

# Protection of Human Subjects

Confidentiality of patient records will be maintained always. All study reports will contain aggregate data only and will not identify individual patients or physicians. At no time during the study will the sponsor receive patient identifying information except when it is required by regulations in case of reporting adverse events.

# Plans for Disseminating & Communicating Study Results

This work will be submitted to a high impact journal in the field of mental health

# Tables & Figures

## Incidence Rate of Target & Outcome

*<< add incidence here. >>*

## Characterization

*<< add characterization table here. >>*

*<< add results here. >>*

# Appendices

## Study Generation Version Information

Skeleton Version: PatientLevelPredictionStudy - v0.0.1

Identifier / Organization: Janssen Research and Development

## Code List

***Concept Set #1 - Bipolar disorder***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 436665 | 13746004 | Bipolar disorder | Condition | Standard | Clinical Finding | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 7746 | [OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder |

***Concept Set #2 - Major depressive disorder***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 4152280 | 370143000 | Major depressive disorder | Condition | Standard | Clinical Finding | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #3 - Depressive disorder***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 440383 | 35489007 | Depressive disorder | Condition | Standard | Clinical Finding | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #4 - Major mental illness***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 436665 | 13746004 | Bipolar disorder | Condition | Standard | Clinical Finding | V | FALSE | TRUE |
| Valid | 436073 | 69322001 | Psychotic disorder | Condition | Standard | Clinical Finding | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #5 - Antipsychotics***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 21604490 | N05A | ANTIPSYCHOTICS | Drug | Classification | ATC 3rd | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #6 - [plp tutorial 2018] antidepressants drug/measurement***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 710062 | 704 | Amitriptyline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 3017597 | 3333-2 | Amitriptyline [Mass/volume] in Serum or Plasma | Measurement | Standard | Lab Test | V | FALSE | TRUE |
| Valid | 4288159 | 69652002 | Amitriptyline measurement | Measurement | Standard | Procedure | V | FALSE | TRUE |
| Valid | 713109 | 722 | Amoxapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 750982 | 42347 | Bupropion | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 797617 | 2556 | Citalopram | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 798834 | 2597 | Clomipramine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 716968 | 3247 | Desipramine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 3000167 | 3531-1 | Desipramine [Mass/volume] in Serum or Plasma | Measurement | Standard | Lab Test | V | FALSE | TRUE |
| Valid | 4012481 | 113085002 | Desipramine measurement | Measurement | Standard | Procedure | V | FALSE | TRUE |
| Valid | 717607 | 734064 | Desvenlafaxine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 738156 | 3638 | Doxepin | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 3013265 | 3579-0 | Doxepin [Mass/volume] in Serum or Plasma | Measurement | Standard | Lab Test | V | FALSE | TRUE |
| Valid | 4218297 | 72234007 | Doxepin measurement | Measurement | Standard | Procedure | V | FALSE | TRUE |
| Valid | 715259 | 72625 | duloxetine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 715939 | 321988 | Escitalopram | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 755695 | 4493 | Fluoxetine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 751412 | 42355 | Fluvoxamine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 778268 | 5691 | Imipramine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 4022365 | 105213004 | Imipramine measurement | Measurement | Standard | Procedure | V | FALSE | TRUE |
| Valid | 781705 | 6011 | Isocarboxazid | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 43560354 | 1433212 | levomilnacipran | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 794147 | 6646 | Maprotiline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 19080226 | 588250 | milnacipran | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 725131 | 15996 | Mirtazapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 721724 | 7531 | Nortriptyline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 3007857 | 3872-9 | Nortriptyline [Mass/volume] in Serum or Plasma | Measurement | Standard | Lab Test | V | FALSE | TRUE |
| Valid | 722031 | 32937 | Paroxetine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 733896 | 8123 | Phenelzine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 754270 | 8886 | Protriptyline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 766209 | 9639 | Selegiline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 739138 | 36437 | Sertraline | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 703470 | 10734 | Tranylcypromine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 705755 | 10834 | Trimipramine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 743670 | 39786 | venlafaxine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 40234834 | 1086769 | vilazodone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 44507700 | 1455099 | vortioxetine | Drug | Standard | Ingredient | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #7 - [plp tutorial 2018] antidepressants procedures/observations***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 2108573 | 4064F | Antidepressant pharmacotherapy prescribed (MDD, MDD ADOL) | Observation | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257553 | 80338 | Antidepressants, not otherwise specified | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257696 | 80332 | Antidepressants, serotonergic class; 1 or 2 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257552 | 80333 | Antidepressants, serotonergic class; 3-5 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257738 | 80334 | Antidepressants, serotonergic class; 6 or more | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257739 | 80335 | Antidepressants, tricyclic and other cyclicals; 1 or 2 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257410 | 80336 | Antidepressants, tricyclic and other cyclicals; 3-5 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257697 | 80337 | Antidepressants, tricyclic and other cyclicals; 6 or more | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 2617574 | G8129 | Patient documented as being treated with antidepressant medication for at least 6 months continuous treatment phase | Observation | Standard | HCPCS | V | FALSE | TRUE |
| Valid | 44786399 | G9194 | Patient with a diagnosis of major depression documented as being treated with antidepressant medication during the entire 180 day (6 month) continuation treatment phase | Observation | Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2617571 | G8126 | Patient with a diagnosis of major depression documented as being treated with antidepressant medication during the entire 84 day (12 week) acute treatment phase | Observation | Standard | HCPCS | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #8 - [plp tutorial 2018] antipsychotic drug/measurement/observation/procedure***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 2108577 | 4065F | Antipsychotic pharmacotherapy prescribed (MDD) | Observation | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257488 | 80342 | Antipsychotics, not otherwise specified; 1-3 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257654 | 80343 | Antipsychotics, not otherwise specified; 4-6 | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 46257555 | 80344 | Antipsychotics, not otherwise specified; 7 or more | Procedure | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 757688 | 89013 | aripiprazole | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 40164052 | 784649 | Asenapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 46275300 | 1658314 | brexpiprazole | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 35603277 | 1667655 | cariprazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 794852 | 2403 | Chlorpromazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 19095002 | 2406 | Chlorprothixene | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 44816350 | 80159 | Clozapine | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 800878 | 2626 | Clozapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 2720963 | S0136 | Clozapine, 25 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 756018 | 4496 | Fluphenazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 766529 | 5093 | Haloperidol | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 2212118 | 80173 | Haloperidol | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 19017241 | 73178 | iloperidone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 44786557 | J0401 | Injection, aripiprazole, extended release, 1 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718258 | J0400 | Injection, aripiprazole, intramuscular, 0.25 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718605 | J3230 | Injection, chlorpromazine hcl, up to 50 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718549 | J2680 | Injection, fluphenazine decanoate, up to 25 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718425 | J1631 | Injection, haloperidol decanoate, per 50 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718424 | J1630 | Injection, haloperidol, up to 5 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 40664583 | J2358 | Injection, olanzapine, long-acting, 1 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 40664472 | J2426 | Injection, paliperidone palmitate extended release, 1 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718621 | J3310 | Injection, perphenazine, up to 5 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718315 | J0780 | Injection, prochlorperazine, up to 10 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718584 | J2950 | Injection, promazine hcl, up to 25 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718568 | J2794 | Injection, risperidone, long acting, 0.5 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718633 | J3400 | Injection, triflupromazine hcl, up to 20 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 2718648 | J3486 | Injection, ziprasidone mesylate, 10 mg | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 792263 | 6475 | Loxapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Invalid | 44786380 | C9497 | Loxapine, inhalation powder, 10 mg | Drug | Non-Standard | HCPCS | U | FALSE | TRUE |
| Valid | 40230761 | 1040028 | lurasidone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 703083 | 6779 | Mesoridazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 19005147 | 6852 | Methotrimeprazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 709699 | 7019 | Molindone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 2007724 | 94.23 | Neuroleptic therapy | Procedure | Non-Standard | 4-dig billing code | V | FALSE | TRUE |
| Valid | 785788 | 61381 | olanzapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 703244 | 679314 | paliperidone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 19131663 | 8042 | Perazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 733008 | 8076 | Perphenazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 745790 | 8331 | Pimozide | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 752061 | 8704 | Prochlorperazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 2721001 | S0183 | Prochlorperazine maleate, oral, 5 mg (for circumstances falling under the medicare statute, use q0164) | Drug | Non-Standard | HCPCS | V | FALSE | TRUE |
| Valid | 19052903 | 8742 | Promazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 766814 | 51272 | quetiapine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 735979 | 35636 | Risperidone | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 700299 | 10502 | Thioridazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 700465 | 10510 | Thiothixene | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 704984 | 10800 | Trifluoperazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 19005104 | 10805 | Triflupromazine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 712615 | 115698 | ziprasidone | Drug | Standard | Ingredient | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #9 - [plp tutorial 2018] lithium drug/procedure/measurement***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 2212121 | 80178 | Lithium | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 751246 | 42351 | Lithium Carbonate | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 2007723 | 94.22 | Lithium therapy | Procedure | Non-Standard | 4-dig billing code | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

***Concept Set #10 - [plp tutorial 2018] mood stabilizers drug/measurement***

| INVALID\_REASON\_CAPTION | CONCEPT\_ID | CONCEPT\_CODE | CONCEPT\_NAME | DOMAIN\_ID | STANDARD\_CONCEPT\_CAPTION | CONCEPT\_CLASS\_ID | INVALID\_REASON | isExcluded | includeDescendants |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Valid | 740275 | 2002 | Carbamazepine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 45889818 | 1011157 | Carbamazepine | Measurement | Classification | CPT4 Hierarchy | V | FALSE | TRUE |
| Valid | 2212109 | 80157 | Carbamazepine; free | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 2212108 | 80156 | Carbamazepine; total | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 44816347 | 80175 | Lamotrigine | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 705103 | 28439 | lamotrigine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 718122 | 32624 | oxcarbazepine | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 44816361 | 80183 | Oxcarbazepine | Measurement | Standard | CPT4 | V | FALSE | TRUE |
| Valid | 745466 | 40254 | Valproate | Drug | Standard | Ingredient | V | FALSE | TRUE |
| Valid | 46257591 | 1022260 | Valproic acid (dipropylacetic acid) | Measurement | Classification | CPT4 Hierarchy | V | FALSE | TRUE |
| Valid | 2212113 | 80164 | Valproic acid (dipropylacetic acid); total | Measurement | Standard | CPT4 | V | FALSE | TRUE |

Cohorts that use this Concept Set:

| Cohort ID | Cohort Name |
| --- | --- |
| 12292 | [PLP tutorial 2018] first MDD aged 10 or older |

## Complete Analysis List

Below is a complete list of analysis that will be performed. Definitions for the column 'Covariate Settings ID' can be found above in the 'Covariate Settings' section. Definitions for the 'Population Settings Id' can be found above in the 'Additional Population Settings' section.

| ID | Target Cohort Name | Outcome Cohort Name | Model Settings Id | Model Settings Description | Covariate Settings ID | Population Settings ID |
| --- | --- | --- | --- | --- | --- | --- |
| 1 | [PLP tutorial 2018] first MDD aged 10 or older | [OHDSI18 Best Prediction Ever] O: Persons newly diagnosed with bipolar disorder | 1 | Lasso Logistic Regression | 1 | 1 |

*<< add models here >>*

# References

*<< To be completed outside of ATLAS. >>*