**SUPPLEMENTAL MATERIAL**

**Identifying Medicare Beneficiaries with Delirium: A Classification Algorithm**

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# A. Supplementary Tables

## Table S1. International Classification of Diseases Diagnosis Codes (ICD-9 & ICD-10) for Delirium (Base Definition) and Codes Removed for Refined definition

|  |  |  |
| --- | --- | --- |
| **Diagnosis Codes** | **Description** | **Refined Definition** |
| **ICD-9 version** | |  |
| 293 | Delirium due to conditions classified elsewhere |  |
| 293.1 | Subacute delirium |  |
| 292.81 | Drug-induced delirium |  |
| 290.11 | Presenile dementia with delirium |  |
| 290.3 | Senile dementia with delirium |  |
| 290.41 | Vascular dementia, with delirium |  |
| 291 | Alcohol withdrawal delirium |  |
| 293.9 | Unspecified transient mental disorder in conditions classified elsewhere |  |
| 780.09 | Other alteration of consciousness |  |
| 293.81 | Psychotic disorder with delusions in conditions classified elsewhere |  |
| 293.82 | Psychotic disorder with hallucinations in conditions classified elsewhere |  |
| 293.83 | Mood disorder in conditions classified elsewhere | Remove |
| 293.84 | Anxiety disorder in conditions classified elsewhere | Remove |
| 293.89 | Other specified transient mental disorders due to conditions classified elsewhere | Remove |
| 290.12 | Presenile dementia with delusional features |  |
| 290.13 | Presenile dementia with depressive features |  |
| 290.43 | Vascular dementia, with depressed mood |  |
| 292.11 | Drug-induced psychotic disorder with delusions |  |
| 292.12 | Drug-induced psychotic disorder with hallucinations |  |
| 292.2 | Pathological drug intoxication |  |
| 780.02 | Transient alteration of awareness |  |
| 290.2 | Senile dementia with delusional features |  |
| 290.42 | Vascular dementia, with delusions |  |
| 290.8 | Other specified senile psychotic conditions |  |
| 290.9 | Unspecified senile psychotic condition |  |
| 292 | Drug withdrawal | Remove |
| 292.82 | Drug-induced persisting dementia | Remove |
| 348.3 | Encephalopathy, unspecified |  |
| 348.31 | Metabolic encephalopathy |  |
| 348.39 | Other encephalopathy |  |
| 349.82 | Toxic encephalopathy |  |
| 780.97 | Altered mental status |  |
| **ICD-10 version** | |  |
| F05 | Delirium due to known physiological condition |  |
| F10121 | Alcohol abuse with intoxication delirium |  |
| F10221 | Alcohol dependence with intoxication delirium |  |
| F10231 | Alcohol dependence with withdrawal delirium |  |
| F10921 | Alcohol use, unspecified with intoxication delirium |  |
| F11121 | Opioid abuse with intoxication delirium |  |
| F11221 | Opioid dependence with intoxication delirium |  |
| F11921 | Opioid use, unspecified with intoxication delirium |  |
| F12121 | Cannabis abuse with intoxication delirium |  |
| F12221 | Cannabis dependence with intoxication delirium |  |
| F12921 | Cannabis use, unspecified with intoxication delirium |  |
| F13121 | Sedative, hypnotic, or anxiolytic abuse with intoxication delirium |  |
| F13221 | Sedative, hypnotic, or anxiolytic dependence with intoxication delirium |  |
| F13231 | Sedative, hypnotic, or anxiolytic dependence with withdrawal delirium |  |
| F13921 | Sedative, hypnotic, or anxiolytic use, unspecified with intoxication delirium |  |
| F13931 | Sedative, hypnotic, or anxiolytic use, unspecified with withdrawal delirium |  |
| F14121 | Cocaine abuse with intoxication with delirium |  |
| F14221 | Cocaine dependence with intoxication delirium |  |
| F14921 | Cocaine use, unspecified with intoxication delirium |  |
| F15121 | Other stimulant abuse with intoxication delirium |  |
| F15221 | Other stimulant dependence with intoxication delirium |  |
| F15921 | Other stimulant use, unspecified with intoxication delirium |  |
| F16121 | Hallucinogen abuse with intoxication with delirium |  |
| F16221 | Hallucinogen dependence with intoxication with delirium |  |
| F16921 | Hallucinogen use, unspecified with intoxication with delirium |  |
| F18121 | Inhalant abuse with intoxication delirium |  |
| F18221 | Inhalant dependence with intoxication delirium |  |
| F18921 | Inhalant use, unspecified with intoxication with delirium |  |
| F19121 | Other psychoactive substance abuse with intoxication delirium |  |
| F19221 | Other psychoactive substance dependence with intoxication delirium |  |
| F19231 | Other psychoactive substance dependence with withdrawal delirium |  |
| F19921 | Other psychoactive substance use, unspecified with intoxication with delirium |  |
| F19931 | Other psychoactive substance use, unspecified with withdrawal delirium |  |
| A812 | Progressive multifocal leukoencephalopathy | Remove |
| E512 | Wernicke's encephalopathy | Remove |
| G0430 | Acute necrotizing hemorrhagic encephalopathy, unspecified | Remove |
| G0431 | Post-infectious acute necrotizing hemorrhagic encephalopathy | Remove |
| G0432 | Post-immunization acute necrotizing hemorrhagic encephalopathy | Remove |
| G0439 | Other acute necrotizing hemorrhagic encephalopathy | Remove |
| G92 | Toxic encephalopathy |  |
| G9340 | Encephalopathy, unspecified |  |
| G9341 | Metabolic encephalopathy |  |
| G9349 | Other encephalopathy |  |
| I673 | Progressive vascular leukoencephalopathy | Remove |
| I674 | Hypertensive encephalopathy | Remove |
| I6783 | Posterior reversible encephalopathy syndrome | Remove |
| J1081 | Influenza due to other identified influenza virus with encephalopathy | Remove |
| J1181 | Influenza due to unidentified influenza virus with encephalopathy | Remove |
| P9160 | Hypoxic ischemic encephalopathy, unspecified | Remove |
| P9161 | Mild hypoxic ischemic encephalopathy | Remove |
| P9162 | Moderate hypoxic ischemic encephalopathy | Remove |
| P9163 | Severe hypoxic ischemic encephalopathy | Remove |

## Table S2. Lists of Antipsychotic Drugs included in the Claims-based definition

|  |  |
| --- | --- |
| **Drug** | **Note** |
| Aripiprazole (ABILIFY) |  |
| Haloperidol |  |
| Quetiapine |  |
| Olanzapine |  |
| Risperidone |  |
| Thorazine |  |
| Ziprasidone | add for liberal definition |
| Latuda | add for liberal definition |
| Perphenazine | add for liberal definition |
| Seroquel |  |
| Trifluoperazine HCL |  |
| Chlorpromazine |  |

## Table S3. Detailed Description of Variables in Each Model (M8-M11)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Models | Count of Visits & Stays with Dx | Count of In-patient Stays with Dx | Count of Out-patient Visits with Dx | Count of Antipsychotic Fills - Conservative | Count of Antipsychotic Fills - Liberal | Age | Dementia Indicator | Sex | Any Dx | Any Antipsychotic Fill - liberal |
| M8 |  | Refined | Refined |  | X | continuous | X |  |  |  |
| M8v2 |  | Refined | Refined |  | X | categories | X |  |  |  |
| M9 |  | Refined | Refined |  | X | continuous | X | X |  |  |
| M9v2 |  | Refined | Refined |  | X | categories | X | X |  |  |
| M10 |  |  |  |  |  | continuous |  |  | Refined | X |
| M10v2 |  |  |  |  |  | categories |  |  | Refined | X |
| M11 |  |  |  |  |  | continuous | X |  | Refined | X |
| M11v2 |  |  |  |  |  | categories | X |  | Refined | X |

**Legend:** description of variable included in each model, where “count of antipsychotic fills – conservative” means thoughtful prescribing attitudes and behaviors vs “count of antipsychotic fills – liberal”, being the opposite**, and where “Any Diagnosis” refers to any diagnosis within the Refined List.**

Abbreviations: Dx, diagnosis

## Table S4. Example of Delirium Prediction Algorithm Performance: Preferred Model (Model 8)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Metric** | **95%** | **CI** | |
| CV AUC | 0.88 | 0.84 | 0.91 | |
| CV CITL | 0.00 | -0.22 | 0.22 | |
| CV Slope | 0.94 | 0.78 | 1.09 | |
|  | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 47.2 | 2.7 | 38.8 | 55.9 |
| Specificity | 93.1 | 0.8 | 90.3 | 95.4 |
| Positive predictive value (PPV) | 57.3 | 3.1 | 47.9 | 66.4 |
| Negative predictive value (NPV) | 90.0 | 0.5 | 88.7 | 91.6 |
|  | **Coeff** | **95%** | **CI** | |
| Count of hospitalizations with a delirium dx | 2.2 | 1.5 | 2.9 | |
| Count of outpatient visits with a delirium dx | 0.5 | -0.2 | 1.2 | |
| Count of antipsychotic drug fills | 0.0 | 0.0 | 0.0 | |
| Age | 0.1 | 0.0 | 0.1 | |
| Dementia status | 1.2 | 0.5 | 1.8 | |
| Constant | -10.2 | -13.4 | -7.1 | |

**Footnote:** The above model has both high levels of performance and includes relatively simple inputs available in Medicare administrative datasets, thus we describe this as the preferred model. CV refers to 10-fold cross-validation. AUC refers to the Area under the ROC Curve. CITL refers to Calibration-in-the-large. The table is based primarily on the reconstructed sample, but CV metrics are shown for the original (analytic) sample. Cross-validation was repeated with reconstructed sample for sensitivity analysis, which yielded similar results. The Mean, Min, and Max from the 1000 Monte Carlo samples is reported for each performance characteristic. We used Medicare Part D claims data to identify all dispensations of an antipsychotic drug (i.e., fills). We used a previously validated claims-based algorithm to identify dementia status. **Coeff refers to logistic regression model coefficients.**

## Table S5. Performance Characteristics of Claims-based Diagnoses in Ascertaining Delirium: Base Definition (Models 1-2)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 1** | | | | **Model 2** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.772 | 0.719 | 0.825 |  | 0.762 | 0.708 | 0.816 |  |
| CV CITL | -0.009 | -0.224 | 0.205 |  | 0.000 | -0.214 | 0.213 |  |
| CV Slope | 0.927 | 0.758 | 1.096 |  | 0.954 | 0.781 | 1.127 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 39.3 | 2.6 | 30.9 | 47.4 | 39.4 | 2.7 | 30.3 | 48.7 |
| Specificity | 94.2 | 0.7 | 91.7 | 96.0 | 94.2 | 0.8 | 91.8 | 96.4 |
| PPV | 57.2 | 3.6 | 46.1 | 67.7 | 57.1 | 3.7 | 44.7 | 68.5 |
| NPV | 88.8 | 0.4 | 87.6 | 90.1 | 88.9 | 0.5 | 87.3 | 90.4 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |
| Count of Visits | 1.9 | 1.2 | 2.5 |  | 1.9 | 1.2 | 2.5 |  |
| Count of Antipsychotic Fills - Conservative definition |  |  |  |  | 0.0 | 0.0 | 0.0 |  |
| Constant | -3.2 | -3.5 | -2.9 |  | -3.2 | -3.5 | -2.9 |  |

**Legend:** performance characteristics of claims-based diagnoses in ascertaining delirium using a base definition (Models 1 and 2). **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

## Table S6. Performance Characteristics of Claims-based Diagnoses in Ascertaining Delirium: Refined Definition (Models 3-5)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 3** | | | | **Model 4** | | | | **Model 5** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.765 | 0.712 | 0.817 |  | 0.756 | 0.702 | 0.810 |  | 0.758 | 0.704 | 0.812 |  |
| CV CITL | 0.004 | -0.207 | 0.215 |  | -0.008 | -0.220 | 0.204 |  | -0.003 | -0.215 | 0.208 |  |
| CV Slope | 0.973 | 0.795 | 1.152 |  | 0.950 | 0.777 | 1.122 |  | 0.966 | 0.791 | 1.141 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Mean** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 38.0 | 2.6 | 28.9 | 48.7 | 38.3 | 2.6 | 30.9 | 46.1 | 38.3 | 2.7 | 28.9 | 46.7 |
| Specificity | 94.1 | 0.7 | 91.8 | 96.3 | 94.1 | 0.8 | 91.7 | 96.2 | 94.1 | 0.8 | 91.5 | 96.4 |
| PPV | 55.9 | 3.6 | 45.5 | 67.3 | 56.1 | 3.7 | 44.1 | 67.0 | 56.0 | 3.8 | 43.4 | 68.8 |
| NPV | 88.6 | 0.4 | 87.3 | 90.3 | 88.7 | 0.4 | 87.5 | 90.0 | 88.7 | 0.4 | 87.1 | 90.1 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |  |  |  |  |
| Any claim with Dx | 1.9 | 1.2 | 2.5 |  | 1.9 | 1.2 | 2.5 |  | 1.9 | 1.2 | 2.5 |  |
| Any Antipsychotic Fill, Conservative definition |  |  |  |  | 0.01 | 0.00 | 0.02 |  |  |  |  |  |
| Count of Antipsychotic Fills - Liberal definition |  |  |  |  |  |  |  |  | 0.01 | 0.00 | 0.02 |  |
| Constant | -3.2 | -3.5 | -2.9 |  | -3.2 | -3.5 | -2.9 |  | -3.2 | -3.5 | -2.9 |  |

**Legend:** performance characteristics of claims-based diagnoses in ascertaining delirium using a refined count of visits and stays with a diagnosis, count of antipsychotic fill (both liberal and conservative definition) as variables (Models 3 through 5). **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value; Dx, diagnosis

## Table S7. Performance of Simpler Claims-based Definitions with of Service and Clinical Factors (Models 10-11)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 10** | | | | **Model 11** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.867 | 0.832 | 0.902 |  | 0.871 | 0.837 | 0.905 |  |
| CV CITL | 0.003 | -0.225 | 0.230 |  | 0.000 | -0.228 | 0.229 |  |
| CV Slope | 0.974 | 0.835 | 1.112 |  | 0.959 | 0.823 | 1.096 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 45.1 | 2.9 | 36.2 | 55.3 | 47.7 | 2.9 | 38.2 | 55.9 |
| Specificity | 93.8 | 0.7 | 91.7 | 96.0 | 93.0 | 0.8 | 90.4 | 95.4 |
| PPV | 58.7 | 3.3 | 49.6 | 70.2 | 57.1 | 3.1 | 47.8 | 68.1 |
| NPV | 89.8 | 0.5 | 88.3 | 91.5 | 90.1 | 0.5 | 88.5 | 91.6 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |
| Any In-patient Claim with Dx | 3.2 | 2.5 | 4.0 |  | 3.2 | 2.4 | 3.9 |  |
| Any Out-patient Claim with Dx | 1.6 | 0.1 | 3.1 |  | 1.4 | -0.1 | 3.0 |  |
| Any Antipsychotic Fill, Liberal def | 1.6 | 0.8 | 2.4 |  | 1.4 | 0.6 | 2.1 |  |
| Age | 0.1 | 0.1 | 0.1 |  | 0.1 | 0.0 | 0.1 |  |
| Dementia |  |  |  |  | 1.0 | 0.3 | 1.7 |  |
| Constant | -10.6 | -13.8 | -7.4 |  | -9.8 | -13.2 | -6.4 |  |

**Legend:** performance characteristics of claims-based definitions using any diagnosis, age, dementia indicator and any antipsychotic fill (liberal definition) as variables (Models 10 to 11). **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

## Table S8. Performance of Models Incorporating Age as Categorical (Models 8-9v2)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 8v2** | | | | **Model 9v2** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.845 | 0.802 | 0.889 |  | 0.855 | 0.816 | 0.895 |  |
| CV CITL | -0.008 | -0.229 | 0.214 |  | -0.012 | -0.233 | 0.209 |  |
| CV Slope | 0.921 | 0.769 | 1.072 |  | 0.914 | 0.763 | 1.065 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 46.7 | 2.7 | 38.8 | 57.2 | 46.6 | 2.7 | 36.8 | 54.6 |
| Specificity | 93.1 | 0.8 | 90.8 | 95.4 | 93.0 | 0.8 | 90.5 | 95.1 |
| PPV | 56.9 | 3.2 | 47.8 | 67.6 | 56.7 | 3.1 | 46.9 | 64.8 |
| NPV | 90.0 | 0.5 | 88.6 | 91.8 | 89.9 | 0.5 | 88.2 | 91.3 |
|  | **Coeff** | **100%** | **CI** |  | **Coeff** | **1.0** | **CI** |  |
| Count of In-patient Stays with Dx | 2.2 | 1.5 | 2.8 |  | 2.2 | 1.5 | 2.8 |  |
| Count of Out-patient Visits with Dx | 0.5 | -0.3 | 1.3 |  | 0.5 | -0.3 | 1.3 |  |
| Count of Antipsychotic Fills - Liberal def | 0.0 | 0.0 | 0.0 |  | 0.0 | 0.0 | 0.0 |  |
| vs Age < 75: Age 75 -79 | 0.7 | -0.1 | 1.6 |  | 0.7 | -0.2 | 1.6 |  |
| Age 80-84 | 0.8 | -0.1 | 1.6 |  | 0.8 | -0.1 | 1.6 |  |
| Age 85 + | 1.7 | 0.8 | 2.5 |  | 1.7 | 0.8 | 2.5 |  |
| Dementia | 1.3 | 0.6 | 1.9 |  | 1.3 | 0.6 | 1.9 |  |
| Female |  |  |  |  | 0.2 | -0.5 | 0.8 |  |
| Constant | -4.0 | -4.5 | -3.4 |  | -4.1 | -4.6 | -3.5 |  |

**Legend:** performance characteristics of claims-based diagnoses in ascertaining delirium using a refined definition of count of in-patient stays and out-patient visits with a diagnosis, count of antipsychotic fill (liberal definition), age, dementia indicator and sex as variables (Models 8 and 9 v2). **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

## Table S9. Performance of Models Incorporating Age as Categorical (Models 10-11v2)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 10v2** | | | | **Model 11v2** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.843 | 0.800 | 0.885 |  | 0.852 | 0.811 | 0.894 |  |
| CV CITL | 0.006 | -0.221 | 0.233 |  | 0.001 | -0.228 | 0.229 |  |
| CV Slope | 0.953 | 0.816 | 1.091 |  | 0.950 | 0.814 | 1.086 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 44.5 | 2.8 | 36.2 | 52.0 | 47.6 | 2.8 | 36.2 | 56.6 |
| Specificity | 93.8 | 0.7 | 91.2 | 96.2 | 93.0 | 0.7 | 90.3 | 95.9 |
| PPV | 58.6 | 3.2 | 48.4 | 71.2 | 57.1 | 2.9 | 48.7 | 68.6 |
| NPV | 89.7 | 0.5 | 88.2 | 91.0 | 90.1 | 0.5 | 88.2 | 91.6 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |
| Any In-patient Claim with Dx | 3.2 | 2.5 | 3.9 |  | 3.1 | 2.4 | 3.9 |  |
| Any Out-patient Claim with Dx | 1.7 | 0.2 | 3.3 |  | 1.5 | -0.1 | 3.1 |  |
| Any Antipsychotic Fill, Liberal def | 1.6 | 0.8 | 2.4 |  | 1.4 | 0.6 | 2.1 |  |
| vs Age<75: Age 75-79 | 0.8 | -0.1 | 1.6 |  | 0.7 | -0.2 | 1.6 |  |
| Age 80-84 | 0.9 | 0.1 | 1.7 |  | 0.8 | 0.0 | 1.6 |  |
| Age 85+ | 1.7 | 0.9 | 2.6 |  | 1.5 | 0.6 | 2.5 |  |
| Dementia |  |  |  |  | 1.1 | 0.4 | 1.8 |  |
| Constant | -4.1 | -4.6 | -3.5 |  | -4.1 | -4.6 | -3.5 |  |

**Legend:** performance characteristics of claims-based definitions using any diagnosis, age, dementia indicator and any antipsychotic fill (liberal definition) as variables (Models 10 and 11 v2), where age categories are as follows: age 75-7 years, 80-84 years or 85 and older. **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

## Table S10. Performance of Model 8 Stratifying by Age Groups

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Refined set of diagnosis codes** | **Model 8** | | | | | | | |
|  | **Age < 80** | | | | **Age 80+** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.794 | 0.719 | 0.869 |  | 0.806 | 0.746 | 0.867 |  |
| CV CITL | 0.021 | -0.314 | 0.356 |  | 0.006 | -0.295 | 0.306 |  |
| CV Slope | 0.785 | 0.584 | 0.985 |  | 0.781 | 0.564 | 0.998 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 43.2 | 3.6 | 32.8 | 54.1 | 51.6 | 3.7 | 39.6 | 63.7 |
| Specificity | 96.3 | 0.7 | 93.9 | 98.2 | 85.0 | 2.0 | 77.2 | 92.0 |
| PPV | 56.6 | 5.1 | 38.9 | 73.7 | 58.4 | 3.7 | 45.7 | 73.1 |
| NPV | 93.9 | 0.4 | 92.9 | 95.0 | 81.2 | 1.2 | 77.6 | 85.5 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |
| Count of In-patient Stays with Dx | 2.8 | 1.9 | 3.7 |  | 1.9 | 1.1 | 2.6 |  |
| Count of Out-patient Visits with Dx | 0.8 | 0.3 | 1.4 |  | -1.1 | -2.7 | 0.5 |  |
| Count of Antipsychotic Fills - Liberal def | 0.0 | -0.1 | 0.1 |  | 0.1 | 0.0 | 0.2 |  |
| Age | 0.2 | 0.0 | 0.3 |  | 0.1 | 0.0 | 0.2 |  |
| Dementia | 0.8 | -0.8 | 2.4 |  | 1.3 | 0.5 | 2.0 |  |
| Constant | -15.0 | -24.1 | -6.0 |  | -11.0 | -18.4 | -3.6 |  |

**Legend:** performance characteristics of claims-based definitions by age groups, younger than 80 years, and 80 years and older, for Model 8. **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

## Table S11. Performance of Model 11 Stratifying by Age Groups

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Model 11** | | | | | | |  |
|  | **Age < 80** | | | | **Age 80+** | | | |
|  | **Metric** | **95%** | **CI** |  | **Metric** | **95%** | **CI** |  |
| CV AUC | 0.814 | 0.744 | 0.885 |  | 0.808 | 0.746 | 0.870 |  |
| CV CITL | -0.008 | -0.352 | 0.337 |  | -0.006 | -0.317 | 0.306 |  |
| CV Slope | 0.919 | 0.736 | 1.102 |  | 0.916 | 0.709 | 1.123 |  |
|  | **Mean** | **SD** | **Min** | **Max** | **Mean** | **SD** | **Min** | **Max** |
| Sensitivity | 41.7 | 4.4 | 27.9 | 57.4 | 54.3 | 4.0 | 39.6 | 68.1 |
| Specificity | 95.9 | 0.7 | 93.3 | 97.8 | 85.8 | 2.0 | 79.5 | 91.5 |
| PPV | 53.1 | 5.1 | 36.7 | 71.1 | 60.9 | 3.8 | 50.6 | 73.7 |
| NPV | 93.7 | 0.4 | 92.4 | 95.3 | 82.2 | 1.3 | 77.8 | 87.1 |
|  | **Coeff** | **95%** | **CI** |  | **Coeff** | **95%** | **CI** |  |
| Any In-patient Claim with Dx | 3.6 | 2.6 | 4.6 |  | 2.9 | 1.9 | 4.0 |  |
| Any Out-patient Claim with Dx | 2.8 | 1.6 | 4.0 |  | -0.6 | -2.3 | 1.1 |  |
| Any Antipsychotic Fill, Liberal def | 0.9 | -0.4 | 2.1 |  | 1.6 | 0.7 | 2.5 |  |
| Age | 0.1 | 0.0 | 0.3 |  | 0.1 | 0.0 | 0.2 |  |
| Dementia | 0.5 | -1.0 | 2.0 |  | 1.2 | 0.5 | 2.0 |  |
| Constant | -14.4 | -23.5 | -5.2 |  | -10.1 | -17.8 | -2.4 |  |

**Legend:** performance characteristics of claims-based definitions by age groups, younger than 80 years, and 80 years and older, for Model 11. **For simplicity, we chose to display the best performing models (i.e., models 6 and 7 not included).**

Abbreviations: CV, cross validation; AUC, area under the curve; CITL, calibration-in-the-large; PPV, positive predictive value; NPV, negative predictive value

# B. Supplementary Text

## a. Supplementary Text: Methods

We examined a total of eleven predictive models corresponding to different combinations of the indicator or count variables. **In this supplementary text we describe those models not included in the main text.** The simplest model (Model 1) regressed clinician-adjudicated delirium (i.e., the reference standard) on the “Base” variable for the count of any delirium ICD-10 diagnostic code. Model 2 added a count of any fill (i.e., drug prescription filled by the patient or administered by a healthcare provider) of commonly prescribed drugs associated with the care of a patient with delirium. Model 3 used the “Refined” indicator variable for the presence of any delirium ICD-10 diagnostic code, and Model 4 included the variable for the count of any fill of commonly prescribed drugs. The Table S3 details the variables included in each of the models.

Model 6 includes variables for the place of service in which the delirium code was obtained (i.e., count of outpatient visits with diagnosis, count of inpatient stays with diagnosis), and the less restrictive list of delirium-associated drugs. Model 7 adds age as continuous variable.

For the base claims-based definition of delirium (Model 1), we observed good calibration with the reference standard with CV CITL of <0.001 and CV slope of 0.93. discrimination, and fair discrimination (CVAUC 0.77; 95% CI 0.72-0.82).

The model for the refined claims-based definition of delirium (Model 3), was well-calibrated to the reference standard with CV CITL of <0.001 and CV slope of 0.97 and a modest increase in discrimination (CVAUC of 0.76; 95% CI 0.71-0.82) compared to Models 1-2. There was negligible improvement with incorporation of counts of associated delirium-associated drugs in a restricted (Model 4) or less restrictive list (Model 5).

## b. Supplementary Text: Protocol for Electronic Health Record Based Ascertainment of Delirium

**Index:**

A. Demographic variables obtained from linked dataset [Medicare-Partners ACO]

B. Clinical variables for clinicians to extract from EHR [Epic] (i.e., “Clinical data” in REDCap”]

C. Tables

### A. Demographic Variables Obtained from Linked Dataset

**EMPI**

* Number (unique patient ID number)

**Date Of Birth**

* Date

**Age2016**

* Number

**cur\_age**

* Number

### B. Clinical Variables for Clinicians to Extract from EHR

**MINIMUM PROCESS:**

1. Set Timeframe: Review EHRs only between dates: 01/01/2016 – 12/31/2018. Filter notes by date in Epic.
   1. Open patient’s EHR -> open “Chart Review” tab on left
   2. Open “Notes” tab in “Chart Review” ribbon
   3. Click “Filters” button in top left corner -> set “From:” date at “01/01/2016” and “To:” date to “12/31/2018”
   4. Click “Save as New Filter” and name it whatever you want -> This will automatically start filtering for this patient and will continue to use this filter until 1) you close out of Epic; 2) you manually uncheck this as a filter; 3) you manually hit “Clear Filters”, which is to the right of all available filters
   5. To use the same filter again after closing Epic: follow steps a and b -> then check the filter you named and saved from your prior session in the top filter ribbon.
   6. If you’re feeling up to it, you can additionally add another filter function to your filter. E.g., “department Specialty” -> Neurology -> “Save ok”; OR “Author Specialty” -> “Neurology”, “Psychiatry”, etc. This will update your previously created filter
   7. Alternatively, if you don’t like filter functions, you can just sort notes by “Service Date” or “Specialty” once you open “Chart Review” -> Notes

2. First, review primarily (but not limited to) notes from primary care providers, psychiatry, psychology, social workers, neurology, neuropsychology, and geriatric medicine (e.g., by using the filter and sorting functions indicated in steps a-g above). Annual Medicare wellness visits may also have at least minimum evaluations.

a. To search for notes from Care Coordination, generic primary care provider, Annual Medicare Wellness Visits (if the note was titled as such in Epic), try explicitly searching for “Annual Wellness” or “PE/Wellness” or “Medicare Wellness” in the search function (i.e., the magnifying glass) in upper right corner of a patient’s opened chart.

b. To review current medication list [ideally should consider medications used during timeframe of 01/01/2016 – 12/31/2018. If not possible, then current medication list assuming no major changes from 2018 to early 2019]

3. If diagnoses cannot be made by reviewing key notes, follow instructions of searching for key terms in Table 1 using the search function (i.e., the magnifying glass in the top right corner of a patient’s chart)

4. Make note of any case in which you are unsure of the diagnosis, sorely guessing on coding, find difficult to classify, etc. Bring these cases to our weekly meeting for peer review and final coding based on consensus (isn’t science great?). Similarly, bring cases with questions concerning variables that initially demonstrated less than desirable agreement (e.g., rare **delirium** subtype, psychosis, wandering, etc.) to the weekly meetings for peer review.

**5. To access REDCap database:**

**Redcap.partners.org -> log in using partners username and password -> My Projects -> Record Status Dashboard -> Click into Demographics to obtain MRN and DOB -> Click into patient Clinical Data to edit delirium data-> Once all info is completed for patients, use Complete? Dropdown box and code as complete.**

6. If a patient has no notes or encounters in Epic (i.e., missing data), then code “No data for abstraction” under first data variable. No other coding on REDCap is necessary beyond this point. If you desire, make a note under the NOTES variable to say data is missing in Epic. These cases were originally coded as “barely guessing” under cognitive concern.

**VARIABLES LIST:**

**1. Data Available**

* 0- No data for abstraction (e.g., no notes, one email)
* 1- Data for abstraction

Notes: This question replaces "NO DATA" that we normally documented under notes.

\*\*For variables related to delirium, please refer to published manuscript.(18)

**17. Delirium Episode**

* 0- No evidence of delirium in the study time frame. Go to “18. Delirium\_Episode\_Certainty”
* 1- At least one episode of delirium in the study time frame Go to “18. Delirium\_Episode\_Certainty”
* 9- Unknown Go to “19. Rationale\_Unknown\_Delirium\_Episode”

Notes: See Table 5 for diagnostic criteria for delirium3. *We are looking for delirium within the study timeframe regardless of syndromic diagnosis* (i.e., even if a patient does not have delirium or MCI, you will still be directed to this variable to abstract information concerning an episode of delirium within the study timeframe).

Clarification: Always code for this variable (i.e., even if patient has no cognitive concern, you still code 0 under syndromic diagnosis AND this variable).

**18. Delirium\_Episode\_Certainty**

* 1 - Not at all confident If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”
* 2- Mildly confident If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”
* 3- Moderately confident If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”
* 4- Highly confident If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”

IF SYNDROMIC DIAGNOSIS=0, 1, or 2, END HERE

**19. Rationale\_Unknown\_Delirium\_Episode**

* 1- Limited data If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”
* 2- Conflicting data If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”
* 3- Both If syndromic diagnosis=3 or 4 Go to “20. Psychosis\_or\_Agitation”

IF SYNDROMIC DIAGNOSIS=0, 1, or 2, END HERE

Notes: For this variable, you may search in discharge notes, admission notes, follow-up notes after institutionalization, and any pertinent information within the timeframe.

**20. Psychosis\_or\_Agitation** [given syndromic diagnosis of 3 or 4]

* 0- No psychotic/agitated behavioral disturbance observed after delirium diagnosis Go to “21. Psychosis\_or\_Agitation\_Certainty”
* 1- Psychotic/agitated behavioral disturbance observed after delirium diagnosis Go to “21. Psychosis\_or\_Agitation\_Certainty”
* 9- Unknown Go to “12. Rationale\_Unknown\_Psychosis\_or\_Agitation”

Notes: Examples include positive symptoms such as paranoia, delusions, A/V hallucinations, psychosis, agitation, combativeness that appear separate from an episode of delirium.Evaluate among those with a cognitive concern or delirium. If the behavioral disturbance is part the continuum of unsolved delirium, then code “Psychosis\_or\_Agitation” positive and rate your degree of certainty as not at all confident. If we see this only in the setting that we believe is delirium, just code as delirium. If we see some evidence that this is delirium, call delirium (e.g., Immediately post-op, part of ED visit). If not sure and suspicion of both, then code both. Document specific disturbance under NOTES variables.

Clarification: When Unknown, please add some information in the “Note” about why you are Unknown (give examples). E.g., no notes at all vs conflicting information [poor description vs. incomplete information].

Clarification: Do not include mood/affective symptoms (e.g., depression, anxiety, apathy, labile mood) or sleep disturbances; rationale is that there is generally not enough evidence to link these disturbances directly to delirium and are common in the general elderly population.

Clarification: If you find the patient hallucinates, code the patient as having a psychotic/agitated behavioral disturbance unless proved otherwise through appropriate testing.

Clarification: Only code this variable if the patient **has delirium (syndromic diagnosis of 3 or 4)**. As noted above, we are interested in psychosis/agitation behavioral disturbances following a delirium diagnosis because this can help predict severity.

**21. Psychosis\_or\_Agitation\_Certainty**

* 1 - Not at all confident Go to “23. Wandering”
* 2- Mildly confident Go to “23. Wandering”
* 3- Moderately confident Go to “23. Wandering”
* 4- Highly confident Go to “23. Wandering”

**22. Rationale\_Unknown\_Psychosis\_or\_Agitation**

* 1- Limited data
* 2- Conflicting data
* 3- Both

Notes: Same as above - search can be all available data within the timeframe.

**23. Wandering** [given syndromic diagnosis of 3 or 4]

* 0- Wandering behavioral disturbance not present after delirium diagnosis Go to “24. Wandering Certainty
* 1- Wandering behavioral disturbance present after delirium diagnosis Go to “24. Wandering Certainty
* 9- Unknown Go to “25. Rationale\_Unknown\_Wandering”

Notes: A patient that gets lost *does not necessarily* qualify as “wandering” (i.e., getting lost while driving, or while walking somewhere, is not considered wandering). One example of a case that might qualify as wandering is if the individual got lost due to disorientation that is clearly associated with delirium.

Clarification: Wandering can include an incident of waking up, getting dressed and wandering around the home in the middle of the night.

Clarification: This should be coded ONLY FOR THOSE WITH DELIRIUM (SYNDROMIC DIAGNOSIS OF 3 OR 4). We are collecting this because this can help predict delirium severity.

**24. Wandering Certainty**

* 1 - Not at all confident END OF NECESSARY VARIABLES
* 2- Mildly confident END OF NECESSARY VARIABLES
* 3- Moderately confident END OF NECESSARY VARIABLES
* 4- Highly confident END OF NECESSARY VARIABLES

**25. Rationale\_Unknown\_Wandering**

* 1- Limited data END OF NECESSARY VARIABLES
* 2- Conflicting data END OF NECESSARY VARIABLES
* 3- Both END OF NECESSARY VARIABLES

Notes: Same as above - search can be all available data within the timeframe.

**26. Other\_Behavioral\_Instance**

* Free text – type here the specific behavioral disturbance not previously coded.

**27. Notes**

* Free text.

### C. Tables

|  |  |
| --- | --- |
| **Table 1. Systematic search of terms in two phases** | |
| **1 | Search for these terms among all patients** | **Notes** |
| **1.A | Medication search** |  |
| Donepezil |  |
| Rivastigmine |  |
| Galantamine |  |
| Memantine |  |
| **1.B | Diagnosis and symptoms search** |  |
| “Delirium” | Must use “” to avoid garbage like drugs |
| Alzheimer |  |
| Confusion | Very useful for discerning cognitive concern |
| Recall | Very useful |
| Memory | Must use “” to avoid garbage like memorial hospital |
| Cognitive | It gives all subs including “cognition” |
| Forget | Very useful |
| Lost | Very useful |
| Clock | Not sure if useful. |
| MOCA | Not sure if useful. [if full term, then cognitive gets it] |
| MMSE | Very useful as it is |
| Mental | Very useful |
| Parkinson; Parkinson’s; Parkinsonism | Turned out somewhat useful |
| **2 | Search for these terms only among those with cognitive concern; attempt to search for behavioral symptoms** | **Notes** |
| **2.A | Antipsychotic Medication search** | Generic works for all forms |
| Aripiprazole |  |
| Haloperidol |  |
| Clozapine |  |
| Olanzapine |  |
| Quetiapine |  |
| Risperidone |  |
| Ziprasidone |  |
| **2.B | Symptom’s search** |  |
| Agitation | Very useful. It gets all variations like agitated. |
| Aggression | Need to check if it gets aggressive, etc. |
| “Delirium” | Must use “” to avoid garbage like midazolam but need to check with more cases. |
| Hallucination | need to check utility with more cases. |
| Wandering | need to check utility with more cases. |
| Psychosis | need to check utility with more cases. |
| Paranoid; paranoia | need to check utility with more cases. |
| Combative | need to check utility with more cases. |
| Delusions | need to check utility with more cases. |
| Hostility | need to check utility with more cases. |
| Outbursts | need to check utility with more cases. |
| Finances | Can help when searching among MCI and Delirium patients- might help increase sensitivity |
| Cooking | Can help when searching among MCI and Delirium patients |
| Driving | Can help when searching among MCI and Delirium patients |

**Table 1 Notes**: Always search for medications and diagnosis. Only search for additional behavioral symptoms and delirium in patients with cognitive concern.

|  |  |
| --- | --- |
| **Table 4. Delirium Severity3** | **Criteria** |
| Mild | Difficulties with instrumental ADLs (e.g., housework, managing money) only |
| Moderate | Difficulties with basic ADLs (e.g., feeding, dressing) as well |
| Severe | Fully dependent |

|  |
| --- |
| **Table 5. Diagnosis of delirium must meet all the following criteria:(22)** |
| A. A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment) |
| B. The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during a day |
| C. An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception) |
| D. The disturbances in criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma. |