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### Background

- An increased understanding of predictors of hospitalization among patients newly diagnosed with major depressive disorder (MDD) is important so that hospitalizations can be reduced, and depression can be treated and managed in an outpatient setting
- In clinical settings, risk assessment leading to inpatient hospitalization may often be reserved for patients with severe MDD or serious mental illness (bipolar disorder, schizophrenia, etc.)
- Although risk assessment can be embedded into electronic health records (EHRs), these tools often do not include psychosocial stressors (Walsh et al, 2021)
- Moreover, it is not uncommon for behavioral health care providers to lack sufficient training in risk assessment (Schmitz et al, 2012) and a simple summary of predictors of hospitalization could prove useful to clinicians

#### **STUDY OBJECTIVE**

• Examine predictors of hospitalization in patients with newly-diagnosed MDD

### Methods

A retrospective cohort study of electronic health record (EHR)-derived de-identified data from the NeuroBlu Research database was conducted in adults with MDD diagnosed between 09/2000-06/2020. All analyses were performed using R.

NeuroBlu Research is a leading source of behavioral health real-world evidence and contains 20+ years of longitudinal data and records for over 1M patients (MDD: 251,000+) in 30+ geographically diverse psychiatry sites in the US spanning both inpatient and outpatient sites including hospitals, emergency departments, and community psychiatry clinics. NeuroBlu Research utilizes a proprietary natural language processing (NLP) algorithm to extract meaningful clinical information not typically captured in a structured way including a large array of symptoms, side effects, family history, and external psychosocial stressors.

Study schematic and patient attrition are presented in **Fig. 1** and **Fig. 2**. Precipitating factors for patients hospitalized within 30 days of index date were assumed to have already occurred and these patients were excluded from this study. Patients were randomly split (70%/30%) into train and test sets. Time to hospitalization was modeled by Cox models with elastic-net regularization; diagnoses of bipolar disorder, schizophrenia, or schizoaffective disorder were entered as time-varying covariates as transition to these diagnoses represents a distinct clinical phenotype which may have a different clinical trajectory. C-index was estimated by 10-fold cross-validation (CV) in train set; model performance was assessed in the test set.

#### Results

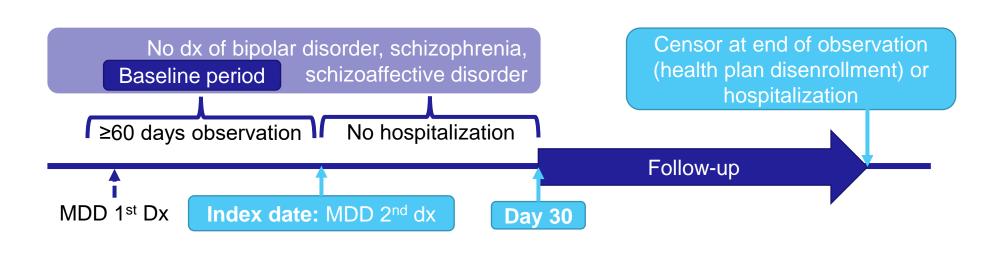


Fig. 1: Study schematic

#### **PATIENT CHARACTERISTICS**

- Train patients were mostly single (39.9%), white (81.2%), females (68.2%) with non-severe MDD (85%), median age 42 years, and median Clinical Global Impression Severity scale (CGIS) 4. Test patients had similar characteristics; see **Table 1**
- Train and test sets were well-balanced in terms of comorbidities, psychosocial stressors, strengths, and family history of mental health issues; Fig. 3
- 43.5% of train set and 41.9% of test patients were hospitalized; median time to hospitalization was 12.6 months and 12.9 months, respectively

Table 1: Demographic and clinical characteristics

	Test set (N=2170) n (%)/M (SD)	Train set (N=5116) n (%)/M (SD)	p-value
Gender (Female)	1468 (67.6%)	3487 (68.2%)	0.67
Age	43.23 (14.05)	42.87 (14.18)	0.35
Race			0.33
White	1730 (79.7%)	4155 (81.2%)	
Black or African American	354 (16.3%)	778 (15.2%)	
Other	86 (4.0%)	183 (3.6%)	
Marital status			0.81
Married	761 (35.1%)	1735 (33.9%)	
Widowed	98 (4.5%)	240 (4.7%)	
Divorced/Separated	456 (21.0%)	1101 (21.5%)	
Single	855 (39.4%)	2040 (39.9%)	
MDD severity			0.88
Not severe	1841 (84.8%)	4350 (85.0%)	
Severe without psychosis	245 (11.3%)	560 (10.9%)	
Severe with psychosis	84 (3.9%)	206 (4.0%)	
CGIS	4.31 (1.16)	4.29 (1.14)	0.35

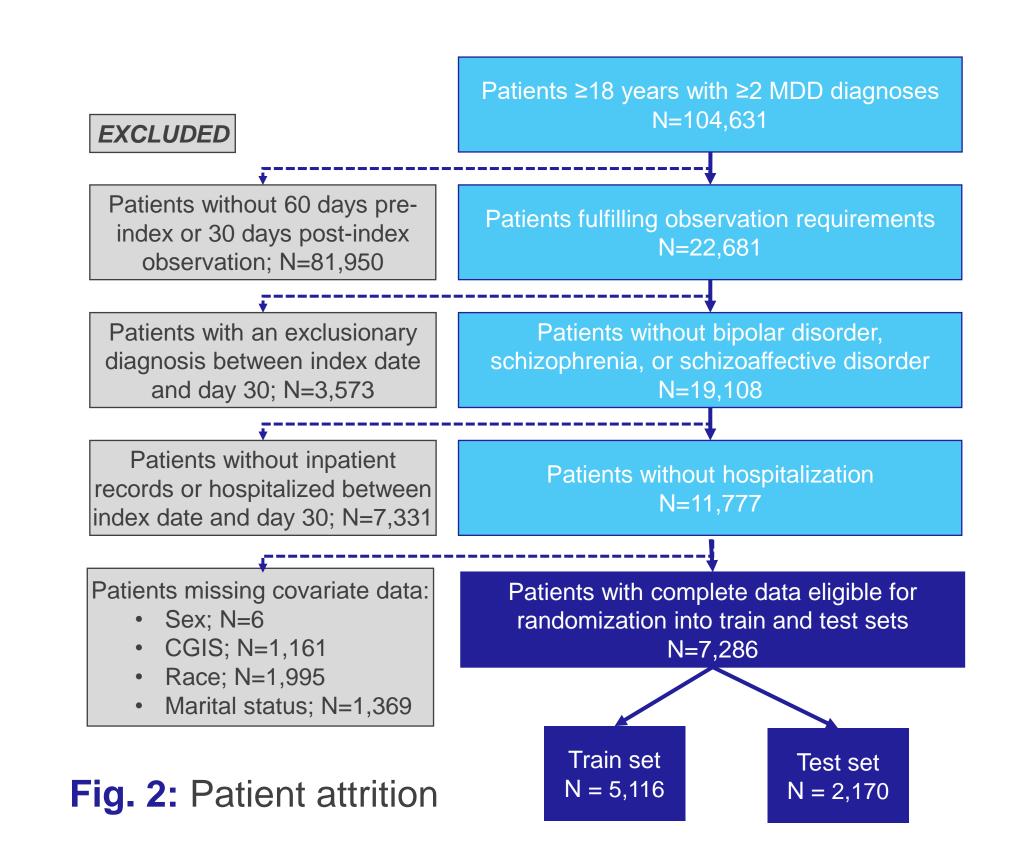
### Limitations

The minimum baseline period of 90 days may not be sufficient to properly select patients with naïve MDD.

The current study did not investigate the effect of pharmacological or non-pharmacological treatments as predictors of hospitalization.

Information such as clinical diagnoses received outside the mental health setting is expected to be missing or under-recorded to the extent that they are not informative for the purposes of this study.

NLP algorithms are good at detecting data when it is recorded, however, a lack of data record doesn't mean 'no', only that it wasn't recorded. Therefore, information on some relevant predictors of MDD-related hospitalizations may be missing or underrecorded.



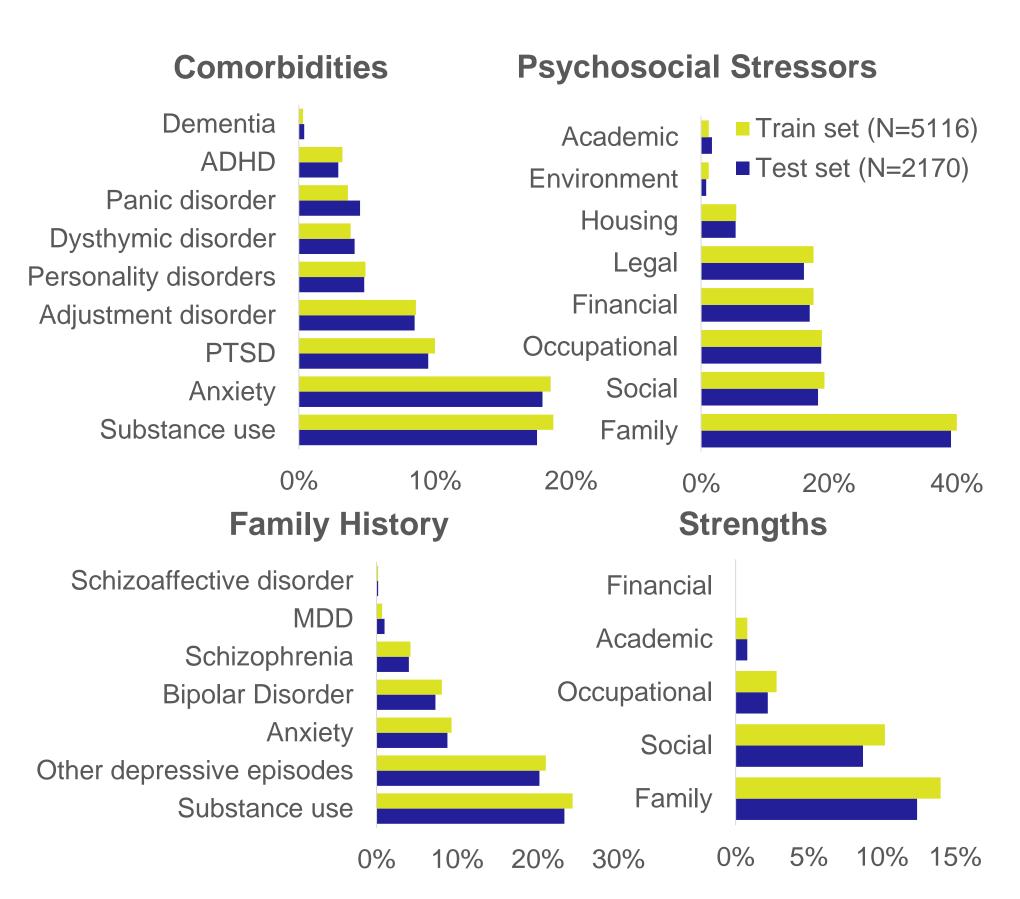


Fig. 3: Baseline clinical characteristics

### Conclusions

Risk assessment may often be reserved for patients with severe MDD or serious mental illness; however, the findings of the present study identified substance use, psychosocial stressors and illness severity as important predictors of hospitalization.

Based on the findings of the present study, substance use (HR 1.70, 95% CI 1.54-1.88), death of a spouse (HR 1.47, 95% CI 1.17-1.84), and family psychosocial stressors (HR 1.35, 95% CI 1.23-1.49) are among the strongest predictors of hospitalization in newly-diagnosed MDD patients.

An EHR tool that allows clinicians to document psychosocial stressors in addition to other risk factors, and systematic training of behavioral health care providers in risk assessment are two areas for improvement.

#### MODEL SELECTION

- 10-fold elastic-net regularized Cox models were fitted, and performance was measured by C-index
- Regularization parameter was chosen such that the CV error is within one standard error (SE) of the minimum and covariates with non-zero coefficients were entered into a final Cox model without regularization; Fig. 4 shows the final model fit in the train set

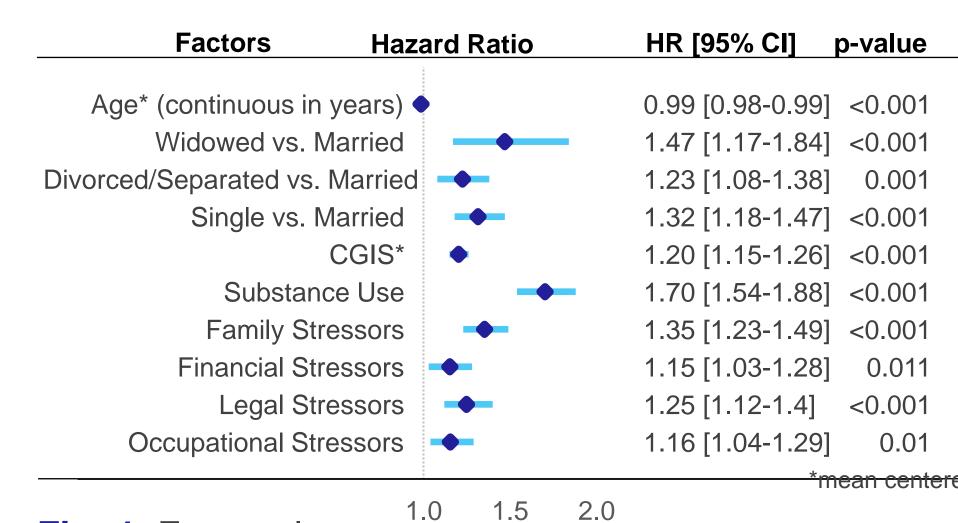


Fig. 4: Forest plot

# MODEL PERFORMANCE

- The model performed well in the train and test sets with C-index 67.8% (CV) and 67.2; Fig. 5
- Calibration slope in the test set was 0.91 (SE= 0.055), close to target value of 1, indicating the model is well-calibrated

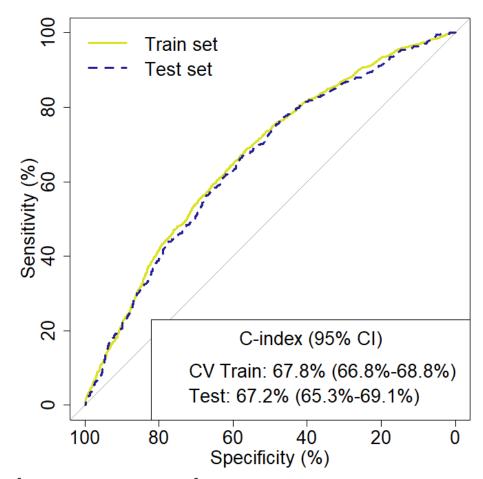


Fig. 5: Receiver operating curves

- Walsh, C. G., Johnson, K. B., Ripperger, M., Sperry, S., Harris, J., Clark, N., Fielstein, E., Novak, L., Robinson, K., & Stead, W. W. (2021. Prospective Validation of an Electronic Health Record-Based, Real-Time Suicide Risk Model. JAMA network open, 4(3, e211428. https://doi.org/10.1001/jamanetworkopen.2021.1428
- 2. Schmitz, W. M., Jr, Allen, M. H., Feldman, B. N., Gutin, N. J., Jahn, D. R., Kleespies, P. M., Quinnett, P., & Simpson, S. (2012. Preventing suicide through improved training in suicide risk assessment and care: an American Association of Suicidology Task Force report addressing serious gaps in U.S. mental health training. Suicide & life-threatening behavior, 42(3, 292–304. https://doi.org/10.1111/j.1943-278X.2012.00090.x

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