DR. LINDSEY COLMAN MCKERNAN (Orcid ID : 0000-0001-9419-8502)

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Outpatient Engagement Lowers Predicted Risk of Suicide Attempts in Fibromyalgia

Lindsey C. McKernan, Ph.D.,[1-2] Matthew C. Lenert, B.A.,[3] Leslie J. Crofford, M.D.,[4] & Colin G. Walsh, M.D., M.A.[1,3,4]

[1]Department of Psychiatry & Behavioral Sciences, Vanderbilt University Medical Center

[2]Department of Physical Medicine & Rehabilitation, Vanderbilt University Medical Center

[3]Department of Biomedical Informatics, Vanderbilt University Medical Center

[4]Department of Medicine, Vanderbilt University Medical Center

RUNNING HEAD: FIBROMYALGIA AND RISK OF SUICIDE

Correspondence concerning this manuscript should be directed to:

Lindsey C. McKernan, Ph.D.

Assistant Professor, Departments of Psychiatry & Behavioral Sciences, Physical Medicine & Rehabilitation

Vanderbilt University Medical Center

Osher Center for Integrative Medicine

3401 West End Avenue, Suite 380

Nashville, TN 37203

Phone: (615) 875-9990 Fax: (615) 936-6144

Email: Lindsey.mckernan@vanderbilt.edu

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Abstract

Objective: Fibromyalgia (FM) patients are 10x more likely to die by suicide than the general population. The purpose of this study was to externally validate published models predicting suicidal ideation and attempts in FM and identify interpretable risk and protective factors for suicidality unique to FM.

Methods: This is a case-control study of large-scale EHR data collected from 1998-2017, identifying FM cases with validated PheKB criteria. Model performance was measured through discrimination including area under the receiver operating characteristic (AUC), sensitivity, specificity, and through calibration including calibration plots. Risk factors were selected by L1-penalized regression with bootstrapping for both outcomes. Secondary utilization analyses converted time-based-billing codes to equivalent minutes to estimate face-to-face provider contact.

Results: We identified 8,879 individuals with FM, with 34 known suicide attempts and 96 documented cases of suicidal ideation. External validity was good for both suicidal ideation (AUC=0.80) and attempts (AUC=0.82) and excellent calibration. Risk factors specific to suicidal ideation included polysomatic complaints such as fatigue (OR=1.29, 95%CI 1.25-1.32), dizziness (OR=1.25, 95%CI 1.22-1.28), and weakness (OR=1.17, 95%CI 1.15-1.19). Risk factors specific to suicide attempt included obesity (OR=1.18, 95%CI 1.10-1.27) and drug dependence (OR=1.15, 95%CI 1.12-1.18). Per utilization analyses, those with FM and no suicidal ideation spent 3.5x more time in follow-up annually, and those without documented suicide attempts spent over 40x more time face-to-face with providers annually.

Conclusion: This is the first study to successfully apply machine learning to reliably detect suicidality in FM, identifying novel risk factors for suicidality and highlighting outpatient engagement as a protective factor against suicide.

Keywords: fibromyalgia, suicide, machine learning, risk factor

Significance and Innovation

- This is the first study to successfully apply machine learning to suicidality in fibromyalgia, identifying novel risk factors for both suicidal ideation and suicide attempts.
- Risk factors for suicidal ideation included polysomatic complaints such as fatigue, dizziness, and weakness.
- Risk factors for suicide attempt include drug dependence and obesity.
- Fibromyalgia patients without documented suicidality spent up to 40x more time with providers annually, highlighting the importance of outpatient engagement as a protective factor against suicide.

Every day, 120 people die from suicide in the United States.[2] At minimum, the presence of chronic pain doubles suicide risk,[31] and evidence suggests that specific pain disorders, such as fibromyalgia (FM) further elevate suicide risk.[3,4] FM is characterized by the presence of widespread pain with cognitive dysfunction, fatigue, and sleep difficulty.[5] Collectively, FM patients are up to 10.5 times more at risk of death from suicide than the general population,[6] and 3.3 times more at risk than other chronic pain patients.[7] Similarly, FM patients have high rates of suicidal ideation, thoughts and behaviors (SITBs) including suicidal ideation (33-48%), ideation with active intent (6-8%),[8,9] and non-fatal suicide attempts by poisoning (17%).[8] The risk factors for SITBs in FM are difficult to study prospectively because of under-reporting worldwide,[10] stigma,[11] or lack of healthcare access.[11] Moreover, SITBs in FM may be misclassified as accidental deaths[7] (e.g., car accidents) if they are reported at all.[10]

A recent comprehensive review indicated that the presence of chronic pain alone, regardless of demographics, pain severity, or mental health, doubles suicide risk. Further, this review suggested that general demographic risk factors for suicide (e.g. gender, age, marital status, education level) may not translate to chronic pain populations, and that it is possible that other modifiable factors specific to pain may increase suicide risk.[31] Very little – and conflicting – information exists detailing risk factors for suicidality in FM patients in part because of reliance on small, prospective cohorts as the mainstay of study in this domain. In FM

populations specifically, risk factors identified thus far include pain severity,[4,7,12,13] widespread pain,[14] disease severity,[6] younger age,[7] depression/anxiety,[8,9,15] sleep dysfunction,[3,8] and mood disorder.[16] A point of debate is the relative contribution of pain severity versus psychiatric co-morbidity to suicidality in FM, and initial (differing) findings may suggest that the presence of psychiatric co-morbidity does not fully explain the increased risk of suicide in FM, may only apply to some patients, and that both pain-specific and general risk factors for elevated suicide risk need to be considered when examining suicide risk in FM.[21] Limitations of existing research include generalizability, small sample sizes, self-reported symptoms and diagnoses, low response rates, or inability to assess individuals over time. Similar to other conditions, risk factors for suicidal ideation and suicidal attempts may differ.[17] The preponderance of studies occur in tertiary specialty clinic settings and may not reflect settings in which large quantities of healthcare are delivered such as primary care. Lastly, population characteristics that are common in FM and known to elevate suicide risk, such as post-traumatic stress[18] and the presence of multiple pain conditions[16] have yet to be investigated.

One path to study SITBs remains large-scale retrospective analyses of clinical electronic health record (EHR) data including predictive modeling. For example, we have validated predictive models of suicide attempt risk on a broad, heterogeneous population of adults[19] and adolescents[20] at a large academic medical center. Generalized models like these may be personalized to high-risk populations (e.g., FM) to 1) predict risk *before* harm occurs and 2) identify risk and protective factors specific to these groups. Research to-date has yet to assess risk factors for SITBs concurrently or longitudinally in routinely collected EHR data in patients with FM. It is unknown whether these general algorithms will accurately identify risk in FM or if the resultant risk patterns differ in FM compared to other groups. Such risk patterns, once quantified, may suggest targets of clinical intervention.

Studies of clinical EHR data are well suited to address these knowledge gaps. Moreover, they also present opportunities to develop clinical tools to identify and prevent SITBs using these same data. To bridge both accurate risk identification with interpretable, *actionable*, intervention, it is paramount to both identify who is at risk and to consider *why* risk profiles look as they do. We hypothesize that in translating existing models of suicide risk to a FM population, novel predictors will need to be considered *specific* to this cohort. Existing evidence notes general risk factors for suicide do not always translate to chronic pain populations,[31] and that pain sub-populations may have different risk factors for suicidality and need to be studied separately to enhance prevention efforts.[21]

Coupling literature- and domain-knowledge of SITBs in FM with validated machine learning algorithms of suicide attempt risk,[19] the purpose of this investigation was to assess the external validity of published models in predicting suicidal ideation and attempts in FM and use novel analyses to identify interpretable risk profiles unique to FM. These latter findings will inform prevention strategies directly.

Materials and Methods

Clinical Predictive Modeling/Clinical Phenotyping (adapted from Walsh et al. 2017)

Data Collection

Clinical data were collected from the electronic health record at Vanderbilt University Medical Center (VUMC) using the de-identified clinical data repository known as the Synthetic Derivative.[22] This repository includes clinical data such as diagnoses, demographics, clinical text, laboratory values, and more collected over twenty years at Vanderbilt on over 2.8 Million individuals with rich data available on over 1 Million patient lives.

Prior model development of the general suicide attempt risk algorithm has been described.[19] In brief, candidate charts were identified using self-injury International Classification of Diseases, version 9 (ICD9) codes (E95x.xx) for adults in the Synthetic Derivative and labeled by multiple experts to establish a reliable gold standard. These 3,250 cases of suicide attempt were compared to a control cohort of 12,695 adults drawn from the general population of VUMC. These charts were identified from a minimum of three visits in the medical center and aged over eighteen years. This cohort defined the published algorithm reported prior with an internal validation c-statistic as high as 0.92 to predict suicide attempt in 7 days. The original algorithm was designed to predict suicide attempt. In this investigation, we seek to extend its reach to predict both suicidal ideation without attempt and suicide attempt in a FM cohort with no additional training.

External Validation Data Collection for this Study

We defined the FM cohort through a validated phenotype publicly available in PheKB.[23] The phenotype uses a combination of diagnostic codes and text phrases to identify cases of true FM. We applied this phenotype to the VUMC population and selected only those 1) meeting PheKB criteria for FM and with 2) more than three visits to VUMC over at least 6 months.

To ensure true external validity testing on the FM cohort, we returned to the initial modeling experiment and removed any patients in the FM cohort from the general model algorithm training set. The general algorithm was then refitted and internally validated after assurance that there were no patients in common in the general cohort.

FM Specific Feature Selection

We combined domain knowledge and existing research to inform feature selection in a FM-specific model of SITBs. First, we conducted a review of existing literature to extrapolate known risk factors (features) and with informatics co-authors (CW and MCL), incorporated those not in the existing model as new risk factors. Second, we used clinical expertise from authors with direct experience working with FM and SITBs (LCM and LJC) to include additional features derived from patient-provider interactions not accounted for in previous research or the existing algorithm. In brief, we added model features using regular expressions from notes and diagnostic codes relevant to FM. These features included post-traumatic stress, trauma exposure, violence exposure, abuse exposure (sexual and non-sexual), sleep dysfunction, marijuana use, abdominal pain, and polysomatic complaints. The Appendix includes a table of novel features added to the model, their basis, and specific codes used to derive them.

Data Preprocessing and Missing Data Handling

Clinical data were preprocessed as reported prior and as described in the Appendix to support external validity testing and replication here. Missing data were rare because the variables measured as counts – diagnoses, medications and visits – were imputed to zeroes if not present. Zip codes were missing in 7.5% of charts and race was missing in 0.05% of charts. Multiple imputation was used to impute missing values in those instances.[24]

External Validity Testing of General Algorithm on FM Cohort

Data on the FM cohort was preprocessed identically to the internal validation sample and included two outcomes and multiple time points of prediction – 1) suicidal ideation, and 2) attempts at 30 days from the last clinical encounter. The general suicide attempt algorithm was then applied to these data to obtain a posterior probability of suicide attempt risk. This

predicted probability was used to validate both suicidal ideation and suicide attempt outcomes in this cohort. External validity testing includes not just testing an algorithm on a new set of input data but also testing its generalizability to predict different outcomes. For example, the Charlson Comorbidity Index, a common risk score originally validated to assess mortality risk, has been used in a panoply of new predictive tasks such as hospital readmission risk. We would not equate suicidal ideation and behaviors like attempts clinically, but we hypothesized that some shared risk factors between ideation and attempts suggest that an algorithm designed to predict suicide attempts specifically would also generalize to predict suicidal ideation.

Recalibration in External Validation

The general model development cohort was enriched to a ratio of four controls for every case in order to optimize model performance. Because outcome prevalence in FM (~1%) was different than that in the enriched, internal development set (~25%), recalibration of external predictions was performed using logistic calibration as we have used in other predictive domains.[25] This method passes the predictions through a logit function trained on the prevalence in the new setting, in this case the FM cohorts. The resultant predictions are subsequently calibrated properly to indicate that a 40% risk of an outcome correlates with 4 of 10 similar individuals in the new setting actually having that outcome. This latter example is the definition of good calibration – whether predictions reflect real outcome rates.

Development and Validation of the Novel Explanatory FM Suicide Risk Algorithm

We used the bootstrapped L-1 penalized regression (BoLASSO[26]) with two levels of bootstrapping to gain insight into which factors may have the most influence on suicide risk for FM patients. In brief, L-1 penalized regression (LASSO) is well-accepted for its ability to select a small number of important predictors across complex data. The BoLASSO enhances this technique with resampling to yield a set of influential predictors and an ability to obtain

interpretable test statistics for those same predictors. We tuned conservatively the BoLASSO to select only those features that were chosen in 80% of bootstraps. Full details can be reviewed in the Appendix.

Performance Evaluation

Performance was measured through discrimination including Area Under the Receiver Operating Characteristic (AUC), sensitivity/recall, specificity, and precision and also through calibration metrics including calibration plots, calibration slope/intercept, and scoring rules.

Utilization Analyses

With preliminary results identifying differential healthcare utilization as protective factors of SITBs (see results), we conducted a secondary analysis of healthcare encounters in study cohorts. We counted Evaluation and Management (E&M) CPT Codes, 99211-99215, Health and Behavior (H&B) Codes, 96150-96154, and Outpatient Psychiatry CPT Codes, 90791-90792, 90832-90840, 90846-90849, 90853, for each study cohort. We linked E&M codes to equivalent minutes in time-based billing to estimate time spent in follow-up.

Results

Using the validated PheKB definition of FM,[23] we identified 14,430 patients from January 1998 – November 2017 with the phenotype. After censoring only those patients with at least three visits over a six month period, there were 8,879 patients with 34 known attempts, 0.4% outcome prevalence, and 96 documented cases of suicidal ideation, 1.1% outcome prevalence. The baseline characteristics of these cohorts are shown in Table 1.

External Validation of Published Model

The general suicide attempt prediction model predicted both suicidal ideation and suicide attempts in a novel FM cohort with good discrimination. The Areas Under the Receiver Operating Characteristic (AUCs, Figure 1) were 0.82 for suicide attempts and 0.8 for suicidal ideation. Sensitivity and specificity varied based on threshold of case positivity and ranged from 0.01 to 1 for specificity for both outcomes and 0 to 1 for sensitivity for attempts and 0 to 0.99 for ideation. Precision and recall/sensitivity were also assessed and precision was low for both outcomes given the extreme case imbalance in this context. Maximum precision was 0.08 for attempts and 0.14 for suicidal ideation (Precision-Recall Curves shown, Figure 2).

Figure 1 Placeholder

Figure 2 Placeholder

Calibration is an important metric to illustrate whether predicted probabilities reflect true prevalence in a population. The externally valid predictions demonstrated excellent calibration performance after recalibration to the outcome prevalence in the novel FM cohort. Risk concentration is the proportion of cases of ideation or attempts by binned quantile of risk. The proportions of cases of suicidal ideation by predicted bin of risk are shown (Figure 3) and indicate the majority of cases of ideation fall into the highest predicted bins of risk, as anticipated.

Figure 3 Placeholder

Risk Factors of Suicidal Ideation and Suicide Attempt in FM

The BoLASSO selected both risk and protective factors for both outcomes. Risk factors are summarized by category in Table 2. The risk categories for suicidal ideation included: polysomatic complaints [fatigue (OR=1.29, 95%CI 1.25-1.32), dizziness (OR=1.25, 95%CI 1.22-1.28), and weakness (OR=1.17, 95%CI 1.15-1.19)], serious and persistent mental illness, [e.g., Bipolar disorder Not Otherwise Specified (OR=1.18, 95%CI 1.17-1.20)], and inpatient utilization (OR=1.5, 95%CI 1.46-1.53). Concomitant categories for suicide attempt were: drug dependence [e.g., Cocaine Dependence (OR=1.18, 95%CI 1.1-1.27)], obesity (BMI 50-59, OR=1.15, 95%CI 1.12-1.18), mental illness [e.g., Recurrent Depression with Psychosis (OR=1.12, 95%CI 1.07-1.18)], and inpatient utilization (OR=1.32, 95%CI 1.27-1.36).

We note that commonly held risk factors such as post-traumatic stress disorder, histories of sexual abuse and trauma, and medications like benzodiazepines were all included as potential predictors of SITBs. However, because of the conservatism of our approach to only report those predictors selected over 80% of the time, they were not finally selected in the models summarized here.

Utilization Analysis

We tallied minutes spent in outpatient follow-up in the cohorts in our study and determined that for suicidal ideation, those patients with FM who did *not* have suicidal ideation spent 3.5x more time in follow-up per year than those with documented suicidal ideation. This ratio was even more pronounced for suicide attempters. Individuals with FM who did *not* have documented suicide attempts spent over 40x more time with outpatient providers than those with documented attempts. We then assessed psychiatry and mental health behavior and intervention codes (CPTs 90791, 90846, 96150-96154) and determined that, while these were

small proportions of the overall study cohort (0.1~2%), none of the patients with these encounters had a documented suicide attempt. Notably, the majority of mental health behavior and intervention codes were billed for those patients with ideation but none with subsequent attempts. These data may suggest a straightforward albeit non-trivial prevention strategy enabled by predictive models that suggest patients on whom outpatient engagement should be established.

Discussion

This study is the first to apply machine learning to suicidality in FM in the context of clinical domain expertise to obtain interpretable patterns of risk. We demonstrated that generalizable predictive models of SITB risk perform well in predicting SITBs in (attempts - AUC ~0.82, maximum precision 0.08, ideation – AUC 0.80, maximum precision 0.14). Notably, the initial algorithm validated externally across a novel cohort and for two different outcomes with no further model refitting. That is, a model predicting suicide attempts alone performed well to predict both suicidal ideation and suicide attempts.

Adding disease-specific risk factors in a rigorous statistical experimental design, the BoLASSO, highlighted different risk patterns for suicidal ideation versus suicide attempts in FM. Both ideation and attempt risk was conferred by younger age, serious and persistent mental illness, comorbid medical illness, and frequent inpatient admission. Polysomatic complaints (e.g., fatigue, dizziness, and weakness) typified risk of suicidal ideation, while drug dependence and comorbid obesity increased the risk of suicide attempt. Of note, we did not have the capability to capture pain severity or duration in this context though it remains a consideration for future work.

This analysis suggests that unique profiles of suicide risk exist in FM. In our sample, profiles of suicide risk in FM combine those indicated in previous investigations 1) in the general population (i.e. obesity, younger age, frequent inpatient admission, severe and persistent mental illness), 2) in chronic pain (illicit drug use, co-morbid health conditions), and 3) in fibromyalgia (mood disorder) with novel risk factors identified in this study (polysomatic complaints including fatigue, dizziness, weakness). Further, our investigation shows that patterns of suicide risk differ for suicidal ideation and suicide attempt in FM, prompting further investigation.

Notably, frequent outpatient utilization (clinic follow-up) and increased rates of outpatient prescriptions for both mental and medical illnesses served as *protective* factors in both groups. Additionally, preventive medications and vaccinations, typical of longitudinal outpatient engagement, lowered risks of SITBs in FM. Subsequent utilization analyses showed a dramatic difference in follow-up time – up to 40x increased time spent with providers in follow-up for the low risk group compared to those with SITBs – across outpatient settings including primary care, medical specialty, and mental health clinics. There was a concomitant increase in use of outpatient resources like health and behavioral interventions in the low risk cohort. Outpatient H&B codes were more likely in those with suicidal ideation without evidence of subsequent attempts, potentially indicating a preventive effect of H&B intervention in this high-risk cohort. These findings suggest further research in patterns of outpatient engagement with respect to suicidality may be indicated.

This work extends existing research by quantifying, characterizing, and predicting SITB risk in a population with clinical data science for the first time. It confirms and builds upon known risk factors of SITBs in FM based on both literature review and clinical expertise. Building on existing research, we also highlight actionable foci of risk management strategies (e.g., polysomatic complaints, pharmacologic therapies) and the buffering effect of outpatient engagement to lower predicted risk.

Strengths of our study include using validated models applied to a valid phenotype of FM in a large EHR cohort. The models were designed to scale to any clinical setting with EHR data, facilitating external validation in this study. Applying these methods to a large academic medical center allowed us to sample patients at all points of care, assessing both known general and disease-specific risk factors concurrently. In addition to reviewing investigations to-date, we combined expertise in machine learning, rheumatology, and psychology to identify additional patient characteristics to clinically-inform risk prediction and interpret results.

These findings should be interpreted in light of study limitations. We relied on a single major academic medical center for study data. Our overall sample size was relatively small; however, this is reasonable given the low base-rate phenomenon of SITB in FM (in our cohort, ~0.4%). External validity results of this investigation are encouraging, but studies of reproducibility and generalizability in new settings are important steps of future work. In working with EHR data, there is always a risk of misclassification. Our reliance on the suicidal ideation codes is typical of this literature, but codes are an imperfect surrogate for true SITBs. Suicidal ideation remains at risk of under-reporting. We report a 1.1% prevalence of documented suicidal ideation in this cohort. Under-documentation occurs from multiple potential sources: 1) patient hesitancy to report symptoms; 2) lack of provider inquiry; 3) billing workflows failing to document diagnostic codes even if the latter two have occurred. Other studies in fibromyalgia reliant on patient self-report have been associated with higher rates. Future analyses should address whether these differences in prevalence result from differences in self-report compared to retrospective EHR analyses, under-reporting, incomplete documentation, or innate differences in our cohort compared to those in other health systems or countries. An existing limitation of replicable machine learning methods is the reliance on structured data within the health record to assess for patient characteristics that inform outcomes. While this permits replicability/reproducibility and the potential for larger-scale

investigations across networks, nuance can be lost in additional risk factors that may exist in "unstructured" data such as text of patient notes (versus a diagnostic code, for example). Experts are addressing this limitation by processing clinical text through natural language,[27] which remains a future direction for this work.

While our current efforts focus on identifying risk, the ultimate goal is to translate these findings to actionable methods in clinical settings to enhance suicide prevention. A clear signal from this investigation is the importance of simply maintaining outpatient contacts over time to reduce risk of SITBs. Predictive models like ours may play a role in identifying those patients who are both at risk of SITBs and who have been lost to follow-up. Enhancing outpatient continuity with at-risk patients is an active area of prevention in military and civilian settings and in diverse diseases.[20,28,29] The gold standard for pain treatment is multimodal therapy, including psychological approaches to pain management.[32] Cognitive behavioral therapy in particular has shown to improve outcomes in FM by improving mood, pain-related disability, and pain severity at follow-up.[33] Given our findings that outpatient engagement of any type including mental health engagement may attenuate risk of suicide attempt in those with suicidal ideation, we suggest connection to mental health resources such as cognitive-behavioral therapy for FM patients with suicidal ideation to enhance outpatient engagement and provider connection.

Providers have expressed helplessness and frustration being unable to "intervene" with complex FM patients.[30] This work shows that the contact itself may have intrinsic benefits that decrease the likelihood of suicidality in this population.

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Table 1

Baseline Patient Characteristics

	Suicide Attempts		**Suicidal Ideation**	
	Cases, No. (%); N = 34	**Controls, No. (%); N = 8,845**	**Cases, No. (%); N = 96**	**Controls, No. (%); N = 8,788**
Gender				
Male	3 (9)	805 (9.5)	15 (16)	796 (9)
Female	31 (91)	8,040 (90.5)	81 (84)	7,992 (91)
Race				
White	30 (88)	7,768 (88)	86 (90)	7,719 (88)
Black	4 (12)	796 (9)	10 (10)	788 (9)
Asian	0 (0)	141 (1.5)	0 (0)	42 (0.5)
Alaskan/Native American	0 (0)	0 (0)	0 (0)	20 (0.2)
Declined to Respond	0 (0)	0 (0)	0 (0)	140 (1.5)
Unknown/Not Recorded	0 (0)	140 (1.5)	0 (0)	79 (0.8)
Age				
Median (Standard Deviation), in years	45 (9.0)	57 (14.2)	50 (13.7)	57 (14.1)
Utilization Mix in Preceding Year				
Outpatient, Mean Visits (Percentile)	7.1 (73)	14.6 (66)	23.3 (60)	14.5 (65)
Inpatient, Mean Visits (Percentile)	5.8 (62)	1.3 (84)	10.7 (72)	1.2 (84)
Comorbidity Mix				
Attention Deficit Disorders with Hyperactivity	0 (0)	149 (1.7)	10 (10)	466 (5)
Post-traumatic Stress Disorder	6 (18)	525 (6)	31 (32)	498 (6)

Oppositional Defiant Disorder	0 (0)	3 (0.03)	0 (0)	2 (0.02)
Generalized Anxiety Disorder	3 (9)	679 (8)	13 (14)	633 (7)
Asthma	8 (24)	1,693 (19)	25 (26)	1,676 (19)
Episodic Mood Disorders	3 (9)	446 (5)	96 (100)	431 (5)
Bipolar	6 (18)	522 (6)	35 (36)	496 (6)
Schizophrenia	1 (3)	91 (1)	8 (8)	82 (1)
CHF	1 (3)	643 (7)	12 (13)	639 (7)
DM	0 (0)	84 (1)	2 (2)	80 (1)
COPD	1 (3)	467 (5)	11 (11)	464 (5)
Malignancy	0 (0)	89 (1)	0 (0)	89 (1)
Liver Dz	0 (0)	29 (0.3)	0 (0)	29 (0.3)

Table 2

Risk Factors for Attempts and SITBs

	Factor Source	Suicidal Attempts Odds Ratio 95% CI	Suicidal Ideation Odds Ratio 95% CI	Examples
Comorbid Medical Illness				
Anti-Infective Drugs	Medication List	[1.16, 1.20]	-	E.g., ciprofloxacin, gentamycin
Thiazolidinediones	Medication List	[1.12, 1.15]	-	E.g., pioglitazone
Non-Nucleoside Reverse Transcriptase	Medication List	[1.11, 1.14]	-	E.g., etravirine
Selective Estrogen Receptor Modulator	Medication List	[1.05, 1.11]	-	E.g., raloxifene
Antiepileptics - Hydantion Derivatives	Medication List	[1.01, 1.06]	-	E.g., phenytoin, fosphenytoin
Atrial flutter	ICD-10 Diagnosis	-	[1.11, 1.15]	ICD-9, 427.32
Obstructive Chronic Bronchitis without Exacerbation	ICD-10 Diagnosis	-	[1.09, 1.13]	ICD-9, E.g., 491.21-491.22
Diabetic Retinopathy	ICD-10 Diagnosis	-	[1.08, 1.14]	ICD-9, E.g., 362.01
Chemotherapy - Pyrimidine Analogues	Medication List	-	[1.08, 1.11]	E.g., gemcitabine, fluorouracil, cytarabine
Ulcer of Lower Limb	ICD-10 Diagnosis	-	[1.05, 1.14]	ICD-9, 707.10
Ulcer of Ankle	ICD-10 Diagnosis	-	[1.05, 1.11]	ICD-9, 707.13
History of Septic Shock	ICD-10 Diagnosis	-	[1.04, 1.12]	ICD-9, 785.52
Diabetes with Other Specified Manifestations, Type I	ICD-10 Diagnosis	-	[1.04, 1.11]	ICD-9, 250.81
Immune Thrombocytopenic Purpura	ICD-10 Diagnosis	-	[1.03, 1.14]	ICD-9, 287.31
Blood Clots - AC DVT/Embolism in Lower Extremities	ICD-10 Diagnosis	-	[1.03, 1.07]	ICD-9, 453.41
Cerebral Embolism with Infarction	ICD-10 Diagnosis	-	[1.01, 1.09]	ICD-9, 434.91
Hypersensitivity Angiitis	ICD-10 Diagnosis	-	[1.01, 1.09]	ICD-9, 446.20

Drug Dependence				
Cocaine Dependence, Unspecified	ICD-10 Diagnosis	[1.10, 1.27]	-	ICD-9, 304.20
Inpatient Utilization				
Inpatient Visits Within the Past Year	Visit Count	[1.27, 1.36]	[1.46, 1.53]	
Mental Illness				
Borderline Personality Disorder	ICD-10 Diagnosis	[1.16, 1.20]	-	ICD-9, 301.83
Indole Derivatives (Anti-Psychotics)	ICD-10 Diagnosis	[1.10, 1.15]	-	E.g., clomipramine, imipramine
Recurrent Depression with Psychotic Features	ICD-10 Diagnosis	[1.07, 1.18]	-	ICD-9, E.g., 296.31, 296.16
Bipolar Disorder NOS	ICD-10 Diagnosis	-	[1.17, 1.20]	ICD-9, E.g., 296.80
Bipolar I Disorder - Manic, with Psychotic Features	ICD-10 Diagnosis	-	[1.13, 1.17]	ICD-9, E.g., 296.43-296.44
Monoamine Oxidase Inhibitors	ICD-10 Diagnosis	-	[1.04, 1.06]	E.g., tranylcypromine, phenelzine
Obesity				
BMI 50.0-59.9	ICD-10 Diagnosis	[1.12, 1.18]	-	
Morbid Obesity	ICD-10 Diagnosis	[1.01, 1.12]	-	
Polysomatic Complaints				
Fatigue	ICD-10 Diagnosis	-	[1.25, 1.32]	ICD-9, 780.7; ICD-10, R53%
Dizziness	ICD-10 Diagnosis	-	[1.22, 1.28]	ICD-9, 780.4, 438.85; ICD-10 R42%
Weakness	ICD-10 Diagnosis	-	[1.15, 1.19]	ICD-9, 728.87; ICD-10 M62.81

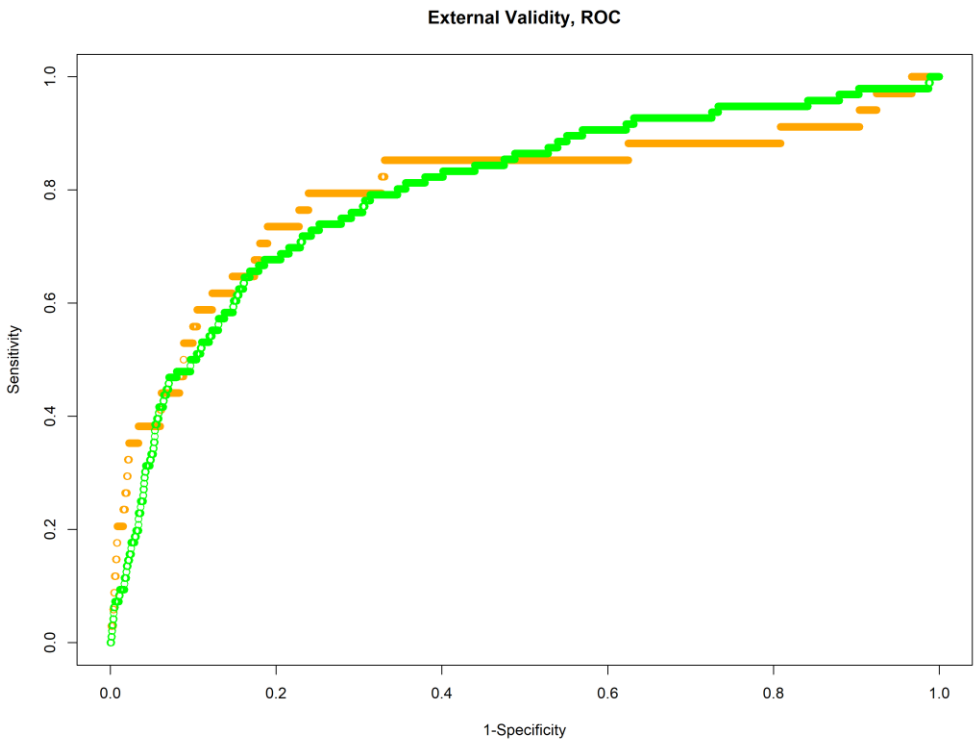

Figure 1: Discrimination Performance: Receiver Operating Characteristic Curves

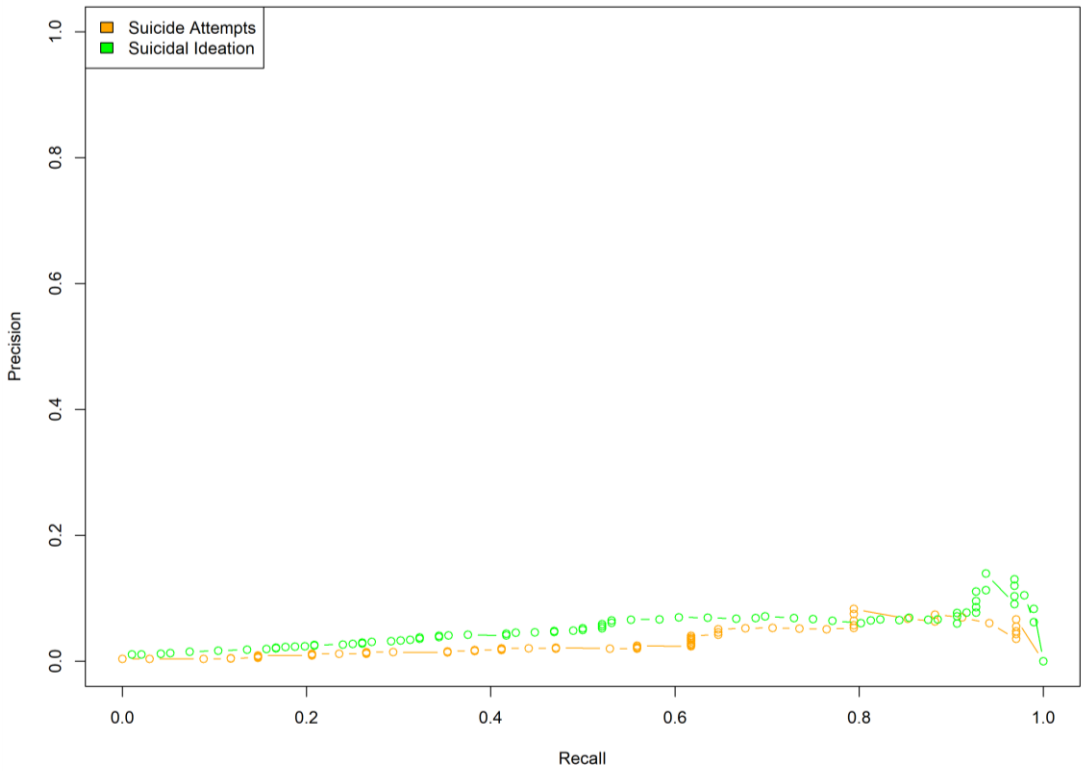

Figure 2: Precision-Recall Curves

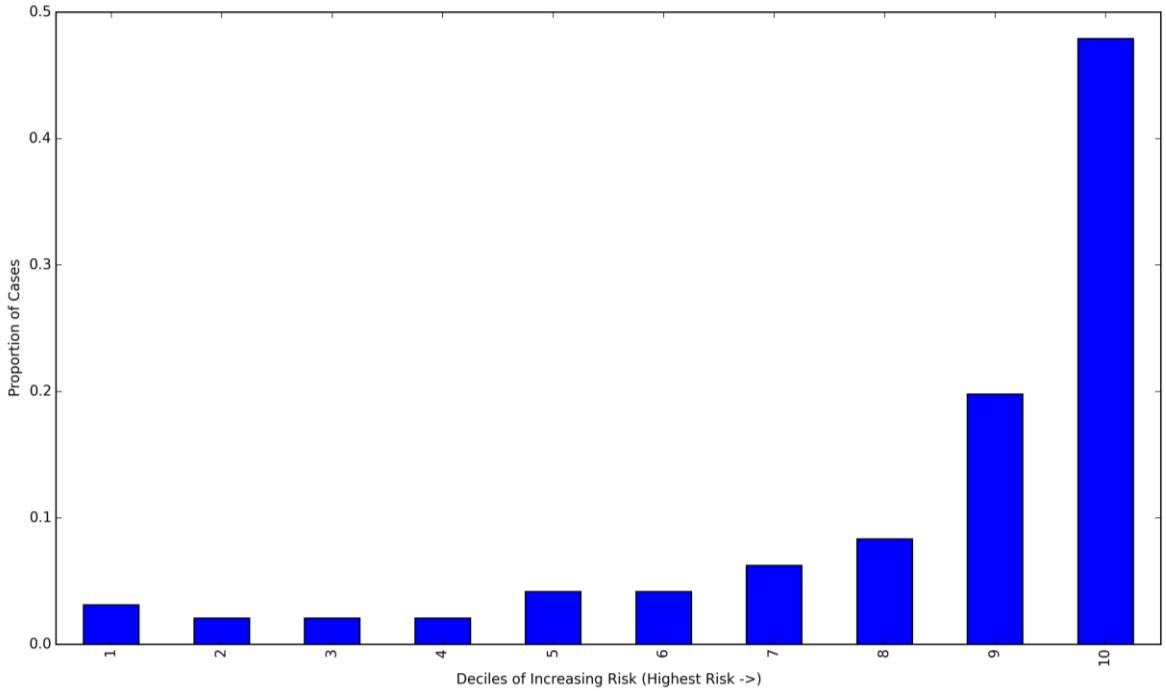

Figure
3: Proportions of Cases of Ideation by Predicted Bin of Risk