The influence of mental health disorders on diabetic neuropathy pain

INTRODUCTION

Diabetic neuropathy (DN) is a condition characterized by the compression or damage to nerves due to prolonged hyperglycemia. It is a significant complication of diabetes, both type 1 and type 2, appearing in nearly 50% of all diagnosed patients (Feldman et al., 2019). Risk factors for diabetic neuropathy include poor glycemic control, hypertension, hyperlipidemia, and smoking. The most common form of diabetic neuropathy is peripheral, with numbness, tingling, and burning sensations affecting the feet, arms, hands, and legs (Tesfaye et al., 2010). The intensity and nature of the pain from these sensations are often chronic enough to interfere with patients on a daily basis.

Similarly, in patients diagnosed with mental health disorders, there is a frequent report of chronic pain, which causes disruptions to daily life. This chronic pain can even exist without any physical damage, and can manifest as headaches, muscle tension, body aches, etc. With mental health disorders commonly altering the way in which the brain processes signals, there is an increased sensitivity to pain (Kioskli et al., Callaghan et al.,Feldman et al). Due to the lack of clarity of origin, it is difficult to treat chronic pain in individuals with mental health disorders.

One common way this pain is assessed in clinical settings and research is through using the Numeric Rating Scale (NRS). This is a standardized 11-point scale measuring pain intensity consisting of a number from 0 through 10–0 indicating “no pain” and 10 indicating the “worst imaginable pain” (Schiurring, n.d., Jacques, 2023).

Chronic pain associated with DN has been closely linked to patients’ physical health, mental health, and emotional well-being. Individuals with chronic pain are at a higher risk of developing depression and anxiety (Rhode et al., 2022). The physiological mechanisms underlying this interaction are explained by evidence showing that neuropathy damages the autonomic nervous system while stimulating the sympathetic nervous system (Speer, 2023). This dysregulation can cause symptoms of mental health disorders to present in patients. Mental health conditions such as depression can intensify the perception of pain through negative thinking and hyperactivation of pain pathways (Thompson et al., 2016). This co-occurrence of chronic pain from diabetic neuropathy and symptoms from mental health disorders complicates pain management efforts in case treatment.

Current literature illustrates the complex nature of DN and co-occurring mental health disorders. In patients with DN and depression, there may be a phenomenon in which a feedback loop is created where chronic pain increases depressive symptoms, which in turn heightens pain sensitivity (Puhalla, 2016, Thompson et al., 2016). In patients with DN and anxiety experience, there may be increased distress and disturbances leading to greater difficulty in managing symptoms (Speer, 2023). Additionally, in patients with DN and bipolar disorder, some show that changes in mood complicate pain perception and treatment response (Tesfaye et al., 2010). The coexistence of DN and mental health conditions poses many difficulties with the relationship

between the two, highlighting the need for increased clarity to improve treatment strategies and patient outcomes (Rhode et al., 2022).

The prevalence of diabetic neuropathy has increased since 2015 on a global level, nearly tripling the number of those affected (Speer, 2023). Similarly, the prevalence of mental health disorders has seen a similar increase of about 25% since 2015 (World Health Organization, 2022). The growth in both areas is particularly concerning from a treatment standpoint as both pose their own challenges to pain management (Feldman et al., 2019). Investigating the influence mental health conditions have on pain-related outcomes in patients with diabetic neuropathy can prove to be critical in improving patient outcomes.

For these reasons, there is a likelihood that patients with comorbid DN and depression exhibit increased pain scores and impairment in quality of life (Thompson et al., 2016). Patients with comorbid DN and anxiety exhibit increased pain severity over time (Speer, 2023), whereas patients with comorbid DN and bipolar disorder will exhibit inconsistency in pain-related outcomes (Keck, 2010 ,Tesfaye et al., 2010). The objective of this study is to evaluate the influence of mental health diagnoses on pain outcomes in patients with diabetic neuropathy. Additionally, this study aims to determine if there is a difference in pain-related outcome measures based on a comorbid mental health condition. Gaining insight into these topics will help inform more effective pain management strategies for the physical, emotional and psychological aspects of diabetic neuropathy.

2. METHODS

2.1 Design and Data Structure

This study used retrospective electronic health record data from the Altman Clinical and Translational Research Institute NIGHTINGALE Platform database. The data used was de-identified. From the repository, patient demographics, medical conditions, and patient observations were pulled. The data used for this study was organized on a patient level, with each patient only being represented once, featuring recordings over a 12-month period from the first comorbid diagnosis date. The inclusion criteria for this study were patients diagnosed with type 1 or type 2 diabetic neuropathy and with depression, anxiety, or bipolar disorder with a 12-month record of pain-related outcomes from the earliest comorbid diagnosis date. The exclusion criteria for this study were patients diagnosed with other conditions, such as cancers, cardiovascular disease, and cognitive impairment, that could influence pain, and patients who had surgery within the 12-month period of interest. The available data was selected from patient visits to the UC Health System between January 2015 and July 2024.

Diabetic neuropathies were defined using condition concept IDs 45605403 for type 2 and 45600638 for type 1. Mental health disorders were defined using condition IDs such as 35207157 for depression, 35207170 for anxiety disorder, and 44829925 for bipolar disorder; however, more condition IDs were used. Dates of diagnosis for these conditions are recorded as DN_date and MH_date. The variable DN_MH_date represented the first date both conditions

were recorded in a patient's visit information. The pain-related data, NRS pain score, collected was measured using observational data where the observation concept ID was 4137083. The primary outcome was recorded through the variables month_#_pain_score representing the averaged pain score rating per that month, where # represented the time in month since the DN_MH_date. Furthermore, demographic information was collected for each patient. This information was self-identified by patients during their patient registration. Gender was defined using concept IDs, with 8532 representing females and 8507 representing males. Race was defined using concept IDs, with values including 8516 for black, 8557 for native Hawaiian, 8522 for other, 8515 for Asian, 8657 for Native American, 8527 for white, 646371142 for multiracial, and 8552 for unknown. Ethnicity was defined using concept IDs 38003563 for Hispanic or Latino and 38003564 for Not Hispanic or Latino.

2.2 Statistical Analysis

The statistical analysis for this study involves a longitudinal comparative analysis consisting of multiple parts: descriptive statistics, between group analysis, and within group analysis to evaluate how the presence of a mental health diagnosis influences changes in pain scores over time , from initial comorbid diagnosis through the 12-month period. All statistics analyses were conducted using the cloud platform DataBricks. Patient data was extracted, organized, and filtered using SQL. Analyses were performed using Python and R using a statistical significance of $p < 0.05$.

The mean pain scores used for statistical analysis in this study were calculated monthly per patient based on the average of available NRS pain scores recorded during visits. This calculated variable was used to reduce bias from the frequency of visits a patient may have versus another.

Mixed-effects linear regression was employed to model NRS pain outcomes while accounting for repeated measures in individuals. Participants were organized into groups first based on the type of diabetic neuropathy they were diagnosed with. Patients then were organized into groups based on their comorbid mental health disorder. NRS pain scores were the dependent variablewhile the mental health conditions were the fixed effect.

Pairwise comparisons were conducted to examine differences in mean NRS pain scores across three comorbid diagnosis groups: DN and depression, DN and anxiety, DN and bipolar. This method evaluated if the mean NRS pain scores over 12 months varied by group. Post-hoc analyses were performed to determine which groups differed from each other.

Further, One-way ANOVA and pairwise comparisons were conducted within subgroups to assess how pain outcomes differed across the significant covariates gender, race, and diabetes type.

RESULTS

3.1 Participant characteristics

This study included 1754 patients in the UC Health database who met the inclusion criteria. For each of these individuals, complete data for age, race, gender, diabetes type, and mental health health diagnosis were described (Table 1).

Participants in this study represented four ethnic groups. The highest number of patients identified as White (n = 904, 51.5%) followed by Hispanic or Latino (n = 413, 23.5%), Black (n = 154, 8.8%), Asian (n = 89, 5.1%), and other (n = 194, 311.1 The gender distribution was relatively even between Female (n = 928, 53%) and Male (n = 826, 47%)(Table 1).

Regarding diabetes type, the majority of patients had type 2 (n = 1558, 89%), with the minority having type 1 diabetes (n=196, 11%)(Table 1).

Regarding mental health conditions, those with a depression diagnosis made up the majority of patients (n = 1158, 66%), while anxiety disorders (n = 421, 24%) and bipolar disorder (n = 175, 10%) were less prevalent(Table 1).

3.2 Pain outcomes by mental health condition

To examine the differences in pain scores across the mental health conditions, mean NRS scores were calculated across all time points and compared. The distribution of scores was determined to be not normally distributed, but the residuals were normally distributed and so the Kruskal-Wallis test was used (Fig 1). The Kruskal-Wallis test showed that there was a significant difference in NRS pain scores across patients with different mental health conditions (Figure 2). At baseline ,the first month of comorbid diagnosis, patients with DN and bipolar disorder had a mean NRS score of 4.61 and at month 12, a mean NRS score of 6.32. This trend was similarly seen in those with depressive disorders (4.07 – 5.23) and anxiety disorders (3.63 – 4.15) (Table 3, Fig 3).

A mixed effects model was used to evaluate the relationship between mental health disorders and NRS pain scores over a 12-month observation period. The model was fit using the mental health condition as a fixed effect and the outcome was the NRS over time. The model took into consideration age, gender, diabetes type, and race as covariates. Additionally, random intercepts were used to account for individual variability in groups. Patients with comorbid DN and bipolar disorder reported the highest mean NRS score with a 5.12 and (SE 0.13),followed by patients with comorbid DN and depressive disorders with a mean NRS score of 4.54 (SE 0.04), while patients with comorbid DN and anxiety disorder had a mean NRS score of 4.17 (SE 0.03) (Table 5). Pairwise comparisons with Bonferroni correction showed that those with comorbid DN and bipolar had significantly higher NRS score than those with anxiety (p=0.0007) and those with depression(p=0.024) (Table 4). Pairwise comparisons also showed that there

was a statistically significant difference between those with DN/anxiety and DN/depression. The model identified interactions with the gender, race, and diabetes type covariates. Female patients in this model had significantly higher mean NRS scores than males with a difference of MD = -0.37 ($p < 0.001$) . White patients in this model had significantly lower pain scores (MD = 0.47, $p < 0.001$) than other races. Patients with Type 2 diabetes reported having lower mean NRS scores (MD = -0.26, $p < 0.001$) than those with Type 1 diabetes (Table 2).

3.3 Pain outcomes within groups

The significance in difference across groups suggests that there may be difference in pain trajectories within groups. To explore this, we computed the differences in NRS scores from baseline to month 12 within each mental health group. Paired t-tests were then run to determine if differences within groups are statistically significant. Over the 12-month period, patients with DN and anxiety experienced the smallest increase in NRS scores from month to month, with a MD = 0.042 ($p < 0.001$) increase per month (Fig 4). Patients with DN and depressive disorders experienced an increase in NRS scores with a MD = 0.097 ($p < 0.001$)(Table 3). Those with DN and bipolar disorder reported an increase in NRS scores with a MD = 0.142 ($p < 0.001$) per month. This data suggests that patients with a higher increase in NRS scores over time may be more susceptible to worsening pain perception potentially reflecting underlying challenges in progression or treatment response.

3.4 Pain outcomes by subgroups

Based on both the between and within group analysis, it is likely covariates influence pain across groups. To confirm the presence of significant interaction terms, a reduced model was compared to a full model using the likelihood ratio test. The results of the likelihood ratio test (421.94, df = 24, $p < 0.0001$) encourage further exploration of the relationships between the covariates, mental health conditions, and NRS scores. For each of the covariates, a one-way ANOVA was conducted to examine the differences in subgroups of the mental health conditions.

In regard to race in those with depression, Black patients reported significantly higher NRS scores than White patients (MD = 0.39, $p < 0.001$). Hispanic patients also reported significantly higher pain scores than White patients (MD = 0.33, $p < 0.001$). A similar trend was seen in patients with bipolar disorder, where Black patients had significantly higher pain scores compared to Hispanic (MD = 1.76, $p < 0.001$) and White (MD = 1.10, $p < 0.001$) patients. In those with anxiety, White patients had significantly higher NRS scores compared to Asian (MD = 1.13, $p < 0.001$), Hispanic (MD = 1.41, $p < 0.001$), and Other (MD = 0.66, $p < 0.001$) race groups (Table 6)(Fig 5).

In regard to gender in those with depression, females had an average NRS score 0.34 points higher than males ($p < 0.001$). This difference was most prevalent in patients with bipolar disorder, where females reported pain scores 0.99 points higher than males ($p < 0.001$). In those with anxiety, females again reported higher NRS scores than males with 0.33 ($p < 0.001$)(Table 7)(Fig 6).

In regard to diabetes type in those with depression, those with Type 1 diabetes reported significantly higher pain scores compared to those with Type 2 diabetes (MD = 0.31, $p < 0.001$). Similarly, patients with anxiety and Type 1 diabetes had significantly higher pain scores than those with Type 2 diabetes (MD = 0.42, $p < 0.001$). No significant differences were observed between diabetes types among patients with bipolar disorder (Table 8)(Fig 7).

Further analysis was considered to determine the effect interactions within subgroups had on NRS pain scores. There were many combinations and comparisons with many being statistically significant, but for the purposes of this study, looking into each and every interaction is not feasible (Tables 10,11,12). Instead, future directions may consider this an avenue to explore.

DISCUSSION

Over the observation period for this study, the interplay between mental health disorders and DN proved to be a significant determinant of pain outcomes. Patients with bipolar disorder reported the highest baseline pain scores and demonstrated the worsening over time, compared to those with depression or anxiety. These findings are consistent with studies linking bipolar disorder to heightened pain sensitivity and poorer treatment outcomes in chronic pain conditions (Kioskli et al., 2019). Patients with comorbid depression and DN also exhibited significant increases in pain scores over time, aligning with prior research that suggests depression alters pain perception and contributes to poorer pain outcomes by amplifying pain sensitivity (Cherif et al., 2020). Conversely, patients with anxiety showed the smallest increase over the 12-month period, which aligns with the assumption that coping mechanisms associated with anxiety disorders are tied to more active symptom management or treatment responsiveness (Jain et al., 2011). There was a significant interaction between the mental health group and time, which emphasizes the importance of designing pain management strategies based on patients' combined mental health and DN symptom profiles.

Over the 12-month period, certain patient characteristics showed significance in influencing pain outcomes. Female patients reported higher pain scores than males, which is consistent with prior studies highlighting gender differences in pain perception and reporting (Bartley & Fillingim, 2013). Similarly to gender differences, racial differences in pain outcomes were also observed. For example Racial differences in pain outcomes were also observed. Black and Hispanic patients reported higher pain scores compared to White patients in certain mental health groups, particularly among those with depression and bipolar disorder. In contrast, within the anxiety subgroup, White patients had significantly lower pain scores than other racial groups. These demographic differences along with others may highlight disparities in the healthcare administration and healthcare system practices that may contribute to variations in pain experiences across racial groups (Anderson, 2009).

Diabetes type was another significant factor influencing pain outcomes. Across mental health conditions, patients with Type 1 diabetes reported significantly higher NRS pain scores compared to those with Type 2 diabetes. This is consistent with prior research indicating that neuropathic pain may present differently depending on diabetes type, with Type 1 diabetes potentially leading to more severe neuropathy-related pain due to differences in disease onset

and progression (Callaghan et al., 2012). Overall, the results of this study support the need for a more comprehensive approach to managing pain in DN patients based on comorbid mental health conditions.

Limitations

Despite the results of this study, there are several limitations. First, as a retrospective cohort study using electronic health records, navigating the database introduces a number of challenges. The findings of the study rely on the accuracy and completeness of recorded data. Varying documentation across healthcare providers may result in measurement bias. The data extracted from the database may be subject to coding errors and incomplete or misclassified data. Secondly, the number of patients in this study was limited to those enrolled in the UC Health System, which may not be generalizable to other populations. The selected sample population includes participants from varying distributions of mental health conditions, diabetes types, and races. Further, though the NRS pain scale is a validated measure, it is subjective and may not capture the full complexity of pain patients experience as part of comorbid diagnosis. Lastly, the design of this study limits the ability to establish causality between comorbid diagnoses and changes in pain outcomes. Though the longitudinal nature of the study allowed for the observation of trends over time, there are many confounding factors that may influence results. Efforts to control confounding in analyses included adjusting for these factors; however, they cannot account for all potential confounding. Future research should consider prospective studies with more comprehensive assessments. Future directions should also consider specifically focusing on differences within one mental health group, adjusting for treatments, study length, and quality of life measures specific to conditions.

Conclusion

This study represents a way to utilize EHR databases to understand the impact of comorbid mental health conditions on patient outcomes with diabetic neuropathy. The findings indicate the differences in pain trajectories in individuals with diabetic neuropathy and coexisting mental health diagnoses. Patients with bipolar disorder experienced the highest and most persistent pain scores, followed by those with depression and anxiety. Gender, race, and diabetes type were shown to be significant contributors to pain variability. The results emphasize the importance of addressing complex interactions diagnoses as part of a comprehensive approach to managing chronic pain in patients. Future studies prospective in nature should explore these relationships further to evaluate the effectiveness of targeted interventions that can address both the pain outcomes related to mental health conditions and diabetic neuropathy.

Tables & Figures

Tables:

Table 1:Patient Characteristics

Patient Characteristics[1]					
	Race				
Characteristic	Other	asian	black	hispanic	white
Total Participants 1754	**NA**	**NA**	**NA**	**NA**	**NA**
female	105	53	96	218	456
male	89	36	58	195	448
18-24	0	0	0	1	0
25-34	6	2	4	15	11
35-44	13	4	8	39	37
45-54	15	8	19	36	79
55-64	53	14	43	128	193
65-74	43	18	46	121	265
75-84	46	27	31	47	232
85+	18	16	3	26	87
1	28	7	17	48	96
2	166	82	137	365	808
Anxiety	38	29	32	111	211
Bipolar Disorder	22	3	34	39	77
Depression	134	57	88	263	616

[1] This table presents the distribution of patient demographics and health conditions across racial groups.

Table 2: Linear Mixed Model Results

Predictor	Estimate	SE	95% CI Lower	95% CI Upper	t-value	p_value
(Intercept)	**4.095**	**0.588**	**2.943**	**5.247**	**6.968**	**0.000**
poly(time, 3)1	**23.650**	**3.024**	**17.723**	**29.577**	**7.821**	**0.000**
poly(time, 3)2	**−30.861**	**3.024**	**−36.788**	**−24.934**	**−10.206**	**0.000**
poly(time, 3)3	**15.672**	**3.024**	**9.746**	**21.599**	**5.183**	**0.000**
main_mental_healthDepression	**0.392**	**0.033**	**0.326**	**0.457**	**11.729**	**0.000**
main_mental_healthBipolar Disorder	**0.906**	**0.053**	**0.802**	**1.011**	**17.035**	**0.000**
age_category25-34	0.258	0.592	−0.902	1.417	0.436	0.663
age_category35-44	0.323	0.587	−0.826	1.473	0.551	0.581
age_category45-54	0.308	0.586	−0.841	1.456	0.525	0.600
age_category55-64	0.265	0.585	−0.881	1.411	0.454	0.650
age_category65-74	0.227	0.585	−0.919	1.373	0.388	0.698
age_category75-84	0.216	0.585	−0.931	1.363	0.369	0.712
age_category85+	0.162	0.586	−0.987	1.310	0.276	0.783
gendermale	**−0.374**	**0.028**	**−0.430**	**−0.319**	**−13.309**	**0.000**
diabetes_type2	**−0.268**	**0.044**	**−0.354**	**−0.181**	**−6.044**	**0.000**
raceasian	**0.389**	**0.065**	**0.261**	**0.517**	**5.973**	**0.000**
raceblack	**0.581**	**0.052**	**0.480**	**0.682**	**11.276**	**0.000**
racehispanic	**0.490**	**0.035**	**0.421**	**0.559**	**13.870**	**0.000**
raceOther	**0.435**	**0.046**	**0.344**	**0.526**	**9.381**	**0.000**
poly(time, 3)1:main_mental_healthDepression	2.482	3.531	−4.439	9.403	0.703	0.482
poly(time, 3)2:main_mental_healthDepression	**30.188**	**3.531**	**23.267**	**37.109**	**8.549**	**0.000**
poly(time, 3)3:main_mental_healthDepression	3.232	3.531	−3.689	10.152	0.915	0.360
poly(time, 3)1:main_mental_healthBipolar Disorder	**31.827**	**5.581**	**20.889**	**42.764**	**5.703**	**0.000**
poly(time, 3)2:main_mental_healthBipolar Disorder	**22.405**	**5.581**	**11.468**	**33.343**	**4.015**	**0.000**
poly(time, 3)3:main_mental_healthBipolar Disorder	**−24.376**	**5.581**	**−35.314**	**−13.438**	**−4.368**	**0.000**

Note: Estimates represent the effect of each predictor on pain scores.

Table 3: Paired t-test Results for Baseline to Month 12 Change

Mental Health Condition	Baseline Mean	Baseline SD	Month 12 Mean	Month 12 SD	Mean Difference	t(df)	p-value	Cohen's d
Anxiety	**3.636**	**2.146**	**4.152**	**1.934**	**−0.516**	**-3.765 (420)**	**<0.001**	**−0.252**
Depression	**4.071**	**1.929**	**5.232**	**1.510**	**−1.161**	**-16.534 (1157)**	**<0.001**	**−0.670**
Bipolar Disorder	**4.615**	**2.200**	**6.321**	**1.940**	**−1.707**	**-8.423 (174)**	**<0.001**	**−0.822**

Note: Mean values represent average pain scores at baseline and Month 12. Paired t-tests are within each mental health condition.

Table 4: Pairwise Comparisons of Change Scores

Comparison Group 1	Comparison Group 2	Mean Difference	Standard Error	p-value (Unadjusted)	p-value (Bonferroni Adjusted)
Depression	**Anxiety**	**0.646**	**0.061**	**NA**	**<0.001**
Bipolar Disorder	**Anxiety**	**1.191**	**0.061**	**NA**	**<0.001**
Bipolar Disorder	**Depression**	**0.545**	**0.061**	**NA**	**<0.05**

Note: Mean differences are from the comparison of baseline to month-12 changes.

Table 5: Overall Pain Score Summary

Mental Health Condition	Mean (SD)	Sample Size (n)
Anxiety	4.17 (1.7)	5,052
Depression	4.54 (1.5)	13,896
Bipolar Disorder	5.12 (1.89)	2,100

Note: Values represent the overall mean pain scores for each mental health condition.

Table 6: ANOVA Comparisons of Pain Scores by Race

Mental Health Condition	Race Comparison	Mean Difference	p-value
Depression	asian - black	−0.232	0.1
Depression	asian - hispanic	−0.175	0.238
Depression	**asian - Other**	**−0.364**	**<0.001**
Depression	asian - white	0.154	0.363
Depression	black - hispanic	0.057	1
Depression	black - Other	−0.132	0.692
Depression	**black - white**	**0.386**	**<0.001**
Depression	**hispanic - Other**	**−0.189**	**<0.01**
Depression	**hispanic - white**	**0.329**	**<0.001**
Depression	**Other - white**	**0.518**	**<0.001**
Bipolar Disorder	**asian - black**	**−1.433**	**<0.05**
Bipolar Disorder	asian - hispanic	0.326	1
Bipolar Disorder	asian - Other	0.056	1
Bipolar Disorder	asian - white	−0.334	1
Bipolar Disorder	**black - hispanic**	**1.759**	**<0.001**
Bipolar Disorder	**black - Other**	**1.489**	**<0.001**
Bipolar Disorder	**black - white**	**1.098**	**<0.001**
Bipolar Disorder	hispanic - Other	−0.270	1
Bipolar Disorder	**hispanic - white**	**−0.661**	**<0.001**
Bipolar Disorder	Other - white	−0.390	0.317
Anxiety	**asian - black**	**0.472**	**<0.01**
Anxiety	asian - hispanic	−0.281	0.08
Anxiety	**asian - Other**	**0.461**	**<0.01**
Anxiety	**asian - white**	**1.125**	**<0.001**
Anxiety	**black - hispanic**	**−0.753**	**<0.001**
Anxiety	black - Other	−0.012	1
Anxiety	**black - white**	**0.653**	**<0.001**
Anxiety	**hispanic - Other**	**0.741**	**<0.001**
Anxiety	**hispanic - white**	**1.406**	**<0.001**
Anxiety	**Other - white**	**0.665**	**<0.001**

Note: Post-hoc pairwise comparisons were conducted within each mental health condition.

Table 7: ANOVA Comparisons of Pain Scores by Gender

Mental Health Condition	Gender Comparison	Mean Difference	p-value
Depression	**female - male**	**0.336**	**<0.001**
Bipolar Disorder	**female - male**	**0.989**	**<0.001**
Anxiety	**female - male**	**0.328**	**<0.001**

Note: Post-hoc pairwise comparisons were conducted within each mental health condition.

Table 8: ANOVA Comparisons of Pain Scores by Diabetes Type

Mental Health Condition	Diabetes Type Comparison	Mean Difference	p-value
Depression	**diabetes_type1 - diabetes_type2**	**0.309**	**<0.001**
Bipolar Disorder	diabetes_type1 - diabetes_type2	−0.076	0.715
Anxiety	**diabetes_type1 - diabetes_type2**	**0.425**	**<0.001**

Note: Post-hoc pairwise comparisons were conducted within each mental health condition.

Table 9: Race-Adjusted Linear Mixed Model Results

Predictor	Estimate	Standard Error	95% CI Lower	95% CI Upper	t-value	p_value	p-value
(Intercept)	**4.675**	**0.221**	**4.242**	**5.107**	**21.165**	**2.017063e-90**	**<0.001**
time	**0.092**	**0.025**	**0.042**	**0.141**	**3.628**	**2.913879e-04**	**<0.001**
main_mental_healthDepression	**−0.773**	**0.257**	**−1.276**	**−0.270**	**−3.013**	**2.626560e-03**	**<0.01**
main_mental_healthBipolar Disorder	−0.475	0.682	−1.813	0.863	−0.696	4.865421e-01	0.487
raceblack	**0.577**	**0.288**	**0.012**	**1.143**	**2.001**	**4.551507e-02**	**<0.05**
racehispanic	−0.102	0.235	−0.562	0.358	−0.435	6.639394e-01	0.664
raceOther	**−0.601**	**0.278**	**−1.145**	**−0.057**	**−2.166**	**3.044706e-02**	**<0.05**
racewhite	−0.425	0.223	−0.862	0.012	−1.908	5.659389e-02	0.057
gendermale	**−0.374**	**0.024**	**−0.421**	**−0.328**	**−15.754**	**3.225635e-53**	**<0.001**
diabetes_type2	**−0.236**	**0.037**	**−0.310**	**−0.163**	**−6.311**	**3.315176e-10**	**<0.001**
age	**−0.003**	**0.001**	**−0.004**	**−0.001**	**−3.158**	**1.608462e-03**	**<0.01**
time:main_mental_healthDepression	**0.091**	**0.031**	**0.031**	**0.152**	**2.943**	**3.281247e-03**	**<0.01**
time:main_mental_healthBipolar Disorder	0.092	0.083	−0.069	0.254	1.119	2.632727e-01	0.263
time:raceblack	**−0.165**	**0.035**	**−0.234**	**−0.097**	**−4.730**	**2.369578e-06**	**<0.001**
time:racehispanic	**0.062**	**0.028**	**0.006**	**0.117**	**2.168**	**3.028641e-02**	**<0.05**
time:raceOther	0.030	0.034	−0.035	0.096	0.903	3.664513e-01	0.366
time:racewhite	**−0.102**	**0.027**	**−0.155**	**−0.049**	**−3.769**	**1.676180e-04**	**<0.001**
main_mental_healthDepression:raceblack	0.563	0.346	−0.115	1.242	1.628	1.036679e-01	0.104
main_mental_healthBipolar Disorder:raceblack	0.809	0.736	−0.634	2.252	1.098	2.721589e-01	0.272
main_mental_healthDepression:racehispanic	**1.159**	**0.286**	**0.597**	**1.720**	**4.045**	**5.451269e-05**	**<0.001**
main_mental_healthBipolar Disorder:racehispanic	0.326	0.714	−1.073	1.724	0.456	6.483146e-01	0.648
main_mental_healthDepression:raceOther	**1.402**	**0.330**	**0.756**	**2.048**	**4.255**	**2.200162e-05**	**<0.001**
main_mental_healthBipolar Disorder:raceOther	0.749	0.746	−0.713	2.212	1.004	3.152891e-01	0.315
main_mental_healthDepression:racewhite	**1.267**	**0.272**	**0.735**	**1.800**	**4.662**	**3.360571e-06**	**<0.001**
main_mental_healthBipolar Disorder:racewhite	**1.389**	**0.699**	**0.020**	**2.759**	**1.989**	**4.688513e-02**	**<0.05**
time:main_mental_healthDepression:raceblack	0.017	0.042	−0.065	0.099	0.405	6.857952e-01	0.686
time:main_mental_healthBipolar Disorder:raceblack	0.163	0.089	−0.012	0.338	1.828	6.765155e-02	0.068
time:main_mental_healthDepression:racehispanic	**−0.200**	**0.035**	**−0.268**	**−0.132**	**−5.759**	**9.510169e-09**	**<0.001**
time:main_mental_healthBipolar Disorder:racehispanic	−0.154	0.086	−0.323	0.016	−1.777	7.575499e-02	0.076
time:main_mental_healthDepression:raceOther	**−0.100**	**0.040**	**−0.179**	**−0.022**	**−2.517**	**1.191036e-02**	**<0.05**
time:main_mental_healthBipolar Disorder:raceOther	−0.081	0.090	−0.258	0.096	−0.901	3.674878e-01	0.367
time:main_mental_healthDepression:racewhite	−0.049	0.033	−0.114	0.015	−1.495	1.349899e-01	0.135
time:main_mental_healthBipolar Disorder:racewhite	−0.003	0.085	−0.169	0.163	−0.036	9.709828e-01	0.971

Note: Estimates represent the effect of each predictor on pain scores.

Table 10: Gender-Adjusted Linear Mixed Model Results

Predictor	Estimate	Standard Error	95% CI Lower	95% CI Upper	t-value	p_value	p-value
(Intercept)	**4.675**	**0.221**	**4.242**	**5.107**	**21.165**	**2.017063e-90**	**<0.001**
time	**0.092**	**0.025**	**0.042**	**0.141**	**3.628**	**2.913879e-04**	**<0.001**
main_mental_healthDepression	**−0.773**	**0.257**	**−1.276**	**−0.270**	**−3.013**	**2.626560e-03**	**<0.01**
main_mental_healthBipolar Disorder	−0.475	0.682	−1.813	0.863	−0.696	4.865421e-01	0.487
raceblack	**0.577**	**0.288**	**0.012**	**1.143**	**2.001**	**4.551507e-02**	**<0.05**
racehispanic	−0.102	0.235	−0.562	0.358	−0.435	6.639394e-01	0.664
raceOther	**−0.601**	**0.278**	**−1.145**	**−0.057**	**−2.166**	**3.044706e-02**	**<0.05**
racewhite	−0.425	0.223	−0.862	0.012	−1.908	5.659389e-02	0.057
gendermale	**−0.374**	**0.024**	**−0.421**	**−0.328**	**−15.754**	**3.225635e-53**	**<0.001**
diabetes_type2	**−0.236**	**0.037**	**−0.310**	**−0.163**	**−6.311**	**3.315176e-10**	**<0.001**
age	**−0.003**	**0.001**	**−0.004**	**−0.001**	**−3.158**	**1.608462e-03**	**<0.01**
time:main_mental_healthDepression	**0.091**	**0.031**	**0.031**	**0.152**	**2.943**	**3.281247e-03**	**<0.01**
time:main_mental_healthBipolar Disorder	0.092	0.083	−0.069	0.254	1.119	2.632727e-01	0.263
time:raceblack	**−0.165**	**0.035**	**−0.234**	**−0.097**	**−4.730**	**2.369578e-06**	**<0.001**
time:racehispanic	**0.062**	**0.028**	**0.006**	**0.117**	**2.168**	**3.028641e-02**	**<0.05**
time:raceOther	0.030	0.034	−0.035	0.096	0.903	3.664513e-01	0.366
time:racewhite	**−0.102**	**0.027**	**−0.155**	**−0.049**	**−3.769**	**1.676180e-04**	**<0.001**
main_mental_healthDepression:raceblack	0.563	0.346	−0.115	1.242	1.628	1.036679e-01	0.104
main_mental_healthBipolar Disorder:raceblack	0.809	0.736	−0.634	2.252	1.098	2.721589e-01	0.272
main_mental_healthDepression:racehispanic	**1.159**	**0.286**	**0.597**	**1.720**	**4.045**	**5.451269e-05**	**<0.001**
main_mental_healthBipolar Disorder:racehispanic	0.326	0.714	−1.073	1.724	0.456	6.483146e-01	0.648
main_mental_healthDepression:raceOther	**1.402**	**0.330**	**0.756**	**2.048**	**4.255**	**2.200162e-05**	**<0.001**
main_mental_healthBipolar Disorder:raceOther	0.749	0.746	−0.713	2.212	1.004	3.152891e-01	0.315
main_mental_healthDepression:racewhite	**1.267**	**0.272**	**0.735**	**1.800**	**4.662**	**3.360571e-06**	**<0.001**
main_mental_healthBipolar Disorder:racewhite	**1.389**	**0.699**	**0.020**	**2.759**	**1.989**	**4.688513e-02**	**<0.05**
time:main_mental_healthDepression:raceblack	0.017	0.042	−0.065	0.099	0.405	6.857952e-01	0.686
time:main_mental_healthBipolar Disorder:raceblack	0.163	0.089	−0.012	0.338	1.828	6.765155e-02	0.068
time:main_mental_healthDepression:racehispanic	**−0.200**	**0.035**	**−0.268**	**−0.132**	**−5.759**	**9.510169e-09**	**<0.001**
time:main_mental_healthBipolar Disorder:racehispanic	−0.154	0.086	−0.323	0.016	−1.777	7.575499e-02	0.076
time:main_mental_healthDepression:raceOther	**−0.100**	**0.040**	**−0.179**	**−0.022**	**−2.517**	**1.191036e-02**	**<0.05**
time:main_mental_healthBipolar Disorder:raceOther	−0.081	0.090	−0.258	0.096	−0.901	3.674878e-01	0.367
time:main_mental_healthDepression:racewhite	−0.049	0.033	−0.114	0.015	−1.495	1.349899e-01	0.135
time:main_mental_healthBipolar Disorder:racewhite	−0.003	0.085	−0.169	0.163	−0.036	9.709828e-01	0.971

Note: Estimates represent the effect of each predictor on pain scores.

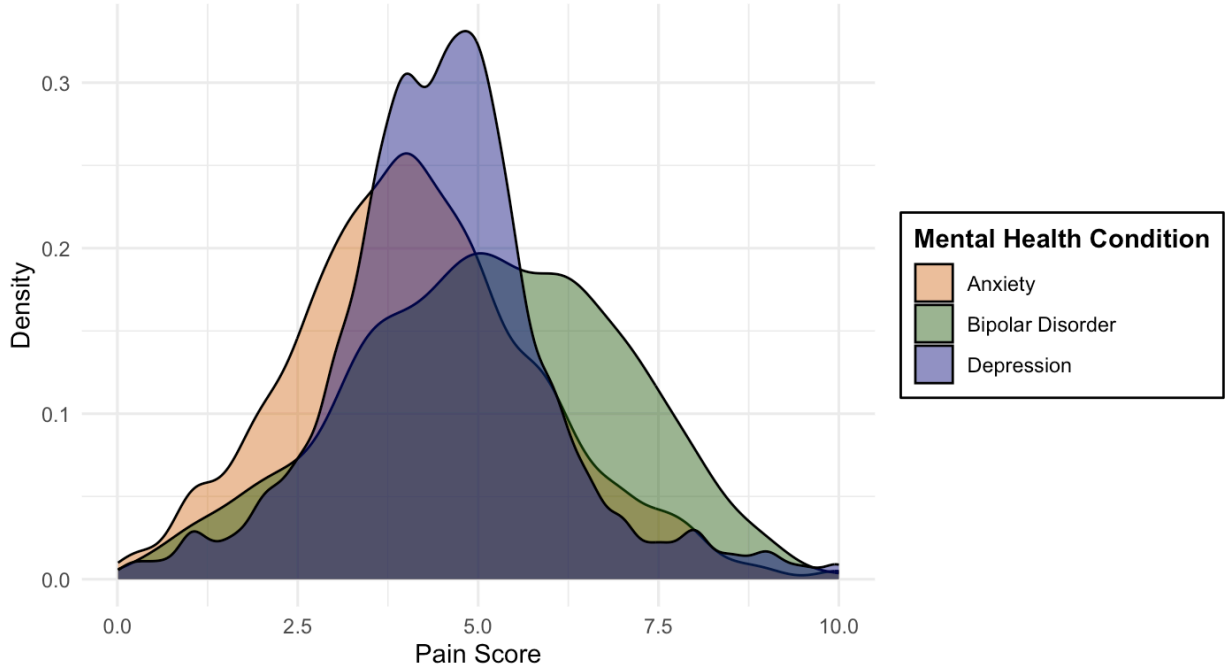
Table 11: Diabetes-Adjusted Linear Mixed Model Results

Predictor	Estimate	Standard Error	95% CI Lower	95% CI Upper	t-value	p_value	p-value
(Intercept)	**4.675**	**0.221**	**4.242**	**5.107**	**21.165**	**2.017063e-90**	**<0.001**
time	**0.092**	**0.025**	**0.042**	**0.141**	**3.628**	**2.913879e-04**	**<0.001**
main_mental_healthDepression	**−0.773**	**0.257**	**−1.276**	**−0.270**	**−3.013**	**2.626560e-03**	**<0.01**
main_mental_healthBipolar Disorder	−0.475	0.682	−1.813	0.863	−0.696	4.865421e-01	0.487
raceblack	**0.577**	**0.288**	**0.012**	**1.143**	**2.001**	**4.551507e-02**	**<0.05**
racehispanic	−0.102	0.235	−0.562	0.358	−0.435	6.639394e-01	0.664
raceOther	**−0.601**	**0.278**	**−1.145**	**−0.057**	**−2.166**	**3.044706e-02**	**<0.05**
racewhite	−0.425	0.223	−0.862	0.012	−1.908	5.659389e-02	0.057
gendermale	**−0.374**	**0.024**	**−0.421**	**−0.328**	**−15.754**	**3.225635e-53**	**<0.001**
diabetes_type2	**−0.236**	**0.037**	**−0.310**	**−0.163**	**−6.311**	**3.315176e-10**	**<0.001**
age	**−0.003**	**0.001**	**−0.004**	**−0.001**	**−3.158**	**1.608462e-03**	**<0.01**
time:main_mental_healthDepression	**0.091**	**0.031**	**0.031**	**0.152**	**2.943**	**3.281247e-03**	**<0.01**
time:main_mental_healthBipolar Disorder	0.092	0.083	−0.069	0.254	1.119	2.632727e-01	0.263
time:raceblack	**−0.165**	**0.035**	**−0.234**	**−0.097**	**−4.730**	**2.369578e-06**	**<0.001**
time:racehispanic	**0.062**	**0.028**	**0.006**	**0.117**	**2.168**	**3.028641e-02**	**<0.05**
time:raceOther	0.030	0.034	−0.035	0.096	0.903	3.664513e-01	0.366
time:racewhite	**−0.102**	**0.027**	**−0.155**	**−0.049**	**−3.769**	**1.676180e-04**	**<0.001**
main_mental_healthDepression:raceblack	0.563	0.346	−0.115	1.242	1.628	1.036679e-01	0.104
main_mental_healthBipolar Disorder:raceblack	0.809	0.736	−0.634	2.252	1.098	2.721589e-01	0.272
main_mental_healthDepression:racehispanic	**1.159**	**0.286**	**0.597**	**1.720**	**4.045**	**5.451269e-05**	**<0.001**
main_mental_healthBipolar Disorder:racehispanic	0.326	0.714	−1.073	1.724	0.456	6.483146e-01	0.648
main_mental_healthDepression:raceOther	**1.402**	**0.330**	**0.756**	**2.048**	**4.255**	**2.200162e-05**	**<0.001**
main_mental_healthBipolar Disorder:raceOther	0.749	0.746	−0.713	2.212	1.004	3.152891e-01	0.315
main_mental_healthDepression:racewhite	**1.267**	**0.272**	**0.735**	**1.800**	**4.662**	**3.360571e-06**	**<0.001**
main_mental_healthBipolar Disorder:racewhite	**1.389**	**0.699**	**0.020**	**2.759**	**1.989**	**4.688513e-02**	**<0.05**
time:main_mental_healthDepression:raceblack	0.017	0.042	−0.065	0.099	0.405	6.857952e-01	0.686
time:main_mental_healthBipolar Disorder:raceblack	0.163	0.089	−0.012	0.338	1.828	6.765155e-02	0.068
time:main_mental_healthDepression:racehispanic	**−0.200**	**0.035**	**−0.268**	**−0.132**	**−5.759**	**9.510169e-09**	**<0.001**
time:main_mental_healthBipolar Disorder:racehispanic	−0.154	0.086	−0.323	0.016	−1.777	7.575499e-02	0.076
time:main_mental_healthDepression:raceOther	**−0.100**	**0.040**	**−0.179**	**−0.022**	**−2.517**	**1.191036e-02**	**<0.05**
time:main_mental_healthBipolar Disorder:raceOther	−0.081	0.090	−0.258	0.096	−0.901	3.674878e-01	0.367
time:main_mental_healthDepression:racewhite	−0.049	0.033	−0.114	0.015	−1.495	1.349899e-01	0.135
time:main_mental_healthBipolar Disorder:racewhite	−0.003	0.085	−0.169	0.163	−0.036	9.709828e-01	0.971

Note: Estimates represent the effect of each predictor on pain scores.

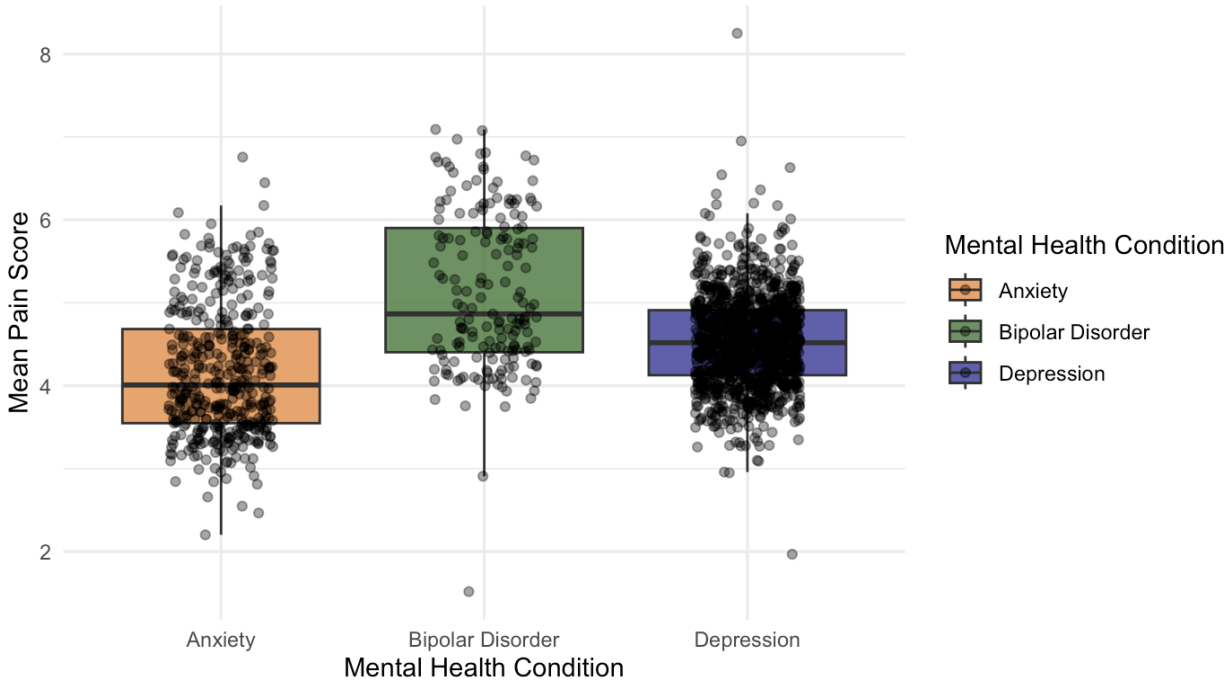
Figures:

Figure 1: Distribution of pain scores across mental health conditions



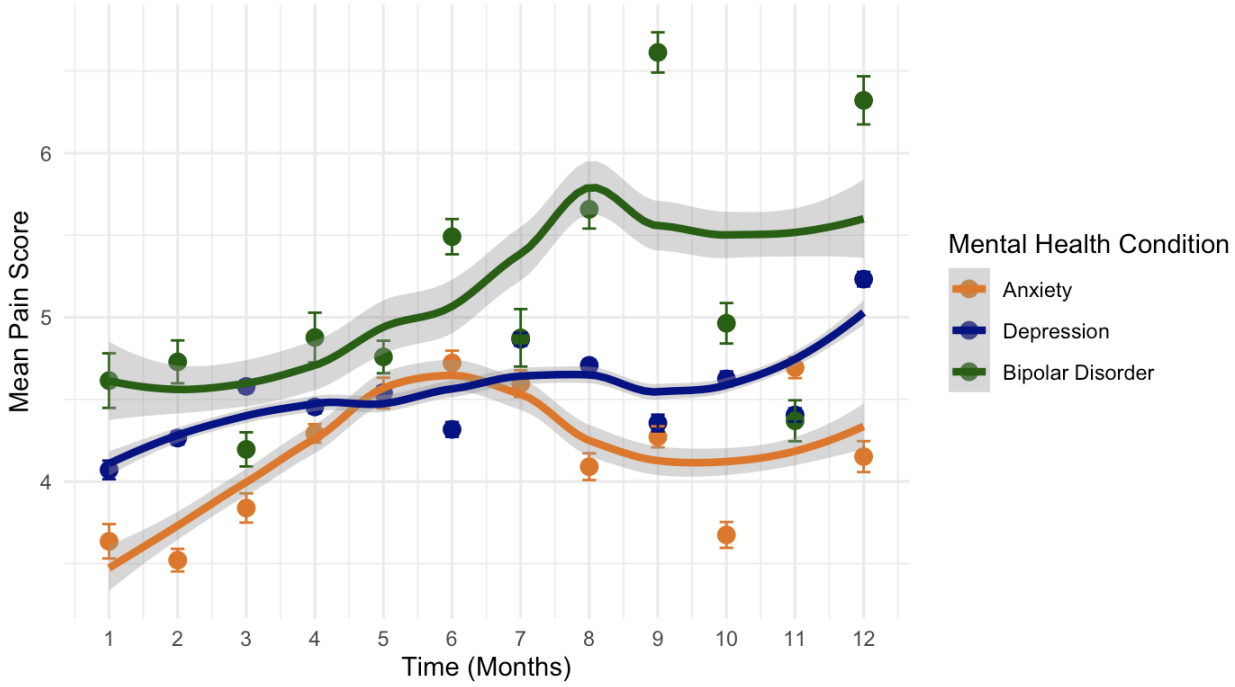
Note: Density curves represent distributions of pain scores for each mental health condition.

Figure 2: Boxplot of mean NRS by mental health



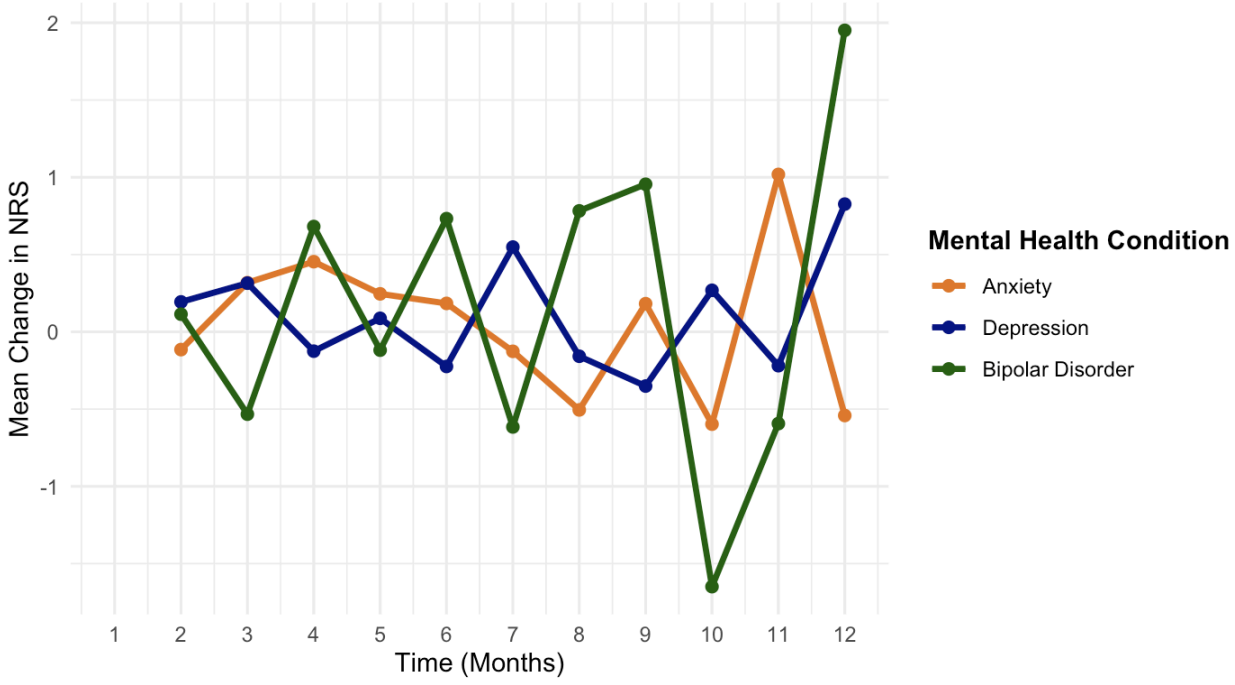
Note: Boxplots represent the distribution of mean pain scores for each mental health condition.

Figure 3: Pain Trends Over 12 Months by Mental Health Condition



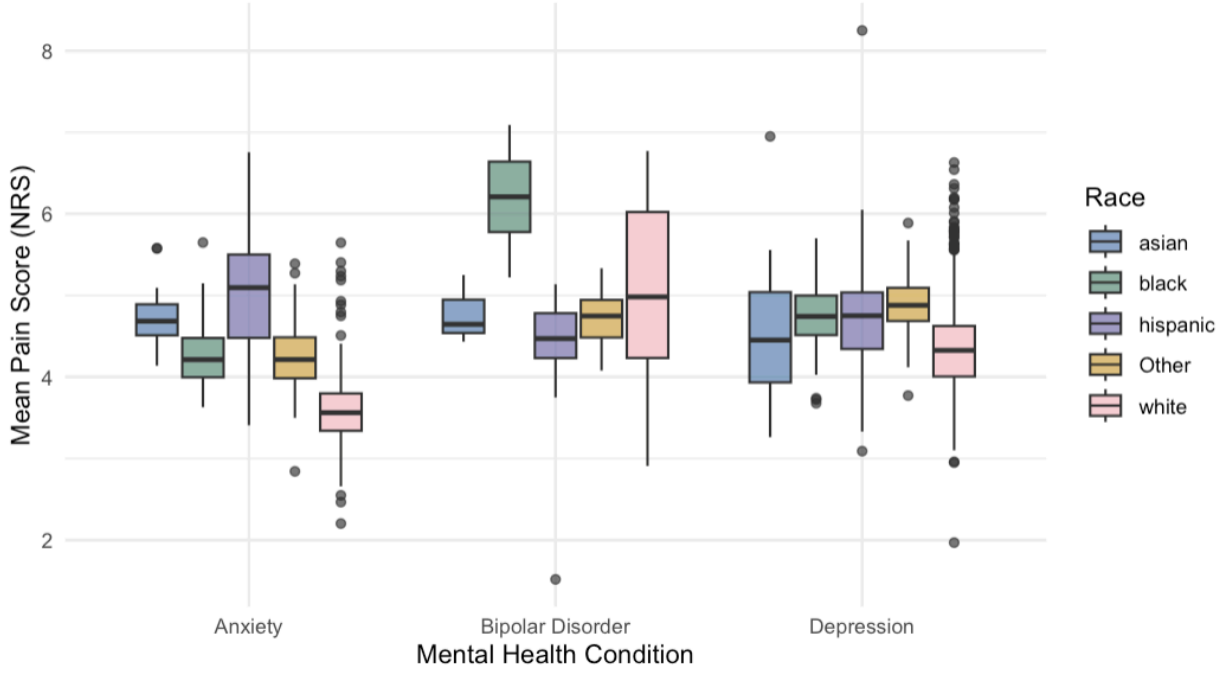
Note: This plot shows the trend of NRS scores over 12 months by mental health condition.

Figure 4: Monthly Change in Pain Score



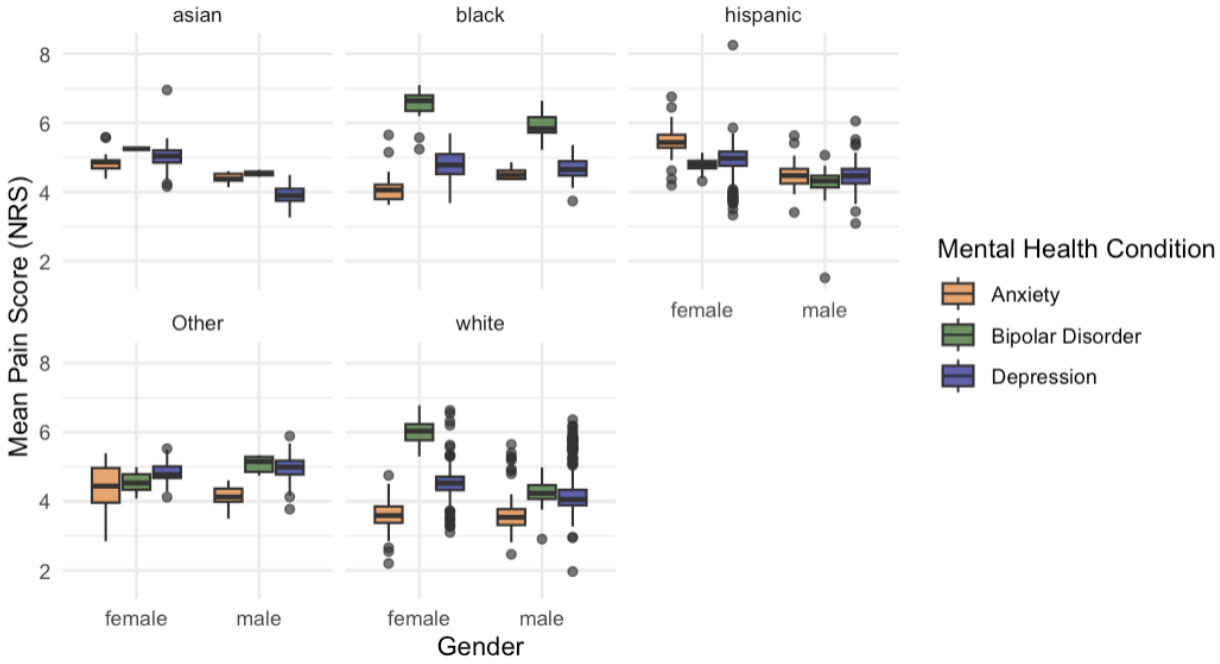
Note: Mean monthly difference in pain scores over 12 months

Figure 5: Mean NRS score by Mental Health Type & Race



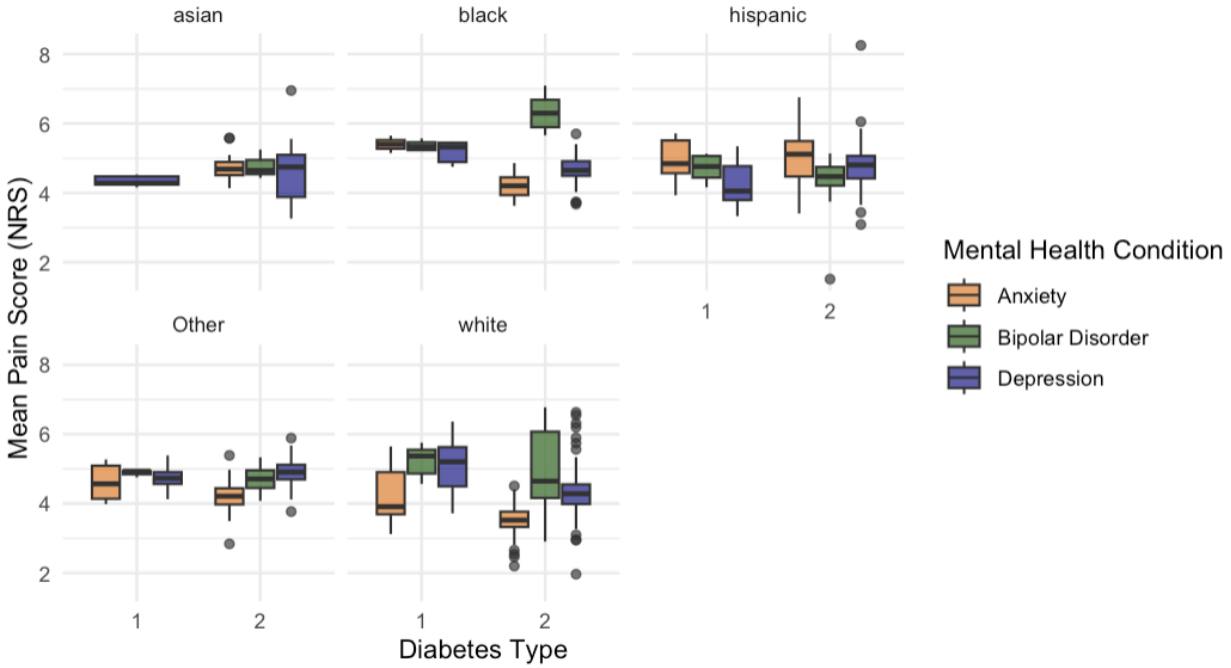
Note: Boxplots represent the distribution of mean pain scores within each race

Figure 6: Mean NRS score by Gender (Stratified by Race)



Note: Each panel represents a different racial group comparing gender in pain scores.

Figure 7: Mean NRS score by Diabetes Type (Stratified by Race)



Each panel represents a different racial groupco mparing diabetes type in pain scores.

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