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# Impact of the COVID-19 pandemic on adults with current and prior depression: initial findings from the longitudinal Texas RAD study

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A R T I C L E I N F O	A B S T R A C T				
<i>Keywords:</i> Coronavirus COVID-19 Depression adults	Background: Emerging work has suggested worsening mental health in the general population during the COVID- 19 pandemic, but there is minimal data on individuals with a prior history of depression. Methods: Data regarding depression, anxiety and quality of life in adult participants with a history of a depressive disorder ( $n = 308$ ) were collected before and during the COVID-19 pandemic. Mixed effects regression models were fit for these outcomes over the period May – August 2020, controlling for pre-pandemic depressive groups (none, mild, moderate-to-severe), demographic characteristics, and early COVID-19 related experiences (such as disruptions in routines, mental health treatment, and social supports). Results: In pre-to-early pandemic comparisons, the 3 pre-pandemic depressive categories varied significantly in anxiety ( $F_{df=2,197} = 7.93$ , $p < 0.0005$ ) and psychological QOL ( $F_{df=2,196} = 8.57$ , $p = 0.0003$ ). The mildly depressed group ( $F_{df=1,201} = 6.01$ , $p = 0.02$ ) and moderate-to-severely depressed group ( $F_{df=1,201} = 38.51$ , $p < 0.0001$ ) had a significant reduction in anxiety. There were no changes among the groups in any outcome from May to August 2020. However, early impact on mental health care access and disruption in routines predicted worse outcomes during this time. Limitations: Follow-up data were self-reported. Furthermore, the duration was a relatively short span into the 				

### 1. Introduction

Since the onset of the COVID-19 pandemic in early 2020, there have been growing concerns about the potential negative impact on mental health from the disease itself and the related disruption of psychosocial routines(S. Galea et al., 2020). Most cross-sectional population surveys world-wide have shown increased prevalence of depressive and anxiety symptoms since March 2020(J. Xiong et al., 2020). In the UK, GHQ-12 surveys from the years immediately prior to the pandemic were compared to data collected in April 2020 (n = 17,452). While they note an overall increase in scores even prior to the pandemic, a disproportionate increase is observed between 2019 and 2020(M. Pierce et al., 2020).

Given the potential mental health crisis, other studies have attempted to understand factors associated with vulnerability to worsening mood symptoms. Online survey results from 1005 United States participants in late March 2020 indicated a high prevalence of mood and anxiety symptoms, and these symptoms were associated with loss of job, loneliness and history of hospitalization(Kantor and Kantor, 2020). Recent results from the a Dutch longitudinal population-based study (n = 3983) between 2019 and March 2020 found prior symptoms, non-native ethnic background, work disability and lung problems were

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associated with symptoms in March 2020(van der Velden et al., 2020). In contrast to other studies however, they noted anxiety/depressive symptoms and emotional support did not significantly increase. In a follow up analysis from the same cohort but through June 2020, authors found an increase in loneliness(van der Velden et al., 2021) but again no change in mood symptoms. Together, these mixed results indicate a possibility of a looming mental health crisis, but given the unprecedented nature of the pandemic, it remains unclear who are most vulnerable and the intra-pandemic trajectory of mental illness.

Further limiting these findings, nearly all studies have mostly relied on self-reported data of psychiatric diagnoses, rather than semistructured clinician interviews and severity data on the same participants pre- and intra- pandemic is minimal. To address these gaps in knowledge, we examined pre- and intra-pandemic data from the ongoing longitudinal depression cohort study Texas Resilience Against Depression (T-RAD), in which all participants have received a prepandemic semi-structured psychiatric interview(M.H. Trivedi et al., 2020). First, we asked whether pre-pandemic depressive symptom severity moderated changes in depressive, anxiety or quality of life during the early pandemic. Second, we examined longitudinal symptom severity from May to August 2020 (intra-pandemic) based on pre-pandemic symptom severity. Finally, we explored whether three items from a newly developed COVID-19 impact scale (mental health care access, disruption in routines, social support) were associated with different symptom trajectories.

### 2. Methods

### 2.1. Study design and participants

The Texas Resilience Against Depression study(M.H. Trivedi et al., 2020) is an ongoing (2016-present) natural history, longitudinal study that follows participants with current or past diagnosis of a unipolar or bipolar depressive disorder (aged 10 and older), as well as youth and young adults (aged 10 to 24) at risk for depression but not yet suffering from the disease. At study enrollment, participants receive comprehensive demographic and psychiatric assessment through a combination of self-report surveys and clinician-rated measures. Then participants are followed every 3 months with follow up self-reported surveys and clinician-rated measures. Additional study details have been previously reported(M.H. Trivedi et al., 2020). Shortly after the onset of the pandemic (April 2020, marked by local stay-at-home orders), participants were asked to complete biweekly remote surveys about symptoms of depression, anxiety, quality of life and the impact of COVID-19. These surveys were emailed to participants via the REDCap electronic data capture system. For this analysis, we focused on adult participants (age  $\geq$  18) with a history of a prior depressive disorder and completed biweekly symptom severity surveys during the pandemic (n = 308).

### 2.2. Measures

Exposure to the COVID-19 pandemic was defined as the time from the start of the local stay-at-home orders (March 16, 2020 in North Texas) to the time that any follow-up measures were completed. Prepandemic depression severity was assessed using the QIDS-C<sub>16</sub>, a 16item clinician-rated assessment that measures the presence and severity of depressive symptoms within the last seven days(A.J. Rush et al., 2003). Score interpretation ranges are as follows: 0 to 5 indicates no depression, 6 to 10 for mild depression, 11 to 15 for moderate depression, 16 to 20 for severe depression, and 21 to 27 for very severe depression. In our analyses, we combined the categories with scores  $\geq$ 11 as being moderate to severe depression. In the T-RAD project, this measure is completed by a qualified assessor every three months. The last available assessment in 2019 (prior to the COVID-19 pandemic) was considered as the pre-pandemic measure of depressive symptom severity.

We assessed 6 outcomes over time in this paper, namely, depression, anxiety and 4 quality of life subscales. Participants completed a series of surveys as part of the T-RAD study at three-month intervals prior to the pandemic, and via biweekly surveys thereafter. These surveys are ongoing, but for the purposes of this analysis, we limited survey data from April 2020 to August 2020. For the depression severity outcome, we used the Patient Health Questionnaire-9 (K. Kroenke et al., 2001), a widely utilized self-report of depressive symptom severity, where higher score indicates higher depression severity. Measures of anxiety and quality of life were collected at similar intervals using the Generalized Anxiety Disorder-7 (GAD-7) scale(R.L. Spitzer et al., 2006) and World Health Organization Quality of Life-BREF (WHOQOL-BREF) scale(C. The WHOQOL Group, 1998) respectively. Higher score in GAD-7 represents higher anxiety levels whereas higher scores on the 4 domain scores of WHOQOL-BREF, namely, physical, psychological, social and environmental QOL (all measured on the WHOQOL recommended transformed scale 4-20) suggest better quality of life in the respective domains.

Participants were also asked about their experiences with COVID-19 during the same period. The impact of COVID-19 was assessed by the Coronavirus Impact Scale (J. Kaufman and Stoddard, 2020). This 12-item scale measures how much the coronavirus pandemic has changed the respondent's life across multiple domains. We focused specifically on questions related to COVID-19 impact on routines, mental health treatment access, and access to extended family and non-family social supports. These were measured on a 0 to 3 Likert scale, with 0 as "no change" or "none", 1 as "mild", 2 as "moderate", and 3 as "severe." We used participants' responses to these questions from the first time they completed this survey in the analyses.

Additional variables of interest, such as age, sex (male/female), race (White/Black/Other), and ethnicity (Hispanic/non-Hispanic) were obtained from a demographic self-report.

### 2.3. Statistical methods

Continuous data were summarized by means and standard deviations for continuous outcomes while frequency and percentages were used for categorical variables. To assess the differences in outcomes from pre-pandemic to early pandemic time, repeated measures analysis of covariance models was used with time (pre-pandemic versus early pandemic) as a within subject factor, pre-pandemic depression severity categories as a between-subject factor, along with their interaction in the model. The inference of interest was the interaction between depression severity categories and time to assess if the participants in depression severity groups experienced differential changes in the outcomes from pre-pandemic to early pandemic periods.

To test if participants had differential changes in their outcomes during the first few months of the pandemic, we used separate mixed effects regression models that controlled for participants' demographic characteristics, COVID-related experiences and group (i.e., prepandemic depressive symptom categories) for each outcome of interest. In the general statistical model for the analysis for each outcome, we denote the response at the *t*<sup>th</sup> time-point for the *i*<sup>th</sup> subject by *Y*<sub>it</sub>, the value of the *j*<sup>th</sup> demographic predictor for the *i*<sup>th</sup> subject by *X*<sub>ij</sub>, the value of the *k*<sup>th</sup> COVID-related predictor for the *i*<sup>th</sup> subject at first survey point by *C*<sub>ik</sub>, and the pre-pandemic depressive symptom category of the *i*<sup>th</sup> subject by *G*<sub>i</sub>. Time was modeled as log (number of days) from March 15, 2020 when the pandemic related lockdowns and social distancing measures were implemented in the Dallas-Fort Worth (DFW) area.

Then the mixed effects model can be presented as follows:

$$Y_{it} = \beta_{0i} + \beta_1 T_{it} + \beta_2 G_i + \beta_3 (G_i \times T_{it}) + \beta_j X_{ij} + \gamma_k C_{ik} + v_{0i} + e_{ik}$$

where  $v_{0i} \sim N(0, \sigma_v^2)$  and  $e_{it} \sim N(0, \sigma^2)$ .

Separate models were fit for each outcome using MIXED procedure in SAS with the intercept specified as random effect and within-subject

residuals specified to have autoregressive structure of degree 1 (AR1). The statistical software SAS version 9.4 was used for the analyses and p < 0.05 was considered as statistically significant.

### 3. Results

#### 3.1. Sample characteristics

The study sample included 71% (n = 218) females, and a majority (n = 239, 77.6%) were white participants with a mean age of 45.4 (SD = 16.4). Twelve percent (n = 38) of participants identified as Hispanic or Latinx. There were no demographic differences among participants across the three depressive symptom categories (none, mild or moderate-to-severe). However, there were significant differences across the three groups by all of the baseline outcome measures, i.e., self-reported depression, anxiety, and all four domains of QOL (physical, psychological, environmental, and social). Participants in the moderate-to-severe depressive symptom group had significantly higher self-reported depression and anxiety on average and significantly lower QOL measures on average than the other depressive symptom groups. Details can be found in table 1.

Table 1	l
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Demographics of participants in T-RAD based on depression severity in 2019 (n = 308).

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	Overall sample % (n)	No depressive symptom% (n)	Mild depressive symptom% (n)	Moderate to severe depressive symptom% (n)	p- value
Sex Male	29.22 (90)	30.43 (42)	25.84 (23)	30.86 (25)	0.71
Female	70.78 (218)	69.57 (96)	74.16 (66)	69.14 (56)	
Race					
White	77.60 (239)	75.36 (104)	76.40 (68)	82.72 (67)	0.75
Black	13.96 (43)	15.94 (22)	14.61 (13)	9.88 (8)	
Other	8.44 (26)	8.70 (12)	8.99 (8)	7.41 (6)	
Hispanic					0.91
Yes	12.34 (38)	11.59 (16)	12.36 (11)	13.58 (11)	
No	87.66 (270)	88.41 (122)	87.64 (78)	86.42 (70)	
	Mean (SD, n)	Mean (SD, n)	Mean (SD, n)	Mean (SD, n)	
Age	45.4 (16.4, 308)	45.4 (16.5, 138)	44.0 (16.8, 89)	46.8 (15.8, 81)	0.54
GAD-7	8.6 (7.5, 308)	4.8 (5.8, 138)	9.2 (6.4, 89)	14.3 (7.4, 81)	< 0.0001
PHQ-9	9.1 (6.3, 301)	5.3 (4.7, 137)	10.2 (4.8, 89)	14.4 (5.7, 81)	< 0.0001
QOL					
Physical	13.7 (3.2,	15.3 (2.5, 128)	13.2 (3.2, 83)	11.7 (2.8, 80)	< 0.0001
	291)	ŕ			
Psychological	12.2	14.0 (2.8,	11.7 (2.4,	9.6 (2.7,	<
i oj enorogreai	(3.2, 292)	128)	83)	81)	0.0001
Environmental	14.9	15.9 (2.5,	14.9 (2.7,	13.5 (3.0,	< 0.0001
	(2.9, 291)	128)	82)	81)	0.0001
Social	12.3 (3.5, 292)	13.3 (3.3, 128)	12.4 (3.3, 83)	10.5 (3.5, 81)	< 0.0001

## 3.2. Are there differences from pre-pandemic to early pandemic in depression severity, anxiety, and quality of life?

We compared the outcomes from pre-pandemic to early pandemic (Fig. 1). At a significance level of 0.05, there was no evidence of difference in the mean self-reported depression severity among the 3 groups at pre versus early pandemic, (F = 1.57, d.f. = 2, 197, p = 0.21). There was, however, a significant main effect of group on self-reported depression, (F = 38.85, d.f. = 2, 197, p < 0.0001), indicating the 3 groups continued to represent different levels of depressive severity in the early pandemic. With regard to anxiety, there was a significant interaction between group and time, (*F* = 7.93, d.f. = 2, 197, *p* < 0.0005) suggesting that the participants in the three groups experienced different levels of change from pre- to early pandemic periods. The mildly depressed group (F = 6.01, d.f. = 1, 201, p = 0.02) and moderateto-severely depressed group (F = 38.51, d.f. = 1, 201, p < 0.0001) had significant reductions in anxiety from pre-pandemic to early pandemic on average. There was no evidence of difference among the 3 groups pre versus early pandemic for physical QOL (F = 1.83, d.f. = 2193, p =0.16), social QOL (F = 0.06, d.f. = 2, 195, p = 0.95), and environmental OOL (F = 0.14, d.f. = 2, 194, p = 0.87). However, for psychological QOL, there was a significant group by time interaction (F = 8.57, d.f. = 2, 196, p = 0.0003) indicating different levels of change among the 3 categories from pre- to early pandemic periods. Average psychological QOL decreased significantly from pre to early pandemic for the notdepressed group (F = 11.36, d.f. = 1197, p = 0.0009) but increased significantly for the moderate-to-severely depressed group (F = 6.71, d. f. = 1193, p = 0.01). Post-hoc calculations showed power > 0.90 for all these tests.

## 3.3. Are there differential changes in outcomes for participants in the three depression severity groups during the early months of the pandemic?

Longitudinal models were fit for each outcome from May 2020 to August 2020, controlling for age, sex, race and ethnicity as well as COVID's impact on routines, mental health treatment access, and access to extended family and non-family social supports. At alpha = 0.05, there was no evidence of significant pre-pandemic severity category by time interaction, i.e., no difference in the mean outcomes among the 3 groups over time, for any of the 6 outcomes (see Table 2). At a significance level of 0.05, there were also no significant main effects of group or time for any of the 6 outcomes. After controlling for factors in the model, older participants experienced significantly higher anxiety (estimate=-0.06, p = 0.0002) and lower physical QOL (-0.02, p =0.04) (Table 2).

There was evidence however that disruption in routines and access to mental healthcare affected both symptom and two quality of life outcomes. Participants who experienced mild changes in their routines due to COVID-19 (in only one area such as work, education, social life, hobbies, religious activities) experienced significantly higher depression (estimate=2.22, p-value=0.02), lower physical QOL (-0.96, p = 0.03) and lower psychological QOL (-1.33, p = 0.001) compared to those without change in routine, controlling for other factors in the model. Significantly greater depression (1.98, p = 0.03) and anxiety (1.85, p = 0.04) symptoms were observed for those who experienced severe changes in routine (in three or more areas) compared to those without changes in routine (Table 2).

Regarding COVID's impact on access to mental health treatment, those who experienced severe changes in their mental health treatment (such as being unable to access needed care) indicated significantly higher depression (5.48, p = 0.002) and higher anxiety (5.34, p = 0.001) as well as lower physical QOL (-1.66, p = 0.03) and lower psychological QOL (-2.24, p = 0.001). These effects were also observed for those who experienced moderate changes in their mental health treatment compared to those who did not. Access to social support was not associated with any of the outcome measures, regardless of severity.



Fig. 1. Self-reported depression (PHQ-9), anxiety (GAD) and QOL in 2019 versus April 2020, stratified by 2019 depressive severity.

### 4. Discussion

In this study, we report the pre- and intra-pandemic longitudinal course of depressive and anxiety symptoms in individuals with a history of a depressive disorder. We found these symptoms, as well as quality of life, have been mostly stable from 2019 to August 2020. This was generally consistent regardless of pre-pandemic depressive symptom severity. Notably however, early pandemic (May 2020) disruption in routines and access to mental healthcare were associated with greater depressive and anxiety symptoms throughout May-August 2020 relative to prior to the pandemic.

To our knowledge, this is the first longitudinal report on the impact of the COVD-19 pandemic in those with extensive pre-pandemic psychiatric characterization. Prior work reporting the impact of COVID-19 on mental health is limited mostly to population surveys, cross-sectional data or comparisons of individuals with and without self-reported mental illness. A systematic review of cross-sectional studies during the pandemic in eight countries representing 93,569 participants noted the prevalence of depressive symptoms between 14.6% to 48.3% of participants – a marked increase over the previous year prevalence(J. Xiong et al., 2020). They note the presence of psychiatric illness was a strong predictor of depressive symptoms during the pandemic, but did not assess whether said history contributed to worsening symptoms during the pandemic.

Few studies have examined longitudinal data within the pandemic and most have focused on the very early pandemic. In China, a survey of these anxiety and depressive symptoms was completed in February and March 2020 with minimal change(Wang et al., 2020). In the Netherlands, a group found mood homeostasis was disrupted immediately following local lockdown mandates, but only in those with a history of mental illness (M. Taquet et al., 2020). To our knowledge, the largest longitudinal study to date (the Dutch Longitudinal Internet

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#### Table 2

Fixed effects for the linear mixed effects models for depression, anxiety and QOL outcomes (n = 295) between May and August 2020.

	Outcomes					
Parameters	Depression	Anxiety	QOL-Physical	QOL-Psych	QOL-Social	QOL-Enviror
Regression coefficients	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate
(fixed effects)						(SE)
Intercept	5.41	8.72	17.32	14.11	13.55	15.74
•	(3.51)	(3.14)*	(1.47)***	(1.33)***	(2.16)***	(1.54)***
Log (days)	-0.16	-0.61	-0.32	-0.11	-0.01	0.05
	(0.72)	(0.63)	(0.29)	(0.27)	(0.44)	(0.30)
Demographics factors	(0.) _)	(0000)	(0)	(0.2.)	(011)	(0.00)
Age	-0.02 (0.02)	-0.06	-0.02	-0.003	-0.01	0.01
0		(0.02)**	(0.01)*	(0.007)	(0.01)	(0.01)
Sex		(000_)	(000-)	(((((((((((((((((((((((((((((((((((((((	(0.02)	(010-)
Female	0.42	-0.19	-0.10	0.37	1.51	0.97
vs Male	(0.58)	(0.58)	(0.28)	(0.26)	(0.38)***	(0.34)*
Race	(0.30)	(0.50)	(0.20)	(0.20)	(0.50)	(0.34)
Non-White	-1.00 (0.63)	-1.13	-0.20	0.63	0.12	-0.74
vs White	-1.00 (0.03)	(0.62)	(0.30)	(0.28)*	(0.41)	(0.36)*
Hispanic		(0.02)	(0.00)	(0.20)	(0.71)	(0.50)
Non-Hispanic	-0.07 (0.78)	0.002	-0.11	-0.45	0.09	-0.22
•	-0.07 (0.78)		(0.38)			-0.22 (0.45)
vs Hispanic		(0.78)	(0.36)	(0.34)	(0.51)	(0.43)
Pre-pandemic factors						
Pre-pandemic depressive severity	1.00	0.60	1.45	0.07	1.07	0.00
Mild vs None	1.80	2.63	-1.47	-2.06	-1.87	-0.30
	(5.29)	(4.67)	(2.17)	(1.97)	(3.23)	(2.21)
Mod/severe vs None	7.90	-0.14	-3.03	-3.22	-1.47	-1.53
	(5.41)	(4.77)	(2.22)	(2.01)	(3.30)	(2.25)
Log (days) x Depressive severity						
Mild vs None	0.19	-0.08	0.03	0.22	0.24	-0.11
	(1.14)	(1.01)	(0.47)	(0.42)	(0.70)	(0.47)
Mod/severe vs None	-0.52	0.98	0.20	0.29	-0.16	-0.09
	(1.16)	(1.03)	(0.48)	(0.43)	(0.71)	(0.48)
Experiences with COVID-19						
Routine						
Mild	2.22	1.52	-0.96	-1.33	-0.50	-0.56
vs No change	(0.91)*	(0.91)	(0.44)*	(0.40)**	(0.60)	(0.53)
Moderate	1.46	1.49	-0.62	-0.79	-0.80	-0.17
vs No change	(0.80)	(0.80)	(0.39)	(0.36)*	(0.53)	(0.47)
Severe	1.98	1.85	-0.59	-0.43	-0.71	-0.60
vs No change	(0.89)*	(0.89)*	(0.43)	(0.39)	(0.58)	(0.52)
Access to Mental Health Treatment						
Mild	0.19	0.81	-0.19	-0.06	0.43	-0.17
vs No change	(0.60)	(0.60)	(0.29)	(0.26)	(0.39)	(0.35)
Moderate	2.97	3.07	-0.68	-0.87	-0.75	-1.28
vs No change	(0.93)**	(0.92)**	(0.44)	(0.41)*	(0.61)	(0.54)*
Severe	5.48	5.34	-1.66	-2.24	-1.88	-1.69
vs No change	(1.55)**	(1.53)**	(0.74)*	(0.68)**	(1.02)	(0.89)
Access to extended family and non-family social supports						
Mild vs No change	-0.13 (0.71)	-1.10 (0.71)	-0.17 (0.34)	0.29 (0.32)	-0.17 (0.47)	-0.32 (0.42
Moderate vs No change	1.40 (0.82)	0.86 (0.81)	-0.76 (0.39)	-0.06 (0.36)	-0.89 (0.54)	-0.61 (0.47
Severe vs No change	2.15 (1.13)	0.04 (1.12)	-1.68 (0.54)	-0.93 (0.50)	-2.11(0.74)*	-1.07 (0.66

\* *p*<0.05; \*\* *p*<0.001; \*\*\* *p*<0.0001.

studies for the Social Sciences) found relatively stable symptoms of depression and anxiety between 2019 and March 2020, and noted worked disability as among the few vulnerabilities to worsening symptoms (van der Velden et al., 2020). These results mirror our data showing relatively stable symptoms, except in those with significant disruption in routines.

Since our study only included individuals with a history of depression, we cannot directly compare our results to prior work in the general population. Given the relative stability of symptoms in our population, and the general worsening of symptoms in other broader population surveys, it is plausible that pre-pandemic mental illness confers some protective factor during the pandemic. In those with moderate-to-severe pre-pandemic symptoms, this may be a ceiling effect (little room for individuals to get worse) or that disruption in employment or social routines had less impact if they were already severely disrupted. For individuals with minimal pre-pandemic symptoms, prior struggle with mental illness may have primed individuals to better cope with pandemic distress relative to those who have never suffered from mental illness. For example, these individuals may be faster to connect with mental healthcare. Both of these are supported by our data showing early pandemic disruption in routines and access to mental healthcare were associated with worse symptoms during the pandemic

Limitations of this study relate primarily to the naturalistic design of this study and potential sampling bias. While this study draws on an existing (pre-pandemic) observational study with actively engaged participants, it is possible individuals with whom the pandemic had a greater impact were more eager or able to participate. For example, those in quarantine or those recently unemployed may have been more able to participate. It is also worth noting that our COVID-19 Impact Scale, by the nature of this novel pandemic, is novel itself, and must be interpreted with caution. . Finally, this study is limited to participants with a history of a depressive disorder and may not generalized to those without a history of depression.

Nonetheless, these data suggest general stability of symptom severity during the pandemic in those with a history of a depressive disorder. Future work will continue to follow these same participants as the pandemic progresses and further explore factors that moderate worsening or improvement over time.

### Author contribution statement

Andrew H. Czysz: Conceptualization, Methodology, Validation, Investigation, Writing - original draft, Writing - review & editing, Supervision. Karabi Nandy: Methodology, Validation, Formal analysis, Data curation, Writing - original draft, Writing - review & editing, Supervision. Jennifer L. Hughes: Conceptualization, Methodology, Writing - original draft.

Abu Minhajuddin: Conceptualization, Methodology, Validation, Formal analysis, Datation curation, Writing - review & editing. Cherise R. Chin Fatt: Conceptualization, Methodology, Writing - review & editing. Madhukar H. Trivedi: Conceptualization, Writing - review & editing, Project administration, Supervision

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### **Declaration of Competing Interest**

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