Title: Evidence-Based Therapist-Supported Digital Mental Health Intervention for Patients Experiencing Medical Multimorbidity: A Retrospective Cohort Intent-to-Treat Study

Running Title: Digital Mental Health Intervention for Patients with Multimorbidity

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Abstract

Objective: Multimorbidity or the co-occurrence of multiple health conditions is increasing globally and associated with significant psychological complications. It is unclear whether digital mental health (DMH) interventions for patients experiencing medical multimorbidity (MMB) are effective, particularly given that this patient population faces more treatment resistance.

Therefore, there is a need for initial preliminary research to examine whether DMH interventions are associated with reductions on depressive and anxiety symptoms in the context of MMB.

Methods: This preregistered retrospective cohort intent-to-treat study with 2,819 patients enrolled in a therapist-supported DMH (TS-DMH) intervention examined the associations between MMB and mental health.

Results: Results indicated that more MMB was significantly associated with greater presenting mental health symptom severity. MMB did not have a deleterious influence on depressive symptom trajectories across treatment, although having one medical condition was associated with a steeper decrease in anxiety symptoms compared to patients with no medical conditions. Finally, MMB was not associated with time to dropout, but was associated with higher dropout and was differentially associated with fewer beneficial treatment outcomes, although this is likely attributable to higher presenting symptom severity, rather than lesser symptom reductions during treatment.

Conclusions: The MHP showed preliminary effectiveness as an evidence-based treatment for patients experiencing depression and anxiety in the context of MMB. Future DMH treatments and research might investigate tailored barrier reduction and extended treatment lengths for patients experiencing MMB to allow for greater treatment dose to reduce symptoms below clinical outcome thresholds.

Introduction

Multimorbidity, or the co-occurrence of two or more health conditions, including both psychiatric and physical health disorders¹, has been described as a “defining challenge”² and an “emerging priority” for health systems³. Currently, around 60% of adults experience two or more conditions, while approximately 40% of adults experience three or more conditions⁴ and the global prevalence has increased in recent years³. Multimorbidity is particularly disabling and impairing⁵, detrimental to quality of life⁶, clinically complex and hard to treat⁴, and disproportionately influential on healthcare utilization and cost³. Psychiatric and physical health conditions are bidirectional, such that greater medical multimorbidity (MMB) or the co-occurrence of multiple physical health disorders are associated with greater psychiatric complaints⁷, while individuals experiencing depression and anxiety are at significantly elevated risk for various deleterious health outcomes and premature mortality⁸. In fact, the predictive power of an affective disorder rivals well-known biomedical risk factors, such as smoking, inactivity, and obesity⁹, such that individuals with affective disorders lose a median of 10 years off their lives due to all-cause mortality¹⁰. Therefore, the need for effective, accessible, and scalable psychiatric treatments for patients experiencing MMB it is of utmost importance.

Currently, less than half of patients experiencing psychiatric complications receive treatment¹¹. A constellation of factors including significant structural barriers¹², shortage of providers¹³, and affordability¹² culminate in significant unmet psychiatric needs. Digital mental health (DMH) interventions have gained popularity for their purported ability to ameliorate several of these limitations. Initial evidence for DMH interventions indicates that these treatments have comparable effectiveness at reducing depressive symptoms when compared to in-person Cognitive Behavioral Therapy (CBT) and superior effects when compared to treatment

as usual and waitlist controls¹⁴. DMH interventions have also been found to be superior at reducing anxiety symptoms when compared to active controls and waitlist controls¹⁵. Evidence suggests that these treatments may be more cost-effective compared to myriad alternatives, including waitlist, group CBT, telephone counseling, and unguided internet CBT for depression and anxiety^{16,17}. Despite the promise of DMH interventions, recent meta-analytic estimates of dropout in smartphone-delivered interventions for depressive symptoms (47.8%)¹⁸ appear higher than meta-analytic dropout estimates for in-person psychotherapy for major depression (19.9%)¹⁹.

Currently, there is a dearth of research examining the effectiveness of these DMH app-based interventions for treating patients with internalizing symptoms that also experience MMB. The majority of research has focused on medical telehealth interventions for specific chronic diseases with supplementary psychiatric components with two recent meta-analyses largely examining remote telehealth interventions (e.g., phone, video, email, and web-based consultation) for depressive and anxiety symptoms that co-occur, with secondary medical conditions^{20,21}. Therefore, there is a pressing need to comprehensively examine the impact of smartphone-delivered DMH interventions for patients presenting with elevated internalizing symptoms that also are experiencing multiple medical conditions.

Current Study

This retrospective single-arm cohort intent-to-treat (ITT) study, preregistered on Open Science Framework (<https://osf.io/vh2et/>), was devised to examine associations between 1) number of medical conditions, here on referred to as MMB, and presenting depressive and anxiety symptom severity, 2) influence of MMB on both depressive and anxiety symptom trajectories across the course of an evidence-based DMH treatment, and 3) MMB and various

treatment outcomes. First, we hypothesized that more MMB would show a positive dose-response association with higher presenting depressive and anxiety symptoms. Second, we hypothesized that more MMB would moderate the association between treatment week and depressive and anxiety symptoms, such that patients with more MMB would have flatter depressive and anxiety trajectories as compared to patients with no MMB. Lastly, we hypothesized that patients with more MMB would have significantly worse treatment outcomes, as indexed by lower treatment response, clinically significant improvement, minimally clinically important difference (MCID), and remission at post-treatment; and have both increased dropout and earlier dropout.

Methods and Materials

Participants.

The present study included patients treated with the Meru Health Program (MHP), an evidence-based therapist-supported DMH (TS-DMH) intervention. All data came from 2,819 patients, aged 18-77 (see Table 1) recruited in the United States and who started the program on or after 03/30/2020 and ended treatment on or before 09/01/2021. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Recruitment.

Patients entered the MHP via referrals from employee assistance programs or via their healthcare providers. Patients consented to participate and have their collected and deidentified data used for research purposes when accepting the MHP privacy practices. Data collected as part of care is stored in Health Insurance Portability and Accountability Act-compliant electronic medical records that includes protected health information. All data are encrypted in transit, and

at rest. Institutional review board exemption for this analysis was obtained from the Pearl Institutional Review Board (21-MERU-114) for analyses of previously collected and de-identified data. Inclusion/exclusion criteria of the MHP required patients to be at least 18 years of age or older, have at least mild levels of depression, anxiety, or burnout, own a smartphone, and not have an active substance use disorder, severe active suicidal ideation with a specific plan, severe active self-harm, or a history of psychosis or mania.

Meru Health Program (MHP) Treatment.

The MHP has been described in detail in prior publications²². In sum, the MHP is a 12-week treatment composed of several different therapist-supported components of evidence-based therapies delivered via a smartphone app.

Measures. All measures examined in this study were collected in the MHP app at baseline and biweekly during the MHP including at end-of-treatment.

Patient Health Questionnaire-9 (PHQ-9). Patients completed the PHQ-9 to screen for depression²³, which is comprised of a list of nine depressive symptoms with response options ranging from 0 (not at all) to 3 (nearly every day) with total scores ranging from 0-27. The PHQ-9 has excellent internal consistency (Cronbach's $\alpha=0.89$ in primary care settings), and excellent test-retest reliability (ICC=0.84)²³.

Generalized Anxiety Disorder-7 (GAD-7). Patients completed the GAD-7 to screen for anxiety²⁴, which is comprised of a list of seven anxiety symptoms with response options ranging from 0 (not at all) to 3 (nearly every day) with total scores ranging from 0-21. The GAD-7 has excellent internal consistency (Cronbach's $\alpha=0.92$), and excellent test-retest reliability (ICC=0.83)²⁴.

Lifetime Medical Conditions. At intake, patients completed an assessment of lifetime medical (i.e., physical health) conditions, including diabetes, anemia, hyper or hypothyroidism, liver disease, heart disease, asthma/chronic bronchitis/emphysema/COPD, cancer, chronic pain/fibromyalgia, kidney disease, arthritis, lupus/IBS/MS, dementia/Alzheimer's, and any other physical health condition. Self-reported medical conditions and medical records have acceptable agreement²⁵ and checklists have higher accuracy and are more complete when compared to data collected from routine sources²⁶. The checklist created a MMB categorical variable of increasing number of medical conditions (0- none, 1- one, 2- two, 3- three or more).

Treatment Outcomes.

- Treatment Response (TR) refers to a clinically significant degree of symptom reduction following treatment initiation and was defined as a 50% reduction in PHQ-9²⁷ and GAD-7²⁷ for patients with a 5 or above starting PHQ-9 and GAD-7 score, respectively.
- Minimally Clinically Important Difference (MCID) refers to smallest change in scores that are of “perceived benefit” to the patient and was defined as a PHQ-9 score reduction of ≥ 5 ²⁸ and a GAD-7 score reduction of ≥ 4 ²⁹ for patients with a 5 or above starting PHQ-9 and GAD-7 score, respectively.
- Clinically Significant Improvement (CSI) was defined as a 50% PHQ-9 reduction from the pretreatment score combined with an end-of-treatment PHQ-9 score that was less than 10²³ for patients with a 10 or above starting score. Due to a lack of a clear definition for CSI for GAD-7, we used this same definition as we used for the PHQ-9.

- Remission was defined as a PHQ-9 < 5³⁰ for patients with a 5 or above starting PHQ-9. Like the CSI definition above, due to a lack of a clear definition for remission for the GAD-7 we used the same definition as that for the PHQ-9.
- Dropout was defined as any patient that did not complete at least 50%—or 6 of 12—of the treatment week introductory videos, which unlocked treatment week materials.

Covariates. Participant age, gender, psychotropic medication use, days actively engaged with app during each two-week period during treatment, dropout status (all hypotheses, except for dropout model), and baseline PHQ-9 and GAD-7 symptom severity (hypothesis 2 and 3) were used as covariates. Age was categorized into 18-25, 26-34, 35-44, 45-54, and 55 and over.

Role of the funding source.

The funder of the study had no role in the study design, interpretation, or writing of the manuscript. All decisions about the research were taken by the investigative team and were unrestricted.

Statistical Analysis.

All statistical analyses were conducted with RStudio, Version 1.3.959. Statistical significance was defined using *p*-values. Descriptive statistics were calculated for each patient demographic and clinical variable (see Table 1). Outcome measures were analyzed using ITT analysis in which all participants with outcome measures at baseline were included, regardless of intervention engagement or attrition (see Supplemental Material for more information on imputation and missing data). All main effect and covariate estimates as well as unadjusted models can be found in Supplemental Materials.

First, we examined the association between more MMB and presenting baseline depressive and anxiety symptom severity by running two linear regressions for the association between MMB and baseline depression and anxiety symptom severity controlling for covariates.

Second, we examined the impact of treatment week on depressive and anxiety symptoms across the 12-week treatment by conducting a multilevel model that nested treatment week (Level-1) within individuals (Level-2). Fixed effects including MMB, and covariates were tested at the level of participants (Level-2). Further, to determine whether more MMB had an impact on depressive and anxiety symptom trajectories across treatment, we examined the cross-level interaction between MMB and treatment week in separate models for depression and anxiety symptoms, while controlling for covariates.

Third, to quantify the clinical significance of the treatment outcomes, we first ran a series of paired-sample *t*-tests to examine pre-post changes in PHQ-9 and GAD-7 scores by MMB to examine whether there were significant reductions in depressive and anxiety symptoms across treatment. Next, we ran a series of logistic regressions with MMB predicting treatment outcomes including, dropout, TR, CSI, MCID, and remission controlling for covariates. Finally, to rule out differential attrition among individuals with MMB as a potential confound for treatment outcomes, we performed a Kaplan-Meier Survival Analysis and Cox proportional hazard (PH) model to examine time to dropout (i.e., last active day of app use) and examined the interaction between MMB and patient age, as age was significantly associated with MMB, $X^2(df=168, N=2,819)=378, p<0.001$). Treatment completers (i.e., completed at least 50%—or 6 of 12—of the treatment weeks) were considered right censored.

Results

Demographic and Clinical Characteristics

Table 1 presents patient demographic and clinical characteristics. Most patients were female (79.78%) with an average age of 39.40 (standard deviation [SD]=11.10). The mean baseline PHQ-9 was 11.40 (SD=6.02) and the mean baseline GAD-7 was 11.40 (SD=4.84), indicating moderate levels of depression and anxiety, respectively, which fall above the diagnostic cutoffs indicative of likely depression and anxiety diagnosis^{23,24}. 27.60% of the sample reported taking psychiatric medication at intake.

Multimorbidity and Baseline Symptom Severity.

MMB was significantly positively associated with baseline depressive in a dose-response relationship, such that having one condition (Std.beta=0.10, $p=0.022$, 95%CI[0.01-0.18]), two conditions (Std.beta=0.18, $p<.001$, 95%CI[0.07-0.29]), or three or more conditions (Std.beta = 0.36, $p<.001$, 95%CI[0.23-0.50]) was associated with greater presenting depressive symptom severity when compared to patients with no medical conditions, albeit these effects were small ($R^2 < .10$) after controlling for covariates. Similarly, MMD was significantly positively associated with baseline anxiety, such that having one condition (Std.beta=0.14, $p =0.002$, 95%CI[0.05-0.22]), two conditions (Std.beta = 0.11, $p =0.043$, 95%CI[0.004-0.22]), or three or more conditions (Std.beta=0.26, $p<.001$, 95%CI[0.12-0.40]) was associated with greater presenting anxiety symptom severity when compared to patients with no medical conditions, albeit these effects were small ($R^2<.10$) after controlling for covariates.

Depressive and Anxiety Symptom Trajectories by Multimorbidity

Treatment week was significantly and inversely associated with PHQ-9 scores (Std.beta=-0.32, $p<.001$, 95%CI[-0.34- -0.31]) and GAD-7 (Std.beta=-0.41, $p<.001$, 95%CI[-0.42- -0.39]). More MMB was associated with depressive and anxiety symptom levels across treatment. Specifically, having one medical condition was significantly associated with higher

PHQ-9 (Std.beta=0.02, $p=.008$, 95%CI [-0.03-0.07]) and GAD-7 (Std.beta=0.06, $p<.001$, 95%CI[0.004-0.120]) scores when compared to patients with no medical conditions and having three or more medical conditions were significantly associated with higher PHQ-9 (Std.beta=0.11, $p<.001$, 95%CI[0.03-0.20]) and GAD-7 (Std.beta=0.22, $p<.001$, 95%CI[0.13-0.32]) scores when compared to patients with no medical conditions, although these effects were not found for patients with two medical conditions ($p\geq.05$). For depressive symptom trajectory, there were no interaction effects between treatment week and multimorbidity ($p\geq.05$), indicating no effect of multimorbidity on depressive symptom trajectories across treatment. In contrast for anxiety symptom trajectories, there was one interaction effect between treatment week and having one medical condition (Std.beta=-0.04, $p=.003$, 95%CI [-0.07- -0.01]), such that those with one medical condition had a steeper decrease in anxiety symptoms across treatment, although this effect was not found for any other interaction ($p\geq .05$). These models had substantial explanatory power (PHQ-9 Model conditional $R^2=0.87$, GAD-7 Model conditional $R^2=0.75$) and the marginal R^2 or part related to the fixed effects (e.g., MMB and covariates) alone was 0.62 for the PHQ-9 Model and 0.32 for the GAD-7 Model.

Multimorbidity and Treatment Outcomes

The MHP was associated with significant improvements in depressive symptoms conditions for patients with no (mean-decrease=-6.11), $t(1302)=42.61$, $p<0.001$, $\hat{g}_{\text{hedges}}=1.18$, 95% CI [1.11-1.25]; one (mean-decrease=-6.64), $t(831)=35.56$, $p<0.001$, $\hat{g}_{\text{hedges}}=1.23$, 95% CI [1.14-1.32]; two (mean-decrease=-5.79), $t(438)=25.43$, $p<0.001$, $\hat{g}_{\text{hedges}}=1.21$, 95% CI [1.09-1.34]; and three or more (mean-decrease=-6.90), $t(244)=20.72$, $p<0.001$, $\hat{g}_{\text{hedges}}=1.32$, 95% CI [1.15-1.49) medical conditions. The MHP was also associated with significant improvements in anxiety symptoms conditions for patients with no (mean-decrease=-6.41), $t(1302)=50.92$,

$p < 0.001$, $\hat{g}_{\text{hedges}} = 1.41$, 95% CI [1.33-1.49]; one (mean-decrease=-6.98), $t(831) = 44.42$, $p < 0.001$, $\hat{g}_{\text{hedges}} = 1.54$, 95% CI [1.44-1.64]; two (mean-decrease=-6.28), $t(438) = 27.70$, $p < 0.001$, $\hat{g}_{\text{hedges}} = 1.32$, 95% CI [1.19-1.45]; and three or more (mean-decrease=-6.54), $t(244) = 20.28$, $p < 0.001$, $\hat{g}_{\text{hedges}} = 1.29$, 95% CI [1.12-1.46) medical conditions.

PHQ-9 Treatment Outcome Categories. While having one medical condition was not associated with differential treatment outcomes when compared to patients with no medical conditions; having two conditions was not associated with TR, CSI, or remission, but was significantly associated with reduced MCID when compared to patients with no medical conditions; and having three or more conditions wasn't associated with TR or remission, but was significantly associated with reduced MCID and CSI when compared to patients with no medical conditions. These effects were associated with various effect sizes ($R^2 = 0.037-0.309$) (see Table 2).

GAD-7 Treatment Outcomes Categories. While having one medical condition wasn't associated with differential treatment outcomes when compared to patients with no medical conditions; having two medical conditions was significantly associated with fewer beneficial treatment outcomes of interest as compared to patients with no medical conditions; and having three or more medical conditions wasn't associated with CSI, but it was significantly associated with reduced TR, MCID, and remission when compared to patients with no medical conditions. These effects were smaller than those for PHQ-9 ($R^2 = 0.054-0.292$) (see Table 2).

Dropout. Having one or three or more medical conditions were associated with higher dropout than those with no medical conditions ($R^2 = 0.76$) (see Table 3).

Survival Analysis. The Cox PH Model indicated that there were no main effects for MMB on time to patient dropout, but there were significant protective effects for those aged 45-

54 and those aged 55 and above in models controlling for gender, medication use, and baseline depressive or anxiety symptom severity (see Table 4). In addition, there were no interaction effects for number of MMB and age, except patients that had two medical conditions and were 35-44 years old, had a lower risk of dropout. In line with these results, Kaplan-Meyer curves, showed that there were no significant effects of MMB on time to dropout (Figure 1). See Supplementary Materials for Kaplan-Meyer curves by age.

Discussion

This preregistered retrospective single-arm ITT study was devised to investigate the association between MMB and psychiatric outcomes during an evidence-based TS-DMH intervention among 2,819 patients. Overall, this study showed preliminary effectiveness and feasibility for a TS-DMH intervention for strongly improving depressive and anxiety symptoms among patients experiencing MMB.

Our hypotheses verify that MMB is an important and growing concern for DMH to consider. First, more MMB was significantly associated with greater severity of baseline depressive and anxiety symptoms, although these were small effects in adjusted analyses. These findings replicate past research indicating that multimorbidity is more disabling and impairing⁵, detrimental to quality of life⁶, clinically complex, and hard to treat⁴.

Second, and in contrast to our hypotheses, more MMB did not influence the trajectory of depressive or anxiety symptoms across treatment and only individuals that experienced one medical condition had a steeper decrease in anxiety symptom trajectory across treatment when compared to patients with no medical conditions. These findings are particularly hopeful from a clinical perspective, such that more MMB did not negatively influence the trajectory of depressive and anxiety symptoms across treatment.

In terms of treatment outcomes, results were pleasantly surprising, in that they did not uphold the hypotheses that MMB would blunt the overall reduction in depressive and anxiety symptoms. Overall, the MHP was associated with large effect size decreases in depressive and anxiety symptoms regardless of the number of MMB. For depressive symptom outcomes, although having one medical condition was not associated with differential treatment outcomes when compared to patients without any medical conditions, having two conditions was associated with reduced MCID and having three or more conditions was associated with reduced MCID and CSI when compared to patients with no medical conditions. Interestingly, MMB had no relationship with depressive symptom remission; however, these findings are not surprising when considering that more MMB was associated with higher baseline depressive symptoms, but not depressive symptom trajectory as compared to those with no MMB. That is, those with more MMB had similar depressive symptom decreases as those with no MMB, but due to higher starting symptom severity they were less likely to pass defined thresholds.

For anxiety outcomes, having one medical condition was not associated with differential treatment outcomes when compared to patients with no medical conditions. This finding may have been due to beneficial effects of more healthcare system contact, but not experiencing enough MMB that it overpowered potential beneficial effects of having greater healthcare system contact. In contrast, as compared with those with no MMB, having two medical conditions was significantly associated with reduction in all treatment outcomes when compared to patients with no medical conditions; and having three or more medical conditions was associated with significantly reduced TR, MCID, and remission when compared to patients with no medical conditions, which may relate to the point above and indicate that once patients pass having one

medical condition, the detrimental effects of MMB overpower any beneficial effect of increased contact with the healthcare system.

Lastly, having one or three or more medical conditions was associated with higher dropout, compared to those with no conditions. Interestingly, this was not found for the comparison between those with no versus two medical conditions. In addition, survival analyses examining the time to dropout indicated that more MMB didn't influence dropout timing, while older age was associated with lower risk of earlier drop out. Again, there was only one multimorbidity interaction with age (patients that had two medical conditions and were 35-44 years old had a lower dropout risk). Again, findings provide a hopeful clinical message that those with more MMB were no more likely to have earlier dropout when compared to patients with no MMB.

Limitations and Future Directions

While this study had several significant strengths including a large patient sample with an ITT study design, the study findings should be interpreted considering several limitations. Most limitations are related to real-world data collection as part of continuous TS-DMH intervention improvement. First, this single-arm observational study precluded the ability to conclude that treatment effects were due to MHP as opposed to unspecified factors. We plan to conduct blinded randomized control trials to examine MHP effectiveness when compared to other evidence-based in-person interventions. Second, we started collecting race/ethnicity data after we began collecting medical conditions leading to high rates of demographic missingness that prevented their use as covariates. This currently limits the generalizability of these findings to specific racial and ethnicity groups; however, we now collect this important information and will include these variables as future covariates. Finally, although we didn't collect medical condition

severity, impairment, or the full spectrum of possible medical conditions, these limitations are common¹ and these variables may be important to consider in future research.

Conclusion

This study replicated the association between more MMB and higher psychiatric symptoms, while advancing this research to an evidence-based TS-DMH intervention. Results indicated that more MMB wasn't associated with a psychiatric symptom trajectories or time to dropout, although there were differential treatment outcomes depending on MMB, however, these outcomes may be attributable to starting with higher symptoms, rather than experiencing lesser symptom reductions during treatment. Future research should account for MMB in DMH interventions as they have a diverse impact on patient outcomes.

Author Contributions.

B.N., N.C.P, K.A., and V.L.F.H. contributed to the interpretation of the results, provided critical feedback, and helped shape the research, analysis, and manuscript. B.N. conceived, wrote the initial draft of the manuscript, and ran analyses for the manuscript.

Role of Funding Source

Meru Health Inc. provided the funding to conduct the research. The funder of the study had no role in the study design, data interpretation, or writing of the manuscript. All decisions about the research were taken by the investigative team and were unrestricted as the study was preregistered.

Conflicts of Interest

Meru Health is the full-time employer of the authors. Meru Health had no role in the conceptualization or design of the study, analysis or interpretation of these data, writing of the manuscript, or in the decision to publish these findings.

Ethics Committee Approval

Institutional review board exemption for this analysis was obtained from the Pearl Institutional Review Board (21-MERU-114).

Guarantor.

B.N. and V.L.F.H.

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Table 1. Patient Demographics and Treatment Outcomes.

Variable		N (Percent)	Mean (SD), Range
Patient Demographics			
Age		2,819	39.4 (11.1), 18-77
Gender	Male	541 (19.19%)	
	Female	2,249 (79.78%)	
	Non-Binary	29 (1.03%)	
Taking Psychiatric Medication	Yes	778 (27.60%)	
	No	2,041 (72.40%)	
Baseline PHQ-7 Severity	Minimal		
	Mild	370 (13.13%)	
	Moderate	816 (28.95%)	
	Moderately Severe	582 (20.68%)	
Baseline GAD-7 Severity	Severe	308 (10.93%)	
	Minimal	370 (13.13%)	
	Mild	816 (28.95%)	
	Moderate	742 (26.32%)	
Medical Multimorbidity	Severe	891 (31.61%)	
	None	1303 (46.22%)	
	One Condition	832 (29.51%)	
	Two Conditions	439 (15.57%)	
	Three or More Conditions	245 (8.69%)	
Treatment Outcomes			
Treatment Response	PHQ-9	1665 (67.00%)	
	GAD-7	1790 (68.19%)	
MCID	PHQ-9	1679 (68.56%)	
	GAD-7	1998 (76.11%)	
Clinically Significant Change	PHQ-9	1144 (70.06%)	
	GAD-7	1320 (74.66%)	
Remission	PHQ-9	1216 (49.65%)	
	GAD-7	1458 (55.54%)	
Dropout	Completer	2,082 (73.86%)	

Note: MCID = minimally clinically important difference.

Table 2. PHQ-9 and GAD-7 Treatment Outcomes.

Predictors	Treatment Response				MCID				CSI				Remission			
	PHQ-9		GAD-7		PHQ-9		GAD-7		PHQ-9		GAD-7		PHQ-9		GAD-7	
	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value	Standardized Beta (SE)	P-Value
(Intercept)	0.94 (0.19)	0.264	0.66 (0.18)	<0.001	1.21 (0.23)	<0.001	1.61 (0.24)	<0.001	0.68 (0.22)	<0.001	0.89 (0.23)	0.293	0.39 (0.19)	<0.001	0.44 (0.18)	<0.001
MMB- one condition	-0.12 (0.11)	0.269	0.15 (0.11)	0.153	-0.22 (0.12)	0.071	0.08 (0.13)	0.560	-0.05 (0.14)	0.720	0.07 (0.14)	0.602	-0.01 (0.11)	0.947	0.06 (0.10)	0.568
MMB- two conditions	-0.20 (0.13)	0.121	-0.28 (0.13)	0.031	-0.32 (0.15)	0.036	-0.54 (0.16)	0.001	-0.28 (0.16)	0.080	-0.39 (0.16)	0.016	-0.23 (0.13)	0.093	-0.34 (0.13)	0.007
MMB- three or more conditions	-0.32 (0.16)	0.051	-0.35 (0.17)	0.039	-0.52 (0.20)	0.010	-0.62 (0.21)	0.003	-0.50 (0.19)	0.010	-0.38 (0.20)	0.062	-0.25 (0.17)	0.145	-0.47 (0.16)	0.004
Age- 26-34	-0.06 (0.17)	0.709	0.15 (0.17)	0.384	0.15 (0.21)	0.485	0.09 (0.22)	0.664	0.29 (0.20)	0.149	0.38 (0.20)	0.058	-0.25 (0.18)	0.158	-0.05 (0.16)	0.778
Age- 35-44	0.02 (0.17)	0.892	0.16 (0.17)	0.356	0.15 (0.21)	0.485	0.23 (0.22)	0.298	0.46 (0.20)	0.022	0.33 (0.21)	0.108	-0.31 (0.18)	0.085	-0.03 (0.16)	0.863
Age- 45-54	0.21 (0.19)	0.275	0.30 (0.18)	0.109	0.36 (0.23)	0.108	0.35 (0.24)	0.135	0.49 (0.22)	0.028	0.51 (0.23)	0.026	-0.11 (0.19)	0.565	0.17 (0.18)	0.333
Age- 55 and above	0.37 (0.21)	0.075	0.64 (0.21)	0.002	0.41 (0.25)	0.094	0.67 (0.26)	0.010	0.92 (0.25)	<0.001	0.94 (0.27)	<0.001	0.04 (0.21)	0.849	0.41 (0.20)	0.041
Sex- female	-0.04 (0.12)	0.726	0.09 (0.11)	0.432	0.16 (0.13)	0.241	0.10 (0.14)	0.455	-0.12 (0.15)	0.408	-0.06 (0.16)	0.698	0.08 (0.12)	0.505	-0.07 (0.11)	0.515
Sex- non-binary	-1.75 (0.45)	<0.001	-1.24 (0.42)	0.003	-1.75 (0.47)	<0.001	-1.41 (0.49)	0.004	-1.78 (0.48)	<0.001	-1.48 (0.48)	0.002	-1.57 (0.64)	0.015	-2.09 (0.56)	<0.001
Completion-drop-out	0.13 (0.13)	0.321	0.30 (0.13)	0.023	0.10 (0.16)	0.516	0.35 (0.17)	0.036	0.45 (0.17)	0.008	0.57 (0.18)	0.001	-0.50 (0.14)	<0.001	-0.07 (0.13)	0.555
Total days active	-0.08 (0.06)	0.168	0.11 (0.06)	0.071	-0.09 (0.07)	0.206	0.08 (0.07)	0.271	-0.17 (0.07)	0.020	-0.02 (0.07)	0.757	0.01 (0.06)	0.817	0.06 (0.06)	0.331

Psychotropic Medication- Present	-0.37 (0.10)	<0.001	-0.52 (0.10)	<0.001	-0.46 (0.12)	<0.001	-0.29 (0.12)	0.018	-0.28 (0.12)	0.024	-0.54 (0.12)	<0.001	-0.35 (0.10)	0.001	-0.28 (0.10)	0.003
Baseline PHQ-9	0.33 (0.05)	<0.001			1.70 (0.08)	<0.001			-0.16 (0.06)	0.006			-0.98 (0.05)	<0.001		
Baseline GAD-7			0.59 (0.05)	<0.001			1.73 (0.08)	<0.001			0.30 (0.06)	<0.001			-0.70 (0.04)	<0.001
Observations	2449		2625		2449		2625		1633		1768		2449		2625	
R ² Tjur	0.037		0.082		0.309		0.292		0.051		0.054		0.209		0.131	

Note- CSI = clinically significant improvement; GAD-7 = Generalized Anxiety Disorder-7; MCID = minimally clinically important difference; MMB = medical multimorbidity; PHQ-9 = Patient Health Questionnaire-9; SE = standard error. Bold = significant.

Table 3. Multimorbidity and Treatment Dropout.

<i>Predictors</i>	Dropout Unadjusted			Dropout Adjusted		
	<i>Standardized Beta (95% CI)</i>	<i>Standardized SE</i>	<i>P-Value</i>	<i>Standardized Beta (95% CI)</i>	<i>Standardized SE</i>	<i>P-Value</i>
(Intercept)	-0.96 (-1.08 – -0.84)	0.06	<0.001	-6.56 (-7.52 – -5.65)	0.48	<0.001
MMB- one condition	-0.09 (-0.28 – 0.11)	0.10	0.389	0.43 (0.02 – 0.84)	0.21	0.040
MMB- two conditions	-0.28 (-0.54 – -0.03)	0.13	0.032	0.07 (-0.46 – 0.61)	0.27	0.784
MMB- three or more conditions	-0.19 (-0.52 – 0.12)	0.16	0.233	0.77 (0.03 – 1.52)	0.38	0.044
Age- 26-34				-0.61 (-1.24 – 0.00)	0.32	0.054
Age- 35-44				-0.43 (-1.07 – 0.20)	0.32	0.181
Age- 45-54				-0.66 (-1.36 – 0.03)	0.35	0.062
Age- 55 and above				-0.61 (-1.48 – 0.25)	0.44	0.164
Sex- female				0.22 (-0.20 – 0.64)	0.22	0.309
Sex- non-binary				-0.43 (-2.33 – 1.89)	1.07	0.685
Total days active				-8.23 (-9.06 – -7.47)	0.41	<0.001
Psychotropic Medication- Present				-0.39 (-0.79 – 0.02)	0.21	0.060

Baseline PHQ-9		0.15 (-0.04 – 0.35)	0.10	0.129
Baseline GAD-7		-0.05 (-0.24 – 0.14)	0.10	0.611
Observations	2819	2819		
R ² Tjur	0.002	0.756		

Note- CI = confidence interval; GAD-7 = Generalized Anxiety Disorder-7; MMB = medical multimorbidity; PHQ-9 = Patient Health Questionnaire-9; SE = standard error. Bold = significant.

Table 4. Cox Proportional Hazard Ratio Model

Variable	coef	exp(coef)	se(coef)	z	p
MMB- one condition	0.013	1.013	0.232	0.100	0.950
MMB- two conditions	0.562	1.754	0.336	1.700	0.090
MMB- three or more conditions	0.884	2.421	0.725	1.200	0.220
Age- 26-34	-0.129	0.879	0.168	-0.800	0.440
Age- 35-44	-0.216	0.806	0.173	-1.200	0.210
Age- 45-54	-0.534	0.586	0.217	-2.500	0.010
Age- 55 and above	-1.163	0.313	0.324	-3.600	< 0.001
Gender- female	-0.057	0.945	0.094	-0.600	0.540
Gender- non-binary	-0.023	0.978	0.348	-0.100	0.950
Psychotropic Medication- present	0.091	1.095	0.086	1.100	0.290
Baseline PHQ-9	0.024	1.024	0.007	3.300	< 0.001
Baseline GAD-7	0.000	1.000	0.009	0.000	0.990
MMB- one condition x Age- 26-34	0.026	1.026	0.274	0.100	0.920
MMB- two conditions x Age- 26-34	-0.759	0.468	0.394	-1.900	0.050
MMB- three or more conditions x Age- 26-34	-0.913	0.401	0.779	-1.200	0.240
MMB- one condition x Age- 35-44	-0.253	0.776	0.278	-0.900	0.360
MMB- two conditions x Age- 35-44	-0.887	0.412	0.393	-2.300	0.020
MMB- three or more conditions x Age- 35-44	-1.046	0.352	0.770	-1.400	0.170
MMB- one condition x Age- 45-54	0.101	1.106	0.326	0.300	0.760
MMB- two conditions x Age- 45-54	-0.718	0.488	0.431	-1.700	0.100
MMB- three or more conditions x Age- 45-54	-1.008	0.365	0.784	-1.300	0.200
MMB- one condition x Age- 55 and above	-0.022	0.978	0.463	0.000	0.960
MMB- two conditions x Age- 55 and above	-0.534	0.586	0.554	-1.000	0.340
MMB- three or more conditions x Age- 55 and above	-0.527	0.591	0.827	-0.600	0.520

Note- GAD-7 = Generalized Anxiety Disorder-7; MMB = medical multimorbidity; PHQ-9 = Patient Health Questionnaire-9; SE = standard error. Bold = significant.

Figure 1. Kaplan-Meier Curve by Number of Medical Conditions.