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Digital Interventions to Improve Treatment Adherence in Generalized Anxiety Disorder: A Randomized Clinical Trial

Carolina Benedetto Gallois

carolinagallois@gmail.com

Federal University of Rio Grande do Sul

Mairon Matheus Machado

Universidade Federal de Ciências da Saúde de Porto Alegre

Gabrielle Terezinha Foppa

Federal University of Rio Grande do Sul

Rafael Ataides Lopes de Oliveira

Universidade Federal de Ciências da Saúde de Porto Alegre

Angélica Cerveira de Baumont

Federal University of Rio Grande do Sul

Alice Barbieri Ebert

Universidade Federal de Ciências da Saúde de Porto Alegre

Leonardo Arruda Zanelatto

Federal University of Rio Grande do Sul

Carolina Cassiano Rangel

Federal University of Rio Grande do Sul

Bruno Lodi

Pontifical Catholic University of Rio Grande do Sul

Luciano Ronchi dos Santos

Federal University of Rio Grande do Sul

Mirian Raquel Fachinetto

Universidade Luterana do Brasil

Ana Laura Gehlen Walcher

Federal University of Rio Grande do Sul

Ives Cavalcante Passos

Federal University of Rio Grande do Sul

Gisele Gus Manfro

Federal University of Rio Grande do Sul

Research Article

Keywords: generalized anxiety disorder, treatment adherence, digital psychiatry, mobile health, measurement-based care, GAD-7, psychoeducation

Posted Date: May 28th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9727754/v1

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Additional Declarations: No competing interests reported.

Abstract

Digital mental health interventions (DMHIs) and measurement-based care (MBC) are increasingly used in clinical practice, yet their combined effectiveness in generalized anxiety disorder (GAD) remains underexplored. This study evaluated the impact of simple and scalable digital interventions—consisting of brief psychoeducational videos and routine symptom monitoring using the Generalized Anxiety Disorder 7-item scale (GAD-7)—as adjuncts to Treatment as Usual (TAU) in patients with GAD.

In this 12-week randomized clinical trial with blinded raters, 60 participants received either TAU alone or TAU plus digital interventions delivered via a mobile application. TAU consisted of biweekly online consultations including symptom assessment, pharmacological management, and general clinical guidance. Outcomes included changes in GAD-7 and Hamilton Anxiety Rating Scale (HAM-A) scores at endpoint and 3 and 6-month follow up assessment, dropout rates, and usability and satisfaction measures.

Both groups showed significant symptom improvement over time. No significant between-group differences were observed in the primary outcome (GAD-7), and differences in HAM-A scores (-7.05, 95% CI -13.5 to -0.56, p=0.034) were not sustained after adjustment for depression comorbidity and at 3 and 6 months follow up evaluation. On the other hand, the intervention group demonstrated a markedly lower dropout rate compared to the control group (6.1% vs. 37%; p = 0.004) and usability of digital intervention was rated as excellent.

These findings highlight that integrating simple, low-cost digital strategies into routine clinical care may substantially improve treatment adherence, addressing a critical gap in mental health services. Given their scalability and ease of implementation, such interventions may represent a scalable and clinically relevant strategy to optimize real-world care for patients with GAD, even when additional symptomatic gains are modest.

Trial registration: ClinicalTrials.gov (NCT05375851). Initial release: 04/14/2022.
Available at: https://clinicaltrials.gov/ct2/show/NCT05375851

Introduction

Generalized Anxiety Disorder (GAD) is a common anxiety disorder with a lifetime prevalence of approximately 5% to 7% (Slee et al., 2019). It is characterized by persistent and excessive anxiety and worry about everyday matters and is often underdiagnosed by healthcare professionals (Slee et al., 2019). GAD has a chronic course with periods of remission and relapse. Treatment includes psychotherapy, pharmacotherapy, or a combination of both (Slee et al., 2019). However, inadequate access to specialized treatment delays diagnosis and exacerbates the condition. Despite advances, many GAD patients remain symptomatic after adequate treatment and experience multiple relapses, leading to significant functional impairments, which underscores the need for new treatment modalities

(Slee et al., 2019; Bandelow et al., 2023; Bisby et al., 2022; Firth et al., 2020; Graham et al., 2020; Pauley et al., 2023).

In an increasing digital era, the use of digital tools as adjuncts in GAD treatment warrants further study. Digital Mental Health Interventions (DMHIs), which refer to mental health services delivered electronically (Soobiah et al., 2020), have gained traction in recent years. However, their implementation and evaluation in routine clinical settings remain challenging due to the complex interactions between users, technology, and healthcare teams. While some studies highlight the benefits of combining DMHIs with usual psychiatric treatment (Lam et al., 2024), a gap remains between research findings and their translation into real-world clinical practice (Borghouts et al., 2021; Seegan et al., 2023), underscoring the need for evidence-based and scalable strategies to integrate DMHIs effectively within routine care (Graham et al., 2020; Stirman et al., 2016).

Data on GAD and DMHIs are limited, with few robust studies available. Most compare DMHIs to waiting list controls, which may offer weak evidence or a nocebo effect (Saramago et al., 2021). These studies often have small sample sizes and focus primarily on web-based treatments, overlooking mobile apps, which are more practical and accessible (Saramago et al., 2021). Christensen et al. (2014) found both web-based interventions and sertraline effective for GAD but did not assess whether combining them improves outcomes. Roy et al. (2021) tested app-delivered mindfulness added to Treatment as Usual (TAU) and observed anxiety reduction. Despite growing research, we found no other studies evaluating the combination of DMHIs with TAU for GAD, underscoring the need for further investigation.

In line with the need to improve and refine psychiatric treatments, psychometric scales have increasingly been used beyond research settings to enhance treatment outcomes. Measurement-Based Care (MBC), which involves the systematic use of symptom assessment scales to guide clinical decisions in routine care, has shown promising results in improving clinical outcomes and reducing response/remission times for psychiatric disorders (Lam et al., 2024; Resnick et al., 2020; Scott & Lewis, 2015; Trivedi et al., 2006). A 24-week study found that adding MBC to usual treatment significantly improved response rates, remission, and time to achieve these outcomes in depressed patients (Guo et al., 2015). However, the impact of MBC on anxious patients remains underexplored, highlighting the need for additional research in this area.

Another effective and accessible strategy to improve mental health outcomes is adding psychoeducational materials to usual treatments. Studies have demonstrated the efficacy of these interventions across various contexts and pathologies (Fusar-Poli et al., 2021; Ghanbari et al., 2021; Powell et al., 2022; Shaygan et al., 2021). Combining these materials with technology can expand their availability and accessibility, promising to enhance psychiatric and psychological treatments (Rigabert et al., 2020).

Treatment adherence remains a major challenge in psychiatric care, with high dropout rates consistently reported across mental health services (Fernández et al., 2021; Swift & Greenberg, 2012; Grover et al., 2021; Wells et al., 2013). Studies suggest that a substantial proportion of patients discontinue treatment

prematurely, particularly within the first few sessions, limiting the effectiveness of otherwise evidence-based interventions and contributing to poor long-term outcomes (Fernández et al., 2021; Swift & Greenberg, 2012). This issue is especially relevant in routine psychiatric care, where premature treatment discontinuation may compromise clinical outcomes and reduce the effectiveness of otherwise evidence-based interventions (Fernández et al., 2021). Therefore, identifying simple, scalable strategies that can improve engagement and retention in treatment is a critical priority in mental health care.

The aim of this study was to evaluate whether the use of simple and scalable digital interventions delivered via a mobile app (including systematic psychometric assessments and psychoeducational videos), as an adjunct to treatment as usual (TAU), could improve clinical outcomes and treatment adherence in patients with GAD within routine outpatient psychiatric care. We hypothesized that integrating these digital adjunct tools into routine clinical care would improve clinical outcomes and treatment adherence.

Methods

Study Design

This was a randomized clinical trial (RCT) with blinded raters, designed to approximate real-world clinical practice conditions, conducted between June 2022 and January 2024 at Hospital de Clínicas de Porto Alegre in Brazil. The control group received TAU, consisting of symptom assessment, fluoxetine prescription, and general guidance. The intervention group received TAU plus psychoeducational videos and self-administered Generalized Anxiety Disorder 7-item scale (GAD-7) at each consultation accessed through "+PSI" app. The trial was registered under ClinicalTrials.gov ID: NCT05375851. This study was reported in accordance with CONSORT guidelines to ensure clear and comprehensive reporting of the study's data. No changes to the research protocol were made after the commencement of the study.

Participants and Randomization

We recruited participants through digital media advertisements from the Hospital de Clínicas de Porto Alegre (including their website and social media), Brazilian psychiatrists' WhatsApp groups, and team members' social media accounts. People from across the country could participate in the study, which was conducted entirely online. This design allowed the inclusion of a geographically diverse sample, reflecting real-world access to care. Recruitment began on June 1, 2022, and ended on March 23, 2023.

The inclusion criteria for the study required participants to be 18 years or older, have a confirmed diagnosis of GAD as verified by the Mini International Neuropsychiatric Interview (MINI), and access to the internet and a mobile phone or tablet with internet connectivity. Exclusion criteria comprised those at risk of suicide, pregnant or lactating women, and individuals currently undergoing psychological or psychiatric treatment or who had received such treatment in the past three months. Regarding comorbidities, individuals with bipolar disorder, psychotic conditions, anorexia nervosa, and substance

use disorders (except for mild tobacco and alcohol use) were excluded from the study. However, other conditions such as depression, other anxiety disorders, obsessive-compulsive disorder, post-traumatic stress disorder, mild alcohol and tobacco use disorder, and mild bulimia nervosa were not excluded, as long as they were not more severe than the GAD diagnosis (as assessed using the Clinical Global Impression Scale - CGI). This approach allowed the inclusion of a heterogeneous sample, consistent with real-world clinical populations.

Interested individuals contacted the study's WhatsApp number or email for initial screening. Those not excluded underwent a psychiatric evaluation using MINI (adapted for DSM-5) and CGI. Included participants underwent a sociodemographic evaluation (Brazil Economic Classification Criteria of 2015) and were assessed with GAD-7 and HAM-A. All blinded raters were trained, and the REDCap platform facilitated the process, including randomization after enrollment. The randomization table was prepared and implemented in REDCap by trained research assistants.

Randomization was stratified by sex and age. After allocation, participants were assigned to one of four psychiatrists for the 12-week treatment. Two psychiatrists managed the control group and two the intervention group (one woman and one man in each). To prevent application bias, psychiatrists attended only their assigned group. Psychiatrists were aware of treatment allocation and were not blinded to group assignment.

Sample Size

The sample size was calculated to detect a 5-point difference in mean GAD-7 score change between the intervention and control groups. Using PSS Health version 0.1.6 (Borges et al., 2020) with 80% power, a 5% significance level,assuming a two-tailed test, and a standard deviation of 6 points (Spitzer et al., 2006), a total of 46 subjects (23 per group) was needed. Accounting for a 30% dropout rate, the sample size was adjusted to 60 (30 per group).

A 5-point change on the GAD-7 scale was chosen to reflect a difference that would be not only statistically significant but also clinically meaningful. The GAD-7 categorizes symptom severity in 5-point increments (mild = 5, moderate = 10, severe = 15), and a 5-point change may indicate a shift between severity categories. While some studies suggest that the minimal clinically important difference (MCID) for GAD-7 lies between 3 and 4 points (Toussaint et al., 2020; Kroenke et al., 2019), we opted for a more conservative and robust estimate to ensure that observed changes would reflect clinically relevant improvements.

Interventions

The research protocol consisted of a 12-week intervention, during which patients had biweekly consultations with their psychiatrist. Thirty-three participants were allocated to the intervention group

(TAU + digital interventions) and twenty-seven to the control group (TAU).

Treatment as Usual (TAU)

The standardized protocol for TAU involved biweekly online consultations (via WhatsApp or Google Meet) lasting 20-30 minutes with a trained psychiatrist. Psychiatrists were instructed to assess symptoms, provide general guidance on the condition, and prescribe medication. Fluoxetine was the medication of choice, as it is the available treatment for GAD provided free of charge by our healthcare system. All Selective Serotonin Reuptake Inhibitors (SSRIs), including fluoxetine, have demonstrated efficacy for GAD in various RCTs and meta-analyses (Slee et al., 2019). The clinician could also opt for the fixed use of clonazepam during the first two weeks of treatment or, after this period, restrict its use to clinically justified cases, aligning with standard care procedures. Its initial fixed use served as a short-term strategy to manage early anxiety symptoms and mitigate initial SSRI-related side effects, given the latency of fluoxetine's therapeutic onset (Bandelow et al., 2023; Bushnell et al., 2021; Gomez et al., 2018). Patients who did not tolerate fluoxetine or for whom it was not indicated were excluded from the study and referred to their local healthcare unit for alternative treatment options. This approach was designed to mirror routine psychiatric care as delivered in real-world clinical settings.

Digital Interventions

The digital interventions were designed to be simple, scalable, and easily integrated into routine care. The digital interventions consisted of two parts. The first part involved five psychoeducational videos on mental health and GAD, produced specifically for the study. These videos, approximately 3 minutes long, featured animations and educational content, and were designed to be watched by patients between sessions. They were freely accessible on the "+PSI" app by Artmed, available on both the Apple Store and Google Play. The video topics included Normal Anxiety vs. Pathological Anxiety (consultation 1), Sleep Hygiene (consultation 2), Healthy Eating and Mental Health (consultation 3), Physical Exercise and Mental Health (consultation 4), and Excessive Alcohol and Drug Consumption (consultation 5). The content of the videos was carefully grounded in robust scientific evidence from lifestyle medicine supporting their relevance to GAD(Firth et al., 2020; Ghanbari et al., 2021; Munro et al., 2026)**.** Each video integrates general health information with targeted strategies tailored to GAD-specific symptoms. Examples include techniques to manage anxiety-driven eating behaviors (highlighted in "Healthy Eating and Mental Health"), guidance on coping with sleep disturbances commonly associated with GAD ("Sleep Hygiene"), strategies to avoid reliance on alcohol or psychoactive substances as anxiety coping mechanisms, and education on how excessive use of these substances can worsen GAD symptoms over the long term ("Excessive Alcohol and Drug Consumption"), as well as evidence-based information about physical exercise as a healthy, effective method to alleviate anxiety ("Physical Exercise and Mental Health"). The video titles intentionally reflect broader health concepts (which are fully covered in the content), given that many GAD patients—in this study as well as in real-world settings—often have

psychiatric comorbidities. Nevertheless, each video provides specific, practical guidance tailored to common symptoms experienced by individuals with GAD.

The second part involved the GAD-7 scale, which was completed at each consultation. This self-administered tool was available for free on the "+PSI" app and was used to guide clinical practice. Patients completed the scale shortly before or at the beginning of each session. Responses were not stored in the app; instead, they were shared verbally with the psychiatrist, who reviewed each item individually and recorded the answers in REDCap.

Adherence Monitoring

Medication adherence was monitored through pill counts at each session to avoid bias from incorrect use. Patients were instructed to set aside the necessary number of pills until the next visit, where the remaining pills were counted and recorded. This was done for both groups. In the intervention group, at the first visit, the clinician helped the patient download the app and provided instructions on video viewing and scale completion. Video adherence was monitored through discussions during consultations, with unviewed videos watched during the appointment.

Outcomes

The study's outcomes included clinical improvement measured by the GAD-7 scale score (primary outcome) and the HAM-A scale score assessed by a blinded rater. Additional outcomes included treatment dropout rates, reflecting real-world treatment adherence, satisfaction levels with the system and treatment received, speed of improvement, and variation in symptom scales and protocol dropout at 3 and 6 months.

Assessments and Blinding

Since we used a digital tool as an adjunct to treatment and the clinician also needed to guide the patient during this intervention and discuss the content of the videos and the results of the scales, blinding was not possible for these parties. However, a blind evaluator conducted the baseline, mid-term, and final assessments. Blinded raters were three psychiatrists from the research team, trained in rating scales assessment, who were blinded to participants’ group allocation. All patients were instructed not to reveal which group they were participating in during the interview with the blinded rater.

Between the third and fourth consultations, patients from both groups were contacted by one of the blinded raters to complete the HAM-A. The purpose of administering this scale midway through the study was to assess any differences in response time between the digital intervention group and the control group. To avoid potential bias, we deliberately chose not to use the GAD-7 as an assessment tool during the treatment period, given that it was employed as a therapeutic strategy in the intervention

group. Applying it to the control group at mid-point could have inadvertently introduced bias by exposing them to an element of the intervention—even though assessments were conducted by blinded assessors. At the end of the study, patients were re-evaluated by the blinded raters using the GAD-7, HAM-A, and CGI-Change scales. Additionally, they completed a satisfaction survey regarding the treatment received, assessed through the Net Promoter Score (NPS). The intervention group also evaluated the usability of the mobile app by completing the System Usability Scale (SUS).

Follow-up

Patients were re-contacted at 3 and 6 months after the study's conclusion to complete GAD-7 and HAM-A scales. This follow-up aimed to evaluate the maintenance of response and adherence under real-world conditions after the end of the intervention.

Ethical Concerns

The study was approved by the ethics committee at the Hospital de Clínicas de Porto Alegre (CAAE: 54357621.7.0000.5327) and conducted in accordance with the principles outlined in the Declaration of Helsinki. Participants provided informed consent and could withdraw at any time. The consent form was sent to participants via WhatsApp and subsequently read to them during the final step of the screening assessment. Participant consent was verbal and recorded in the research protocol records. Data was securely stored, with access limited to the research team, ensuring privacy in compliance with Brazil's General Data Protection Law (Law No. 13.709, August 14, 2018). Confidentiality was maintained through anonymization, and participants were informed of potential data publication with privacy safeguards. Those not meeting inclusion criteria were referred to primary care, and urgent cases were directed to psychiatric emergency services.

Statistical Analysis

Statistical analysis included descriptive statistics (mean, median, interquartile range, standard deviation, frequencies, and percentages). Student's t-test and Mann-Whitney U test were used for continuous variables, and Chi-square or Fisher's exact test for categorical variables,all using two-tailed tests. Analyses followed the *intention-to-treat* principle, preserving the benefits of randomization and avoiding biases due to the exclusion or loss of patients during the study; the method of handling missingness was Last Observation Carried Forward (LOCF). The Analysis of Covariance (ANCOVA) was used to control outcomes based on psychiatric comorbidities and Generalized Estimating Equations (GEE) assessed differences in symptom improvement speed (by comparing HAM-A scale results over time). Robust (sandwich) standard errors were used in the GEE models to account for within-subject correlations. We also calculated the relative risk (RR) of dropout incidence between groups, with a 95% confidence interval (CI), to provide a more precise estimate of the magnitude of the difference in

participant losses. A 5% significance level ($p < 0.05$) was applied, and analyses were performed using SPSS, version 29 (IBM Corp., Armonk, NY, USA).

Results

Participants Flow and Characteristics

Recruitment began in June 2022 and concluded in March 2023. Of the 131 individuals who expressed interest in participating in the study, 31 were excluded after the initial screening. The remaining 100 underwent clinical evaluation by the psychiatrists, and of these, 60 were included for randomization. The participants were randomized into the intervention group (n=33) and the control group (n=27). (see Fig. 1) By July 2023, all participants had completed the 12-week protocol, and the follow-up was concluded in January 2024.

Fig. 1. CONSORT flow diagram of participant recruitment, allocation, and follow-up.

The baseline characteristics of the participants are presented in Table 1. Descriptive comparisons suggest that the groups were broadly similar in terms of sociodemographic characteristics and symptom severity.

Table 1. Baseline characteristics of randomized patients

	Control group (*n* = 27)	Intervention group (*n* = 33)	*p value*
Median age, years (IQR)	29 (23 - 40)	34 (27 - 40)	0.21[α]
Gender			0.74[β]
Female	22 (81.5)	28 (84.8)	
Male	5 (18.5)	5 (15.5)	
Ethnicity			0.93[β]
White	19 (70.4)	24 (72.7)	
Black	5 (18.5)	5 (15.2)	
Others	3 (11.1)	4 (12.1)	
Marital status			0.39[β]
Single	18 (66.7)	21 (63.6)	
Married	7 (25.9)	5 (15.2)	
Separated/Divorced	2 (7.4)	6 (18.2)	
Widow	0	1 (3)	
Religion Practice			0.68 [β]
Yes	8 (29.3)	10 (30.3)	
No	9 (33.3)	14 (42.4)	
No religion	10 (37)	9 (27)	
Level of education			0.61 [β]
Incomplete elementary education	1 (3.7)	0	
Complete high school	8 (29.6)	7 (21.2)	
Incomplete higher education	8 (29.6)	9 (27.3)	
Complete higher education	6 (22.2)	12 (36.4)	
Postgraduate	4 (14.8)	5 (15.2)	
Work			0.46 [β]
Yes	20 (74.1)	27 (81.8)	
No	7 (25.9)	6 (18.2)	

Comorbidities			
Major depression	15 (55.6)	24 (72.7)	0.26 β
Panic disorder	3 (11.1)	8 (24.2)	0.31 β
Agoraphobia	4 (14.8)	10 (30.3)	0.22 β
Social Anxiety	3 (11.1)	3 (9.1)	1.00 β
Posttraumatic stress disorder	0	2 (6.1)	0.49 β
Obsessive compulsive disorder	2 (7.4)	1 (3)	0.58 β
Alcohol use disorder	1 (3.7)	1 (3)	1.00 β
Mean Baseline GAD-7 score (SD)	15.26 (2.99)	14.64 (3.45)	0.46Ω
Mean Baseline HAM-A score (SD)	23.33 (10.51)	26 (9.89)	0.31Ω
Mean Baseline GAD CGI score (SD)	2.78 (0.69)	2.88 (0.69)	0.57Ω

Values express n (%), unless otherwise indicated. IQR, interquartile range; SD, standard deviation; GAD-7, Generalized Anxiety Disorder 7-item scale; HAM-A, Hamilton Anxiety Rating Scale; CGI Clinical Global Impression Scale. α = Mann-Whitney; β = Chi-square; Ω = Student's t-test. Baseline comparisons are presented for descriptive purposes.

Losses and Exclusions

Of the 33 participants in the intervention group, 2 did not complete the full evaluation protocol. One participant was prescribed pregabalin for pain by another doctor and had to be excluded. Another participant did not adhere to the medication and did not download the app.

Of the 27 patients allocated to the control group, 10 did not complete the evaluation protocol. Six abandoned the treatment and stopped responding to contacts, two discontinued due to issues related to fluoxetine, one started psychotherapy, and one was excluded due to suicide risk.

At the 3-month follow-up assessment after the study endpoint, there were an additional 2 dropouts in the intervention group (cumulative n = 4) and 2 in the control group (cumulative n = 12). At the 6-month follow-up, there was only 1 dropout in the control group (cumulative n = 13) and no dropouts in the intervention group (cumulative n = 4).

In the intervention group, significantly fewer dropouts were observed compared to the control group (6.1% in the intervention group vs. 37% in the control group; p = 0.004). This difference remained

statistically significant at both the 3-month follow-up (12.1% vs. 44.4%; p = 0.008) and the 6-month follow-up (12.1% vs. 48.1%; p = 0.003), even though by this time, patients were no longer in treatment, and the dropouts were considered from the study follow-up rather than from the treatment. This may reflect a stronger engagement with the treatment previously received. (see Fig. 2) To provide a more precise estimate of this difference, we additionally calculated the relative risk (RR) of dropout between groups. The intervention group had an RR of 0.16 (95% CI: 0.04–0.68), suggesting an 84% lower risk of dropout compared to the control group.

Fig. 2. Dropout rates between groups.

The analysis of dropouts revealed no differences in symptom severity or most of the evaluated sociodemographic characteristics, except for a statistically significant difference related to unemployment (unemployed individuals were more likely to drop out; p = 0.04).

Outcomes

A significant reduction in symptoms was observed in both groups. When evaluating the difference between final and initial scores (delta), a statistically significant difference favoring the intervention group was found in the HAM-A delta (MD = -7.05; 95% CI: -13 to -0.6; p = 0.034). However, no statistically significant difference was found regarding our primary outcome, the GAD-7 delta (MD = 2.63; 95% CI: -4.46 to 2.12; p = 0.481). In follow-up evaluations, there were no statistically significant differences between the groups in the GAD-7 and HAM-A delta scores. (see Table 2)

Table 2. Comparison of delta scores between groups *(intention-to-treat analysis)*

	Mean	SD	Mean Difference	95% CI	p-value*
GAD-7 Delta (endpoint)					
Intervention	- 9.13	5.68	2.63	-0.60 to 5.80	0.108
Control	-11.76	4.58			
GAD-7 Delta (3-month follow-up)					
Intervention	-7.18	6.78	-0.62	-4.01 to 2.76	0.713
Control	-6.55	6.31			
GAD-7 Delta (6-month follow-up)					
Intervention	-6.15	6.57	0.62	-2.66 to 3.91	0.705
Control	-6.77	6.13			
HAM-A Delta (endpoint)					
Intervention	-14.75	13.16	-7.05	-13.5 to -0.56	**0.034****
Control	-7.70	11.61			
HAM-A Delta (3-month follow-up)					
Intervention	-13.90	13.99	-5.90	-12.62 to 0.80	0.083
Control	-8.00	11.47			
HAM-A Delta (6-month follow-up)					
Intervention	-11.39	10.98	-3.76	-9.52 to 1.99	0.196
Control	-7.62	11.21			

GAD-7, Generalized Anxiety Disorder 7-item scale; HAM-A, Hamilton Anxiety Rating Scale; SD, standard deviation; CI, confidence interval; Δ = Endpoint – Baseline.
**Student's t-test; **p < 0.05.*
Sample size was consistent across all comparisons: n = 33 (intervention), n = 27 (control).

To assess whether there was a difference in the speed of symptom improvement between the groups, we compared the HAM-A scale results, including the mid-term evaluation (between sessions 4 and 5), using a Generalized Estimating Equations (GEE) model to examine the interaction between time and group. The analysis did not reveal a statistically significant interaction effect (Wald χ^2 (2) = 2.656, p = 0.265), indicating no difference in the rate of symptom improvement between the intervention and control groups.

The groups did not differ statistically in their scores on the NPS, which aimed to assess participants' satisfaction with the treatment received by asking how likely they were to recommend the treatment to a friend, scored on a scale from 1 to 10. The intervention group had a mean score of 9.44 (SD = 1.01), and the control group had a mean score of 9.70 (SD = 0.80). The mean difference was -0.26 (95% CI: -0.80 to 0.28; p = 0.31), indicating similar levels of treatment satisfaction across both conditions.

The average final score on SUS, administered to participants in the intervention group, was 89.3 (SD = 11.4), indicating excellent acceptability among users. The scores ranged from 65 to 100, with a median of 92.5 and 75% of participants scoring above 80, reinforcing the strong usability of the digital tools employed.

Ancillary Analyses

We conducted an ANCOVA to evaluate the delta scores of the anxiety scales while controlling for psychiatric comorbidities. When adjusting for the presence of any psychiatric comorbidity, the effect of group remained statistically significant (F (1, 57) = 4.25, p = 0.04) for the HAM-A delta, as well as when adjusting for the presence of any other anxiety disorders (F (1, 55) = 4.00, p = 0.05). However, when adjusting specifically for the presence of depression, the difference between groups did not reach statistical significance (F (1, 57) = 3.26, p = 0.07). No significant differences were observed between groups after adjustment for any of the comorbidity variables for the GAD-7 delta (all $p > 0.05$).

When analyzing the use of fluoxetine between the groups, we found a statistically significant increase in the medication dosage in the intervention group (Mann-Whitney U = 619.00, p = 0.004). In a separate analysis including only the patients who completed the study (per protocol analysis), there appears to be a trend toward this same difference in dose increase. However, our sample lacks the power to confirm this analysis. The maximum dose of fluoxetine used in the study was 60 mg/day.

Another interesting finding related to medication use is that only one patient (3.7%) in the control group was prescribed clonazepam, whereas 72.7% (n = 24) of the intervention group received a prescription for it ($p < 0.001$), despite all clinicians having the freedom to prescribe this medication. Actual clonazepam use (across the full study period) was recorded in 48.5% of the intervention group (n = 16) and 3.7% of the control group (n = 1). Most clonazepam prescriptions and use occurred during the first two weeks of the study—62.5% of all prescriptions and 58.8% of actual use. The maximum dose of clonazepam used in the study was 0.5 mg/day.

Harms

No serious adverse events occurred. Mild and transient side effects related to fluoxetine were reported, with one control group participant excluded for intolerance and another refusing to use fluoxetine. No harms were associated with the use of “+PSI” app.

Discussion

Although the addition of digital interventions to TAU did not result in superior symptomatic outcomes, a marked and clinically meaningful improvement in treatment adherence was observed. Given the well-established impact of adherence on long-term outcomes in psychiatric care, this finding represents a

highly relevant contribution. Adherence to treatment among psychiatric patients tends to be very low, which limits therapeutic efforts and negatively impacts treatment outcomes (Fernández et al., 2021; Swift & Greenberg, 2012). Dropout rates among mental health patients are high, with rates of 30% in high-income countries and 45% in low- and middle-income countries, mostly occurring during the first two visits (Fernández et al., 2021). As our study found a dropout rate of only 6.1% (including 6 appointments) and Brazil is considered a middle-income country, this is a significant difference that could lead to substantial improvements in the treatment of GAD, especially within routine psychiatric care. It is important to note that the dropout rate in the control group was 37%, a figure that closely aligns with data from the literature (Fernández et al., 2021; Grover et al., 2021; Wells et al., 2013). These findings suggest that relatively simple and low-cost digital strategies may play a key role in addressing one of the most persistent challenges in mental health care.

We observed that the increase in fluoxetine dosage was significantly higher in the intervention group. This finding may reflect the use of systematic symptom monitoring (MBC), which may have facilitated more timely and informed clinical decision-making, which is consistent with previous findings on the use of MBC in the clinical management of psychiatric disorders (Lam et al., 2024; Resnick et al., 2020; Scott & Lewis, 2015; Fortney et al., 2017). Although all clinicians had the freedom to prescribe clonazepam as an adjunct to fluoxetine treatment, only one patient (3.7%) in the control group received this prescription, compared to 72.7% (n = 24) of patients in the intervention group. This may also be related to better symptom evaluation and more attentive care due to MBC. This study may have lacked sufficient power and observational time to adequately assess the full impact of MBC on GAD, leaving room for future research in this area.

In addition to the aspects related to MBC, the psychoeducational videos were discussed during the sessions, allowing patients to share which elements they identified with and the specific symptoms they associated with the topic addressed in each video. This process enabled clinicians to gather more individualized information about each patient's needs, potentially leading to quicker and more confident decisions regarding dose adjustments or the use of clonazepam. In this way, these findings suggest that the structured nature of these digital tools may have contributed to strengthening the therapeutic alliance. Patients may have felt more supported and understood, while clinicians may have felt better informed and more confident in tailoring treatment decisions, including the careful titration of fluoxetine or the temporary use of clonazepam. As both components were delivered within a single digital intervention arm, it was not possible to isolate their individual effects. However, their combined use may have contributed in distinct ways to the observed differences in medication adjustments between groups. Future studies with separate intervention arms may help clarify the individual impact of each component.

The absence of superior symptomatic outcomes is consistent with previous studies evaluating digital interventions as adjuncts to standard treatment (Clarke et al., 2002). This may reflect the already established effectiveness of TAU, particularly when combined with pharmacological treatment, making additional gains more difficult to detect. There are very few studies in the recent literature that consider

DMHIs as adjuncts, particularly in patients with GAD (Deady et al., 2017). However, Clarke et al. (2002), who evaluated a web-based intervention program as an add-on treatment to reduce depression, also did not find a significant difference, which aligns with our findings. On the other hand, a study that added mindfulness practice via an app to TAU (Roy et al., 2021) showed some benefit, likely because the digital intervention used a more specific and well-established technique for GAD (reinforcement learning using mindfulness training). This suggests that a more targeted approach focused on the core symptoms of GAD could lead to more effective symptom improvement. However, it is important to note that this study did not include active medication control within the study; participants followed their usual treatments as recommended by their doctors outside the study environment, which may have favored the intervention.

The main driving force behind this project was its potential for clinical applicability. Although digital interventions can be useful for most psychiatric disorders, we chose to focus on a single diagnosis for feasibility reasons and to better isolate the impact of the intervention. The study presents strong external validity, as we compared usual treatment (Slee et al., 2019), which is already routinely practiced by psychiatrists, with adjunctive treatment using DMHIs, which are simple and easy to implement. Additionally, digital tools are increasingly present in the daily lives of both doctors and patients, allowing for the exploration of their utility in clinical settings (Bisby et al., 2022). Since GAD is also a very common disorder, this study highlights the potential clinical utility of integrating simple digital interventions into routine care (Bisby et al., 2022; Firth et al., 2020; Graham et al., 2020). This disorder has had a significant impact on health systems, with demands exceeding care capacities in most places. Although the observed clinical improvements were not statistically significant, the results related to treatment adherence are quite relevant and crucial for the treatment of GAD.

This study has several strengths, most notably the inclusion of a "real-world" sample (individuals with comorbid disorders, given that GAD has an approximately 80% comorbidity rate) (Ruscio et al., 2017) and the comparison of the digital intervention as an add-on to TAU (including medication use), rather than relying on the isolated use of a digital intervention compared to a wait-list control, which is a common study design in most DMHIs studies (Pauley et al., 2023; Saramago et al., 2021). Moreover, the use of 3 and 6-months follow-up assessment is another strength considering the evaluation of maintenance and increasing outcome effects in longer-term. One of the primary limitations of this study is the small sample size, which may affect the generalizability of the findings to a broader population. Since we chose to add two digital interventions together, we were unable to isolate the impact of each one individually. Although a four-arm study—evaluating each intervention individually (psychoeducational videos plus fluoxetine; symptom monitoring plus fluoxetine) and in combination (videos plus symptom monitoring plus fluoxetine) versus a control group (TAU with fluoxetine)—would have provided a more precise understanding of each component's contribution, logistical and resource constraints limited the feasibility of implementing a more complex trial structure in the present study. Given that all participants in the intervention group were uniformly exposed to both digital components, it was not possible to assess whether higher engagement (e.g., viewing more videos or completing more scales) was associated with better outcomes. Additionally, the use of DMHIs required participants to have access to

technology and internet, potentially excluding those without such resources and limiting the applicability of the findings to more digitally connected populations (Lam et al., 2023; Gallois et al., 2024; Perumalswami et al., 2024). Lastly, the lack of blinding for the intervention could introduce performance bias, as participants and clinicians were aware of the treatment allocation, potentially influencing the results.

Our findings suggest that integrating simple, safe, and cost-effective digital interventions into standard treatment for GAD may improve treatment adherence and optimize the use of healthcare resources. Given their scalability and low implementation burden, such strategies may represent a pragmatic and clinically applicable strategy to address persistent challenges in psychiatric clinical practice.

Statements and Declarations

Acknowledgements

None.

Funding

This study was supported by the National Council for Scientific and Technological Development (CNPq) and by the Fundo de Incentivo à Pesquisa e Eventos (FIPE) of Hospital de Clínicas de Porto Alegre (HCPA). Artmed supported the production of the psychoeducational videos and provided free access to the psychometric assessment scales on the “+PSI” app used in this study. The study was also conducted as part of a doctoral research project at the Federal University of Rio Grande do Sul (UFRGS). The funding sources had no role in the study design, data collection, analysis, interpretation of the data, or preparation of the manuscript.

Competing Interests

The authors declare that the “+PSI” mobile application used in this study was developed by Artmed Publishing, which provided technical support for the implementation of the digital interventions. The authors report no other competing interests.

Ethics Approval

This study was approved by the Ethics Committee of Hospital de Clínicas de Porto Alegre (HCPA) and conducted in accordance with the Declaration of Helsinki.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Data Availability

The dataset generated and analyzed during the current study has been deposited in a public repository. The access link has been omitted from the manuscript to preserve double anonymous peer review and will be provided upon acceptance.

Authors' Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by the research team. The first draft of the manuscript was written by the first author, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Use of Artificial Intelligence

The authors used an artificial intelligence-based language tool (ChatGPT, OpenAI) to assist with language editing, clarity, and organization of the manuscript. This use was limited to AI-assisted copy editing of human-generated text, including improvements in readability, grammar, spelling, punctuation, and style. No generative content was produced by the tool, and all scientific content, interpretations, and conclusions were developed by the authors. All authors reviewed and approved the final version of the manuscript and take full responsibility for its content.

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Figures

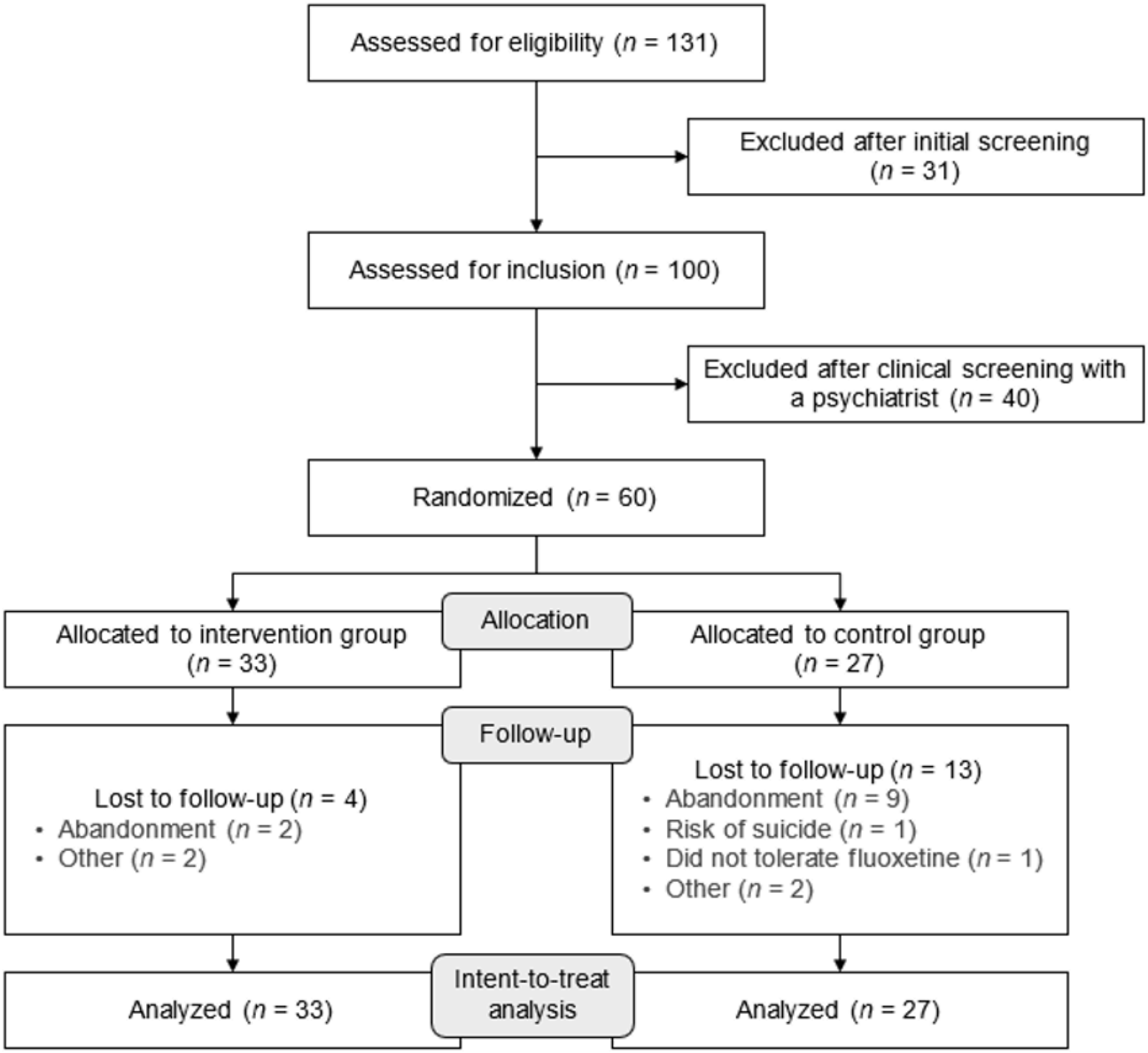


Figure 1

CONSORT flow diagram of participant recruitment, allocation, and follow-up.

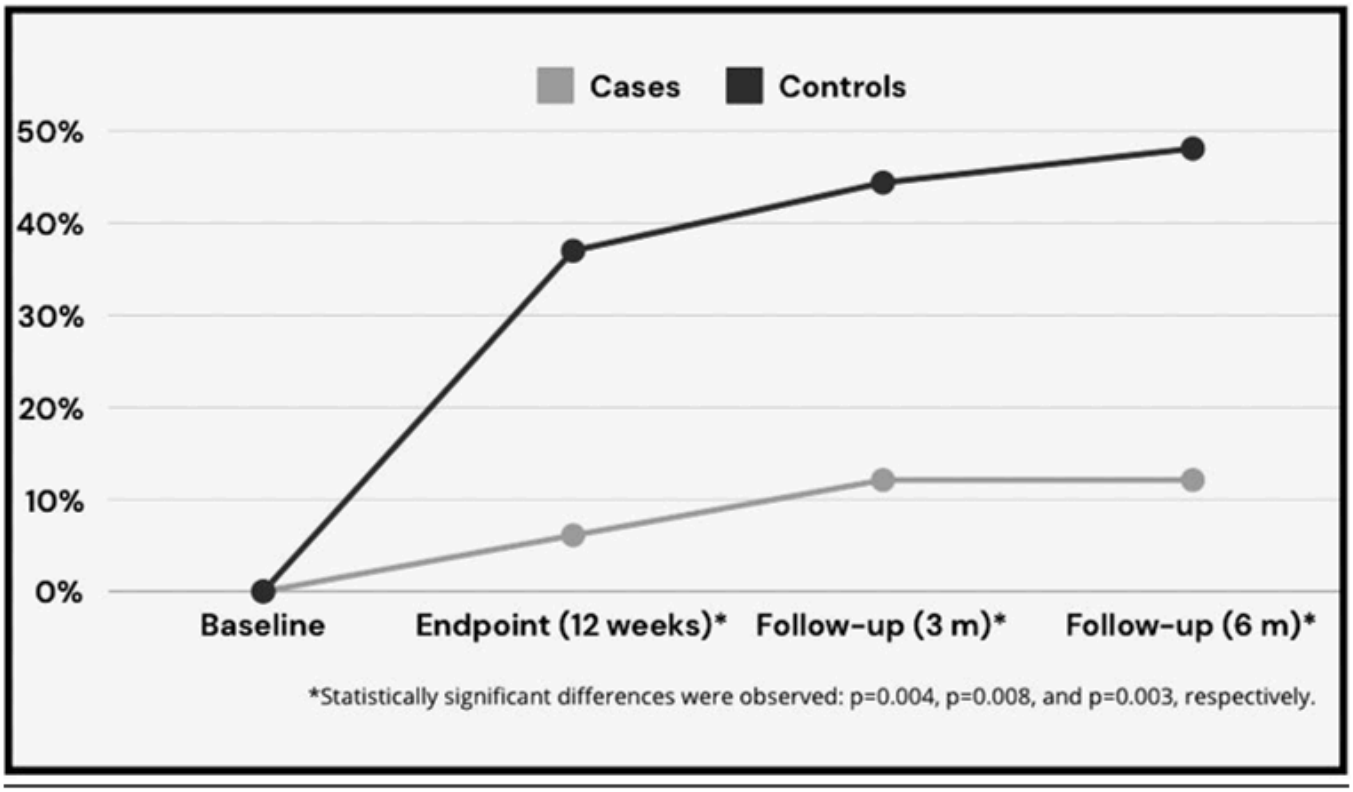


Figure 2

Dropout rates between groups.