Efficacy of a Digital Therapeutic Intervention for Generalised Anxiety Disorder: A Pre-Post Study

Ravindranath Janapureddy, Yosef Koffler, Jowinn Chew, Daniel Frings, Krishna Swetha Gummuluri

Submitted to: JMIR Formative Research
on: March 01, 2024

Table of Contents

Efficacy of a Digital Therapeutic Intervention for Generalised Anxiety Disorder: A Pre-Post Study

Ravindranath Janapureddy[1] BSc, BTECH, MBA; Yosef Koffler[1] DPhil; Jowinn Chew[2]; Daniel Frings[2] PhD; Krishna Swetha Gummuluri[3] MBBS, DPM

[1]Resony Health (registered as RCube Health Ltd.) London GB
[2]London South Bank University London GB
[3]Novartis Healthcare Pvt Ltd Hyderabad IN

Corresponding Author:
Ravindranath Janapureddy BSc, BTECH, MBA
Resony Health (registered as RCube Health Ltd.)
20-22 Wenlock Road
London
GB

Abstract

Background: Generalised Anxiety Disorder(GAD) is estimated to affect 1 in 8 people in the UK seeking help from their GP in primary care; where treatment options may either be unacceptable to patients (e.g. medication), or may be delayed (e.g. psychotherapy delivered through NHS Talking Therapy services). These barriers leave an important treatment gap that may be filled by Digital Mental Health Interventions, offering immediate, evidence-based care.

Objective: This study aimed to evaluate the efficacy,d user acceptability and safety of the Resony Anxiety app, a digital therapeutic intervention for individuals with self-reported anxiety using a pre-post study design.

Methods: A total of 86 UK-based participants were recruited and underwent a 6-week intervention using the Resony Anxiety app as a standalone unguided intervention. Primary and secondary outcome measures included the GAD-7 and DASS-21 questionnaires.

Results: The participants reported a significant reduction in anxiety of 3.27 points on the GAD-7 after six weeks, with continued improvement during the follow-up period. The effect size was medium for GAD-7 and small for DASS-21 as measured using Hedge's g. Qualitative feedback indicated that 95% of participants enjoyed using the app, and 64% found it effective in managing their anxiety. 77% of the participants would recommend the app to a friend or family member with anxiety.

Conclusions: This study indicates that the Resony Anxiety app is effective and safe in reducing anxiety in adults. Future studies with larger samples and more robust experimental designs, such as randomised controlled trials, are needed to confirm these initial promising findings.

(JMIR Preprints 01/03/2024:57993)
DOI: https://doi.org/10.2196/preprints.57993

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**
Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Original Paper

Ravindranath Janapureddy[1], Yosef Koffler[1], Jowan Chew[2], Daniel Frings[2] Krishna Swetha Gummuluri[3]
[1] Resony Health
[2] London South Bank University
[3] Novartis Healthcare Pvt Ltd

Corresponding Author:
Ravindranath Janapureddy
Resony Health,
20 - 22 Wenlock Road, London, N17GU
Email: ravi@resony.health
Ph: +447946386093

Efficacy of a Digital Therapeutic Intervention for Generalised Anxiety Disorder: A Pre-Post Study

Abstract

Background: Generalised Anxiety Disorder(GAD) is estimated to affect 1 in 8 people in the UK seeking help from their GP in primary care; where treatment options may either be unacceptable to patients (e.g. medication), or may be delayed (e.g. psychotherapy delivered through NHS Talking Therapy services). These barriers leave an important treatment gap that may be filled by Digital Mental Health Interventions, offering immediate, evidence-based care.
Objective: This study aimed to evaluate the efficacy,d user acceptability and safety of the Resony Anxiety app, a digital therapeutic intervention for individuals with self-reported anxiety using a pre-post study design.
Methods: A total of 86 UK-based participants were recruited and underwent a 6-week intervention using the Resony Anxiety app as a standalone unguided intervention. Primary and secondary outcome measures included the GAD-7 and DASS-21 questionnaires.
Results: The participants reported a significant reduction in anxiety of 3.27 points on the GAD-7 after six weeks, with continued improvement during the follow-up period. The effect size was medium for GAD-7 and small for DASS-21 as measured using Hedge's g. Qualitative feedback indicated that 95% of participants enjoyed using the app, and 64% found it effective in managing their anxiety. 77% of the participants would recommend the app to a friend or family member with anxiety.
Conclusions: This study indicates that the Resony Anxiety app is effective and safe in reducing anxiety in adults. Future studies with larger samples and more robust experimental designs, such as randomised controlled trials, are needed to confirm these initial promising findings.

Keywords:

Digital health; online intervention; anxiety; smartphone intervention; digital therapeutics; generalized anxiety disorder; gad

Introduction

Generalised anxiety disorder (GAD) is a common and debilitating mental health condition

characterised by excessive and persistent worry, often accompanied by physical symptoms such as fatigue, muscle tension, and sleep disturbances [1]. GAD affects millions of people worldwide and has a significant impact on individuals' quality of life, social functioning, and occupational productivity [1]. Despite the availability of evidence-based treatments, such as cognitive-behavioural therapy (CBT) and pharmacological interventions, many individuals with GAD do not receive adequate care due to barriers such as limited access to mental health professionals, stigma, and cost [2,3].

Digital therapeutics, which encompass a broad range of technology-based interventions, have been used as an alternative or supplement to traditional treatments to address the unmet needs of individuals with GAD by improving access, patient choice and clinical outcomes [4]. These interventions can be delivered through various platforms, such as mobile apps, online programs, and virtual reality systems. Digital therapeutics offer several advantages, including increased accessibility, personalised care, and the potential for real-time monitoring and feedback. Moreover, recent studies have demonstrated promising results in the efficacy of digital therapeutics for GAD and other mental health conditions [5,6,7]. However, it is inconclusive whether these interventions are better than no intervention and further research is needed to compare digital therapeutics to the current standard of care including one-to-one therapy and medication [4].

Majority of the literature regarding digital health interventions for GAD including digital therapeutics, focus on the digital delivery of cognitive behavioural therapy (CBT), which is emerging as an efficacious treatment for GAD [4,8,9]. In the UK, the NHS recommends incorporating evidence-based digital health interventions in the delivery of Improving Access to Psychological Therapies (IAPT) services (currently called NHS Talking Therapies) [10]. There are also other approaches such as transdiagnostic psychological treatments which have been used for treatment of anxiety disorders [11]. There are some calls for further studies to study non-CBT models as well. This will help provide patient choice and inform health care policy on the best form of therapy to treat GAD [12].

The current intervention Resony Anxiety [13] is a smartphone-based digital therapeutic intervention intended for the improvement of worry, anxiety, and GAD in adults. Resony has an equal emphasis on a variety of physiological and psychological (CBT) interventions such as resonance breathing, applied relaxation, gratitude journaling and cognitive reframing. It thereby can be seen an offering a novel option of therapeutic interventions for GAD, which are not exclusively focused on CBT [14].

The primary objective of this study is to evaluate the safety, efficacy and user acceptability of the Resony Anxiety app for individuals living with self-reported anxiety using a pre-post study design. Specifically, we aimed to assess the impact of the intervention on anxiety and GAD symptoms as measured by GAD-7 and DASS-21 questionnaires. In addition, we assessed if Resony Anxiety is safe to use, whether any side-effects were observed and if users enjoyed using Resony Anxiety.

This study contributes to the growing body of literature on digital therapeutics for GAD by providing evidence on the safety and efficacy of Resony Anxiety. The findings of this study have the potential to inform the development of more effective and personalised digital therapeutics for GAD, ultimately improving access to care and clinical outcomes for individuals affected by this debilitating condition.

Methods

Design

This study is a pre-post study examining the efficacy of a novel smartphone-based digital therapeutic intervention, Resony Anxiety, for adults with symptoms of anxiety and GAD. This study is decentralised and therefore conducted entirely online.

Participants and recruitment

A total of 86 participants living in the UK were recruited for this study. Recruitment was managed by an independent platform talkhealth, an online health community. Talkhealth promoted a pre-qualifier questionnaire on their platform for 8 weeks to recruit participants. Promotion of the study included details about what the study would entail, how the app works, and guidance regarding the app's potential benefits for the user. All questionnaires used in this study also included a link to talkhealth's privacy policy which is accessible directly from their website at any time should trial participants have any queries or concerns. The following consent was obtained during recruiting and before the study commenced.

- talkhealth consent form [15]
- Resony Health Terms of service [16]
- Resony Health Privacy Policy [17]

Eligible participants were aged 18 years and above, owned a smartphone, were living in the UK/Europe; living with symptoms of anxiety or been diagnosed with generalised anxiety disorder and had already discussed anxiety with a healthcare professional.

Candidates were excluded from the study if they were diagnosed with schizophrenia, bipolar disorder, or dementia; were suffering from epilepsy and/or were currently pregnant.

Procedures

First, participants were screened against the inclusion and exclusion criteria based on their self-reported information in the pre-qualifier questionnaire. Then, informed consent was collected from eligible and interested participants. Consented participants received an email with a link to download the Resony Anxiety app and asked to use the app for 6 weeks. Data was collected on a weekly basis via Qualtrics and In-app. Follow-up data was also collected at Week 10 and Week 12 via Qualtrics and In-app. After the study concluded, a focus group was conducted in a virtual setting with 15 study participants to get in depth qualitative feedback. The results of this study are included as qualitative evidence.

Intervention

Resony Anxiety is a smartphone-based digital therapeutic intended for the improvement of worry, anxiety, and GAD in adults. It is a 6-week treatment programme consisting of evidence-based exercises drawn from cognitive behavioural therapy (CBT) and physiological techniques. These include applied relaxation, and non-directive resonance breathing [18,19,20,21,22]. Users had three ten-minute exercises to complete daily - a breathing exercise called resonant breathing, gratitude journaling & reframing exercise, and progressive muscle relaxation. There are three

psychoeducational videos to help users understand what the app does and how it works. Users also have access to two acute exercises, a shorter breathing exercise and an anxiety balance sheet, to use when they experience moments of intense anxiety or panic. The rationale behind the intervention is to build skills and techniques which can be used to manage low levels of anxiety, as well as provide techniques to manage high levels of acute anxiety.

Outcomes

Primary outcome measures

The primary outcome is anxiety severity after a 6-week intervention
GAD-7: The General Anxiety Disorder 7-Item (GAD-7) Scale is a self-report scale that measures symptoms of generalised anxiety disorder (GAD). It has been validated in adult populations and shown to have good psychometric properties among adolescents as well [23, 24]. The GAD-7 demonstrates good internal consistency (Cronbach's $\alpha = 0.91$) and unidimensional factor structure and is associated with self-report measures of depression and social anxiety, indicating construct validity. The GAD-7 also appears to have good psychometric validity across different cultures, with adequate internal consistency (Cronbach's alpha of 0.77) and desired convergent validity. Additionally, GAD-7 has been found to have acceptable psychometric properties among adolescents with persistent post-concussive symptoms (PPCS) [25]. Overall, the GAD-7 is a reliable and valid tool for measuring symptoms of GAD in various populations.

Secondary outcome measures

- DASS-21: The Depression, Anxiety and Stress Scale is a validated self-reported questionnaire consisting of 21 items, 7 items per subscale: depression, anxiety, and stress. The DASS-21 Scale has demonstrated [26] sufficient high-quality evidence for bifactor structural validity, internal consistency (bifactor), criterion validity (specifically for the Depression subscale), and hypothesis testing for construct validity. However, there is inconsistent moderate-quality evidence for measurement invariance across gender, insufficient low-quality evidence for the reliability of each subscale, and sufficient low-quality evidence for responsiveness for only the Depression and Stress subscales [27,28,29].
- Autonomic Balance questionnaire: These are 8 questions about the physiological aspects of anxiety which could help determine if the user exhibits sympathetic dominance and parasympathetic dominance.
- Semi-structured interviews focused on the content, frequency, and user experience of intervention. (Figure 1)

Statistical Analysis

The analysis plan was pre-registered [30]

Effect sizes (Hedge’s g) were used to examine the magnitude of change from pre- to post-treatment. Hedge’s g was interpreted as >0.2=small, >0.5=medium and >0.8=large. Hedge's g is a popular effect size measure used in meta-analyses and systematic reviews. It is a standardised mean difference that corrects for potential bias in small sample sizes, making it more appropriate for studies with unequal or small sample sizes. Hedge's g is used to compare the difference between two group means, taking

into account the pooled standard deviation. In the context of digital health interventions, Hedge's g can be used to estimate the effect size of a particular intervention. It helps researchers to quantify the effectiveness of the intervention and compare it across different studies in a meta-analysis.

A correlation matrix was used to examine the relationships among different variables and assess the strength and direction of these relationships [see Appendix 1]

Results

Main outcomes

The study enrolled a total of 86 participants and the demographics are presented in Table 1.

Table 1. Age demographics of study participants

Age range	**N (%)**
21-29	3
30-39	10
40-49	24
50-59	33
60-69	14
70+	2

All participants were living with anxiety and 18.5% of participants (n=16) had self-reported to be diagnosed with generalised anxiety disorder, 28% (n=24) were currently on anxiolytic or antidepressant medication; 67.5% (n=58) of participants had previously consulted their general physician (GP) for anxiety and 47.5% (n=41) had previously undergone CBT either digitally or with a therapist. 73% (n=63) of the participants have never used a mental health app before. Additional details of participants can be found in the Appendix 2.

The In-app GAD7 assessment was filled in by 51 participants, before the start of Week 1; while 24 participants completed the GAD7 assessment at 6 weeks. A GAD-7 follow up was done at the end of Week 10 and 12 respectively. All 86 participants filled out the DASS-21 assessment before the start of Week 1 with 59 participants completing the DASS-21 assessment at 6 weeks (Table 2).

Table 2. GAD7 and DASS-21 assessments in participants

	Time point	**N**	**Mean ± SD**	**Min-Max**
GAD-7				
	Week 1	51	13.02 ± 4.79	5-21
	Week 6	24	9.75 ± 8.55	1-21
	Week 10	30	7.83 ± 5.56	0-21
	Week 12	20	6.9 ± 5.84	0-21
DASS-D				
	Week 1	86	8.27 ± 5.11	0-19
	Week 6	59	6.56 ± 4.75	0-20
DASS-A				
	Week 1	86	6.40 ± 3.87	0-17
	Week 6	59	5.22 ± 4.02	0-17
DASS_S				

	Week 1	86	9.88 ± 4.16	0-20
	Week 6	59	8.08 ± 4.43	1-20
Autonomic Questionnaire Score 1				
	Week 1	86	3.10 ± 1.50	0-6
Autonomic Questionnaire Score 2				
	Week 1	86	2.23 ± 1.57	0-7
Autonomic Questionnaire Score 1				
	Week 6	86	1.81 ± 1.85	0-6
Autonomic Questionnaire Score 2				
	Week 6	86	1.53 ± 1.69	0-6
Autonomic Questionnaire Score 1				
	Week 10	86	0.90 ± 1.51	0-6
Autonomic Questionnaire Score 2				
	Week 10	86	0.65 ± 1.29	0-6
Autonomic Questionnaire Score 1				
	Week 12	86	0.60 ± 1.32	0-5
Autonomic Questionnaire Score 2				
	Week 12	86	0.48 ± 1.18	0-6

DASS: Depression, Anxiety and Stress Scale; GAD: Generalized Anxiety Disorder; Min: Minimum; Max: maximum; SD: Standard deviation.

Anxiety symptoms reduced over a 6-week period. There was a significant reduction in anxiety of 3.27 points as measured on the GAD-7, from 13.02 to 9.75, after 6 weeks. This improvement continued in the follow-up period, with a further 1.92-point reduction from week 6 to week 10. (Figure 2)

Effect sizes (Hedge's g) were used to examine the magnitude of change from pre- to post-treatment. Hedge's g was interpreted as ≥0.2=small, >0.5=medium and ≥0.8=large. The effect sizes were medium for GAD-7 and small for DASS-21 (Table 3).

Table 3: Within-group effect sizes over time

Measure	Week 1 to Week 6 within-group effect size (Hedges' g (95% CI))	Week 1 to Week 10 within-group effect size (Hedges' g (95% CI))	Week 1 to Week 12 within-group effect size (Hedges' g (95% CI))
GAD-7			
	-0.53 (-1.02 - -0.03)	-1.02 (-1.50 - -0.54)	-1.2 (-1.75 - -0.65)
DASS21-D			
	-0.34 (-0.68 - -0.01)	n/a	n/a
DASS21-A			
	-0.3 (-0.63 – 0.03)	n/a	n/a
DASS21-S			
	-0.40 (-0.74 - -0.07)	n/a	n/a
Autonomic Questionnaire			

score 1			
	-0.77 (-1.08 - -046)	-1.46 (-1.80 – 1.13)	-1.77 (-2.12 - -1.42)
Autonomic Questionnaire score 2			
	-0.43 (-0.73 - -0.13)	-1.1 (-1.42 - -0.78)	-1.26 (1.59 - -0.93)

CI: Confidence interval

In terms of Recovery, the analysis included 24 participants who completed the GAD-7 at the end of week 6 and found that 10 had reduced their GAD-7 score to 7 or less. This represents a recovery rate of 41.6%. In terms of Improvement, the analysis included the same 24 participants and found that 12 had reduced their GAD-7 score by 3.53 points or more and met the criteria of caseness at the start of intervention, representing a Reliable Improvement rate of 50%. Reliable recovery (if participants meet both criteria for reliable improvement and recovery) was obtained by 9 participants and is calculated at 37.5%.

Qualitative analysis

At 6 weeks post-intervention, a Qualtrics survey was conducted with the following results based on data from 56 participants who completed the Satisfaction questionnaire
The following are the highlights with the detailed results available in the Appendix 3.

- 87.5% of participants said that Resony Anxiety app helped them with their anxiety
- 64% said that the App was effective in managing their anxiety
- 66% said that the App met or exceeded their expectations
- 53% said they were satisfied with the App, 34% were neither satisfied nor dissatisfied, 13% were dissatisfied
- 95% of participants said that they enjoyed using the Resony app with 75% mentioning that they found the App easy to use and 76% mentioned that they found the App convenient to use
- 77% of participants would recommend Resony Anxiety to a friend or family member who has anxiety

Discussion

On the GAD-7, at baseline participants were reporting moderate levels of anxiety. By post-intervention, they were reporting mild levels of anxiety which was sustained at follow up 1 and follow up 2. On the DASS21 scales, participants reported normal levels at baseline and post intervention. Participants may have experienced sympathetic dominance at baseline, post-intervention, follow up 1 and follow up 2 as measured by the autonomic questionnaire.

Small-to-large within group effects favouring the Resony Anxiety app on all variables were observed. The severity of GAD symptoms within-group was decreased with medium-to-large effects from baseline to post-intervention, and these improvements were sustained at both follow ups.

Qualitative feedback received from participants post-study indicated that the program was helpful in

managing their anxiety, and most participants reported they enjoyed using the app, found it easy and convenient to use, and would recommend it to a friend or family member with anxiety. The intervention was found to be safe by participants, even by those who suffered with severe anxiety.

The results observed and reported in this pre-post study have been achieved using Resony as an unguided intervention. In that respect, it can also be seen to be a real world study. It opens up the benefit of Resony being used independently by people who suffer from anxiety but who do not present to their GP or self-refer to NHS Talking Therapies. There are many patients who don't interact with the NHS but self-diagnose and self-manage their anxiety. It also opens up the possibility for Resony to be offered to patients who have been assessed but are awaiting a therapeutic intervention i.e. on a waiting list.

In terms of limitations, a relatively low percentage of participants completed the assessments in the study due to an absence of external intervention in the digital only anxiety program. In addition, there were no notifications in the App to remind participants to complete the assessments. Both points above were evidenced in the qualitative feedback received from participants post study. The lack of notifications may have reduced the effectiveness of Resony and also influenced the low completion rate of the assessments. In the qualitative feedback, participants proactively suggested adding notifications into the App to assist them in following the programme and completing the assessment questionnaires.

Limitations

Despite the promising potential for Resony Anxiety that this data shows, the study is not without limitations. The lack of a comparator condition, including the study design which was an unblinded study, that may have affected the results. Further, there was no evaluation of the participants' self-reported scores by a healthcare professional and the evaluation completion rate was low, partly due to the fact that no notifications were sent out to participants. It is necessary to conduct a larger study with a multicentre, parallel-design randomised control trial to better assess the effectiveness of the Resony Anxiety App.

Conclusions

The results suggest that the Resony Anxiety app is effective and safe for use in reducing anxiety in adults. This result was achieved by Resony as an unguided intervention, while participants used the app for a six-week program at their own discretion. Further studies with larger sample sizes and more robust experimental designs (i.e. randomised controlled trial) should be undertaken to validate these initial promising findings.

Acknowledgements

The authors would like to thank talkHealth, who supported the study and London South Bank University, who did the data analysis of the study results.

The authors would like to thank Malika Bouazzaoui, who designed the study and supported with conduct of the study.

Author's contributions

JC and DF performed statistical analysis, and interpreted the data, and drafted the manuscript. RJ oversaw the design and creation of the study intervention. YK, GKS critically reviewed the

manuscript and contributed to drafting the manuscript. All authors revised the manuscript and approved the final content.

Funding

The study was funded by Resony Health (registered as RCube Health), the manufacturer of the Resony Anxiety app.

Conflicts of Interest

GKS is an employee of Novartis Healthcare Pvt Ltd and the views and opinions expressed in this manuscript are those of the author and do not necessarily reflect the official policy or position of Novartis. All other authors have confirmed they have no conflicts of interest to declare.

Abbreviations

CBT: Cognitive Behavioral Therapy
DASS-21: Depression, Anxiety and Stress Scale
GAD: Generalized Anxiety Disorder
GAD-7: General Anxiety Disorder 7-Item
NHS: National health services
PPCS: Persistent post-concussive symptoms

References

1. Ruscio AM, Hallion LS, Lim CCW, Aguilar-Gaxiola S, Al-Hamzawi A, Alonso J, et al. Cross-sectional comparison of the epidemiology of DSM-5 Generalized Anxiety Disorder across the globe. JAMA Psychiatry. 2017 May 1;74(5):465-475. [https://doi.org/10.1001/jamapsychiatry.2017.0056] [PMID: 28297020]
2. Salaheddin K, Mason B. Identifying barriers to mental health help-seeking among young adults in the UK: a cross-sectional survey. Br J Gen Pract. 2016 Oct;66(651):e686-92. [doi: 10.3399/bjgp16X687313.] [PMID: 27688518]
3. Andrade LH, Alonso J, Mneimneh Z, Wells JE, Al-Hamzawi A, Borges G, et al. Barriers to mental health treatment: results from the WHO World Mental Health surveys. Psychol Med. 2014 Apr;44(6):1303-17. [doi: 10.1017/S0033291713001943.] [PMID: 23931656]
4. Saramago P, Gega L, Marshall D, Nikolaidis GF, Jankovic D, Melton H, et al. Digital Interventions for Generalized Anxiety Disorder (GAD): Systematic Review and Network Meta-Analysis. Front Psychiatry. 2021 Dec 6;12:726222. [doi: 10.3389/fpsyt.2021.726222] [PMID: 34938209]
5. Păsărelu CR, Andersson G, Bergman Nordgren L, Dobrean A. Internet-delivered transdiagnostic and tailored cognitive behavioral therapy for anxiety and depression: a systematic review and meta-analysis of randomized controlled trials. Cogn Behav Ther. 2017 Jan;46(1):1-28.
[doi: 10.1080/16506073.2016.1231219] [PMID: 27712544]
6. Torous J, Bucci S, Bell IH, Kessing LV, Faurholt-Jepsen M, Whelan P, Carvalho AF, Keshavan M, Linardon J, Firth J. The growing field of digital psychiatry: current evidence and the future of apps, social media, chatbots, and virtual reality. World Psychiatry. 2021 Oct;20(3):318-335.

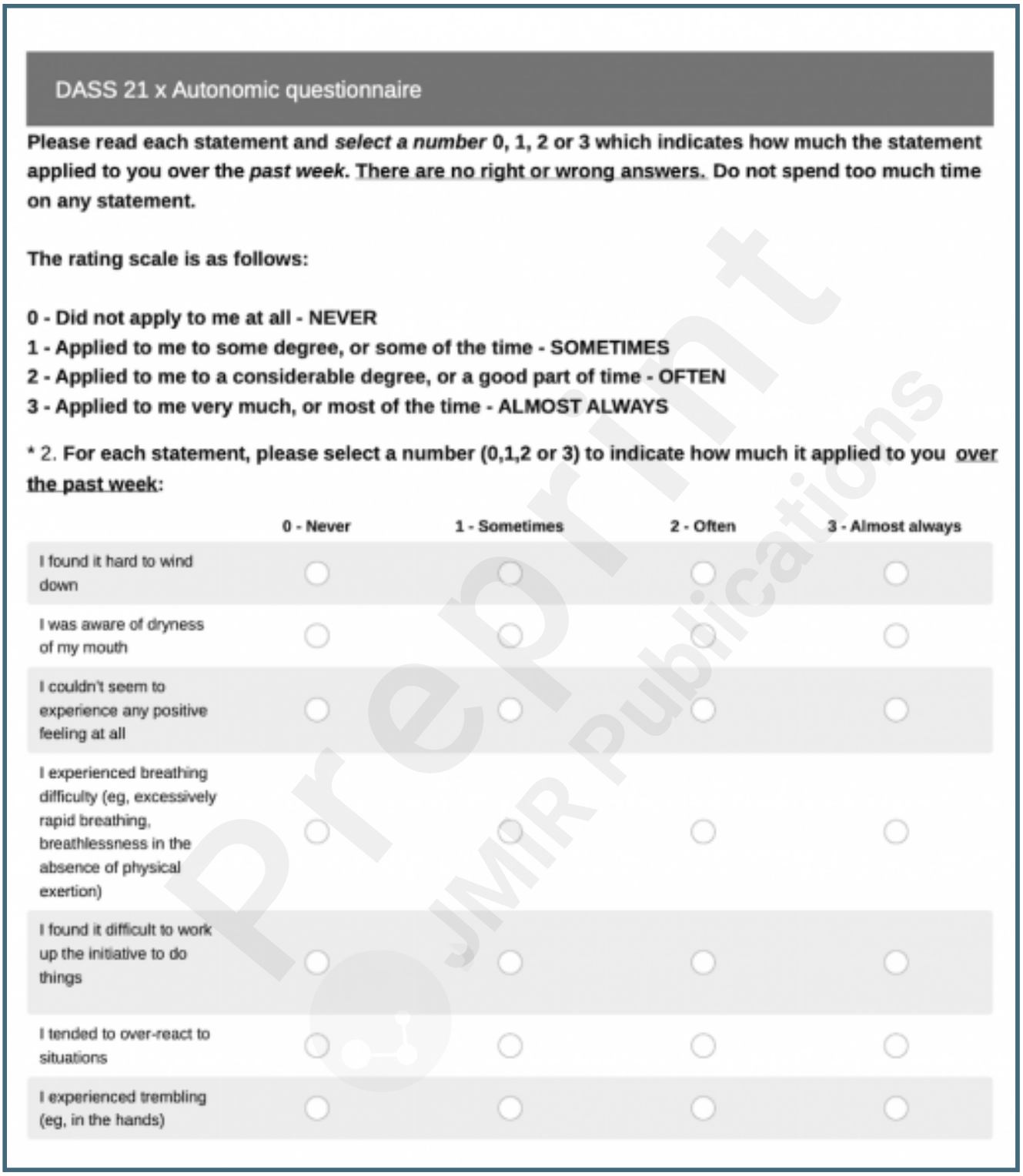
[doi: 10.1002/wps.20883] [PMID: 34505369]
7. Dear, BF, Staples, LG, Terides, MD, Fogliati, VJ, Sheehan, J, Johnston, L, et al. (2016). Transdiagnostic versus disorder-specific and clinician-guided versus self-guided internet-delivered treatment for Social Anxiety Disorder and comorbid disorders: A randomized controlled trial. Journal of Anxiety Disorders, 2016 Aug; 42: 30–44. [doi: 10.1016/j.janxdis.2016.05.004] [PMID: 27261562]
8. Eilert N, Enrique A, Wogan R, Mooney O, Timulak L, Richards D. The effectiveness of Internet-delivered treatment for generalized anxiety disorder: An updated systematic review and meta-analysis. Depression and Anxiety. 2021 Nov; 38: 196–219. [doi: https://doi.org/10.1002/da.23115]
9. Trenoska Basile V, Newton-John T, Wootton BM. Remote cognitive-behavioral therapy for generalized anxiety disorder: A preliminary meta-analysis. J Clin Psychol. 2022 Dec;78(12):2381-2395. [doi: 10.1002/jclp.23360] [PMID: 35403706]
10. NHS England Improved Access to Psychological Therapy Manual URL: https://www.england.nhs.uk/wp-content/uploads/2018/06/the-nhs-talking-therapies-manual-v6.pdf [accessed on 11 January 2024]
11. Barlow DH, Farchione TJ, Bullis JR, Gallagher MW, Murray-Latin H, Sauer-Zavala S, et al. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders Compared With Diagnosis-Specific Protocols for Anxiety Disorders: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Sep 1;74(9):875-884. [doi: 10.1001/jamapsychiatry.2017.2164] [PMID: 28768327]
12. Hunot V, Churchill R, Silva de Lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. Cochrane Database Syst Rev. 2007 Jan 24;2007(1):CD001848. [doi: 10.1002/14651858.CD001848.pub4] [PMID: 17253466]
13. Resony Anxiety URL: https://www.resony.health/resonyanxiety
14. Fincham GW, Strauss C, Montero-Marin J, Cavanagh K. Effect of breathwork on stress and mental health: A meta-analysis of randomised-controlled trials. Sci Rep. 2023 Jan 9;13(1):432. [doi: 10.1038/s41598-022-27247-y] [PMID: 36624160]
15. talkhealth consent form URL: Link
16. Resony Health Terms of service URL: https://www.resony.health/terms-of-service
17. Resony Health Privacy Policy URL: https://www.resony.health/privacy-policy
18. Brown RP, Gerbarg PL, Muench F. Breathing practices for treatment of psychiatric and stress-related medical conditions. Psychiatr Clin North Am. 2013 Mar;36(1):121-40. [doi: 10.1016/j.psc.2013.01.001] [PMID: 23538082]
19. Ma X, Yue ZQ, Gong ZQ, Zhang H, Duan NY, Shi YT, et al. The Effect of Diaphragmatic Breathing on Attention, Negative Affect and Stress in Healthy Adults. Front Psychol. 2017 Jun 6;8:874. [doi: 10.3389/fpsyg.2017.00874] [PMID: 28626434]
20. Martha S. McCallie BSW , Claire M. Blum RN & Charlaine J. Hood. Progressive Muscle Relaxation, Journal of Human Behavior in the Social Environment. 2006; 13(3): 51-66. [doi: 10.1300/J137v13n03_04]
21. Fekete EM, Deichert NT. A Brief Gratitude Writing Intervention Decreased Stress and Negative Affect During the COVID-19 Pandemic. J Happiness Stud. 2022;23(6):2427-2448. [doi: 10.1007/s10902-022-00505-6] [PMID: 35228834]

22. Keng SL, Smoski MJ, Robins CJ. Effects of mindfulness on psychological health: a review of empirical studies. Clin Psychol Rev. 2011 Aug;31(6):1041-56. [doi: 10.1016/j.cpr.2011.04.006] [PMID: 21802619]
23. Tiirikainen K, Haravuori H, Ranta K, Kaltiala-Heino R, Marttunen M. Psychometric properties of the 7-item Generalized Anxiety Disorder Scale (GAD-7) in a large representative sample of Finnish adolescents. Psychiatry Res. 2019 Feb;272:30-35. [doi: 10.1016/j.psychres.2018.12.004] [PMID: 30579178]
24. Manzar MD, Salahuddin M, Alghadir A, Anwer S, Peter S, Bahammam AS, Pandi-Perumal SR. Psychometric properties of the Generalized Anxiety Disorder-7 Scale in Ethiopian university students. Bull Menninger Clin. 2021 Fall;85(4):405-427. [doi: 10.1521/bumc.2021.85.4.405] [PMID: 34851681]
25. Marcynyszyn LA, McCarty CA, Chrisman SPD, Zatzick DF, Johnson AM, Wang J, et al. Psychometric Properties and Validation of the General Anxiety Disorder 7-Item Scale Among Adolescents With Persistent Post-Concussive Symptoms. Neurotrauma Rep. 2023 Apr 27;4(1):276-283. [doi: 10.1089/neur.2022.0075] [PMID: 37139182]
26. Lee J, Lee EH, Moon SH. Systematic review of the measurement properties of the Depression Anxiety Stress Scales-21 by applying updated COSMIN methodology. Qual Life Res. 2019 Sep;28(9):2325-2339. [doi: 10.1007/s11136-019-02177-x] [PMID: 30937732]
27. Thapa DK, Visentin D, Kornhaber R, Cleary M. Psychometric properties of the Nepali language version of the Depression Anxiety Stress Scales (DASS-21). Nurs Open. 2022 Nov;9(6):2608-2617. [doi: 10.1002/nop2.959] [PMID: 34161668]
28. Osman A, Wong JL, Bagge CL, Freedenthal S, Gutierrez PM, Lozano G. The Depression Anxiety Stress Scales-21 (DASS-21): further examination of dimensions, scale reliability, and correlates. J Clin Psychol. 2012 Dec;68(12):1322-38. [doi: 10.1002/jclp.21908] [PMID: 22930477]
29. Kakemam E, Navvabi E, Albelbeisi AH, Saeedikia F, Rouhi A, Majidi S. Psychometric properties of the Persian version of Depression Anxiety Stress Scale-21 Items (DASS-21) in a sample of health professionals: a cross-sectional study. BMC Health Serv Res. 2022 Jan 26;22(1):111. [doi: 10.1186/s12913-022-07514-4] [PMID: 35078477]
30. Statistical analysis plan registered at URL: https://osf.io/rgwuh/.

Supplementary Files

Figures

DASS21 x Autonomic Questionnaire.



DASS 21 x Autonomic questionnaire

Please read each statement and *select a number* 0, 1, 2 or 3 which indicates how much the statement applied to you over the *past week*. There are no right or wrong answers. Do not spend too much time on any statement.

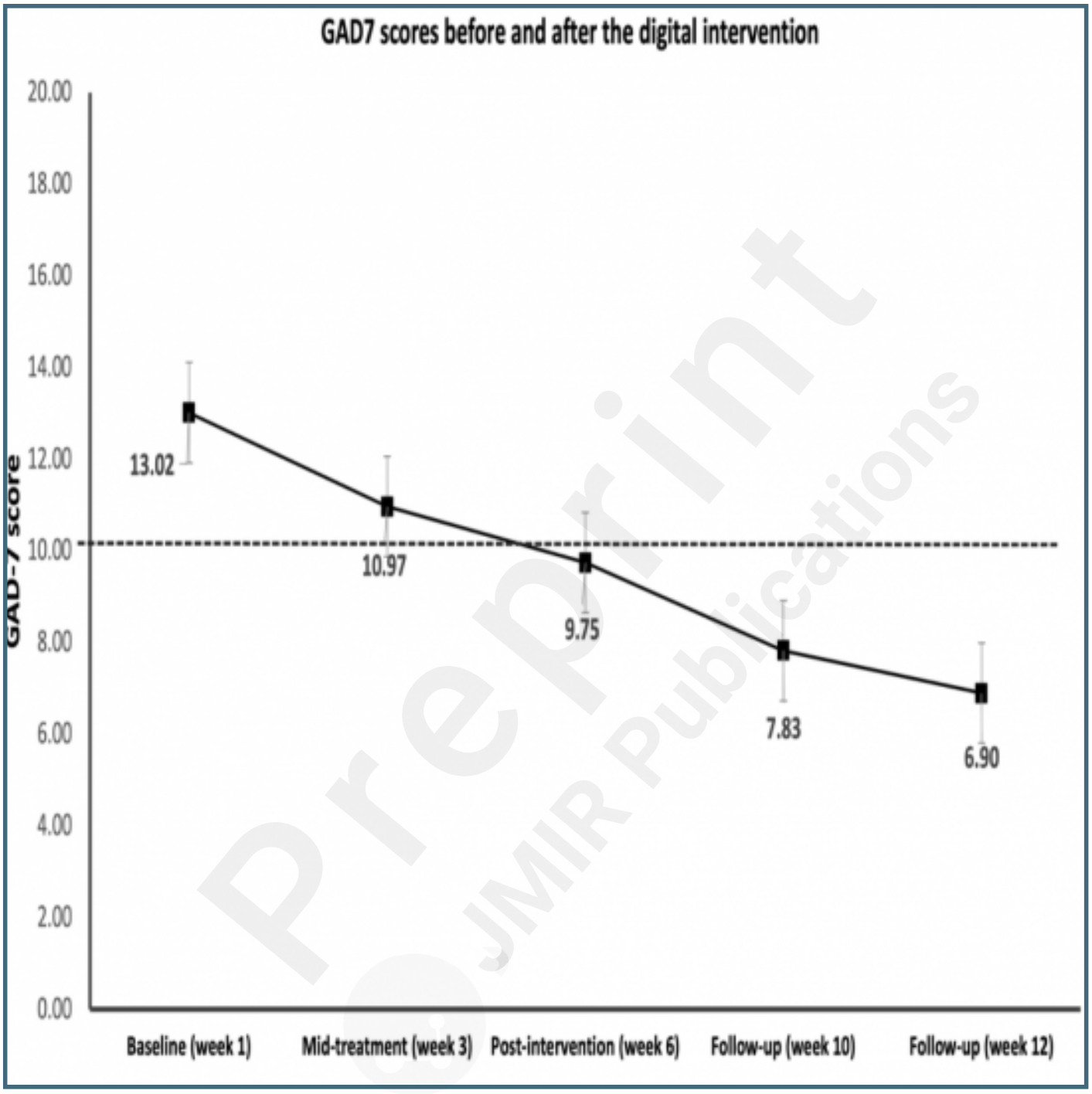
The rating scale is as follows:

0 - Did not apply to me at all - NEVER
1 - Applied to me to some degree, or some of the time - SOMETIMES
2 - Applied to me to a considerable degree, or a good part of time - OFTEN
3 - Applied to me very much, or most of the time - ALMOST ALWAYS

* 2. **For each statement, please select a number (0,1,2 or 3) to indicate how much it applied to you over the past week:**

	0 - Never	1 - Sometimes	2 - Often	3 - Almost always
I found it hard to wind down	○	○	○	○
I was aware of dryness of my mouth	○	○	○	○
I couldn't seem to experience any positive feeling at all	○	○	○	○
I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	○	○	○	○
I found it difficult to work up the initiative to do things	○	○	○	○
I tended to over-react to situations	○	○	○	○
I experienced trembling (eg, in the hands)	○	○	○	○

Anxiety symptoms over time measured with GAD-7 questionnaire.



Multimedia Appendixes

Correlation Matrix.
URL: http://asset.jmir.pub/assets/d69c28a6871e0f99231f897c8c96df08.docx

Health Questionnaire at Baseline.
URL: http://asset.jmir.pub/assets/065f1c116417ef51b7f5ffc6118c9a22.pptx

Post Intervention Questionnaire.
URL: http://asset.jmir.pub/assets/6d062eae436e61135b461294619565fa.pptx