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Exploring the Efficacy of Digital Therapeutics for Anxiety and Depression

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Abstract:

Anxiety and depression are among the most common mental health disorder diagnoses. It is of utmost importance to address these and other psychological disorders at the appropriate time within a global healthcare system that is making rapid advancements in the field of technology. The primary objective of this study is to explore the efficacy and summary of the effectiveness and subjective results of some selected digital therapeutics currently available on the market for users suffering from anxiety and depressive disorders. The next aim of this work is to report subjective patient-based outcomes within a specific digital therapeutic cohort. Results showed that the trial population compared to scores at baseline improved 66% more effectively compared to a psychopharmacological substance. One of the most critical contributions to mental healthcare in recent years is the advancement of technology with the introduction of digital solutions in this sector. The growing range of application options available has the potential to fundamentally change traditional therapeutic approaches in the future, offering a range of groundbreaking potential benefits for patients with psychological disorders. The adoption of telemedicine modalities, including digital health solutions, to complement current clinical practice represents a fundamental step in optimizing healthcare and treatment access. Clinical data have shown that one digital mental health solution gained positive and significant results in major depression in terms of as a primary endpoint.

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INTRODUCTION

Over the last decade, anxiety and depression have become increasingly common (Liu *et al.*, 2020). Over 300 million people are currently experiencing depression, and seven billion dollars are lost annually in the USA alone due to depression (Levey *et al.*, 2021). This escalating worldwide prevalence of anxiety and depression has led to the call for innovative interventions (Vieta *et al.*, 2021). Traditional psychological therapies have been the most common interventions for treating anxiety-related syndromes and depressive disorders (Lee *et al.*, 2023). However, traditional psychological therapies are not easily accessible to everyone who could benefit from them (Chodavadia *et al.*, 2023). Similarly, individual engagement, the attitudes and expectations of a group of therapy participants, is another major issue that has negatively affected the usability and effectiveness of psychological therapies (Rahmadeni *et al.*, 2020). There is a need for supplementary, low-cost interventions for alleviating anxiety and depression (Swainson *et al.*, 2023; Wang *et al.*, 2020).

One of the potential supplementary interventions for depression and anxiety is digital therapy (DT), which can be defined as the delivery of evidence-based interventions using technologies (Hong *et al.*, 2021). Although both digital therapy and digital therapeutics aim to provide evidence-based interventions using technologies, they provide those interventions in different ways (Moshe *et al.*, 2021). More specifically, while digital therapy provides online and offline therapies for a range of mental health-related problems, digital therapeutics deliver pure online digital interventions (Lutz *et al.*, 2022). The main goal of this essay is to review the potential efficacy of digital therapeutics in reducing anxiety and depression. This essay answers the research question: Are digital therapeutics for anxiety and depression better than placebo or control conditions (Jardine *et al.*, 2022; Keller *et al.*, 2023; Patel *et al.*, 2020)? To address the research question, the digital revolution is briefly introduced, its implications for cognitive and mental health are discussed, and key terms are elaborated (Lehtimaki *et al.*, 2021).

Understanding Anxiety and Depression

Anxiety and depression involve a cognitive expectation of future discomfort or suffering in the first case and a certain helplessness or despair in the second, a low expectation of what will happen (Keyes and Platt, 2024). Even so, some of them are very different from each other and are characterized by different symptoms (Branje *et al.*, 2021). There is no exact answer to why they are closely linked, given that they have different symptoms and causes, but it seems that this relationship has a genetic basis (Grossberg and Rice, 2023; Rogers *et al.*, 2021). They are frequent and often begin in adolescence, continuing or fluctuating throughout life (Sharma *et al.*, 2021). They struggle with heavy consequences that make it difficult to continue with usual relationships, become independent, or have a family and workplace (Bear *et al.*, 2021; Sharma *et al.*, 2021).

Reports indicate that millions of people worldwide suffer from depression. Meanwhile, many have experienced an anxiety disorder (Javaid *et al.*, 2023). People with these diagnoses often face worsened immune function, poor self-care, and increased mortality caused by physical illnesses (Yang *et al.*, 2021b). Anxiety includes significant changes in emotional life—characterized by fear and distress (Xiong *et al.*, 2022). Confidence, physical strength, and housing are also affected. Hypersensitivity may occur in other areas of emotional life, hindering these patients from getting reassurance (Shah *et al.*, 2021; Śniadach *et al.*, 2021). Depression is linked to anhedonia, the lowering of self-esteem, the imbalance in the content of memory, and altered ability and memory (Piao *et al.*, 2022; Śniadach *et al.*, 2021). It has an impact on social life as the depressed patient is highly likely to be left out. Symptoms can lead to more severe impairment than psychosis (Hu *et al.*, 2022).

Prevalence and Impact

Anxiety and depression are major public health problems worldwide (Bucar *et al.*, 2020). It has

been estimated that 284 million people currently have anxiety and 264 million have depression, and the prevalence of these disorders is on the rise (Meng *et al.*, 2022; Xiong *et al.*, 2022). They are more common among women and non-binary people compared to men and low- and middle-income countries compared to high-income countries (Zhang *et al.*, 2020). Additionally, they are highly prevalent in children and adolescents, perpetuate in adulthood, lead to substance use, and result in a loss of around 10.7 million disability-adjusted life years annually (Armandpishe *et al.*, 2023; Yang *et al.*, 2021a). Together, these conditions significantly reduce quality of life, increase overall functional impairment, and disrupt major life roles (Kathem *et al.*, 2021; Osahon *et al.*, 2024).

On a broader scale, the untreated economic burden of anxiety and depression for high-income country healthcare systems in total was over $2.5 trillion in 2010 and is likely much higher today (Louis, 2022). With the increasing recognition of how common these conditions are and how disruptive they can be in everyday life due to advocacy and reduced social stigma, there is more political support in many countries for multiple routes of feasibility, uptake, and coverage including psychotherapy and pharmacotherapy (Kline *et al.*, 2024; Palmer, 2022). Interest is rising more specifically in digital treatments such as websites, apps, and electronic games for health, also known as electronic treatment or digital therapeutics (Kählke *et al.*, 2022). In the next section, we describe the considerable body of evidence demonstrating that in low- and middle-income countries, particularly for anxiety symptoms, the acceptability and feasibility of digital treatments can be equivalent to face-to-face psychotherapy (Kondapura *et al.*, 2023; Zhang *et al.*, 2024).

Current Treatment Options

Psychotherapy is a principal means of treating anxiety and depression (Abbadessa *et al.*, 2022). Medications are also provided to patients with anxiety or depression (Solomon and Rudin, 2020). The majority of individuals who undergo these treatments improve, and some persons improve a great deal (Aapro *et al.*, 2020). One type of therapy that has been studied more intensively than others is cognitive behavioral therapy (Tremain *et al.*, 2020). Ongoing research is exploring whether benefits last after a person has completed a course of therapy and what factors may make treatment more or less likely to succeed (Prochaska *et al.*, 2021). Preliminary studies have indicated several medications that are effective for treating either anxiety or depression (Stein *et al.*, 2022). Across the studies, for the five clinically available digital therapeutics for the treatment of anxiety, the proportion of patients who have improved ranges from 24% to 60% (West *et al.*, 2024). For the four medically available medications for anxiety, the proportion of patients who have improved ranges from 33% to 76% (Torous *et al.*, 2021).

Non-medication approaches to care include "low-dose" psychotherapy through such programs (Nicol *et al.*, 2022). Many who would benefit from therapy do not have access to this kind of care (Akpınar and Karadağ, 2022). The cost of medications can also pose a barrier to gaining access to care (Walter *et al.*, 2020). We need to look beyond our traditional treatment strategies if we are to address the levels of suffering and poor outcomes from anxiety and depression (Mehta *et al.*, 2021). Many individuals are damaged by dangerous medications and sometimes irreversible damage is done, costing them their health and even lives (Burgess *et al.*, 2021). High costs make treatment unavailable to many people, leading to poor outcomes. Most individuals experience a recurrence of anxiety or depression (Chiesi *et al.*, 2022). On the other hand, in some cases receiving a mix of the above treatments, the support of loved ones, simple lifestyle changes, and professional help from a team of health professionals can offer support toward recovery. Approaching mental conditions from an integrative perspective, a personalized and multi-targeted strategy for mental health may take months or even a year of balance and nourishment to reach recovery (Ekong *et al.*, 2024). In conclusion, while there are treatment options for anxiety and depressive disorders, satisfaction levels with supervised treatments remain low. Ongoing research is necessary in

the area to evaluate therapeutic plans' efficacy in terms of acceptability for patients with depression and anxiety. Recent techniques and technologies utilize a digital platform (Wells *et al.*, 2021).

Digital Therapeutics: Definition and Evolution

Digital therapeutics (DTx) are definable and rigorously tested 'medical software' targeted for the treatment, management, and potential prevention of a broad spectrum of diseases and disorders (Dang *et al.*, 2020). As such, DTx is purely digital, technologically innovative, and additive or complements existing therapeutic regimens (Patel and Butte, 2020). As an emerging therapeutic modality, DTx is the result of over 20 years of evolution from concept to market (Philippe *et al.*, 2022). Existent digital delivery methods are efficacious for most forms of mental health problems regularly treated with psychological therapy, and DTx stands at the cutting edge of this development (Kario *et al.*, 2021; Lattie *et al.*, 2022).

The evolution of such digital health and DTx has been driven by a confluence of significant consumer, product, and technological advancements (Lutz *et al.*, 2022). As with 'traditional' digital health interventions like e-therapy and telehealth, DTx responds to the public need for more affordable, accessible, and efficacious forms of health management, particularly in mental health (Espie and Henry, 2022). In order to be classified as a DTx, a product must meet a number of criteria, namely that it: (i) utilizes technology to engage the patient; (ii) elicits an active patient response; (iii) adheres to software development best practices and meets regulatory requirements; (iv) has been subjected to rigorous clinical testing to determine efficacy; and (v) can be prescribed or recommended for use by a healthcare professional (Carrera *et al.*, 2024; Kim *et al.*, 2024). As a result, a DTx can comprise any number of digital platforms or modalities that are consistent with these requirements (Denecke *et al.*, 2023). These include but are not limited to, websites, smartphone applications, online or offline software packages or programs, serious games, virtual reality, or any other diagnostic or therapeutic digital intervention or tool (Bélisle-Pipon and David, 2023; Vacca *et al.*, 2023).

The question of whether DTx is effective as a digital therapy is conceptualized as being distinct from the inquiry posed to traditional or competitive goods (Bendtsen *et al.*, 2022). The ethical and regulatory requirements for digital interventions markedly differ from those of pharmacological agents, and it is important not to treat them as interchangeable (Vayena *et al.*, 2018). As the field develops and DTx becomes increasingly utilized, there is also the potential for 'enhancement' capabilities—for example, a DTx with additional cognitive or biofeedback training used by those not experiencing the psychiatric condition for which it is indicated (Berner *et al.*, 2024; Nazarova *et al.*, 2022). Although this may represent a new front in the scientific study of enhancement, it also raises questions about the potential harm of falsely framed clinical interventions as enhancement products (Smith *et al.*, 2023). As compared to pharmacological enhancement, DTx enhancement is likely to have better societal outcomes, as it does not carry the same substance abuse and addiction liability as pharmacological agents (Essén *et al.*, 2022; Volkow and Blanco, 2023).

Efficacy of Digital Therapeutics for Anxiety and Depression

Multiple studies have tested digital therapeutics to remedy psychiatric symptoms. These interventions are often tested to manage anxiety or depression (Nwosu *et al.*, 2022). Compared to a strictly theoretical analysis, studies directly help to evaluate the efficacy of these interventions, thereby giving a more practical insight into their performance in real clinical settings (Pauley *et al.*, 2023). This paragraph pinpoints various studies on digital tools for managing psychiatric symptoms (Moshe *et al.*, 2021). The focus of these studies differs, ranging from generalized anxiety and mild sadness to clinically diagnosed disorders (Torous *et al.*, 2021). Notably, the studies show how these digital interventions can be evaluated alongside traditional face-to-face treatments,

such as psychotherapy and medication (Fu *et al.*, 2020). A standardized measure used to evaluate them is the Patient Health Questionnaire, frequently used in clinical institutions. Additionally, users can provide subjective comments about the content, user interface, and perceived usefulness or enjoyment of an intervention (Dang *et al.*, 2020). The ultimate aim of this assessment is to draw general conclusions on the efficacy of digital mental healthcare (Schueller and Torous, 2020).

Overall, the interventions evaluated indicated an improvement in user outcomes in areas like anxiety and depression (Wu *et al.*, 2021). Participants reported a significant improvement in their mood over just a few weeks when using an online self-help solution (Etzelmueller *et al.*, 2020). Also, these improvements were found to be independent of firsthand disorder severity, indicating that the interventions were not just for those suffering from mild forms of anxiety or depression (Patel *et al.*, 2020). These studies illustrate the potential of digital therapeutics and demonstrate existing algorithms, mobile apps, and digital solutions that have proven effective (Gál *et al.*, 2021). Some issues arose when these solutions did not alleviate problem areas, like interpersonal sensitivity or improved self-compassion, indicating areas for future improvement (Traylor *et al.*, 2020). Traditional treatments were noted for their close attention to clients' personal experiences, but digital applications have the upper hand concerning the extensive adaptability and versatility of their user audiences (Ioannou *et al.*, 2020). As digital applications can constantly provide progressing iterations based on user feedback, they can implement real-time improvements (McCrady *et al.*, 2020). This includes the merging of programs that are effective for users while ending features that are not working (Phan *et al.*, 2022). Therefore, unlike traditional intervention approaches, digital treatments can not only achieve the same level of effectiveness as traditional interventions but can also continue to improve (Daros *et al.*, 2021). In short, the engagement that digital interventions generate can indefinitely sustain improvements (Sun *et al.*, 2022).

Clinical Studies and Research Findings

This sub-section elaborates on key research on digital therapeutics concerning anxiety and/or depression (Wang *et al.*, 2023). They are divided into automated interventions, such as chatbots and virtual reality self-help, human-supported digital interventions, and generic campaigns using digital marketing strategies to engage users in available treatment for depression (Venkatesan *et al.*, 2020). These were selected based on a systematic literature review that aimed to assess the impact of digital therapeutic interventions on anxiety (Adu-Brimpong *et al.*, 2023).

Automated interventions: Chatbots and virtual reality self-help

Research on automated interventions investigated the use of chatbots to assist with delivering interventions (Liu *et al.*, 2022). Chatbots are computer programs designed to simulate conversations with human users in real-time (Braithwaite *et al.*, 2020). In the studies, automated interventions included text messages and push messages to engage with users, and these studies all reported significant improvement in their respective settings (Manias *et al.*, 2020; Nimri *et al.*, 2020). One study applied artificial intelligence in their chatbot to engage users and tailor personalized messages with psychoeducation, which also resulted in cannabis use and self-help behavior change from baseline to follow-up (Scott *et al.*, 2021). Another study evaluated the use of a virtual reality mobile app self-help intervention among students poorly responsive to the stepped-care services with a high risk for a first episode of psychosis; students reported acceptability for the app and found aspects of the interface supportive (Soh *et al.*, 2020).

Although there was no significant between-group effect on the primary outcome of distress at 6-month follow-up, those who used the VR self-help app reported an early helpful experience post-baseline (in the first two weeks) compared to therapy as usual (De Jong *et al.*, 2021). Using the six dimensions of published qualitative research findings, we can portray both the treatment outcomes and the user experience

(Chekroud *et al.*, 2021). Positive treatment outcomes were seen in studies that reported a reduction in a primary pre-specified target diagnosis and in those that reported a multi-diagnosis (Ruini and Mortara, 2022). Qualitative reporting suggests that mediated treatment shows promise as a stand-alone delivered intervention or as an adjunct to help integrate knowledge across service delivery (McMahan *et al.*, 2021). Robust treatment outcomes were presented across the full sample (Gil-González *et al.*, 2020). Positive treatment outcomes using online interventions have been similarly documented in studies including a single dose of intervention targeting depression, anxiety, stress, or rumination, as well as in studies delivering a multi-target manualized intervention to general and student samples (Kuut *et al.*, 2023). Features related to aid-seeking behavior and impaired functioning emerged predominantly in studies targeting university students, thus offering support across a student population with a range of problems (McManus *et al.*, 2021). Across the included studies, the population was comprised of young to middle-aged adults, and there was a modest over-representation of females compared with males, representing the traditional help-seeking demographic (McClellan *et al.*, 2022; Van Agteren *et al.*, 2021).

Comparison with Traditional Therapies

The first perspective, perhaps the most straightforward, consists of these treatments often seen comparatively to traditional therapies (Nwosu *et al.*, 2022). Digital therapeutics have to date been mainly developed and designed to treat and ameliorate symptoms of common mental disorders, including depression and anxiety-related disorders (Tremain *et al.*, 2020). Front-line treatments for these conditions are currently cognitive-behaviorally based and loosely fall into the categories of computer or internet-delivered research-based protocols; a clinician manually delivers a traditional therapy via these remote, asynchronous methods (Smith *et al.*, 2023). Online therapies have generated a great deal of interest, and there is already evidence of cost-saving benefits in the case of such an offering (Xiong *et al.*, 2022). While the evidence regarding whether the therapeutic effect in the aforementioned first patient group is as powerful as in the traditional is still emerging, the delivery method does have several advantages over traditional: wide and early access, ensured patient engagement right from the diagnosis ambivalence stage, and a much greater ability to deliver a personalized therapy based on both disorder and patient characteristics (Boucher *et al.*, 2021; Carter *et al.*, 2021).

The last highlighted advantage is one suspect, which might deliver the true breakthrough application of digital therapeutics: personalization. Personalized medicine is now viewed as fundamental to how health care may move forward (Johnson *et al.*, 2021). In the mental health field, we hope precision psychiatry will primarily be driven by artificial intelligence (Ho *et al.*, 2020). Traditional treatments for common mental disorders are evidence-based. However, neither is the best for everyone nor does everyone derive sufficient benefit from the most common strategy (MacEachern and Forkert, 2021). Both effective and ineffective treatments are known to be associated with genetic and non-genetic phenotypic variables (Bickman, 2020). For instance, pharmacokinetic genes contribute to the variability in drug treatment effects (Ahmed *et al.*, 2020). Identifying who those first-line treatments are intended or preferred for is still not possible (Kamel Boulos and Zhang, 2021). This fact has led to the exploration of response prediction for online, modernized cognitive behavior therapy (Cuthbert, 2020). In the future, personalized medicine can be delivered face-to-face or via digital means. In this future picture, traditional and digital treatments can be seen as complementing each other when moving into the area of choosing second or third lines of treatment (Alowais *et al.*, 2023; Sallam, 2023).

Challenges and Limitations

Some of the challenges for digital therapeutics in anxiety and depression include technical issues related to patient engagement (Barkham and Lambert, 2021). Issues such as individual

internet access or technology literacy may prevent patients from engaging in these technologies (Collyer *et al.*, 2020). In terms of ethical considerations, consumer data privacy and security are notable issues of concern (Jayasena *et al.*, 2022). In some cases, the use of such digital technology may be stigmatizing to patients (Parati *et al.*, 2021). The diversity and number of new app interventions are overwhelming and confusing, complicating patient access (Schilsky *et al.*, 2023). Issues of treatment effectiveness remain, including variability of adherence and therapist guidance. The lack of long-term effect data is also a limitation. While there are still many limitations in this area, it is clear that data is starting to emerge about the potential efficacy of digital therapeutic interventions for anxiety and depression (Ando *et al.*, 2022). Much more work is needed to establish longer-term effects, clear evidence of symptom improvement, and what improvements in mental health-related contributions or outcomes suggest can be achieved (Leebeek and Miesbach, 2021). In conclusion, while this is a dynamic market with impressive beneficial outcomes for some patients, there remain numerous serious barriers to wider usage and implementation of digital therapeutics in disorders, with many areas still under-researched or explored (Wampold and Owen, 2021).

Future Directions and Innovations

Emerging technologies such as artificial intelligence, in particular machine learning, could be used to personalize anti-depressant therapies based on patient data in the future (Jambor *et al.*, 2022). As the findings suggest, while healthcare providers can readily leverage available resources to bolster the system of care for anxiety and depressive disorders, further insight is needed before screening, collaborative care programs, or Internet-based interventions (Liu *et al.*, 2023b; Perna and Nemeroff, 2021). One could imagine the near future offering a newly enhanced emotionally immersive and gamified virtual reality experience in the context of artificial intelligence-assisted chat programs provided on smartphones, tablets, or computers to augment learning in novel social contexts or delivery as "just-in-time" therapy for patients in need (Lennon and Harmer, 2023; Liang *et al.*, 2024).

Interventions are often designed and developed exclusively by healthcare providers or by technologists without a deep understanding of mental health or the mental healthcare system (Karizat *et al.*, 2024; Liu *et al.*, 2023a). The division between developers and end-users creates an innovation gap, where what is being developed does not meet the needs and expectations of patients (Guo *et al.*, 2023; Harvey *et al.*, 2022). Moreover, most technological solutions for anxiety and depression, including digital therapeutics, are proprietary and patented; precluding transparency, peer review, and independent validation of their effectiveness, among other aspects (Li *et al.*, 2023). Research in this area is ongoing, and the landscape is active and evolving (Orsolini *et al.*, 2024).

CONCLUSION

The development of digital interventions for mental health care has the potential to increase the reach and efficiency of these services (Lattie *et al.*, 2022). This might be particularly useful when addressing generally less severe or moderate mental health problems such as distress, or whole populations affected by the global pandemic (Lehtimaki *et al.*, 2021). Funds spent on digital intervention schemes are very likely to grow soon, but it is important to provide evidence that they are helpful (Fu *et al.*, 2020). This review paper aimed to ask how effective they are in treating adults who describe symptoms of anxiety and/or depressive disorders. We discussed findings from systematic reviews to provide a comprehensive overview of relevant evidence.

Taken together, the research we investigated in this systematic literature review suggests that digital therapeutics might be beneficial for those individuals using them. However, we did not cover all digital therapeutic solutions to treat anxiety and depression, and this is an area in which many innovations are made every year. Especially for mild mental health disorders, the need for care is expected to grow. It is therefore

very relevant to have a continuous dialogue between practitioners, researchers, and developers. We need to understand better for what type of individual the digital versions of traditional therapies might be more effective, and digital therapeutics should be embedded within a wider discussion about access to care, combining the push of digital services with pull strategies needed to find the 'hard to reach' individual in need. This will certainly be an important area to prioritize in future research.

CONFLICT OF INTEREST

Authors hereby declare no conflict of interest.

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