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Digital therapeutics for digestive health

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A 'Zemedy' For Irritable Bowel Syndrome: Case Report On The Use Of A Digital Therapeutic For The Management Of A Functional Bowel Disorder

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ABSTRACT

Introduction Irritable bowel syndrome is a functional bowel disorder thought to be underpinned by the dysregulation of the gut-brain axis. IBS places a significant burden on healthcare systems, and deficient care pathways hinder patient access to efficient and cost-effective treatments – namely, psychological interventions such as cognitive behavioural therapy (CBT). In clinical practice, CBT is known to produce significant and sustained reductions in IBS symptom severity, with up to 80% of patients responding to these therapies. While access to these therapies is both limited and expensive, advancements in digital therapeutics are granting IBS patients the independence to effectively manage their condition.

Case Description Three white females at 29-, 62-, and 66-years old were formally diagnosed with IBS-D, IBS-C, and IBS-D (respectively) after a number of general practitioner (GP) visits and medical examinations ruled out presence of other organic causes for their symptoms. Upon diagnosis, the patients were offered lifestyle advice, introduced to the low FODMAP diet, and given pharmacological agents to control their symptoms, but continued to suffer with recurring bowel events and persistent psychiatric/gastrointestinal comorbidities. Later, patients were referred to non-specialized group CBT sessions for anxiety and stress management, and noticed some improvement in the severity of their IBS symptoms. Upon the completion of their group therapy sessions, the patients sought specialized CBT for IBS courses. After an online search, all three patients independently came across Zemedly – a multi-component mobile application with a core 10-week CBT programme, designed for IBS.

Results Using Zemedly since September 2019, the patients saw vast and global improvement in the state of their IBS – particularly, developments in the frequency and severity of their gastrointestinal symptoms, as well as in their overall psycho-social wellbeing. The patients appreciated the flexibility in the delivery of the CBT sessions and enjoyed the interactive manner in which they learned about cognitive restructuring and behavioural change in IBS. The patients also emphasized the quality and clarity of the information disseminated through Zemedly around the dysregulation of the gut-brain axis in IBS. Additionally, the patients consistently highlighted the efficiency of the symptom management tools available on the app. Importantly, the patients lauded the utility of breathing exercises available, as well as the accessibility of ‘flare mode’ feature during an IBS flare-up of symptoms. Finally, the patients valued the availability of symptom, thought, stool, and food diaries, and commented on their helpfulness in recalling events at doctor visits as well as their advantage in delineating lifestyle-

symptom correlations. Today, with the exception of the 66-year old patient who is still on the low FODMAP diet, the patients exclusively use Zemedly for the management of their IBS. All three have completed the core CBT programme, but continue use Zemedly for sudden-onset flare-ups and overall maintenance of their IBS symptoms and mental health.

Discussion Real-world evidence shows that the use of a digitally-delivered CBT programme for the treatment of IBS is both effective and cost-efficient, producing significant improvements to patient physical health and psycho-social wellbeing.

Conclusion Zemedly is a novel and innovative pipeline for the dissemination of care and information around IBS, allowing patients to track and manage their own condition, at their own comfort.

KEYWORDS

Digital therapeutics (Dtx); functional bowel disorder (FBD); irritable bowel syndrome (IBS); cognitive behavioural therapy (CBT); gastrointestinal (GI) tract; gut-brain axis.

INTRODUCTION

A functional bowel disorder (FBD) is a medical disorder associated with the chronic dysfunction of the gastrointestinal (GI) tract – albeit such dysfunction is not directly attributable to an apparent cause. The symptoms of an FBD vary with the segment of the GI tract affected¹, but usually worsen with stress and appear alongside other conditions – commonly, comorbid psychiatric conditions. For this reason, FBDs are thought to be driven by the dysregulation of the gut-brain axis². Irritable bowel syndrome, or IBS, is a commonly diagnosed FBD. With a global prevalence rate of 10-20%¹, IBS develops in almost two times more females than males, and manifests in young adulthood. What causes IBS to develop in certain individuals, but not others, is poorly understood. Rather, current research indicates that multiple factors, including

patient age, gender, socioeconomic background, genetics, clinical history of gastrointestinal infection, and alterations to the gut microbiota, all contribute to the onset and progression of IBS in patients³.

Clinically, IBS is associated with a range of symptoms of the lower gastrointestinal tract – mainly, characteristic changes to the form and frequency of bowel movements. The Rome IV Criteria subtype IBS patients according to the predominant mode in which the syndrome affects their bowel movements: constipation-predominant (IBS-C), diarrhoea-predominant (IBS-D), mixed (IBS-M), or unsubtyped (IBS-U)¹. Such alterations to patients' bowel movements are in turn associated with a variety of other symptoms, including abdominal pain, discomfort, and bloating – although these are typically relieved with defecation³. Regardless, symptom onset can occur suddenly, post-prandially, or continuously¹. Yet across the IBS patient population, symptom severity also varies: 25% of IBS patients are classed with severe symptoms, 35% with moderate symptoms, and 40% with mild symptoms⁴. Still, arguably the most marked clinical variability lies in the onset of other conditions alongside the patient's IBS: comorbidities range from psychiatric to gastrointestinal and non-gastrointestinal conditions³. The most common comorbidities in IBS, however, are psychiatric conditions such as anxiety and depression – which appear in up to 90% of IBS cases⁵. Moreover still, patients with IBS commonly exhibit anxiety-related behaviours such as catastrophizing and somatisation, which have in themselves been shown to increase the severity of abdominal symptoms. Both the nature of IBS symptoms and the development of anxiety-related fear and avoidance behaviours have been known to drive patients into social reclusion⁶. Therefore, the IBS patient suffers with both physical symptoms and the associated psycho-social implications.

The diagnosis and treatment of the syndrome are also complicated in clinical practice. To date, no definitive clinical tests have been developed for the diagnosis of IBS; instead, an IBS diagnosis is made in the absence of evident structural changes to the gut and by the exclusion of other functional disorders³. Besides, the Rome Foundation suggests that IBS symptoms must appear daily for at least three days a week, and continue over the course of six months, for an IBS diagnosis to be made with a degree of clinical certainty. While the Rome IV criteria aim to provide a simplistic model for the diagnosis and treatment of IBS, the guidelines are not found to be as easily deployable in practice as they were developed to be⁷. Physicians struggle with implementing the criteria in a clinical setting due to the varied and subjective nature of IBS symptoms⁸.

Finally, once an IBS diagnosis has been reached, there remains obstacles in providing the patient with an efficient and cost-effective treatment. Today, IBS patients are first offered lifestyle and dietary advice, and then prescribed medication to help ease symptoms and control bowel movements^{9,10}. These treatments remain suboptimal, and both the IBS patient and their treating physician often report feeling dissatisfied with the availability of options. Ultimately, the disgruntled patient may not want to receive lifestyle and dietary advice after a long period of suffering and distress; whereas the discouraged physician does not have much to offer for clear answers or curative treatments⁸. If symptoms persist (i.e. in refractory IBS), the patient is then referred for psychological therapy¹⁰. In theory, psychological interventions adapted for use in IBS address the dysregulation of the gut-brain axis – dampening signals from the brain to the gut that are thought to amplify bodily symptoms. In themselves, psychological therapies are fundamentally designed to resolve anxiety-related behaviours (i.e. catastrophizing and somatisation), which are prevalent in the IBS patient population⁶. Popular in the IBS community, psychological therapies such as cognitive behavioural therapy (CBT) and hypnotherapy have been vetted for their effectiveness in reducing the patient’s symptoms and improving psycho-social wellbeing^{11,12,13,14,15}. Although up to 80% of IBS patients have been shown to respond to these psychological interventions¹⁶, shortages in the availability of qualified therapists and difficulties in programme adherence heavily limit treatment provision¹². This heavily disadvantages patients from receiving a therapy that produces significant and sustained improvements in their physical and mental health, and health-related quality of life.

Altogether, IBS is a widespread, complex, and chronic condition that is difficult to diagnose, treat, and live with. With no effective cure, IBS places a large economic and public health burden on healthcare systems⁴. To resolve the discrepancy between patient needs and physician resources, developing an innovative solution for the delivery of a comprehensive treatment for IBS is necessary⁸. Such a treatment must validate the legitimacy of IBS and its impact on the patient; provide clear and comprehensive information about IBS; address the physical, psychological, chronic, and abrupt facets of IBS symptoms; and allow patients to self-manage their condition. Today, advances in mobile health systems provide a one-to-many model of care that promises to alleviate the burden of the syndrome. In particular, digital therapeutics (Dtx) can facilitate the delivery of comprehensive, efficient, and cost-effective therapies to patients at scale¹⁷. This report presents the case for a novel and innovative approach to the treatment of IBS outside the clinic, using a digital therapeutic – Zemedy.

Zemedy is a multi-component mobile application with a core 10-week CBT programme, designed for IBS. Combining digitized CBT, hypnotherapy, stress-management techniques, and symptom tracking features, Zemedy offers IBS patients an innovative and inclusive treatment plan in managing their symptoms. Answering to the shortages of CBT for IBS specialists, Zemedy simulates the face-to-face therapy sessions sought by patients as a non-pharmacological approach for their symptoms. The 10-week CBT programme contains interactive learning modules that serve to educate the patient on a variety of IBS-related topics, including the influence of the gut-brain axis and the effect of stress on the course of IBS. In turn, patients are taught cognitive restructuring techniques to dissociate between the maladaptive thoughts and behaviours surrounding their IBS. A variety of symptom management tools are also available through Zemedy, including breathing techniques, hypnotherapy, and exercise plans. An additional feature, called 'Flare Mode', adapts and integrates breathing and calming exercises to relieve patients during a flare up – i.e. during the sudden onset of IBS symptoms. Patients are additionally offered the use of symptom tracking features: the 'Healthcheck' page allows patients to assess their physical, digestive, and mental health status, the 'Thought Diary', 'Symptom Diary', 'Food Diary', and 'Stool Diary' logs allow patients to track symptom onset and symptom-related thoughts in real time, and the 'Goals' feature allows patients to set performance and health targets. Importantly, patients are assisted through the core CBT programme and the additional therapeutic features by an AI-enabled chatbot named Elle; Elle monitors patient progress, provides patients with feedback, and reminds patients to complete their weekly CBT modules. Moreover, community and expert forums are also available on the app for discussion threads between patients and experts.

Developed by the team at Bold Health, Zemedy is an evidence-based, multi-component psychotherapeutic application that IBS patients can use to self-manage their condition. In this case report, we describe the rapid improvement of symptoms and health-related quality of life in three IBS patients who completed the core CBT programme available on Zemedy. Additionally, we discuss how the implementation of Zemedy in the clinical approach to IBS can be seen to disrupt an unsustainable care system: offering a more efficient and perhaps cost-effective approach to the management of IBS.

CASE DESCRIPTIONS

Three white females at ages 29-, 62-, and 66-years first presented with abdominal pains, abdominal spasms, and marked changes in bowel movements – all of which worsened during periods of heightened stress. The 62- and 66-year old patients had additionally been clinically diagnosed with anxiety and depression. The patients each frequented the GP, particularly when symptoms became worse and bowel movements uncontrolled. Due to the non-specific nature of their symptoms, all three patients received exploratory investigations to identify potential underlying causes. The 29-year old patient (patient 1) took blood tests and a stool test, while the 62- and 66-year old patients (patient 2 and patient 3, respectively) undertook stool tests, blood tests, and colonoscopies to eliminate other diagnoses. Two and four exploratory colonoscopies for each of patient 2 and patient 3, respectively, were prompted due to the patients' family histories. In particular, patient 2 has a family history of bowel cancer, and also presented with a hiatus hernia and gastroesophageal acid reflux (GERD). Patient 3 has a history of high blood pressure and bowel disorders, with her older sister diagnosed with IBS-D. However, the results of all blood tests, stool tests, and colonoscopies for all three patients were inconclusive. After prolonged investigations, patients 1, 2, and 3 were formally diagnosed with IBS-D, IBS-C, and IBS-D around 2, 30, and 10 years ago – respectively.

In their initial treatment plans, all three patients were offered formal nutritional and dietary advice, and patients 1 and 3 were put on the low FODMAP diet. However, only patient 3 was able to adhere to the diet, and has been on it for the past 10 years; patient 1 found the diet too restrictive and chose to discontinue its course during the reintroduction phase. Patients 2 and 3 were additionally prescribed pharmacological agents to control for their gastrointestinal and psychiatric symptoms. In particular, patient 2 was given Mebevrine (antispasmodic) for her IBS, Omeprazole for her GERD, and Seroxat (selective serotonin reuptake inhibitor, SSRI) for her depression. Patient 3 has taken Loperamide (antidiarrheal) and IBAID (probiotics) for her IBS, statins for her cholesterol, and Sertraline (SSRI) for her depression. While the patients' IBS statuses were expected to improve, their symptoms remained refractory even with the dietary/lifestyle changes and pharmacological agents introduced. As a second line approach to treatment, all three patients were referred by their GPs to either attend group session cognitive behavioural therapy (CBT; patient 3) or take online CBT courses (patients 1 and 2) – in an attempt to manage the stress and anxiety surrounding their conditions. All three patients noticed marked improvements in the severity of their IBS symptoms upon completion of their respective CBT sessions. After

discussing these improvements with their GP, all three patients then actively sought specialist CBT courses for IBS. While all three patients considered face-to-face therapy with a CBT for IBS specialist, they found the privately-held sessions to be expensive and inconvenient. All three patients then independently came across Zemedly during their ongoing online search for alternative treatment plans.

Using Zemedly since September 2019, the patients saw vast and global improvement in the state of their IBS – particularly, developments in the frequency and severity of their gastrointestinal symptoms, as well as in their overall psycho-social wellbeing. Notably, the patients emphasized the quality and clarity of the information disseminated through Zemedly around the dysregulation of the gut-brain axis in IBS, and enjoyed the interactive manner in which they learned about cognitive restructuring and behavioural change in IBS. The patients report that this helped them understand the relationship between their mental and emotional wellbeing and abdominal symptoms, where reframing their illness-related thoughts and behaviours contributed to improving their pains. The patients also appreciated the flexibility in the pace of delivery of the CBT sessions. For example, patient 3 began by using Zemedly every day, and towards the end of the 10-week programme, was using Zemedly on average twice a week.

Additionally, the patients consistently highlighted the efficiency of the symptom management tools available on the app. Patient 2 describes how the breathing exercises in particular help her at night during periods of stress, where at the onset of symptoms she is able to practice the techniques and “go to sleep within 30 minutes, otherwise [she] would have tossed and turned all night.” Importantly, the patients lauded the accessibility of ‘flare mode’ feature during an IBS flare-up, saying that they often used it after the sudden onset of symptoms. Patient 2 comments on how when she has an attack, she is “keen on using the deep breathing exercises and the (guided imagery) visualizations of the beach to help calm her down.”

Moreover, the patients appreciated the availability of symptom, thought, stool, and food diaries, and commented on their advantage in delineating patterns between lifestyle changes, dietary changes, and symptom patterns. Patients 2 and 3 also raised an important comment, stating that the diaries are helpful in recalling the occurrence IBS-related events at doctor. Patient 3 further commented on the use of the thought diary, how writing her feelings down “clarifies how her thoughts fit into her IBS, resolving her stress.”

Finally, patients 2 and 3 commented on the use of the Zemedly community page and forums – where the feature allows them to be heard, and to discuss with others their triumphs and pitfalls in IBS. Patient 3 further adds that she felt Zemedly and the Zemedly community were there for her when “everyone else was fed up with listening to her talk about her IBS.”

In general consensus between the three patients, Zemedly has dramatically improved their health-related quality of life. Patient 3 has even shared that, by way of Zemedly, she has even stopped carrying around spare clothes in anticipation of untimely bowel events. Today, with the exception of the 66-year old patient who is still on the low FODMAP diet, the patients exclusively use Zemedly for the management of their IBS. All three patients have completed the core CBT programme, but continue use Zemedly for sudden-onset flare-ups and overall maintenance of their IBS symptoms and mental health. The patients commented that they are “no longer suffering with the impact of IBS” after using Zemedly. Importantly, none of the patients experienced any adverse effects from using the therapy.

DISCUSSION

This case report introduces real world evidence indicating the effectiveness of using a Dtx for the treatment of IBS. In the cases of three patients suffering with refractory IBS symptoms, introducing Zemedly to their treatment plan produced significant improvements in patient physical health and psycho-social wellbeing. These cases are important to recognize in moving beyond diets and pills in IBS. The preliminary data provided in this case report guides the IBS patient and research community towards better solutions in an disadvantaged system – particularly in improving patient access to efficacious therapies. The information obtained from these patients is in line with previously published reports in IBS on two levels. First, the results document the effectiveness of digitally-delivered CBT in controlling the frequency and severity of IBS symptoms^{11,12,13,14,15,16}. Second, the results corroborate the hypothesis that the effects of CBT on reducing IBS symptom severity are mediated through the improvement of patient quality of life¹⁵. Importantly, the implementation of Zemedly in the clinic can also minimize the risk of recall bias in IBS research¹⁸. Through the use of diary features, patients can better report on their symptoms both in real time and retrospectively –

assisting physicians and informing studies with more accurate data. In turn, this may improve the diagnostic capacity of the current criteria, and guide the personalization of treatment strategies.

Rooted in scientific evidence, Zemedi provides the patient with a quantity of treatment options – without compromising quality. Digitizing the delivery of CBT, hypnotherapy, and other stress management techniques also allows patients to personalize their treatment course – choosing what features to use, and when. In effect, the digital nature of Zemedi and the availability of tracking features additionally serve to make this treatment modality data-driven – providing patients and physicians with the data necessary to map lifestyle/symptom patterns. Finally, Zemedi encapsulates the advantage of using digital technologies to reach and treat a larger number of individuals suffering from manageable conditions. The platform gives individuals with IBS the autonomy and flexibility in managing their own disease.

Digital therapeutics lend themselves well to inefficient healthcare systems, promising to alleviate the public health burden of disease. A growing body of academic research supports the efficiency and cost-effectiveness of digitally-delivered therapies in IBS^{11,12,13,14,15,16,19}. This report presents real world evidence around the premise and promise of Zemedi to improve IBS patient access to effective treatments. What remains is the validation of this treatment in a clinical research context through randomized controlled trials: quantifying the degrees of change comparatively, methodically, and statistically. In future directions, measuring the effect of Zemedi on known scales in IBS, such as the IBS Symptom Severity Scale, Work and Social Adjustment Scale, and the Gastrointestinal Symptom Rating Scale for IBS, will be essential to establishing the use of the therapeutic in clinical practice.

CONCLUSION

Zemedi is a novel and innovative pipeline for the dissemination of care and information around IBS, a prevalent FBD. Zemedi allows patients to track and manage their own condition, at their own comfort. The patients presented in this case report represent a larger population of enduring IBS sufferers whose struggles have been ignored due to logistical considerations. Zemedi validates the legitimacy of IBS and its impact on the

patient, providing patients with a comprehensive solution as a first-line treatment. The Zemedi platform also disseminates standardized and up-to-date information about IBS, allowing patients to discern fact from fiction around their syndrome. Finally, the features available on Zemedi address all the physical, psychological, chronic, and abrupt facets of IBS symptoms, and allow patients to effectively self-manage their condition. Therefore, by way of Dtx solutions, immediate access to impactful treatments may become the answer for all.

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