A Coached Digital Cognitive Behavioral Intervention Reduces Anxiety and Depression in Adults With Functional Gastrointestinal Disorders

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INTRODUCTION: **Traditional cognitive behavioral interventions (CBIs) improve mood and gastrointestinal symptom severity in patients with functional gastrointestinal disorders (FGIDs) but face substantial barriers to implementation. Integrating behavioral health technology into medical clinic workflows could overcome these barriers. We evaluated the feasibility and impact of a coached digital CBI (dCBI) as a first-line intervention in a prospective cohort of emotionally distressed patients with FGID.**

METHODS: **Patients with anxiety and/or depressive symptoms were offered a dCBI (an app called RxWell) during routine clinic visits. RxWell provides cognitive behavioral techniques enhanced by within-app text messaging with a health coach. Both gastroenterology and behavioral health-care providers electronically prescribed RxWell. We tracked patient interactions with RxWell, and patients completed anxiety (General Anxiety Disorder-7) and depression (Personal Health Questionniare Depression Scale) measures through the app. Our primary study outcome was the change in General Anxiety Disorder-7 and Personal Health Questionniare Depression Scale scores.**

RESULTS: **Of 364 patients with FGID (mean age 43 years [SD 16 years]; 73.1% women) prescribed the dCBI, 48.4% enrolled (median use, 3 techniques [interquartile range 1–14]). About half of RxWell enrollees communicated with health coaches. The mean baseline anxiety score was 11.4 (SD 5.5), and the depression score was 11.5 (SD 6.1). RxWell users experienced improvements in anxiety (mean change 2.71 [$t = 3.7$, $df = 58$; $P < 0.001$]) and depression (mean change 2.9 [$t = 4.2$, $df = 45$; $P < 0.001$]) at 4 months.**

DISCUSSION: **Patients with FGIDs and moderately severe anxiety and depressive symptoms are willing to use dCBI tools recommended by their providers. Our pilot data demonstrate that dCBI usage is associated with clinically and statistically significant mood symptom reductions.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/CTG/A733

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INTRODUCTION

Functional gastrointestinal disorders (FGIDs) are common conditions, with a worldwide prevalence of approximately 40% of adults (1), and collectively, FGIDs constitute most gastrointestinal (GI) consultations in both primary and specialty clinics (2,3). The pathophysiological basis of FGIDs is understood to be dependent on dysregulated interactions within the brain-gut-microbiota axis (4–6). Indeed, this concept has led to a reframing of FGIDs as disorders of brain-gut interaction (DGBI) (7). It is widely recognized that patients with FGIDs experience not only GI symptoms but also significant burdens from stress and coexistent mood disorders. As many as two-thirds of patients with FGIDs will at some point exhibit symptoms of anxiety or depression (2), and patients with irritable bowel syndrome (IBS) have more than a 3-fold increased odds of experiencing anxiety or depressive symptoms compared with the general population (8). Patients with FGIDs who experience heavier psychological burdens experience poorer quality of life and more severe GI symptoms (7,9,10). Clearly, the management of treatment of patients with FGIDs would benefit from an integrative

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approach that addresses psychological burdens and disordered mood regulation.

Given the wide appreciation for brain-gut interactions in the expression of FGID illness, there has been growing interest in cognitive behavioral interventions (CBIs) for treating patients with FGIDs. Multiple investigations using a variety of CBIs, such as mindfulness meditation, cognitive behavioral therapy, and other stress reduction techniques, have demonstrated a positive impact not only in mood and stress but also in GI symptom severity in patients with FGIDs (11–17). However, despite these promising data, traditional CBIs are resource-intensive endeavors that require ongoing, direct contact between behavioral health-care providers and patients. In addition, traditional CBIs face substantial barriers to broader implementation because of poor access, substantially limited numbers of behavioral health-care providers, challenges with affordability, and even patients' willingness to engage in face-to-face psychological care.

There is intense interest in developing digital CBIs (dCBIs) as potentially cost-effective, scalable, and effective treatments that address many of the barriers of traditional CBIs. The dCBIs have demonstrated efficacy for those with mood disorders (18–20) and for those with FGIDs such as IBS (21,22). Digital mental health interventions offer an attractive approach to deliver evidence-based psychological care to patients unable or unlikely to seek in-person treatment. However, to date, the evidence for effectiveness of CBIs and dCBIs has been limited to clinical trial settings involving patients with specific FGID diagnoses. Furthermore, although some commercial dCBI products are available, these lack medical oversight. Integrating monitored dCBIs into medical clinic workflows could potentially overcome several barriers faced by traditional CBIs. Yet, there is a clear knowledge gap regarding the real-world feasibility and efficacy of dCBIs in the care of heterogeneous cohorts of patients with FGID.

To address this knowledge gap, we evaluated the feasibility and effects of a coached dCBI for treating anxiety and depression, nested in an integrated behavioral-neurogastroenterology clinical program dedicated to treating patients with FGIDs. The primary goals of the study were to evaluate the initial effects of a dCBI as a lower-barrier, first-line intervention or as an adjunct intervention for reducing emotional distress in patients with FGID. The primary outcomes were a reduction of anxiety and depressive severity across a 4-month period after the dCBI was prescribed as part of routine GI outpatient care. We also evaluated an exploratory, secondary outcome of the change in emergency department (ED) visits over 6 months following the dCBI prescription compared with 6 months before the dCBI prescription.

METHODS

Study cohort

Patients seen during routine care at an integrated behavioral-neurogastroenterology clinic at the University of Pittsburgh Medical Center (UPMC), who exhibited or reported symptoms of anxiety and/or depression during their encounter, were considered for access to a dCBI app called RxWell. The clinic is staffed by 4 neurogastroenterologists and an advanced practice provider, and patient encounters occurred either through in-person or telemedicine clinic visitations between March 1, 2020, and February 11, 2021. Once patients consented to accept the dCBI, an order was placed through the electronic medical record (Epic Systems). Patients were instantly texted a code to download the RxWell app from either Google or Apple app stores. Patients completed anxiety General Anxiety Disorder-7 (GAD-7) and depression Personal Health Questionniare Depression Scale (PHQ-8) measures in RxWell, thereby completing the enrollment process. Patients were prompted, through the app, to complete GAD-7 and PHQ-8 assessments starting at 30 days from the date of their previous GAD-7 and/or PHQ-8 assessment. Patients may have completed those assessments at later dates, but within the 3-month window of analysis after the enrollment in RxWell. Because of the variation in the timing of the postassessment data entry, some patients may not have completed all 3 possible postenrollment assessments. Thus, to capture more postassessment data points, we allowed up to 4 months of time from enrollment to enhance the likelihood of collecting a third assessment. The study outcomes focused on changes in GAD-7 and PHQ-8 scores compared with baseline that were recorded over the 4-month period after the download of RxWell. The app prescription was used as a first-line behavioral intervention by gastroenterologist providers. A subgroup of patients received RxWell as an adjunct tool that supplemented sessions with behavioral health-care providers (2 psychiatrists and 2 therapists), as clinically indicated.

Description of the coached dCBI (RxWell)

RxWell is a health coach–enhanced, dCBI app available for use on both iOS and Android phones. It is housed within the UPMC Health Plan. UPMC is a large, integrated delivery and finance system that offers both medical care and health-care coverage to more than 3.9 million members. The mobile app (Figure 1) provides users with a brief (5–10 minutes), skill-building intervention with techniques, such as relaxation, behavioral activation and exposure, distress tolerance, cognitive reframing, and mindfulness meditation, for treating depression and anxiety. The content of RxWell was developed based on standard cognitive behavioral therapy techniques for treating anxiety disorders and depression using unique anxiety and depression programs. Patients initially chose either the "Anxiety Track" or the "Depression Track" program, which were composed of 53 and 40 techniques, respectively. Based on interactions with digital health coaches (Figure 1c), the app could be individualized to include some techniques from either track.

Digital health coaches. RxWell includes an integrated digital health coach who is assigned to each user. Coaches are bachelor's-level graduates who complete additional training in motivational interviewing techniques and cognitive behavioral theory for treating anxiety and depression. Each health coach is supervised by a licensed mental health-care provider (E.S.). The health coach communicates with RxWell users through asynchronous, secure, within-app messaging. The health coach reinforces CBI principles, guides patients through goal setting, and helps patients work through challenges and recognize successes.

Risk escalation protocol. An additional feature of the app is risk escalation protocol. Patients appearing to be at risk or displaying signs of increased distress within the app are flagged by their digital health coach, who notifies the licensed behavioral health supervisor. Patient text messages, write-in techniques, and worsening mood ratings, or GAD-7 and PHQ-8 assessments could all form the basis for a risk escalation. Coaches contact their supervisor and message the patient encouraging them to reach out to their medical provider or 911, depending on the severity of the escalation. The licensed supervisor determines the need for patient outreach or outreach to the patient's referring clinician.

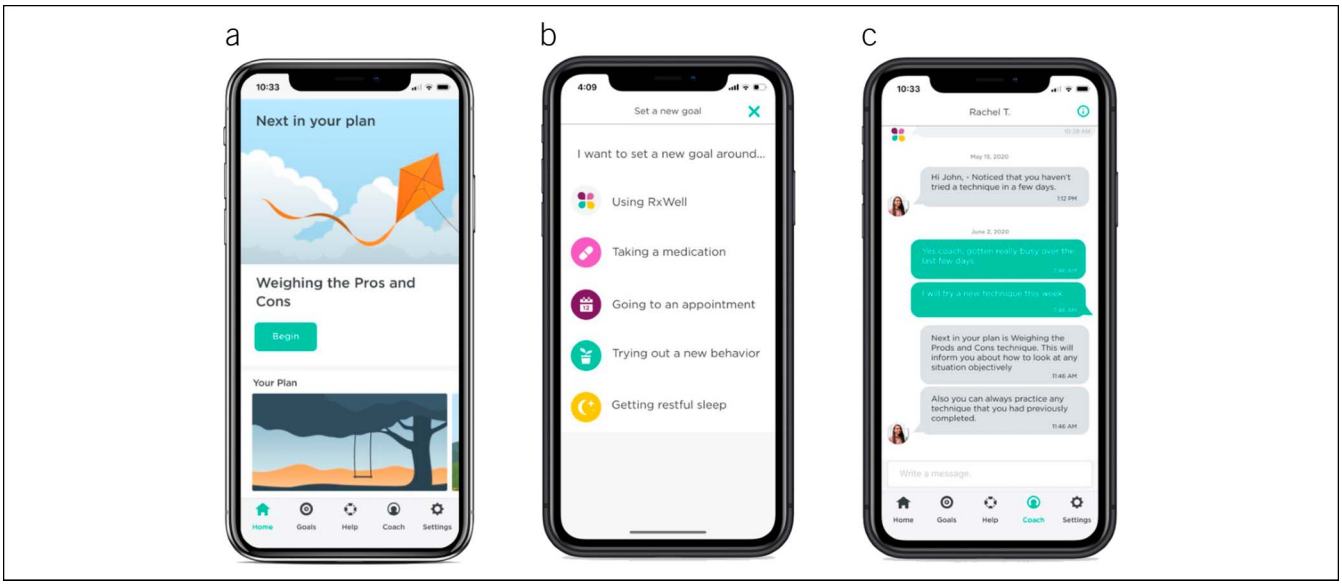

Figure 1. Screenshots of the RxWell app. (**a**) RxWell home page, (**b**) task selection interface, (**c**) platform for health coach interactions.

Patient engagement. Within-app information was collected and included de-identified demographic information (age, sex), app usage information (anxiety vs depression tracks), periodic assessments of anxiety severity (GAD-7) (23) and depression severity (PHQ-8) (24), number of techniques completed, and the number of within-app text messages sent to a patient's digital coach. Meaningful patient engagement was operationally defined *a priori* as a patient enrolling in the app and completing at least 3 techniques (25). Information about demographics (sex, race), diagnoses and *International Classification of Diseases 10th revision (ICD-10)* codes, antidepressant medication use, behavioral health-care provider utilization, and ED visits were obtained from the electronic medical record chart review. Although not a condition for receiving and ordering RxWell, all patients included in this study had separately consented to join an institutional review board (IRB)-approved "FGID Research Registry" (University of Pittsburgh IRB No. STUDY19050107) that allows for retrospective medical chart review.

Primary outcome measures

The GAD-7 is a validated, self-report questionnaire used to identify probable cases of anxiety disorders by evaluating the severity of 7 diagnostic anxiety symptoms during the past 2 weeks (23). Total GAD-7 scores range from 0 to 21, with scores >10 consistent with at least moderate levels of anxiety. The PHQ-8 is a valid measure of depression severity (24). Total PHQ-8 scores range from 0 to 24, with scores >10 consistent with at least moderate depression. Effects over time from baseline to first assessment (i.e., at least 30 days later) and across the 4-month postintervention period were evaluated by paired *t* tests. We also determined the proportion of patients achieving clinically significant outcomes (defined by a reduction of 3 or greater GAD-7 or PHQ-8 scores).

Exploratory secondary outcome measures

We assessed the number of all-cause ED visits in the 6 months before and in the 6 months after the date on which RxWell was ordered. These ED visits were manually counted by directly reviewing the electronic medical record of each patient in which RxWell was electronically ordered. We identified the proportion of RxWell users and nonusers who made at least 1 ED visit in the 6 months before and 6 months after the date on which RxWell was electronically ordered.

Statistical analyses

We used descriptive statistics to characterize the sample population through proportional assessment for categorical data, median (interquartile range [IQR]) when ordinal data were skewed, and mean (SD) when ordinal data were normally distributed. Effects over time were assessed using the Wilcoxon signed rank test for skewed data and paired *t* tests for normally distributed data. All tests for statistical significance were 2-sided analyses, with a *P* value less than 0.05 considered statistically significant. Owing to anticipated loss to follow-up, we used unweighted complete case analysis for the first assessment follow-up data (which was completed at a minimum of 30 days from enrollment), and the last observation carried forward method for any additional follow-up data recorded within 4 months of enrollment. In *post hoc* analyses, we used Spearman correlations to assess the relationship between anxiety and depression change scores, techniques completed, and number of messages to the coach. In addition, we used logistic regression to assess risk of having at least 1 ED visit in the 6 months after RxWell prescription between those enrolled and not enrolled in RxWell. All analyses were conducted using either SPSS software, version 27 (IBM, Armonk, NY) or Stata software, version 13.1 (StataCorp, College Station, TX).

RESULTS

Study cohort

A total of 2,823 clinic visits were staffed by gastroenterology providers (n = 2,002) or behavioral health-care providers (n = 821) during the observation period. A total of 364 patients with FGID consented and were prescribed RxWell during one of these clinic visits (n = 285 [78%] from gastroenterology providers, n = 79 [22%] from behavioral health-care providers). Thus, approximately14% of all gastroenterology provider visits and approximately10% of behavioral health-care provider visits were associated with an RxWell prescription. Of the 364 patients who

were prescribed RxWell, 176 (48.4%) ultimately enrolled in the app, in doing so also completing baseline GAD-7 or PHQ-8 measures. Of the patients who were prescribed RxWell, 188 (51.6%) did not complete the enrollment process. RxWell users were divided into the Anxiety (n = 126 [71.6%]) and Depression Tracks (n = 50 [28.4%]), as shown in Figure 2. The clinical characteristics of those who enrolled in RxWell and those who did not and the total study population that had RxWell ordered are summarized in Table 1. A proportion of RxWell users did not complete any follow-up assessments (n = 71), with 31 (43.7%) of these patients meeting our *a priori* definition of engagement with the app (Figure 2). The distribution of FGID diagnoses in the study cohort, based on review of *ICD-10* codes at the clinical encounter associated with the RxWell order, revealed that approximately equal proportions of the cohort had upper GI or lower GI disorders as their dominant clinical problem (Figure 3). Table 2 lists the most prominent GI diagnoses of the patients included in the study. A full account of all *ICD-10* codes and their assignment to the diagnostic categories are listed in Supplemental Tables 1A and 1B (see Supplemental Material, Supplementary Digital Content 1, http://links.lww.com/CTG/A719).

Patient engagement with RxWell

A total of 176 patients enrolled in RxWell (Figure 2) and used a median of 3 techniques (IQR 1–14), with 100 RxWell users (56.8%) completing 3 or more techniques, sufficient to be deemed engaged with the program. A total of 86 RxWell users (48.9%) messaged their coach at least once (median of 3 messages [IQR 1–11]), and 26.7% (n = 47) sent 3 or more messages to their coach during the observation period.

Risk escalations

There were a total of 66 risk escalations from 27 individuals (range 1–16 per individual) during the study period, with most of them (n = 44, 67%) deemed of low to moderate risk severity. Each risk escalation was characterized by a health coach notifying the licensed supervisor (E.S.), and prescribing providers were notified in each case. For the 22 risk escalations that were deemed of more serious severity, the users were additionally messaged to call 911 or provided with a local crisis phone line. There were no serious adverse risk events (e.g., suicide attempts or involuntary commitment to psychiatric inpatient care) during the course of this pilot study.

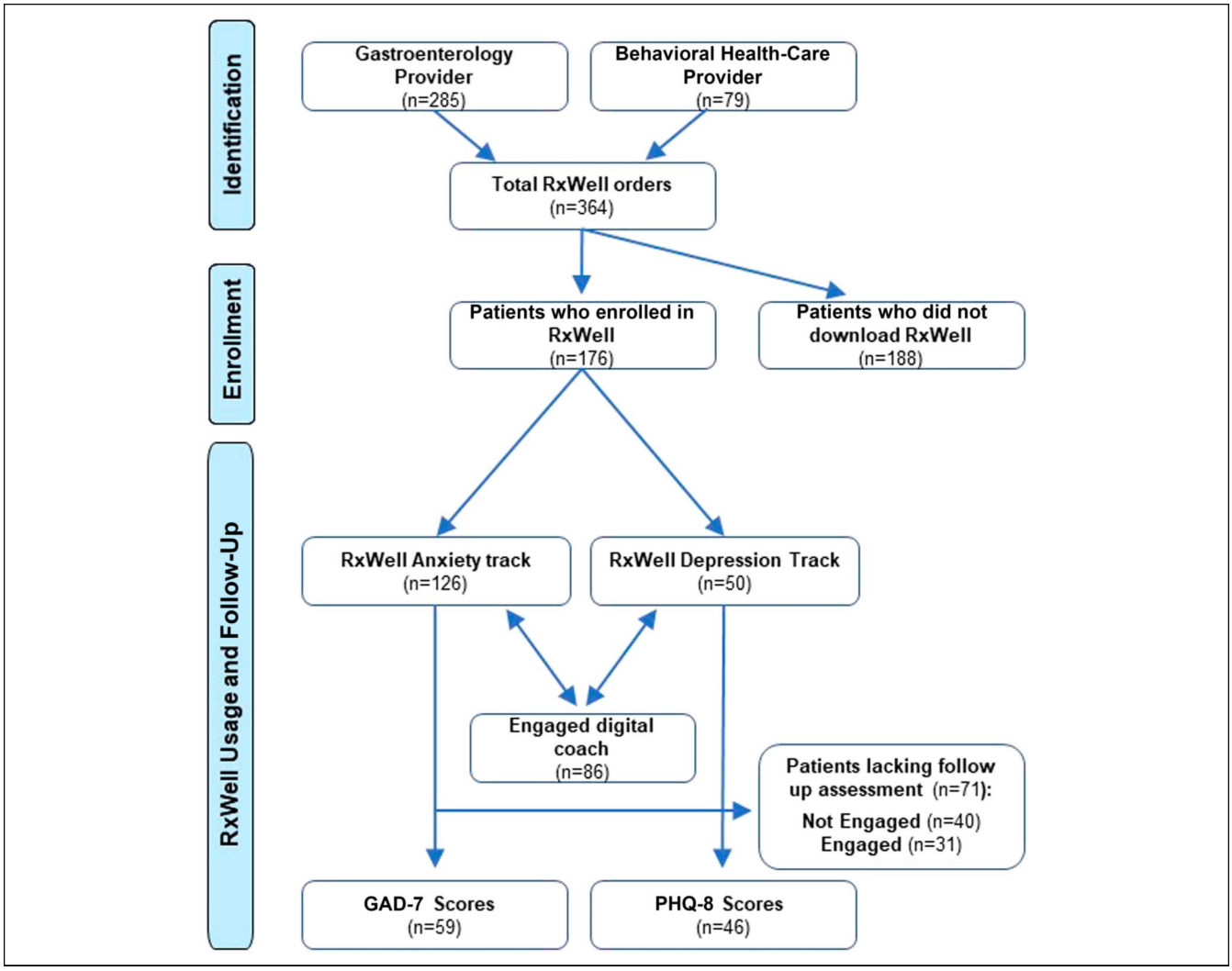

Figure 2. Schematic of the study flow.

Table 1. Clinical characteristics of the total study cohort, those with did not enroll in RxWell, and those who did enroll in RxWell

	Total cohort (n = 364)	Not enrolled (n = 188)	Enrolled (n = 176)
Women, n (%)	266 (73.1)	136 (72.3)	130 (73.9)
Race, n (%)			
White	328 (90.1)	120 (88.3)	162 (92.1)
Black	30 (8.2)	13 (9.6)	12 (6.8)
Other	4 (1.1)	2 (1.1)	2 (1.1)
Decline	2 (0.6)	2 (1.1)	0 (0)
RxWell track, n (%)			
Anxiety	—	—	126 (71.6)
Depression	—	—	50 (28.4)
Age (mean yr [SD])	43.3(16.3)	44.2(16.6)	42.3(15.8)
Baseline antidepressant use, n (%)	237 (65.1)	119 (63.3)	118 (67.0)
Baseline use of neurogastroenterology behavioral health-care provider	143 (39.3)	54 (28.7)	89 (50.8)
GAD-7 and PHQ-8 scores, mean (SD)			
Baseline GAD-7	—	—	11.4(5.51)
GAD-7 (after the first assessment)	—	—	9.47(6.87)
GAD-7 (up to 4 mo)	—	—	9.17(5.6)
Baseline PHQ-8	—	—	11.53(6.08)
PHQ-8 (after 1 mo)	—	—	10.15(6.03)
PHQ-8 (up to 4 mo)	—	—	8.43(5.42)
RxWell utilization, median (IQR)			
No. of completed techniques (median [IQR])	—	—	3(1,14)
No. of messages to health coach (median [IQR])	—	—	0(0,3)
ED utilization, n (%)			
≥1 ED visit 6 mo before RxWell order[a]	146 (40.1)	77 (41.0)	69 (39.2)
≥1 ED visit 6 mo after RxWell order[a]	94 (26.9)	57 (32.4)	37 (21.3)

ED, emergency department; FGID, functional gastrointestinal disorder; GAD-7, General Anxiety Disorder-7; IQR, interquartile range; PHQ-8, Personal Health Questionniare Depression Scale.
[a]n = 350 total; n = 176 not enrolled, n = 174 enrolled.

Effects on anxiety and depression

We found that RxWell use was associated with statistically and clinically significant differences between baseline anxiety scores and anxiety scores at the first assessment and up to 4 months of follow-up (Table 3). The differences between baseline depression scores and follow-up scores were not statistically different at the first assessment but were statistically and clinically significant different at up to 4 months (Table 3). Among enrolled users with sufficient follow-up data for analysis, approximately 70% (41 of 59 Anxiety Track users) experienced some reduction in anxiety scores, with approximately 44% (26 of 59 Anxiety Track users) experiencing clinically significant reductions of 3 points or more on the GAD-7 scores. Similarly, approximately 65% (30 of 46 Depression Track users) experienced some reduction in depression scores, with ~52% (24 of 46 Depression Track users) experiencing clinically significant reductions of 3 points or more on the PHQ-8 scores.

In an exploratory secondary analysis, we sought to clarify the relationship between user engagement with RxWell, the number of interactions with their digital health coach, and the change in anxiety and depression scores. Our analysis demonstrated that anxiety scores improved in all RxWell users, whether or not they either engaged with their digital health coach (Table 4). However, we observed that depression scores improved only in those RxWell users who did engage with their digital health coach (Table 4). We found that neither the absolute number of techniques used nor the number of messages with digital health coaches correlated with the magnitude of anxiety or depression score changes at the first assessment or up to 4 months (see Supplementary Table 1, Supplementary Digital Content 1, http://links.lww.com/CTG/A719). However, there was a strong, positive association between the number of completed techniques and number of messages to the health coach (Spearman correlation 0.729; $P < 0.001$) (see Supplementary Table 2, Supplementary Digital Content 1, http://links.lww.com/CTG/A719).

We performed an additional subgroup analysis of the first assessment and 4-month outcomes in patients referred by gastroenterology providers (see Supplementary Table 3A, Supplementary Digital Content 1, http://links.lww.com/CTG/A719)

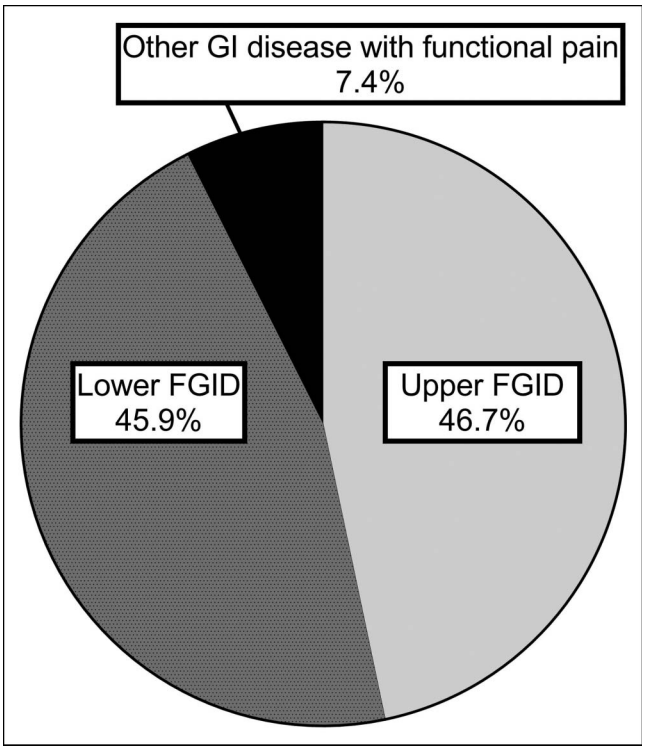

Figure 3. Proportion of study patients with upper or lower functional gastrointestinal disorders.

and those referred by behavioral health-care providers (see Supplementary Table 3B, Supplementary Digital Content 1, http://links.lww.com/CTG/A719). In both subgroups, RxWell users experienced statistically significant reductions in the 4-month depression scores, but there were only modest reductions in anxiety scores in the patients referred by behavioral health-care providers.

ED visits

The proportion of patients with at least 1 ED visit in the 6 months before and after their RxWell prescription is summarized in Table 1. We found a significantly decreased odds ratio of having 1 or more ED visits among those enrolled in RxWell in the 6 months after their RxWell prescription compared with those not enrolling in RxWell (odds ratio 0.503, $P < 0.012$). In other words, patients enrolled in RxWell had an ~50% reduction in the odds of visiting an ED in the 6-month postenrollment.

DISCUSSION

Our findings have several major implications for the future role of digital behavioral health tools in real-world gastroenterological care. First, our study demonstrates the feasibility of incorporating a health coach–supported, digital CBI (RxWell) into real-time gastroenterology clinic workflows for patient with FGIDs. There is growing evidence to support behavioral health-care interventions as key components of integrative care for patients with DGBI, but substantial barriers to implementation due to poor access, provider shortages, and time and financial costs have limited their widespread practice. Thus, it is not surprising that there has been intense interest in developing digital platforms to deliver behavioral interventions to a broader range of patients because these tools could conceivably overcome many of these barriers to face-to-face therapy (25–29). Our study found that providers were willing to prescribe RxWell and many patients were willing to engage with the program. A key advantage of our implementation strategy was the provision for providers to e-prescribe the digital intervention directly from the electronic health record, in real time, during direct patient encounters (either virtually or in face-to-face clinic visits). Electronic prescription likely lowered barriers for physicians to implement the program, and it is likely that direct orders from a physician in the context of doctor-patient interaction increased patients' views of the credibility of the RxWell intervention. Furthermore, the availability of asynchronous human interaction using within-app text messaging from digital health coaches was another advantage of our program, potentially boosting patients' motivation to engage with the tool. Another notable benefit for patients using the dCBI intervention was the continual, 24/7 access to evidence-based behavioral health techniques. The population of patients used in this intervention had elevated baseline anxiety and depression scores and substantial medical complexity common to patients often referred to academic neurogastroenterology clinics. Despite this mental health burden, and amid the backdrop of societal upheaval due to the COVID-19 pandemic (which has intensified mental health issues for many patients with FGIDs) (30), it is impressive that a substantial proportion of patients accessed and engaged with the dCBI program. Our preliminary evidence clearly highlights the feasibility of incorporating dCBI platforms that use paraprofessionals as digital health coaches into routine gastroenterological workflows with a population of complex patients. Our experience suggests that this intervention could be a cost-efficient and scalable model to provide wide access to behavioral treatments for patients in a wider range of practice settings.

The second implication of our findings is that short-term patient use of the dCBI platform may improve anxiety and depression. Many patients experienced mood improvements within the first month of use and those who continued to engage with the program and interact with digital health coaches made more

Table 2. Characterization of FGID diagnoses in the study cohort

FGID categories	FGID diagnoses[a]	N (%)
Upper FGID	Gastroparesis, functional dyspepsia, cyclic vomiting syndrome, GERD, and dysphagia	170 (46.7%)
Lower FGID	Irritable bowel syndrome, functional constipation, functional diarrhea, abdominal pain, pelvic floor dysfunction, and anorectal dyssynergia	167 (45.9%)
Other GI disease with functional pain	Crohn disease, ulcerative colitis, and chronic pancreatitis	27 (7.4%)

FGID, functional gastrointestinal disorder; GERD, gastroesophageal reflux disease; GI, gastrointestinal.
[a]Determined based on primary *International Classification of Diseases 10th revision* diagnosis linked to the encounter in which RxWell was ordered; if not specified (n = 11), then FGID diagnosis was assigned by review of clinic notes.

Table 3. Change in GAD-7 and PHQ-8 scores within the RxWell-enrolled population

	N	Mean change (SD)	CI	t (df)	*P* value (2-tailed)	Cohen d effect size
Baseline GAD-7—the first assessment GAD-7	59	2.64 (5.25)	(1.28, 4.01)	3.87 (58)	<0.001	0.47
Baseline GAD-7—the 4-mo GAD-7	59	2.71 (5.68)	(1.23, 4.19)	3.67 (58)	0.001	0.46
Baseline PHQ-8—the first assessment PHQ-8	46	1.13 (4.89)	(−0.32, 2.58)	1.568 (45)	0.124	0.19
Baseline PHQ-8—the 4-mo PHQ-8	46	2.85 (4.58)	(1.49, 4.21)	4.22 (45)	<0.001	0.51

CI, confidence interval; GAD-7, General Anxiety Disorder-7; PHQ-8, Personal Health Questionniare Depression Scale.

extensive use of the program and experienced greater improvements in depression than those who did not engage with the coaches. This finding is consistent with other studies demonstrating that coached digital platforms generally outperform purely self-guided ones (31–34). Thus, our study provides additional signal that hybrid interventions (i.e., digital + human interaction) yield higher engagement levels than purely self-guided digital apps. Without control groups or more robust comparisons with non-RxWell user groups, we cannot strictly conclude that the improvements in mood we observed were solely due to RxWell use. However, the fact that engagement with RxWell health coaches was associated with greater improvements in depression certainly suggests a causal link. Future work will analyze outcomes with RxWell users over longer time scales and compare mental health outcomes with patients who do not engage with the app. Nonetheless, our results provide a clear signal that health coach–supported digital behavioral interventions could become a generalizable strategy to influence mood across broad populations of patients.

Third, it is also worth noting that our implementation trial of dCBI was agnostic to the patients' underlying GI diagnosis. Past clinical trials of CBI or dCBI have focused on specific patient groups, such as those with functional dyspepsia or IBS (17,21,22,35,36). Our data showed broad-based improvements in mood that were not restricted to patients with specific GI disorders, suggesting that dCBI could be effective for patients with a broad range of digestive issues.

Fourth, this exploratory pilot study can only report real-world outcome data. A randomized controlled trial design would be better positioned to assess the clinical efficacy of the app. Most real-world data demonstrate decreased clinical responses and lessened adherence to interventions compared with the reference randomized controlled trials due to heterogeneity in the patient populations and other confounding variables. Yet, our results are in league with the results reported in the Assessing Cognitive Behavioural Therapy for IBS trial (21,22), which evaluated a treatment strategy that included a digital behavioral health tool intervention for patients with IBS. Furthermore, the improvement of GAD-7 and PHQ-8 scores we observed in our study was compatible with the effect sizes reported in other dCBI trials (37). Our patient population was more heterogeneous than that included in the Assessing Cognitive Behavioural Therapy for IBS trial, and patients were often referred specifically to our clinic because of being refractory to conventional treatments. In this light, it is encouraging to see that many of our patients experienced benefits from using RxWell even outside of a formal clinical trial setting, with rates of adherence to the dCBI tool only slightly inferior to those observed in controlled trials (37).

Fifth, our dCBI had a unique functionality that used the content of interactions between health coaches and patients in a robust risk escalation protocol triggered by troublesome encounters. These safety features were built into the design of the intervention, with algorithms for communication between digital coaches, their clinical supervisors, and in turn the prescribing providers to alert more severe behavioral and emotional disturbances that should warrant more intensive behavioral treatments. Thus, widespread use of RxWell could function as a behavioral health warning system capable of identifying issues and proactively triaging patients to appropriate levels of behavioral healthcare interventions.

Finally, our initial exploratory analysis of health outcomes found a significant association of RxWell use with reductions in

Table 4. Change in GAD-7 and PHQ-8 scores based on engagement with RxWell coach (defined as ≥ 3 messages)

Category	Interval	N	Mean change (SD)	CI	t (df)	*P* value (2-tailed)	Cohen d effect size
Coach	Baseline GAD-7—the first assessment GAD-7	40	2.05 (4.96)	(0.46, 3.64)	2.61 (39)	0.013	0.371
	Baseline GAD-7—the 4-mo GAD-7	40	3.18 (5.64)	(0.37, 3.98)	2.44 (39)	0.019	0.372
	Baseline PHQ-8—the first assessment PHQ-8	33	1.24 (5.27)	(−0.63, 3.11)	1.35 (32)	0.185	0.173
	Baseline PHQ-8—the 4-mo PHQ-8	33	3.64 (4.53)	(2.03, 5.24)	4.62 (32)	<0.001	0.631
Without coach	Baseline GAD-7—the first assessment GAD-7	19	3.89 (5.74)	(1.13, 6.66)	2.96 (18)	0.009	0.290
	Baseline GAD-7—4-mo GAD-7	19	4.00 (5.63)	(1.29, 6.71)	3.10 (18)	0.006	0.309
	Baseline PHQ-8—the first assessment PHQ-8	13	0.85 (3.93)	(−1.53, 3.22)	0.78 (12)	0.453	0.241
	Baseline PHQ-8—the 4-mo PHQ-8	13	0.85 (4.22)	(−1.70, 3.40)	0.72 (12)	0.484	0.258

CI, confidence interval; GAD-7, General Anxiety Disorder-7; PHQ-8, Personal Health Questionniare Depression Scale.

all-cause ED utilization. This suggests that improved mood associated with RxWell use may mediate better symptom control and/or health-care seeking behaviors. One limitation of our analysis is that we could only track UPMC ED visits and not ED visits in other health-care systems. Nonetheless, the early signal of benefit of the RxWell intervention with a reduction in ED visits is an encouraging and conspicuous preliminary result that implies potentially significant health-care cost savings. Our use of paraprofessionals as digital coaches in a stepped care model would enable a cost-efficient, scalable model of CBI for a broad population of patients. Our findings have implications for health-care system and health insurance funding models that could justify sustained, expanded investments in digital behavioral platforms (i.e., costs of behavioral health coaches, information technology support and app development, etc.) based solely on a robust health-care savings value proposition through decreasing utilization of unplanned care.

There are a number of limitations of our work. First, our study was an open, nonrandomized implementation trial performed largely under a quality assurance framework. We would require an IRB-approved, prospective, randomized controlled trial or adaptive clinical trial design to truly evaluate the efficacy of the RxWell dCBI compared with a defined control group. Second, our trial did not restrict RxWell access to patients who met diagnostic criteria for anxiety disorder or clinical depression but rather was triggered by the patients' expression of anxiety or depression symptoms in a real-time clinic visit. Thus, the resulting study population had a range of mood disorder severity, and it is not clear whether some baseline characteristics (mood severity, true anxiety, or depression diagnosis) would predict treatment response to RxWell. This is an important issue to address in future work because it would help determine whether RxWell is best suited as an agnostic first-line intervention in a stepped behavioral health-care paradigm for all patients regardless of severity or whether RxWell is more appropriate for those with mild-to-moderate emotional distress to prevent the progression to a more severe mental health disorder. This broad range of baseline anxiety and depressive symptom stability and severity likely contributed to the lack of correlation between dCBI dosage (e.g., number of techniques and coach interactions completed) and the observed change in emotional distress scores observed in our cohort. Third, we were limited in assessing the app effects on health-care outcomes and GI symptom improvements because of the variety of GI disorders and the nonrandomized design. We could not easily track metrics of DGBI symptom severity or general GI symptom severity to assess the impact of RxWell on GI functioning. Future studies that incorporate standardized GI symptom surveys (i.e., the Patient-Reported Outcomes Measurement Information Syste GI tools) (38) into the clinical workflows will allow for such outcomes to be assessed. Fourth, because the anxiety and depression metrics were obtained through the engagement with the RxWell platform, we were not able to track the changes in mood of patients who were prescribed RxWell but who did not use it. This limited our ability to ascribe the mental health benefits that we observed directly to the use of RxWell. Future studies that incorporate more frequent mental health assessments similar to those obtained in RxWell could create a suitable comparison cohort to address this issue. Another limitation of our study is that there was substantial attrition in patient engagement with the app, and we could meaningfully measure only GAD-7 or PHQ-8 score outcomes over 4 months. Ideally, longer follow-up would be needed to assess the durability of the clinical improvements we observed over a shorter time frame. Finally, 1 potential confound in our study was that some patients had additional behavioral resources available to them (i.e., a private practice psychologist) that we did not record, and many patients used the techniques but did not fill out the symptom surveys. Thus, we could have underestimated and overestimated the treatment effects ascribed to RxWell using our methodology. Finally, our study population was derived from a tertiary care specialty neurogastroenterology clinic, and thus, our results may differ from those derived from a general GI population.

Our study also has a number of strengths. We were able to readily recruit a large cohort of diverse patients to a health coach–supported dCBI. In doing so, we were able to capture clinically relevant, real-world, quantitative data on mental health outcomes in the process of ongoing clinical care. Our patient population was similar to other academic centers with a referral population of patients with more severe FGIDs. We were able to offer cognitive behavioral and mindfulness techniques to a wide patient population. Our intervention was scalable and easy to implement. The techniques used in RxWell were evidence-based and safe, and the app was available for the patients to practice techniques on their own time. The addition of the risk escalation protocol allowed our app to be an adjunct to patients with severe anxiety and depression and as a method to capture high-risk patients with anxiety or depression who need additional services. By embedding the app within the electronic medical record, clinicians could easily order this dCBI and track their patient's progress. Finally, access to health coaches provided an additional source of instruction and encouragement for patients to engage with the app.

A coached dCBI can be feasibly and effectively incorporated into routine medical care for patients with DGBIs and is associated with improvements in anxiety and depressive symptom severity. Our preliminary observations also suggest that our intervention was associated with reduced ED utilization. These initial findings strongly argue for the further development of coached dCBI applications for broad application in gastroenterology care. Future randomized controlled studies are needed to determine the magnitude of the impact of coached dCBIs on anxiety, depression, functional GI symptoms, and health-care utilization.

CONFLICTS OF INTEREST

Guarantor of the article: David J. Levinthal, MD, PhD.
Specific author contributions: E.S.: planned the study, conducted statistical analyses, interpreted data, and drafted the manuscript. A.T. planned the study, conducted statistical analyses, interpreted data, and drafted the manuscript. A.N.P. conducted the study and drafted the manuscript. M.A.M. conducted the study. C.D.S. planned the study and drafted the manuscript. V.S. planned the study and drafted the manuscript. M.L.W. conducted statistical analysis. M.J.K. planned the study and drafted the manuscript. D.J.L. planned the study, interpreted data, and drafted the manuscript.
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Potential competing interests: D.J.L. is a consultant for Takeda Pharmaceuticals and Alexza Pharmaceuticals. None of the other authors have any conflicts of interest to declare.

Study Highlights

WHAT IS KNOWN

- ✓ Functional gastrointestinal disorders (FGIDs) are common disorders with high prevalence of comorbid anxiety and depression.
- ✓ Cognitive behavioral interventions (CBIs) reduce anxiety and depression and also improve gastrointestinal symptoms in those with FGIDs.

WHAT IS NEW HERE

- ✓ Patients with FGIDs are willing to use a coached, digital CBI tool recommended by their medical provider in the course of real-world, clinical care.
- ✓ Patient use of the digital CBI was associated with statistically and clinically significant improvements in anxiety and depression lasting up to 4 months.

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