An Office-Based, Point-of-Care Test Predicts Treatment Outcomes With Community-Based Pelvic Floor Physical Therapy in Patients With Chronic Constipation

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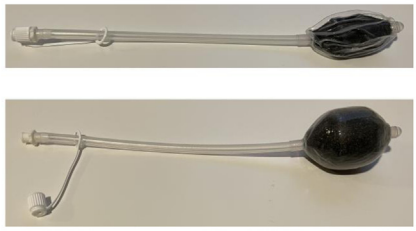
RED (Investigational, Point-of-Care Device to Predict Outcomes with Community-Based Pelvic Floor Physical Therapy to Treat Constipation)

1) Device inserted into rectum
2) Cap removed to inflate device
3) Patient attempts to defecate balloon in left lateral position



Expulsion time	Likelihood of response
<5 seconds or >120 seconds	48.9%
5-120 seconds	8.9%

Clinical Gastroenterology and Hepatology

BACKGROUND & AIMS: Rectal evacuation disorders are common among constipated patients. We aimed to evaluate the accuracy of an investigational point-of-care test (rectal expulsion device [RED]) to predict outcomes with community-based pelvic floor physical therapy.

METHODS: We enrolled patients meeting Rome IV criteria for functional constipation failing fiber/laxatives for more than 2 weeks. RED was inserted and self-inflated, and then time-to-expel was measured in a left lateral position. All patients underwent empiric community-based pelvic floor physical therapy in routine care with outcomes measured at 12 weeks. The primary end point was global clinical response (Patient Assessment of Constipation Symptoms score reduction, >0.75 vs baseline). Secondary end points included improvement in health-related quality-of-life (Patient Assessment of Constipation Quality of Life score reduction, >1.0) and complete spontaneous bowel movement frequency (Food and Drug Administration complete spontaneous bowel movement responder definition).

RESULTS: Thirty-nine patients enrolled in a feasibility phase to develop the use-case protocol. Sixty patients enrolled in a blinded validation phase; 52 patients (mean, 46.9 y; 94.2% women) were

Abbreviations used in this paper: CSBM, complete spontaneous bowel movement; FC, functional constipation; gAUC, generalized area under the curve; HRQoL, health-related quality-of-life; PAC-SYM, Patient Assessment of Constipation Symptoms instrument; RED, rectal expulsion device.

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included in the intention-to-treat analysis. In the left lateral position, RED predicted global clinical response (generalized area under the curve [gAUC], 0.67; 95% CI, 0.58–0.76]), health-related quality-of-life response (gAUC, 0.67; 95% CI, 0.58–0.77; $P < .001$), and complete spontaneous bowel movement response (gAUC, 0.63; 95% CI, 0.57–0.71; $P < .001$). As a screening test, a normal RED effectively rules out evacuation disorders (expected clinical response, 8.9%; $P = .042$). Abnormal RED in the left lateral position (defined as expulsion within 5 seconds or >120 seconds) predicted 48.9% clinical response to physical therapy. A seated maneuver enhanced the likelihood of clinical response (71.1% response with seated RED retained >13 seconds) but likely is unnecessary in most settings.

CONCLUSIONS: **RED offers an opportunity to disrupt the paradigm by offering a personalized approach to managing chronic constipation in the community (Clinicaltrials.gov: NCT04159350).**

Keywords: Pelvic Rehabilitation; Pelvic Floor Dysfunction; Dyssynergic Defecation; Diagnostic Test Accuracy; Predictive Accuracy; Medical Technology; Innovation; Chronic Idiopathic Constipation; Rural.

See editorial on page 902.

Chronic constipation affects 10% to 20% of the population and can impact quality of life to a similar degree as congestive heart failure or rheumatoid arthritis.[1] Notably, 700,000 individuals present to the emergency department for constipation each year in the United States, and $10 billion is spent annually on laxative therapies.[2,3] For symptomatic chronic constipation refractory to fiber or laxative therapy, clinical practice guidelines recommend physiological testing to identify abnormalities in anorectal function as the next step.[4–7] Abnormal anorectal function testing identifies patients with rectal evacuation disorders. Identifying patients with an evacuation disorder is essential because therapy is no longer focused on laxative therapies. For example, evacuation disorders preferentially respond to pelvic rehabilitation therapy that includes biofeedback training and typically is rendered by pelvic floor physical therapists in the community (subsequently called *pelvic floor physical therapy*).[8,9] On the other hand, constipated patients without evacuation disorders are less likely to respond to pelvic floor physical therapy.[10] Anorectal function testing is not readily available to community gastroenterologists outside of specialized centers, often resulting in many constipated patients repeatedly being exposed to unnecessary diagnostic procedures and trials of ineffective and costly laxative therapies.[11]

To enable standardized, accessible, chronic constipation testing for community gastroenterologists, we developed an easy-to-use, office-based, point-of-care rectal expulsion device (RED) (Figure 1).[12] RED was designed to prioritize usability so that community-based gastroenterologists have a simple tool to predict clinical outcomes for their patients with available resources.[13] By incorporating RED into a general gastroenterologist's outpatient visit, chronically constipated individuals with an evacuation disorder can be identified quickly and triaged directly to pelvic floor physical therapy. Thus, RED offers the possibility of disrupting the current treatment paradigm by enabling an initial biomarker-based strategy to engage patients with personalized, guideline-based care in community settings. Before such a process of care can be realized, there is a critical need for prospective data to evaluate whether RED can meaningfully change management in a general, community care setting.

We report the findings of a prospective, pragmatic clinical trial that evaluated the clinical utility of RED among adults with chronic constipation referred to a regional gastroenterology practice after failing a usual and empiric trial of soluble fiber supplementation and/or osmotic laxatives. These patients underwent RED followed by empiric, high-quality pelvic rehabilitation therapy focused on improving bowel function provided by community-based physical therapists specializing in pelvic floor rehabilitation across northern New England. The objective of our study was to test the hypothesis that RED could predict the likelihood of clinical improvement with pelvic floor physical therapy.

Methods

Study Design

Our prospective cohort study (ClinicalTrials.gov: NCT04159350) was conducted in accordance with regulatory requirements, the International Conference on Harmonization, Good Clinical Practice, and the ethical principles of the Declaration of Helsinki. Our nonrandomized study and its reporting adhered to the Strengthening the Reporting of Observational Studies in Epidemiology statement. This study was reviewed by the Dartmouth-Hitchcock Institutional Review Board (approval #02000107). All authors had access to the study data and reviewed and approved the final manuscript. A separate report will be published to detail outcomes based on traditional anorectal function tests.

We recruited adult patients (age, 18–80 y) referred to general gastroenterology clinics at Dartmouth-Hitchcock Health between June and December 2020 (feasibility phase) and January and June 2021 (validation phase)

meeting Rome IV criteria for functional constipation.[14] Our enrollment criteria (Supplement) were designed to identify typical populations referred to community practice rather than patients who typically are referred to quaternary settings. As such, eligible patients had failed to improve with a usual trial of daily soluble fiber and/or osmotic laxative therapy and were otherwise relatively diagnostic- and treatment-naïve. They agreed to undergo outpatient anorectal function testing at the Dartmouth-Hitchcock Gastrointestinal Motility Laboratory to provide an objective assessment of anorectal function followed by a coordinated referral for empiric pelvic floor physical therapy that is standard in our practice as part of routine clinical care (consistent with patient preferences for effective behavioral treatments in light of increasing prescription drug costs).[15] All patients received empiric soluble fiber supplementation and/or laxatives for at least 2 weeks (if not already taken) to confirm failure of empiric treatment before scheduling their anorectal function testing.

Informed consent subsequently was obtained at the anorectal function testing appointment, consistent with legal/regulatory requirements. Patients meeting all inclusion criteria and none of our exclusion criteria underwent RED before undergoing anorectal function testing as part of routine care as an objective baseline assessment of pelvic floor defecatory mechanics and to avoid the potential for laboratory-based anorectal function tests to influence the results of RED. All patients were given a clinical educational handout containing information on maintenance of daily soluble fiber supplementation (if already taken), basic advice on toileting habits, and a rescue regimen consisting of secretory laxatives and suppositories/enemas. Patients began physical therapy within 2 weeks of the baseline anorectal function testing. Patients agreed to maintain stable dietary intake and their stable soluble fiber supplement or osmotic laxative regimen and to limit use of rescue stimulant laxatives or magnesium supplementation to no more than 2 d/wk. Patient-reported outcomes were assessed at baseline and at 12 weeks (post-treatment) after the first visit with physical therapy. Data were managed using REDCap (Vanderbilt University, Nashville, TN). We conducted our study in 2 phases: an initial unblinded feasibility phase designed to facilitate the development and testing of a standard, scripted protocol for the use of RED, followed by a blinded validation phase to evaluate the predictive accuracy of RED. Recognizing the intrinsic nature of this work in academic-based innovation and related intellectual property around RED co-held with the Regents of The University of Michigan, during the validation phase, motility nurses performed RED, and the results were blinded to the patient, investigators, and physical therapists; patient-reported outcome assessments remained blinded during the study and housed separately. Only the

What You Need to Know

Background

Ninety-eight percent of chronically constipated patients never undergo pelvic floor physical therapy despite rectal evacuation disorders being common causes of chronic constipation. This is largely owing to limited access to diagnostics and perceived limitations on access to pelvic floor physical therapists.

Findings

In a prospective study of patients with chronic constipation, we showed that a rectal expulsion device called RED appears capable of predicting global symptom response, improvement in bowel movement frequency, and improvement in health-related quality-of-life with pelvic floor physical therapy delivered in the community.

Implications for patient care

RED is an investigational tool that offers an opportunity to disrupt the management paradigm by offering an initial biomarker-based approach to managing chronic constipation.

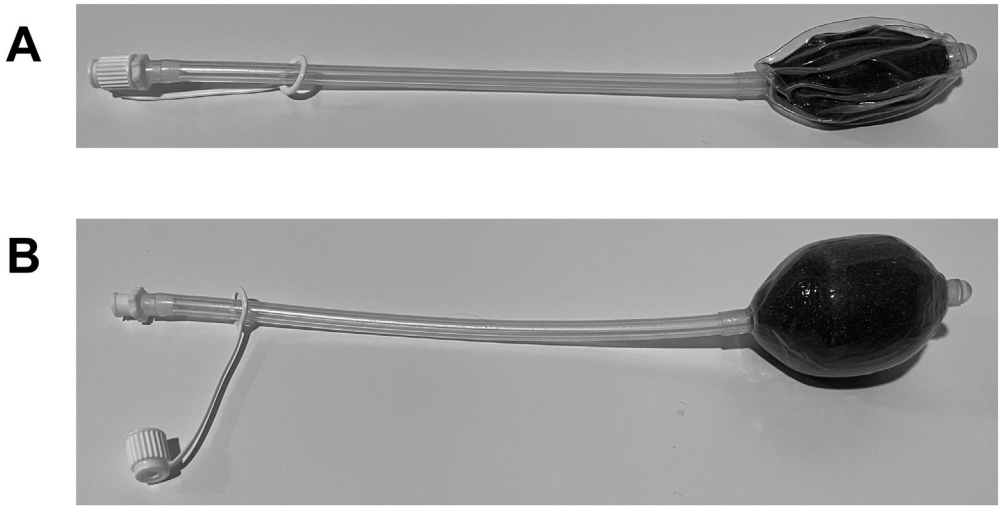

Figure 1. The rectal expulsion device (RED) is inserted in a (*A*) compressed state and subsequently (*B*) self-inflated in the rectum by removing a cap on the end of the device.

biostatistician (P.M.-C.) had access to the entire data set before the completion of statistical analysis. The motility nurses performing RED also were blinded to the results of the feasibility phase and any associated diagnostic interpretation or patient outcomes.

All authors had access to the study data and reviewed and approved the final manuscript. This study was funded by the AGA Research Foundation and University of Michigan Fast Forward Medical Innovation, which had no role in the direct conduct of this study.

Protocol for Use of Rectal Expulsion Device

During the initial visit, the patient was positioned in the left lateral decubitus position. After a digital rectal examination, RED (In2Being, LLC, Saline, MI) was lubricated and inserted into the rectum by the primary investigator (E.D.S.) during the feasibility phase, and by the motility laboratory nurse (E.A.P. or C.G.) during the validation phase. The internal rectal portion of the device subsequently was inflated by removing a cap on the end of the extracorporeal portion of the device. After insertion and inflation, the device was pulled back slightly and rotated to ensure that the insufflated rectal portion rested freely in the rectum within approximately 1 cm of the proximal border of the anal canal. The operator instructed the patient to defecate the device in the left lateral position and ring a bell if the device was expelled successfully. The patient then attempted expulsion privately with the operator outside of the room. If the RED was not expelled within 2 minutes, the patient moved to a private toilet to attempt device expulsion in a seated position. If RED still was not expelled within 2 minutes, the device was safely removed.[16] The time to expel RED was recorded in the left lateral and seated positions.

Protocol for Pelvic Floor Physical Therapy

Our protocol was designed to capture the essence of evidence-based treatment paradigms in tertiary centers in a manner that can be rapidly adopted across community-based settings (Supplement). Our regional network of pelvic floor physical therapists anchored therapy on biofeedback training (simplified and adapted from the American Neurogastroenterology and Motility Society/European Society for Neurogastroenterology and Motility treatment protocol) incorporated into a broader evaluation and management plan for evacuation disorders.[17] We ensured reliable adoption of this standard protocol over a series of quarterly meetings across the Northern New England Pelvic Floor Collaborative and monitored adherence during the feasibility phase of this study. Patients were encouraged to attend at least 3 biweekly visits with the goal of promoting self-practice of pelvic floor exercises at home.

Outcomes

The primary outcome was the percentage of patients who met the threshold for clinically meaningful improvement in global symptom experience of patients with chronic constipation, as measured by the validated Patient Assessment of Constipation Symptoms instrument (PAC-SYM) (score range, 0–4). The response was defined according to a minimal clinically important difference in global symptom severity corresponding to a reduction in PAC-SYM score of 0.75 or greater at 12 weeks vs baseline.[18,19] Our secondary outcomes were the percentage of patients reporting meaningful improvement in disease-specific, health-related quality of life (HRQoL) (PAC Quality of Life; score range, 0–4; minimal clinically important responder threshold = reduction in score $\geq$1.0 at 12 weeks compared with baseline) and the percentage of patients meeting the responder definition at 12 weeks on the Food and Drug Administration end point used in chronic idiopathic constipation drug trials that focuses on bowel movement frequency and form (among the subgroup of patients reporting fewer than 3 weekly complete spontaneous bowel movements [CSBMs] at baseline).[20] Per Food and Drug Administration guidance, a final question to assess for inadvertent patient unblinding toward their perceived interpretation of RED was included in the 12-week assessment.[21] Safety was assessed according to the nature, severity, and incidence of adverse events either spontaneously reported by the patient or by the nurse/investigator.

Statistical Plan

Our sample size of 60 patients was informed by constructing a 2 $\times$ 2 cell (responder status vs RED result) under assumptions of 80% power and a 5% type 2 error rate with a 10% expected study withdrawal rate using a chi-square test informed by our feasibility phase, based on assumptions of 60% likelihood of an abnormal RED and a 25% increase in clinical response with abnormal RED.

In the blinded validation phase, patients were stratified into 2 analysis groups based on the outcome of RED performed at the baseline assessment (normal RED vs abnormal RED). Therefore, the assignment to and size of analysis groups changed dynamically on varying the cut-off value used to define an abnormal RED result.

Our analysis was based on predictive accuracy with regard to outcomes with community-based pelvic floor physical therapy. The generalized area under the curve (gAUC) was calculated to assess trade-offs between sensitivity and specificity to inform predictive accuracy for our primary responder analysis.[22] The gAUC is capable of evaluating simultaneous interpretation cut-off values in different directions and is not reliant on preconceived assumptions on appropriate interpretation (such as that prolonged time to expel might be the only

useful indicator of treatment outcome). The 95% bootstrap-based CIs were calculated. We applied the Youden index criterion (the point maximizing sensitivity+specificity) in our data analysis to optimize the predictive accuracy of RED in choosing appropriate cut-off values for test interpretation in a typical referral population and use-case setting.[23] A chi-square test was performed to evaluate differences in the observed frequency of response rates between patients with normal and abnormal RED at optimal cut-off values. Exploratory statistical analyses also were performed using a chi-square test for dichotomous measures.

Results

Study Participants and Baseline Demographics

Sixty patients were enrolled (Table 1 lists patient characteristics). Enrolled patients were predominantly women, similar to the population characteristics in national cross-sectional surveys and drug trials for chronic constipation. A total of 21.7% (13 of 60 patients) reported having at least 3 weekly CSBMs at baseline despite meeting Rome IV functional constipation criteria. All 60 patients were included in the safety analysis.

Our intention-to-treat population was the primary population on which we evaluated predictive accuracy. This population included 52 patients who underwent RED and attended at least 1 visit with physical therapy without loss to follow-up evaluation (88.1% compliance; median of 3.0 physical therapy appointments attended; range, 1–7 appointments). Referrals to physical therapy were balanced among the regional consortium partners based on patient convenience, recognizing the wide geographic catchment area across northern New England.

Predictive Accuracy

The primary outcome was to evaluate clinical response with community-based pelvic floor physical therapy as defined by a minimal clinically important difference in global symptom severity corresponding to a reduction in PAC-SYM score of 0.75 or greater at 12 weeks vs baseline informed by achieving statistical significance on gAUC. This outcome was achieved in both the left lateral (gAUC, 0.67; 95% CI, 0.58–0.76; $P < .001$) and seated position (AUC, 0.69; 95% CI, 0.54–0.83; $P = .009$) (Figure 2). The left lateral position also predicted significant improvements in secondary outcomes of CSBM response among the subgroup of patients with fewer than 3 weekly CSBMs at baseline (gAUC, 0.63; 95% CI, 0.57–0.71; $P < .001$) and improvement in HRQoL response in the left lateral position (gAUC, 0.67; 95% CI, 0.58–0.77; $P < .001$). In the seated position, there were

Table 1. Baseline Demographics

	Intention-to-treat population (N = 52)	Safety population (N = 60)
Age, *y*, average ± SD (range)	46.9 ± 18.2 (18–79)	46.4 ± 17.6 (18–79)
Sex (% women)	49 (94.2)	56 (93.3)
Average CSBM per week	1.46 ± 1.97	1.38 ± 1.89
Percentage of patients with <3 CSBM/wk	40 (76.9%)	47 (78.3%)
Average SBM/wk	3.42 ± 4.40	3.20 ± 4.20
Average stool consistency by Bristol Stool Scale	2.60 ± 1.61	2.58 ± 1.67
Average straining severity score, Likert 1–5[a]	3.38 ± 1.22	3.47 ± 1.18
Average abdominal discomfort score, Likert 1–5[a]	3.15 ± 1.18	3.22 ± 1.19
Average bloating score, Likert 1–5[a]	3.19 ± 1.16	3.38 ± 1.21
Average constipation severity score, Likert 1–5[a]	3.53 ± 1.09	3.60 ± 1.09
Baseline anorectal manometry testing[a]		
Average resting pressure, *mm Hg*	64.6 ± 21.1	64.9 ± 20.9
Maximum squeeze pressure, *mm Hg*	165.9 ± 76.0	163.7 ± 71.9
Dyssynergia pattern by London consensus		
Paradoxic anal contraction or incomplete relaxation	28 (53.8% of patients)	32 (53.3% of patients)
Normal pattern	24 (46.2% of patients)	28 (46.7% of patients)
Average balloon expulsion time, *s*	60.02 ± 49.9	59.68 ± 49.9

NOTE. Symptom scores were evaluated on Likert scale ranging from 1 to 5.
CSBM, complete spontaneous bowel movement; SBM, spontaneous bowel movement; SD, standard deviation.
[a]Anorectal function testing was performed according to the standardized London consensus protocol. Anorectal manometry was performed using 3-D high-definition anal manometry (Medtronic PLC, Minneapolis, MI). Balloon expulsion testing was performed using part# SR1B (Mui Scientific, Mississauga, Ontario, Canada).

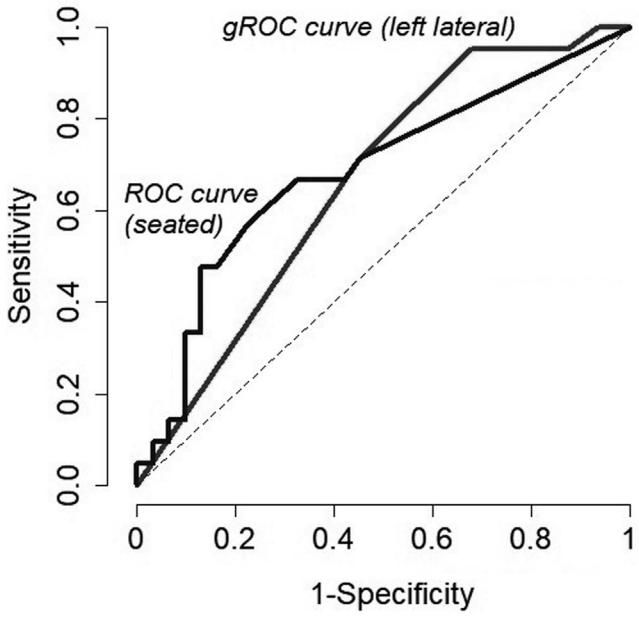

Figure 2. Accuracy of the rectal expulsion device (RED) to predict 12-week clinical response outcomes with pelvic floor physical therapy. Data are presented on a generalized receiver-operator characteristic curve (left lateral position) and the receiver-operator characteristic curve (seated position). Clinically meaningful response is defined by achieving a score reduction of at least 0.75 compared with baseline on the Patients' Assessment of Constipation Symptoms global symptom measure. ROC, receiver operating characteristic; gROC, generalized receiver operating characteristic.

nonsignificant trends toward a benefit in CSBM response (AUC, 0.63; 95% CI, 0.43–0.81; $P = .095$) and HRQoL response (AUC, 0.65; 95% CI, 0.46–0.81; $P = .058$).

Optimal Thresholds to Define an Abnormal Test and Expected Patient Outcomes

In the left lateral position, the optimal threshold to predict global symptom improvement with pelvic floor physical therapy was to classify abnormal device expulsion as occurring either within 5 seconds (suggesting a weak pelvic floor) or in longer than 120 seconds (suggesting dyssynergic defecation). This cut-off value had a sensitivity of 95.2% and a specificity of 32.3% to predict clinical response to pelvic floor physical therapy (the P value associated with the relationship between these variables was $P = .042$) (Table 2). In a typical referral population of patients with chronic constipation meeting Rome IV functional constipation criteria and failing empiric fiber/laxatives, 78.8% of patients undergoing RED would be expected to test abnormal. A total of 48.8% of patients with RED classified as abnormal would be expected to achieve clinically meaningful improvement in global constipation symptoms with pelvic floor physical therapy. In conceptualizing RED as a screening test, a normal RED is an important result that identifies patients for whom pelvic floor physical therapy is unlikely to benefit (expected treatment response of 8.9%) (Figure 3).

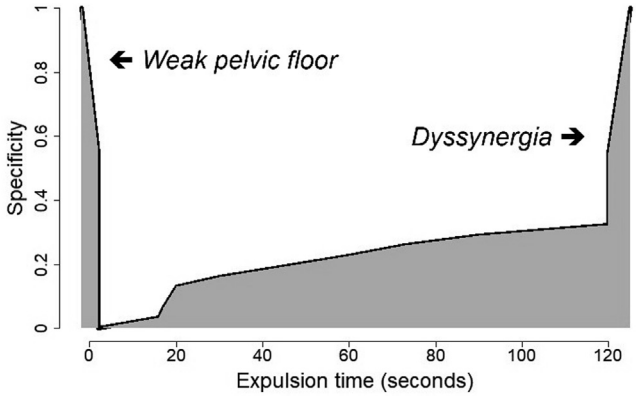

Figure 3. The predicted clinical response to pelvic floor physical therapy using the rectal expulsion device (RED) in the left lateral position is bimodal. Expelling RED within 5 seconds or more than 120 seconds predicts a higher likelihood of response to physical therapy.

By adding a subsequent seated maneuver for patients who failed to expel RED within 2 minutes in a left lateral position, the optimal cut-off value to define abnormal was longer than 13 seconds in a seated position. This maneuver enhanced the predicted response to pelvic floor physical therapy (71.4% with abnormal seated RED vs 28.9% expected response with a normal RED at this cut-off time). At this cut-off time, 26.9% of patients would test abnormal in a typical referral population.

Safety

No serious adverse events occurred during our study. One patient experienced transient anal pain during the placement of RED, which was aborted because of a suspected anal fissure. This patient then experienced similar transient anal pain during anorectal manometry and balloon expulsion but was able to complete pelvic floor physical therapy.

Discussion

We performed a prospective pragmatic clinical trial to evaluate the predictive accuracy of an investigational, easy-to-use, office-based, point-of-care, anorectal function test to identify patients with chronic constipation who are more likely to improve with pelvic floor physical therapy in a real-world regional clinical practice setting. Our study was designed primarily to evaluate the most pertinent question in practice: Does the test inform management?

In our trial, we showed that RED can be safely and quickly performed in the left lateral position immediately after a rectal examination. As a simple screening test for patients who fail a typical trial of soluble fiber supplementation or osmotic laxatives taken daily, RED is able to reliably identify patients for whom pelvic floor physical

Table 2. Accuracy of Predicted Clinical Response to Pelvic Floor Physical Therapy and Expected Clinical Response Rates at Optimal Cut-Off Values Using RED at Baseline in Left Lateral and Seated Positions

Definition of an abnormal RED	Patients who test positive based on the chosen definition	Sensitivity	Specificity	Likelihood of clinical response among patients with an abnormal test (PPV)	Likelihood of clinical response among patients with a normal test (1-NPV)	*P* value
Left lateral position Expulsion time <5 s or >120 s (ie, weak pelvic floor or dyssynergia)	78.8% likelihood of testing positive (41/52 patients)	95.2% sensitivity (20/21 patients)	32.2% specificity (10/31 patients)	48.8% expected likelihood of response (20/41 patients)	8.9% expected likelihood of response (1/11 patients)	.042
Seated position Expulsion time >13 s	26.9% likelihood of testing positive (14/52 patients)	47.6% sensitivity (10/21 patients)	87.1% specificity (27/31 patients)	71.4% expected likelihood of response (10/14 patients)	28.9% expected likelihood of response (11/38 patients)	.014

NPV, negative predictive value; PPV, positive predictive value; RED, rectal expulsion device.

therapy is unlikely to provide substantial benefit (ie, patients who might be more likely to benefit from intensifying medical therapy).[4] Patients with an abnormal RED in the left lateral position can be referred directly to pelvic floor physical therapy. Failure of empiric physical therapy could indicate a more complex evacuation disorder, and formal anorectal function testing or referral to multidisciplinary clinical programs that treat benign anorectal disorders can be considered for these patients.[5] Although adding a subsequent seated maneuver identifies patients with an enhanced likelihood of clinical response, this extra maneuver is likely unnecessary in most cases given increasing patient preferences toward empiric behavioral interventions (considering the out-of-pocket costs with repeated courses of laxatives).[15]

RED is an innovative, disposable, single-use device that was developed to meet the needs of community practitioners by focusing on simplicity, cost, and integration into routine workflow.[12] Indeed, the optimal cut-off time of the resulting design for RED was only 13 seconds in a seated position, compared with the traditional 60-second (or longer) cut-off time for balloon expulsion test, recognizing that: RED is based on the compressibility of stool rather than water, and straining for 59 seconds to initiate defecation of stool would not likely be considered normal to most people. Furthermore, RED is designed to be performed in the left lateral position and does not require a commode or specialized equipment that likely would impede usual clinical workflow or incur significant capital investment.[24]

Similarly, our trial end points were designed to answer the most salient questions from community-based gastroenterologists. As the recent London consensus recognizes, most clinical trials on anorectal function tests are designed with the needs of anorectal physiology experts and their patients in mind (ie, an AUC of >0.9 on diagnostic accuracy to detect dyssynergia was not an acceptable goal).[25] As such, the gAUC/AUC on predictive accuracy within 0.6 to 0.7 was anticipated and should be viewed as consistent with our design priorities: RED shows very high sensitivity (>95%) to broadly detect evacuation disorders as a simple screening tool at the expense of specificity.[25] Low specificity is inherent to our broadly defining a reference standard on clinical response, in contrast to the mere presence of dyssynergia. The broad differential of evacuation disorders includes functional evacuation disorders (higher expected response) and structural disorders (lower expected response).[5,14] Recognizing variability in expected outcomes across the differential diagnosis for evacuation disorders, gastroenterology and surgical specialty society guidelines uniformly advise an initial trial of pelvic floor physical therapy for all affected patients.[4–7]

There are several limitations to consider in the context of conducting behavioral intervention trials vs drug trials. First, our study shows that Rome IV criteria encompass more than simply bowel movement frequency and form.[14] In our study, 21.7% of patients meeting Rome IV criteria for functional constipation already met the CSBM responder definition applicable to a chronic idiopathic constipation drug trial at study enrollment. Second, although RED and patient-reported outcomes were blinded, anorectal manometry and balloon expulsion test results were not. However, anorectal function tests do not substantially impact the decision to try empiric pelvic floor physical therapy in our practice.[26] Understanding the limitations in blinding patients toward expelling a rectal device, we found no significant influence on outcomes with pelvic floor physical therapy by patients' preconceived notions on

the interpretation of their anorectal function tests (including RED) using a standard unblinding question in the final assessment ($P = .722$).[21]

In summary, RED is an office-based investigational test that appears safe and simple to perform during a routine visit and appears promising as an initial point-of-care biomarker to triage patients with chronic constipation to community-based pelvic floor physical therapy from any gastroenterologist's office. It is hoped that RED will disrupt the current empiric treatment paradigm for patients with chronic constipation by providing community gastroenterologists with a tool that allows them to choose the right treatment for the right patient.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2022.03.022.

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Conflicts of interest
These authors disclose the following: William D. Chey has consulted for AbbVie, Allakos, Alnylam, Arena, Biomerica, Gemelli, Ironwood, Isothrive, QOL Medical, Nestle, Phathom, Progenity, Redhill, Salix, Urovant, and Vibrant, has received research grants from Commonwealth Diagnostics International, QOL Medical, and Salix, and has stock options from GI on Demand, Isothrive, and Modify Health; Jason R. Baker has consulted for Diversatek Healthcare, Medtronic, GI Supply, and Coloplast; Eric D. Shah has consulted for GI Supply/Laborie, Mahana, and Bausch Health; and William D. Chey, Eric D. Shah, Jason Baker, Adrienne Harris, and the Regents of the University of Michigan are holders of patent PCT/US2019/050155, related to the rectal expulsion device. The remaining authors disclose no conflicts.

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Data Transparency Statement
Individual de-identified participant data corresponding to primary and secondary responder analyses will be shared upon reasonable request to the corresponding author and according to relevant legal requirements and institutional policies.