Cognitive Behavior Therapy Tailored to Anxiety Symptoms Improves Pediatric Functional Abdominal Pain Outcomes: A Randomized Clinical Trial

Natoshia R. Cunningham, PhD[1], Anne Kalomiris, MA[2], James Peugh, PhD[2,3], Michael Farrell, MD[3,4], Scott Pentiuk, MD[3,4], Daniel Mallon, MD[3,4], Christine Le, BA[2], Erin Moorman, MS[2], Lauren Fussner, PhD[2], Richa Aggarwal Dutta, PhD[2], and Susmita Kashikar-Zuck, PhD[2,3]

Objectives To evaluate the feasibility of a stepped care model, and establish the effect of a tailored cognitive behavioral therapy, the Aim to Decrease Anxiety and Pain Treatment (ADAPT), compared with standard medical treatment as usual on pain-related outcomes and anxiety.

Study design Eligible patients between the ages of 9 and 14 years with functional abdominal pain disorders (n = 139) received enhanced usual care during their medical visit to a gastroenterologist. Those that failed to respond to enhanced usual care were randomized to receive either a tailored cognitive behavioral therapy (ADAPT) plus medical treatment as usual, or medical treatment as usual only. ADAPT dose (4 sessions of pain management or 6 sessions of pain and anxiety management) was based on presence of clinically significant anxiety. Outcomes included feasibility, based on recruitment and retention rates. Response to ADAPT plus medical treatment as usual vs medical treatment as usual on pain-related outcomes and anxiety measures was also investigated using a structural equation modeling equivalent of a MANCOVA. Anxiety levels and ADAPT dose as moderators of treatment effects were also explored.

Results Based on recruitment and retention rates, stepped care was feasible. Enhanced usual care was effective for only 8% of youth. Participants randomized to ADAPT plus medical treatment as usual showed significantly greater improvements in pain-related disability, but not pain levels, and greater improvements in anxiety symptoms compared with those randomized to medical treatment as usual only. Anxiety and ADAPT treatment dose did not moderate the effect of treatment on disability nor pain.

Conclusions Tailoring care based on patient need may be optimal for maximizing the use of limited psychotherapeutic resources while enhancing care. *(J Pediatr 2021;230:62-70)*.

Trial registration ClinicalTrials.gov: NCT03134950.

Pediatric functional abdominal pain disorders (FAPD) are common,[1,2] debilitating,[3-5] and can persist for years.[6,7] Youth with FAPD can experience psychological problems[8-11] and social and academic difficulties.[4,5] Anxiety corresponds to higher pain and disability[10,12,13] over the long term.[14,15] Early psychological intervention could improve patient outcomes[16]; however, it is infrequently offered during standard medical care.

Stepped care may be a feasible method for receiving psychological treatment during routine care. Stepped care approaches initially provide less intensive treatments to the majority of patients, which are brief and fully embedded within the medical visit.[17,18] For patients that do not respond, care can be "stepped up" (eg, more intensive intervention outside of a medical visit with a trained provider). Stepped care has been shown to be feasible[18]; however, it has not yet been tested in pediatric FAPD.

For those requiring stepped-up care, cognitive behavior therapy (CBT) is effective for treating pediatric chronic pain,[19] including FAPD.[20-22] CBT includes cognitive and behavioral approaches to improve pain-related functioning.[19] However, a substantial proportion (~40%) of youth with FAPD fail to respond.[20] This may be because anxiety attenuates the effect of pain-focused CBT.[23] Bolstering pain-focused CBT with anxiety management techniques for those with anxiety may enhance treatment outcomes. Our research team has initiated anxiety screening

ADAPT	Aim to Decrease Anxiety and Pain Treatment
ADIS	Anxiety Disorder Interview Schedule
CBT	Cognitive behavior therapy
FAPD	Functional abdominal pain disorders
FDI	Functional Disability Inventory
GI	Gastrointestinal
SCARED	Screen for Child Anxiety Related Disorders
VAS	Visual Analog Scale

From the [1]Department of Family Medicine, Michigan State University, Grand Rapids, MI; [2]Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, [3]Department of Pediatrics, University of Cincinnati College of Medicine and [4]Division of Gastroenterology, Hepatology, and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

All phases of this study were supported by the Sharon S. Keller American Pain Society grant and the Cincinnati Children's Hospital Place Outcomes Award (both awarded to N.C.). In addition, the PI (N.C.) is currently supported by an NIH/NCCIH K23 award, AT009458, and a past NIH/NICHD F32 award, HD078049, that enabled the development of the ADAPT intervention. The other authors declare no conflicts of interest.

Portions of this study were presented at the American Pain Society conference, April 3-6, 2019, Milwaukee, Wisconsin.

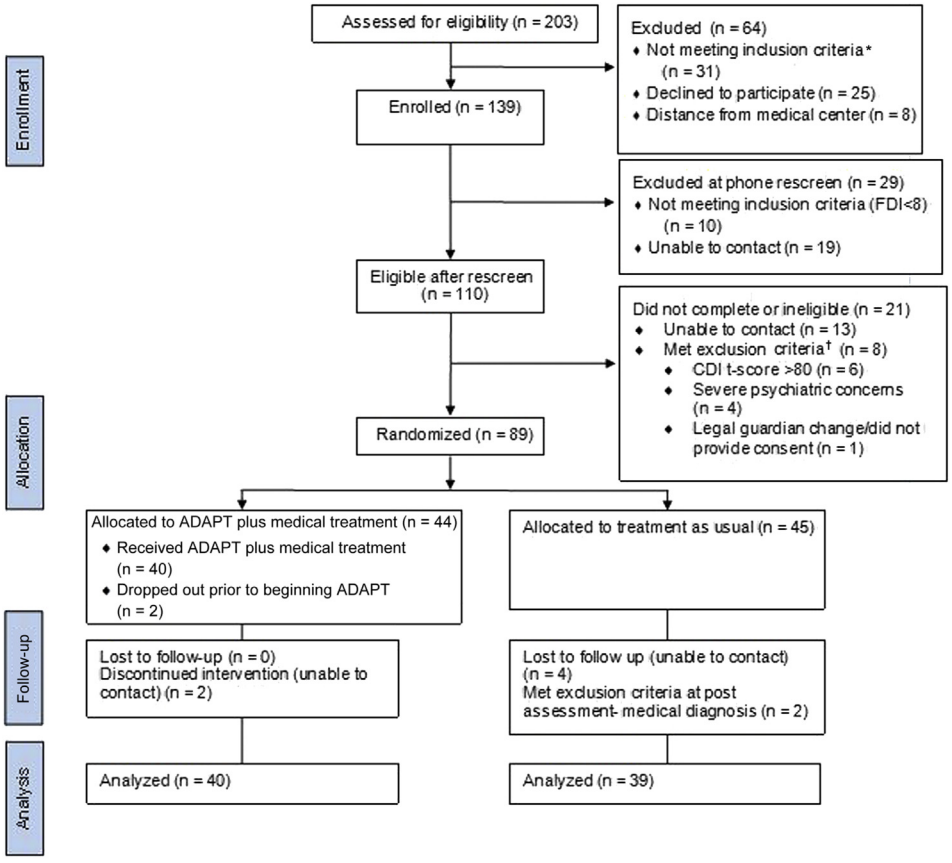
https://doi.org/10.1016/j.jpeds.2020.10.060

and enhanced usual care processes into gastroenterology clinics of a large children's hospital.[12] The team also developed and pilot tested the Aim to Decrease Anxiety and Pain Treatment (ADAPT),[21] a tailored CBT to target pain and anxiety in youth with FAPD. In the present study, those who failed to respond to enhanced care were eligible to receive ADAPT plus medical treatment as usual.

We examined feasibility (recruitment and retention rates) of stepped care, and response to ADAPT plus medical treatment as usual. We predicted that those who completed ADAPT plus medical treatment as usual would show greater reductions in functional disability, pain intensity, and anxiety than the medical treatment as usual group.

Methods

Patients were recruited from outpatient pediatric gastroenterology clinics of a large academic medical center (**Figure 1**). Consent/assent from the primary caregiver and child were obtained for this institutional review board-approved study. Children ages 9- to 14-years-old with FAPD diagnosed by a pediatric gastroenterologist using Rome IV guidelines[24] were eligible. To qualify, participants also had to show evidence of more than minimal disability (defined as a score of >7 on the Functional Disability Inventory - Child Version [FDI]). This cut-off was previously established as a criterion for enrollment in prior pediatric pain behavioral trials.[25] After study enrollment, gastroenterologists continued to offer medical treatment as usual to all participants, which could include a referral for CBT. Given the wait for CBT generally exceeded the anticipated study period, this was not a barrier to participating, and study staff ensured clinical CBT and ADAPT did not overlap. The study was registered on ClinicalTrials.gov (NCT03134950).



Note.
*Inclusion criteria: 1) Between 9-14 years of age, 2) Diagnosed with FAPD by a gastroenterologist or primary care provider, and 3) More than minimal disability as evidenced by a total score of ≥7 on the FDI
†Participants meeting inclusion criteria were deemed ineligible due to mental health concerns if they demonstrated severe depressive symptoms or psychiatric concerns. Three of the 8 participants excluded demonstrated evidence of both of these mental health exclusionary criteria. We note 4 participants ("severe psychiatric concerns") were deemed ineligible after baseline the psychological assessment and prior to randomization.

Figure 1. Consort study diagram. Two hundred three children were approached, 139 were enrolled, and 110 remained eligible for stepped-up care after rescreening. Of those, 89 were randomized to ADAPT plus medical treatment as usual (n = 40 completing) or medical treatment as usual (medical treatment as usual; n = 39 completing).

Procedures

This study evaluated the feasibility of a stepped care approach. All participants received step 1. Participants that did not demonstrate a clinical response then received step 2.

Step 1: Screening and Enhanced Usual Care. Patients were introduced to the study by a medical staff.[12] A research coordinator then met with interested families. After consent, participants received step 1, enhanced usual care (**Table I**; available at www.jpeds.com): a brief pain-focused psychoeducation/relaxation training administered during their medical visit by a research coordinator or trained nurse (https://steppedcare.research.cchmc.org/).[12] This website was also provided to participants for home practice. Usual care (part of enhanced usual care and medical treatment as usual) at this center also consisted of use of pharmacotherapies that demonstrate at least some evidence-base for the management of FAPD pain (eg, antispasmodic agents) by the gastrointestinal (GI) provider. As part of usual care, providers had the autonomy to tailor treatment based on the needs of the patient. Two weeks later, participants were rescreened by a research coordinator via telephone. Those reporting low levels of disability (FDI ≤7) were considered enhanced usual care "responders" and completed the study. "Nonresponders" (FDI >7) were invited to complete the next phase.

Step 2: Assessment and ADAPT. Qualifying participants underwent an assessment consisting of a diagnostic interview (Anxiety Disorder Interview Schedule for the DSM-IV, Child Version [ADIS-IV][26]) and additional psychosocial measures (described in the Measures section). If participants qualified following the assessment, they were randomized to either stepped-up care, consisting of ADAPT, a tailored CBT treatment (**Table I** and below) + medical treatment as usual, or medical treatment as usual alone. Eight weeks after randomization, all participants completed a follow-up assessment to re-assess outcomes.

ADAPT. ADAPT is a brief, tailored intervention to treat pain and anxiety, and uses a blend of in-person visits and web modules with phone support to ensure consistent delivery.[21] ADAPT was developed with National Institutes of Health funding (F32HD078049, Cunningham PI) to address the unique needs of youth with FAPD. ADAPT teaches evidence-based cognitive behavioral strategies to cope with pain[25] and anxiety,[27,28] given that anxiety commonly co-occurs in this population[9-12,16,29] and is predictive of poor outcomes.[14,15] Pilot testing indicated good evidence of feasibility.[21] ADAPT was delivered by doctoral psychologists supervised by licensed providers.

For this study, ADAPT (**Table I**) was delivered in a stratified manner to be optimally tailored to the needs of youth with FAPD. All youth received coping skills training for pain as part of ADAPT, and additional components for anxiety management were offered if indicated. Specifically, youth with FAPD without evidence of clinical anxiety received four weekly sessions of pain-focused ADAPT (Measures section provides additional information). Two sessions were delivered in-person, and 2 were delivered via web modules with weekly psychologist telephone support. Youth with clinical anxiety received 6 weekly sessions total (2 in-person and 4 web-based with weekly telephone support) consisting of pain management and anxiety management.

Treatment Integrity. Treatment integrity was assessed using audio recordings of the in-person sessions by independent evaluators (eg, doctoral and postdoctoral psychology trainees). Integrity scores (0%-100%) were obtained. Items assessed included delivery of session-specific skills and assessment of participant comprehension.

Measures

Demographic and background information (including medication/supplement usage) were collected from the parent and from the patient's electronic medical chart. Furthermore, clinically sensitive and psychometrically validated child informant measures were used, as youth with FAPD are more sensitive informants of their own symptoms.[10]

Outcome Measures

Pain-Related Disability. The child-report version of the FDI is a 15-item measure of difficulty in performing activities in the past several days,[30] is valid for youth with chronic pain,[31] and is used in FAPD.[10,12,21,32] Higher scores indicate greater disability. Healthy youth on average have a total FDI score of 3.5.[30] Therefore, a score of >7 (double that value) was determined to be indicative of at least some disability because of pain for enrollment in the current study. An FDI score decrease of ≥7.8 points denotes a clinically meaningful treatment response,[33] which was used for comparing ADAPT plus medical treatment as usual vs medical treatment as usual outcomes, and there are cut-offs categorizing mild (<13), moderate (13-29), and severe (30+) disability.[31] The FDI (all αs ≥.85) was completed at screening, re-screening, and post-treatment.

Pain Intensity. Average pain over the past 2 weeks was assessed via a visual analog scale (VAS), anchored with the words, "no pain," and "worst pain."[34] This was collected at screening, baseline, and post-assessment. A score of ≥3/10 is clinically significant.[35]

Clinical Anxiety Measures

The Screen for Child Anxiety Related Disorders Report, Child Version (SCARED) is a 41-item, measure of anxiety over 3 months[36,37] and is widely used in pediatric pain research.[12,38-41] Higher scores indicate greater anxiety. A cut-off of ≥25 is clinically significant.[37] The SCARED was administered at screening (α = .93) and post-assessment (α = .95). A 50% reduction in scores at post-treatment is considered a clinically meaningful indictor of improvement/remission.[42]

The ADIS-IV is a clinician-administered interview assessing psychiatric disorders in childhood.[26,43] Trained-to-criterion, blind-to-treatment-condition clinicians administered the ADIS-IV. Diagnoses and clinician severity ratings ranging

from 0 to 8 (scores ≥4 indicate a diagnosable condition) were obtained. The ADIS-IV was administered at baseline and post-assessment. Inter-rater reliabilities were examined by reviewing audio recordings based on established guidelines.[44] Agreement for no diagnosis (κ range = .67-1.0) and the presence of an anxiety disorder at both pre- and post-treatment were appropriate (κ range = .83-1.0). The κ coefficients obtained for matching principal anxiety disorders (generalized anxiety disorder, social phobia, separation anxiety disorder, and specific phobias) were in the good to excellent range at pre- (κ = .64-1.0) and post-treatment (κ = .87-1.0).

Other Measures

Depressive Symptoms. The Childhood Depression Inventory, Second Edition (CDI-2) is a 28-item self-report measure of depression.[45] Those with severe symptoms (CDI-2, t score >80), or active suicidal ideation at baseline (α = .89) were excluded and referred for treatment.

Power and Analytic Plan

Power (.80) to detect a treatment effect difference (d = .50 for FDI) was n = 40 per group. Descriptive statistics using SPSS v 25 (SPSS Inc) were computed to assess youth participation and response rate to the initial dose of stepped care. Missing data were minimal (≥96% of item-level data obtained) and were handled using maximum likelihood estimation[46] in Mplus. A structural equation modeling equivalent of a MANCOVA was conducted to assess differences between ADAPT plus medical treatment as usual vs medical treatment as usual completers on the primary outcome (FDI), and secondary outcome (VAS pain intensity), controlling for baseline outcome scores and age, as age has been shown to be positively correlated with higher FDI scores.[10] Differences in anxiety symptoms controlling for baseline anxiety scores were also explored. Indicators of clinically significant change were also used to estimate the strength of the treatment effects.

Treatment effect moderation by anxiety and by number of sessions was also explored via a structural equation modeling equivalent MANCOVA and independent samples *t* tests. Effect sizes (95% CI) were calculated to understand effect magnitude. Differences in types and numbers of medications/supplements prescribed between ADAPT plus medical treatment as usual and medical treatment as usual groups was also examined via χ^2 tests and an independent samples *t* test.

Results

Demographic information is presented in **Table II** (available at www.jpeds.com). The total sample (N = 139) ranged from ages 9 to 14 years (mean = 11.65, SD = 1.68), and included 84 female participants (60%). The most common diagnoses based on the Rome IV checklist[24] completed by the medical provider were FAPD, not otherwise specified (n = 85, 61%) and irritable bowel syndrome (n = 50, 36%). Most primary caregivers were mothers who completed high school. On average, youth presented with moderate levels of pain, functional disability, and anxiety (**Table III**; available at www.jpeds.com).

Stepped Care

Step 1: Enhanced Usual Care. A total of 203 youth were approached between 2015 and 2018, and 139 (68.5%) enrolled and underwent enhanced usual care. The average FDI score was 17.9 (SD = 8.3). Research staff re-screened 120 youth via telephone approximately 2 weeks after their screening/gastroenterology clinic visit. Of those, only 10 (8%) reported their FDI levels reduced to no more than minimal (ie, FDI ≤ 7; Measures section). Those with more than minimal disability (ie, FDI >7) after 2 weeks were scheduled for a baseline assessment (n = 110), of which 89 completed and remained eligible for randomization.

Step 2: ADAPT plus Medical Treatment as Usual vs Medical Treatment as Usual. Qualifying youth were randomized (based on computer-generated list) to ADAPT plus medical treatment as usual (n = 44) or medical treatment as usual alone (n = 45), and 79 of those youth completed the study by the end of 8 weeks (ADAPT plus medical treatment as usual, n = 40; medical treatment as usual, n = 39). The assignment was provided to research coordinators by the study statistician. There were no significant group differences in baseline variables.

Study outcome data are presented in **Table IV**. Participants who received ADAPT plus medical treatment as usual demonstrated significantly lower FDI levels at post-assessment compared with those randomized to medical treatment as usual ($b = -4.26$, SE = 2.04, $t = -2.09$, $P = .036$; **Figure 2**). The effect size difference was moderate (Cohen $d = 0.45$). Moreover, there was an average 9.7-point reduction in FDI scores for ADAPT completers (compared with a 2.9-point reduction in the medical treatment as usual group), which is indicative of clinically meaningful change (eg, >7.8-point decrease).[33] In addition, 60% of those completing ADAPT plus medical treatment as usual had a clinically significant reduction in FDI scores compared with 28.1% of those completing medical treatment as usual. Similarly, ADAPT plus medical treatment as usual completers had a 12.3% average VAS pain reduction, whereas medical treatment as usual completers had a 5.5% average VAS pain reduction. The effect size difference was moderate (Cohen $d = 0.30$). However, the differences between groups on pain intensity was not statistically significant ($b = -0.67$, SE = 0.41, $t = -1.61$, $P = .108$; **Figure 3**).

Anxiety at post-treatment, controlling for pre-treatment anxiety, was also explored (**Table IV** and **Figure 4** [available at www.jpeds.com]). Children receiving ADAPT plus medical treatment as usual reported lower SCARED scores at post-treatment as compared with those who received medical treatment as usual ($b = -6.36$, SE = 2.85, $t = -2.23$, $P = .026$). The effect size was moderate (Cohen $d = 0.39$). The average SCARED score percent decrease was 33% for ADAPT plus medical treatment as usual vs 16.5% for medical treatment as usual; 13 out of 40 (32.5%) youth experienced at least a 50% reduction in SCARED scores after ADAPT plus medical treatment as usual compared with 6 out of 39 (15.4%) after medical treatment as usual. There were not significant differences in the clinican severity rating of the primary anxiety disorder diagnosis at post-treatment when comparing the ADAPT plus medical

Table IV. Post-treatment changes in child symptoms following ADAPT plus medical treatment as usual

Descriptions	$\bar{X}_{Difference}$	SE	t value	P
Primary study aims				
Functional disability at post-treatment				
Age	−0.15	0.59	−0.26	.792
FDI (pretreatment)	0.46	0.14	3.22	.001
ADAPT plus medical treatment as usual subgroup	−4.26	2.04	−2.09	.036
Pain at post-treatment				
Age	−0.17	0.12	−1.43	.153
VAS pain (pretreatment)	0.60	0.10	6.13	.000
ADAPT plus medical treatment as usual subgroup	−0.67	0.41	−1.61	.108
Exploratory study aims				
Anxiety severity at post-treatment				
CSR anxiety diagnosis (pretreatment)	0.29	0.20	1.46	.145
ADAPT plus medical treatment as usual subgroup	−0.51	0.55	−0.93	.350
Anxiety symptoms at post-treatment				
SCARED (pretreatment)	0.62	0.08	7.33	.000
ADAPT plus medical treatment as usual subgroup	−6.36	2.85	−2.23	.026

CSR, clinician severity rating.
ADAPT plus medical treatment as usual subgroup represents dummy coded variable with 0 = medical treatment as usual only and 1 = ADAPT plus medical treatment as usual. FDI assesses child report of functional disability. VAS assesses child report average pain intensity. SCARED assesses child report of anxiety symptoms. CSR measures clinician perception of severity of the primary anxiety diagnosis during the ADIS-IV.

treatment as usual and medical treatment as usual groups ($b = -0.51$, SE = 0.55, $t = -0.93$, $P = .350$). However, the effect was in the expected direction, suggesting severity of the primary anxiety disorder tended to decrease following ADAPT plus medical treatment as usual compared with medical treatment as usual.

Treatment Integrity. Treatment integrity for ADAPT was found to be excellent (mean = 98%, range = 88%-100%).

Adherence. Of the 44 individuals assigned to ADAPT, 4 were lost to attrition (9%). Of these individuals, 2 participated in at least 1 in-person session and 2 did not complete any component of ADAPT treatment. Of ADAPT completers (n = 40), 75% (n = 30) were assigned the 6-session version and 25% (n = 10) were assigned the 4-session version.

All 40 ADAPT completers participated in the 2 in-person sessions and weekly therapist telephone calls. Adherence data to the web portion of ADAPT were calculated based on previously established guidelines.[21] The percentage of available videos and handouts viewed, and forms completed was calculated for each patient: Participants watched, on average, over one-half of the available videos (mean = 57%, SD = 37%, range = 0%-100%). On average, patients also downloaded 21% (SD = 29%, range = 0%-100%) of the handouts and completed 29% (SD = 22%, range = 0%-64%) of the online forms. Eight patients did not complete any online content.

Moderation Analyses. Analyses showed baseline SCARED scores did not moderate effects on FDI and average pain intensity at post. Further, ADAPT dose (4 vs 6 sessions) did not moderate effects on FDI and average pain intensity at post. There was a significant difference in SCARED scores at post between those who were stratified to the 6 session (mean SCARED = 26.67) versus the 4 session (mean SCARED = 8.67; t [37] = −5.36, P <.001). These differences were expected given that ADAPT treatment dose was assigned based on SCARED anxiety levels.

Medication Usage. In the ADAPT plus medical treatment as usual group, the most common medications and supplements prescribed by the GI provider were antispasmodic agents (n = 24, 60%), acid reduction therapies (n = 14, 35%), laxatives (n = 12, 30%), peppermint oil (n = 6, 15%), probiotics (n = 5, 12.5%), low dose psychotropic agents (n = 3, 7.5%), and antinausea medications (n = 2, 5%). Antidiarrheal medication, antiulcer/protectants, and gas reducing medication were also infrequently prescribed (all ns = 1, 2.5%). The average number of GI medications/supplements prescribed was 1.75 (SD = 1.0, range

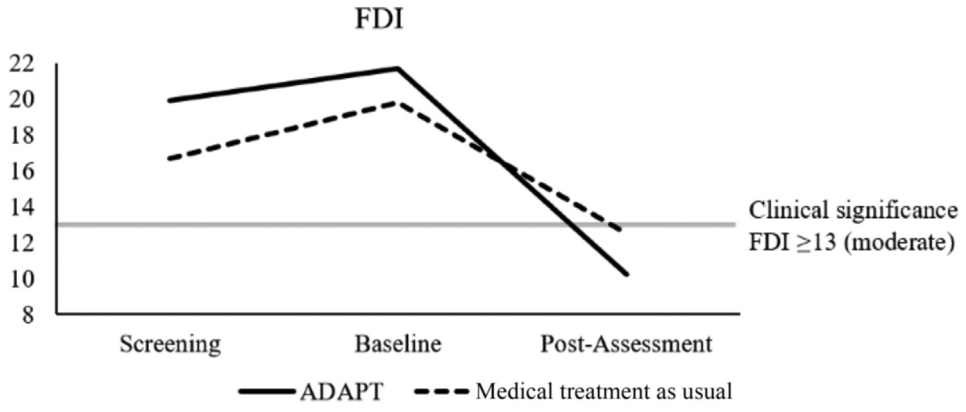


Figure 2. FDI scores from screening to re-screening generally remained within the moderate range of disability. After randomization to ADAPT plus medical treatment as usual or medical treatment as usual, both groups experienced a reduction in FDI scores, with the ADAPT plus medical treatment as usual group experiencing the most pronounced improvement. The ADAPT plus medical treatment as usual group had significantly lower FDI scores at post compared with the medical treatment as usual group.

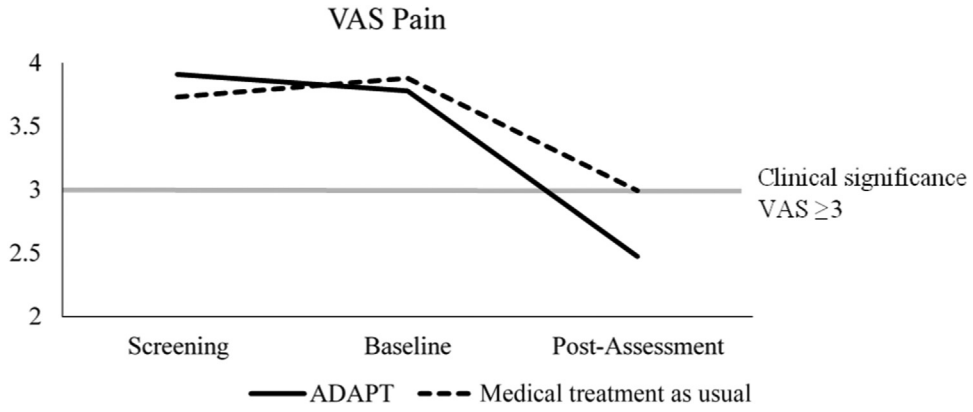


Figure 3. Average scores on the VAS for pain remained in the moderate range from screening to baseline. At post assessment, both ADAPT plus medical treatment as usual and medical treatment as usual groups experienced a reduction in pain symptoms. For ADAPT plus medical treatment as usual completers, the reduction in pain symptoms was clinically significant but was not statistically different compared with those completing medical treatment as usual.

0-5). In the medical treatment as usual group, the most common medications and supplements prescribed by the GI provider were antispasmodic agents (n = 19, 48.7%), acid reduction therapies (n = 19, 48.7%), laxatives (n = 13, 33.3%), low dose psychotropic agents (n = 4, 10.3%), anti-nausea medications (n = 4, 10.3%), peppermint oil (n = 3, 7.7%), and probiotics (n = 2, 5.1%). The average number of GI medications/supplements prescribed was 1.82 (SD = 0.98, range 0-4). There were no significant differences between ADAPT plus medical treatment as usual and medical treatment as usual groups on types of medications prescribed nor numbers of medications prescribed.

Discussion

Findings of this randomized clinical trial of ADAPT suggest that a brief, stepped care approach is highly feasible for managing pain and anxiety in youth with FAPD within the context of standard medical care. Moreover, the easily accessible tailored CBT intervention (ADAPT) plus medical treatment as usual may be effective for reducing pain-related disability and anxiety symptoms. These findings are critically important because FAPD are among the most common childhood pain conditions[1,2]; yet, there is currently limited evidence to support the use of pharmacologic treatments.[47,48] The most potent intervention for the management of pediatric FAPD[22] and other pediatric chronic pain conditions[19] involves the use of nonpharmacologic treatments such as CBT, which are often difficult to provide due to limited access and the need for multiple in-person visits. CBT for pain management also does not always directly target anxiety, which is highly prevalent in FAPD[8-11] and adversely impacts response to CBT.[23] Thus, the ADAPT intervention, which targets pain and anxiety when appropriate, has the potential to substantially improve patient outcomes. The stepped care approach,[17,18] which begins by targeting all-comers, is practical to employ in a medical setting and provides flexibility, recognizing that patients with FAPD may require varying levels of care.[15]

Based on the study findings, it may be feasible for patients with FAPD to receive psychoeducation and basic relaxation strategies for pain management as part of standard medical treatment. For those who fail to respond to the initial treatment, which in this investigation constituted the vast majority of patients, additional care may be warranted. For such patients, a brief CBT, such as ADAPT, which includes both in-person and web-based/telehealth sessions,[21] may bolster patient outcomes.

Youth with FAPD demonstrated improvements in pain-related functional disability and anxiety symptoms following ADAPT plus medical treatment as usual. This is important because the presence of anxiety in conjunction with FAPD is quite common.[8-12,16] Further, anxiety is associated with increased pain and disability,[10,12-14] and adverse outcomes in youth with FAPD in cross-sectional[10,13] and longitudinal studies.[14,49] Left untreated, youth with FAPD are prone to long-term mental health issues.[49] This tailored approach to simultaneously address pain-related disability and anxiety in FAPD may improve patient outcomes over the long term. Indeed, the goal of CBT is to teach youth coping strategies that will allow them to function despite pain. Therefore, prior literature supports the notion that disability outcomes tend to improve before pain improves,[50] which is congruent with the study results.

The importance of using a CBT treatment approach integrated into medical care and includes telehealth delivery should not be understated, particularly given the coronavirus disease 2019 pandemic and the increasing demand for telehealthcare. Such an approach provides increased accessibility to care (particularly for vulnerable families, and those living far from the medical center) and has important implications for the future of psychological treatments for youth with chronic pain. Indeed, ADAPT offers some advantages over exclusively web-based approaches for pain management by allowing patients to build rapport with a therapist. Direct provider-patient contact for both medical and psychological needs is important for non-specific therapeutic effects, and there is support that remote patient-provider contact (eg, phone or live

video-conferencing) achieves a therapeutic bond comparable with traditional in-person delivery of psychological treatments.[51] In the current investigation, adherence to both the live in-person and telehealth/phone portions of ADAPT was quite high, whereas the variability in the completion of the web components of ADAPT was consistent with adherence rates generally observed during web-based interventions.[52]

Given psychological providers with expertise in the management of pediatric chronic pain are limited, additional research would be valuable to determine if ADAPT can be delivered completely remotely (eg, in person sessions converted to telehealth sessions), and if components of ADAPT can be delivered independently by a member of the medical team (eg, nurse delivered) in certain cases. In addition, given ADAPT plus medical treatment as usual appears to be effective, it is important to explore mechanisms to better understand *why* such a treatment works. Examination of underlying neural mechanisms, for example,[53] may allow for further tailoring and enhancement of treatment approaches.

Integration of behavioral health within standard medical care provides youth with increased access to the most effective treatment for pain management, de-stigmatizes mental health concerns, increases patient/family buy-in, and offers a systematic and evidence-based approach to treating youth with FAPD. For these reasons, it would be valuable to test such a treatment model in other settings, such as primary care, where behavioral health integration for the management of mental health concerns, such as anxiety, has already shown benefits.[54] It would also be valuable to test and adapt such models with other pediatric chronic health conditions involving pain, such as migraines. In our study, enhanced usual care demonstrated limited benefits, but it would be helpful to explore if this "enhancement" offered any additional improvement for patients over and above standard care. It may also be beneficial to extend the length of enhanced usual care from 2 weeks to 4 weeks in a future large-scale trial. It may also be helpful to consider an approach that is initially stratified (vs stepped) as patients would immediately be eligible to receive more intensive treatment rather than waiting until they failed stepped care if they presented with more severe levels of disability/anxiety from the outset.

This single-site pilot randomized controlled trial did not have an active treatment control beyond medical treatment as usual, and our sample consisted mostly of white female participants, which limits generalizability; however, findings offered preliminary evidence of the positive effects of this innovative approach to care. We offered this intervention to younger youth (9-14 years of age) with a goal of offering a targeted intervention to prevent adverse outcomes over the longer term but believe a similar program could be beneficial for older adolescents as well.[21] A larger-scale, multisite study with longitudinal exploration of outcomes (including testing if refresher/maintenance sessions would enhance outcomes) would allow for further understanding of treatment effects. It would also be informative to compare components of ADAPT to determine if certain strategies (eg, cognitive vs behavioral) are more effective than others and if the inclusion of additional components (eg, attention bias training) would further enhance treatment. Finally, it would be informative to compare other active treatments such as standard CBT for pain to ADAPT, in addition to accounting for the use of specific pharmacotherapies in treatment. In the current examination, there were no differences in types of medications or supplements prescribed across ADAPT plus medical treatment as usual and medical treatment as usual groups. Although there was not an effect based on the ADAPT dose received, the treatment dose varied within the CBT arm (25% received 4 sessions, 75% received 6 sessions). This stratified approach to treatment allowed for the heterogenous FAPD patient population to receive an intervention that was appropriately tailored to the unique symptom presentation (eg, with or without clinical levels of anxiety), and therefore has optimal clinical utility.

Although a stepped care approach is feasible, youth with FAPD appear to benefit from the stepped-up (CBT) approach for pain and anxiety management. This approach is feasible for improving health- and mental-health related outcomes in youth with FAPD. By offering tailored CBT to affected youth, accessibility to care is enhanced for those with greatest need. Further, tailoring care based on symptoms and need may enhance outcomes while maximizing the use of limited therapeutic resources. ■

We thank the study staff in the Division of Behavioral Medicine and Clinical Psychology at Cincinnati Children's Hospital Medical Center who contributed to the successful execution of this research, including Anjana Jagpal (research coordinator), Dr Sarah Nelson (study interventionist), and Dr Jacqueline Newman Warner (study interventionist). We also owe our utmost thanks to the patients and families who participated in the study.

Submitted for publication May 27, 2020; last revision received Oct 12, 2020; accepted Oct 23, 2020.

Reprint requests: Natoshia R. Cunningham, PhD, Department of Family Medicine, Michigan State University, College of Human Medicine, 628 Secchia Center, 15 Michigan St NE, Grand Rapids, MI 49503. E-mail: natoshia@msu.edu

References

1. King S, Chambers CT, Huguet A, MacNevin RC, McGrath PJ, Parker L, et al. The epidemiology of chronic pain in children and adolescents revisited: a systematic review. Pain 2011;152:2729-38.
2. Korterink JJ, Diederen K, Benninga MA, Tabbers MM. Epidemiology of pediatric functional abdominal pain disorders: a meta-analysis. PLoS One 2015;10:e0126982.
3. Campo JV, Di Lorenzo C, Chiappetta L, Bridge J, Colborn DK, Gartner JC Jr, et al. Adult outcomes of pediatric recurrent abdominal pain: do they just grow out of it? Pediatrics 2001;108:E1.
4. Greco LA, Freeman KE, Dufton L. Overt and relational victimization among children with frequent abdominal pain: links to social skills, academic functioning, and health service use. J Pediatr Psychol 2007;32:319-29.
5. Claar RL, Walker LS, Smith CA. Functional disability in adolescents and young adults with symptoms of irritable bowel syndrome: the role of academic, social, and athletic competence. J Pediatr Psychol 1999;24:271-80.
6. Walker LS, Guite JW, Duke M, Barnard JA, Greene JW. Recurrent abdominal pain: a potential precursor of irritable bowel syndrome in adolescents and young adults. J Pediatr 1998;132:1010-5.
7. Stødal K, Nygaard EA, Bentsen BS. Recurrent abdominal pain: a five-year follow-up study. Acta Pædiatr 2005;94:234-6.
8. Campo JV, Bridge J, Ehmann M, Altman S, Lucas A, Birmaher B, et al. Recurrent abdominal pain, anxiety, and depression in primary care. JAMA Pediatr 2004;113:817-24.

9. Dorn LD, Campo JC, Thato S, Dahl RE, Lewin D, Chandra R, et al. Psychological comorbidity and stress reactivity in children and adolescents with recurrent abdominal pain and anxiety disorders. J Am Acad Child Adolesc Psychiatry 2003;42:66-75.
10. Cunningham NR, Cohen MB, Farrell MK, Mezoff AG, Lynch-Jordan A, Kashikar-Zuck S. Concordant parent-child reports of anxiety predict impairment in youth with functional abdominal pain. J Pediatr Gastroenterol Nutr 2014;60:312-7.
11. Dufton LM, Dunn MJ, Compas BE. Anxiety and somatic complaints in children with recurrent abdominal pain and anxiety disorders. J Pediatr Psychol 2009;34:176-86.
12. Cunningham NR, Moorman E, Brown CM, Mallon D, Chundi PK, Mara CA, et al. Integrating psychological screening into medical care for youth with abdominal pain. Pediatrics 2018;142:e20172876.
13. Wendland M, Jackson Y, Stokes LD. Functional disability in paediatric patients with recurrent abdominal pain. Child Care Health Dev 2010;36:516-23.
14. Mulvaney S, Lambert EW, Garber J, Walker LS. Trajectories of symptoms and impairment for pediatric patients with functional abdominal pain: a 5-year longitudinal study. J Am Acad Child Adolesc Psychiatry 2006;45:737-44.
15. Cunningham NR, Jagpal A, Peugh J, Cohen MB, Farrell MK, Mezoff AG, et al. Using a simple risk categorization to predict outcomes in pediatric functional abdominal pain at 6 months. J Pediatr Gastroenterol Nutr 2017;64:685-90.
16. Cunningham NR, Lynch-Jordan A, Mezoff AG, Farrell MK, Cohen MB, Kashikar-Zuck S. Importance of addressing anxiety in youth with functional abdominal pain: suggested guidelines for physicians. J Pediatr Gastroenterol Nutr 2013;56:469-74.
17. Bower P, Gilbody S. Stepped care in psychological therapies: access, effectiveness and efficiency. Narrative literature review. Br J Psychiatry 2005;186:11-7.
18. Von Korff M, Tiemens B. Individualized stepped care of chronic illness. W J Med 2000;172:133-7.
19. Fisher E, Law E, Dudeney J, Palermo TM, Stewart G, Eccleston C. Psychological therapies for the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev 2018;9. CD003968.
20. van der Veek SM, Derkx BH, Benninga MA, Boer F, de Haan E. Cognitive behavior therapy for pediatric functional abdominal pain: a randomized controlled trial. Pediatrics 2013;132:e1163-72.
21. Cunningham NR, Nelson S, Jagpal A, Moorman E, Farrell M, Pentiuk S, et al. Development of the aim to decrease anxiety and pain treatment for pediatric functional abdominal pain disorders. J Pediatr Gastroenterol Nutr 2018;66:16-20.
22. Rutten JM, Korterink JJ, Venmans LM, Benninga MA, Tabbers MM. Nonpharmacologic treatment of functional abdominal pain disorders: a systematic review. Pediatrics 2015;135:522-35.
23. Cunningham NR, Jagpal A, Tran ST, Kashikar-Zuck S, Goldschneider KR, Coghill RC, et al. Anxiety adversely impacts response to cognitive behavioral therapy in children with chronic pain. J Pediatr 2016;171:227-33.
24. Koppen IJ, Nurko S, Saps M, Di Lorenzo C, Benninga MA. The pediatric Rome IV criteria: what's new? Expert Rev Gastroenterol Hepatol 2017;11:193-201.
25. Kashikar-Zuck S, Ting T, Arnold L, Bean J, Powers S, Graham T, et al. Cognitive behavioral therapy for the treatment of juvenile fibromyalgia: a multisite, single-blind, randomized, controlled clinical trial. Arthritis Rheum 2012;64:297-305.
26. Silverman WK, Albano A. The Anxiety disorders interview schedule for children for DSM-IV (child and parent versions). San Antonio, TX: Psychological Corporation; 1996.
27. Lyneham HJ, Abbott MJ, Wignall A, Rapee RA. The Cool kids anxiety treatment program. Sydney, Australia: MUARU, Macquarie University; 2003.
28. Hudson JL, Rapee RM, Deveney C, Schniering CA, Lyneham HJ, Bovopoulos N. Cognitive-behavioral treatment vs an active control for children and adolescents with anxiety disorders: a randomized trial. J Am Acad Child Adolesc Psychiatry 2009;48:533-44.
29. Campo JV, Comer DM, Jansen-Mcwilliams L, Gardner W, Kelleher KJ. Recurrent pain, emotional distress, and health service use in childhood. J Pediatr 2002;141:76-83.
30. Walker L, Greene J. The functional disability inventory: measuring a neglected dimension of child health status. J Pediatr Psychol 1991;16:39-58.
31. Kashikar-Zuck S, Flowers S, Claar R, Guite J, Logan D, Lynch-Jordan A, et al. Clinical utility and validity of the functional disability inventory among a multicenter sample of youth with chronic pain. Pain 2011;152:1600-7.
32. Cunningham NR, Lynch-Jordan A, Barnett K, Peugh J, Sil S, Goldschneider K, et al. Child pain catastrophizing mediates the relation between parent responses to pain and disability in youth with functional abdominal pain. J Pediatr Gastroenterol Nutr 2014;59:732-8.
33. Sil S, Arnold LM, Lynch-Jordan A, Ting TV, Peugh J, Cunningham N, et al. Identifying treatment responders and predictors of improvement after cognitive-behavioral therapy for juvenile fibromyalgia. Pain 2014;155:1206-12.
34. McGrath PJ, Walco GA, Turk DC, Dworkin RH, Brown MT, Davidson K, et al. Core outcome domains and measures for pediatric acute and chronic/recurrent pain clinical trials: PedIMMPACT recommendations. J Pain 2008;9:771-83.
35. Kelly A. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. Emer Med J 2001;18:205-7.
36. Birmaher B, Khetarpal S, Brent D, Cully M, Balach L, Kaufman J, et al. The screen for child anxiety related emotional disorders (SCARED): scale construction and psychometric characteristics. Am Acad Child Adolesc Psychiatry 1997;36:545-53.
37. Birmaher B, Brent D, Chiappetta L, Bridge J, Monga S, Baugher M. Psychometric properties of the screen for anxiety related emotional disorders (SCARED): a replication study. J Am Acad Child Adolesc Psychiatry 1999;38:1230-6.
38. Tran ST, Jastrowski Mano KE, Anderson Khan K, Davies W, Hainsworth KR. Patterns of anxiety symptoms in pediatric chronic pain as reported by youth, mothers, and fathers. Clin Pract Pediatr Psycho 2016;4:51.
39. Khan KA, Tran ST, Jastrowski Mano KE, Simpson PM, Cao Y, Hainsworth KR. Predicting multiple facets of school functioning in pediatric chronic pain: examining the direct impact of anxiety. Clin J Pain 2015;31:867-75.
40. Jastrowski Mano KE, Evans JR, Tran ST, Anderson Khan K, Weisman SJ, Hainsworth KR. The psychometric properties of the screen for child anxiety related emotional disorders in pediatric chronic pain. J Pediatr Psychol 2012;37:999-1011.
41. Cunningham NR, Jagpal A, Nelson S, Jastrowski Mano KE, Tran ST, Lynch-Jordan AM, et al. Clinical reference points for the screen for child anxiety-related disorders in 2 investigations of youth with chronic pain. Clin J Pain 2019;35:238-46.
42. Caporino NE, Sakolsky D, Brodman DM, McGuire JF, Piacentini J, Peris TS, et al. Establishing clinical cutoffs for response and remission on the screen for child anxiety related emotional disorders (SCARED). J Am Acad Child Adolesc Psychiatry 2017;56:696-702.
43. Silverman WK, Saavedra LM, Pina AA. Test-retest reliability of anxiety symptoms and diagnoses with the anxiety disorders interview schedule for dsm-iv: child and parent versions. J Am Acad Child Adolesc Psychiatry 2001;40:937-44.
44. Mannuzza S, Fyer AJ, Martin LY, Gallops MS, Endicott J, Gorman J, et al. Reliability of anxiety assessment: I. Diagnostic agreement. Arch Gen Psychiatry 1989;46:1093-101.
45. Kovacs M. Children's depression inventory 2nd edition: Self Report. North Tonawanda, NY: Multi-Health systems, Inc.; 2011.
46. Enders CK. Applied missing data analysis. New York: Guilford; 2010.
47. Martin AE, Newlove-Delgado TV, Abbott RA, Bethel A, Thompson-Coon J, Whear R, et al. Pharmacological interventions for recurrent abdominal pain in childhood. Cochrane Database Syst Rev 2017;3:CD010973.
48. Korterink JJ, Rutten JM, Venmans L, Benninga MA, Tabbers MM. Pharmacologic treatment in pediatric functional abdominal pain disorders: a systematic review. J Pediatr 2015;166:424-31.e6.

49. Shelby GD, Shirkey KC, Sherman AL, Beck JE, Haman K, Shears AR, et al. Functional abdominal pain in childhood and long-term vulnerability to anxiety disorders. JAMA Pediatr 2013;132:475-82.
50. Lynch-Jordan AM, Sil S, Peugh J, Cunningham N, Kashikar-Zuck S, Goldschneider KR. Differential changes in functional disability and pain intensity over the course of psychological treatment for children with chronic pain. Pain 2014;155:1955-61.
51. Simpson SG, Reid CL. Therapeutic alliance in videoconferencing psychotherapy: a review. Aust J Rural Health 2014;22:280-99.
52. Kelders SM, Kok RN, Ossebaard HC, Van Gemert-Pijnen JE. Persuasive system design does matter: a systematic review of adherence to web-based interventions. J Med Internet Res 2012;14:e152.
53. Cunningham NR, Kashikar-Zuck S, Coghill RC. Brain mechanisms impacted by psychological therapies for pain: identifying targets for optimization of treatment effects. Pain Rep 2019;4:e767.
54. Walter HJ, Vernacchio L, Trudell EK, Bromberg J, Goodman E, Barton J, et al. Five-year outcomes of behavioral health integration in pediatric primary care. Pediatrics 2019e20183243.

50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Association of Type 1 Diabetes Mellitus and Celiac Disease: Then and Now

Penny R, Thompson RG, Polmar SH, Schultz RB. Pancreatitis, malabsorption, and IgA deficiency in a child with diabetes. J Pediatr 1971;78:512-6.

Fifty years ago, the medical community recognized 2 distinct types of diabetes mellitus, one mostly diagnosed in childhood and another with an adult-onset. Contemporaneously, the first set of diagnostic criteria for celiac disease established the causal relationship between dietary gluten and villous atrophy on intestinal biopsy. However, the autoimmune etiologies of these 2 diseases had not yet been elucidated.

A pattern emerged of children with diabetes with coexistent malabsorption. In 1971, Penny et al published a case report of a 5-year-old girl diagnosed with diabetes at the age of 2 years. One year after diagnosis, she began experiencing abdominal pain, foul-smelling stools, and weight loss. After 11 months of symptoms, she was hospitalized with ascites, pancreatitis, and steatorrhea. She was discharged on pancreatic enzymes but was re-hospitalized for no weight gain. A duodenal biopsy revealed absence of villi and chronic inflammation consistent with celiac disease. She was placed on a gluten-free diet, and after 1 year, had gained 13 pounds.

Fifty years later, the association between celiac disease and type 1 diabetes (T1D) is well recognized. Now, children newly diagnosed with T1D are screened at regular intervals for celiac disease, and most cases develop within 5 years of their diabetes diagnosis. Research continues to better understand the autoimmune etiologies of T1D and celiac disease and their pathophysiologic relationship; studies describe genetic susceptibilities for both with the HLA-DR3-DQ2 and HLA-DR4-DQ8 gene loci.[1] Therapy for T1D has evolved significantly in the past 50 years, although as environmental triggers are still unclear, prevention strategies remain elusive. Awareness and diagnosis of celiac disease also has increased, and a gluten-free diet successfully treats celiac disease. However, the burden of this co-diagnosis continues and requires expanded therapies,[2] prevention, and a cure.

Jennifer Ni, MD
Division of Pediatric Endocrinology
School of Medicine

Chaitan Khosla, PhD
Stanford ChEM-H

David M. Maahs, MD, PhD
Division of Pediatric Endocrinology
School of Medicine
Stanford University
Palo Alto, California

References

1. Kozhakhmetova A, Wyatt RC, Caygill C, Williams C, Long AE, Chandler K, et al. A quarter of patients with type 1 diabetes have co-existing non-islet autoimmunity: the findings of a UK population-based family study. Clin Exp Immunol 2018;192:251-8.
2. Syage JA, Green PHR, Khosla C, Adelman DC, Sealey-Voyksner JA, Murray JA. Latiglutenase treatment for celiac disease: symptom and quality of life improvement for seropositive patients on a gluten-free diet. GastroHep 2019;1:293-301.

Table I. Stepped care and ADAPT intervention components for youth with FAPD

Interventions	Provider	Platform	Protocol used (focus of skill)
Step 1: Enhanced usual care*	Clinic nurse or research coordinator	In-person Web	• Psychoeducation (pain) • Relaxation (pain)
Step 2: ADAPT intervention			
Session 1	Psychologist	In-person	• Program overview • Psychoeducation (pain and anxiety) • Parent guidelines (pain) • Deep breathing/guided imagery (pain)
Session 2	Psychologist	In-person	• Progressive muscle relaxation (pain) • Calming statements (pain) • Activity pacing (pain)
Session 3	Psychologist	Web and phone	• Pleasant activity scheduling (pain) • Problem solving (pain)
Session 4†	Psychologist	Web and phone	• Cognitive restructuring (anxiety)
Session 5†	Psychologist	Web and phone	• Guided exposure (anxiety) • Assertiveness training (anxiety)
Session 6	Psychologist	Web and phone	• Maintenance planning (pain and anxiety)

All ADAPT sessions were approximately 60 minutes. Web sessions of ADAPT were completed by child participant independently (30 minutes) followed by phone support (15-30 minutes), with the patient's psychologist. Phone sessions were conducted primarily between the interventionist and child participant, with a brief portion of time reserved to update summarized content with the parents.

*https://steppedcare.research.cchmc.org.

†Optional modules administered over 2 sessions depending on presence of clinically significant anxiety. Participants without clinical anxiety received 4 weekly sessions of pain-focused ADAPT intervention only (ie, 2 in-person and 2 web-based modules with interventionist phone support). Participants with clinical levels of anxiety received 6 weekly sessions (ie, 2 in-person and 4 web-based with interventionist phone support) consisting of both pain and anxiety management strategies.

Table II. Sample characteristics

Demographics	Total enrolled (N = 139)	Treatment completers (n = 79)
Sex		
Female	84 (60%)	47 (59%)
Male	55 (40%)	32 (41%)
Age		
9 y	21 (15%)	12 (15%)
10 y	21 (15%)	13 (16%)
11 y	17 (12%)	9 (11%)
12 y	28 (20%)	12 (15%)
13 y	30 (22%)	18 (23%)
14 y	22 (16%)	15 (19%)
Race		
White or European American	129 (93%)	71 (90%)
Asian American	0 (0%)	0 (0%)
American Indian	1 (1%)	1 (1%)
African American	4 (3%)	3 (4%)
Biracial	2 (1%)	1 (1%)
Other	1 (1%)	1 (1%)
Ethnicity		
Hispanic/Latino	2 (1%)	2 (3%)
Pain diagnosis		
FAPD	85 (61%)	45 (57%)
IBS	50 (36%)	31 (39%)
Functional dyspepsia	2 (1%)	1 (1%)
Abdominal migraine	2 (1%)	2 (3%)
Participating caregiver		
Mother	108 (78%)	64 (81%)
Father	13 (9%)	7 (9%)
Grandmother	13 (9%)	5 (6%)
Grandfather	2 (1%)	1 (1%)
Foster parent	3 (2%)	2 (3%)
Caregiver high school completion		
Mother	—	79 (100%)
Father	—	75 (95%)

IBS, irritable bowel syndrome.
"Treatment" indicates completion of ADAPT plus medical treatment as usual or medical treatment as usual. Parent high school completion was only assessed at baseline (not enrollment).

Table III. Descriptive statistics and bivariate correlations of study outcome variables

Measures	M	SD	Range	2	3	4	5	6	7	8
Pre										
1. FDI	17.87	8.17	8-47	.38*	.28†	.05	.39‡	.25†	.30*	.21
2. VAS	3.75	1.86	0-8.7	–	.08	−.12	.27†	.53‡	.04	.29†
3. SCARED	35.12	15.68	4-67		–	.34†	.24†	.02	.62‡	.31†
4. CSR	6.08	1.31	4-8			–	.18	.13	.36*	.23§
Post										
5. FDI	11.33	9.48	0-41				–	.54‡	.67‡	.25§
6. VAS	2.73	2.22	0-8.6					–	.26†	.32†
7. SCARED	25.46	16.56	1-63						–	.43*
8. CSR	3.79	2.23	0-8							–

CSR, clinician severity rating; *M*, mean.
FDI assesses child report of functional disability. VAS assesses child report average pain intensity. SCARED assesses child report of anxiety symptoms. CSR measures clinician perception of severity of the primary anxiety diagnosis during the ADIS. Table contains means and standard deviations for participants used in primary and exploratory analyses.
*$P < .01$.
†$P < .05$.
‡$P < .001$.
§$P < .10$.

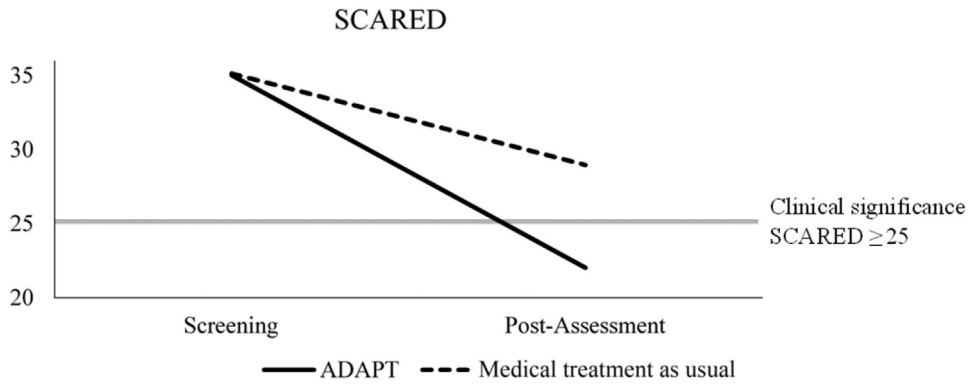


Figure 4. Patients with FAPD generally presented with clinically elevated levels of anxiety. Those who completed ADAPT plus medical treatment as usual were more likely to have statistically and clinically significant reductions in anxiety symptoms at post-assessment. The SCARED was not readministered at baseline because scores are valid for 3 months following administration.