Efficacy of a Digital Personalized Elimination Diet for the Self-Management of Irritable Bowel Syndrome and Comorbid Irritable Bowel Syndrome and Inflammatory Bowel Disease

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INTRODUCTION: **Most patients with irritable bowel syndrome (IBS) and dual-diagnosis IBS and inflammatory bowel disease (IBD) report that symptoms originate from or are exacerbated by trigger foods. Despite patient interest and need, there is no consensus on what diet is optimal. Popular diets have notable limitations including cost, length, implementation complexity, and lack of personalization.**

METHODS: **This pilot study evaluated the feasibility, desirability, and effect on gastrointestinal symptoms of a digitally delivered personalized elimination diet for patients with IBS and comorbid IBS/IBD, powered by machine learning. Participants were recruited online and were provided access to a digital personalized nutrition tool for 9 weeks (N = 37; IBS only = 16, Crohn's disease and IBS = 9, and ulcerative colitis and IBS = 12).**

RESULTS: **Significant symptom improvement was seen for 81% of participants at study midpoint and persisted for 70% at end point, measured by the relevant symptom severity score (IBS symptom severity score, Patient Simple Clinical Colitis Activity Index, or Mobile Health Index for Crohn's disease). Clinically significant symptom improvement was observed in 78% of participants at midpoint and 62% at end point. Twenty-five participants (67.6%) achieved total symptomatic resolution by the end of study. Patient-reported quality of life improved for 89% of participants. Ninety-five percentage daily engagement, 95% retention, 89% adherence and 92% satisfaction with the program were reported.**

DISCUSSION: **Dietary elimination can improve symptoms and quality of life in patients with IBS and comorbid IBS/IBD. Digital technology can personalize dietary interventions and improve adherence. Randomized controlled trials are warranted.**

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INTRODUCTION

One of the most frequent questions patients with chronic gastrointestinal (GI) disorders such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) ask their physicians is how to modify their diet to manage their condition and improve their quality of life (QoL) (1–7). Unfortunately, data supporting particular approaches is weak, and dietary recommendations largely remain based on trial and error (1).

Recent technological advances in multiomics platforms for data collection and analysis have provided evidence of the relationships between dietary intake, gut microbiome composition, mucosal homeostasis, immune responses, and microbial metabolite production (1,3,6,8–10). Removing dietary triggers has been shown to provide symptomatic relief in IBS and be as effective as medical therapy for the management of IBD in certain populations (11–15). Other studies have indicated further relationship between diet, clinical outcomes, and patient QoL (1).

It has historically been difficult to personalize, simplify, and scale dietary interventions while maintaining their potential symptomatic and QoL benefits (16,17). One major challenge is that IBS and IBD are heterogeneous conditions, and patients often respond differently to the same food. One-size-fits-all dietary recommendations are

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therefore not optimal. Nutrition plans must be tailored to the biological, lifestyle, and clinical characteristics of individual patients (1). An emerging field of interdisciplinary study, precision nutrition, may offer a potential solution: using digital technology, behavioral science, metabolomics, microbiomics, and genetics to build a personalized diet for each patient based on the measurement and/or prediction of individual responses to foods (18,19).

In this context, elimination diets such as the low-fermentable oligosaccharide, disaccharide, monosaccharide, and polyol diet (FODMAP) are often used to personalize a nutrition plan for symptomatic amelioration (17). These diets involve the sequential elimination and reintroduction of common foods associated with gastrointestinal distress, such as lactose, fructose, and polyols (9). Through this experimentation, patients identify personal trigger foods that exacerbate symptoms and then remove them from daily intake. Studies on elimination diets show evidence of IBS and IBD symptom amelioration: 50%–80% of patients experience some benefits compared with using a habitual diet (20). However, these diets are time-consuming, highly complex to implement, nutrient-restrictive, and often do not meet the personalization goals patients have come to expect in a digital world (16,20–22). Combined, these factors contribute to partial (<40%) or complete noncompliance in clinical practice (20,21).

Digital tools are increasingly being leveraged in clinical practice to improve adherence, optimize care, and gather and analyze critical data to provide the right care to the right patient at the right time. However, the application of these technologies to gastroenterology remains largely unstudied (23–25). In addition, and despite the significant (~40%) overlap between IBS and IBD diagnosis reported in the literature, the effect of diet on comorbid IBS/IBD is also underexamined (26,27). Recent advances in smartphone-based digital technologies and machine learning analysis tools present an opportunity to modernize, simplify, and increasingly personalize the standard approaches to elimination-based dietary intervention for patients with GI (1,23,28). This study investigated the effect of an interactive, mobile-delivered elimination diet program powered by machine learning on IBS and comorbid IBS/IBD symptoms, QoL, and diet adherence.

METHODS

This was a decentralized, single-center, open-labeled, uncontrolled, prospective cohort study conducted over 9 weeks. Participants were recruited online through social media (Facebook, Reddit, and Instagram). All participants provided written informed consent and received financial compensation. The study and all associated materials were approved by the Advarra Institutional Review Board (protocol #50728).

Two study populations were eligible for inclusion: adults aged 18–65 years previously diagnosed by a gastroenterologist with IBS (Rome III criteria for any subtype) and patients with comorbid IBS and IBD with Crohn's disease (CD) or ulcerative colitis (UC) established by endoscopic, histologic, and radiologic criteria. Both study populations were required to self-report their diagnosis and report experiencing active symptoms; patients with comorbid IBS/IBD were required to report both active IBS and IBD symptoms, measured by the appropriate symptom severity score. Minimum symptom activity was determined by the appropriate condition-specific symptom severity score: IBS symptom severity score (IBS-SSS) ≥150 for IBS, Simple Crohn's Disease Activity Index (sCDAI) ≥175 for CD, and Patient Simple Clinical Colitis Activity Index (P-SCCAI) ≥2 for UC (29–32). Exclusion criteria included pregnancy, significant comorbidities, disease duration <1 year, current use of tobacco, narcotics, or cannabis, a history of eating disorder, ostomy, pouch or known symptomatic intestinal stricture, current use of a restricted diet (e.g., low FODMAP or other), and recent (within 6 months) start or change of GI prescription medication. Patients with dual IBS/IBD currently on steroids were excluded. A minimum of 20 participants was estimated to provide 80% power to detect clinically significant symptom improvement; 39 participants were recruited (14,15,33,34).

Intervention

Over 9 weeks, participants were guided through 4 experimental phases of the personalized elimination diet: identification, elimination, reintroduction, and maintenance. A secure digital survey was sent to patients each morning of the study period through

Table 1. Tabular representation of the study protocol, indicating the activities conducted in each phase, length of each phase, and how each machine learning algorithm is used

Sample timeline		
Phase	**Week**	**Activity**
Machine learning algorithm 1: suggests a unique list of 21 likely trigger foods for each participant, using clinical and demographic data		
1: Identify	1 2 3	Patients eat normally and complete daily symptom and diet surveys
Machine learning algorithm 2: identify 3–5 foods that may be associated with an individual study participant's IBS/IBD symptoms and suggest they remove these from their diet in phase 2		
2: Eliminate	1 2	Patients remove the suggested foods from their diet and complete daily symptom and diet surveys
3: Reintroduce	1–2 (3 d per reintroduction)	Every 3 days, study participants reintroduce another potential trigger food and complete daily symptom and diet surveys throughout
Output: final description of a low-restriction diet that may measurably improve a participant's IBS or comorbid IBS/IBD symptoms		
4: Maintenance	1 2	Patients eat modified diet from study and complete daily symptom and diet surveys

IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

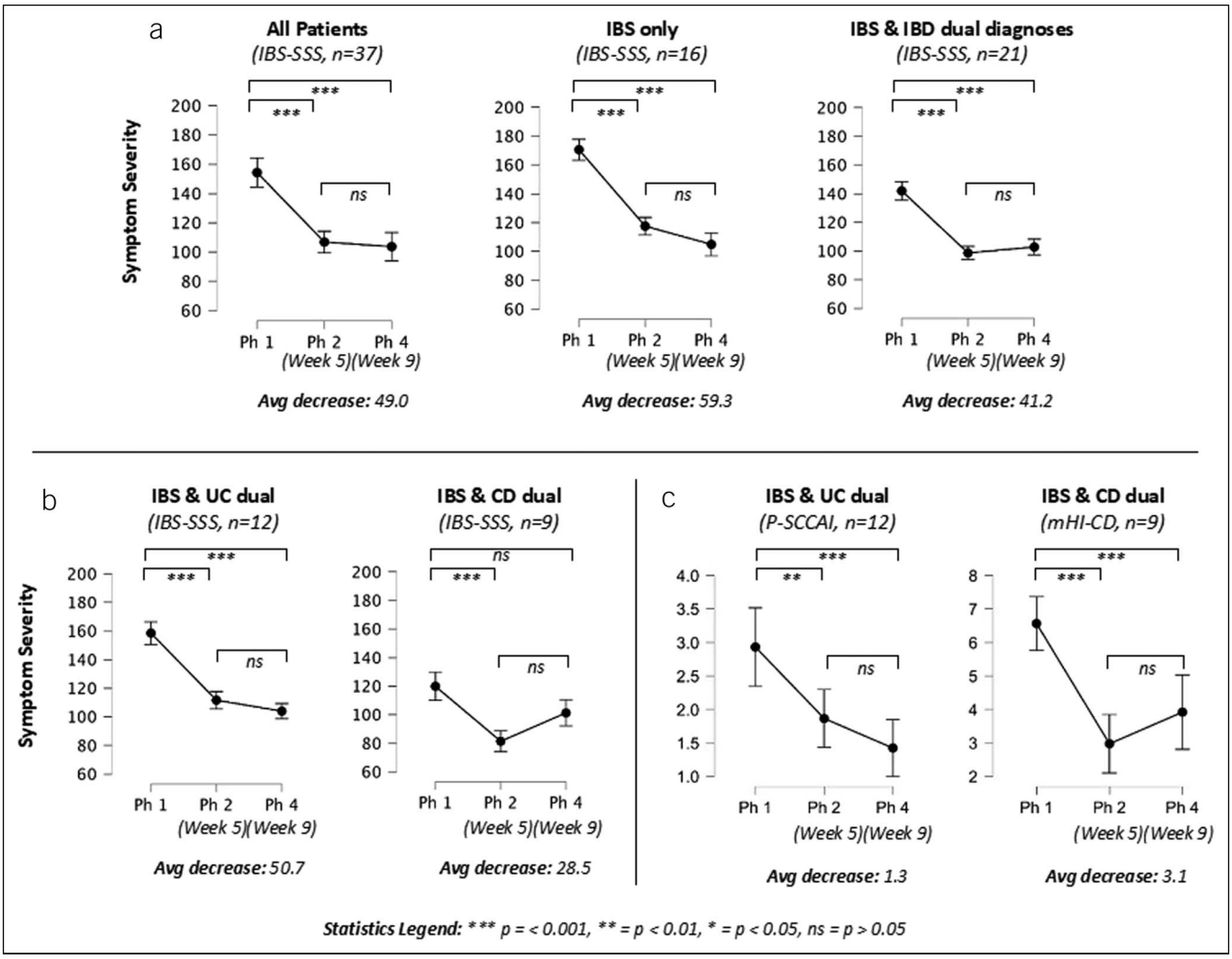

Figure 1. Symptom severity scores measured at phases 1 (baseline), 2 (study midpoint), and 4 (study conclusion) for all patients and for IBS, dual IBS/UC, and dual IBS/CD patient subgroups. In (**a**) IBS symptom severity scores for all patients (n = 37), patients with single IBS diagnosis (n = 16), and patients with dual diagnoses (n = 21) show significant improvement, and this symptom relief was maintained over 9 weeks. In (**b**) IBS symptom severity scores for patients with dual IBS/UC and IBS/CD show significant improvement only in IBS/UC participants, maintained for 9 weeks. In (**c**) UC and CD symptom severity scores show significant improvement relative to baseline, maintained over 9 weeks. Statistical significance of symptom improvement measured by 1-way repeated measures ANOVA and Bonferroni-corrected post hoc analyses; error bars represent 95% confidence intervals. Symptom severity represented as absolute score for the appropriate symptom severity score (IBS-SSS, mHI-CD, and P-SCCAI). CD, Crohn's disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Score; mHI-CD, Mobile Health Index for CD; P-SCCAI, Patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.

encrypted text message/SMS (35). Patient-reported outcomes, clinical symptom severity scores, dietary intake, and demographic data were analyzed using machine learning to dynamically guide patients from phase to phase.

A systematic literature review was conducted by 2 authors using efficacy studies on the diets previously described, clinical practice guidelines, meta-analyses on dietary approaches to IBS and IBD management, and survey studies on the daily dietary practices of patients with IBS and IBD (3–5,10,16,17,21). Data from a total of 4,565 patients with IBS, 1,560 patients with IBD, and 2,993 health controls were included in the analysis. Using these pooled records, we generated an aggregated list of 246 frequently eliminated trigger foods (e.g., alliums, legumes, cultured dairy, and caffeine), mapped to the aggregated clinical and demographic characteristics (e.g., diagnosis, disease subtype, age, and length of disease course) reported in each study. Guiding principles derived by this relational database were used to supervise a set of sequential weighing, sorting and downsampling algorithms (leveraging feedback-based recursion) to assign each patient a unique set of 21 high-potential trigger foods they would track in phase 1. Each unique list of trigger foods was reviewed by a dietitian for nutritional adequacy.

During phase 1 (3 weeks), participants ate their regular diet and completed a daily digital survey with questions about GI symptoms and a 24-hour recall of their unique list of 21 trigger foods eaten (30,31,36). Patients with IBS completed the IBS-SSS; patients with comorbid IBS/IBD completed both the daily IBS-SSS and appropriate IBD score (P-SCCAI for UC or the Mobile Health Index for CD, mHI-CD) (26,27).

Using diet and symptom data gathered in phase 1, a supervised machine learning algorithm (using a combination of gradient

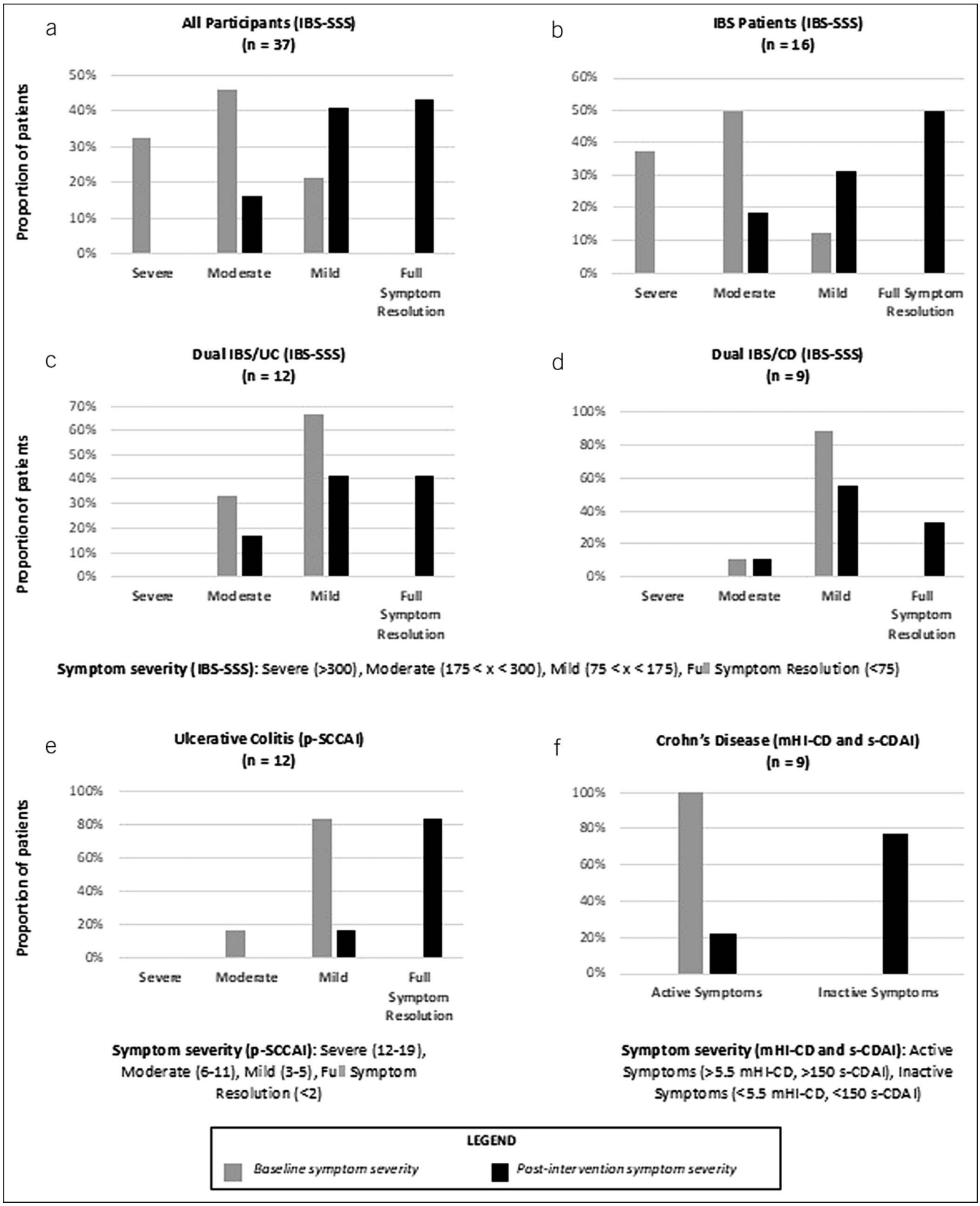

Figure 2. Analysis of clinical symptom improvement from baseline for all patients (**a**, n = 37), patients with IBS only (**b**, n = 16), patients with dual IBS/UC (**c** and **e**, n = 12), and patients with dual IBS/CD (**d** and **f**, n = 9). Proportion of participants classified by severity of GI symptoms at baseline in gray are compared with their postintervention symptom severity classification in black. Relative to baseline, clinical symptom improvement was seen in each diagnosis subgroup, and 25 participants (67.6%) achieved symptomatic remission by end of study. CD, Crohn's disease; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Score; mHI-CD, Mobile Health Index for CD; P-SCCAI, Patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.

Table 2. Demographics and baseline clinical characteristics of study participants (n = 37)

Baseline characteristic	
Age, avg (range)	37 (19–57)
Sex, n (%)	
Female	23 (62)
Male	14 (38)
Ethnicity, n (%)	
White	27 (73)
African American	5 (14)
Hispanic	2 (5)
Native Hawaiian/Pacific Islander	1 (3)
Asian American	2 (5)
Diagnosis, n (%)	
IBS only	16 (44)
Crohn's disease and IBS	9 (24)
Ulcerative colitis and IBS	12 (32)
IBS subtype	
IBS-diarrhea	25 (68)
IBS-constipation	4 (11)
IBS-mixed	8 (21)
Baseline symptom severity, avg (95% CI)	
All patients, IBS-SSS	154 (±18)
Patients with IBS only, IBS-SSS	171 (±29.7)
IBS and CD, IBS-SSS	120 (±20.1)
IBS and ulcerative colitis, IBS-SSS	160 (±27.6)
CD, CDAI	214 (±70)
CD, mHI-CD	6.6 (±0.9)
UC, P-SCCAI	2.9 (±0.7)

Descriptive statistics defined in the table.
CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Score; mHI-CD, Mobile Health Index for CD; P-SCCAI, Patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.

descent, regularization, and recursive elements) predicted the 3–5 trigger foods most strongly associated with adverse symptoms. In phase 2 (2 weeks), participants eliminated these foods from their diets and completed the same daily survey to measure adherence and effect on symptomatology. Subsequently, participants were guided to reintroduce eliminated foods in phase 3, 1 at a time, every 3 days, each day increasing food intake by 1 serving (~1–2 weeks) (17). Participants continued to complete daily surveys; if daily symptom scores increased by ≥25%, participants paused their reintroduction until symptoms abated to phase 2 baseline values. After reintroduction, participants implemented their modified diet (removing trigger foods identified in phase 1–3) for an additional 2 weeks in phase 4. A tabular view of the protocol is summarized in Table 1.

At study midpoint and end, participants completed qualitative assessments of their energy/alertness, stress, physical activity, QoL, other patient-reported outcomes, and subjective evaluations of the program's desirability using a 5-point Likert scale through secure digital survey (37).

Outcome measures

Primary and secondary endpoints were collected at midpoint (week 5) and study completion (week 9). The primary outcome was symptomatic improvement measured in 4 ways: statistical and clinical significance of symptom improvement, achievement of total symptomatic resolution, and persistence of symptom amelioration.

Symptoms were measured by the appropriate symptom severity score (IBS-SSS for IBS, P-SCCAI for comorbid IBS/UC, and mHI-CD for comorbid IBS/CD). Statistically significant changes were evaluated by appropriate statistical analysis. Clinically significant symptom improvement was defined as a ≥1-point reduction in P-SCCAI, a ≥30% reduction of mHI-CD, and a ≥35-point reduction of IBS-SSS (31,36,38). Symptomatic resolution was defined as a P-SCCAI <2, mHI-CD <5.5, and an IBS-SSS <75 (30–32,36). Neither inflammatory biomarkers nor endoscopic data were gathered for patients with comorbid IBS/IBD; the concurrent measurement of IBS and IBD symptoms were used to indicate net effect on QoL and indicate areas for further research. Maintenance of symptom improvement from baseline to end of study was measured to evaluate persistence. Additional self-reported outcomes were also measured, including effect on disease knowledge and overall well-being. For these metrics, a majority (≥60%) of participants responding "agree" or "strongly agree" in a 5-point Likert scale was considered successful (37).

Secondary endpoints related to this program's feasibility and desirability. Feasibility was measured by participant engagement, retention, and adherence. Engagement was measured by daily completion of surveys and participant retention. Adherence to study protocol was measured by the percentage reduction of trigger food intake and number of days compliant with program recommendations.

Desirability was measured through the net promoter score (NPS), which categorizes responders into 3 groups: "promoters" who recommend the tool, "passives" who are happy but would not actively promote it, and "detractors" who actively discourage others to use it. NPSs were calculated by subtracting the percentage of detractors from the percentage of promoters (score range −100 to +100) (39). An NPS ≥0 and a patient satisfaction score >50% was defined as "desirable" (39).

Statistical analysis

A P value of <0.05 was considered statistically significant for primary and secondary outcomes. Descriptive statistics were reported as averages, medians, counts, or percentages. Analyses included those who completed all baseline and follow-up assessments.

To evaluate primary end points, repeated measures ANOVAs with post hoc, Bonferroni-corrected, 2-tailed paired-sample t tests were used to compare symptom severity in phase 1 with symptom severity following trigger food elimination and maintenance (phases 2 and 4). Effect size of symptomatic relief was measured using partial eta squares (petasq), which can be benchmarked against Cohen criteria of small (0.01), medium (0.06), and large (0.14) effects (40,41). Statistical analysis was conducted at both the individual level and group level (age quartile, sex, ethnicity, GI condition, and symptom severity at intake). Qualitative data were analyzed using the McNemar χ^2

test with Yates continuity correction. Descriptive statistics were used to measure secondary end points. All statistical analyses were conducted on a local copy of STATA (Release 17 for MacOS) and JASP (version 0.16 for MacOS) (42,43).

RESULTS

Participants

Sixty-seven potential participants were screened. Twenty-six failed to meet eligibility criteria, and 2 eligible individuals elected not to participate. Thirty-nine eligible participants started the study. Two patients withdrew (at week 2 and week 3) because they no longer wished to participate. Nine-week retention was 95%. Analysis was conducted on the 37-member cohort that completed the study (16 IBS-only, 12 IBS/UC, and 9 IBS/UC). Participant characteristics are detailed in Table 1; no changes to medications or other confounding variables were observed during the study period.

Primary outcomes

The digital personalized elimination diet program improved IBS and comorbid IBS/IBD symptoms statistically and clinically significantly for most participants. Most participants achieved total symptomatic resolution; symptom relief persisted for the entire study period.

Statistically significant symptom improvement ($P < 0.001$ Bonferroni-corrected 2-tailed *t* test) was seen for 81% of participants at week 5 and persisted for 70% of participants at week 9, measured by the relevant symptom severity score (note: week 5 vs 9 $P = 0.34$, the McNemar test). By the end of the study, patients with IBS (n = 16) improved symptoms by an average 59.3 points (IBS-SSS, $P < 0.001$, petasq = 0.62). Patients with dual IBS/UC (n = 12) improved by an average 1.3 points on the P-SCCAI ($P < 0.001$, petasq = 0.53) and 50.7 points on the IBS-SSS ($P < 0.001$, petasq = 0.65). Patients with dual IBS/CD (n = 9) improved by an average 3.1 points on the mHI-CD ($P < 0.001$, petasq = 0.72) and 28.5 points on the IBS-SSS ($P = 0.02$, petasq = 0.37), evaluated by 1-way repeated-measures ANOVA (Figure 1).

IBD symptom scores in dual-diagnosis patients were significantly more sensitive to the intervention than IBS scores (55% P-SCCAI improvement vs 36% IBS-SSS improvement, $P < 0.05$; 41% mHI-CD improvement vs 15% IBS-SSS improvement, $P < 0.05$). Symptom improvement was maintained successfully 4 weeks after the identification and elimination of trigger foods for patients in each condition group (Figure 1). In patients with IBS only, symptom improvement was maintained from study midpoint to end (average IBS-SSS 117.6 and 104.9, respectively, compared with 170.6 at baseline, $P < 0.001$). Both IBS and UC symptom improvement in patients with dual IBS/UC were maintained over 4 weeks (average P-SCCAI 2.9, 1.9, 1.4 at baseline, midpoint, and end point, respectively, $P < 0.007$; average IBS-SSS 158.5, 111.7, and 104.0, at baseline, midpoint, and end point, respectively, $P < 0.001$). In patients with dual IBS/CD, CD symptom improvement was maintained (mHI-CD 6.6, 3.0, 3.9 at baseline, midpoint, and end point, respectively, $P < 0.001$), but IBS symptom relief was not (120.0, 81.4, and 101.3, at baseline, midpoint, and end point, respectively, $P = 0.47$), calculated through Bonferroni-corrected post hoc analysis.

Seventy-eight percentage of participants saw clinically significant symptom improvement at week 5 and 62% at week 9 (week 5 vs 9 $P = 0.18$, the McNemar test). Twenty-five participants (67.6%) achieved symptomatic resolution by the end of the study (50%, 62.5%, and 77.8% of IBS, IBS/UC, and IBS/CD cohorts, respectively) (Figure 2). Patients were 14 times more likely to have fully resolved symptoms at study end compared with those during baseline ($P < 0.001$, the McNemar test). No significant difference was observed between study midpoint and end point ($P = 0.15$), indicating a persistence of clinically significant symptomatic relief. Statistically and clinically significant symptom improvement was observed regardless of sex, age quartile, severity at intake, and ethnicity (Table 2). Patient-reported outcomes related to disease

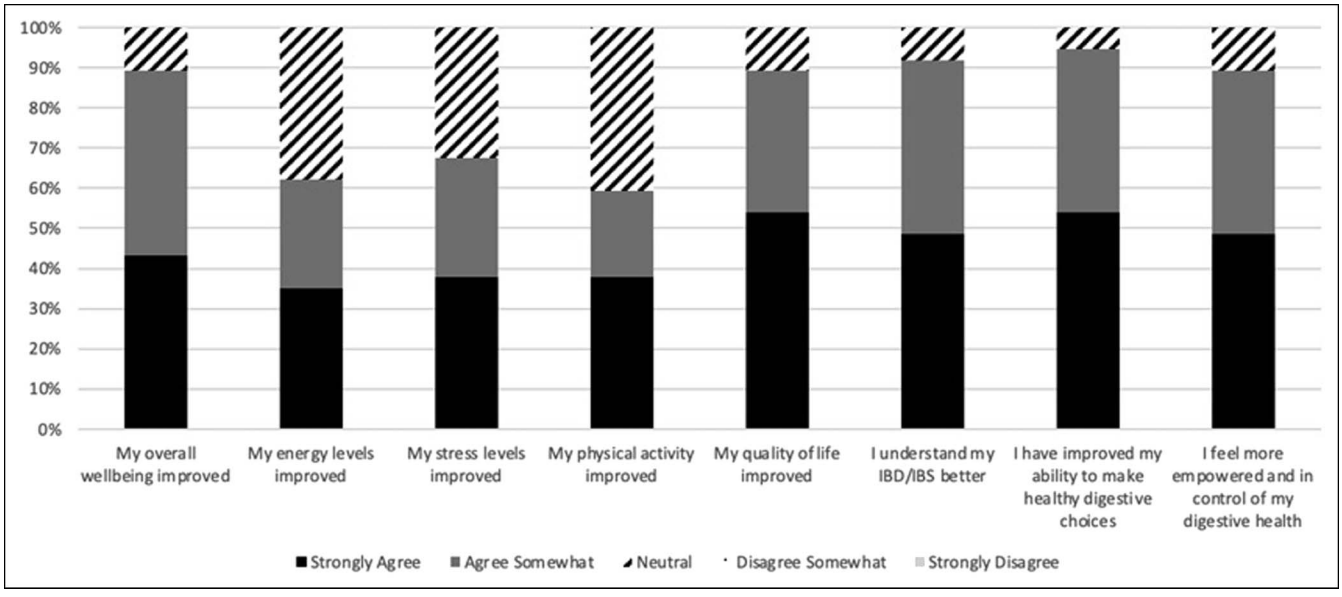

Figure 3. Analysis of 5-point Likert scale (strongly agree, agree somewhat, neutral, disagree somewhat, and strongly disagree) responses of participants to key patient-reported outcomes statements. Reponses are represented as percentage of responses by Likert category. A large majority of study participants reported improved outcomes (ability to make healthy digestive choices, understanding of their GI condition, control over their digestive health, quality of life, etc). No participant selected Likert categories related to disagreement. GI, gastrointestinal.

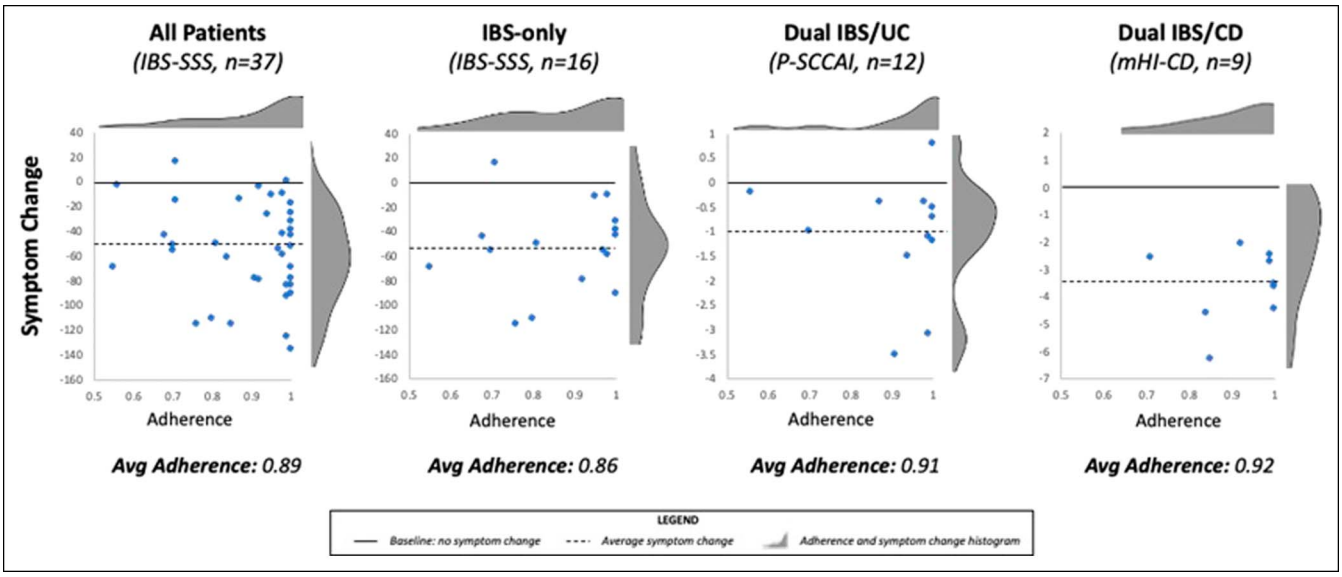

Figure 4. Analysis of adherence to study protocol (phase 2, elimination) and associated symptom change for all patients and each diagnosis subgroup (IBS, dual IBS/UC, and dual IBS/CD). Symptom change reported in absolute numbers (negative represents symptom improvement, positive represents symptom exacerbation). Adherence reported as normalized percentage (0–1) where 0 = no reduction of trigger food intake and 1 = total elimination of trigger food intake. Distribution of symptom change (y axis) and protocol adherence (x axis) are reported in a histogram for each analysis. Participants eliminated most of their trigger foods from their diet during phase 2 (89%–92% reduction of intake). Higher adherence to the elimination of trigger foods in phase 2 was not associated with increased symptom improvement due to the homogeneity in adherence. CD, Crohn's disease; GI, gastrointestinal; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Score; mHI-CD, Mobile Health Index for CD; P-SCCAI, Patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.

knowledge, QoL, overall well-being, and 5 other factors also demonstrated strong improvement (Figure 3).

Secondary outcomes

Patients reported the diet program was feasible and desirable. Ninety-five percentage daily engagement (completed surveys) and 89% adherence with the protocol were observed. Participants reduced their intake of suggested trigger foods by 89.3% on average during the elimination phase (89% ± 13%); adherence was significantly left-skewed (skewness = −1.3, SE = 0.39). Higher adherence during trigger food elimination was not associated with increased symptom improvement ($P = 0.62$, 0.70, and 0.76 for IBS, UC, and CD, respectively) due to homogeneous adherence (Figure 4). Eighty-nine percentage of participants (n = 33) were fully or partially adherent to the reintroduction protocol. Eighty-five percentage of those participants (n = 28) were able to

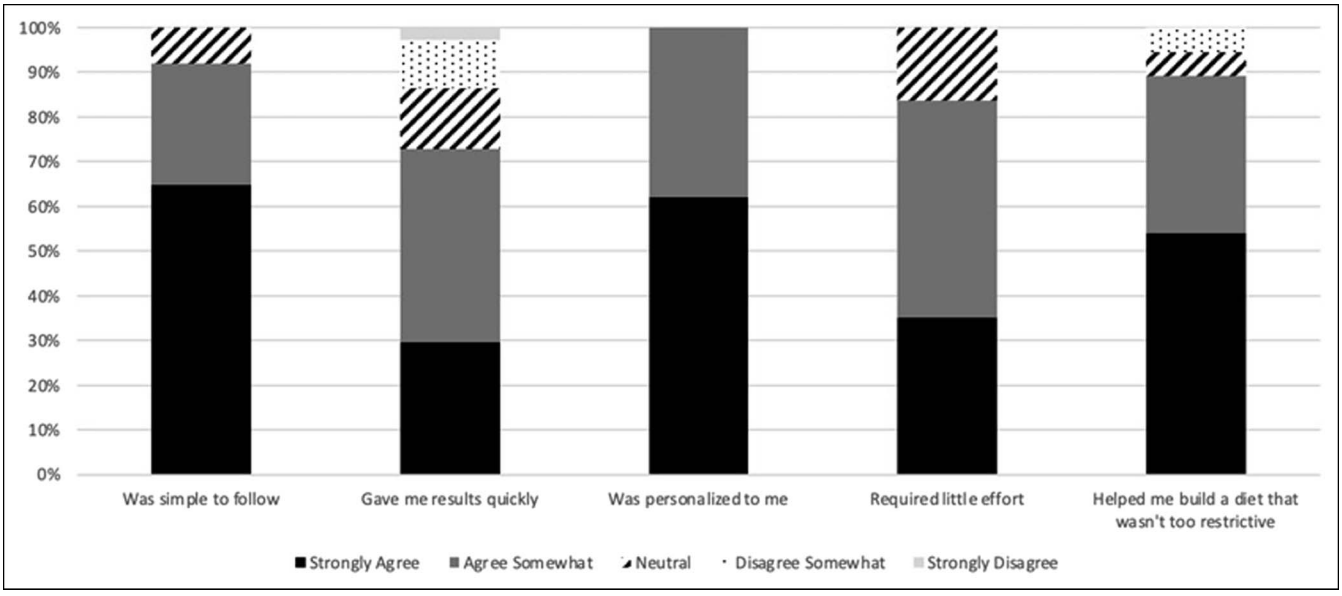

Figure 5. Analysis of 5-point Likert scale (strongly agree, agree somewhat, neutral, disagree somewhat, and strongly disagree) responses of participants to key desirability and feasibility statements. Reponses are represented as percentage of responses by Likert category. Most of the study participants reported the program was low effort, quick to execute, personalized to their unique characteristics, and generated a low-restriction diet.

Table 3. Analysis of symptom improvement by cohort (age, gender, and symptom severity at baseline and ethnicity) using the appropriate symptom severity score (IBS-SSS, mHI-CD, and P-SCCAI)

Participant cohort	Average net change (phases 1–4)	Average percentage change (phases 1–4)	*P* value
All participants (IBS-SSS)	−62.13[a]	−38.42	<0.001[b]
Gender			
All male participants (IBS-SSS)	−50.79[a]	−34.00	<0.001[b]
All female participants (IBS-SSS)	−57.04[a]	−33.51	<0.001[b]
IBS-only male (IBS-SSS)	−31.00[a]	−22.00	<0.01[b]
IBS-only female (IBS-SSS)	−61.50[a]	−35.51	<0.001[b]
Dual IBS/CD male (mHI-CD)	−4.13	−65.00[a]	<0.001[b]
Dual IBS/CD female (mHI-CD)	−0.80	−27.59	0.148
Dual IBS/UC male (p-SCCAI)	−1.20[a]	−41.00	<0.001[b]
Dual IBS/UC female (p-SCCAI)	−3.32[a]	−49.88	<0.001[b]
Age quartile (IBS-SSS)			
First quartile	−49.33[a]	−27.26	<0.001[b]
Second quartile	−55.18[a]	−34.75	<0.001[b]
Third quartile	−52.80[a]	−41.12	<0.001[b]
Fourth quartile	−63.43[a]	−33.56	<0.001[b]
IBS severity at intake (IBS-SSS)			
First quartile	−36.33[a]	−35.16	<0.001[b]
Second quartile	−54.64[a]	−39.31	<0.001[b]
Third quartile	−43.25[a]	−24.91	<0.001[b]
Fourth quartile	−83.22[a]	−35.08	<0.001[b]
UC severity at intake (P-SCCAI)			
First quartile	−0.17	−11.63	0.67
Second quartile	−0.97	−43.28	<0.01[b]
Third quartile	−1.57[a]	−43.93	<0.05[b]
Fourth quartile	−1.57[a]	−34.81	<0.05[b]
CD severity at intake (mHI-CD)			
First quartile	−3.10	−67.07[a]	<0.001[b]
Second quartile	−4.35	−66.31[a]	<0.001[b]
Third quartile	−3.59	−50.06[a]	<0.001[b]
Fourth quartile	−2.99	−37.47[a]	<0.005[b]
Ethnicity (IBS-SSS)			
White	−52.00[a]	−30.91	<0.001[b]
Non-White	−61.90[a]	−42.96	<0.001[b]

CD, Crohn's disease; CI, confidence interval; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-SSS, IBS Symptom Severity Score; mHI-CD, Mobile Health Index for CD; P-SCCAI, Patient Simple Clinical Colitis Activity Index; UC, ulcerative colitis.
[a]Clinically significant.
[b]Statistically significant.

reidentify at least 1 trigger food during reintroduction; these individuals reduced intake of trigger foods in the maintenance phase by an average of 65% relative to baseline.

Participants indicated this program was highly desirable: 92% of patients were satisfied with the program, and the NPS was 79. All other desirability sentiments were well-reviewed (Figure 5).

Every participant indicated the program was personalized to their unique characteristics; indeed, no significant trends were observed regarding trigger foods commonly identified by participant groups. Statistical analysis by condition, sex, age, and severity of symptoms at intake indicated every diet created by participants was entirely unique to that participant ($P = 0.67$, 0.92, 0.98, and 0.92, respectively). The algorithm was successfully able to identify a single diet recommendation for each patient from 2,441,880 possible combinations (Table 3).

DISCUSSION

This study investigated the effect, feasibility, and desirability of a novel personalized, digital elimination diet program powered by machine learning. Over 9 weeks, patients were guided through 4 experimentation phases to identify and eliminate a personalized set of trigger foods hypothesized to be exacerbating their IBS and/or IBD symptoms. A majority (>70%) of participants showed statistically significant, clinically significant, and persistent improvement in symptoms; most participants achieved total resolution of symptoms. These results seem to improve on other studies on elimination diets and suggest the machine learning algorithms were useful in this context (20,21,44).

This is the first example of a precision dietary intervention for patients with IBS and dual IBS/IBD that personalizes nutrition recommendations to an individual's unique biological, lifestyle, and clinical profile (23,24). The digital nature of the program and the degree of personalization offer several crucial advantages over existing dietary interventions.

First, digitizing program delivery enables a greater degree of personalization than manual techniques. This program's machine learning algorithm identified unique patient-level patterns from large, complex dietary and symptom data sets to predict personal responses to foods. No 2 final diets generated by the program were the same, providing further evidence that individuals likely respond to foods heterogeneously and emphasizing the need to personalize nutritional interventions to an individual rather than a group level (1,17,28). For example, 1 patient identified onions, cashews, and cream as triggers; another identified artificial sweeteners, apples, and carbonated beverages. Personalization also made the final diets less restrictive, which allowed patients to eat a more nutritionally diverse set of foods compared with elimination diets such as FODMAP (20,45,46).

Second, the program's personalization and digitization contributed to considerably higher levels of compliance (89%) relative to other dietary interventions (16%–50%) (46,47). This was likely related to lower diet restrictions and automated guidance, both of which reduced cognitive burden on patients (1). Compliance may also be due to participants interacting with the tool to create a diet for themselves; the active involvement of patients in their own medical decision-making has a positive impact on adherence and outcomes (48–51).

Finally, this program showed strong engagement, satisfaction, and usability metrics. The NPS for this program was 79, significantly higher than commercial and healthcare benchmarks (39). Although the basis for these results is multifactorial, frequent feedback from the digital platform seems to be a meaningful contributor.

This study has several limitations. As a small, single-center, uncontrolled pilot study, suggestibility effects cannot be ignored; the use of patient-reported outcomes, broad inclusion criteria, and the 9-week duration of this study help reduce the potential effect of this variable (52–54). The small sample size of this pilot study limits the ability to generalize these results to a broader population, but the large effect sizes observed is compelling evidence that this tech-enabled approach to diet is a promising future direction for clinical research. Self-reporting bias may also be a limitation, but primary outcomes were measured based on clinically validated symptom severity scores rather than self-reported symptom improvement. Furthermore, inflammatory markers were not included in this analysis; consequently, it is difficult to determine whether the benefit seen in patients with dual IBS/IBD was due to an anti-inflammatory effect. Despite this, IBD symptom scores were significantly more sensitive to this intervention than the IBS-SSS, indicating potential effect on inflammation. Furthermore, both IBS and IBD symptom scores improved significantly from baseline, indicating an improvement in QoL for dual-diagnosis patients. Finally, patients were recruited online, potentially selecting for people already comfortable with digital tools and interested in dietary modification.

This program is a step forward in the evaluation and implementation of precision nutrition for IBS and comorbid IBS/IBD. Further research, including randomized controlled trials over longer durations with larger sample sizes, is warranted to determine the effectiveness and durability of digital and personalized dietary interventions.

CONFLICTS OF INTEREST

Guarantor of the article: Samuel N. Jactel, MBA.
Specific author contributions: All authors contributed to study design. Study was conducted by J.O. and S.N.J. under the supervision of K.W., V.J., J.B., and J.K. Data analysis was conducted by J.O. and M.P. Manuscript was written by J.B., J.O., S.N.J., and M.P., with input from all coauthors. All authors had access to the study data and have reviewed and approved the final manuscript. All authors have reviewed and approved the final draft of this manuscript.
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Potential competing interests: S.N.J. is an officer at Ayble Health with stock options. The remaining authors disclose no conflicts.

Study Highlights

WHAT IS KNOWN

- ✓ A majority of patients with irritable bowel syndrome (IBS) and comorbid IBS/inflammatory bowel disease (IBD) report symptomatic exacerbation due to diet.
- ✓ Personalized elimination diets can improve symptoms for patients with IBS and comorbid IBS/IBD.
- ✓ No previous research has investigated the application of digital tools to improve elimination diets.

WHAT IS NEW HERE

- ✓ This is the first example of a digitally delivered elimination diet program that personalizes nutrition recommendations.
- ✓ The program was associated with improved symptoms and symptomatic resolution in patients with IBS and comorbid IBS/IBD.
- ✓ Patients reported high levels of engagement, satisfaction, and adherence to the program.

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