Virtual Gastrointestinal Care Solutions — Appendices

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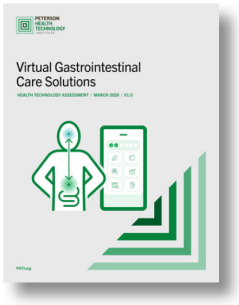
Accessing PHTI's Full Report

You can access the full report here.



Appendix A – Methodology Overview

This evaluation of virtual solutions for gastrointestinal (GI) conditions followed the Peterson Health Technology Institute's (PHTI) published assessment methodology, using the ICER-PHTI Assessment Framework for Digital Health Technologies, and stakeholder engagement process. Additional information about PHTI's process and advisors can be found at phti.org.

Assessment Framework

PHTI partnered with the Institute for Clinical and Economic Review (ICER), a leader in health technology assessment, to develop the ICER-PHTI Assessment Framework for Digital Health Technologies that guides this and all other PHTI evaluations. The assessment framework prioritizes products' clinical benefits and economic impact, while also considering effects on health equity and user experience. The selection process for which technologies are evaluated are based on several factors, including market relevance, disease burden, level of spend and claimed savings, and evidence quality and availability.

PHTI's goal is to provide decision makers with relevant information to inform digital health purchasing and innovation that improves overall health system performance and delivers better health outcomes at lower costs. By helping purchasers identify bright spots in digital health innovation, PHTI aims to raise the bar for technology-driven advances in healthcare delivery, including superior outcomes, convenience, access, and affordability. The assessment framework can also guide technology developers and investors about performance standards, and the evidence needs required to demonstrate stated clinical and economic benefits.

Clinical Assessment

A systematic literature review (SLR), including online database searches, data screening and extraction, and evidence quality ratings, was conducted by a third-party health technology assessment partner to identify all relevant published literature evaluating clinical impact of virtual solutions for OUD. The SLR was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This SLR followed the methods and standard set forth in the ICER-PHTI Assessment Framework to provide a rigorous evaluation of digital health technologies. The SLR was registered a priori with PROSPERO (CRD420251066790).

Data from two literature databases, MEDLINE and EMBASE, were systematically searched for inclusion into the SLR. Conference proceedings were hand-searched to retrieve relevant publications. Potentially eligible studies were identified via the search strategy outlined in Table 1 and Table 2 below. Studies were considered for inclusion in the SLR based on the population, intervention, comparators, outcomes, and setting/study design (PICOS) criteria presented in Table 3 below.

The SLR included a review of the "grey" literature, which captured data from sources not indexed and that are available from scientific conferences, the US Food and Drug Administration (FDA) website, and 510 clearances, company websites, and information provided by companies under review.

Table 1. Medline Search Strategy

Search	Terms	Citations
#1 – Clinical Indications (GI)	("abdominal pain" or "abdominal discomfort" or "gut pain" or "constipat*" or "diarrhea" or "bloat*" or "cramp*" or "flatulence" or "bowel habit*" or "gas" or "reflux" or "nausea" or "vomit*" or "bowel control" or "FGID" or "functional gastrointestinal disorder*" or "gastrointestinal disease*" or "gastrointestinal disorder*" or "gastroenterology" or "weight?loss" or "rectal bleed*" or "fecal incontinence" or "bowel incontinence" or "belch*" or "regurgitat*" or "eructat*" or "heartburn" or "malnutrition" or "tenesmus" or "epigastric pain" or "epigastric burning" or "FODMAP" or "steatosis" or "dyspepsia" or "steatorrhea" or "hepatic fibrosis").ti,ab	904,197
#2 – Clinical Indications (IBD)	*irritable bowel disease/ or *crohn disease/ or *ulcerative colitis/ or *inflammatory bowel disease/ or ("irritable bowel disease" or "IBD" or "ulcerative colitis" or "crohn* disease" or "inflammatory bowel disease").ti,ab	143,640
#3 – Clinical Indications (IBS)	*irritable bowel syndrome/ or ("irritable bowel" or "IBS" or "irritable colon").ti,ab	21,311
#4 – Indication Combination	**1** or **2** or **3**	1,043,711
#5 – Digital or Virtual Solution	("digital care" or "digital health" or "digitial digestive chronic care" or "digital digestive care" or "digital therapeutic* care" or "digital therap*" or "ai?enabled" or "artifical intelligence" or "mobile application" or "virtual care" or "diet planning" or "diet logging" or "patient?facing app*" or "patient?facing portal*" or "symptom tracking" or "health coach*" or "personali?ed medical nutrition" or "subscription?based" or "holistic medicine" or "tele?health" or "digital technolog*").ti,ab	36,871
#6 – Artificial Intelligence	*artificial intelligence/	33,910
#7 – Mobile Application	*mobile application/	12,251
#8 – Telemedicine	*telemedicine/	37,402
#9 – Solution Combination	**5** or **6** or **7** or **8**	105,977
#10 – Publication Type Exclusions	NOT ("case report" or "comment" or "editorial" or "letter" or "review" or "clinical trial protocol").pt.	5,736,104
#11 – Nonhuman Studies Exclusions	NOT ("animal*" or "non?human" or "animal experiment*" or "animal model*" or "in vitro study" or "menstrual" or "pregnan*" or "chemotherap*" or "cancer" or "transplant*" or "colonoscop*" or "thyroid*" or "covid" or "coronavirus" or "oil and gas" or "gas industr*" or "greenhouse gas*" or "diabetes" or "vaccine*" or "chatbot" or "chatgpt" or "urinary tract infection" or "UTI").ti,ab	6,466,970
#12 – Total Exclusions	10 or 11	11,063,248
#13 – Final Combination	**4** (Indication Combination) and **9** (Solution Combination)	1,260
#14 – Final Combination + Exclusions	**13** NOT **12** (Indication + Solution Combinations + NOT Exclusion Combination)	642
#15 - Date Filter	Filter 2015 – 2025	515
#16 - Language Filter	Filter Language: English	504
#17 - Remove Duplicates	FINAL COUNT	497

Table 2. EMBASE Search Strategy

Search	Terms	Citations
#1 – Clinical Indications (GI)	("abdominal pain" or "abdominal discomfort" or "gut pain" or "constipat*" or "diarrhea" or "bloat*" or "cramp*" or "flatulence" or "bowel habit*" or "gas" or "reflux" or "nausea" or "vomit*" or "bowel control" or "FGID" or "functional gastrointestinal disorder*" or "gastrointestinal disease*" or "gastrointestinal disorder*" or "gastroenterology" or "weight?loss" or "rectal bleed*" or "fecal incontinence" or "bowel incontinence" or "belch*" or "regurgitat*" or "eructat*" or "heartburn" or "malnutrition" or "tenesmus" or "epigastric pain" or "epigastric burning" or "FODMAP" or "steatosis" or "dyspepsia" or "steatorrhea" or "hepatic fibrosis").ti,ab	1,321,588
#2 – Clinical Indications (IBD)	*irritable bowel disease/ or *crohn disease/ or *ulcerative colitis/ or *inflammatory bowel disease/ or ("irritable bowel disease" or "IBD" or "ulcerative colitis" or "crohn* disease" or "inflammatory bowel disease").ti,ab	236,789
#3 – Clinical Indications (IBS)	*irritable bowel syndrome/ or ("irritable bowel" or "IBS" or "irritable colon").ti,ab	37,110
#4 – Indication Combination	1 or 2 or 3	1,539,460
#5 – Digital or Virtual Solution	("digital care" or "digital health" or "digitial digestive chronic care" or "digital digestive care" or "digital therapeutic* care" or "digital therap*" or "ai?enabled" or "artifical intelligence" or "mobile application" or "virtual care" or "diet planning" or "diet logging" or "patient?facing app*" or "patient?facing portal*" or "symptom tracking" or "health coach*" or "personali?ed medical nutrition" or "subscription?based" or "holistic medicine" or "tele?health" or "digital technolog*").ti,ab	51,092
#6 – Artificial Intelligence	*artificial intelligence/	55,799
#7 – Mobile Application	*mobile application/	14,090
#8 – Telemedicine	*telemedicine/	28,737
#9 – Solution Combination	5 or 6 or 7 or 8	138,416
#10 – Publication Type Exclusions	("case report" or "comment" or "editorial" or "letter" or "review" or "clinical trial protocol").pt.	5,569,166
#11 – Nonhuman Studies Exclusions	("animal*" or "non?human" or "animal experiment*" or "animal model*" or "in vitro study" or "menstrual" or "pregnan*" or "chemotherap*" or "cancer" or "transplant*" or "colonoscop*" or "thyroid*" or "covid" or "coronavirus" or "oil and gas" or "gas industr*" or "greenhouse gas*" or "diabetes" or "vaccine*" or "chatbot" or "chatgpt" or "urinary tract infection" or "UTI").ti,ab	8,965,637

Table 2. EMBASE Search Strategy

Search	Terms	Citations
#12 – Total Exclusions	10 or 11	13,462,878
#13 – Final Combination	4 and 9	2,797
#14 – Final Combination + Exclusions	13 not 12	1,391
#15 - Date Filter	Filter 2015 - 2025	1,283
#16 - Language Filter	Filter Language: English	1,248
#17 - Remove Duplicates	FINAL COUNT	1,237

Table 3. PICOS Inclusion and Exclusion Criteria

Criteria	Inclusion Criteria	Exclusion Criteria
Population	• Adults (≥18 years) who are managing digestive disorder symptoms based on a self-report or validated measure, or clinician judgement • Adults (≥18 years) who are experiencing symptoms of at least two of the following: abdominal pain, constipation, diarrhea, bloating, cramping, flatulence, nausea/vomiting, weight loss, rectal bleeding, fecal incontinence, heartburn/reflux, malnutrition, or steatorrhea	• Individuals < 18 years of age • Individuals who are pregnant • Urgent care telehealth • GI conditions or symptoms secondary to another condition (e.g. GLP-1 use, trauma, pregnancy, antibiotic use, cancer)
Subgroup(s)	• Race/ethnicity, sex, age ≥ years, urban/rural location, LGBTQ+, socioeconomic status	N/A
Intervention(s)	• Virtual care team access (including telehealth only) OR • Virtual personalized symptom management or treatment (e.g., diet planning/elimination, activity, sleep, or stool logging) OR • Virtual behavioral health service integration (e.g. CBT, hypnotherapy) OR • Virtual medication management OR • Virtual care navigation to virtual or in-person care	• Direct-to-consumer, self-pay models • Digital tools for screening/diagnosis/gut microbiome testing without an active management care plan
Comparator(s)	• Standard of care • In-person GI treatment (provider agnostic), diet recommendations, medication management, self-management coaching, interventional care as needed • No care for GI-related symptoms (i.e., not on any treatment, waitlisted, or delayed) • Comparison to baseline • None	N/A

Table 3. PICOS Inclusion and Exclusion Criteria

Criteria	Inclusion Criteria	Exclusion Criteria

Outcome(s)	**Primary Outcomes**
	• Score change over time on self-reported or validated outcome measures, including (but not limited to):
	  ○ Patient Simple Clinical Colitis Activity Index (P-SCCAI)
	  ○ Mobile Health Index for Crohn's Disease (mHI-CD)
	  ○ Mayo Score
	  ○ CDAI
	  ○ Bristol Stool Scale (BSS)
	  ○ Irritable Bowel Syndrome Symptom Severity Scale (IBS-SSS)
	  ○ Patient Health Questionnaire (PHQ-9)
	  ○ Generalized Anxiety Disorder-7 (GAD-7)
	  ○ PROMIS GI scales
	  ○ Likert scale
	  ○ Virtual solution-specific symptom tracking
	
	Secondary Outcomes
	• Increased rate of diagnosis; reduced time to diagnosis
	• Increased medication adherence
	• Improvement in behavioral health outcomes
	• Increased employee productivity; decreased absenteeism
	• Reduction in wait time to see provider (by provider type)
	• Symptom control
	• Activity impairment
	• Safety/Adverse outcomes
	• Change in HCRU (e.g. inpatient/emergency utilization, specialty visits, imaging, procedures, high-cost medications and tests)
	
	User Experience
	• Treatment satisfaction or acceptability (e.g. NPS)
	• Retention in program/treatment adherence
	• Engagement with virtual solution (e.g. duration/frequency of usage, communications, other)
	
	Health Equity
	• Access and accessibility
	• Distribution
		NA

Setting	• Virtual only OR • Outpatient setting and virtual AND • United States (US)	• Inpatient/ED setting only • In-person only (no virtual component) • Outside of US
Study Design	• Randomized control trials • Nonrandomized control trials • Observational studies • Budget impact models, cost-effectiveness models	• Editorials, letters, commentaries, study protocols, case reports, qualitative reports, animal and pre-clinical studies, narrative reviews, systematic literature reviews*, and meta-analyses • Studies with ≤ 20 participants
Language	• English	N/A

Table 3. PICOS Inclusion and Exclusion Criteria

Criteria	Inclusion Criteria	Exclusion Criteria
Data Sources	• MEDLINE (via Ovid) • EMBASE (via Ovid) • Clinicaltrials.gov	N/A
Conferences	• American College of Gastroenterology (ACG) Annual Conference • American Gastroenterology Association (AGA) Annual Conference (Digestive Disease Week) • AGA Tech Summit • Food and Nutrition Conference and Expo	N/A
Date of Publication	• Databases: 2015 – 2025 • Conferences: 2022 – 2025	N/A
Language	• English	• Non-English

Notes: N/A = not applicable. SLR = systematic literature review. ED = emergency department. *SLRs were included for manual reference checks for studies published between 2015 to 2025 and were not included in the qualitative evidence synthesis.

Screening

All publications identified by the systematic literature searches were reviewed against the predefined selection criteria (Table 3). Study selection followed a two-stage screening process based on the review of titles and abstracts (stage I) and full-text articles (stage II). Following completion of title/abstract review, all full-texts of publications identified for inclusion during this stage were retrieved for further review. For conference abstracts without available associated posters and for database abstracts without a full-text available, the report was screened based on the available information within the abstract. Title/abstract and full-text screening for each report were conducted by a human researcher and a trained AI-assisted tool, with any disagreements resolved by discussion with a third human investigator, if needed.

All screening was conducted using both Microsoft Excel and a Python-based command-line AI tool. The AI tool supports the literature screening process by identifying potentially relevant studies from biomedical literature using large language models (LLMs). During both screening stages, abstracts and articles were excluded if they had populations, interventions, outcomes, settings, study designs, or publication types that were out of scope based on the PICOS criteria. Studies published in languages other than English were also excluded.

Data Extraction

Data were extracted by one investigator, with quality assurance against the original source publication completed by another independent investigator. Table 4 lists the reported data captured (if available) for each included study.

Table 4. Data Collected

Study Information
Publication citation
Study identifier or trial name
Study design
Source of data
Timeframe of data collection
Follow-up duration
Patient Information
Sample size
Age (in years)
Sex and/or Gender
Race/Ethnicity
Employment status
Insurance type (Commercial, Medicaid, Medicare, Uninsured)
Housing type
Location (Urban/Rural)
Comorbidities
Other notable characteristics
Interventions
Digital intervention (including definition)
Control intervention (including definition)
Outcomes
Primary Clinical Outcomes • Symptoms (including name and/or description of scale used) • Quality of life (including name and/or description of scale used)
Secondary Clinical Outcomes • Mental health (including name and/or description of scale used) • Safety/Adverse events (including definition) • Patient knowledge and self-efficacy (including name and/or description of scale used)
User Experience • Program engagement • Satisfaction/Usability • Program completion/Adherence
Health Equity • Access and accessibility • Distribution • Outcomes by subgroups of interest (e.g. Race/Ethnicity, Sex/Gender, Age)

Notes: For outcomes reported across multiple timepoints, results were recorded separately for each timepoint.

Evidence Quality Assessment

All included randomized control trials (RCTs) were assessed for potential bias using the Cochrane Collaboration Risk of Bias in Randomized Trials Version 2 (RoB2).[1] The RoB2 includes a maximum of 22 questions that considers the following domains:

Domain 1: Risk of bias arising from the randomization process
Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment or adherence to intervention)
Domain 3: Missing outcome data
Domain 4: Risk of bias in measurement of the outcome
Domain 5: Risk of bias in selection of the reported result

Possible ROB2 ratings are shown in Table 5.

Table 5. Risk of Bias Categories for RoB2

Rating	Criteria
Low risk of bias	The trial is judged to be at low risk of bias for all domains for this result.
Some concerns	The trial is judged to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain.
High risk of bias	The trial is judged to be at high risk of bias in at least one domain for this result OR The trial is judged to have some concerns for multiple domains in a way that substantially lowers confidence in the result.

Notes: RoB2 = Risk of bias in randomized trials, Version 2

Non-randomized and observational studies were assessed using the Newcastle-Ottawa Scale (NOS).[2] Studies were evaluated for multiple criteria within three categories: selection of groups, comparability of groups, and either exposure or outcome, depending on the type of study. Possible NOS ratings are shown in Table 6.

Table 6. Risk of Bias Categories for NOS

Rating	Criteria
++ (Good study quality)	All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter.
+ (Fair study quality)	Some of the checklist criteria have been fulfilled, where they have not been fulfilled or not adequately described, the conclusions are unlikely to alter.
- (Poor study quality)	Few or no checklist criteria have been fulfilled, and the conclusions are likely or very likely to alter.

Notes: NOS = Newcastle Ottawa Scale

[1] Julian PT Higgins, Jelena Savović, Matthew J Page, et al., "Chapter 8: Assessing Risk of Bias in a Randomized Trial," in *Cochrane Handbook for Systematic Reviews of Interventions*, Version 6.5 (Cochrane, 2024). https://www.cochrane.org/authors/handbooks-and-manuals/handbook/current/chapter-08.
[2] GA Wells, B Shea, D O'Connell, et al., *The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-Analyses* (Ottawa Hospital Research Institute, 2025). https://ohri.ca/en/who-we-are/core-facilities-and-platforms/ottawa-methods-centre/newcastle-ottawa-scale.

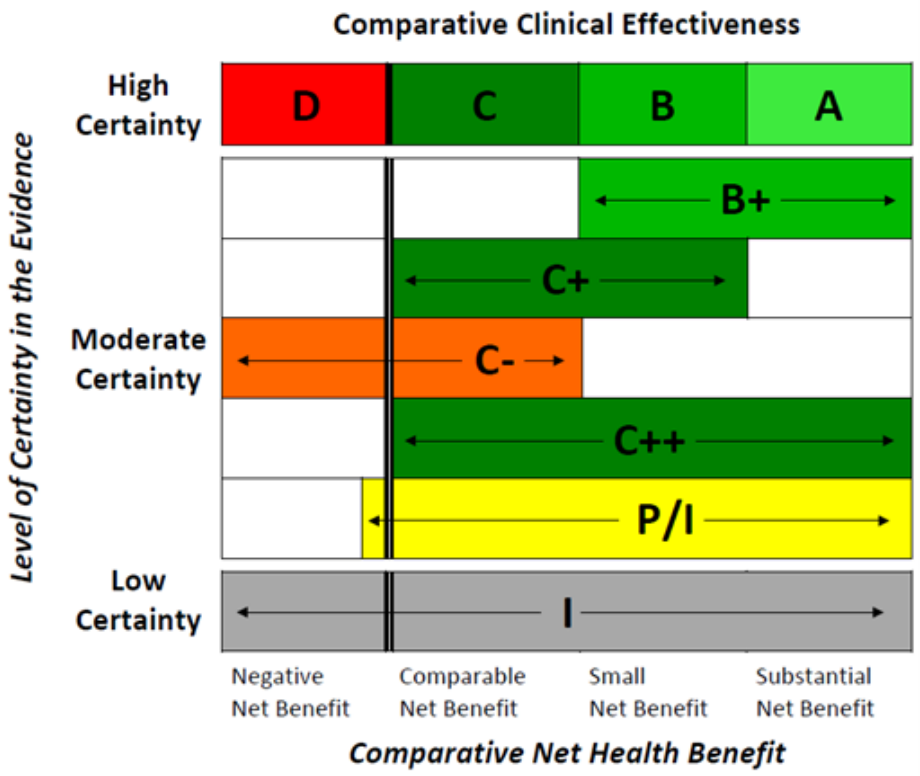
For ease of interpretation, scales from the two risk of bias tools were converted to the following single scale:

- "Low" – Original ratings of "Low risk of bias" (RoB2) or "Good study quality" (NOS)
- "Moderate" – Original ratings of "Some concern" (RoB2) or "Fair study quality" (NOS)
- "High" – Original ratings of "High risk of bias" (ROB2) or "Poor study quality" (NOS)

ICER-PHTI Assessment Framework Evidence Standards: The body of research that comprised the clinical effectiveness section was assessed against the minimum evidence requirements set forth in the ICER-PHTI framework based on the level of risk that the digital intervention presents to a user. Most interventions in this assessment qualify as Tier 3 because they are professionally directed therapeutic services used in consultation with a medical professional. The minimum evidence requirement for Tier 3 are randomized clinical trials (RCTs) demonstrating clinical efficacy, while other real-world comparative evidence and single-arm studies may be considered as additional supporting data.

ICER Evidence Rating Matrix: The body of evidence for each digital solution approach was evaluated based on effectiveness and safety, following the ICER Evidence Rating Matrix™ (see Figure 1).

Figure 1. The ICER Evidence Rating Matrix™



- **A = "Superior"** – High certainty of a substantial (moderate-large) net health benefit
- **B = "Incremental"** – High certainty of a small net health benefit
- **C = "Comparable"** – High certainty of a comparable net health benefit
- **D = "Negative"** – High certainty of an inferior net health benefit

- **B+ = "Incremental or Better"** – Moderate certainty of a small or substantial net health benefit, with high certainty of at least a small net health benefit
- **C+ = "Comparable or Incremental"** – Moderate certainty of a comparable or small net health benefit, with high certainty of at least a comparable net health benefit
- **C- = "Comparable or Inferior"** – Moderate certainty that the net health benefit is either comparable or inferior, with high certainty of at best a comparable net health benefit
- **C++ = "Comparable or Better"** – Moderate certainty of a comparable, small, or substantial net health benefit, with high certainty of at least a comparable net health benefit
- **P/I = "Promising but Inconclusive"** – Moderate certainty of a small or substantial net health benefit, small likelihood of a negative net health benefit
- **I = "Insufficient"** – Any situation in which the level of certainty n the evidence is low

Evidence Evaluation Approach

The PHTI evaluation approach is informed by expert advisors in the healthcare space, clinical advisors, and patients with a goal of producing meaningful evaluations that inform purchasing decisions.

Virtual Solutions for Gastrointestinal (GI) Conditions: The solutions included in this assessment are all designed to improve clinical outcomes and reduce costs for GI patients. Most studies focused on populations of patients with a specific diagnosis or collection of diagnoses (e.g. IBS, IBD), while several included patients with any GI diagnosis (and patients with GI symptoms, without a formal diagnosis).

Comparator Interventions: This assessment prioritized studies that include comparators over single-arm studies, to assess the incremental impact of digital interventions relative to usual care and/or traditionally delivered interventions. Control groups in comparator studies fell into two categories: comparisons to usual care or no intervention (e.g. waitlist controls), and comparisons to an active control (e.g. traditional patient education, in-person multidisciplinary care).

Clinical Outcomes: The primary outcomes of clinical effectiveness were change over time and between group differences in symptoms and quality of life. A mix of self-report scales, both validated and unvalidated, were used to measure symptoms and quality of life across studies (see Table 7). Validated measures of symptoms and quality of life were disease-specific and included a range of domains. For ease of cross-study comparison, validated measures were prioritized over non-validated measures. Secondary clinical outcomes included behavioral health, measured using validated, self-reported scales, and safety, defined as the occurrence and frequency of any adverse events.

Table 7. Summary of Validated Symptom and QoL Scales for IBS and IBD

Scale	Domain(s)	Description	Scoring	MCID	# Studies
IBS					
IBS Visual Analogue Scale (100mm VAS)[3]	Abdominal pain, diarrhea, constipation, bloating and flatulence, vomiting and nausea, psychological well-being, quality of life	Questionnaire designed to measure treatment response of symptoms and well-being of IBS patients.	0 – 100	N/A	5
IBS Symptom Severity Scale (IBS-SSS)	Abdominal pain, abdominal distention, bowel habits (frequency and quality), quality of life	Questionnaire developed to assess the frequency and severity of IBS symptoms in the past 10 days. Each domain is rated on a 100-point scale and then summed. [4]	0 – 500; < 75: no symptoms; 75 – 174: mild symptoms; 175 – 299: moderate symptoms; 300 ≤: severe symptoms	>50pt Change	7
Gastrointestinal Symptom Rating Scale for IBS (GSRS-IBS)	Abdominal pain, bloating, constipation, diarrhea, satiety	13-item questionnaire assessing severity of IBS symptoms over the past 7 days. Each item is graded on a 7-point scale and then summed.[5]	13 – 91	N/A	1
IBS Quality of Life (IBS QOL)	Quality of life: Dysphoria, Interference with Activity, Body Image, Health Worry, Food Avoidance, Social Reaction, Sexual, Relationships	34-item quality of life measure designed to assess the impact of IBS and treatments. Each item is rated on a 5-point scale and then summed, averaged and transformed to a 100-point scale.[6]	0 – 100	N/A	3

[3] Mariette Bengtsson, Bodil Ohlsson, and Kerstin Ulander, "Development and Psychometric Testing of the Visual Analogue Scale for Irritable Bowel Syndrome (VAS-IBS)," *BMC Gastroenterology* 7, no. 1 (2007): 16. https://doi.org/10.1186/1471-230X-7-16.
[4] Elyse R Thakur, Mark Kunik, Maria Ellionore Jarbrink-Sehgal, et al., *Behavioral Medicine Management of Irritable Bowel Syndrome: A Referral Toolkit for Gastroenterology Providers*, n.d.
[5] Brjánn Ljótsson, Michael Jones, Nicholas J Talley, et al., "Discriminant and Convergent Validity of the GSRS-IBS Symptom Severity Measure for Irritable Bowel Syndrome: A Population Study," *United European Gastroenterology Journal* 8, no. 3 (2020): 284–92. https://doi.org/10.1177/2050640619900577.
[6] David A Andrae, Donald L Patrick, Douglas A Drossman, et al., "Evaluation of the Irritable Bowel Syndrome Quality of Life (IBS-QOL) Questionnaire in Diarrheal-Predominant Irritable Bowel Syndrome Patients," *Health and Quality of Life Outcomes* 11, no. 1 (2013): 208. https://doi.org/10.1186/1477-7525-11-208.

Table 7. Summary of Validated Symptom and QoL Scales for IBS and IBD

Scale	Domain(s)	Description	Scoring	MCID	# Studies
IBD					
Inflammatory Bowel Disease Questionnaire (IBDQ)[7]	Quality of life: bowel symptoms, emotional health, systemic systems, and social function.	32-item questionnaire designed to assess disease-related quality of life. Each item is rated on a 7-point scale and summed.	32 – 224	N/A	2
Short Inflammatory Bowel Disease Questionnaire (SIBDQ)	Quality of life: bowel symptoms, emotional health, systemic systems, and social function.	Shortened version of the IBDQ, consisting of 10 items rated on a 7-point scale and then summed.	10 – 70	N/A	2
Harvey-Bradshaw Index (HBI)[8]	Abdominal pain, abdominal mass, complications, number of soft / liquid stools per day, general well-being	Index developed to assess the severity of Crohn's disease.	0 – 16+; <5: remission; 5 – 7: mild activity; 8 – 16: moderate activity; 16 <: severe activity	N/A	5
Simple Clinical Colitis Activity Index (SCCAI)[9]	Blood in stool, bowel frequency at day/night, extracolonic manifestation, general well-being, urgency	Index developed to assess ulcerative colitis patients.	0 – 19; ≤2: remission; <5: mild or no disease activity	N/A	5

Comparator Studies Data: Among studies, the most complete data across all study articles were selected for interpretation of the findings. For studies missing between-group difference data points, values were calculated based on data provided in the study articles or, when available, digitized data values from figures and graphs. Between-group comparison values were based on differences in change from baseline when reported, or when calculation was possible.

Minimum Clinically Important Difference (MCID): Only one validated instrument included in this study, the IBS-SSS, had a universally defined MCID (defined as a ≥50 point change on the 500-point scale). Because most validated scales did not have a universally defined MCID, statistical significance was used as a proxy for meaningful change/improvement across studies and scales.

User Experience and Health Equity: To be clinically effective, virtual solutions for GI conditions must engage patients and deliver strong user experience. The assessment includes data on patients' user experience, satisfaction, and engagement with solutions. In addition, patient

[7] Aaron Yarlas, Stephen Maher, Martha Bayliss, et al., "The Inflammatory Bowel Disease Questionnaire in Randomized Controlled Trials of Treatment for Ulcerative Colitis: Systematic Review and Meta-Analysis," *Journal of Patient-Centered Research and Reviews* 7, no. 2 (2020): 189–205. https://doi.org/10.17294/2330-0698.1722.
[8] Reena Khanna, Surim Son, Guangyong Zou, et al., "Estimation of the Harvey Bradshaw Index from the Patient-Reported Outcome 2 in Crohn's Disease: Results Based on a Large Scale Randomized Controlled Trial," *Inflammatory Bowel Diseases* 31, no. 8 (2025): 2097–2105. https://doi.org/10.1093/ibd/izae281.
[9] R S Walmsley, R C S Ayres, R E Pounder, et al., "A Simple Clinical Colitis Activity Index," *Gut* 43, no. 1 (1998): 29–32. https://doi.org/10.1136/gut.43.1.29.

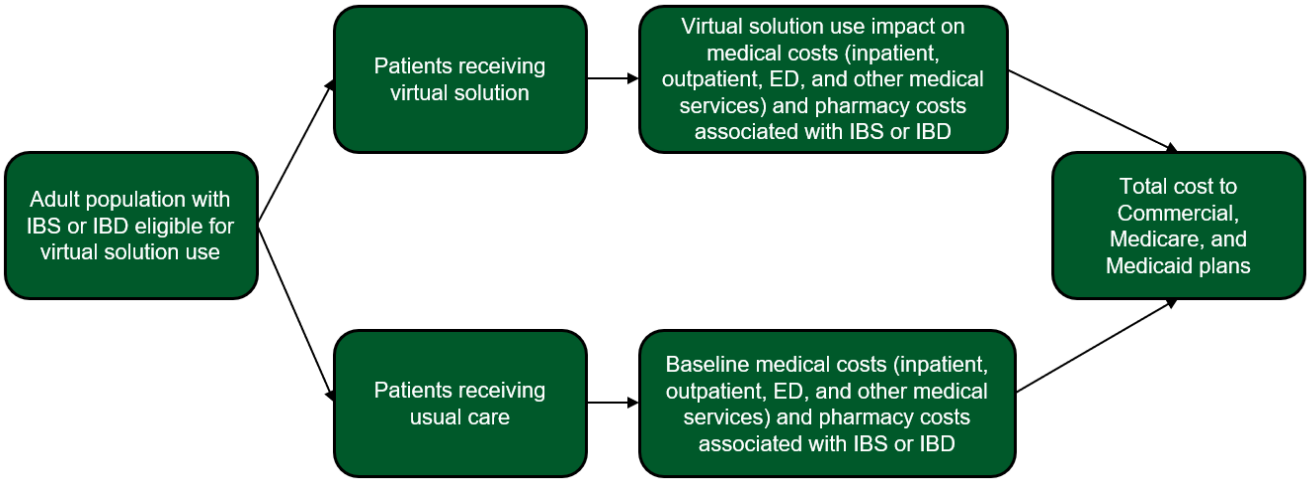
sociodemographic characteristics were reviewed to understand how solutions performed across different patient subgroups.

Economic Assessment

PHTI developed a de novo budget impact analysis for virtual solutions for United States (US) adults with GI disorders, specifically IBS and IBD. The model captured all major IBS clinical subtypes, including IBS-Constipation (IBS-C), IBS-Diarrhea (IBS-D), IBS-Mixed (IBS-M), and IBS-Unspecified (IBS-U), and both primary forms of IBD, ulcerative colitis and Crohn's disease. For IBD, both an average patient population and a moderate-to-severe patient population were evaluated.

The model assumed a hypothetical 1,000,000 member US health plan, where eligible patients initiated a virtual solution compared to usual care and were followed over one year (Figure 2). The model estimated the healthcare spending between the two groups. Additional details on model components are presented below in Table 8.

Figure 1. Budget Impact Model Schematic



Notes: ED = emergency department; IBD = inflammatory bowel disease; IBS = irritable bowel syndrome.

Table 8. Budget Impact Model Components

Category	Details
Intervention	The model considered two virtual solution categories: clinician-led and wraparound
Comparator	Usual care without virtual solution use
Costs considered	• Total cost of service for virtual solution and usual care PPPY (with breakdown by inpatient, outpatient, ED, other medical, and pharmacy services) • Annual cost of virtual solution
Results	• Total costs for virtual solution and usual care scenarios • Incremental budget impact, total • Incremental budget impact PMPM • Incremental budget impact PUPY

Table 8. Budget Impact Model Components

Model assumptions and limitations	• The model only considered costs related to IBS and IBD, and did not consider other GI disorders for which virtual solutions may be used • The model assumed 25% of patients seeking treatment would utilize a virtual solution • Where needed, payer-specific costs were derived by applying published Commercial-to-Medicare and Medicare-to-Medicaid cost ratios to Commercial cost inputs from the literature • The model did not account for age-related expenditure differences for IBS/IBD • Due to lack of evidence, clinician-led and wraparound virtual solutions were modeled as having equal impact across all cost categories for IBS • The impact and cost of each virtual solution were assumed to be equal across health plans, given the lack of evidence supporting differential effects or reimbursement by plan type

Notes: ED = emergency department; GI = gastrointestinal; IBD = inflammatory bowel disease; IBS = irritable bowel syndrome; PMPM = per member per month; PPPY = per patient per year; PUPY = per user per year.

Analysis Inputs

Patient Population: The eligible patient population for the analysis was US adults seeking treatment for IBS or IBD. Enrollment data for Commercial, Medicare, and Medicaid plans were adjusted to estimate the adult population. For the Commercial population, age distributions were sourced from US Census health insurance coverage data and re-proportioned using 2024 US Census population estimates to reflect adults aged ≥18 years.[10,11] For Medicare, age distributions were obtained from the Centers for Medicare and Medicaid Services (CMS) Chronic Conditions Warehouse and re-proportioned using 2024 US Census population data and Census health insurance coverage estimates to reflect adults aged ≥18 years.[12,13,14] Multiple data sources were required due to limited age granularity in individual datasets. For Medicaid, the proportion of adults was sourced from 2023 CMS Medicaid and Children's Health Insurance Program enrollment data and adjusted to exclude dually eligible Medicare-Medicaid enrollees using CMS enrollment data.[15,16]

Literature-based age-specific disease prevalence rates were then applied. The model estimated age-specific prevalence of IBS from a multi-national survey across 33 countries comprising of adults who met the Rome IV diagnostic criteria for IBS.[17] The age-specific global prevalence of IBS, which included IBS-C, IBS-D, IBS-U, and IBS-M was converted to US specific estimates using a scaling factor of 150.5%, derived from the ratio of overall US to global IBS

[10] Lisa N. Bunch and Halelujha Ketema, "Health Insurance Coverage in the United States: 2024," United States Census Bureau, September 9, 2025. https://www.census.gov/library/publications/2025/demo/p60-288.html
[11] United States Census Bureau, "National Population by Characteristics: 2020–2024," 2025. https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html
[12] *National Population by Characteristics: 2020-2024*.
[13] *Health Insurance Coverage in the United States: 2024*.
[14] *Chronic Conditions Data Warehouse. Medicare Enrollment by Age Group, 2013-2022* (Centers for Medicare & Medicaid Services, 2024). https://www2.ccwdata.org/web/guest/medicare-charts/medicare-part-d-charts.
[15] *2023 Medicaid and CHIP Beneficiaries* (Center for Medicaid and CHIP Services, 2023). https://www.medicaid.gov/medicaid/quality-of-care/downloads/beneficiary-ataglance-2023.pdf.
[16] *CMS Program Statistics - Medicare-Medicaid Dual Enrollment* (Centers for Medicare & Medicaid Services, 2023). https://data.cms.gov/summary-statistics-on-beneficiary-enrollment/medicare-and-medicaid-reports/cms-program-statistics-medicare-medicaid-dual-enrollment.
[17] Ami D. Sperber, Shrikant I. Bangdiwala, Douglas A. Drossman, et al., "Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study," *Gastroenterology* 160, no. 1 (2021): 99-114.e3. https://doi.org/10.1053/j.gastro.2020.04.014.

prevalence.[18,19] Given the underlying age distributions of each health plan, the prevalence of IBS within a Commercial, Medicare, and Medicaid plan varied.

Age-specific prevalence of IBD was estimated from an analysis of the 2015 National Health Interview Survey data, a nationally representative US health survey from the Centers for Disease Control and Prevention.[20] Adult patients were classified as having IBD based on a self-reported diagnosis. Similarly to IBS, variations in the prevalence of IBD by health plan reflected the underlying age distribution of each plan.

The proportion of patients seeking treatment for IBS or IBD was derived from analyses reporting the share of patients who sought care in the past 12 months, based on self-reported data.[21,22] For IBS, model inputs were derived from an online survey of adults meeting Rome IV diagnostic criteria, which reported treatment patterns for IBS-C, IBS-D, and IBS-M.[23] The model calculated the overall care-seeking proportion as a prevalence-weighted average across these subtypes. For IBD, the proportion seeking care was taken from an analysis of healthcare utilization among patients with IBD in the 2015 and 2016 National Health Interview Surveys.[24]

Consistent with prior PHTI reports, the model assumes that 25% of patients in the usual care arm would shift to use virtual solutions.

The model also included the capability to generate results for a combined IBS and IBD population. To avoid double-counting, the model accounted for patients with comorbid IBS and IBD. Approximately 32.5% of patients with IBD experience concurrent IBS symptoms.[25] These patients were removed from the IBS patient flow before combining the IBS and IBD populations. Due to limited data, the model does not assume separate healthcare spending or impact of virtual solution use for patients with comorbid IBS and IBD. The excess patients were excluded solely to prevent double-counting in the combined results.

Patient population funnel inputs are presented in Table 9. Patient funnel diagrams are presented in Figure 3 and Figure 4.

[18] Sperber et al., "Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study," 99-114.e3.
[19] Christopher V. Almario, Eden Sharabi, William D. Chey, et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States: Results From a Nationwide Cross-Sectional Study," *Gastroenterology* 165, no. 6 (2023): 1475–87. https://doi.org/10.1053/j.gastro.2023.08.010.
[20] James M. Dahlhamer, Emily P. Zammitti, Brian W. Ward, et al., "Prevalence of Inflammatory Bowel Disease Among Adults Aged ≥18 Years — United States, 2015," *Morbidity and Mortality Weekly Report* 65, no. 42 (2016): 1166–69. https://doi.org/10.15585/mmwr.mm6542a3.
[21] Almario et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States," 1475–87.
[22] *NHSR 152: Health Care Utilization Among U.S. Adults With Inflammatory Bowel Disease, 2015–2016* (Centers for Disease Control and Prevention, 2021). https://doi.org/10.15620/cdc:100471.
[23] Almario et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States," 1475–87.
[24] *Centers for Disease Control and Prevention, 2021.*
[25] Keeley M Fairbrass, Sarah J Costantino, David J Gracie, et al., "Prevalence of Irritable Bowel Syndrome-Type Symptoms in Patients with Inflammatory Bowel Disease in Remission: A Systematic Review and Meta-Analysis," *The Lancet Gastroenterology & Hepatology* 5, no. 12 (2020): 1053–62. https://doi.org/10.1016/S2468-1253(20)30300-9.

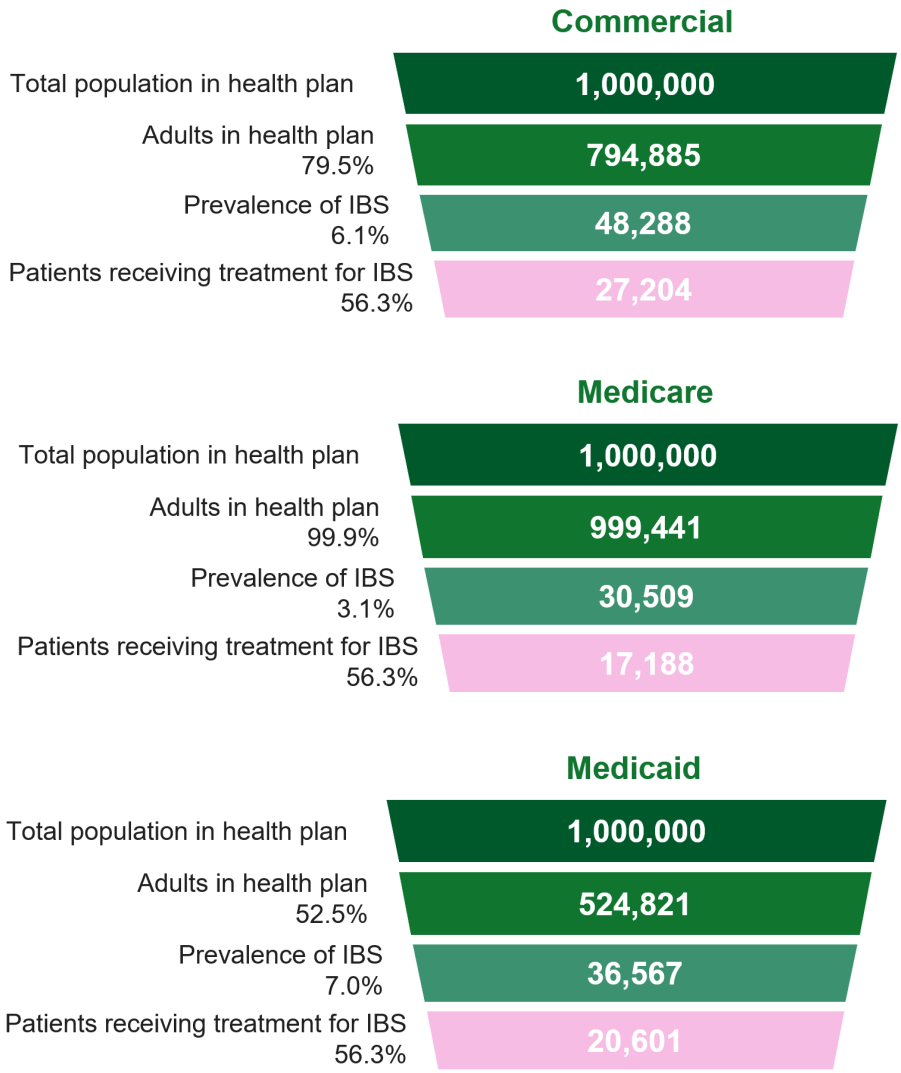
Table 9. Eligible Population Inputs for Patients with IBS and IBD

		Commercial	Medicare	Medicaid	Source
Plan population		1,000,000	1,000,000	1,000,000	Assumption
Proportion of plan that is adults		79.5%	99.9%	52.5%	US Census health insurance coverage and population estimates data; CMS enrollment data[26,27,28,29,30]
Prevalence of GI Condition	IBS	6.1%	3.1%	7.0%	Sperber 2021[31] and Almario 2023[32]; adjusted by age distribution for each health plan[33,34]
	IBD	1.2%	1.6%	1.0%	Dahlhamer 2016[35]; adjusted by age distribution for each health plan[36,37]
Proportion of patients receiving treatment	IBS	56.3%			Almario 2023[38]
	IBD	92.6%			National Health Interview Survey[39]
Proportion of treated patients utilizing virtual solution		25%			Assumption

Notes: IBD = inflammatory bowel disease; IBS = irritable bowel syndrome.

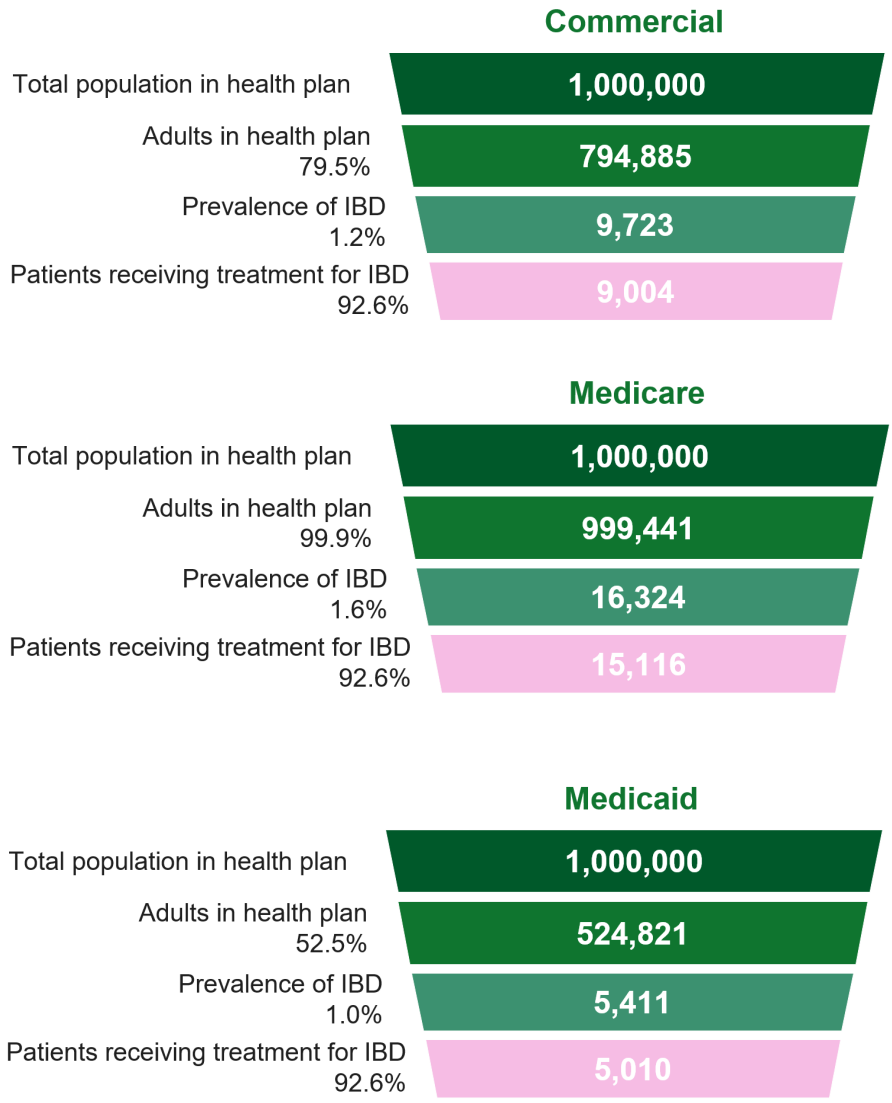
[26] *Health Insurance Coverage in the United States: 2024*.
[27] *National Population by Characteristics: 2020-2024*.
[28] *Chronic Conditions Data Warehouse. Medicare Enrollment by Age Group, 2013-2022*.
[29] *2023 Medicaid and CHIP Beneficiaries*.
[30] *CMS Program Statistics - Medicare-Medicaid Dual Enrollment*.
[31] Sperber et al., "Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study," 99-114.e3.
[32] Almario et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States," 1475–87.
[33] *Health Insurance Coverage in the United States: 2024*.
[34] *National Population by Characteristics: 2020-2024*.
[35] Dahlhamer et al., "Prevalence of Inflammatory Bowel Disease Among Adults Aged ≥18 Years — United States, 2015," 1166–69.
[36] *Health Insurance Coverage in the United States: 2024*.
[37] *National Population by Characteristics: 2020-2024*.
[38] Almario et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States," 1475–87.
[39] *Centers for Disease Control and Prevention, 2021.*

Figure 2. IBS Population Funnels for a 1 Million-Member Health Plan



Notes: IBS = irritable bowel syndrome.

Figure 4. IBD Population Funnels for a 1 Million-Member Health Plan



Notes: IBD = inflammatory bowel disease.

Cost: Cost inputs for the budget impact analysis were informed by a targeted literature review. All inputs were inflated to 2024 US dollars, where needed, using the annual Consumer Price Index for medical care.[40] Costs were converted between payer types using cost conversion factors specific to each service category. Conversion factors for emergency department (ED) costs and other medical costs were assumed to be the same as outpatient costs. The model did

[40] *Consumer Price Index for All Urban Consumers: Medical Care in U.S. City Average* (Federal Reserve Bank of St. Louis, 2025). https://fred.stlouisfed.org/series/CPIMEDSL.

not account for age-specific differences in expenditures because robust current data were unavailable, although there is some limited evidence that potential differences may exist.[41]

Table 10. Payer Type Cost Conversions

Payer Type	Inpatient Services	Outpatient Services	ED Services	Other Medical Costs	Pharmacy Services	Source
Medicare to Commercial	182%	240%	240%	240%	111%[a]	Congressional Budget Office[42]
Medicare to Medicaid	78.0%	72.0%	72.0%	72.0%	85.4%[b]	Commonwealth Fund[43]; CMS[44]

Notes: ED = emergency department. [a] In the absence of clearly reported Medicare-to-Commercial pharmacy price differentials, commercial pharmacy costs were assumed to be 111% of Medicare pharmacy costs. [b] Medicaid pharmacy costs were assumed to be 85.4% of Medicare pharmacy costs, based on the standard Medicaid drug rebate for branded drugs.

Usual Care Costs: For both IBS and IBD, annual usual care costs were estimated using total per-patient service costs across inpatient, outpatient, ED, and pharmacy settings. Patients with IBD were reported to incur additional medical expenditures beyond these core service categories, categorized as other medical costs.

IBS: Usual care costs for IBS were derived from two retrospective US claims analyses conducted in commercially-insured populations with IBS-D and IBS-C.[45,46] In both studies, total annual healthcare costs were estimated for IBS patients and their matched controls and categorized into inpatient, outpatient, ED, and pharmacy costs. Outpatient costs included those for office visits and other outpatient services such as diagnostic testing, and laboratory and radiology services. The model inputs for annual usual care service costs, by category, were calculated as the difference between annual costs for IBS-D and IBS-C cohorts and their matched controls. Among individuals with IBS-D, mean annual cost was $17,292 compared with $5,665 for matched controls, resulting in an incremental cost of $11,627. [47] Among individuals with IBS-C, mean annual cost was $16,232 versus $4,523 for controls, yielding an incremental cost of $11,709. [48] The model applies the distribution of IBS subtypes—28.1% IBS-D, 33.6%

[41] Omar Dabbous, H Thompson, Ramesh Arjunji, et al., "Impact of Age on Healthcare Costs and Resource Utilization in Patients With Crohn's Disease From a Payer Perspective," *Inflammatory Bowel Diseases* 13, no. 5 (2007): 660, https://doi.org/10.1097/00054725-200705005-00060.
[42] *The Prices That Commercial Health Insurers and Medicare Pay for Hospitals' and Physicians' Services* (Congressional Budget Office, 2022). https://www.cbo.gov/publication/57778.
[43] *How Differences in Medicaid, Medicare, and Commercial Health Insurance Payment Rates Impact Access, Health Equity, and Cost* (Commonwealth Fund, 2022). https://www.commonwealthfund.org/blog/2022/how-differences-medicaid-medicare-and-commercial-health-insurance-payment-rates-impact.
[44] *Unit Rebate Amount Information* (Centers for Medicare & Medicaid Services, 2025). https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/unit-rebate-amount-calculation.
[45] Jessica L. Buono, Kush Mathur, Amelia J. Averitt, et al., "Economic Burden of Irritable Bowel Syndrome with Diarrhea: Retrospective Analysis of a U.S. Commercially Insured Population," *Journal of Managed Care & Specialty Pharmacy* 23, no. 4 (2017): 453–60. https://doi.org/10.18553/jmcp.2016.16138.
[46] Jalpa A. Doshi, Qian Cai, Jessica L. Buono, et al., "Economic Burden of Irritable Bowel Syndrome with Constipation: A Retrospective Analysis of Health Care Costs in a Commercially Insured Population," *Journal of Managed Care Pharmacy* 20, no. 4 (2014): 382–90. https://doi.org/10.18553/jmcp.2014.20.4.382.
[47] Buono et al., "Economic Burden of Irritable Bowel Syndrome with Diarrhea," 453–60.
[48] Doshi et al., "Economic Burden of Irritable Bowel Syndrome with Constipation," 382–90.

IBS-C, and 38.3% categorized as IBS Other (IBS-M and IBS-U)—to estimate an overall incremental cost for IBS. [49] Patients classified as having IBS-Other were assumed to incur the same costs as those with IBS-C, the higher-cost subtype (Table 9).

Compared with IBD, patients with IBS had lower total annual healthcare costs per patient; however, ED costs were higher and accounted for a larger share of overall spending. This pattern likely reflects differences in diagnosis, management, and care-seeking behavior between the two conditions. For example, IBS is often treated as a diagnosis of exclusion, which may lead patients to undergo extensive and costly diagnostic testing in emergency care to rule out organic disease.[50] In addition, patients with IBS frequently can present with acute, distressing symptoms that require ED visits in the absence of effective outpatient management.[51] In contrast, IBD flares may more often be managed with established, targeted therapies in outpatient settings.[52]

Table 11. Annual Usual Care Costs for Patients with IBS, PPPY (2024 USD)

Cost Category	Calculated Cost, Commercial
Inpatient costs	$2,280
Outpatient costs	$6,429
ED costs	$732
Other medical costs	--[a]
Pharmacy costs	$2,245

Notes: ED = emergency department; IBS = irritable bowel syndrome; PPPY = per patient per year; USD = US dollars. [a] Patients with IBS did not incur other medical costs.

IBD: Usual care costs for IBD were derived from two US claims analyses of commercially-insured populations with ulcerative colitis and Crohn's disease.[53,54] In both claims analyses, total annual healthcare costs for inpatient, outpatient, ED, other medical, and pharmacy costs were reported for the ulcerative colitis and Crohn's disease populations and their matched controls. The outpatient cost category captured key components of outpatient care, including office visits, endoscopic procedures, radiographic imaging, and laboratory tests. Other medical costs were

[49] Almario et al., "Prevalence and Burden of Illness of Rome IV Irritable Bowel Syndrome in the United States," 1475–87.
[50] Brennan M. R. Spiegel, Mary Farid, Eric Esrailian, et al., "Is Irritable Bowel Syndrome a Diagnosis of Exclusion?: A Survey of Primary Care Providers, Gastroenterologists, and IBS Experts," *American Journal of Gastroenterology* 105, no. 4 (Apr 2010): 848-58, https://doi.org/10.1038/ajg.2010.47.
[51] Xiao Jing Wang, Elyse Thakur, and Jordan Shapiro, "Non-pharmaceutical Treatments for Irritable Bowel Syndrome," *BMJ* 387 (Dec 16 2024): e075777, https://doi.org/10.1136/bmj-2023-075777; Jessica L. Buono, Kush Mathur, Amelia J. Averitt, et al., "Economic Burden of Irritable Bowel Syndrome With Diarrhea: Retrospective Analysis of a U.S. Commercially Insured Population," *Journal of Managed Care & Specialty Pharmacy* 23, no. 4 (2017): 453–60, https://doi.org/10.18553/jmcp.2016.16138.
[52] Emily P Terlizzi, James M Dahlhamer, Fang Xu, et al., "Health Care Utilization Among U.S. Adults With Inflammatory Bowel Disease, 2015-2016," *National Health Statistics Report*, no. 152 (Feb 2021): 1–7, https://stacks.cdc.gov/view/cdc/100471.
[53] Dominic Pilon, Zhijie Ding, Erik Muser, et al., "Long-Term Direct and Indirect Costs of Ulcerative Colitis in a Privately-Insured United States Population," *Current Medical Research and Opinion* 36, no. 8 (2020): 1285–94. https://doi.org/10.1080/03007995.2020.1771293.
[54] Ameur M. Manceur, Zhijie Ding, Erik Muser, et al., "Burden of Crohn's Disease in the United States: Long-Term Healthcare and Work-Loss Related Costs," *Journal of Medical Economics* 23, no. 10 (2020): 1092–1101. https://doi.org/10.1080/13696998.2020.1789649.

defined as expenditures for healthcare services not captured within the established service categories. Annual usual care service costs for IBD were estimated by subtracting the annual costs of matched controls from those of patients with IBD. Among individuals with Crohn's disease, mean annual cost was $29,063 compared with $8,668 for matched controls, yielding an incremental cost of $20,395.[55] Among individuals with ulcerative colitis, mean annual cost was $21,587 compared with $8,505 for matched controls, resulting in an incremental cost of $13,082.[56] Applying a distribution of patients with IBD that have Crohn's (44.6%) and ulcerative colitis (55.4%), the model assumes a prevalence-weighted average annual incremental cost of $16,490 (Table 12).[57]

Table 12. Annual Usual Care Costs for Patients with IBD, PPPY (2024 USD)

Cost Category	Calculated Cost, Commercial
Inpatient costs	$5,316
Outpatient costs	$5,250
ED costs	$568
Other medical costs[a]	$270
Pharmacy costs	$5,087

Notes: ED = emergency department; IBD = inflammatory bowel disease; PPPY = per patient per year; USD = US dollars. [a] Defined as expenditures for healthcare services not captured within the established service categories.

Moderate-to-Severe IBD: To estimate annual costs of service for the moderate-to-severe population, total medical and pharmacy costs were adjusted to reflect greater disease severity. In addition, the relative distribution of inpatient, outpatient, and ED costs within total medical costs was adjusted to account for differences in utilization patterns among moderate-to-severe patients.

The prevalence of moderate-to-severe IBD was estimated using the two claims-based analyses among patients with ulcerative colitis and Crohn's disease described earlier.[58,59] Approximately 40% of adult patients with ulcerative colitis have moderate-to-severe disease, and 58% of adult patients with Crohn's disease have moderate-to-severe disease. A weighted average prevalence for a patient population with moderate-to-severe IBD was calculated based on the relative distribution of ulcerative colitis (55.4%) and Crohn's disease (44.6%) within the IBD population.[60]

For ulcerative colitis, total medical and pharmacy costs for moderate-to-severe patients were used to derive cost ratios relative to the overall ulcerative colitis population (2.42-fold for medical costs and 3.15-fold for pharmacy costs).[61] Adjusted medical costs, excluding other medical costs, were

[55] Manceur et al., "Burden of Crohn's Disease in the United States," 1092–1101.
[56] Pilon et al., "Long-Term Direct and Indirect Costs of Ulcerative Colitis in a Privately-Insured United States Population," 1285–94.
[57] James D. Lewis, Lauren E. Parlett, Michele L. Jonsson Funk, et al., "Incidence, Prevalence, and Racial and Ethnic Distribution of Inflammatory Bowel Disease in the United States," *Gastroenterology* 165, no. 5 (2023): 1197-1205.e2. https://doi.org/10.1053/j.gastro.2023.07.003.
[58] Manceur et al., "Burden of Crohn's Disease in the United States," 1092–1101.
[59] Pilon et al., "Long-Term Direct and Indirect Costs of Ulcerative Colitis in a Privately-Insured United States Population," 1285–94.
[60] Lewis et al., "Incidence, Prevalence, and Racial and Ethnic Distribution of Inflammatory Bowel Disease in the United States," 1197-1205.e2.
[61] Pilon et al., "Long-Term Direct and Indirect Costs of Ulcerative Colitis in a Privately-Insured United States Population," 1285–94.

allocated across inpatient, outpatient, and ED settings using a relative distribution derived from a retrospective claims analysis of patients with ulcerative colitis and differing disease severity.[62] In the moderate-to-severe population with ulcerative colitis, 48.0% of total medical costs were attributed to inpatient services, 49.5% to outpatient services, and 2.5% to ED services. Due to limited data availability, unadjusted cost data were used to inform the distribution across place-of-service.

For Crohn's disease, medical and pharmacy costs were adjusted to reflect the moderate-to-severe population using cost ratios relative to the overall Crohn's disease population (1.71-fold for medical costs and 2.14-fold for pharmacy costs).[63] To apportion medical costs across care settings, healthcare resource utilization by place of service reported by an analysis of National Health and Wellness Survey data of patients with Crohn's disease and differing disease severity was combined with average service costs for each service category.[64] In the moderate-to-severe population with Crohn's disease, inpatient services accounted for 74.5% of total medical costs, followed by outpatient services (19.1%), and ED services (6.4%). Due to lack of control group, the resulting cost distribution reflects utilization patterns among moderate-to-severe Crohn's disease patients only and does not represent incremental differences relative to controls. Applying a distribution of patients with IBD that have Crohn's (44.6%) and ulcerative colitis (55.4%), the model assumes a prevalence-weighted average annual cost of $36,184 (Table 9).[65]

Table 13. Annual Usual Care Costs for Patients with Moderate-to-Severe IBD, PPPY (2024 USD)

Cost Category	Calculated Cost for a Commercial Health Plan
Inpatient costs	$13,642
Outpatient costs	$7,911
ED costs	$979
Other medical costs	$547
Pharmacy costs	$13,104

Notes: ED = emergency department; IBD = inflammatory bowel disease; PPPY = per patient per year; USD = US dollars.

Healthcare Resource Use and Productivity Costs: Changes in healthcare resource utilization reported in published literature were used to estimate the impact of virtual solutions on healthcare spending relative to usual care. For IBS, although most studies reported utilization for emergency department visits and hospitalizations, outpatient utilization data were limited and inconsistent. Including changes in outpatient costs is especially important for IBS, as patients often undergo frequent noninvasive tests to monitor symptoms and guide management. Thus, outpatient services is a major contributor to total spending—representing more than 50% of total

[62] Russell Cohen, Martha Skup, A. Burak Ozbay, et al., "Direct and Indirect Healthcare Resource Utilization and Costs Associated with Ulcerative Colitis in a Privately-Insured Employed Population in the US," *Journal of Medical Economics* 18, no. 6 (2015): 447–56. https://doi.org/10.3111/13696998.2015.1021353.
[63] Manceur et al., "Burden of Crohn's Disease in the United States," 1092–1101.
[64] Sabree C Burbage, Kathryn L Krupsky, M Janelle Cambron-Mellott, et al., "Racial and Ethnic Disparities in Health-Related Outcomes in Crohn's Disease: Results From the National Health and Wellness Survey," *Crohn's & Colitis 360* 6, no. 2 (2024): otae021. https://doi.org/10.1093/crocol/otae021.
[65] Lewis et al., "Incidence, Prevalence, and Racial and Ethnic Distribution of Inflammatory Bowel Disease in the United States," 1197-1205.e2.

cost of care for IBS. [66,67] Given the variability and gaps in the available outpatient data, the model applies the reported difference in healthcare spending between the intervention and controls arms, rather than category-specific utilization reductions. This approach avoids over- or underestimating changes in costs by service category where data are sparse.

Clinician-led: For IBS, the percent reduction in annual costs due to the virtual solution was estimated from a prospective, 9-month study of 234 patients with IBS and functional gastrointestinal disorders that reported changes in health resource utilization and costs associated with Oshi's virtual integrated care program.[68] Using a difference-in-differences methodology, the study reported savings across three index date scenarios that varied by whether GI spending in the three months prior to a GI visit were captured in baseline or follow-up costs. These scenarios produced varying savings estimates, with differences of as much as $700 (5%) per patient across scenarios based on index date selection. PHTI considers the index date that was defined as a visit to a new GI provider to be the most reliable because it consistently applies spending before and after a new GI provider visit for both the control and intervention group. The percent change was estimated as a between-group difference in all-cause costs, calculated as the difference of the within-group percent changes between baseline and follow-up for virtual solution users and controls. In the intervention arm, pre-intervention costs were $14,878 and decreased by 36% to a post-intervention cost of $9,508. In the control arm, pre-intervention costs were $12,688 and decreased by 15% to a post-intervention cost of $10,800. This resulted in a 21% between group change. The model applied this overall percent change in costs from the virtual solution uniformly across inpatient, outpatient, ED, and pharmacy cost categories and therefore did not assume category-specific differential effects. Changes to other medical costs were not applied to the IBS population.

For IBD, changes in annual service costs were calculated from a randomized trial of 348 participants with IBD, receiving either multidisciplinary telemedicine weekly, telemedicine every other week, or in-person multidisciplinary care over 12 months.[69] Participants were a mix of 67.9% Crohn's disease and 32.2% ulcerative colitis and randomized to a control group or two telemedicine intervention groups. The intervention groups received regular symptom monitoring via text messages with automated alerts and nurse-provider management of symptoms between office visits either weekly or every other week. The percent change in healthcare resource utilization for the telemedicine weekly and every other week arms were aggregated into a weighted average and the percent difference compared to the control arm was applied for each corresponding service cost category. Virtual multidisciplinary care was assumed to reduce inpatient costs by 105.6%, increase outpatient costs by 2.7%, and increase ED costs by 58.4%. Given a reduction greater than 100% is not feasible, the model capped the inpatient cost

[66] Buono et al., "Economic Burden of Irritable Bowel Syndrome with Diarrhea," 453–60.
[67] Doshi et al., "Economic Burden of Irritable Bowel Syndrome with Constipation," 382–90.
[68] Sameer K Berry, Jeffrey A Berinstein, David J Cook, et al., *Virtual Integrated Care Improves Patient Outcomes at Lower Costs: Prospective Pilot Study on GI Care*, 2022.
[69] Raymond K. Cross, Patricia Langenberg, Miguel Regueiro, et al., "A Randomized Controlled Trial of TELEmedicine for Patients with Inflammatory Bowel Disease (TELE-IBD)," *American Journal of Gastroenterology* 114, no. 3 (2019): 472–82. https://doi.org/10.1038/s41395-018-0272-8.

reduction at 100%, effectively reducing costs to $0. Other medical costs and pharmacy costs were assumed to remain unchanged between usual care and the virtual solution.

Wraparound*:* Due to limited evidence on the impact of wraparound solutions in patients with IBD, its impact was modeled exclusively for the IBS population. The percent change in cost of service was estimated from a retrospective, controlled cohort study of 347 participants with chronic gastrointestinal disorders (5% of patients had IBS) and 1,041 matched controls.[70] The analysis reported changes in costs associated with Cylinder's digital digestive health program consisting of symptom tracking, personalized medical nutrition therapy, health coaching, and targeted education. The calculated percent change in costs due to the virtual solution represented the difference in total medical and pharmacy costs between groups, estimated as the difference of the within-group percent changes between baseline and follow-up for virtual solution users and controls. In the intervention arm, pre-intervention costs were $8,884 and increased by 6% to a post-intervention cost of $9,442. In the control arm, pre-intervention costs were $8,757 and increased by 30% to a post-intervention cost of $11,341. Under this assumption, wraparound solutions were modeled as reducing all cost categories by 23%. In the model, the overall percent change was applied uniformly across all service categories and did not account for category-specific variation in the impact of the virtual solution. Changes to other medical costs were not applied to the IBS population.

Table 14. Percent Change in Usual Care Costs Associated with Virtual Solutions in IBS and IBD

Service Category	Clinician-led	Wraparound[a]
IBS		
Inpatient costs	-21.2%	-23.2%
Outpatient costs	-21.2%	-23.2%
ED costs	-21.2%	-23.2%
Other medical costs	--	--
Pharmacy costs	-21.2%	-23.2%
IBD		
Inpatient costs	-105.6%	--
Outpatient costs	2.7%	--
ED costs	58.4%	--
Other medical costs	--	--
Pharmacy costs	--	--

Notes: ED = emergency department; IBD = inflammatory bowel disease; IBS = irritable bowel syndrome.
[a]Wraparound solutions were only modeled for use in the IBS population.

Virtual Solution Program Costs: The model assumed a one-time, annual cost of $1,025 for the clinician-led virtual solution in IBS and IBD. For wraparound virtual solutions in IBS, the model assumed a one-time, annual cost of $825. All virtual solution costs were assumed to be the same across health plans due to a lack of evidence supporting differential reimbursement by market type.

[70] Shepherd et al,, "A Health Economic Evaluation," e5–e10..

Appendix B – SLR Studies, Company-specific Clinical Citations, HCRU Data, and Contracting Details

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Ayble Health				
Jactel 2023 A	Full text	O	Online Databases & Conference Proceedings	Samuel N. Jactel, Joseph M. Olson, Kathleen Y. Wolin, et al., "Efficacy of a Digital Personalized Elimination Diet for the Self-Management of Irritable Bowel Syndrome and Comorbid Irritable Bowel Syndrome and Inflammatory Bowel Disease," Clinical and Translational Gastroenterology 14, no. 1 (2023): e00545. https://doi.org/10.14309/ctg.0000000000000545
Jactel 2023 B	Abstract/poster	O	Company Data Submission	Samuel N. Jactel, Joseph M. Olson, Jordan Brown, et al., "Efficacy of a Digitally Delivered Personalized Elimination Diet for the Self-Management of Inflammatory Bowel Disease and Irritable Bowel Syndrome," Gastroenterology 162, no. 3 suppl. (2021): S25. https://www.gastrojournal.org/article/S0016-5085(21)03871-3/fulltext
Jactel 2023 C	Abstract/poster	O	Company Data Submission	Samuel Jactel et. al., "Efficacy of a Digitally Delivered Personalized Elimination Diet for the Self-Management of Inflammatory Bowel Disease and Irritable Bowel Syndrome," Inflammatory Bowel Diseases 28, no. 1 suppl. (2022): S25. https://doi.org/10.1093/ibd/izac015.039
Lupe 2025 A	Full text	I	Company Data Submission	Stephen E. Lupe, Joseph M. Olson, Kendra Kamp, et al., "First Real-World Evidence of an AI-Enhanced Digital Collaborative Care Model to Improve IBS Symptoms," Neurogastroenterology & Motility 37, no. 11 (2025): e70144. https://doi.org/10.1111/nmo.70144
Lupe 2025 B	Abstract/poster	I	Company Data Submission	Stephen Lupe, Joseph Olson, Tiffany Taft, et al., "First Real-World Evidence of an AI-Enhanced Digital Collaborative Care Model to Improve IBS Symptoms," abstract presented at Digestive Disease Week, San Diego, CA, May 3, 2025.
Lupe 2025 C	Abstract/poster	I	Company Data Submission	Stephen Lupe, Joseph Olson, Tiffany Taft, et al., "42: First Real-World Evidence of an AI-Enhanced Digital Collaborative Care Model to Improve IBS Symptoms," Gastroenterology 169, no. 1 suppl. (2025): S-16–S-17. https://doi.org/10.1016/S0016-5085(25)01003-0

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Cylinder Health				
Bravata 2024 A	Full text	O	Online Databases & Conference Proceedings	Dena Bravata, Hau Liu, Meghan M Colosimo, et al., "Digital Disease Management Programme Reduces Chronic Gastrointestinal Symptoms Among Racially and Socially Vulnerable Populations," *BMJ Open Gastroenterology* 11, no. 1 (2024): e001463. https://doi.org/10.1136/bmjgast-2024-001463
Bravata 2024 B	Full text	O	Online Databases & Conference Proceedings	Dena M. Bravata, Hau Liu, Meghan M. Colosimo, et al., "Improvements in Digestive Symptoms After Participation in an App-Based Chronic Digestive Disease Management Program: A Prospective Cohort Evaluation," *Cureus* 16, no. 8 (2024): e66941. https://doi.org/10.7759/cureus.66941
Bravata 2024 C	Abstract/poster	O	Online Databases & Conference Proceedings	Dena Bravata, Hau Liu, Alex Bullock, et al., "696 Participation in a Digital Digestive Chronic Care Program Improves Health Outcomes in Demographically Diverse and Socially Vulnerable Populations," *Gastroenterology* 166, no. 5 suppl. (2024): S-162. https://doi.org/10.1016/S0016-5085(24)00865-5
Commons 2023	Abstract/poster	O	Online Databases & Conference Proceedings	Erin Commons, Hau Liu, and Rachel Sepulveda, "Deployment and Evaluation of an Integrated Digital Digestive Solution Deploying App-Based Telenutrition Services for a Commercially-Insured Population with Chronic Digestive Conditions," *Journal of the Academy of Nutrition and Dietetics* 123, no. 9 (2023): A81. https://doi.org/10.1016/j.jand.2023.06.008
Commons 2024 A	Abstract/poster	O	Online Databases & Conference Proceedings	Erin Commons, Alicen Black, Pen-Che Ho, and Hau Liu, "Addressing Health Inequities in Gastroenterology: The Impact of a Digital Digestive Health Program with Virtual Dietitian and Health Coach Support for Socially Vulnerable Populations." *Journal of the Academy of Nutrition and Dietetics* 124, no. 10 (2024): A63. https://doi.org/10.1016/j.jand.2024.07.092
Commons 2024 B	Abstract/poster	O	Online Databases & Conference Proceedings	Erin Commons, Alicen Black, Pen-Che Ho, and Hau Liu, "Addressing Health Inequities in Gastroenterology: The Impact of a Digital Digestive Health Program with Virtual Dietitian and Health Coach Support for Socially Vulnerable Populations," poster presented at 2024 Food & Nutrition Conference & Expo, Minneapolis, MN, October 5–8, 2024. https://cylinderhealth.com/wp-content/uploads/Cylinder-FNCE2024-poster-addressing-health-inequities-in-GI.pdf
Liu 2023 A	Abstract/poster	O	Online Databases & Conference Proceedings	Hau Liu, Meghan M. Colosimo, Alex Bullock, et al., "P1236 Improvements in Digestive Symptoms After Participation in a Digital Digestive Chronic Care Program," poster presented at the American College of Gastroenterology Annual Scientific Meeting, Vancouver, BC, October 20-25, 2023.
Liu 2023 B	Abstract/poster	O	Online Databases & Conference Proceedings	Hau Liu, Meghan M. Colosimo, Alex Bullock, et al., "S1731 Improvements in Digestive Symptoms After Participation in a Digital Digestive Chronic Care Program," American Journal of Gastroenterology 118, no. 10S (2023): S1290. https://doi.org/10.14309/01.ajg.0000956564.98996.92

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Shepherd 2025	Full text	O	Company Data Submission	Martha Shepherd, Pen-Che Ho, Jon Harris-Shapiro, et al., "The Effects of a Digital Digestive Care Management Program on Employee Absenteeism: A Case-Control Study," *Journal of Occupational & Environmental Medicine* 67, no. 9 (2025): e612–e615. https://doi.org/10.1097/JOM.0000000000003441
Shepherd 2026	Full text	O	Company Data Submission	Martha Shepherd, Pen-Che Ho, David Hines, et al., "A Health Economic Evaluation of Digital Digestive Care Management," *American Journal of Managed Care* 32, no. 1 (2026): e5–e10. https://doi.org/10.37765/ajmc.2026.89872
Varma 2025 B	Full text	O	Company Data Submission	Sanskriti Varma, Alicen Black, Erin Commons, et al., "The Impact of a Digital Digestive Health Program and Telehealth Visits in Socially Vulnerable Populations: Cohort Evaluation," *JMIR Formative Research* 9 (September 2025): e70748. https://doi.org/10.2196/70748
Digbi Health				
Almonacid 2022	Abstract/poster	O	Online Databases & Conference Proceedings	Daniel E. Almonacid, Shreyas V. Kumbhare, Patricia Francis-Lyon, et al., "Digital Therapeutics Care Utilizing Genetic and Gut Microbiome Signals for the Management of Functional Gastrointestinal Disorders: Results From a Preliminary Retrospective Study," Gastroenterology 162, no. 7 (2022): S1010. https://dx.doi.org/10.1016/S0016-5085%2822%2962398-9
Kumbhare 2022	Full text	O	Online Databases & Conference Proceedings	Shreyas V. Kumbhare, Patricia A. Francis-Lyon, Dashyanng Kachru, et al., Digital Therapeutics Care Utilizing Genetic and Gut Microbiome Signals for the Management of Functional Gastrointestinal Disorders: Results from a Preliminary Retrospective in *Microbiology* 13 (March 2022): 826916. https://doi.org/10.3389/fmicb.2022.826916
Nerva Health*				
Anderson 2024	Abstract/poster	I	Company Data Submission	Ellen Anderson, Simone L. Peters, Peter R. Gibson, and Emma P. Halmos, "244 App-Delivered Gut-Directed Hypnotherapy Is Superior to Psychoeducation in Reducing Symptoms Associated with Irritable Bowel Syndrome: A Randomised Control Trial," *Gastroenterology* 166, no. 5 suppl. (2024): S-55. https://doi.org/10.1016/S0016-5085(24)00623-1
Anderson 2025	Full text	I	Company Data Submission	Ellen J. Anderson, Simone L. Peters, Peter R. Gibson, et al., "Comparison of Digitally Delivered Gut-Directed Hypnotherapy Program with an Active Control for Irritable Bowel Syndrome," *American Journal of Gastroenterology* 120, no. 2 (2025): 440–448. https://doi.org/10.14309/ajg.0000000000002921
Pathipati 2023	Abstract/poster	O	Online Databases & Conference Proceedings	Mythili Pathipati, Luisa Scott, Allen Griser, et al., "Efficacy of a Digital Prescription Mobile Application for Adults With Irritable Bowel Syndrome," The American Journal of Gastroenterology 118, no. 10 (2023): S453. https://doi.org/10.14309/01.ajg.0000952108.09469.6d

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Pathipati 2024	Full text	O	Online Databases & Conference Proceedings	Mythili P. Pathipati, Luisa L. Scott, Allen Cameron Griser, and Kyle Staller, "Real-World Outcomes for a Digital Prescription Mobile Application for Adults with Irritable Bowel Syndrome," *Neurogastroenterology & Motility* 36, no. 7 (2024): e14811. https://doi.org/10.1111/nmo.14811
Peters 2021	Abstract/poster	O	Company Data Submission	Simone L. Peters, Peter R. Gibson, and Emma P. Halmos, "654 Mobile App-Delivered Gut-Directed Hypnotherapy Significantly Improves Symptoms of Irritable Bowel Syndrome: Is This the Way of the Future?" *Gastroenterology* 160, no. 6 (2021): S-128.
Peters 2022	Abstract/poster	O	Company Data Submission	Simone Peters, Peter Gibson, and Emma Halmos, "S515 App-Delivered Gut-Directed Hypnotherapy Program Nerva Improves Symptoms in Patients with Irritable Bowel Syndrome but How Can We Ensure Users Are Compliant?" *American Journal of Gastroenterology* 117, no. 10 suppl. (2023): e365–e366. https://doi.org/10.14309/01.ajg.0000858700.31768.51
Peters 2023 A	Abstract/poster	O	Company Data Submission	Simone L. Peters, Peter R. Gibson, and Emma P. Halmos, "App-Delivered Gut-Directed Hypnotherapy Halves the Long-Term Costs Associated with Managing Irritable Bowel Syndrome and Improves Work Productivity," *Gastroenterology* 164, no. 6 suppl. (2022): S-137. https://doi.org/10.1016/s0016-5085(23)01293-3
Peters 2023 B	Abstract/poster	O	Company Data Submission	Simone Peters, Peter Gibson, and Emma Halmos, "S694 Improvements in Psychological Outcomes Following App-Delivered Gut-Directed Hypnotherapy: Highlighting the Importance of the Biopsychosocial Model of Care in IBS," *American Journal of Gastroenterology* 118, no. 10 suppl. (2023): S508. https://doi.org/10.14309/01.ajg.0000952416.43527.3d
Peters 2023 C	Full text	O	Online Databases & Conference Proceedings	Simone L. Peters, Peter R. Gibson, and Emma P. Halmos, "Smartphone App-Delivered Gut-Directed Hypnotherapy Improves Symptoms of Self-Reported Irritable Bowel Syndrome: A Retrospective Evaluation," *Neurogastroenterology & Motility* 35, no. 4 (2023): e14533. https://doi.org/10.1111/nmo.14533
Simicich 2024	Full text	O	Online Databases & Conference Proceedings	Lauren Simicich, Vanessa Muniz, Katherine Scheffrahn, and Gary Elkins, "Nerva, a Mobile Application of Gut-Directed Hypnotherapy for Irritable Bowel Syndrome: User Characteristics, Patterns of Use, and Predictors of Persistence," *Digital Health* 10 (2024). https://doi.org/10.1177/20552076241263257
Varma 2024	Abstract/poster	O	Online Databases & Conference Proceedings	Sanskriti Varma, Luisa L. Scott, Allen C. Griser, et al., "Digital Gut-directed Cognitive Behavioral Therapy May Improve Fecal Incontinence In Irritable Bowel Syndrome," Gastroenterology 166, no. 5 (2024): S493–S494. https://dx.doi.org/10.1016/S0016-5085%2824%2901611-1
Varma 2025	Full text	O	Online Databases & Conference Proceedings	Sanskriti Varma, Luisa L. Scott, Alice Sibelli, et al., "Digital Gut-Directed CBT May Improve Fecal Incontinence in IBS," *Digestive Diseases and Sciences* 70, no. 4 (2025): 1441–1448. https://doi.org/10.1007/s10620-025-08871-w
Oshi Health				

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Berry 2022	Abstract/poster	O	Company Data Submission	Sameer Berry, Jahnavi Curlin, Jeffrey Berinstein, et al., "Reduced ED Utilization in Patients Enrolled in a Provider-Integrated Digital Health Platform: Results from a Prospective Study," abstract presented at the American Public Health Association Annual Meeting and Expo, Atlanta, GA, November 12–15, 2023.
Berry 2023 B	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Jeffrey Berinstein, David J. Cook, et al., "S635 A Virtual Integrated Care Program Improves Patient Outcomes, Engagement, and Satisfaction at Reduced Costs: A Prospective Trial," *American Journal of Gastroenterology* 118, no. 10 suppl. (2023): S465–S466. https://doi.org/10.14309/01.ajg.0000952180.47006.f3
Berry 2023 C	Abstract/poster	O	Online Databases & Conference Proceedings	Sameer Berry, Jeffrey Berinstein, David Cook, et al., "A Virtual Integrated Care Program Improves Patient Outcomes, Engagement, and Satisfaction at Reduced Costs: A Prospective Trial," abstract presented at the American Telemedicine Association Annual Conference & Expo, San Antonio, TX, March 4–6, 2023.
Berry 2023 D	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Jeffrey A. Berinstein, David J. Cook, et al., "A Virtual Integrated Care Program Improves Patient Outcomes, Engagement, and Satisfaction at Reduced Costs: A Prospective Trial," poster presented at the Americal College of Gastroenterology (ACG) Annual Meeting, Vancouver, Canada, October 20–25,2023.
Berry 2023 E	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Lyndsay Solimine, et al., "Outcomes of a Multidisciplinary Care Delivery Model for Gastrointestinal Disorders," poster presented at the American Telemedicine Association, New Orleans, LA, May 3–6, 2025.
Berry 2025 A	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "S2952 Virtual Multidisciplinary GI Clinic Improves Patient Engagement, Satisfaction, and Symptoms at Reduced Costs and Healthcare Utilization: A Propensity-Matched Prospective Observational Study," *The American Journal of Gastroenterology* 120, no. 10S2 (October 2025): S635. https://doi.org/10.14309/01.ajg.0001139268.02765.79
Berry 2025 B	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary Clinic Improves IBD Patient Engagement, Satisfaction, and Symptoms at Reduced Costs and Healthcare Utilization: A Propensity-Matched Prospective Observational Study," poster presented at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.
Berry 2025 C	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary GI Clinic Improves Outcomes in Medicare-Aged Patients with Gastrointestinal Conditions," poster presented at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.
Berry 2025 D	Abstract/poster	O	Company Data Submission	Sameer Berry, Sanskriti Varma, Chamara Basnayake, et al., "S2482 Transforming Liver Care: Patient-Reported Outcomes from a Virtual Multidisciplinary Gastrointestinal Clinic," *American Journal of Gastroenterology* 120, no. 10 suppl. 2 (2025): S533. https://doi.org/10.14309/01.ajg.0001137388.06934.83

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Berry 2025 E	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary Clinic Improves IBD Patient Engagement, Satisfaction, and Symptoms at Reduced Costs and Healthcare Utilization: A Propensity-Matched Prospective Observational Study," *The American Journal of Gastroenterology* 120, no. 10S2 (October 2025): S342. https://doi.org/10.14309/01.ajg.0001133824.17131.72
Berry 2025 F	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary GI Clinic Improves Outcomes in Medicare-Aged Patients with Gastrointestinal Conditions," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S639–S640. https://doi.org/10.14309/01.ajg.0001139356.20270.ed
Berry 2025 G	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary GI Clinic Improves Outcomes in Medicare-Aged Patients with Gastrointestinal Conditions," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S639–S640. https://doi.org/10.14309/01.ajg.0001139356.20270.ed
Berry 2025 H	Abstract/poster	O	Company Data Submission	Sameer K. Berry, Sanskriti Varma, Jeffrey Berinstein, et al., "Transforming Liver Care: Patient-Reported Outcomes From a Virtual Multidisciplinary Gastrointestinal Clinic," poster presented at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.
Berschback 2025 A	Abstract/poster	O	Company Data Submission	Madeline Berschback, Treta Purohit, Sanskriti Varma, et al., "Predictors of Improvement Among Patients with Disorders of Gut-Brain Interaction in a Virtual Multidisciplinary Care Model," poster presented at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.
Berschback 2025 B	Abstract/poster	O	Company Data Submission	Madeline Berschback, Treta Purohit, Sanskriti Varma, et al., "S1166 Predictors of Improvement Among Patients with Disorders of Gut-Brain Interaction in a Virtual Multidisciplinary Care Model," The American Journal of Gastroenterology 120, no. 10S2 (2025): S251. https://doi.org/10.14309/01.ajg.0001132124.76594.5b
Salvo Health				
Nandi 2025 A	Abstract/poster	O	Company Data Submission	Partha Nandi, Naresh T. Gunaratnam, Frank G. Gress, et al., "The Use of Telehealth and Digital Technology In the Multidisciplinary Treatment of Irritable Bowel Syndrome In Patients Within Traditional Gastroenterology Practices," poster presented at Digestive Disease Week (DDW) Annual Meeting, San Diego, CA, May 3–6, 2025.
Nandi 2025 B	Abstract/poster	O	Company Data Submission	Partha Nandi, Naresh T. Gunaratnam, Frank G. Gress, et al., "The Use of Telehealth and Digital Technology in the Multidisciplinary Treatment of Irritable Bowel Syndrome in Patients Within Traditional Gastroenterology Practices," Gastroenterology 169, no. 1 (2025): S1068–S1069. https://doi.org/10.1016/S0016-5085(25)03364-5
Pitman 2023 A	Abstract/poster	O	Company Data Submission	Max Pitman, Erin Hendricks, and Alyssa Guberman, "A Modified Low-FODMAP Diet for the Treatment of Irritable Bowel Syndrome," poster presented at the Institute for Functional Medicine Annual International Conference, Orlando, FL, June 1–3, 2023.

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Pitman 2023 B	Abstract/poster	O	Company Data Submission	Max Pitman, Alyssa Guberman, and Erin Hendriks, "A Modified Low-FODMAP Diet for the Treatment of Irritable Bowel Syndrome (IBS)," abstract presented at American College of Lifestyle Medicine, Boulder, CO, October 29, 2023.
Sachdev 2023 A	Abstract/poster	O	Online Databases & Conference Proceedings	Amit Sachdev, Peter H.R. Green, Alyssa Guberman, et al., "S657 The Use of Telehealth and Digital Technology in the Multidisciplinary Treatment of Irritable Bowel Syndrome," *American Journal of Gastroenterology* 118, no. 10 suppl. (2023): S480–481. https://doi.org/10.14309/01.ajg.0000952268.79111.8b
Sachdev 2023 B	Abstract/poster	O	Company Data Submission	Amit Sachdev, Peter H. R. Green, Alyssa Guberman, et al., "The Use of Telehealth and Digital Technology in the Multidisciplinary Treatment of Irritable Bowel Syndrome," poster presented at the American College of Gastroenterology (ACG), Vancouver, BC, October 20–25, 2023.
SonarMD*				
Kosinski 2024 A	Abstract/poster	O	Company Data Submission	Lawrence R. Kosinski, Omer Shahab, Sachin Singh, et al., "Tu1004 Reduction in Cost of Care in Patients with IBD in a Large Community Practice Using a Proactive Patient Engagement Platform," *Gastroenterology* 166, no. 5 suppl. (2024): S-1215. https://doi.org/10.1016/S0016-5085(24)03248-7
Kosinski 2024 B	Abstract/poster	O	Company Data Submission	Lawrence R. Kosinski, George Pavlou, Nadeem Baig, et al., "Tu1003 Reduction in Utilization in Patients with IBD Enrolled in a Statewide Value Based Care Program Using a Proactive Patient Engagement Model," *Gastroenterology* 166, no. 5 suppl. (2024): S-1214. https://doi.org/10.1016/S0016-5085(24)03247-5
Kosinski 2024 C	Abstract/poster	O	Company Data Submission	Lawrence Kosinski, Sachin Singh, Omer Shahab, et al., "The Importance of Patient Engagement in the Management of Inflammatory Bowel Disease (IBD)," *Gastroenterology* 166, no. 3 suppl. (2024): S72. https://doi.org/10.1053/j.gastro.2023.11.164
Other				
Abutaleb 2017	Abstract/poster	I	Online Databases & Conference Proceedings	Ameer Abutaleb, Andrea G. Buchwald, Kenechukwu Chudy-Onwugaje, et al., "Inflammatory Bowel Disease Telemedicine Clinical Trial: Impact of Educational Text Messages on Disease-Specific Knowledge Over 1 Year," *Inflammatory Bowel Diseases* 24, no. 10 (2018): 2191–2197. https://doi.org/10.1093/ibd/izy149
Berinstein 2024	Abstract/poster	O	Online Databases & Conference Proceedings	Jeffrey Berinstein, Louise Babikow, John I. Allen, et al., "Su1835 A Virtual Multidisciplinary-care Program Improves Outcomes for Patients with Inflammatory Bowel Disease," *Gastroenterology* 166, no. 5 (2024): 18–21. https://doi.org/10.1016/s0016-5085(24)02399-0
Berry 2023 A	Full text	I	Online Databases & Conference Proceedings	Rani Berry, Sameer K. Berry, David Recker, et al., "606 A Randomized Parallel-Group Study of Self-Administered, Digital, Gut-Directed Hypnotherapy vs. Muscle Relaxation

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
				for Irritable Bowel Syndrome," *Gastroenterology* 164, no. 6 (2023): S-112–S-113. https://doi.org/10.1016/s0016-5085(23)01235-0
Bilgrami 2019 A	Full text	I	Online Databases & Conference Proceedings	Zaid Bilgrami, Ameer Abutaleb, Kenechukwu Chudy-Onwugaje, et al., "Effect of TELEmedicine for Inflammatory Bowel Disease on Patient Activation and Self-Efficacy," *Digestive Diseases and Sciences* 65, no. 1 (2019): 96–103. https://doi.org/10.1007/s10620-018-5433-5
Bilgrami 2019 B	Abstract/poster	I	Online Databases & Conference Proceedings	Zaid Bilgrami, Ameer Abutaleb, Kenechukwu Chudy-Onwugaje, et al., "Effect of Telemedicine for Inflammatory Bowel Disease (Tele-IBD) On Patient Activation and General Self-efficacy," *Gastroenterology* 156, no. 6 (2019): S1109–1110. https://dx.doi.org/10.1016/S0016-5085%2819%2939733-1
Chudy-Onwugaje 2017	Abstract/poster	O	Online Databases & Conference Proceedings	Kenechukwu Chudy-Onwugaje, Patricia Langenberg, Miguel Regueiro, et al., "Demographic and Clinical Predictors of Adherence to Self-Testing in Telemedicine for Patients with Inflammatory Bowel Disease (TELE-IBD)," *American Journal of Gastroenterology* 112 (October 2017): S347–S349. https://doi.org/10.14309/00000434-201710001-00632
Chudy-Onwugaje 2018 A	Full text	O	Online Databases & Conference Proceedings	Kenechukwu Chudy-Onwugaje, Ameer Abutaleb, Andrea G. Buchwald, et al., "Age Modifies the Association Between Depressive Symptoms and Adherence to Self-Testing with Telemedicine in Patients with Inflammatory Bowel Disease," *Inflammatory Bowel Diseases* 24, no. 12 (2018): 2648–2654. https://doi.org/10.1093/ibd/izy194
Chudy-Onwugaje 2018 B	Abstract/poster	O	Online Databases & Conference Proceedings	Kenechukwu Chudy-Onwugaje, Ameer Abutaleb, Patricia Langenberg, et al., "Age Modifies the Association Between Depression and Adherence to Self-testing in Patients with Inflammatory Bowel Disease Managed via Telemedicine," *Gastroenterology* 154, no. 6 (2018): S805. https://dx.doi.org/10.1016/S0016-5085%2818%2932761-6
Chugh 2022	Abstract/poster	O	Online Databases & Conference Proceedings	Rishika Chugh, Andrew Liu, Olivia Bigazzi, et al., "A Digital Health Platform for the Clinical Care of Inflammatory Bowel Disease Patients," *Gastroenterology* 162, no. 7 (2022): S257–S258. https://dx.doi.org/10.1016/S0016-5085%2822%2960612-7
Chugh 2023	Full text	O	Online Databases & Conference Proceedings	Rishika Chugh, Andrew W. Liu, Yelena Idomsky, et al., "A Digital Health Intervention to Improve the Clinical Care of Inflammatory Bowel Disease Patients," *Applied Clinical Informatics* 14, no. 5 (2023): 855–865. https://doi.org/10.1055/a-2154-9172
Cross 2017	Abstract/poster	I	Online Databases & Conference Proceedings	Raymond K. Cross, Charlene Quinn, Katharine Russman, et al., "TELEmedicine for Patients with Inflammatory Bowel Disease (Tele-IBD)," *Gastroenterology* 152, no. 5 (2017): S596. https://doi.org/10.1016/S0016-5085(17)32135-2
Cross 2018	Abstract/poster	I	Online Databases & Conference Proceedings	Raymond K. Cross, Patricia Langenberg, Miguel D. Regueiro, et al., "A Randomized Controlled Trial of Telemedicine for Patients With Inflammatory Bowel Disease (Tele-IBD)," *Gastroenterology* 154, no. 6 (2018): S177. https://dx.doi.org/10.1016/S0016-5085%2818%2931005-9

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Cross 2019	Full text	I	Online Databases & Conference Proceedings	Raymond K. Cross, Patricia Langenberg, Miguel Regueiro, et al., "A Randomized Controlled Trial of TELEmedicine for Patients with Inflammatory Bowel Disease (TELE-IBD)," *American Journal of Gastroenterology* 114, no. 3 (2019): 472–482. https://doi.org/10.1038/s41395-018-0272-8
Hunt 2021	Full text	I	Online Databases & Conference Proceedings	Melissa Hunt, Sofia Miguez, Benji Dukas, et al., "The Efficacy of Zemedy, a Mobile Digital Therapeutic for the Self-Management of Irritable Bowel Syndrome: A Cross-Over, Randomized Controlled Trial," *JMIR mHealth and uHealth* 9, no. 5 (2021): e26152. https://doi.org/10.2196/26152
Jing 2024	Abstract/poster	O	Online Databases & Conference Proceedings	Xiao Jing, Anjali Rajagopal, Saam Dilmaghani, et al., "S773 Baseline Severity Correlates with Symptom Improvement on Novel Digital Hypnotherapy Intervention for Bloating," *American Journal of Gastroenterology* 119, no. 10S (2024): S533–S534. https://doi.org/10.14309/01.ajg.0001032460.90402.c3
McDonald 2018	Full text	I	Online Databases & Conference Proceedings	Elizabeth McDonald, Raymond Teets, Caroline Ortiz, et al., "A Randomized Trial of a Group-Based Integrative Medicine Approach Compared to Waitlist Control on Irritable Bowel Syndrome Symptoms in Adults," Explore 14, no. 6 (2018): 406–413. https://doi.org/10.1016/j.explore.2018.04.008
Omeish 2025	Abstract/poster	O	Online Databases & Conference Proceedings	Haya Omeish, Saleh Al-Juburi, Tracey Torosian, et al., "Hypnosis as Adjunctive Therapy to Managing Inflammatory Bowel Disease Is Feasible via Telemedicine and May Decrease Emergency Department Visits," *Gastrointestinal Endoscopy* 101, no. 5 (2025): S335–S336. https://doi.org/10.1016/j.gie.2025.03.599
Pater 2022	Abstract/poster	O	Online Databases & Conference Proceedings	Roeland Pater, Dandyano Zentveld, and Lisa Booth, "Promoting At-Home Disease Management of IBD with a Multidisciplinary Digital Therapy App: Short-Term Results," *Gastroenterology* 162, no. 3 (2022): S94. https://doi.org/10.1053/j.gastro.2021.12.196
Quinn 2019	Full text	I	Online Databases & Conference Proceedings	Charlene Connolly Quinn, Sarah Chard, Erin G. Roth, et al., "The Telemedicine for Patients with Inflammatory Bowel Disease (TELE-IBD) Clinical Trial: Qualitative Assessment of Participants' Perceptions," *Journal of Medical Internet Research* 21, no. 6 (2019): e14165. https://doi.org/10.2196/14165
Rafferty 2021	Full text	I	Online Databases & Conference Proceedings	Aaron J. Rafferty, Rick Hall, and Carol S. Johnston, "A Novel Mobile App (Heali) for Disease Treatment in Participants With Irritable Bowel Syndrome: Randomized Controlled Pilot Trial," *Journal of Medical Internet Research* 23, no. 3 (2021): e24134. https://doi.org/10.2196/24134
Regueiro 2018**	Full text	O	Company Data Submission	Miguel Regueiro, Benjamin Click, Alyce Anderson, et al., "Reduced Unplanned Care and Disease Activity and Increased Quality of Life After Patient Enrollment in an Inflammatory Bowel Disease Medical Home," *Clinical Gastroenterology and Hepatology* 16, no. 11 (2018): 1777–1785. https://doi.org/10.1016/j.cgh.2018.04.007

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
Reich 2019	Full text	O	Online Databases & Conference Proceedings	Jason Reich, Andrew Canakis, Divya Shankar, et al., "The Use of an EHR Patient Portal (MyChart-Epic) in Patients with Inflammatory Bowel Disease," *Crohn's & Colitis* 360 1, no. 3 (2019): otz039. https://doi.org/10.1093/crocol/otz039
Schliep 2019	Abstract/poster	I	Online Databases & Conference Proceedings	Matthew Schliep, Kenechukwu Chudy-Onwugaje, Ameer Abutaleb, et al., "Text Message-based Telemedicine Does not Improve Quality of Life or Depressive Symptoms In Inflammatory Bowel Disease Patients," *Gastroenterology* 156, no. 6 (2019): S608. https://dx.doi.org/10.1016/S0016-5085%2819%2938416-1
Schliep 2020	Full text	I	Online Databases & Conference Proceedings	Matthew Schliep, Kenechukwu Chudy-Onwugaje, Ameer Abutaleb, et al., "TELEmedicine for Patients with Inflammatory Bowel Disease (TELE-IBD) Does Not Improve Depressive Symptoms or General Quality of Life Compared with Standard Care at Tertiary Referral Centers," *Crohn's & Colitis* 360 2, no. 1 (2020): otaa002. https://doi.org/10.1093/crocol/otaa002
Singer 2019	Abstract/poster	O	Online Databases & Conference Proceedings	Jorie Singer, Victoria Rai, Philip Sossenheimer, et al., "P091 Factors Predicting Compliance with Passive and Active Monitoring in Inflammatory Bowel Disease Patients," *American Journal of Gastroenterology* 114 (2019): S24. https://doi.org/10.14309/01.ajg.0000613332.17424.bb
Sivasailam 2018	Abstract/poster	I	Online Databases & Conference Proceedings	Barathi Sivasailam, Raymond K. Cross, Leyla Ghazi, et al., "Telemedicine for Patients with Inflammatory Bowel Disease (Tele-IBD) Decreases Inflammatory Bowel Disease (IBD)-related Hospitalizations," *Gastroenterology* 154, no. 1 (2018): S86–S87. https://doi.org/10.1093/ibd/izy037.034
Szigethy 2021	Full text	O	Online Databases & Conference Proceedings	Eva Szigethy, Aylin Tansel, Alexa N. Pavlick, et al., "A Coached Digital Cognitive Behavioral Intervention Reduces Anxiety and Depression in Adults with Functional Gastrointestinal Disorders," *Clinical and Translational Gastroenterology* 12, no. 12 (2021): e000436. https://doi.org/10.14309/ctg.0000000000000436
Vawdrey 2023	Full text	I	Online Databases & Conference Proceedings	David K. Vawdrey, David Fletcher, Tejal Raichura, et al., "Pandemic Telemedicine Adoption Trends in a Predominantly Rural Integrated Health System," AMIA Annual Symposium Proceedings 2022 (2023): 1101–1107.
Wang 2025	Full text	O	Online Databases & Conference Proceedings	Xiao Jing Wang, Lindsey Philpot, Jon Ebbert, et al., "Digital Therapeutic Combining Hypnosis and Diaphragmatic Breathing Intervention for Functional Abdominal Bloating: A Feasibility Study," *Clinical and Translational Gastroenterology* 16, no. 4 (2025): e00811. https://doi.org/10.14309/ctg.0000000000000811
Weinstein 2022	Full text	O	Online Databases & Conference Proceedings	Milena M. Weinstein, Samantha J. Pulliam, Laura Keyser, et al., "Use of a Motion-Based Digital Therapeutic in Women with Fecal Incontinence: A Pilot Study," *Neurourology and Urodynamics* 41, no. 1 (2021): 475–481. https://doi.org/10.1002/nau.24854
Zand 2020 A	Full text	O	Online Databases & Conference Proceedings	Aria Zand, Audrey Nguyen, Zack Stokes, et al., "Patient Experiences and Outcomes of a Telehealth Clinical Care Pathway for Postoperative Inflammatory Bowel Disease

Appendix B-1: 88 Articles Included in the SLR

Study Articles	Article Type	Study Category	Data Source	Full Reference
				Patients," *Telemedicine and e-Health* 26, no. 7 (2020): 889–897. https://doi.org/10.1089/tmj.2019.0102
Zand 2020 B	Full text	O	Online Databases & Conference Proceedings	Aria Zand, Audrey Nguyen, Courtney Reynolds, et al., "Patient Experience and Satisfaction with an E-Health Care Management Application for Inflammatory Bowel Diseases," *International Journal of Environmental Research and Public Health* 18, no. 22 (2021): 11747. https://doi.org/10.3390/ijerph182211747
Zyczynski 2020	Full text	I	Online Databases & Conference Proceedings	Halina M. Zyczynski, Holly E. Richter, Vivian W. Sung, et al., "Performance, Acceptability, and Validation of a Phone Application Bowel Diary," *Neurourology and Urodynamics* 39, no. 8 (2020): 2480–2489. https://doi.org/10.1002/nau.24520

Notes: I = interventional. O = observational. N/A = not applicable. SLR = systematic literature review. Systematic literature reviews and meta-analyses are not included in the table. *Data included in assessment, company not formally evaluated. ** Clinical protocols described in Regueiro 2018 were exclusively licensed by Ayble Health.

Appendix B-2: 49 Company-specific Clinical Citations Excluded from SLR

Source	Full Reference	Reason for Exclusion	Details on Reason for Exclusion
Ayble Health			
Company Website	Validation Institute, “Ayble Health Outcomes 2024,” accessed September 30, 2025. https://validationinstitute.com/mp-files/ayble_health_outcomes_2024_final.pdf/	Publication type out of scope	Publication is not peer-reviewed
Company Website	Validation Institute, “FoodMed Certified: Ayble Health,” accessed September 30, 2025. https://validationinstitute.com/mp-files/ayble_health_foodmed_tools_2024_final.pdf/	Publication type out of scope	Publication is not peer-reviewed
Cylinder Health			
Company Data Submission	Simon Mathews, Sergey Izmailyan, Frances Brito, et al., “Prevalence and Financial Burden of Digestive Diseases in a Commercially Insured Population,” Clinical Gastroenterology and Hepatology 20, no. 7 (July 2022): 1480–1487. https://doi.org/10.1016/j.cgh.2021.06.047	Intervention out of scope	Intervention does not consist of a DHT/telehealth
Company Data Submission	Simon Mathews, Sandy Templeton, Stephanie K. Taylor, et al., “Evaluation of a Digital Handheld Hydrogen Breath Monitor to Diagnose Lactose Malabsorption: Interventional Crossover Study,” JMIR Formative Research 5, no. 10 (2021): e33009. https://doi.org/10.2196/33009	Population out of scope	Participants with lactose malabsorption or lactose intolerance
Company Website	Cylinder Health, “Nonprofit Organization Achieves Measurable Cost Savings by Focusing on Digestive Health,” accessed September 30, 2025. https://go.hello.cylinderhealth.com/case-study-non-profit-pdf	Publication type out of scope	Publication is not peer-reviewed
Company Website	Cylinder Health, “Robins & Morton Cuts Gut Health Symptoms by 86% with Cylinder,” accessed September 30, 2025. https://go.hello.cylinderhealth.com/case-study-robins-and-morton-pdf	Publication type out of scope	Publication is not peer-reviewed
Company Website	Cylinder Health, “Member Outcomes & Engagement Report,” 2025, accessed October 1, 2025. https://go.hello.cylinderhealth.com/member-outcomes-engagement-report	Publication type out of scope	Publication is not peer-reviewed
Company Website	Cylinder Health, “Improving Employee Health with Innovative Digestive Care,” accessed October 1, 2025. https://go.hello.cylinderhealth.com/accolade-cylinder-case-study-pdf	Publication type out of scope	Publication is not peer-reviewed
Company Website	Cylinder Health, “Digestive Health: The Silent Cost Burden for Health Plans,” accessed October 1, 2025. https://go.hello.cylinderhealth.com/silent-cost-burden-for-health-plans-pdf	Publication type out of scope	Publication is not peer-reviewed
Company Data Submission	Sarah Rotondo-Trivette, Viankail C. Castelan, Kushagra Mathur, et al., "Artificial Intelligence- and Physician-Interpreted Stool Image Characteristics Correlate With C-Reactive Protein Among Inpatients With Acute Severe Ulcerative Colitis: A Pilot Study." Crohns Colitis 360 6, no. 3 (2024): otae043. https://doi.org/10.1093/crocol/otae043	Publication type out of scope	Study includes <20 participants
Company Data Submission	Mark Pimentel, Ruchi Mathur, Jiajing Wang, et al., “A Smartphone Application Using Artificial Intelligence Is Superior to Subject Self-Reporting When Assessing Stool Form,” American Journal of Gastroenterology 117, no. 7 (July 2022): 1118–1124. https://doi.org/10.14309/ajg.0000000000001723	Outcomes out of scope	Primary outcome was accuracy of AI stool assessment
Company Data Submission	Andrew Fagan, Mary Leslie Gallagher, Travis Mousel, et al., "Artificial Intelligence Evaluation of Stool Quality Guides Management of Hepatic Encephalopathy Using a Smartphone App." The American Journal of Gastroenterology 119, no. 5 (2024): 977–981. https://doi.org/10.14309/ajg.0000000000002646	Population out of scope	Participants with cirrhosis

Appendix B-2: 49 Company-specific Clinical Citations Excluded from SLR

Source	Full Reference	Reason for Exclusion	Details on Reason for Exclusion
Company Data Submission	Beatriz Sordi Chara, Kamalpreet S. Hara, Daniel Penrice, et al., "Artificial Intelligence-Enabled Stool Analysis for Lactulose Titration Assistance in Hepatic Encephalopathy through a Smartphone Application." The American Journal of Gastroenterology 119, no. 5 (2024): 982–986. https://doi.org/10.14309/ajg.0000000000002656	Population out of scope	Participants with hepatic encephalopathy
Digbi Health			
Company Data Submission	Shreyas V. Kumbhare, Inti Pedroso, Bharat Joshi, et al., "Longitudinal Gut Microbial Signals Are Associated with Weight Loss: Insights from a Digital Therapeutics Program," Frontiers in Nutrition 11 (2024): 1363079. https://doi.org/10.3389/fnut.2024.1363079	Outcomes out of scope	Primary outcomes were weight loss and gut microbial composition
Company Data Submission	Inti Pedroso, Santosh Kumar Saravanan, Shreyas Vivek Kumbhare, et al., "Economic Impact of a Precision Nutrition Digital Therapeutic on Employer Health Costs: A Multi-Employer and Multi-Year Claims Analysis," Healthcare 13, no. 23 (2025): 3147. https://doi.org/10.3390/healthcare13233147	Outcomes out of scope	Primary outcome was total medical expenditures per patient
Company Website	Digbi Health, "The Path to Good Health is Through the Gut," accessed October 1, 2025. https://cdn.shopify.com/s/files/1/2078/0145/files/Digbi_Whitepaper_Feb2022_V6_Scott.pdf?v=1656689323	Publication type out of scope	Publication is not peer-reviewed
Company Website	Ranjan Sinha, Dashyanng Kachru, Roshni Ray Ricchetti, et al., "Leveraging Genomic Associations in Precision Digital Care for Weight Loss: Cohort Study," Journal of Medical Internet Research 23, no. 5 (May 2021): e25401. https://doi.org/10.2196/25401	Outcomes out of scope	Primary outcome was weight loss
Company Website	Inti Pedroso, Shreyas Vivek Kumbhare, Bharat Joshi, et al., "Mental Health Symptom Reduction Using Digital Therapeutics Care Informed by Genomic SNPs and Gut Microbiome Signatures," Journal of Personalized Medicine 12, no. 8 (2022): 1237. https://doi.org/10.3390/jpm12081237	Outcomes out of scope	Outcomes were association of genetic scores and gut microbiome features with mental health symptoms
Company Website	Blue Shield of California, "More Than 23,500 Blue Shield of California Members Reclaim Their Health in First Year of Reimagined Wellvolution Program," (2020). https://news.blueshieldca.com/2020/07/15/more-than-23-500-blue-shield-of-california-members-reclaim-their-health-in-first-year-of-reimagined-wellvolution-program	Publication type out of scope	Publication is not peer-reviewed
Company Website	Digbi Health, "Blue Collar Employer Case Study: Achieving 12% Employee Utilization with a National Food Distributor," accessed September 30, 2025. https://cdn.shopify.com/s/files/1/2078/0145/files/Blue_Collar_Case_Study_Digbi_Health.pdf?v=1736155367	Publication type out of scope	Publication is not peer-reviewed
Company Website	Digbi Health, "Employer Case Study — Digbi Health," accessed September 30, 2025. https://cdn.shopify.com/s/files/1/2078/0145/files/Employer_Case_Study_Digbi_Health.pdf?v=1736157509	Publication type out of scope	Publication is not peer-reviewed
Company Website	Digbi Health, "Tax Preparation Employer Case (Oct 2023 V2)," (2023), accessed September 30, 2025. https://cdn.shopify.com/s/files/1/2078/0145/files/Tax_Prep_Employer_Case_Oct_2023_V2.pdf	Publication type out of scope	Publication is not peer-reviewed
Nerva Health*			

Appendix B-2: 49 Company-specific Clinical Citations Excluded from SLR

Source	Full Reference	Reason for Exclusion	Details on Reason for Exclusion
Company Data Submission	Simone Peters, Peter Gibson, and Emma Halmos, "App-Delivered Gut-Directed Hypnotherapy Program, Nerva, Improves Gastrointestinal Symptoms and Psychological Outcomes in Pediatric Populations: A Retrospective Audit," poster presented at ESPGHAN, Milan, Italy, May 15–18, 2024.	Population out of scope	Participants are pediatric patients
Oshi Health			
Company Data Submission	Andrea Onstad, Karee Ruth, Brianna Olivieri, et al., "S5142 A Rare Case of Severe Refractory Eosinophilic Gastroenteritis Successfully Treated in a Multidisciplinary Hybrid GI Care Model," American Journal of Gastroenterology 119, no. 10S (October 2024): S3225. https://doi.org/10.14309/01.ajg.0001049936.60489.98	Publication type out of scope	Case study
Company Data Submission	Andrea Onstad, Treta Purohit, Michael Bass, et al., "A Case of Severe and Prolonged Cryptosporidiosis Revealing Human Immunodeficiency Virus, Treated in a Multidisciplinary Hybrid GI Care Model," abstract accepted for presentation at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.	Publication type out of scope	Case study
Company Data Submission	Alyssa Shaffer, Treta Purohit, Michael Bass, et al., "From Virtual to Procedural: A Case of Candy Cane Syndrome Diagnosed Through Hybrid GI Care," abstract presented at the American College of Gastroenterology Annual Scientific Meeting, Phoenix, AZ, October 24–29, 2025.	Population out of scope	Participants with Candy Cane Syndrome
Company Website	Oshi Health, "2024 Oshi Impact Report," accessed September 30, 2025. https://access.oshihealth.com/2024_Oshi_Impact_Report	Publication type out of scope	Publication is not peer-reviewed
Company Website	American Medical Association, "Future of Health: Case Study — Oshi Health," accessed September 30, 2025. https://www.ama-assn.org/system/files/future-health-case-study-oshi-health.pdf	Publication type out of scope	Publication is not peer-reviewed
Company Website	Oshi Health, Inc., "Dietitian and Health Coaching Case Study," accessed September 30, 2025. https://oshihealth.com/wp-content/uploads/2021/03/Dietitian_and_Health_Coaching_CaseStudy.pdf	Publication type out of scope	Publication is not peer-reviewed
Company Submission	Andrea Onstad, Treta Purohit, Michael Bass, et al., "A Case of Severe and Prolonged Cryptosporidiosis Revealing Human Immunodeficiency Virus, Treated in a Multidisciplinary Hybrid GI Care Model," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S1075. https://doi.org/10.14309/01.ajg.0001148072.89823.5f	Publication type out of scope	Case study
Company Submission	Alyssa Shaffer, Treta Purohit, Michael Bass, et al., "From Virtual to Procedural: A Case of Candy Cane Syndrome Diagnosed Through Hybrid GI Care," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S1359. https://doi.org/10.14309/01.ajg.0001153972.76232.7e	Population out of scope	Participants with Candy Cane Syndrome
Company Data Submission	Louise Babikow, Tonks Fawcett, Elizabeth Pfeifer, et al., "Integrated Virtual Care for Irritable Bowel Syndrome: A Qualitative Study," Gastroenterology Nursing 47, no. 2 (2024): 85–91. https://doi.org/10.1097/SGA.0000000000000789	Publication type out of scope	Qualitative report
Salvo Health			

Appendix B-2: 49 Company-specific Clinical Citations Excluded from SLR

Source	Full Reference	Reason for Exclusion	Details on Reason for Exclusion
Company Data Submission	Erin Hendriks, Sheena Batura, Sajal Gunaratnam, et al., "Lifestyle Medicine RPM Program for Metabolic Dysfunction-Associated Liver Disease," abstract accepted at the American College of Lifestyle Medicine, Dallas, TX, November 16–19, 2025.	Population out of scope	Participants with MASLD or obesity
Company Data Submission	Erin Hendriks, Sheena Batura, Sajal Gunaratnam, et al., "Lifestyle Medicine RPM Program for Metabolic Dysfunction-Associated Liver Disease," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S611. https://doi.org/10.14309/01.ajg.0001138840.87337.e6	Population out of scope	Participants with MASLD or obesity
Company Data Submission	Erin Hendriks, Sheena Batura, Sajal Gunaratnam, et al., "Lifestyle Medicine RPM Program for Metabolic Dysfunction-Associated Liver Disease," poster presented at the American College of Lifestyle Medicine, Dallas, TX, November 16–19, 2025.	Population out of scope	Participants with MASLD or obesity
Company Data Submission	Sheena Batura, Naresh Gunaratnam, Partha Nandi, et al., "Lifestyle Medicine RPM Program for Metabolic Dysfunction-Associated Liver Disease (MASLD)," abstract presented at ACG Annual Meeting, Phoenix, AZ, October 20–24, 2025.	Population out of scope	Participants with MASLD or obesity
Company Data Submission	Sheena Batura, Naresh Gunaratnam, Partha Nandi, et al. "Lifestyle Medicine RPM Program for Metabolic Dysfunction-Associated Liver Disease (MASLD)," poster accepted at ACG Annual Meeting, Phoenix, AZ, October 20–24, 2025.	Population out of scope	Participants with MASLD or obesity
Company Website	Amanda Sussex, "New Study Shows 79% Reduction in GI-Related Emergency Room Visits for Salvo Health Patients," accessed September 30, 2025. https://www.salvohealth.com/blog/study-shows-reduction-in-emergency-room-visits-for-salvo-health-patients	Publication type out of scope	Publication is not peer-reviewed
Company Website	Amanda Sussex, "Salvo Health Reduces ER Visits, Creating Path to 3:1 ROI," accessed September 30, 2025. https://www.salvohealth.com/blog	Publication type out of scope	Publication is not peer-reviewed
Company Website	Erin Hendriks, "Digital-First Care Drives Strong Outcomes for IBS in New Research at the ACG," accessed September 30, 2025. https://www.salvohealth.com/blog/digital-first-care-drives-strong-outcomes-for-ibs-in-new-research-at-the-acg	Publication type out of scope	Publication is not peer-reviewed
SonarMD*			
Company Data Submission	Lawrence R. Kosinski, Siddharth Singh, Sachin Singh, et al. "Anxiety is Associated With Increased Inflammatory Bowel Disease Disorder Disease Activity: Use of Retrospective Health Assessment Data and Generalized Anxiety Disorder Can Identify High-Risk Populations of Inflammatory Bowel Disease," The American Journal of Gastroenterology 119, no. 12S (2024): S9. https://doi.org/10.14309/01.ajg.0001082652.92027.8b	Outcomes out of scope	Study does not measure the impact of DHT on outcomes; analysis on the association between anxiety and disease flare-ups
Company Data Submission	Siddharth Singh, Joel V. Brill, James A. Proudfoot, et al. "Project Sonar: A Community Practice-Based Intensive Medical Home for Patients With Inflammatory Bowel Diseases," Clinical Gastroenterology and Hepatology 16, no. 12 (2018): 1847–1850.e1.	Publication type out of scope	Narrative review

Appendix B-2: 49 Company-specific Clinical Citations Excluded from SLR

Source	Full Reference	Reason for Exclusion	Details on Reason for Exclusion
Company Data Submission	Lawrence Kosinski, Siddharth Singh, Joel Brill, et al. "Financial Volatility of Inflammatory Bowel Diseases vs Other Chronic Gastrointestinal Diseases – Using the Beta Coefficient to Categorize GI Disorders," Inflammatory Bowel Diseases 26, no. S1 (2020): S49. https://doi.org/10.1093/ibd/zaa010.124	Intervention out of scope	Intervention does not consist of a DHT/telehealth
Company Data Submission	Beth Houck, Daniel Weintraub, Joel Brill, et al. "Bundled Payments for Care Improvement Advanced (BPCI-A): A Decision-Based Case Study," Clinical Gastroenterology and Hepatology 18 (2020): 2856–2858. https://doi.org/10.1016/j.cgh.2020.06.040	Outcomes out of scope	No relevant outcomes reported.
Company Data Submission	Lawrence R. Kosinski and Joel V. Brill. "The Impact of Cascading Accountability on Specialty Practices: Time for a Nested Solution," Clinical Gastroenterology and Hepatology 21, no. 2 (February 2023): 260–263. https://doi.org/10.1016/j.cgh.2022.11.001	Publication type out of scope	Narrative review
Company Data Submission	Lawrence R. Kosinski, John I. Allen, Sachin Singh, et al. "Mental Health Disorders are Associated with Increased Cost in IBD Patients – Use of Retrospective Claims Data and Phq-2 Can Identify High-risk High-Cost Populations of IBD," Gastroenterology 162, no. 7 (2022): S-678. https://doi.org/10.1016/S0016-5085(22)61590-7	Outcomes out of scope	Primary outcome was total cost of care among patients with IBD, by PHQ-2 score
Company Data Submission	Siddharth Singh, Joel Brill, Derek Blankenship, et al., "Su1786 Reduction in Costs of Care in Patients with Crohn's Disease in a Community Practice-Based Medical Home Over Two Years: A Propensity Score Matched Cohort Analysis," Gastroenterology 156, no. 6 (2019): S–611. https://doi.org/10.1016/S0016-5085(19)38423-9	Publication date out of scope	Abstract was published in 2019 (conference abstracts/posters were included if published between 2022-2025)
Company Data Submission	Lawrence Kosinski, Joel V. Brill, Michael Sorensen, et al. "824 Project Sonar: Reduction in Cost of Care in an Attributed Cohort of Patients With Crohn's Disease," Gastroenterology 150, no. 4 (2016): S173.	Publication date out of scope	Abstract was published in 2016 (conference abstracts/posters were included if published between 2022-2025)
Company Data Submission	Lawrence Kosinski, Charles Baum, Joel Brill, et al. "P-052 Project Sonar: Patient Engagement Reduced Relative Risk and Cost of Care in an Attributed Cohort of Patients with Crohn's Disease," Inflammatory Bowel Diseases 23, suppl. 1 (February 2017): S22.	Publication date out of scope	Abstract was published in 2017 (conference abstracts/posters were included if published between 2022-2025)

Notes: * Company not formally evaluated.

Appendix B-3: 13 Company-specific Economic Citations Included with Healthcare Resource Utilization Claims

Source	Full Reference
Cylinder Health	
Company Data Submission	Martha Shepherd, Pen-Che Ho, Jon Harris-Shapiro, et al., "The Effects of a Digital Digestive Care Management Program on Employee Absenteeism: A Case-Control Study," Journal of Occupational & Environmental Medicine 67, no. 9 (2025): e612–e615. https://doi.org/10.1097/JOM.0000000000003441
Company Data Submission	Martha Shepherd, Pen-Che Ho, David Hines, et al., "A Health Economic Evaluation of Digital Digestive Care Management," American Journal of Managed Care 32, no. 1 (2026): e5–e10. https://doi.org/10.37765/ajmc.2026.89872
Digbi Health	
Company Data Submission	Inti Pedroso, Santosh Kumar Saravanan, Shreyas Vivek Kumbhare, et al., "Economic Impact of a Precision Nutrition Digital Therapeutic on Employer Health Costs: A Multi-Employer and Multi-Year Claims Analysis," Healthcare 13, no. 23 (2025): 3147. https://doi.org/10.3390/healthcare13233147
Nerva*	
Company Data Submission	Simone L. Peters, Peter R. Gibson, and Emma P. Halmos, "App-Delivered Gut-Directed Hypnotherapy Halves the Long-Term Costs Associated with Managing Irritable Bowel Syndrome and Improves Work Productivity," Gastroenterology 164, no. 6 suppl. (2022): S-137. https://doi.org/10.1016/s0016-5085(23)01293-3
Oshi Health	
Company Data Submission	Sameer K. Berry, Jeffrey A. Berinstein, David J. Cook, et al., "Virtual Integrated Care Improves Patient Outcomes at Lower Costs: Prospective Pilot Study on GI Care," poster presented at the Institute for Healthcare Improvement Forum, Orlando, FL, December 4–7, 2022.
Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary GI Clinic Improves Patient Engagement, Satisfaction, and Symptoms at Reduced Costs and Healthcare Utilization: A Propensity-Matched Prospective Observational Study," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S635-S635. https://doi.org/10.14309/01.ajg.0001139268.02765.79.
Company Data Submission	Sameer K. Berry, Sanskriti Varma, Chamara Basnayake, et al., "Virtual Multidisciplinary Clinic Improves IBD Patient Engagement, Satisfaction, and Symptoms at Reduced Costs and Healthcare Utilization: A Propensity-Matched Prospective Observational Study," The American Journal of Gastroenterology 120, no. 10S2 (October 2025): S342. https://doi.org/10.14309/01.ajg.0001133824.17131.72
SonarMD*	
Company Data Submission	Lawrence Kosinski, Joel V. Brill, Michael Sorensen, et al., "824 Project Sonar: Reduction in Cost of Care in an Attributed Cohort of Patients with Crohn's Disease," *Gastroenterology* 150, no. 4 suppl. (2016): S173. https://doi.org/10.1016/S0016-5085(16)30668-0
Company Data Submission	Lawrence Kosinski, Charles Baum, Joel Brill, et al., "P-052 Project Sonar: Patient Engagement Reduced Relative Risk and Cost of Care in an Attributed Cohort of Patients with Crohn's Disease," *Inflammatory Bowel Disease* 23, suppl. 1 (2017): S22. https://doi.org/10.1097/01.MIB.0000512574.75693.b8
Company Data Submission	Lawrence R. Kosinski, Omer Shahab, Sachin Singh, et al., "Tu1004 Reduction in Cost of Care in Patients with IBD in a Large Community Practice Using a Proactive Patient Engagement Platform," Gastroenterology 166, no. 5 suppl. (2024): S-1215. https://doi.org/10.1016/S0016-5085(24)03248-7
Company Data Submission	Lawrence R. Kosinski, George Pavlou, Nadeem Baig, et al., "Tu1003 Reduction in Utilization in Patients with IBD Enrolled in a Statewide Value Based Care Program Using a Proactive Patient Engagement Model," Gastroenterology 166, no. 5 suppl. (2024): S-1214. https://doi.org/10.1016/S0016-5085(24)03247-5

Appendix B-3: 13 Company-specific Economic Citations Included with Healthcare Resource Utilization Claims

Source	Full Reference
Company Data Submission	Lawrence Kosinski, Sachin Singh, Omer Shahab, et al., "The Importance of Patient Engagement in the Management of Inflammatory Bowel Disease (IBD)," Gastroenterology 166, no. 3 suppl. (2024): S72. https://doi.org/10.1053/j.gastro.2023.11.164
Company Data Submission	Siddharth Singh, Joel Brill, Derek Blankenship, et al., "Su1786 Reduction in Costs of Care in Patients with Crohn's Disease in a Community Practice-Based Medical Home Over Two Years: A Propensity Score Matched Cohort Analysis," *Gastroenterology* 156, no. 6 (2019): S-611. https://doi.org/10.1016/S0016-5085(19)38423-9.

Note: * Data included in assessment, company not formally evaluated.

Appendix C – Risk of Bias Ratings for SLR Studies

Appendix C-1: Risk of Bias Ratings using the Cochrane Collaboration Risk of Bias in Randomized Trials Version 2 (RoB2)

Study Articles	Overall Rating	Random Sequence Generation	Deviation from Intended Intervention Bias	Missing Outcome Data	Outcome Measurement Bias	Selective Reporting
Nerva*						
Anderson 2025; Anderson 2024**	Low	Low	Low	Low	Low	Low
Other						
Atreja 2018 A**; Atreja 2018 B**; Atreja 2017**	N/A	N/A	N/A	N/A	N/A	N/A
Berry 2023 A	Moderate	Moderate	Low	Low	Low	Low
Bilgrami 2019 A; Cross 2019; Quinn 2019; Schliep 2020; Abutaleb 2017**; Bilgrami 2019 B**; Cross 2017**; Cross 2018**; Schliep 2019**; Sivasailam 2018**	Moderate	Moderate	Low	Low	Low	Low
Hunt 2021	Moderate	Moderate	Low	Low	Low	Low
McDonald 2018	High	Moderate	High	Low	Low	High
Rafferty 2021	High	Low	High	Low	Low	Low
Reich 2019	High	High	High	Low	Low	Low
Zyczynski 2020	Moderate	Moderate	Low	Low	Low	Low

Notes: N/A = not applicable. See Appendix A for detailed rating information. *Data included in assessment; company not formally evaluated. ** Indicates conference abstract/poster.

Appendix C-2: Risk of Bias Ratings using the Newcastle-Ottawa Scale (NOS)

Study Articles	Overall Rating	Group Selection	Group Comparability	Outcome Exposure/Assessment
Ayble Health				
Jactel 2023 A; Jactel 2023 B**; Jactel 2023 C**	Good	++++	++	+++
Lupe 2025 A; Lupe 2025 B**; Lupe 2025 C**	Good	++++	++	+++
Cylinder Health				
Bravata 2024 A; Bravata 2024 C**; Commons 2023**; Commons 2024 A**; Commons 2024 A**; Varma 2025 B	Good	++++	++	+
Bravata 2024 B; Liu 2023 A**; Liu 2023 B**	Good	++++	++	+
Shepherd 2025; Shepherd 2026	Good	++++	++	+++
Digbi Health				
Kumbhare 2022; Almonacid 2022**	Good	++++	++	++
Nerva*				
Pathipati 2024; Varma 2025; Pathipati 2023**; Varma 2024**	Good	++++	++	++
Peters 2022**	N/A	N/A	N/A	N/A
Peters 2023 A**	N/A	N/A	N/A	N/A
Peters 2023 B**	N/A	N/A	N/A	N/A
Peters 2023 C; Peters 2021**	Good	++++	++	+++
Simichich 2024	Good	++++	++	+++
Oshi Health				
Berry 2022**; Berry 2023 B**; Berry 2023 C**; Berry 2023 D**; Berry 2023 E**; Berry 2025 A**	N/A	N/A	N/A	N/A
Berry 2025 B**; Berry 2025 C**; Berry 2025 D**; Berry 2025 E**; Berry 2025 F**; Berry 2025 G**; Berry 2025 H**	N/A	N/A	N/A	N/A
Berschback 2025 A**; Berschback 2025 B**	N/A	N/A	N/A	N/A
Salvo Health				
Nandi 2025 A**; Nandi 2025 A**	N/A	N/A	N/A	N/A
Pitman 2023 A**; Pitman 2023 B**; Sachdev 2023 A**; Sachdev 2023 B**	N/A	N/A	N/A	N/A
SonarMD*				
Kosinski 2024 A**	N/A	N/A	N/A	N/A
Kosinski 2024 B**	N/A	N/A	N/A	N/A
Kosinski 2024 C**	N/A	N/A	N/A	N/A
Other				
Chudy-Onwugaje 2018; Chudy-Onwugaje 2017**	Good	++++	++	++
Chugh 2023; Chugh 2022**	Good	++++	++	++
Omeish 2025**	N/A	N/A	N/A	N/A
Pater 2022**	N/A	N/A	N/A	N/A
Regueiro 2018 ***	Good	++++	++	+++
Singer 2019**	N/A	N/A	N/A	N/A
Szigethy 2021	Good	++++	++	++
Vawdrey 2023	Fair	++++	0	++
Wang 2025; Jing 2024**	Good	++++	++	+++

Appendix C-2: Risk of Bias Ratings using the Newcastle-Ottawa Scale (NOS)

Study Articles	Overall Rating	Group Selection	Group Comparability	Outcome Exposure/Assessment
Weinstein 2021	Good	++++	++	++
Zand 2020 A	Good	++++	++	+++
Zand 2020 B	Good	++++	++	+

Notes: N/A = not applicable. See Appendix A for detailed rating information. *Data included in assessment; company not formally evaluated. ** Indicates conference abstract/poster. *** Clinical protocols described in Regueiro 2018 were exclusively licensed by Ayble Health.

Appendix D – Key Comparator Studies on IBS and IBD

Publication	Company	Risk of Bias	Total N, Study	Reported Metric	Treatment Arm	Total N, Arm	Timepoint	Baseline Score, Mean	Follow-Up Score, Mean	Within-Group Change from Baseline		Between Group Difference in Change from Baseline
										Mean	p-value	p-value
Irritable Bowel Syndrome (IBS)												
Anderson 2025	Nerva	Low	240	100mm VAS	DHT	121	42 days	67	40	-27	N/R	<0.001
					Control	119	42 days	66	52	-14	N/R	N/A
				IBS-SSS	DHT	121	42 days	321	208	-105	<0.05	0.004
					Control	119	42 days	303	244	-59	<0.05	N/A
				IBS-QoL	DHT	121	42 days	50	36	-14	<0.001	<0.001
					Control	119	42 days	57	50	-7	<0.001	N/A
Hunt 2021	N/A	Moderate	121	GSRS-IBS	DHT	36	8 weeks	36.76	27.56	*-9.2*	0.002	<0.001
					Control	44	8 weeks	37.75	38.18	*0.43*	NR	N/A
					DHT	24	20 weeks	36.76	27.83	*-8.93*	NR	NR
					Control	21	20 weeks	37.75	30.95	*-6.8*	NR	NR
				IBS-QoL	DHT	36	8 weeks	53.63	34.25	*-19.38*	<0.001	<0.001
					Control	44	8 weeks	60.48	58.19	*-2.29*	NR	N/A
					DHT	24	3 months	53.63	38.08	*-15.55*	<0.001	NR
					Control	21	3 months	60.48	43.98	*-16.50*	NR	NR
McDonald 2018	N/A	High	52	IBS-QoL	DHT	30	12 weeks	45.2	26	*-19.2*	NR	0.19
					Control	22	12 weeks	40.8	33	*-7.8*	NR	N/A
				IBS-SSS (proportion of patients with absent / mild symptoms)	DHT	30	12 weeks	18.8%*	45.5%	*26.7*	≤0.05	0.05
					Control	22	12 weeks	9.4%	20.0%	*10.6*	NR	N/A
				IBS-SSS (proportion of patients with moderate / severe symptoms)	DHT	30	12 weeks	81.3%*	54.5%	*-26.8*	≤0.05	0.05
					Control	22	12 weeks	90.6%	80.0%	*-10.6*	NR	N/A
Rafferty 2021	N/A	High	25	IBS-SSS	DHT	14	30 days	272	*107*	-165	NR	0.37
					Control	11	30 days	275	*152*	-123	NR	N/A

Appendix D – Key Comparator Studies on IBS and IBD

Publication	Company	Risk of Bias	Total N, Study	Reported Metric	Treatment Arm	Total N, Arm	Timepoint	Baseline Score, Mean	Follow-Up Score, Mean	Within-Group Change from Baseline		Between Group Difference in Change from Baseline
										Mean	p-value	p-value
				WHO-QoL	DHT	14	30 days	107.4	*128.9*	21.5	NR	0.04
					Control	11	30 days	117.2	*124.2*	7.0	NR	N/A
Inflammatory Bowel Disease (IBD)												
Cross 2019	N/A	Moderate	348	IBDQ	DHT – W**	116	12 months	172.3	179.2	*6.9*	0.42	0.95
					DHT – EOW*	115	12 months	172.3	181.5	*9.2*	0.03	0.95
					Control	117	12 months	168.1	179.3	*11.2*	0.06	N/A
				HBI	DHT – W**	78	12 months	4.2	3.2	*-1.0*	<0.0001	0.18
					DHT – EOW*	79	12 months	4.7	4.2	*-0.5*	<0.0001	0.18
					Control	79	12 months	5.2	3.7	*-1.5*	<0.0001	N/A
				SCCAI	DHT – W**	38	12 months	2.5	2	*-0.5*	0.31	0.25
					DHT-EOW*	36	12 months	2.7	1.7	*-1.0*	0.35	0.25
					Control	38	12 months	2.9	1.4	*-1.5*	<0.01	N/A
Reich 2019	N/A	High	127	SIBDQ	DHT	64	6 months	49.3	58	*8.7*	NR	0.06
					Control	63	6 months	53.7	57.5	*3.8*	0.7	N/A

Notes: IBS = irritable bowel syndrome. IBD = inflammatory bowel disease. DHT = digital health technology. N/A = not applicable. NR = not reported. VAS = visual analogue scale. IBS-SSS = IBS Symptom Severity Scale. IBS-QoL = IBS Quality of Life scale. GSRS-IBS = Gastrointestinal Symptom Rating Scale – IBS. WHO-QoL = World Health Organization Quality of Life scale. IBDQ = IBD Questoinnaire. HBI = Harvey-Bradshaw Index. SCCAI = Simple Clinical Colitis Activity Index. SIBDQ = Short Inflammatory Bowel Disease Questionnaire. Values in italics are calculated from other data provided in article.
*Percentages may not sum to 100.0% exactly due to rounding.
**Cross 2019 included two intervention groups: one which interacted with the DHT weekly ("W"), and one which interacted with the DHT every other week ("EOW").