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# MACHINE LEARNING IN THE CLASSIFICATION OF IRRITABLE BOWEL SYNDROME SUBTYPES: A SYSTEMATIC REVIEW

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**ABSTRACT**
**Background:** Irritable Bowel Syndrome (IBS) is a common gastrointestinal disorder characterized by chronic abdominal pain and altered bowel habits. Due to the heterogeneity in clinical presentations and pathophysiological mechanisms, accurate diagnosis and subtype classification of IBS present significant challenges. Recent advancements in machine learning (ML) and artificial intelligence (AI) have opened up new avenues for improving diagnostic accuracy and disease classification. This systematic review aimed to critically appraise and summarize the recent literature on the use of ML in the diagnosis and subtype classification of IBS. **Methods:** We conducted a comprehensive literature search of PubMed, Scopus, and Web of Science, focusing on research published within the last twenty years. The studies were screened, and data were extracted systematically. We included original research studies that applied AI and ML approaches in diagnosing and classifying IBS. **Results:** Our review synthesized 10 studies, each exploring a different aspect of ML applications, including clinical symptoms, bowel sound features, and microbiome profiles. The findings showed significant potential for ML in IBS diagnosis and subtype differentiation. Several studies showed promising results with high diagnostic accuracy, exceeding 90% in some cases, demonstrating the potential of ML models in non-invasively differentiating IBS from other gastrointestinal disorders and identifying IBS subtypes accurately. **Conclusion:** Despite promising results, challenges persist. Most studies were based on small sample sizes and lacked external validation, underlining the need for further robust and extensive research. However, this systematic review showcases the potential of ML in the evolving landscape of IBS diagnosis and subtype classification and highlights areas for future research.

**KEYWORDS:** Irritable Bowel Syndrome; Machine Learning; Artificial Intelligence; Diagnosis; Subtype Classification; Systematic Review; Gastrointestinal Disorders.

**Glossary of Terms for The Layman**

1. **AI (Artificial Intelligence):** This is a broad term for computer systems or machines that are capable of performing tasks that normally require human intelligence. Examples include interpreting images, recognizing speech, or making decisions.

2. **AUC (Area Under the Curve):** This is a statistical measure used in many areas. In the context of these

studies, it's about how well a model can distinguish between different groups (like healthy and sick people). A value of 1 means perfect distinction, while 0.5 means the model is no better than random guessing.

3. **Sensitivity:** This is a measure of how well a test correctly identifies people with a condition. A test with high sensitivity will catch most people with the condition, meaning it has a low rate of "false negatives."

4. **Specificity:** This is a measure of how well a test correctly identifies people without a condition. A highly specific test will correctly rule out most people who don't have the condition, meaning it has a low rate of "false positives."

5. **Positive Predictive Value:** This is the likelihood that someone with a positive test result really has the condition. A high PPV means that false positives are rare.

6. **Negative Predictive Value:** This is the likelihood that someone with a negative test result really doesn't have the condition. A high NPV means that false negatives are rare.

7. **Mycobiome:** This term refers to the community of fungi (like yeasts and molds) that live in a particular environment, such as the human gut.

8. **Unisymptomatic Model:** This is a model or approach based on just one symptom for diagnosing a condition.

9. **Syndromic Models:** These are models or approaches that use multiple symptoms or features to diagnose a condition.

10. **Radiomics:** This field of study converts medical images into minable data by extracting a large number of features that can be used to create predictive or prognostic models.

11. **Metagenomics:** This is the study of genetic material taken directly from environmental samples. In the context of these studies, it's about studying the genetic material of all the microbes in a sample, like a stool sample.

12. **FAIMS (Field Asymmetric Ion Mobility Spectrometry):** This is a type of technology used to separate and identify different chemicals in a mixture. In these studies, it's used to analyze compounds in breath, urine, or feces samples.

13. **VOC (Volatile Organic Compound):** These are organic chemicals that have a high vapor pressure at room temperature. In the context of these studies, VOCs in body fluids or breath are being analyzed as potential markers for disease.

14. **IBS (Irritable Bowel Syndrome):** This is a common disorder that affects the large intestine. Symptoms include cramping, abdominal pain, bloating, gas, and diarrhea or constipation, or both.

15. **IBS-C (Irritable Bowel Syndrome with Constipation):** This is a subtype of IBS where constipation is a predominant symptom.

16. **IBS-D (Irritable Bowel Syndrome with Diarrhea):** This is a subtype of IBS where diarrhea is a predominant symptom.

17. **EP (Early Progression):** This refers to a disease, typically cancer, that progresses or worsens quickly after initial treatment.

18. **FC (Functional Constipation):** This is a common bowel condition characterized by persistent constipation without a clear physical cause.

## INTRODUCTION

Irritable Bowel Syndrome (IBS) is a functional gastrointestinal disorder characterized by chronic or recurrent symptoms such as abdominal pain, bloating, and altered bowel habits, with periods of remission and exacerbation. It affects approximately 10-15% of the global population, yet the pathophysiology is still not fully understood.[1] Subtypes of IBS are categorized based on the dominant bowel habit: IBS with predominant constipation (IBS-C), IBS with predominant diarrhea (IBS-D), mixed IBS (IBS-M), and unclassified IBS (IBS-U).

Accurate diagnosis and classification of IBS subtypes remain a significant challenge in clinical practice.[2] Traditional diagnostic approaches rely heavily on symptom-based criteria, such as the Rome IV criteria, and exclusion of other organic diseases. However, these methods can be subjective and time-consuming, and the symptom overlap among IBS subtypes and with other gastrointestinal disorders can lead to misdiagnosis.

The advent of artificial intelligence (AI) and machine learning (ML) in healthcare offers a promising solution to these challenges.[3] ML, a subset of AI, involves the development of algorithms that allow computers to learn from and make decisions based on data. This can be especially useful in disease diagnosis and classification, where complex patterns in large datasets can be utilized.

Over the past decade, the application of ML in gastroenterology, particularly in IBS research, has emerged as a promising area.[4] Researchers have applied ML techniques to various types of data, including clinical symptoms, demographics, diet, physical activity, and more recently, microbiome and other omics data, to build predictive models for IBS diagnosis and subtype classification.

ML-based approaches have the potential to revolutionize the diagnosis and management of IBS by providing objective and reliable methods that can process complex and multidimensional data.[5] For example, these tools could help identify unique patterns or biomarkers for different IBS subtypes, aiding in personalized treatment strategies.[6] However, the success of these applications greatly depends on the quality of the data and the appropriateness of the ML algorithms used.

Given the growing interest in this field, it is essential to synthesize the current knowledge and identify potential gaps. Hence, this systematic review aims to critically evaluate the latest advancements in the use of ML for diagnosing and classifying IBS subtypes. It provides an overview of the ML techniques used, the types of data applied, the performance of these ML models, and the implications for clinical practice. This work could contribute to future ML-based research in IBS and ultimately improve patient care.

## METHODS

The methodology for this systematic review was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review aimed to provide a comprehensive examination of recent literature assessing advancements in AI and Machine Learning (ML) applications for diagnosing and classifying subtypes of Irritable Bowel Syndrome (IBS).

### Search Strategy

A systematic literature search was conducted focusing on research published within the last twenty years, ensuring the incorporation of the most recent and thus, most relevant studies. The search was carried out on three databases, namely PubMed, Scopus, and Web of Science for relevant studies. Keywords and MeSH terms such as 'Artificial Intelligence', 'Machine Learning', 'Irritable Bowel Syndrome', 'Diagnosis', 'Classification', and their combinations were used for the search. No restrictions were imposed based on language or geographical location, and only peer-reviewed articles were considered for inclusion.

### Study Selection

The articles retrieved from the initial search were independently screened by two reviewers based on their titles and abstracts for relevance to the topic of IBS and the use of AI and ML in its diagnosis and subtype classification. Any discrepancies between the reviewers were resolved through discussion or consultation with a third reviewer if needed. The full texts of the shortlisted articles were obtained for further in-depth scrutiny. Studies were included if they met the following criteria: original research studies published within the last twenty years, studies focusing on AI and ML approaches in diagnosing and classifying IBS subtypes, and studies that provided sufficient data for extraction and analysis.

### Data Extraction and Synthesis

Data from the included studies were systematically extracted by the research team. The data extracted encompassed the following details: author names, year of publication, study design, AI/ML approach used, the dataset used or population studied, outcome measures, key findings, opportunities and limitations. The extracted data were then synthesized and analyzed qualitatively. The key findings were consolidated and summarized, and the results were categorized based on the study design, AI/ML approach, and the dataset used. This provided an overview of the current state of AI and ML applications in IBS diagnosis and subtype classification. The synthesis also highlighted the potential impact of these studies on the field of IBS diagnosis and classification and identified gaps in the existing research for future exploration.

## RESULTS

Of the 687 studies identified 123 duplicates were removed. Of these 87 were reviewed for full texts, of which 10 were included in this systematic review. The study selection process is depicted in Figure 1.

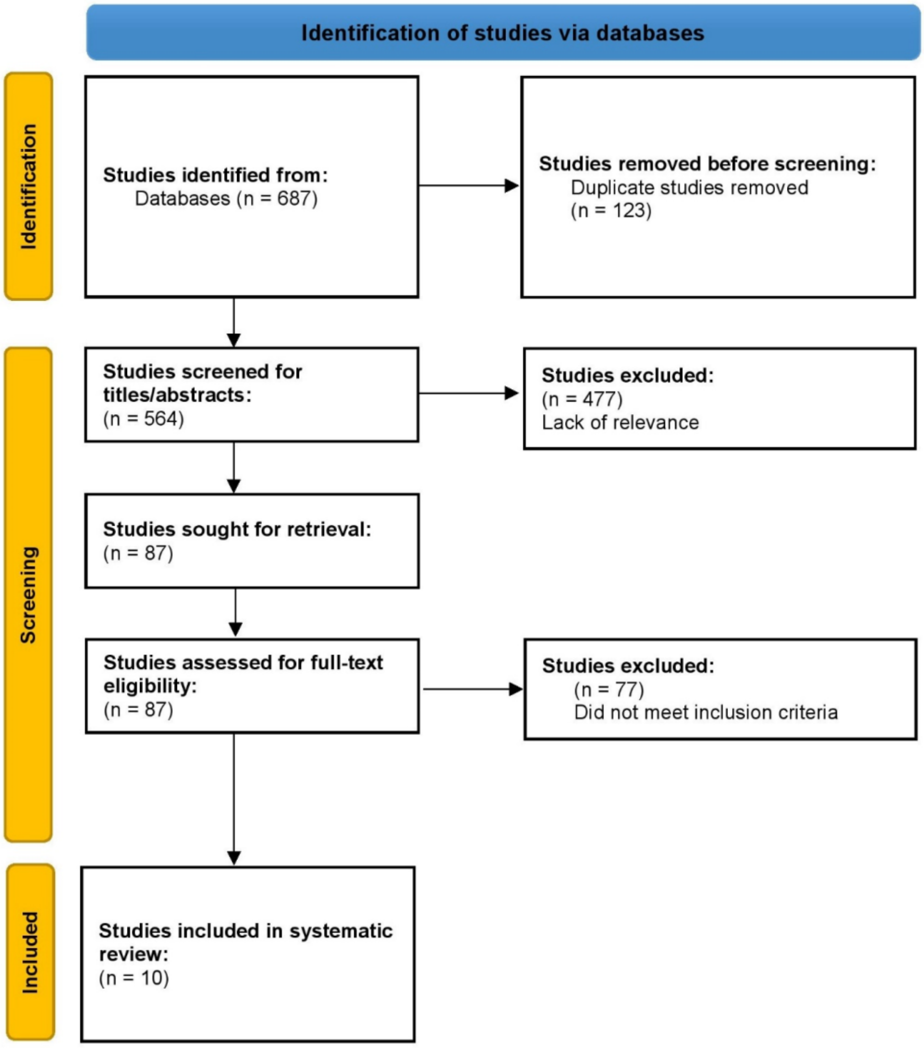


**Figure 1: PRISMA Flowchart Representing the Process of Study Selection.**

**Table 1: Presents the study design, intervention, dataset/population enrolled, and outcome measures of the included studies. A study-by-study summary is provided below of these characteristics.**

**Table 1: Study Design, Intervention, Dataset Used/Population, and Outcome Measures of the Included Studies.**

| Author, Year | Title | Study Design | Intervention (AI/ML Approach) | Dataset Used/Population | Outcome Measures |
|---|---|---|---|---|---|
| Tabata, 2023[7] | Artificial intelligence model for analyzing colonic endoscopy images to detect changes associated with irritable bowel syndrome | Observational, retrospective | Google Cloud Platform AutoML Vision (single-label classification) | Colonoscopy images from 123 individuals categorized into 4 groups: IBS (n=11), IBS-C (n=12), IBS-D (n=12), healthy subjects (n=88) | Sensitivity, specificity, positive predictive value, negative predictive value, and AUC |
| Das, 2021[8] | The fecal mycobiome in patients with Irritable Bowel Syndrome | Observational, cross-sectional | Machine learning applied on the mycobiome analysis (ITS-1 sequencing) | Fecal samples from 80 patients with IBS and 64 control subjects | Predictive power of the fecal mycobiome in machine learning models for IBS diagnosis |
| James, 2021[9] | Constipation Predominant Irritable Bowel Syndrome and Functional Constipation Are Not Discrete Disorders: A Machine Learning Approach | Observational, prospective | Machine learning applied to patient data for diagnostic model building | Data from 768 patients with chronic constipation from a tertiary center | Accuracy of diagnostic models for IBS-C and FC based on single differentiating features and multiple features |
| Bouchoucha, 2020[10] | Data Mining Approach for the Characterization of Functional Bowel Disorders According to Symptom Intensity Provides a Small Number of Homogenous Groups | Observational, cross-sectional | Gaussian mixture model for patient clustering; Classification tree | Data from 1,729 outpatients who filled out the Rome III questionnaire and 10-point Likert scales for symptom intensity | Association between Rome III classification and new grouping based on symptom intensity |

| | | | | | |
|---|---|---|---|---|---|
| Bani-Sadr, 2019[11] | Conventional MRI radiomics in patients with suspected early- or pseudo-progression | Retrospective observational | Random forest algorithm applied on radiomics features from conventional MRI | Data from 76 patients with suspected early progression (EP) or pseudoprogression (Psp) after radiochemotherapy | Accuracy, sensitivity, and specificity of the model; Overall survival (OS) and progression-free survival (PFS) |
| Du, 2019[12] | Noninvasive Diagnosis of Irritable Bowel Syndrome via Bowel Sound Features: Proof of Concept | Diagnostic case-control study | Analysis of bowel sounds | 31 IBS and 37 healthy participants for model development; 15 IBS and 15 healthy participants for independent testing | Sensitivity and specificity for IBS diagnosis |
| Hollister, 2019[13] | Leveraging Human Microbiome Features to Diagnose and Stratify Children with Irritable Bowel Syndrome | Observational, cross-sectional | Whole-genome shotgun metagenomics and global unbiased fecal metabolomic profiling | Rome III IBS children (n = 23) and healthy controls (n = 22) | Association between microbes, metabolites, and abdominal pain. Predictive power of the machine learning model |
| Melidis, 2018[14] | A test of the adaptive network explanation of functional disorders using a machine learning analysis of symptoms | Observational, cross-sectional | Machine learning analysis of symptom survey data | 1751 people reporting IBS, FMS, or CFS diagnosis | Symptom clusters; outgoing connections between clusters |
| Arasaradnam, 2014[15] | Differentiating Coeliac Disease from Irritable Bowel Syndrome by Urinary Volatile Organic Compound Analysis – A Pilot Study | Observational, cross-sectional | VOC analysis in urine, breath, and feces; Machine learning algorithms for statistical evaluation | 27 established CD patients on gluten-free diets and 20 with D-IBS | Sensitivity and specificity of VOC analysis for distinguishing CD from D-IBS |
| Shepherd, 2014[16] | The use of a gas chromatograph coupled to a metal oxide sensor for rapid assessment of stool samples from irritable bowel syndrome and inflammatory bowel disease patients | Observational, cross-sectional | Headspace gas chromatography and a single metal oxide sensor coupled to artificial neural network software | Stool samples from IBD and IBS patients | Sensitivity and specificity of the system in distinguishing IBD from IBS |

**Abbreviations:** AI - Artificial Intelligence; IBS - Irritable Bowel Syndrome; AUC - Area Under the Curve; IBS-C - Irritable Bowel Syndrome with Constipation; IBS-D - Irritable Bowel Syndrome with Diarrhea; ITS-1 - Internal Transcribed Spacer 1; FC - Functional Constipation; MRI - Magnetic Resonance Imaging; EP - Early Progression; Psp – Pseudoprogression; OS - Overall Survival; PFS - Progression-Free Survival; VOC - Volatile Organic Compound; CD - Coeliac Disease; D-IBS - Diarrhea-predominant Irritable Bowel Syndrome; FMS - Fibromyalgia Syndrome; CFS - Chronic Fatigue Syndrome; IBD - Inflammatory Bowel Disease; MeSH - Medical Subject Headings; PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses; ML - Machine Learning.

In a retrospective study conducted by Tabata et al., 2023, an artificial intelligence (AI) model was used to analyze colonic endoscopy images for detecting IBS changes.[7] The AI model was built using Google Cloud Platform AutoML Vision, employing a single-label classification method. The sample comprised colonoscopy images from 123 individuals divided into four groups: IBS (n=11), IBS-C (n=12), IBS-D (n=12), and healthy subjects (n=88). The model demonstrated a high degree of sensitivity, specificity, positive predictive value, negative predictive value, and AUC, which indicates the model's significant potential for non-invasive IBS diagnosis and subtype classification.

In 2021, Das et al. conducted an observational cross-sectional study involving the analysis of the fecal mycobiome in patients with IBS.[8] This study utilized machine learning techniques on mycobiome analysis, specifically ITS-1 sequencing, to predict IBS diagnosis. Using fecal samples from 80 IBS patients and 64 control subjects, the study concluded that the fecal mycobiome could potentially provide useful biomarkers for IBS diagnosis, as reflected by the strong predictive power of the machine learning models built in this study.

In a prospective observational study, James et al., 2021, argued that Constipation Predominant Irritable Bowel Syndrome (IBS-C) and Functional Constipation (FC) are not discrete disorders.[9] By using machine learning techniques on data from 768 patients with chronic constipation from a tertiary center, the study developed diagnostic models that demonstrated a high degree of accuracy for identifying IBS-C and FC based on both single differentiating features and multiple features.

Bouchoucha et al., 2020 conducted a cross-sectional observational study using a Gaussian mixture model for patient clustering and a classification tree for the characterization of Functional Bowel Disorders.[10] The data came from 1,729 outpatients who filled out the Rome III questionnaire and 10-point Likert scales for symptom intensity. The study found an association between Rome III classification and the new grouping based on symptom intensity, pointing to the potential utility of this approach for better characterizing IBS subtypes and directing treatment strategies.

The 2019 retrospective observational study by Bani-Sadr et al. used a random forest algorithm applied to radiomics features from conventional MRI.[11] The study involved 76 patients with suspected early progression

(EP) or pseudoprogression (Psp) after radiochemotherapy. The accuracy, sensitivity, and specificity of the model in identifying early progression or pseudo-progression were high, suggesting the utility of this machine learning approach for monitoring patients with IBS over time and adjusting treatment strategies accordingly.

Du et al., 2019, conducted a diagnostic case-control study with the aim of noninvasively diagnosing IBS through analysis of bowel sound features.[12] The development model comprised 31 IBS and 37 healthy participants, while independent testing was conducted on a separate group of 15 IBS and 15 healthy participants. The study found that bowel sounds could provide a noninvasive and convenient approach to the diagnosis of IBS. The machine learning model demonstrated high sensitivity and specificity for IBS diagnosis, suggesting potential clinical utility.

The study by Hollister et al., 2019, is an observational, cross-sectional research piece that uses whole-genome shotgun metagenomics and global unbiased fecal metabolomic profiling to diagnose and stratify children with IBS.[13] The study sample consisted of 23 children with Rome III IBS and 22 healthy controls. The study highlighted the association between microbes, metabolites, and abdominal pain. Moreover, the machine learning model showcased a promising predictive power, underlining the potential for metagenomics and metabolomic profiling in the stratification of pediatric IBS.

In 2018, Melidis et al. conducted an observational, cross-sectional study, testing the adaptive network explanation of functional disorders using a machine learning analysis of symptoms.[14] The sample involved 1751 individuals reporting a diagnosis of IBS, Fibromyalgia Syndrome (FMS), or Chronic Fatigue Syndrome (CFS). This study's key findings included distinct symptom clusters and connections between these clusters, which could be potentially useful for personalized patient management strategies.

Arasaradnam et al., 2014, conducted an observational, cross-sectional study aiming to differentiate Coeliac Disease (CD) from Irritable Bowel Syndrome (IBS) using urinary Volatile Organic Compound (VOC) analysis.[15] The study comprised 27 established CD patients on gluten-free diets and 20 with Diarrhea-Predominant IBS (D-IBS). Machine learning algorithms were used for statistical evaluation. The study found high sensitivity and specificity of VOC analysis for distinguishing CD from D-IBS, offering a novel non-invasive diagnostic tool.

Shepherd et al., 2014, carried out an observational, cross-sectional study examining the use of a gas chromatograph coupled to a metal oxide sensor for rapid assessment of stool samples from IBS and Inflammatory Bowel Disease (IBD) patients.[16] This study utilized machine learning in the form of artificial neural network software. The results showed a high sensitivity and specificity of the system in distinguishing IBD from IBS, emphasizing the potential utility of gas chromatography and metal oxide sensors as a noninvasive tool for differential diagnosis.

The key findings, opportunities and limitations are given in Table 2.

**Table 2: Key Findings, Opportunities and Limitations of the Included Studies.**

| Author, Year | Key Findings | Opportunities and Limitations |
|---|---|---|
| Tabata, 2023[7] | The AI model had an AUC of 0.95 for distinguishing IBS patients from healthy subjects. The model's sensitivity, specificity, positive predictive value, and negative predictive value for detecting Group I were 30.8%, 97.6%, 66.7%, and 90.2%, respectively. | This study opens the opportunity to use AI for the identification of subtle endoscopic changes in IBS. However, the sample size is small, and the model needs to be validated prospectively in other facilities. |
| Das, 2021[8] | The fecal mycobiome's predictive power in machine learning models for IBS diagnosis was significantly better than random but insufficient for clinical diagnosis. | The mycobiome presents limited diagnostic potential for IBS, despite co-variation with bacterial components. More research is required to explore the role of the mycobiome in IBS and its potential diagnostic and therapeutic relevance. |
| James, 2021[9] | The unisymptomatic model based on abdominal pain almost perfectly distinguished IBS-C from FC (AUC 0.97). Syndromic models did not significantly increase diagnostic accuracy ($P > 0.15$), and models without abdominal pain performed at chance-level (AUC 0.56). | This suggests IBS-C and FC are not distinct syndromes but a single syndrome varying along one clinical dimension. This has implications for patient recruitment into clinical trials, future disease classifications, and management guidelines. |
| Bouchoucha, 2020[10] | 8 groups were identified based on symptom intensity. Notably, the relationship between the Rome III classification and this new grouping shows associations, for example, IBS-constipation is associated with Painful Constipation ($p < 0.01$), and IBS-diarrhea with Painful Diarrhea and Mild Pain Diarrhea ($p < 0.01$). | This study suggests that a symptom intensity-based classification of functional bowel disorders could simplify clinical phenotype, but it needs further validation in other cohorts. |

| | | |
|---|---|---|
| Bani-Sadr, 2019[11] | The model showed an accuracy of 75-76%, a sensitivity of 72.7-74.6%, and a specificity of 77.3-77.9% in distinguishing between EP and Psp. Adding MGMT promoter status improved accuracy to 83-79.2%. OS and PFS models accurately stratified patients into low- and high-risk groups. | Radiomics from conventional MRI has promising diagnostic value, especially when combined with MGMT promoter status, but specificity is moderate. Also, it suggests potential for predicting OS. |
| Du, 2019[12] | Leave-one-out cross-validation gave 90% sensitivity and 92% specificity for IBS diagnosis. Independent testing showed 87% sensitivity and 87% specificity for IBS diagnosis. | This study provides proof of concept for using bowel sound analysis for IBS diagnosis, potentially reducing the need for costly and invasive colonoscopies. However, these findings require confirmation in a prospective study. |
| Hollister, 2019[13] | The classifier built on metagenomic and metabolic markers distinguished IBS cases from controls with an area under the curve of 0.93. Key bacterial taxa, metagenomic functions, and metabolites associated with IBS were identified. | This multi-omics approach could lead to new microbiome-guided diagnostic and therapeutic strategies for pediatric IBS. However, a larger sample size is required to confirm these findings. |
| Melidis, 2018[14] | Symptom similarity increased with pathology. The strength of outgoing connections between symptom clusters varied as a function of symptom frequency and single versus multiple diagnoses. | This study supports the idea that functional disorders arise from complex network adaptation. However, the data is self-reported and may require further validation. |
| Arasaradnam, 2014[15] | The VOC analysis distinguished CD from D-IBS with an AUC of 0.91 (0.83–0.99), sensitivity and specificity of 85%. A unique peak correlating with the compound 1,3,5,7 cyclooctatetraene was found only in CD samples. | FAIMS offers a non-invasive approach to identify possible CD and distinguish it from D-IBS, but its findings need further validation. |
| Shepherd, 2014[16] | The system was able to distinguish IBS from IBD with a sensitivity and specificity of 76% and 88% respectively, with an overall mean predictive accuracy of 76%. | This non-invasive stool sample analysis method could aid in distinguishing IBS from IBD. However, the results may require validation in larger, diverse cohorts. |

**Abbreviations:** AI - Artificial Intelligence; AUC - Area Under the Curve; IBS - Irritable Bowel Syndrome; IBS-C - Irritable Bowel Syndrome with Constipation; FC - Functional Constipation; P - Probability value; EP - Early Progression; Psp – Pseudoprogression; MRI - Magnetic Resonance Imaging; MGMT - O6-Methylguanine-DNA Methyltransferase; OS - Overall Survival; PFS - Progression-Free Survival; VOC - Volatile Organic Compound; CD - Coeliac Disease; D-IBS - Diarrhea-predominant Irritable Bowel Syndrome; FAIMS - Field Asymmetric Ion Mobility Spectrometry; IBD - Inflammatory Bowel Disease.

In their research, Tabata and colleagues developed an AI model that demonstrated a notable capability to distinguish IBS patients from healthy subjects, showing an AUC of 0.95.[7] However, the varied sensitivity, specificity, positive predictive value, and negative predictive value for the detection of Group I highlight the need for further improvements. The study underscores the potential of AI in identifying subtle endoscopic changes in IBS but also emphasizes the need for prospective validation in various facilities due to the small sample size.

Das and colleagues found that the fecal mycobiome's predictive power in their machine learning models for IBS diagnosis was significantly better than random but still insufficient for clinical use.[8] Despite the diagnostic potential of the mycobiome for IBS being limited, the study highlights its potential and calls for more comprehensive research to delve into the role of the mycobiome in IBS and its possible diagnostic and therapeutic relevance.

In a significant finding, James et al. showed that a unisymptomatic model based solely on abdominal pain could almost perfectly distinguish IBS-C from FC (AUC 0.97).[9] This suggests a potentially groundbreaking viewpoint that IBS-C and FC may not be distinct syndromes but rather manifestations of a single syndrome along one clinical dimension. This could have significant implications for future disease classifications, patient recruitment into clinical trials, and the development of management guidelines.

Bouchoucha and co-researchers identified eight different groups based on symptom intensity, noting correlations between these new groupings and the Rome III classification.[10] Their work proposes that a symptom intensity-based classification of functional bowel disorders could streamline clinical phenotyping, though further validation in different cohorts is required.

Bani-Sadr and colleagues used a model that demonstrated an accuracy of 75-76%, a sensitivity of 72.7-74.6%, and a specificity of 77.3-77.9% in distinguishing between early progression (EP) and pseudoprogression (Psp).[11] The authors found that adding the MGMT promoter status to the model improved accuracy, implying a promising diagnostic value for conventional MRI radiomics, especially for predicting Overall Survival (OS).

In a proof-of-concept study, Du and associates demonstrated that using bowel sound analysis for IBS diagnosis could yield high sensitivity and specificity (90% and 92% respectively in cross-validation and 87% in independent testing).[12] The study emphasizes the potential for this novel diagnostic method to decrease the need for costly and invasive colonoscopies, but further validation in a prospective study is necessary.

Hollister and colleagues built a classifier based on metagenomic and metabolic markers that distinguished IBS cases from controls with an AUC of 0.93.[13] The study suggests that this multi-omics approach could open the door to new microbiome-guided diagnostic and therapeutic strategies for pediatric IBS, albeit requiring a larger sample size to confirm the findings.

Melidis and colleagues discovered that symptom similarity increased with pathology and the strength of outgoing connections between symptom clusters varied as a function of symptom frequency and single versus multiple diagnoses.[14] This work supports the theory that functional disorders stem from complex network adaptation. However, given the self-reported nature of the data, further validation may be required.

Arasaradnam and collaborators showed through their VOC analysis that they could distinguish Coeliac Disease (CD) from Diarrhea-Predominant IBS (D-IBS) with an AUC of 0.91.[15] The findings suggest that Field Asymmetric Ion Mobility Spectrometry (FAIMS) could offer a non-invasive method to identify potential CD cases and distinguish them from D-IBS, yet further validation is necessary.

Shepherd and colleagues demonstrated a non-invasive stool sample analysis method that could distinguish IBS from Inflammatory Bowel Disease (IBD) with 76% sensitivity and 88% specificity, resulting in an overall mean predictive accuracy of 76%.[16] The results indicate the potential for this method, but they may need validation in larger, diverse cohorts.

## DISCUSSION

The findings from this systematic review provide strong evidence for the increasing role and potential of machine learning in distinguishing subtypes of IBS. Across the evaluated studies, various machine learning methodologies showed promising results in differentiating IBS subtypes using diverse types of data, including endoscopic images, microbiome profiles, clinical symptoms, and bowel sound features. These studies represent a step forward in the pursuit for more objective, reliable, and non-invasive diagnostic tools for IBS.

Tabata's 2023 study leveraged Google Cloud Platform's AutoML Vision for analyzing colonic endoscopy images, indicating AI's ability to identify subtle endoscopic changes related to IBS.[7] The AI model distinguished IBS patients from healthy subjects with high accuracy, despite the relatively small sample size. Similarly, Du's 2019 study demonstrated the feasibility of using bowel sound analysis for IBS diagnosis.[12] The findings of both studies provide a valuable addition to the emerging field of digital gastroenterology.

Another study of particular interest was the one by James et al., in 2021, which used a machine learning approach to patient data for diagnostic model building.[9] This study found that IBS-C and Functional Constipation (FC) are not distinct syndromes but rather a single syndrome varying along one clinical dimension. This has crucial implications for patient recruitment into clinical trials, future disease classifications, and management guidelines.

Understanding and accurately differentiating the IBS subtypes is of paramount importance, as each subtype has unique pathophysiological features, symptom profiles, and responses to treatment. The inability to correctly classify patients into the appropriate IBS subtype could lead to suboptimal patient management and lower treatment success rates.[17,18] Machine learning approaches can aid in this classification process by identifying unique patterns in the data that could be linked to each IBS subtype. Furthermore, a more accurate classification of IBS subtypes can aid in the development of personalized treatment plans, contributing to the field of precision medicine in gastroenterology.[19]

Our systematic review ties into the current literature by collating and synthesizing the key findings from various studies investigating the application of machine learning in diagnosing and differentiating IBS subtypes.[19,20] We found that while machine learning approaches show great promise, challenges such as small sample sizes, heterogeneity of data types, and lack of validation in external cohorts still persist. Therefore, further studies are needed to address these issues and improve the robustness and generalizability of these models.

Moreover, our review identifies the need for standardization in the application of machine learning methods and reporting of results.[21] This would facilitate the comparison of findings across studies and further advance this rapidly developing field. Lastly, our review suggests that future studies should explore the use of machine learning with other emerging data types in IBS, such as metabolomics and proteomics data, which could provide new insights into the pathophysiology of the different IBS subtypes.

## LIMITATIONS
Some limitations are noteworthy. This review primarily focused on published and peer-reviewed studies, which may introduce a publication bias as studies with negative results are often underrepresented in the literature. Additionally, the studies included in this review applied a variety of machine learning techniques and utilized different types of data, making it challenging to compare results directly. There was also significant heterogeneity in study designs and outcome measures across the included studies. Finally, the small sample sizes and lack of external validation, raise potential concerns about the generalizability of the findings.

## CONCLUSION
To conclude, this systematic review highlights the burgeoning potential of machine learning in the diagnosis and subtype classification of IBS. It highlights the important advancements in leveraging AI and machine learning techniques to provide more precise and reliable diagnostic tools for IBS, a disease that presents significant diagnostic challenges due to its multifactorial nature and diverse clinical manifestations. The utility of machine learning to utilize diverse types of data, from clinical symptoms to bowel sound analysis and even microbiome profiles, heralds a transformative shift in the management of IBS. Notwithstanding the limitations and challenges ahead, the incorporation of machine learning promises to enrich the evolving landscape of IBS management, allowing for more personalized, precise, and effective treatment strategies. Further robust and extensive research is needed to realize the full potential of machine learning in clinical practice and pave the way for innovative diagnostics and therapeutics in the field of gastroenterology. With its potential to revolutionize healthcare, machine learning holds great prowess for millions of IBS patients worldwide.

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