

Irritable Bowel Syndrome

Clinicopathologic mechanisms, clinical diagnosis, and differential reasoning

A symptom-defined syndrome

Clinical reasoning · pathogenesis · differential diagnosis

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Define IBS as a symptom-based syndrome with no characteristic structural lesion.
- Explain the contributions of motility, visceral sensation, gut–brain signaling and luminal factors.
- Apply the Rome V clinical framework while recognizing its distinction from textbook-era wording.
- Distinguish IBS from inflammatory, infectious and microscopic causes of bowel dysfunction.

IBS: A syndrome, not a single lesion

Chronic or recurrent bowel symptoms without a defining macroscopic or microscopic lesion

- A clinical umbrella for potentially heterogeneous mechanisms.
- The symptoms are real even when endoscopy and biopsy are normal.
- Clinical phenotype is more informative than a tissue diagnosis.

Three symptom domains define the phenotype

Abdominal pain

Recurrent discomfort is central to case recognition.

Bloating

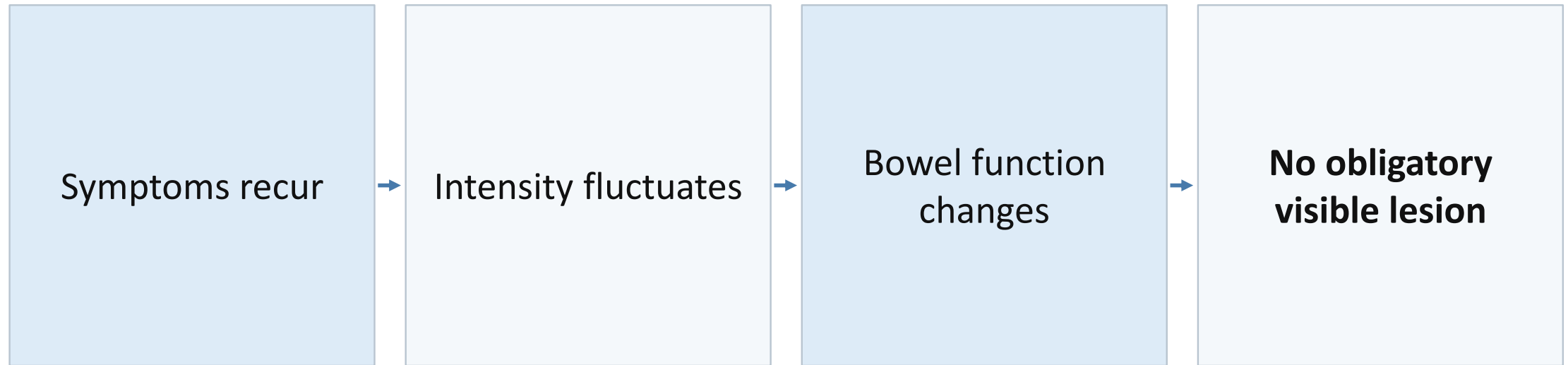
May accompany pain without tissue injury.

Altered bowel habit

Constipation, diarrhea, or both.

The combination—not any isolated symptom—is the clinical clue.

Relapsing symptoms do not imply tissue injury



A relapsing clinical course is compatible with normal structural assessment.

A normal biopsy is expected in uncomplicated IBS

Macroscopic examination

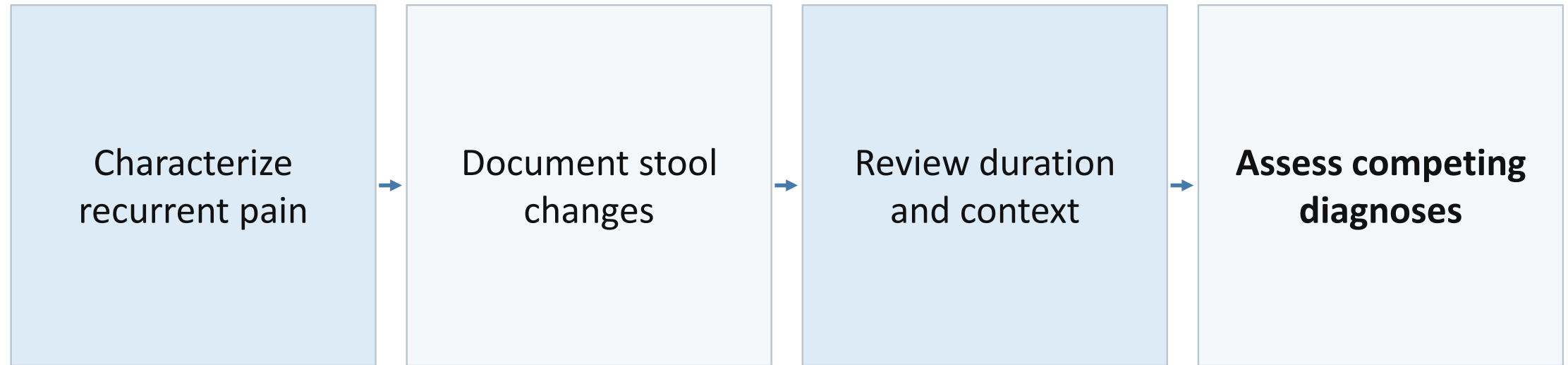
No defining mass, ulcer, or inflammatory lesion

Microscopic examination

No characteristic structural change required for the diagnosis

Normal tissue does not invalidate an abnormal sensation or motility phenotype.

Diagnosis begins with the symptom pattern



IBS does not have a pathognomonic histologic marker.

IBS has recognizable bowel-habit subtypes

IBS-C

Constipation-predominant

IBS-D

Diarrhea-predominant

IBS-M

Mixed abnormal stool forms

Rome V also retains IBS-U for an unclassified bowel-habit pattern.

Subtype and syndrome are different questions

Question 1: Is this IBS?

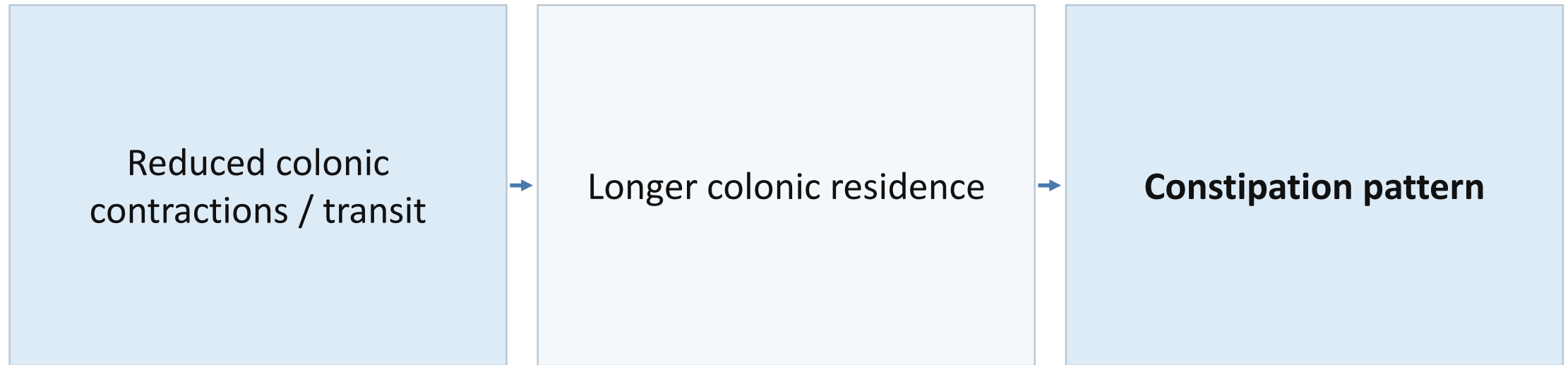
Recurrent pain/discomfort related to bowel function; Duration and associated features.

Question 2: Which subtype?

Determine predominant abnormal stool form, preferably off symptom-altering medication.

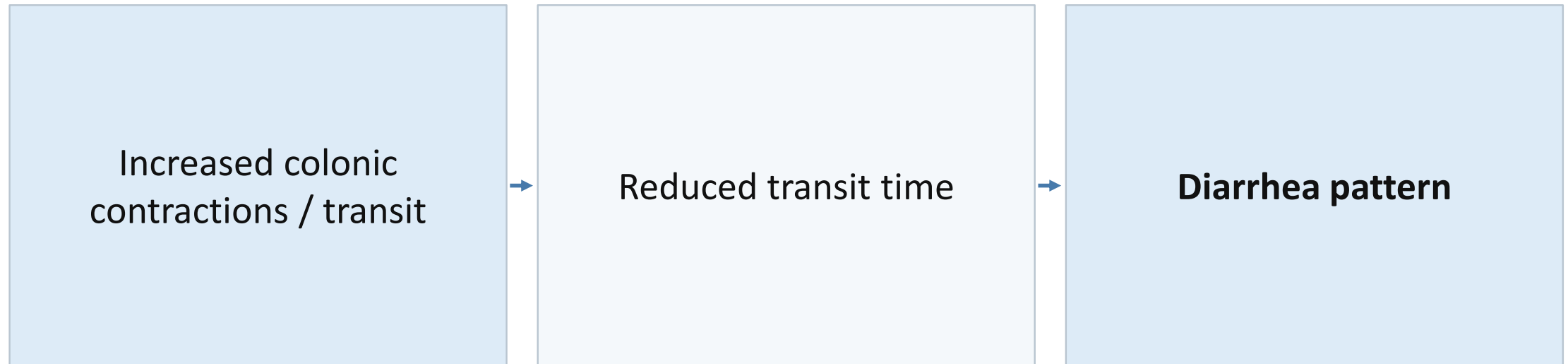
Subtyping follows—rather than replaces—syndrome recognition.

IBS-C: Transit and stool retention



Reduced colonic motility as a tendency, not a universal mechanism.

IBS-D: Accelerated transit



A tendency toward increased motility can coexist with sensory or bile-acid contributions.

IBS-M: Abnormal stool forms coexist

Constipation episodes

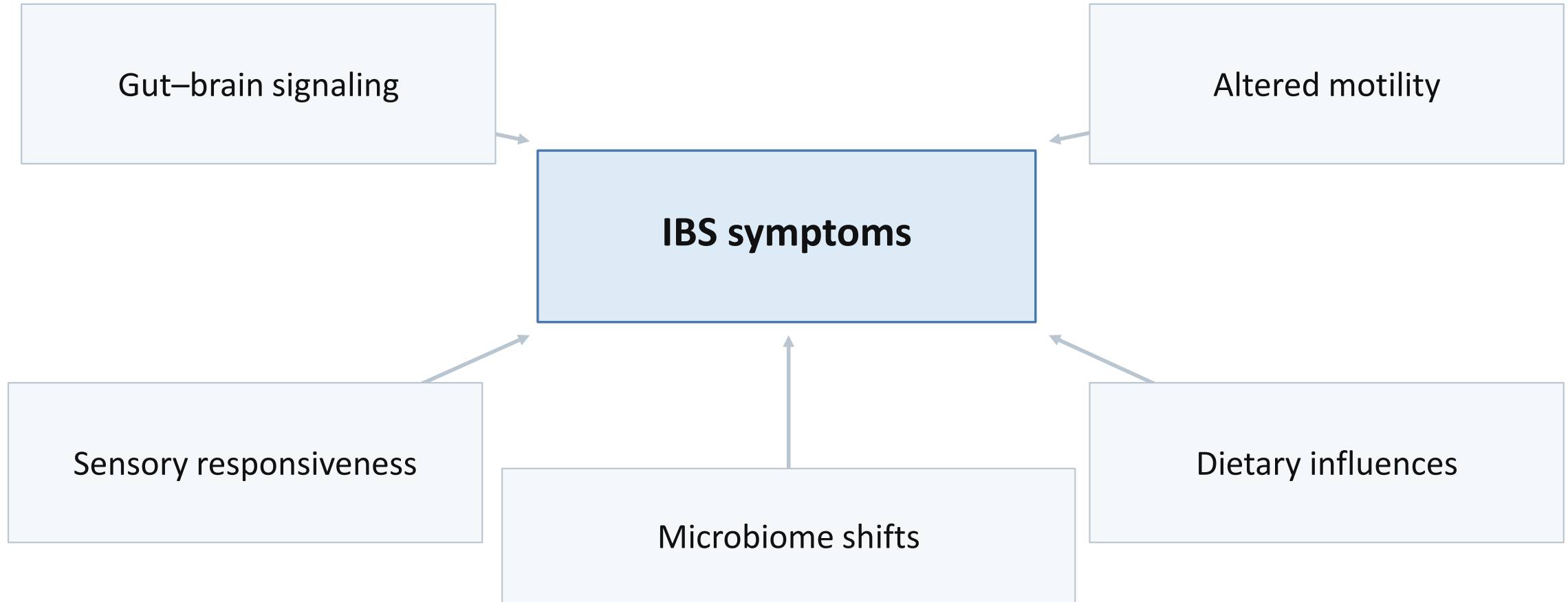
Hard or lumpy stools occur in a substantial fraction of abnormal bowel movements.

Diarrheal episodes

Loose or watery stools also occur in a substantial fraction.

A single stool sample is insufficient to characterize the pattern.

An integrative pathogenesis model



These are interacting contributors; Robbins does not assert one universal causal pathway.

Enteric sensory responses may be heightened



Symptom intensity need not correlate with visible mucosal damage.

Visceral sensitivity explains the pathology paradox

Tissue-level assessment

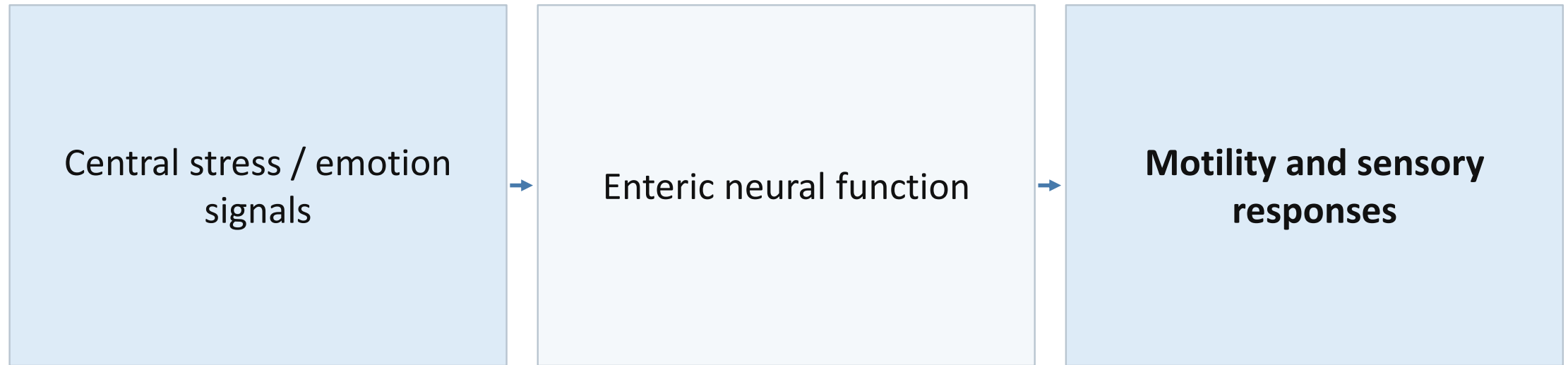
No corresponding diagnostic lesion may be found.

Functional assessment

Responses to gastrointestinal stimuli can nevertheless be amplified.

This is a mechanistic explanation, not a stand-alone diagnostic test.

The gut–brain axis is bidirectional



Enteric signals can also influence central symptom perception; The relationship is not one-way.

Enteric nervous system dysfunction is implicated

- Altered enteric nervous system activity to IBS.
- Disordered signaling can affect both motility and sensory processing.
- The involvement is supported by physiologic and molecular associations.
- No single neural defect is necessary or sufficient for all cases.

Stress modifies symptoms without negating them

Stress-related input

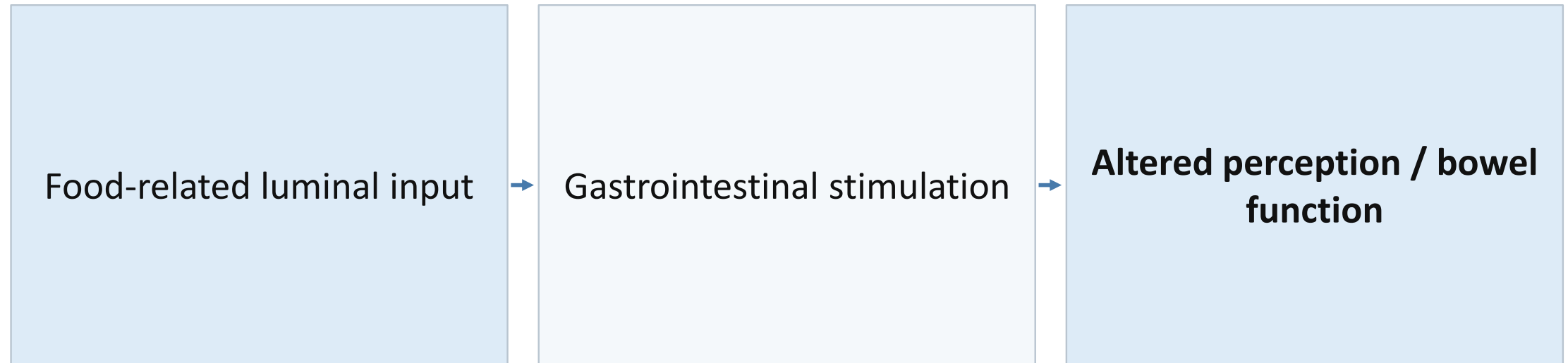
Can modify gut–brain signaling, motility, and sensory responsiveness.

Clinical interpretation

Stress association is not proof that symptoms are imagined or voluntary.

A biopsychosocial mechanism is compatible with biologically mediated symptoms.

Diet is a potential symptom modifier

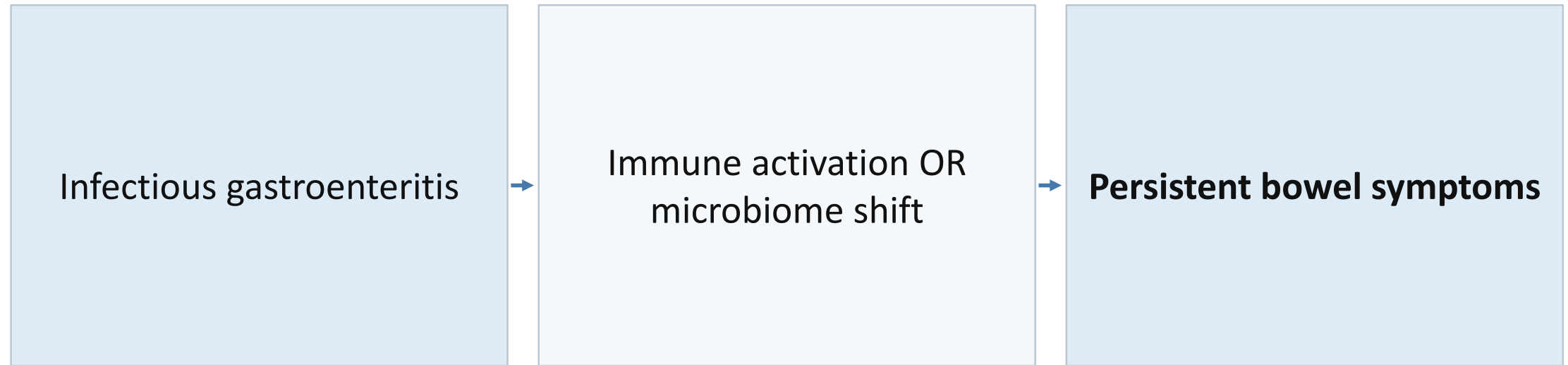


The source identifies diet as one factor; Individual food triggers are not universal.

Microbiome perturbation is one proposed contributor

- A shift in intestinal microbial communities may modify intestinal signaling.
- The microbiome is discussed as part of an interacting pathogenesis model.
- Robbins does not identify a single diagnostic IBS microbial signature.
- Association alone does not establish a treatment target in every patient.

Postinfectious IBS: A clinically identifiable pathway



Immune activation and dysbiosis as alternatives or joint hypotheses.

Postinfectious IBS is not persistent infection by default

Preceding event

Documented or recalled infectious gastroenteritis before symptom onset.

Subsequent syndrome

Ongoing IBS-type symptoms may persist after the acute infection has resolved.

Evaluate active infection separately if clinical evidence indicates it.

Excess bile acids can contribute to IBS-D



A recognized mechanism in a subset of patients—not synonymous with all IBS-D.

Bile acids affect two intestinal functions

Motility

Bile acids can alter intestinal contractile and transit behavior.

Epithelial ion transport

Changes in ion handling can increase luminal water movement.

Both effects provide a biologic route to loose stools.

Not all IBS-D is bile-acid mediated

- IBS-D denotes the stool phenotype rather than one etiology.
- Bile-acid excess or malabsorption accounts for some cases.
- Motility, sensory and gut–brain factors may also be involved.
- A therapeutic or diagnostic approach may need mechanism-specific reasoning.

Serotonin signaling is a candidate pathway



Genetic links to serotonin reuptake transporters are associations, not diagnostic biomarkers.

Other molecular associations remain exploratory

Cannabinoid receptors

Candidate regulatory
signaling.

TNF-related mediators

Candidate inflammatory
signaling.

Serotonin transporters

Candidate neurotransmitter
handling.

Association studies do not establish a single-gene explanation for IBS.

Genetic associations $\neq$ a clinical genetic test

What studies suggest

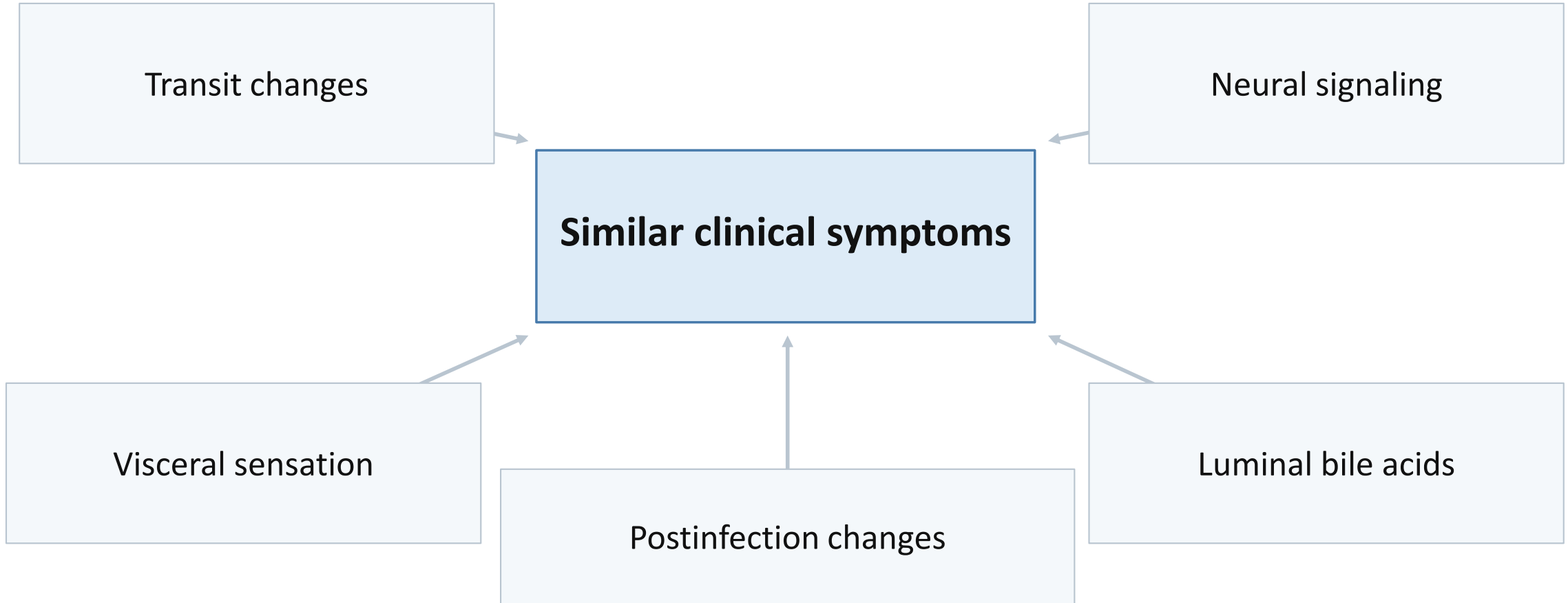
Several candidate gene families may influence susceptibility or phenotype.

What they do not prove

No reported candidate variant is a specific diagnostic test for IBS.

Separate etiologic hypotheses from clinically validated biomarkers.

IBS is best understood as mechanistic heterogeneity



Different mechanisms may converge on a shared symptom-defined syndrome.

5-HT₃ blockade links mechanism and treatment



Treatment response supports pathway relevance but is not proof of etiology in each patient.

Motility-directed agents target a symptom domain

Diarrhea-predominant IBS

Opioid-acting antidiarrheal agents can reduce stool frequency.

Important limitation

Bowel-habit improvement need not resolve abdominal pain or other mechanisms.

Robbins mentions opioid and anticholinergic effects; Specific prescribing needs separate guidance.

IBS prevalence varies with the definition

Approximately 5–10% reported in high-income settings

- Peak prevalence is reported at 20–40 years.
- A female predominance is described.
- Changes in symptom criteria affect prevalence estimates.

Epidemiology: Avoid conflating case definitions

Reported prevalence

Dependent on population, survey method, and diagnostic threshold.

Biologic interpretation

A criteria-driven shift is not automatically a true change in disease occurrence.

State the criteria and population when interpreting an IBS frequency estimate.

The textbook criterion requires interpretation

- The extracted Robbins text describes abdominal pain or discomfort ≥ 3 days/month over 3 months.
- It also mentions improvement with defecation and change in stool frequency or form.
- This wording resembles earlier criteria and is not identical to Rome IV.
- The current adult Rome V framework should be identified by its 2026 edition.

Rome V (2026): Core adult IBS criteria

≥ 3 days per month

Recurrent, not continuous, abdominal pain or discomfort in the last 3 months

- Associated with ≥ 2 bowel-related features.
- Onset must precede diagnosis by ≥ 6 months.

Rome V: The three associated features

Defecation

Symptoms are related to defecation.

Stool frequency

A change in frequency is present.

Stool form

A change in form/appearance is present.

At least two features accompany the recurrent pain or discomfort.

Rome IV to Rome V: Two key revisions

Rome IV · 2016

Abdominal pain ≥ 1 day/week.
The word discomfort was not included.

Rome V · 2026

Pain OR discomfort ≥ 3 days/month.
Symptoms should be recurrent, not continuous.

Both versions require bowel-related features and chronic symptom onset.

Duration matters in Rome V



A brief acute diarrheal illness alone is not established adult IBS.

Defecation can improve or worsen symptoms

What the criterion says

Pain/discomfort is RELATED to defecation.

What not to assume

Improvement after defecation is not obligatory for every patient.

The modern wording is broader than “relieved by defecation.”

Altered stool frequency is one association

Change from the patient's usual bowel movement frequency

- Frequency may increase in a diarrheal phenotype.
- Frequency may decrease in a constipated phenotype.
- Frequency alone does not classify every case or establish IBS.

Stool form is distinct from stool frequency

Frequency

How often bowel movements occur.

Form

Whether stool is hard/lumpy or loose/watery.

Assess both rather than using “diarrhea” and “constipation” imprecisely.

Rome V stool-form subtyping

Subtype	Hard stool (types 1–2)	Loose stool (types 6–7)
IBS-C	>25%	<25%
IBS-D	<25%	>25%
IBS-M	>25%	>25%
IBS-U	Not classifiable by the above patterns	Not classifiable by the above patterns

Applied to bowel movements on days with abnormal stool; Evaluate off bowel-habit medications.

Bristol Stool Form Scale anchors terminology

Types 1–2

Hard / lumpy

Types 3–5

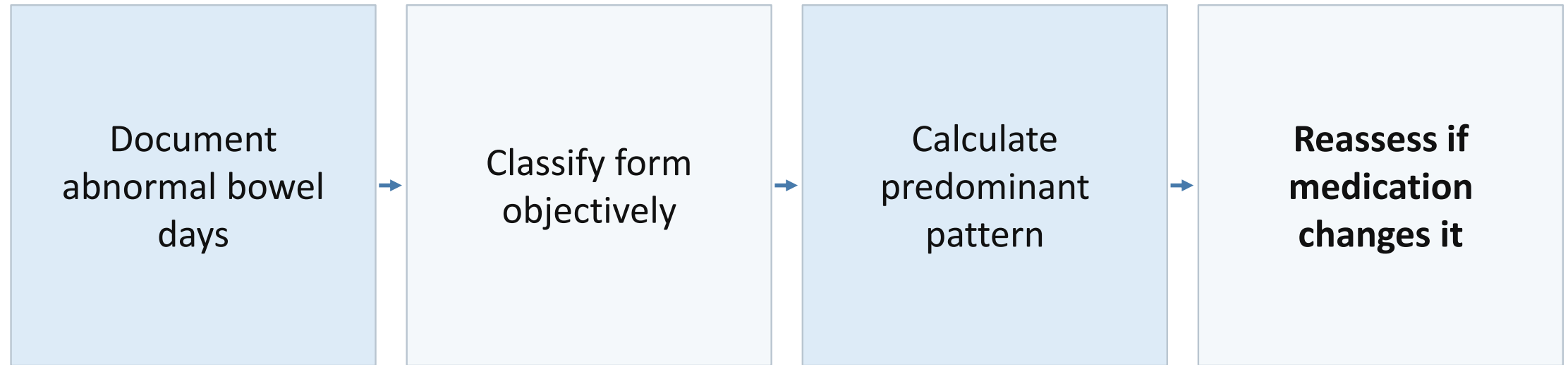
Intermediate formed stools

Types 6–7

Mushy / watery

IBS subtype rules emphasize hard and loose extremes, not an average over all seven types.

Subtype assignment needs representative observations



Rome V advises prospective stool diaries for clinical trial subtyping.

IBS versus chronic constipation

IBS-C

Recurrent bowel-related pain/discomfort
plus constipation pattern.

Chronic constipation

Constipation symptoms without
sufficient IBS criteria.

Pain/discomfort is central to syndromic differentiation.

IBS versus functional diarrhea

IBS-D

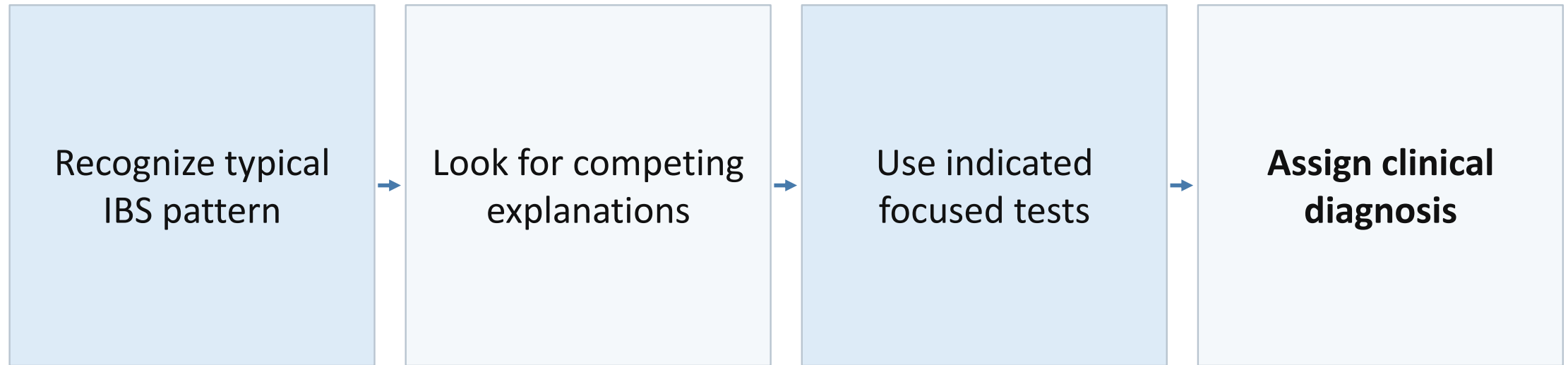
Diarrheal pattern with qualifying recurrent abdominal pain/discomfort.

Functional diarrhea

Predominantly loose/watery stool without the required IBS symptom constellation.

The two labels should not be used interchangeably.

A positive diagnosis still requires judgment



ACG favors positive rather than exhaustive exclusionary diagnostic strategies.

Alarm findings change the diagnostic pathway

Typical pattern

Stable recurrent symptoms with a convincing IBS relationship to stool function.

Concerning finding

Bleeding, anemia, weight loss or other evidence of organic disease demands evaluation.

Do not explain new objective abnormalities by IBS without independent assessment.

Infection can mimic or precede IBS

Active enteric infection

An infectious cause must be considered for relevant acute or persistent diarrhea.

Postinfectious IBS

IBS-like symptoms begin after a gastrointestinal infection has resolved.

The temporal sequence alone does not demonstrate an active pathogen.

IBS versus inflammatory bowel disease

Feature	IBS	Inflammatory bowel disease
Diagnostic basis	Characteristic symptom pattern	Evidence of chronic intestinal inflammation
Endoscopy	No characteristic lesion	May reveal ulcers/inflammatory changes
Histology	No defining inflammatory pattern	May show crypt injury, inflammation or granulomas
Concern	Functional impairment	Tissue injury and complications

Structural inflammation is not expected in uncomplicated IBS.

Microscopic colitis is a crucial trap



Normal endoscopy alone cannot distinguish IBS from microscopic colitis.

Two microscopic-colitis morphologies

Collagenous colitis

A thickened subepithelial collagen band
and inflammation.

Lymphocytic colitis

Increased intraepithelial lymphocytes
without the collagenous band.

These are biopsy-defined entities, unlike IBS.

Normal gross appearance $\neq$ normal histology

IBS

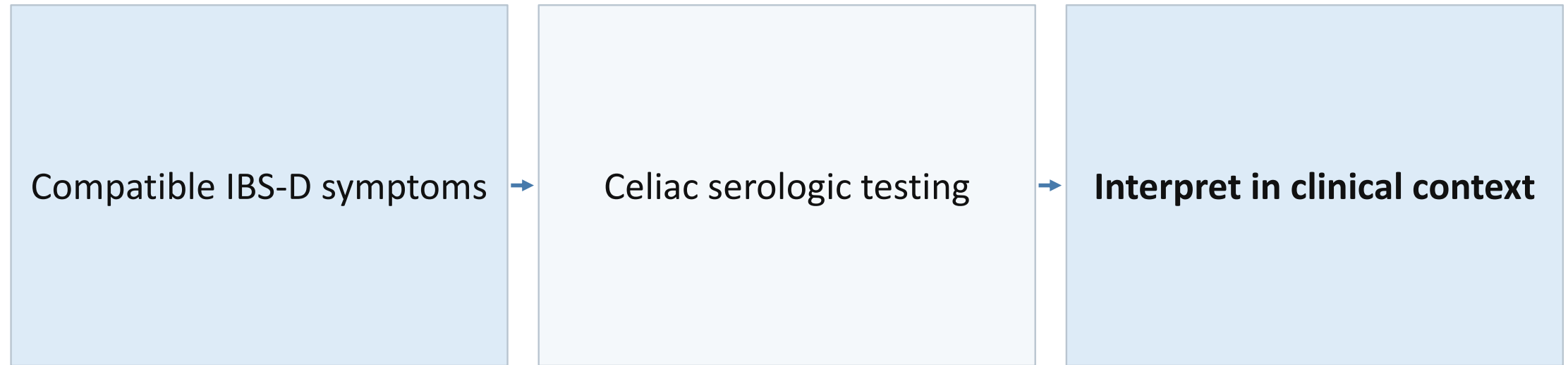
Endoscopy and routine histology may both be normal.

Microscopic colitis

Endoscopy can be normal despite diagnostic microscopic change.

The investigative question determines when sampling adds value.

Targeted testing: Celiac disease in IBS-D



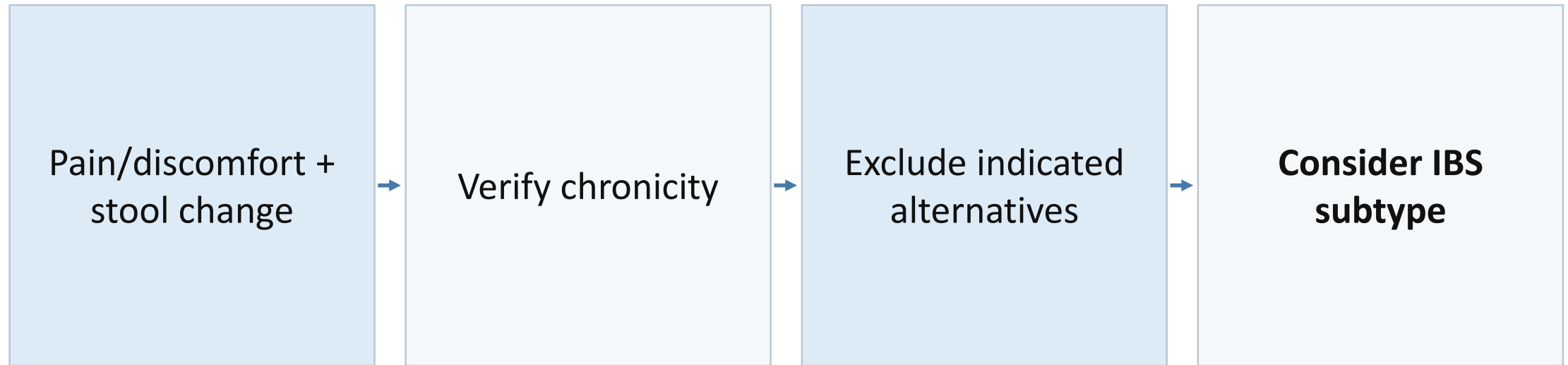
ACG 2021 advises screening for celiac disease in patients with IBS and diarrhea symptoms.

Targeted testing: Inflammatory disease in IBS-D



ACG 2021 suggests fecal calprotectin to help exclude IBD in appropriate patients.

Clinical reasoning: Combine pattern and testing



Do not require normal colonoscopy in every patient as a universal gatekeeper.

Case 1: Recurrent pain and loose stools

Clinical vignette

A 27-year-old reports 10 months of recurrent abdominal discomfort, frequently associated with defecation, and loose stools during episodes. There is no described inflammatory or bleeding feature.

What additional history confirms the symptom criterion, and which subtype is plausible?

Case 1: Reason through the diagnosis

- Establish recurrence on ≥ 3 days/month in the preceding 3 months.
- Confirm at least two bowel-related features.
- Characterize the proportion of loose and hard abnormal stools.
- Consider IBS-D only if the subtype pattern fits and alternatives are assessed.

Case 2: Watery diarrhea with normal endoscopy

Clinical vignette

A 58-year-old has persistent watery nonbloody diarrhea. The colon appears macroscopically normal. Biopsies show a thickened subepithelial collagen band.

Which diagnosis explains the microscopic finding, and why is IBS inadequate?

Case 2: Tissue evidence overrides a symptom label

- The collagen-band finding supports collagenous colitis.
- This is a recognized cause of watery diarrhea with normal endoscopy.
- IBS does not account for this diagnostic histopathology.
- A normal endoscopic appearance must not be mistaken for normal mucosal biology.

Case 3: Bowel symptoms after gastroenteritis

Clinical vignette

An adult recovers from infectious gastroenteritis but subsequently develops chronic episodic pain, bloating and altered stool form. No pathogen persistence is documented.

Which IBS pathway is suggested, and what competing explanation remains important?

Case 3: A mechanism is not a confirmed cause

- Postinfectious IBS is a reasonable clinical hypothesis.
- Immune activation and microbiome shifts are proposed mechanisms.
- Ongoing infection must be reconsidered when findings suggest it.
- The history alone does not specify a microbial or immune biomarker.

Management starts with the dominant problem

Pain / discomfort

Target gut–brain/sensory dimensions.

Diarrhea

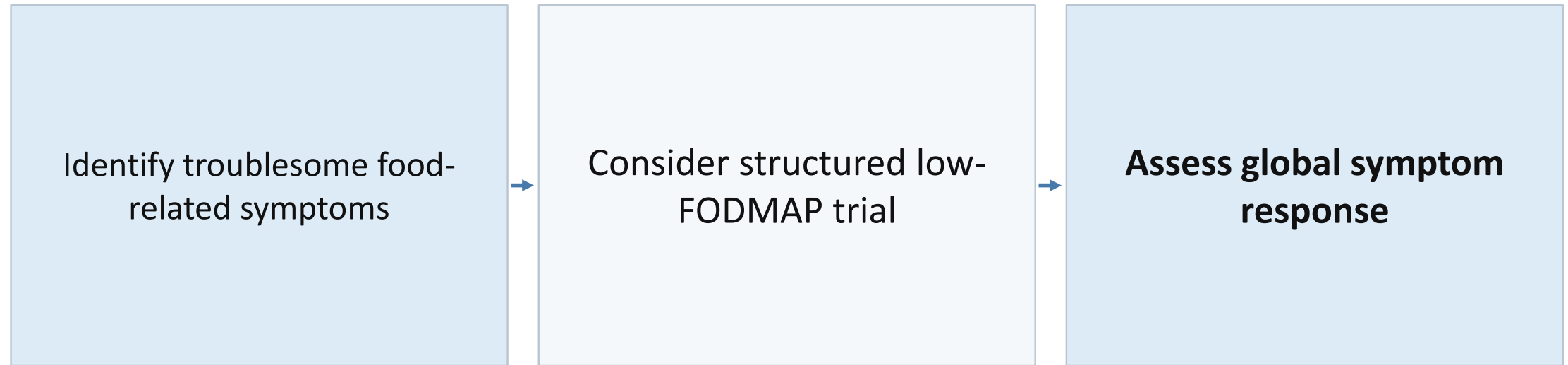
Consider transit and selected mechanism-directed interventions.

Constipation

Consider measures directed at impaired transit or secretion.

Different symptom dimensions may require different approaches.

Dietary intervention is a time-limited trial



ACG 2021 recommends a limited trial; This is guidance beyond the Robbins paragraph.

Gut-directed psychotherapy is biologically coherent



ACG 2021 suggests gut-directed psychotherapy as an IBS treatment option.

IBS-C: Approved secretory targets

Chloride-channel activators

Increase intestinal fluid movement; A guideline-endorsed treatment class.

Guanylate-cyclase activators

Another guideline-endorsed IBS-C treatment class.

ACG 2021 recommendations are treatment evidence, not textbook pathogenesis claims.

IBS-D: Treatment need not imply infection

Rifaximin

ACG 2021 recommends treatment of global IBS-D symptoms in selected patients.

Interpretation

An antibiotic response cannot establish ongoing bacterial infection as the universal IBS-D cause.

Treatment selection requires patient-specific assessment.

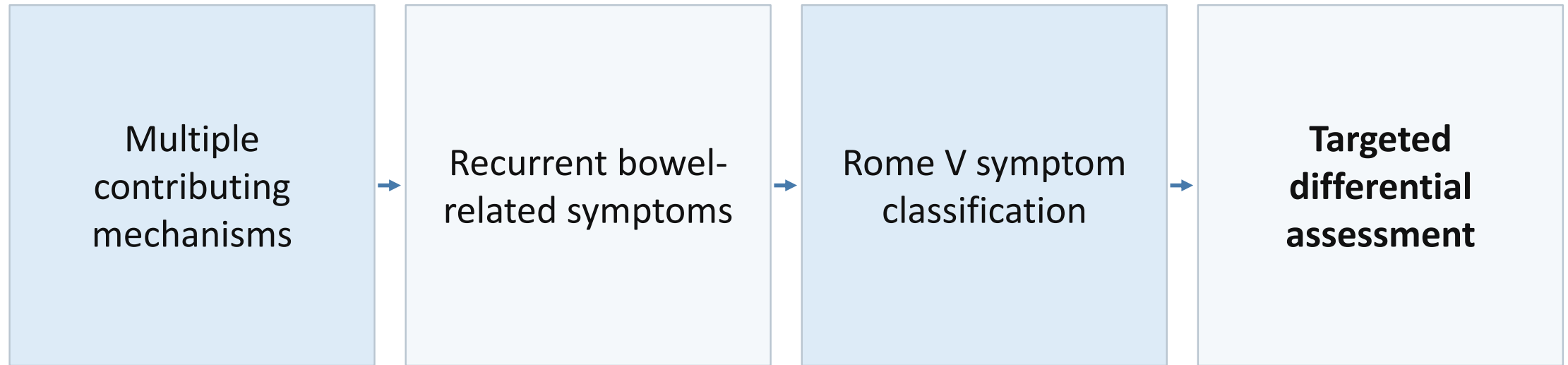
Mechanism-targeted care has limitations

- Clinical subtypes are defined by stool pattern, not unique pathology.
- Several mechanisms may coexist in one patient.
- No single medication addresses all mechanistic contributors.
- Response to intervention does not independently confirm a specific cause.

Four errors to avoid

Error	Better interpretation
“Normal biopsy means no disease.”	IBS can involve sensory/motility dysfunction.
“All watery diarrhea is IBS-D.”	Consider infection, IBD and microscopic colitis.
“Stress proves symptoms are psychological.”	Gut–brain interaction is a physiologic model.
“A genetic association diagnoses IBS.”	Reported gene links are not validated diagnostic tests.

Integrated model: From physiology to diagnosis



The clinicopathologic task is to interpret symptoms without inventing a lesion.

Five clinically important conclusions

- IBS is a heterogeneous symptom-defined syndrome with real functional impairment.
- Endoscopic and microscopic assessments have no defining IBS lesion.
- Motility, sensation, gut–brain signaling, bile acids and postinfection changes may contribute.
- Rome V (2026) broadens the symptom threshold relative to Rome IV.
- A positive diagnosis must remain sensitive to inflammatory and microscopic mimics.

Principal sources

Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. Chapter 17, pp. 727.

Rome Foundation. Rome V Diagnostic Criteria for Adult IBS and IBS Subtypes (2026).

Rome Foundation. Rome IV Diagnostic Criteria for Adult IBS (2016).

Lacy BE, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021;116:17–44.