



Research Summary: SIBO Recurrence

As featured in Dr. Kenny Mittelstadt's video:
SIBO Keeps Coming Back? Here's What You're Missing
Date of Publication: 06/06/2026

Research Context:

This video explores why SIBO comes back so predictably after treatment, and what the research tells us about the conditions that allow it to return. The issue is not usually a failure of the antimicrobial treatment itself. It is that treatment addresses the bacteria without changing the environment that made overgrowth possible in the first place.

The three studies below look at three distinct but connected pieces of that environment: stomach acid, the relationship between SIBO and gut lining integrity, and what happens to the gut's pacemaker cells after infection.

Key Findings from the Research:

Study 1 (PMID 28770351): A 2018 meta-analysis looked at whether proton pump inhibitor use (PPIs are the most commonly used acid-reducing medications) raises the likelihood of SIBO. Researchers pooled data from multiple studies and found that people taking PPIs had roughly twice the odds of having SIBO compared to those not taking them. The proposed reason is straightforward: stomach acid is one of the gut's built-in defenses against bacterial overgrowth. When that acid is suppressed, that defense is weakened, and bacteria that would normally not survive the upper digestive tract can accumulate. This connection between acid-suppressing medication and SIBO risk gives a concrete example of how digestive power shapes the bacterial environment.

Note: This is a meta-analysis of observational studies. It shows a pattern between PPI use and SIBO, but cannot confirm that PPIs directly cause SIBO in every case. The script appropriately frames this as a risk factor, not a guarantee.

Study 2 (PMID 28274108): This 2017 review examined what connects SIBO and irritable bowel syndrome at the level of gut biology. One of its central observations is that SIBO and compromised gut lining integrity tend to co-occur and reinforce one another. When bacteria overgrow in the small intestine, they can damage the mucosal lining. When the lining is damaged, the environment becomes more hospitable to future overgrowth. This two-way relationship helps explain why treating the bacteria alone often produces temporary results: the terrain that supported the overgrowth is still in place. The review also draws attention to how motility, immune tone, and the gut microbiome all interact, framing SIBO not as a single-system problem but as a pattern that runs across multiple connected systems.

Study 3 (PMID 28679338): This study used a post-infectious mouse model to examine what happens to the gut's pacemaker cells after an infection clears. The interstitial cells of Cajal (ICC) are the cells that drive the migrating motor complex, which is the cleansing wave that moves bacteria out of the small intestine between meals. Researchers found that mice who developed SIBO after a gut infection had significantly lower ICC density compared to those who recovered without SIBO. When ICC density in the ileum dropped below a specific threshold, 54% of those mice developed SIBO. When density was low across multiple bowel segments, that number rose to 88%. This suggests that the reduction in these pacemaker cells after infection may be a meaningful driver of why SIBO develops and returns in some people.

Note: This is an animal model study. The specific mechanisms and thresholds observed in mice do not translate directly to human physiology. This study supports the biological plausibility of the post-infectious motility mechanism discussed in the video, but human research on this specific pathway is still developing.



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Functional Medicine Connections:

Here is how these three pieces fit together. Your small intestine has several built-in systems that keep bacteria from accumulating. Stomach acid acts as a filter at the entrance. The migrating motor complex sweeps bacteria toward the colon between meals. The gut lining, when intact, limits bacterial translocation and keeps the immune system from staying in a state of low-grade activation.

When any one of these systems is compromised, the others carry more load. When more than one is compromised at the same time, the conditions for SIBO become more stable and harder to disrupt through antimicrobial treatment alone.

The nervous system layer adds another dimension. The migrating motor complex is regulated partly through vagal signaling. When the nervous system is in a sustained stress state, vagal tone drops, motility slows, and the cleansing wave becomes less reliable. This means that stress chemistry is not just something you feel. It actively shapes the digestive conditions that either prevent or enable bacterial accumulation.

This is why SIBO recurrence is not a mystery. It is a predictable outcome when the terrain has not changed.

Practical Reflections & Takeaways:

When you think about the times your SIBO symptoms have returned, what was happening in your life in the weeks or months before? Was there a change in stress load, sleep, a new medication, or a shift in eating patterns? Those observations may be pointing toward which lever is most relevant to your pattern.

If you have been treated for SIBO more than once, what has been the focus of each treatment? Was the terrain, the digestive environment, or the nervous system ever part of the conversation?

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