Impaired glucose metabolism in irritable bowel syndrome: personalised low-glycaemic diet as potential therapeutic target

We read with great interest the recent study by Gilliam-Vigh *et al* demonstrating significant transcriptomic alterations in the intestinal mucosa of individuals with type 2 diabetes (T2D), particularly increased immune activation, altered barrier function in the large intestine and metabolic dysfunction.[1] These findings provide crucial mechanistic insights that complement observations on metabolic disturbances in patients with irritable bowel syndrome (IBS), supporting the rationale for glucose-targeted interventions.

PERSONALISED LOW-GLYCAEMIC DIET: A NOVEL THERAPEUTIC APPROACH

Given the substantial interindividual variability in glycaemic responses,[2] we investigated the therapeutic potential of a personalised low-glycaemic diet (PLGD) in IBS management. In our nutritional observation study of 20 age and gender-matched patients with IBS, we compared clinical outcomes between those receiving either a PLGD or the established low-FODMAP diet (LFD) over a minimum 3-month period (figure 1).

Remarkably, our personalised nutrition (PN) approach achieved symptom improvement comparable to standard LFD, assessed by the validated IBS Severity Scoring System (IBS-SSS) (online supplemental material). PLGD showed a −100 point reduction in IBS-SSS (p=0.0195), comparing favourably to published data from Nybacka *et al*, where LFD plus dietary advice reduced scores by −117 points, and a low-carbohydrate diet achieved −93 points.[3]

MECHANISTIC RATIONALE

The mechanistic basis for targeting glucose metabolism in IBS is supported by several converging lines of evidence. IBS pathophysiology is characterised by gut-brain axis dysregulation, involving interactions among the central and enteric nervous systems, gut microbiota and mucosal immune system.[4] Impairments in glucose metabolism observed in patients with IBS suggest glycaemic control as a promising therapeutic target that may influence several of these pathways simultaneously.

Furthermore, the transcriptomic signature described by Gilliam-Vigh *et al* in patients with T2D mirrors pathophysiological features observed in IBS. This convergence points to the metabolic-immune axis as a shared pathogenic mechanism across both disorders. Importantly, hyperglycaemia itself drives intestinal barrier dysfunction and increases infection risk,[5] providing direct mechanistic support for glucose-targeted interventions in functional GI disorders.

The regional specificity of transcriptomic changes is particularly noteworthy. The reported immune activation in the ileocaecal region and large intestine corresponds to the anatomical loci most frequently implicated in IBS symptomatology. This regional vulnerability may explain why targeting glucose metabolism through PN yields symptomatic benefit across distinct IBS phenotypes.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

PLGD offers several clinical advantages over traditional dietary strategies. Unlike LFD, which may reduce beneficial short-chain fatty acid production and adversely affect GI microbiota composition and cardiometabolic risk profile with

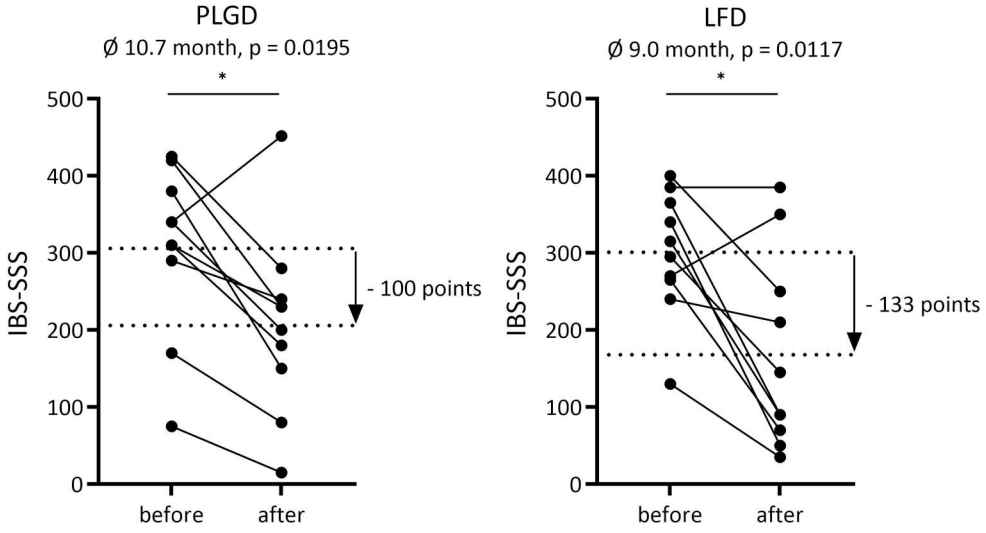

Figure 1 Precomparison and postcomparison in IBS Severity Scoring System (IBS-SSS) between age- and gender-matched patients with IBS receiving either a personalised low-glycaemic diet (PLGD, n=10) or a standard therapy low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) diet (LFD, n=10) using paired Wilcoxon test. The group means are represented by a dashed line, and an arrow represents the reduction in IBS-SSS, with a reduction between 50 and 230 points in PLGD and between 30 and 290 points in LFD. *P<0.05.

long-term use,[6] PLGD could maintain dietary diversity while optimising individual metabolic responses.

Our approach used a 2-week self-directed test phase with continuous glucose monitoring (CGM), followed by app-based dietary recommendations, eliminating the need for intensive dietary counselling while accommodating individual food preferences and intolerances. This approach addresses key limitations of current dietary interventions: the need for specialised dietary counselling, restricted food choices and potential long-term cardiovascular and microbiome alterations.

The integration of CGM with digital therapeutic platforms offers a scalable, personalised approach to IBS management that could be widely implemented in clinical practice. This PN strategy aligns with the growing recognition that 'one-size-fits-all' dietary recommendations have limited efficacy in heterogeneous conditions like IBS.

CONCLUSION

Our findings suggest that patients with IBS exhibit impaired glucose metabolism and that PLGD can achieve therapeutic benefits comparable to established treatments. The mechanistic insights provided by Gilliam-Vigh *et al* underscore the role of metabolic-immune interactions. Combined with evidence that hyperglycaemia could drive intestinal barrier dysfunction, these findings establish a compelling rationale for targeting glucose metabolism in IBS. Therefore, PN, targeting individual glycaemic responses, may represent a paradigm shift in functional GI disorder management, offering both mechanistic rationale and practical advantages over current dietary interventions.

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Funding This work was supported by the German Federal Ministry of Research, Technology and Space (01KD2103A and 01EA2109A).

Disclaimer The views presented in this manuscript are those of the authors and not necessarily those of the company.

Competing interests TS is employed at Perfood Laboratories GmbH. TS is a co-founder of Perfood Laboratories GmbH and a minority shareholder.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and data collection was conducted under the framework of the 'OUTLIVE-CRC study', which was approved by the Ethics Committee of the University of Lübeck (AZ 21-415) and registered in the German Clinical Trials Register (DRKS00031028). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; internally peer reviewed.

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/gutjnl-2025-336797).

To cite Schmelter F, Schröder T, Laumonnier Y, *et al*. *Gut* 2026;**75**:1081–1083.

Received 25 August 2025
Accepted 24 September 2025
Published Online First 5 October 2025

Gut 2026;**75**:1081–1083. doi:10.1136/gutjnl-2025-336797

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