



The Gut Microbiome as a Nutritional Target: Separating Established Mechanism From Commercial Claim

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Abstract

The gut microbiome is offered as a target for nutritional intervention across a large consumer market, and the published evidence supports that framing much less evenly than the marketing implies. The strongest randomised result in the field concerns transplanting a whole community rather than feeding one: donor faeces infusion resolved recurrent infection in 13 of 16 patients against 4 of 13 on vancomycin alone, a trial stopped early for benefit. That intervention is not dietary. The best-supported dietary exposure, fibre, was synthesised across 185 prospective studies and 58 trials and associated with 15 to 30 per cent lower mortality, but its established route runs through fermentation substrate and metabolites rather than through any directed change in community composition. Where supplementation has been examined mechanistically the direction is unfavourable: after antibiotics, probiotics delayed and left incomplete the reconstitution that recovered rapidly with autologous transplant. Regulatory assessment reflects this. Of 4,637 general function claims submitted in the European Union, no probiotic health claim has been authorised, and the single authorised claim involving live cultures concerns lactose digestion in yoghurt. The mechanism is established at one link in the chain and the commercial claim is made about another.

Keywords: Gut microbiome; Probiotics; Dietary fibre; Health claims; Evidence quality

Introduction

That the resident gut community influences host physiology is not in dispute, and the sequencing methods that established it are two decades old [1,2]. What follows from it for nutritional practice is a separate question, and the gap between the two is where a substantial consumer market operates [3,4].

The claim structure is usually the same. A mechanism is demonstrated, generally in animals or in vitro; an association is reported between some dietary exposure and an outcome; and a product is offered on the implication that the first explains the second and can be purchased [3,5]. Each step may be sound in isolation while the chain is not [5,6].

This review separates the links. It asks which parts of the diet-microbiome-outcome chain carry randomised evidence,

which carry association only, and which carry neither.

Objective

This review sets out to establish four things from the published literature. First, where the strongest randomised evidence in the field actually sits and whether it is nutritional. Second, what the best-supported dietary exposure shows and by what route. Third, what happens when supplementation is examined mechanistically rather than by outcome. And fourth, what regulatory assessment of the marketing claims has concluded.

Literature Review

The strongest result is not a diet: A randomised trial in recurrent infection assigned patients to donor faeces infusion after a short vancomycin course and bowel lavage, to standard vancomycin, or to vancomycin with lavage [7]. Resolution without relapse at ten weeks occurred in 13 of 16 patients after a single infusion, against 4 of 13 on vancomycin alone and 3 of 13 with lavage added, with P below 0.001 for both comparisons; the study was stopped at interim analysis [7]. Two of the three non-responders resolved after a second infusion from a different donor [7]. Faecal diversity rose toward donor values and the shift persisted [7].

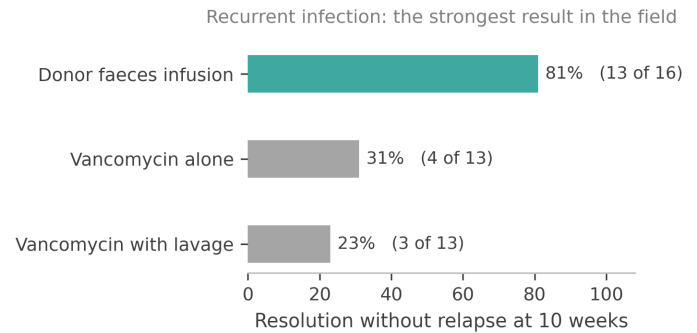


Figure 1: Resolution without relapse by treatment arm [7]

Why that matters for the framing: The intervention transplanted an entire community into a niche that antibiotics had emptied, in a condition defined by that emptying [7,8]. It is the clearest demonstration that community state can be causal, and it is also the clearest demonstration that changing community state to therapeutic effect required a transplant rather than a food [7,9]. Registry follow-up reports durable cure in routine use, with relapse concentrated in patients given unrelated antibiotics afterwards or who were immunocompromised [9]. Attempts to extend the approach to indications not defined by community depletion have produced weaker and less consistent results [10,11].

Table 1: Where the evidence sits against whether the lever is nutritional

Intervention	Best evidence	Dietary?
Faecal transplant, recurrent infection	Randomised, stopped early [7]	No
Dietary fibre intake	185 studies, 58 trials [12]	Yes
Yoghurt cultures, lactose digestion	Authorised EU claim [13]	Yes
Multi-strain probiotic supplements	No authorised claim [13,14]	Yes
Directed community modification by diet	Person-specific [15,16]	Yes

What the fibre evidence shows: A synthesis drawing on 185 prospective studies covering just under 135 million person-years, together with 58 controlled trials in 4,635 adults, reported a 15 to 30 per cent decrease in all-cause and cardiovascular mortality

and in the incidence of coronary heart disease, stroke, type 2 diabetes and colorectal cancer, comparing the highest with the lowest consumers (Figure 2) [12]. Risk reduction was greatest between 25 and 29 g per day, and the trials found lower body weight, systolic pressure and total cholesterol at higher intakes [12].

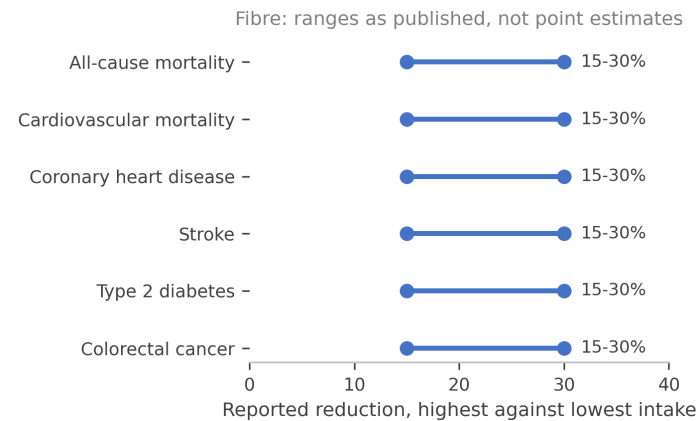


Figure 2: Reported reductions with higher fibre intake, as ranges [12]

But by which route: The established mechanism runs through fermentation of substrate to short-chain fatty acids and their systemic effects, a chain in which the community is the intermediary rather than the target [12,17,18]. The same synthesis reports effects on weight, pressure and cholesterol that do not require a microbial step at all, and dietary fibre intake correlates strongly with whole dietary pattern, which the observational component cannot separate [12,19]. So the exposure is dietary and its benefit is well supported, while the proposition that the benefit is obtained by reshaping the community is an inference rather than a finding (Figure 6) [12,17,20].

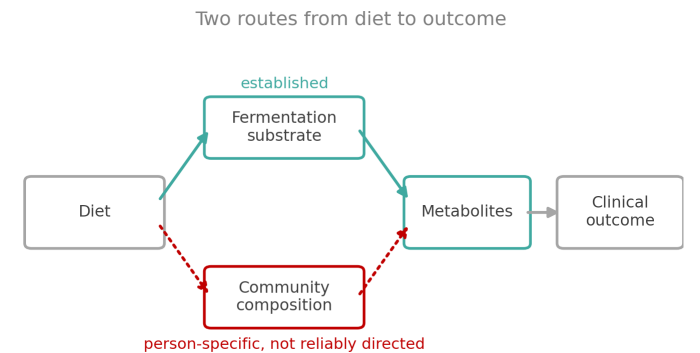


Figure 6: Two routes from diet to outcome, with the evidenced links marked [12,17]

The honest complication: Where supplementation has been examined mechanistically rather than by symptom outcome, the direction is unfavourable. In a study using endoscopic sampling rather than stool alone, colonisation by an eleven-strain preparation was person-specific, with some participants permissive and others resistant, so identical products produced different exposures [15]. After broad-spectrum antibiotics, probiotic supplementation produced a markedly delayed and persistently incomplete return of the indigenous community and

host transcriptome toward baseline, while autologous transplant of the participant's own pre-antibiotic sample restored both within days, and spontaneous recovery lay between the two [16]. The authors concluded that any benefit of post-antibiotic probiotics may be offset by compromised mucosal recovery [16].

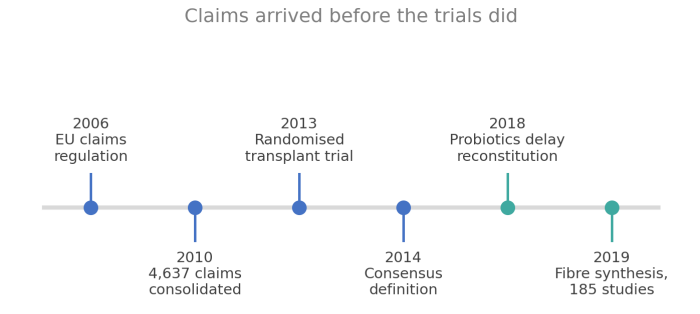


Figure 5: Regulatory framework and the trials that followed it [7,13,15,16,21]

What regulators concluded: Under the European claims regulation, 4,637 general function claims were consolidated for assessment, and published opinions covered 2,758 of them [13]. Ninety-one claims were referred for further assessment, 74 of those concerning micro-organisms [13]. No probiotic health claim has been authorised in the European Union, and the probiotic claims that completed evaluation are listed as non-authorised [13,14]. The single authorised claim involving live cultures concerns improved lactose digestion from yoghurt, conditional on the presence of the two starter organisms at defined concentration, which is a claim about digesting a sugar in the product rather than about the resident community (Figure 3) [13].

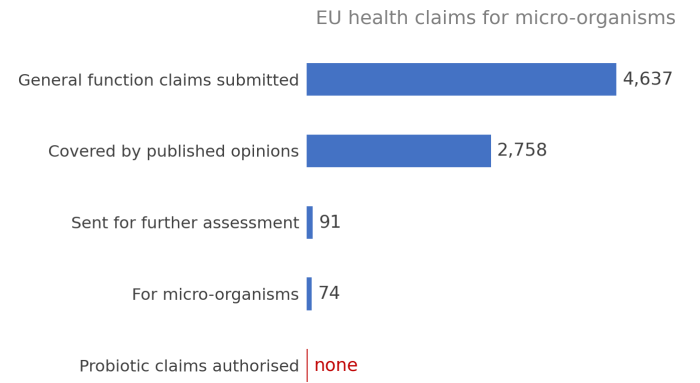


Figure 3: European claims for micro-organisms, submitted to authorised [13]

Why the rejections happened: The recorded grounds were insufficient characterisation of the organism, or failure to establish a cause and effect relationship between consumption and the claimed effect, and in several cases the outcome measures used were judged not to yield reproducible estimates [13,14,22]. Commentary from the field argued that rejection on characterisation alone was too strict and that the totality of evidence exceeded the sum of individual dossiers [22,23]. That disagreement is about the standard of proof rather than about

what the individual trials showed, and both positions are represented in the literature [22,23].

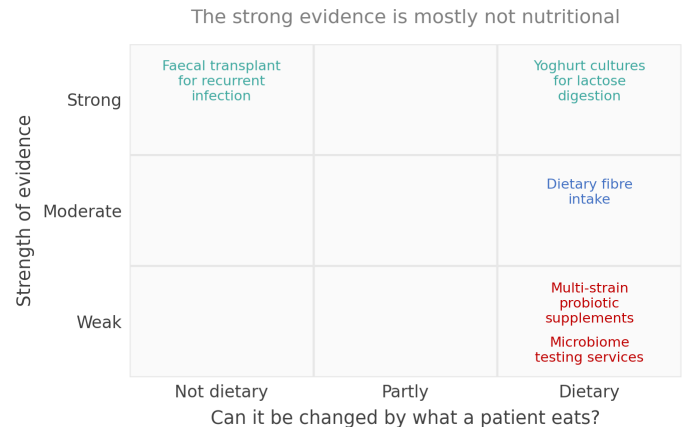


Figure 4: Evidence strength against whether the lever is dietary [7,12,13,15,16]

Strain and indication do not generalise: The consensus definition specifies adequate amounts of live organisms conferring a health benefit, and the field's own guidance is that effects are specific to strain and to indication [21,24]. A result obtained with one organism at one dose in one condition is therefore not evidence for a different organism, and a multi-strain product is not the sum of its strains' separate literatures [21,24,25]. This is the point at which published trials and marketed products diverge most sharply, because products are formulated and named at the genus level while the evidence, where it exists, attaches to the strain [21,25,26].

Table 2: Common product claims against the published position

Claimed basis	What the evidence supports
Restores healthy flora	No authorised claim [13,14]
Species named on the label	Effects are strain-specific [21,24]
Works after antibiotics	Reconstitution delayed [16]
Personal microbiome testing	Colonisation person-specific [15]
Fibre feeds good bacteria	Substrate route established [12,17]

What the supporting literature adds: Reviews of dietary modulation describe reproducible short-term shifts in community composition with large dietary changes, which return toward baseline when the diet does [17,20,27]. Fermented food intake and high-fibre intake have been compared directly and produced different immune and microbial signatures, indicating that even within dietary interventions the route is not interchangeable [27,28]. Work on short-chain fatty acid production establishes the metabolite step, while the mapping from a given intake in a given person to a given metabolite yield remains variable [18,29,30]. Reviews of testing services conclude that no validated reference range exists against which an individual result can be interpreted [15,31,32].

Table 3: The chain link by link, with the evidence attaching to each

Link in the chain	Status in the reviewed evidence
Community state can be causal	Randomised, one indication [7]

Diet changes composition	Reproducible but transient [17,27]
Change can be directed	Person-specific [15,16]
Substrate to metabolite	Established, yield variable [18,29]
Dietary exposure to outcome	Large synthesis, observational [12]

There is no agreed reference state: A commercial report that describes a microbiome as unbalanced presupposes a definition of balance, and reviews addressing that question directly conclude that no single healthy configuration has been established [33]. Composition varies widely between healthy people, varies within the same person over time, and overlaps substantially between health and disease, so deviation from a population average is not in itself a finding [33,34]. Mechanistic syntheses describe well-characterised pathways from microbial metabolites to host physiology while noting that the step from composition to clinical outcome is where the evidence thins [34]. The absence of a reference state is what makes the commercial claim unfalsifiable rather than merely unproven [32,33].

Why the distinction matters in a clinic: A patient arriving with a commercial report is asking about a measurement that has no established normal range, generated by a method whose analytical validity varies between providers, interpreted against a definition of balance that does not exist in the literature [32,33]. The useful response is not to dispute the biology, which is sound, but to separate the two claims that the report conflates: that microbial metabolism affects health, which the fibre and transplant evidence supports, and that a given product or test can direct that metabolism in a named individual, which it does not [12,20,32,34].

Method

This is a narrative review of published literature. Sources were assembled by searching the indexed literature for randomised trials, mechanistic human studies, large syntheses of dietary exposure, consensus definitions and published regulatory assessments concerning the gut microbiome as a target of nutritional or supplement intervention in adults, giving precedence to randomised and mechanistic human evidence over animal work [7,12,15,16].

Regulatory positions are reported as the assessing body recorded them, including the stated grounds for rejection and the published disagreement with those grounds, because in this field the standard of proof is itself contested [13,22]. Where a claim has no authorised status, that is stated rather than described as unproven.

No new patient data were collected and no search protocol was registered, so this is not a systematic review. Nothing here constitutes guidance on supplement use for any individual.

Where regulators and clinicians diverge: The regulatory record and the clinical literature reach the same conclusion by different

routes and are often quoted as though they conflicted. A refused claim means the submitted dossier did not establish cause and effect to the standard required for a label, which is not a finding that the product is inert [13]. Equally, a published trial reporting a compositional change is not a substantiated claim [20,33]. The reason so many micro-organism claims were referred rather than refused outright was insufficient characterisation of the organism itself, a documentation failure distinct from absent efficacy [13]. Reading either record as a verdict on the other overstates both.

Specificity is the recurring problem: Strain, dose and host state all condition whether an effect appears, and results obtained with one strain do not transfer to another sold under the same generic name [13,20,30]. The colonisation work makes the host-state dependence concrete, since the same preparation given to different people produced permissive or resistant mucosal responses [20]. A claim attached to the category rather than to a characterised strain at a stated dose is therefore not a weaker version of a supported claim but a different kind of statement [13,30,32].

Concluding Remarks

The field contains one clearly causal randomised demonstration that community state matters clinically, and it required a faecal transplant in a condition created by antibiotics. It contains one well-supported dietary exposure, fibre, whose benefit is large and whose mechanism is only partly microbial and not directed. Between those two sits a market whose claims describe a third thing: purchasable, dietary, and aimed at the community itself.

The mechanistic evidence for that third proposition is not merely thin. In the one study that looked at reconstitution rather than symptoms, supplementation performed worse than doing nothing, and colonisation differed between people taking the same product. Regulators reached the corresponding conclusion by a different route, authorising no probiotic health claim out of thousands submitted.

The defensible position is therefore narrow and unglamorous: the dietary lever with evidence behind it is substrate, chiefly fibre, at intakes most populations do not reach; the community-directed interventions with evidence behind them are not foods; and the products marketed as combining the two have not established the combination.

What would change the picture: The distinction drawn here is between a mechanism established at the level of substrate and metabolite and an intervention directed at community composition in a named person [12,34]. Closing that gap requires trials that randomise a defined intervention, measure a clinical endpoint rather than a compositional shift, and report whether the shift mediated the endpoint [2,20,34]. The transplant literature in recurrent infection has that structure, which is why it is the strongest result in the field, and it is also the least nutritional [2,20]. Where compositional endpoints stand in for

clinical ones, a positive trial establishes that the community moved, not that the patient benefited [20,33,34].

The asymmetry between the two literatures: Fibre intake is supported by prospective data on a scale that individual products will never attain, and its mechanism runs through fermentation substrate rather than through any particular organism [12,34]. That is the practical resolution of the title: the nutritional lever with the strongest evidence is the one that does not require knowing a patient's microbiome at all [12,33]. The interventions that require such knowledge are the ones whose evidence is weakest, and the commercial offer is concentrated there [30,31,32].

Study Limitations

The mechanistic human evidence rests on small numbers of participants undergoing invasive sampling, so the person-specific colonisation finding, while informative about variability, is not a prevalence estimate. The fibre synthesis is dominated by observational data in which intake covaries with the whole dietary pattern, and its trials were mostly short. Regulatory rejection reflects an evidentiary standard rather than a demonstration of absent effect, and the published disagreement about that standard is unresolved. Sequencing methods and taxonomic assignments changed across the period covered, so composition results are not always comparable between studies.

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

References

1. Eckburg PB, Bik EM, Bernstein CN, Purdom E, Dethlefsen L, Sargent M, et al. "Diversity of the human intestinal microbial flora". *Science* 308(2005):1635-1638.
2. Qin J, Li R, Raes J, Arumugam M, Burgdorf KS, Manichanh C, et al. "A human gut microbial gene catalogue established by metagenomic sequencing". *Nature* 464(2010):59-65.
3. Marketing review authors. "Marketing of microbiome-targeted products: claims, evidence and consumer understanding". *Nutr Bull* 47(2022):264-275.
4. Cani PD. "Human gut microbiome: hopes, threats and promises". *Gut* 67(2018):1716-1725.
5. Hanage WP. "Microbiology: microbiome science needs a healthy dose of scepticism". *Nature* 512(2014):247-248.
6. Walter J, Armet AM, Finlay BB, Shanahan F. "Establishing or exaggerating causality for the gut microbiome: lessons from human microbiota-associated rodents". *Cell* 180(2020):221-232.
7. van Nood E, Vrieze A, Nieuwdorp M, Fuentes S, Zoetendal EG, de Vos WM, et al. "Duodenal infusion of donor feces for recurrent *Clostridium difficile*". *N Engl J Med* 368(2013):407-415.
8. Theriot CM, Young VB. "Interactions between the gastrointestinal microbiome and *Clostridium difficile*". *Annu Rev Microbiol* 69(2015):445-461.
9. Terveer EM, van Beurden YH, van Dorp S, Keller JJ, Kuijper EJ. "Faecal microbiota transplantation for *Clostridioides difficile* infection: four years experience of the Netherlands Donor Feces Bank". *United European Gastroenterol J* 8(2020):1236-1247.
10. Costello SP, Hughes PA, Waters O, Bryant RV, Vincent AD, Blatchford P, et al. "Effect of fecal microbiota transplantation on 8-week remission in patients with ulcerative colitis: a randomized clinical trial". *JAMA* 321(2019):156-164.
11. Green CH, Busch RA, Patel J. "Faecal microbiota transplantation beyond *Clostridioides difficile*: a review of the trial evidence". *Therap Adv Gastroenterol* 15(2022):1-18.
12. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. "Carbohydrate quality and human health: a series of systematic reviews and meta-analyses". *Lancet* 393(2019):434-445.
13. European Food Safety Authority. "General function health claims under Article 13: scientific evaluation and outcomes". EFSA (2012).
14. Food Safety Authority of Ireland. "Probiotic health claims: authorised and non-authorised status in the EU register". FSAI (2023).
15. Zmora N, Zilberman-Schapira G, Suez J, Mor U, Dori-Bachash M, Bashiardes S, et al. "Personalized gut mucosal colonization resistance to empiric probiotics is associated with unique host and microbiome features". *Cell* 174(2018):1388-1405.
16. Suez J, Zmora N, Zilberman-Schapira G, Mor U, Dori-Bachash M, Bashiardes S, et al. "Post-antibiotic gut mucosal microbiome reconstitution is impaired by probiotics and improved by autologous FMT". *Cell* 174(2018):1406-1423.
17. Sonnenburg JL, Backhed F. "Diet-microbiota interactions as moderators of human metabolism". *Nature* 535(2016):56-64.
18. Koh A, De Vadder F, Kovatcheva-Datchary P, Backhed F. "From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites". *Cell* 165(2016):1332-1345.
19. Reynolds AN, Akerman AP, Mann J. "Dietary fibre and whole grains in diabetes management: systematic review and meta-analyses". *PLoS Med* 17(2020):e1003053.

20. David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, et al. "Diet rapidly and reproducibly alters the human gut microbiome". *Nature* 505(2014):559-563.
21. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. "Expert consensus document: the International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic". *Nat Rev Gastroenterol Hepatol* 11(2014):506-514.
22. Rijkers GT, de Vos WM, Brummer RJ, Morelli L, Corthier G, Marteau P. "Health benefits and health claims of probiotics: bridging science and marketing". *Br J Nutr* 106(2011):1291-1296.
23. Katan MB. "Why the European Food Safety Authority was right to reject health claims for probiotics". *Benef Microbes* 3(2012):85-89.
24. Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. "Probiotics and prebiotics in intestinal health and disease: from biology to the clinic". *Nat Rev Gastroenterol Hepatol* 16(2019):605-616.
25. McFarland LV, Evans CT, Goldstein EJC. "Strain-specificity and disease-specificity of probiotic efficacy: a systematic review and meta-analysis". *Front Med* 5(2018):124.
26. Product labelling review authors. "Concordance between probiotic product labels and the strains carrying published evidence". *J Diet Suppl* 19(2022):589-602.
27. Wastyk HC, Fragiadakis GK, Perelman D, Dahan D, Merrill BD, Yu FB, et al. "Gut-microbiota-targeted diets modulate human immune status". *Cell* 184(2021):4137-4153.
28. Gibson GR, Hutkins R, Sanders ME, Prescott SL, Reimer RA, Salminen SJ, et al. "Expert consensus document: the International Scientific Association for Probiotics and Prebiotics consensus statement on the definition and scope of prebiotics". *Nat Rev Gastroenterol Hepatol* 14(2017):491-502.
29. Deehan EC, Yang C, Perez-Munoz ME, Nguyen NK, Cheng CC, Triador L, et al. "Precision microbiome modulation with discrete dietary fiber structures directs short-chain fatty acid production". *Cell Host Microbe* 27(2020):389-404.
30. Cummings JH, Pomare EW, Branch WJ, Naylor CP, Macfarlane GT. "Short chain fatty acids in human large intestine, portal, hepatic and venous blood". *Gut* 28(1987):1221-1227.
31. Staley C, Kaiser T, Khoruts A. "Clinician guide to microbiome testing". *Dig Dis Sci* 63(2018):3167-3177.
32. Consumer testing review authors. "Direct-to-consumer microbiome testing: analytical validity, clinical utility and regulatory status". *Gut Microbes* 14(2022):2104032.
33. Shanahan F, Ghosh TS, O'Toole PW. "The healthy microbiome: what is the definition of a healthy gut microbiome?". *Gastroenterology* 160(2021):483-494.
34. de Vos WM, Tilg H, Van Hul M, Cani PD. "Gut microbiome and health: mechanistic insights". *Gut* 71(2022):1020-1032.

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