The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of synbiotics

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Notable properties of the gut microbiota include its functionality and resilience. A stable gut community protects the host against invading microorganisms and helps maintain homeostasis, including immune regulation. Nonetheless, disruptions occur owing to dietary shifts, antibiotic use, age or infection, leading to a gut microbiota that can contribute to a range of inflammatory, pathogenic and metabolic conditions such as inflammatory bowel diseases, colorectal cancer, metabolic syndrome and atopy. Several strategies have been proposed to modulate the composition and function of the gut microbiota, including faecal microbiota transplants, the application of probiotics and other live microorganisms, and the use of non-digestible dietary substrates such as prebiotics.

When the synbiotic concept was first described 25 years ago, the notion that selectively fermentable non-digestible food ingredients (prebiotics) could be combined with probiotics was envisioned. Thus, synbiotics were loosely defined as mixtures of "probiotics and prebiotics that beneficially affect the host". The term itself was formed from the Greek prefix 'syn', meaning ‘together’ and the suffix ‘biotic’, meaning ‘pertaining to life’. Despite the availability of similarly worded definitions, confusion exists among stakeholders, including scientists, about what constitutes a synbiotic. A general misunderstanding might have been, in part, because the original definition itself — that is, "mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, thus improving host welfare" — was too wordy and lacked precision. In addition, the expansion of the entire ‘–biotics’ category, including terms such as postbiotic and pharmabiotic, almost certainly further contributes to confusion. To provide clarity and guidance regarding appropriate use of the term ‘synbiotic’, in May 2019, the International Scientific Association for Probiotics and Prebiotics (ISAPP) convened an expert panel of academic scientists.
to address the current status of synbiotics, including its
definition. The outcomes of that meeting and subse-
quent discussions comprise this Consensus Statement. A
summary of key conclusions is shown in Box 1. Herein,
we consider applicable efficacy and mechanistic
evidence on combination probiotic plus prebiotic pro-
ducts, we recommend the research needed to establish a
‘synbiotic’ formulation, discuss the safety consider-
tations, and reflect on implications for stakeholders of
the symbiotic concept.

Methods
ISAPP is a non-profit collaboration of scientists dedi-
cated to advancing scientific excellence and providing
objective, science-based information on probiotics and
prebiotics. The organization's activities are funded by
companies involved in the sale of probiotics and prebi-
otics, but ISAPP is guided by an international, all-volunteer
academic board that functions independently. This
ISAPP-organized panel was composed of experts in
microbiology, nutrition and gastrointestinal physiology,
including many who were involved in the latest updates
of the probiotic12 and prebiotic13 definitions according to
ISAPP. Panellists were charged with accomplishing the
following goals: consider what a synbiotic is and pro-
vide a clear, concise and testable definition; suggest the
appropriate experimental conditions necessary to estab-
lish symbiotic activity; describe the evidence required
to demonstrate the health benefits and establish safety; and
provide guidance for stakeholders, including research-
ers, industry, public health professionals and regulatory
agencies.

Prior to the meeting, panellists developed a discus-
sion outline and target questions. During the meeting,
panellists presented the perspectives and evidence
regarding the core issues involved. Debate ensued until
a consensus was achieved. After the meeting, individ-
ual panellists wrote sections of the summary, which
were compiled by K.S.S., G.R.G., R.H. and M.E.S. into
a draft report. This document was edited and agreed
upon by all panel members. The authors would like to
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An updated definition
The panel updated the definition of a synbiotic to
‘a mixture comprising live microorganisms and sub-
strate(s) selectively utilized by host microorganisms
that confers a health benefit on the host’. ‘Host’ micro-
organisms in this context include both autochthonous
microorganisms (resident or colonizing the host) and
allochthonous microorganisms (externally applied,
such as probiotics), which, even if transiently present,
do constitute a component of the host microbiota.

The panel considered defining symbiotics as simply
a mixture of probiotics and prebiotics. Common to
the definition of both probiotics and prebiotics is the
requirement that each independently provides a health
benefit and the dose of each must be adequate to inde-
pendently achieve those benefit(s). However, the panel
recognized the possibility that a functional symbiotic
could be formulated at doses below those at which the
probiotic or prebiotic could independently exert health
benefits. Alternatively, a particular microorganism
might lack probiotic functions even at high dosages
owing to competition or other ecological effects but,
in the presence of a suitable substrate, could provide a
health benefit. Likewise, a novel substrate, again even at
high doses, might not by itself provide benefits but could
do so when combined with a selected live microorgan-
ism(s) that it can enhance. Such formulations comprise
a live microorganism and a substrate that depend on the
presence of one another and function in concert. Simply
put, the microbial component does not necessarily have
to be a standalone probiotic and the non-digestible
substrate does not necessarily have to be a standalone
prebiotic, but, if together they provide a health benefit,
then the mixture can be called a symbiotic. This pro-
posed definition of a symbiotic should encourage inno-
vation in formulations by not requiring that component
parts meet the strict definitions of either a probiotic or
a prebiotic.

However, the panel also recognized that a current
common usage of the term symbiotic includes prod-
ucts that combine a probiotic and a prebiotic. Such a
combination product might not have any evidence of
co-dependent function but is instead designed for
the components to work independently to promote an
observed health benefit(s). The panel agreed that such
a formulation could be considered a symbiotic, pro-
vided that components meet the respective probiotic12
and prebiotic13 definitions (Fig. 1). Thus, the probi-
otic strain(s) is chosen based on the benefits that it
provides to the host, while the prebiotic is designed to
promote the growth and activities of beneficial mem-
ers of the indigenous microbiota and provide a health
benefit14. Furthermore, a combination of probiotic plus
prebiotic must be tested to confirm that a health ben-
efit is conferred by the combined formulation compared
with a placebo. Otherwise, the product should not be
labelled a symbiotic. Based on these qualifiers, the panel

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The definition of synbiotic has been updated to “a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host”.

Within this definition, ‘host’ microorganisms comprise both autochthonous (resident or colonizing the host) and allochthonous (externally applied, such as probiotics) microorganisms, either of which can be targets for the substrate contained in the synbiotic.

Two subsets of synbiotics were defined: complementary and synergistic. A ‘synergistic synbiotic’ is a synbiotic in which the substrate is designed to be selectively utilized by the co-administered microorganism(s). A ‘complementary synbiotic’ is a synbiotic composed of a probiotic combined with a prebiotic, which is designed to target autochthonous microorganisms. Minimum criteria for the existing probiotic and prebiotic must be met for both components of a complementary synbiotic.

Beneficial effect(s) of a synbiotic on health must be confirmed in the target host, which might include humans, companion animals, or agricultural species or a subpopulation (such as different age or developmental stage, health status, sex or living situation) thereof.

For a synergistic synbiotic, evidence of selective utilization of the substrate must be demonstrated in the same study establishing the health benefit. The aim is to demonstrate that the combined effect is better than the estimated effects of each component separately. This step is not required for a complementary synbiotic, as it contains a prebiotic for which selective utilization has already been established.

A synbiotic can be applied to intestinal or extra-intestinal microbial ecosystems and might be formulated into products fitting an array of regulatory categories (such as foods, non-foods, feeds, drugs or nutritional supplements).

Implied in the definition is that safety of the synbiotic for the intended use is established.

‘Symbiotic’ is not a synonym of synbiotic and is incorrect in this context.

The characterization of a synbiotic must be sufficient

Characterization needed for synbiotics

A synbiotic should be characterized to the extent needed to ensure safety and a consistent performance. Live microbial component(s) of the synbiotic should have a publicly available genome sequence and annotation, be assessed for any genes of safety concern (for example, toxin production or transferrable antibiotic resistance), named using current taxonomic nomenclature and carry a traceable strain designation. The strain(s) should also be deposited into a recognized international culture collection that permits access by scientists to conduct research. In short, the safety, identity, purity and potency of the live microorganism should be clearly and accurately described according to the best available methods that meet applicable regulatory standards for the product category.

The structure and purity of the substrate should be stated and characterized by appropriate chemical analyses. This process includes testing for microbial and other contaminants as per regulatory standards for the country of sale. The level of purity required will depend on what is needed to ensure a consistent performance and safety of the product. The level of active substance in commercial preparations of prebiotics available worldwide ranges considerably, often from 35% to 99%.[17-19] The monosaccharides and disaccharides carried over from the production process that are present in prebiotic preparations are typically digested and absorbed by the host in the upper gastrointestinal tract after oral ingestion. A relevant issue is whether the material used in the formulation is sufficient to deliver a consistent dose of the active component and result in reproducible selective utilization by microorganisms and beneficial health effect(s) in the target host. This issue highlights that studies should communicate the content of the active ingredient being tested in addition to the quantity of the overall product. For example, a 6 g dosage of 50% pure galacto-oligosaccharides would provide 3 g of the active substrate and should be reported as such.

The active ingredients of a synbiotic must be sufficient

Current levels of evidence

Numerous randomized controlled trials (RCTs) in humans across a range of populations, from healthy individuals to those with acute and chronic diseases,
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**Synbiotic categories.** Synbiotics can be formulated using two approaches. A complementary synbiotic comprises a probiotic plus a prebiotic (more than one of each can be used), working independently to achieve one or more health benefits. Probiotic and prebiotic components of the complementary synbiotic must meet the minimum criteria, as stipulated previously. A synergistic synbiotic is composed of a live microorganism and a selectively utilized substrate but neither needs to meet the minimum criteria stipulated previously for probiotics and prebiotics. Instead, these components are designed to work together, with the substrate being selectively utilized by the co-administered microorganism. The panel considered whether all synbiotics should be synergistic. However, the absence of such substances today speaks to the difficulty of achieving the required evidence. The panel judged that it was more important for the definition to be useful rather than hypothetical.

**Fig. 1** | Synbiotic categories. A complementary synbiotic comprises a probiotic plus a prebiotic (more than one of each can be used), working independently to achieve one or more health benefits. Probiotic and prebiotic components of the complementary synbiotic must meet the minimum criteria, as stipulated previously. A synergistic synbiotic is composed of a live microorganism and a selectively utilized substrate but neither needs to meet the minimum criteria stipulated previously for probiotics and prebiotics. Instead, these components are designed to work together, with the substrate being selectively utilized by the co-administered microorganism. The panel considered whether all synbiotics should be synergistic. However, the absence of such substances today speaks to the difficulty of achieving the required evidence. The panel judged that it was more important for the definition to be useful rather than hypothetical.

**Necessary evidence for synbiotics**
A synbiotic must contain a live microorganism and a selectively utilized substrate. For complementary synbiotics, the respective components must fulfill the evidence and dose requirements for both a probiotic and prebiotic. Furthermore, the combination must be shown in an appropriately designed trial to confer a health benefit in the target host. A product containing a probiotic and a prebiotic that only has evidence for each component individually, and not as a combination product, should not be called a synbiotic. A key evidentiary requirement for a synergistic synbiotic is that there be at least one appropriately designed study of the synbiotic in the target host that demonstrates both selective utilization of the substrate and a health benefit (Box 2).

Generating this evidence requires appropriately designed, adequately powered experimental trials conducted on the target host. These studies should follow standard human trial design and reporting guidelines and consider best practices for diet–microbiota research. The study should also meet the criteria outlined in CONSORT and should be registered, including a description of all outcomes, prior to recruitment. These CONSORT criteria include guiding principles for microorganisms, microbiota-related compliance and outcome measures, relevant subgroups, and statistical considerations for evaluating the microbiota as a mediator of clinical effects.
Ideally, the health benefit of a synbiotic would be superadditive, that is, it would exceed the benefit observed for the sum of the individual components. However, owing to the difficulties in demonstrating different levels of health benefit in an efficacy trial, the panel did not insist upon this aspect. Instead, we advocate requiring a measurable, confirmed health benefit of the synbiotic, which is conferred, at least in part, through selective utilization of the substrate(s) provided in the synbiotic. Although in vitro and animal models are used frequently to test the effects of probiotics, prebiotics and synbiotics, it is our position that these have not been fully validated as predictive and that definitive tests of these interventions must be performed in the target host. Of course, model experiments can add mechanistic insights, in particular in cases for which available samples from studies in the target host have limited usefulness (for example, faeces, which are not reflective of upstream intestinal microbial or metabolic activities).

As noted, it is required that the health benefit of the synbiotic mixture be confirmed, even when established probiotic(s) and prebiotic(s) (that is, ones that meet criteria stipulated in respective definitions and are used at efficacious doses) are used to formulate components of the synbiotic. This requirement would account for any potential antagonistic effect of the combination that might diminish the health benefits of each component independently. Although unlikely, such antagonism is theoretically possible, as shown in in vitro studies whereby some carbohydrate substrates increased the production of antimicrobial compounds by probiotics. Depending on which microorganism is able to utilize the substrate, which antimicrobial factors are produced, and which taxa are neutralized or killed by them, such a scenario could lead to positive or negative outcomes. Therefore, in the absence of evidence that the combination product provides a health benefit, a product should simply be labelled as “contains probiotics and prebiotics”. Sanders et al. provide a perspective on determining whether evidence from studies using one formulation (for example, a prebiotic or a probiotic alone) can be extrapolated to different formulations (for example, when combining a prebiotic and a probiotic).

**Guiding principles for synbiotic research**

**Design.** A randomized, double-blind, placebo-controlled trial is recommended for synbiotic research. The study should be registered with accepted protocol and results systems such as ClinicalTrials.gov. Study quality factors include, but are not limited to, appropriate blinding, randomization, the allocation concealment mechanism, reporting of inclusion and/or exclusion criteria and adverse events (AEs), completion of intention-to-treat analyses, and adequate statistical power. Crossover designs might be preferred to account for the individualized nature of the gut microbiota. The wash-out period length should be based on the primary outcome with consideration for secondary outcomes; a 2-week wash-out between conditions is generally adequate for gut microbiota outcomes, although longer times might be necessary for some populations (for example, the elderly or for those with constipation or functional bowel disorders). Parallel-arm designs might be required for long-term outcomes (such as weight loss or glycaemia). The number of study groups required depends on whether the researchers intend to demonstrate synergism (Table 2). Health outcomes and selective utilization of the substrate by host microbiota must be demonstrated in the same study. When experimental trials are not feasible or ethical, observational trials, including prospective longitudinal studies, are useful; these studies must accurately capture synbiotic exposure and control for relevant confounders (such as diet or antibiotics).

**Population or participants.** When choosing the study population, many parameters need to be defined, including the target host (including non-human species), target life stage (for example, pregnant women, infants, children, adults or elderly) and health status (for example, healthy, at-risk, or with a diagnosed disease or condition). Furthermore, microbiome-related factors, such as recent probiotic, prebiotic, synbiotic or antibiotic use,

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**Fig. 2 | Design and mechanisms of action of complementary and synergistic synbiotics.** Two approaches to designing synbiotics are represented here. The complementary approach combines a prebiotic and a probiotic that work independently to elicit one or more health benefits. The prebiotic and probiotic must each meet applicable criteria (Table 3). The prebiotic functions by modulating the resident microbiota in a manner associated with an improved health outcome. The synergistic approach selects a substrate that is utilized by the co-administered live microorganism, enhancing its functionality. Synergistic synbiotics work together (not independently) to bring about the resulting health benefits.
### Table 1 | Human trials of orally administered combinations of live microorganisms and a substrate reporting health outcomes

| Health outcome                                             | Population studied          | Substrate used                        | Live microorganism(s) component and dose                                      | Refs |
|-----------------------------------------------------------|----------------------------|---------------------------------------|-------------------------------------------------------------------------------|------|
| Prevention of surgical infections and complications       | Adults, n = 54             | GOS (12 g per day)                    | Bifidobacterium breve strain Yakult (1×10^9/g), Lactobacillus casei strain Shirotai (1×10^9/g) (3 g per day) | 96   |
|                                                           | Adults, n = 79             | FOS (dose not stated, three times per day) | Streptococcus faecalis T-110 (60 million), Clostridium butyricum TO-A (4 million), Bacillus mesentericus TO-A (2 million), Lactobacillus sporogenes* (100 million) (three times per day) | 97   |
|                                                           | Adults, n = 80             | Inulin, β-glucan, pectin and resistant starch (2.5 g of each, twice per day) | Pedioecoccus pentosaceus 5–33:3 (10^9), Leuconostoc mesenteroides 77:1 (10^9), Lactobacillus paracasei subsp. paracasei F19 (10^9), Lactobacillus plantarum 2362 (10^9) (twice per day) | 98   |
|                                                           | Adults, n = 92             | OFS (15 g, twice per day)              | Lactobacillus acidophilus La5, Lactobacillus bulgaricus, Bifidobacterium lactis BB-12, Streptococcus thermophilus (4×10^9 CFU) (three times per day) | 99   |
|                                                           | Adults, n = 46             | FOS (100 mg, twice per day)            | L. acidophilus 10 (1×10^9 CFU), Lactobacillus rhamnosus HS 111 (1×10^8 CFU), L. casei 10 (1×10^8 CFU), Bifidobacterium bifidum (1×10^8 CFU) (twice per day) | 45   |
|                                                           | Adults, n = 61             | GOS (10 g per day)                     | B. breve strain Yakult (1×10^8/g), L. casei strain Shirotai (1×10^8/g) (3 g per day) | 100  |
| Treatment of non-alcoholic fatty liver disease            | Adults, n = 52             | FOS (250 mg per day)                   | L. casei PXN 37, L. rhamnosus PXN 54, S. thermophilus PXN 66, B. breve PXN 25, L. acidophilus PXN 35, Bifidobacterium longum PXN 30, L. bulgaricus PXN 39 (2×10^7 CFU per day) | 101  |
|                                                           | Adults, n = 66             | FOS (dose not provided)                | B. longum (dose not provided) | 102  |
|                                                           | Adults, n = 50             | FOS (125 mg, twice per day)            | L. casei PXN 37, L. rhamnosus PXN 54, S. thermophilus PXN 66, B. breve PXN 25, L. acidophilus PXN 35, B. longum PXN 30, L. bulgaricus PXN 39 (2×10^7 CFU per day) | 103  |
|                                                           | Adults, n = 75             | Inulin HP (10 g per day)               | B. longum, L. acidophilus (2×10^7 CFU per day) | 104  |
| Prevention of sepsis in infants                           | Infants, n = 4,556         | FOS (150 mg per day)                   | L. plantarum ATCC-20195 (~10^6 per day) | 105  |
| Treatment of overweight or obesity and metabolic syndrome | Adults, n = 225 and n = 134 | Litess Ultra polydextrose (12 g per day) | Bifidobacterium animalis subsp. lactis 420 (10^8 CFU per day) | 46,109 |
|                                                           | Adults, n = 38             | FOS (250 mg, twice per day)            | L. casei PXN 37, L. rhamnosus PXN 54, S. thermophilus PXN 66, B. breve PXN 25, L. acidophilus PXN 35, B. longum PXN 30, L. bulgaricus PXN 39 (2×10^7 CFU per day) | 107  |
| Treatment of T2DM and glycaemia                           | Adults, n = 62             | Inulin (0.36 g, three times per day)   | L. sporogenes* (9×10^7 CFU, three times per day) | 108  |
|                                                           | Adults, n = 81             | Inulin (0.07 g/1 g bread) (120 g per day as synbiotic bread) | L. sporogenes* (1×10^8 CFU/g, 120 g per day as synbiotic bread) | 109  |
| Treatment of dyslipidaemia                                | Women with gestational diabetes, n = 70 | Inulin (800 mg per day)               | L. acidophilus, L. casei, B. bifidum (2×10^8 CFU per day of each) | 110  |
|                                                           | Adults with T2DM, n = 78   | Inulin (0.07 g/1 g bread) (120 g per day as synbiotic bread) | L. sporogenes* (1×10^8 CFU/g, 120 g per day as synbiotic bread) | 109  |
|                                                           | Adults with CHD and T2DM, n = 60 | Inulin (800 mg per day)               | L. acidophilus, L. casei, B. bifidum (2×10^8 CFU/g of each per day) | 111  |
|                                                           | Adults with T2DM, n = 62   | Inulin (0.36 g, three times per day)   | L. sporogenes* (9×10^7 CFU, three times per day) | 108  |
| Treatment of inflammation                                | Elderly, n = 37            | GOS (8 g per day)                      | B. lactis Bi-07 (10^8 CFU per day) | 112  |
|                                                           | Adults, n = 36             | FOS (1.4 g per day)                    | L. acidophilus La5, B. animalis ssp. lactis Bb-12, Lactobacillus delbrueckii ssp. bulgaricus, S. thermophilus, L. paracasei ssp. paracasei (2×10^7 CFU per day) | 113  |
|                                                           | Adults with T1DM and T2DM on haemodialysis, n = 60 | Inulin (0.8 g per day)               | L. acidophilus, L. casei, B. bifidum (2×10^8 CFU of each per day) | 114  |
| Treatment of irritable bowel syndrome                     | Adults, n = 85             | FOS (100 mg, three times per day)      | Bacillus coagulans (15×10^7 spores, three times per day) | 115  |
|                                                           | Children, n = 71           | Inulin (900 mg, twice per day)         | B. lactis B94 (5×10^8 CFU, twice per day) | 116  |
| Eradication of Helicobacter pylori                         | Adults, n = 76             | FOS (250 mg per day)                   | L. casei PXN 37, L. rhamnosus PXN 54, S. thermophilus PXN 66, B. breve PXN 25, L. acidophilus PXN 35, B. longum PXN 30, L. bulgaricus PXN 39 (2×10^7 CFU per day) | 117  |
|                                                           | Children, n = 104          | Inulin (900 mg per day)                | B. lactis B94 (5×10^8 CFU per day) | 118  |
microbiota-disrupting medications and diet can be considered as (in)eligibility criteria, depending on primary health and microbiota outcomes. A 2-week wash-in period is generally adequate for probiotics; however, certain populations might require longer wash-in periods (such as 4 weeks for those with slow transit time)\(^{35}\). The time since last antibiotic exposure will vary depending on the dose and purity of the substrate, and the timing and route of administration of the intervention. Subject compliance with an oral intervention can include measurement of adherence and diet diversity. For mother–infant dyads, consider possible vertical transmission of microorganisms from mother to infant in breast milk, microorganisms and substrates naturally present in breast milk, and the unique characteristics of immature infant microbiome.

**Intervention.** The intervention should be fully described to enable replication of the study. This entails an adequate description of substrate and live microorganism dosages, specification of the microbial strain, the structure and purity of the substrate, and the timing and route of administration of the intervention. Subject compliance with an oral intervention can include measurement of the administered microorganisms in stool.

The duration of the intervention will be determined based on outcome; microbiota changes can be rapid but health outcomes will vary from days to weeks (such as constipation, stool frequency) to months (such as reduced fat mass, glycaemia). The background diet must be considered and, if possible, monitored as diet could provide a source of prebiotic substrates that are intrinsic and intact within certain foods (such as onions, wheat) as well as live microorganisms (such as fermented foods). Diet monitoring should include the use of validated methods such as the National Cancer Institute

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**Table 1 (cont.) | Human trials of orally administered combinations of live microorganisms and a substrate reporting health outcomes**

| Health outcome | Population studied | Substrate used | Live microorganism(s) component and dose | Refs |
|----------------|--------------------|----------------|-----------------------------------------|------|
| **Treatment of polycystic ovarian syndrome** | Adults, \(n = 60\) | Inulin (800 mg/day) | \(L.\) *acidophilus* strain T16 (IBRC-M10785), \(L.\) *casei* strain T2 (IBRC-M10783), \(B.\) *bifidum* strain T1 (IBRC-M10771) (2×10\(^7\) CFU/g of each per day) | 119 |
| | Adults, \(n = 60\) | Inulin (800 mg/day) | \(L.\) *acidophilus* strain T16 (IBRC-M10785), \(L.\) *casei* strain T2 (IBRC-M10783), \(B.\) *bifidum* strain T1 (IBRC-M10771) (2×10\(^7\) CFU/g of each per day) | 120 |
| **Treatment of chronic kidney disease** | Adults, \(n = 30\) | Inulin (2.2 g), tapioca-resistant starch (1.3 g) (three times per day) | \(L.\) *plantarum* (5×10\(^9\)), \(L.\) *casei* subsp. *rhamnosus* (2×10\(^9\)), \(L.\) *bulgaricus* gasserii (2×10\(^9\)), \(B.\) *longum* (1×10\(^7\)), \(L.\) *acidophilus* (1×10\(^7\)), \(L.\) *salivarius* (1×10\(^8\)), \(S.\) *thermophilus* (5×10\(^7\)) (3 times per day) | 121 |
| | Adults, \(n = 66\) | FOS (500 mg capsule with undefined FOS dose, two capsules per day) | \(L.\) *casei*, \(L.\) *acidophilus*, \(L.\) *bulgaricus*, \(L.\) *rhamnosus*, \(B.\) *breve*, \(B.\) *longum*, \(S.\) *thermophilus* (500 mg capsule with undefined dose of microorganism, two capsules per day) | 122 |
| | Adults, \(n = 37\) | Inulin, FOS, GOS (7.5 g per day for first 3 weeks then 15 g per day for second 3 weeks) | Nine different strains across \(L.\) *bifidobacterium*, \(B.\) *longum*, \(S.\) *thermophilus* (2×10\(^7\) CFU per day for first 3 weeks then 9×10\(^7\) CFU per day for second 3 weeks) | 123 |
| **Prevention of atopic dermatitis** | Pregnant women, \(n = 1,223\) | Newborn infants received the probiotic: GOS (0.8 g, once per day) | Mothers received only the probiotic twice per day: \(L.\) *rhamnosus* GG (5×10\(^9\) CFU), \(L.\) *rhamnosus* GG LC705 (5×10\(^9\) CFU), \(B.\) *breve* BB9 (2×10\(^9\) CFU), Propionibacterium freudenreichii subsp. *shermanii* JS (2×10\(^7\) CFU); infants received the probiotic once per day | 124 |
| **Treatment of atopic dermatitis** | Infants: 12–36 months of age, \(n = 90\) | FOS (50 mg, twice per day) | \(L.\) *acidophilus* DDS-1, \(B.\) *lactis* UABLA-12 (5×10\(^9\) CFU, twice per day) | 125 |
| | Infants: 3 months to 6 years of age, \(n = 40\) | FOS (958 mg, twice per day) | \(L.\) *casei* PXN 37, \(L.\) *rhamnosus* PXN 54, \(S.\) *thermophilus* PXN 66, \(B.\) *breve* PXN 25, \(L.\) *acidophilus* PXN 35, \(B.\) *infantis* PXN 27, \(L.\) *bulgaricus* PXN 39 (1×10\(^7\) CFU, twice per day) | 126 |
| | Children: 2–14 years of age, \(n = 60\) | FOS (475 mg, twice per day) | \(L.\) *salivarius* PM-A0006 (2×10\(^6\) CFU, twice per day) | 127 |

The selected studies contained in this table represent blinded, randomized, controlled trials that showed a health benefit of the combination product. Studies listed did not necessarily test both the health benefit and selective utilization by the microbiota, so we have avoided the use of the term ‘synbiotic’ in this table. Null trials and studies using the inappropriate term ‘symbiotic’ were excluded. CHD, coronary heart disease; FOS, fructo-oligosaccharides; GOS, galacto-oligosaccharides; OFS, chicory root oligofructose; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus. a Incorrectly by some to refer to *Bacillus coagulans*. b Incorrectly by some to refer to *Bacillus coagulans*. c Incorrectly by some to refer to *Bacillus coagulans*. d Incorrectly by some to refer to *Bacillus coagulans*. e Incorrectly by some to refer to *Bacillus coagulans*. f Incorrectly by some to refer to *Bacillus coagulans*. g Incorrectly by some to refer to *Bacillus coagulans*. h Incorrectly by some to refer to *Bacillus coagulans*.
Dietary History Questionnaire (DHQ), Automated Self-Administered 24-hour dietary assessment tool (ASA24) and nutrient analysis software (such as Nutrition Data System for Research).

**Placebo or control.** Design of a placebo or control is driven by the comparisons of interest. Often, a fully inert control is preferred. For formulations within pills or sachets, a low dose of highly digestible ingredients (such as maltodextrin or corn starch) or slowly fermentable fibre (such as microcrystalline cellulose) are acceptable placebos, which enables double blinding. For interventions composed of a food or beverage, the control group must be carefully considered, including differences in flavour, texture and nutrient content. These factors will also determine whether the study can be considered as a single-blinded or double-blinded design.

**Outcome.** A synbiotic requires both a health outcome and a microbiota outcome in the same study. Primary and secondary health outcome(s) must be clearly specified. The microbiota outcome should be hypothesis-driven and for each individual component. As the materials comprising the mixture, at the dose used, were not established prebiotics or probiotics, it does not meet our definition of a complementary synbiotic.

**Box 2 | Actual and hypothetical examples to illustrate the synbiotic concept**

The qualifier ‘established’ refers to a probiotic or prebiotic that meets the requirements of the globally accepted definitions from International Scientific Association for Probiotics and Prebiotics consensus.

**Example 1**
In a blinded four-arm study, 41 healthy volunteers received either *Bifidobacterium animalis* subsp. *lactis* BI-07 (10⁹ CFU per day), 8 g per day xylo-oligosaccharides (XOS), the combination of both or an inert maltodextrin control for 21 days. XOS enhanced bifidobacteria counts in faeces in both the synbiotic and prebiotic groups compared with the control and improved plasma lipid profiles and modulated markers of immune function in healthy adults. The lowest reported use of analogues was observed during combination supplementation along with a reduced expression of CD19 on B cells (as markers of immune function). Thus, the combination exerted certain benefits that were not afforded by the probiotic or prebiotic alone. This study shows a probiotic status for XOS used at 8 g per day. Previous evidence supports that *Bifidobacterium animalis* subsp. *lactis* BI-07 at 10⁹ CFU per day met criteria for a probiotic. Taken together, this tested product meets our definition of a complementary synbiotic. However, because an increase of *Bifidobacterium* was not observed in individuals fed the combination product, it does not meet our definition of a synergistic synbiotic.

**Example 2**
Krumbeck et al. conducted a parallel multi-arm, double-blinded randomized control trial in people with obesity (17–19 per group) to assess the effects of a synbiotic containing 5 g of galacto-oligosaccharide (GOS) and 10⁴ *Bifidobacterium adolescentis* IVS-1 on gut barrier function. The test strain had been obtained by an in vivo selection strategy intended to select for strains that would be expected to provide synergistic outcomes. In addition to the synbiotic, GOS, *B. adolescentis* IVS-1 and placebo (lactose) controls were also included. After 3 weeks of consumption, genus-specific and strain-specific quantitative real-time PCR were performed to assess changes in absolute abundances of bifidobacteria. To assess intestinal permeability, non-metabolizable sugars were measured in urine following the consumption of a sugar mixture. Although the results showed that all three treatments (GOS only, *B. adolescentis* IVS-1 only and the combination) markedly improved gut barrier function, there was no statistically significant difference among the three groups. The *B. adolescentis* IVS-1 group was significantly enriched but the addition of GOS as a synbiotic did not further increase strain abundance. Likewise, all three treatments significantly increased the absolute abundance of faecal bifidobacteria compared to baseline, but there was no statistically significant difference among the three groups. Although the combination, probiotic and prebiotic arms all improved the markers of colonic permeability and all increased faecal bifidobacteria levels, the study did not support our definition of a synergistic synbiotic.

**Example 3**
In a hypothetical study, an established prebiotic substrate (for example, GOS or inulin) at the dose shown to be both selectively utilized and have a health benefit (primary outcome showing improved probably of response) is combined with an established probiotic at the dose shown to have a health benefit in the same target host. This combination product is tested and shown to confer a health benefit compared with the control (not necessarily the same benefit as previously tested for the probiotic and prebiotic). This product would meet our definition of a complementary synbiotic.

**Example 4**
In a hypothetical study, a substrate (not an established prebiotic) at 1 g per dose is combined with 10⁹ CFU of a live microorganism (not an established probiotic). Preclinical testing suggests that the live microorganism selectively utilizes the substrate. A study tracking both health and microbiota end points in the target host comprises 10⁹ CFU per dose of live microorganism alone, 1 g per dose of substrate, 10⁹ CFU per dose of the live microorganism plus 1 g per dose of the substrate, and an inert control. Microbiota analysis supports selective utilization by the combination. Concomitantly, a health or therapeutic end point is improved by the combination. The combined effect is better than the estimated effects of each component separately. This product would meet our definition of a synergistic synbiotic.

**Example 5**
A substrate (not an established prebiotic) plus a live microorganism (not an established probiotic) is tested against the control. It is found to confer a health benefit and increase levels of bifidobacteria in faeces. This result does not provide evidence for either a synergistic or complementary synbiotic. To fulfil criteria for a synergistic synbiotic, it must be demonstrated that the health benefit and selective utilization of the substrate exceed those observed for the control and for each individual component. As the materials comprising the mixture, at the dose used, were not established probiotics or prebiotics, it does not meet our definition of a complementary synbiotic.
and provide insight into the microbiota-mediated mechanisms underlying the health outcome. Outcomes may include the abundance and viability of the administered live microorganism, changes in overall microbiota and/or microbiome composition, abundance of specific taxa and/or strains, microbial-derived metabolites, or others. Metabolomic analysis could also be performed using liquid chromatography–mass spectrometry, nuclear magnetic resonance or other suitable methods.

**Statistics.** A statistician’s involvement in the design phase of a study will provide confidence that the sample size is sufficient for the defined outcomes using intention-to-treat analysis. Mediation analyses might be useful to assess whether microbiota effects are contributing to the health benefit. Ancillary analyses, which could include population subgroups, responders versus non-responders or exploratory microbiota analyses should be pre-specified.

Finally, as with all trials, funding sources should be transparently reported, AEs must be carefully recorded and reported, and study design, execution and reporting should comply with CONSORT guidelines to minimize study bias.

**Designing a synbiotic trial**

There are multiple ways to design a synbiotic trial intended to examine health effects in the target host. Here, we provide some recommendations based on the criteria established herein to demonstrate complementary or synergistic synbiotics. Pre-specified subgroup analyses should be considered based on the relevant clinical factors (such as sex and age), baseline gut microbiota factors, dietary factors (such as typical dietary fibre intake) or other relevant factors (such as responder analysis). The number of experimental groups or ‘study arms’ required to prove efficacy and support mechanistic understanding will depend on the existing level of evidence for the component live microorganism(s) and selectively utilized substrate(s) as well as the researchers’ intent to determine whether components of the test mixture are complementary or acting as synergistic synbiotics (TABLE 2).

When selecting the study design and determining the duration of the intervention and (if applicable) of the

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**Table 2 | Evidence required for synbiotics using doses delivered in product**

| Composition | Dose | Microbiological evidence from trial in target host | Study design | Evidence of health benefit required from trial in target host |
|-------------|------|---------------------------------------------------|--------------|-------------------------------------------------------------|
| **Complementary synbiotic** | | | | |
| Prebiotic | Sufficient to result in the selective utilization by resident microbiota and a health benefit in the absence of the co-administered probiotic | No additional evidence needed beyond that for the prebiotic component | Two-arm trial of complementary synbiotic and an inert control | Complementary synbiotic is superior to control |
| Probiotic | Sufficient to result in a health benefit in the absence of the co-administered prebiotic | No effect on resident microbiota required | Two-arm trial of complementary synbiotic and an inert control | Complementary synbiotic is superior to control |
| **Synergistic synbiotic** | | | | |
| Substrate selectively utilized by the co-administered live microorganism | Sufficient to result in the selective utilization by the co-administered microorganism | Evidence that the substrate is selectively utilized by the co-administered live microorganism | Trial of live microorganism(s), selectively utilized substrate(s), combination of microorganism(s) plus substrate(s), and control | Combined effect of synergistic synbiotic is better than the estimated effects of each component separately |
| Live microorganism that selectively utilizes the co-administered substrate | Sufficient to selectively utilize the co-administered substrate and result in a health benefit | Evidence that the substrate is selectively utilized by the co-administered live microorganism | Trial of live microorganism(s), selectively utilized substrate(s), combination of microorganism(s) plus substrate(s), and control | Combined effect of synergistic synbiotic is better than the estimated effects of each component separately |

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The unmodified term ‘synbiotic’ can be used on a commercial product label as long as the criteria for either a complementary or synergistic synbiotic are met. There is no restriction on the type of health target but it must be realistic and mechanistically driven. See TABLE 1 for a list of diseases and conditions targeted to date in human trials of putative synbiotics. Microbial, metabolic and health end points (or suitable biomarkers) must be tracked in the same study for a synergistic synbiotic, in the target host. It is not indicated here, but documentation of the safety of the final blended product for the intended use is required. Effective doses delivered in a commercial product must be present through the end of shelf-life. Studies documenting health benefits conferred by probiotic and prebiotic components are also required.
wash-out period, general recommendations are difficult to make. Factors that will impact these decisions include the live microorganism dose and its ability to persist in situ as well as the characteristics of study subjects; for example, in elderly individuals or persons with slow intestinal transit time, a longer wash-out period could be required compared with a study conducted in younger individuals. Parallel arm designs would be appropriate for studies that aim to demonstrate improvements in metabolic health measures, such as adiposity or glycemic control, as these outcomes typically require longer-term interventions (that is, 12 weeks or more). Gut microbiota changes can be rapid (within days), and longer-term interventions (that is, 12 weeks or more) are required compared with a study conducted in younger individuals. Parallel arm designs would be appropriate for studies that aim to demonstrate improvements in metabolic health measures, such as adiposity or glycemic control, as these outcomes typically require longer-term interventions (that is, 12 weeks or more).

Gut microbiota changes can be rapid (within days), and longer-term interventions (that is, 12 weeks or more). Gut microbiota changes can be rapid (within days), and longer-term interventions (that is, 12 weeks or more).

Currently, changes in the gut microbiota and microbial metabolites, such as short-chain fatty acids, are not accepted by regulatory bodies as measures of a health outcome.

Responders and non-responders among study participants in intervention studies with prebiotics and probiotics are commonly observed, which could justify including the probability of a positive response as a study endpoint. In the context of synergistic consortia, non-responders include individuals for whom little or no change in gut microbiota composition and/or clinical endpoints occurs compared with placebo. Various reasons for the non-responder phenotype include limited available niches for desired gut microorganisms (either native or introduced as probiotics), limited substrates to support microbial growth, host immune system expressing intolerance for specific microorganisms or a lack of specific microorganisms in the host microbiota. Although many scenarios of formulations for synbiotics can be conceived, we provide both actual and hypothetical examples to illustrate the concept (Box 2).

**Trials for synergistic synbiotics.** Studies on a synergistic synbiotic that compare the synbiotic to the control can provide supportive evidence but do not constitute the primary evidence needed to confirm a synergistic synbiotic. Instead, a study including the combination, the substrate alone, the live microorganisms alone and a control should be conducted. Using an appropriate statistical model, the aim is to demonstrate that the combined effect is better than the estimated effects of each component separately. Evidence of selective utilization of the substrate by the co-administered live microorganism must be obtained from the same trial demonstrating the health benefit.

**Trials for complementary synbiotics.** A two-arm parallel or crossover study would be sufficient to test a complementary synbiotic. The aim is to demonstrate that the combination is better than the placebo group with a relevant health endpoint. As a demonstrated prebiotic is used to formulate a complementary synbiotic, we do not require that selective utilization by the indigenous microbiota be reconfirmed in this clinical trial.

**Measurement of selective utilization.** Measurement of selective utilization by the microbiota might involve different approaches, including both in vitro model systems and in vivo studies in the target host. For example, selective utilization of a substrate could be demonstrated experimentally using well-established in vitro gut models that include measurement of substrates and products during a prescribed time course. Ultimately, however, studies must be done in the target host to show that specific microorganisms or taxa had been enriched or their activity enhanced by a particular substrate. For synergistic synbiotics, methods that quantify the live microorganism should be used to show that the target strain has indeed been enriched and other suitable methods can be used to show that its function has been enhanced. Microbiota features that are useful to measure include characterization of the overall gut microbial community and microbiota diversity, abundance and/or activity of specific taxa, microorganism-microorganism or microorganism-host proximity, the presence and/or abundance of specific microbial genes or gene clusters of interest, and/or metabolite concentrations.

**Safety measures for synbiotics.** Prebiotics and probiotics tested to date have a strong safety record, and synbiotics formulated with them might also be presumed safe for the same intended uses. However, novel formulations must be suitably assessed for safety. Unfortunately, historically, many probiotic and prebiotic intervention trials have not adequately reported the types and frequency of AEs or serious AEs, perhaps owing to expectations that, as food ingredients, these products were inherently safe or that AEs could be due to failure to comply with norms for reporting harms in RCTs. Nonetheless, clear guidance for reporting AEs and serious AEs is provided by CONSORT and these standards should be followed. Describing such events as “unrelated to the study product”, without justification for this statement, is unacceptable.

A systematic review of 384 interventions involving prebiotics, probiotics and synbiotics found that no safety-related data were reported in 37% of the RCTs and 89 studies only used generic statements to describe AEs. Up to 98% of studies did not provide a definition of AEs or serious AEs, the number of participant withdrawals due to AEs, or the number of AEs and serious AEs per study group. Taken together, these results are evidence that some studies inadequately collect or report data on AEs. van den Nieuwoerden et al. reviewed the AEs reported in studies with probiotic and synbiotic interventions and classified them according to the Common Terminology Criteria for Adverse Events system; they found that the incidence of AEs in each category was either no different from or often lower in the control groups than in the treatment group.

Thorough safety assessment of a synergistic synbiotic requires consideration that the added microorganism will express enhanced functionality in the presence of a targeted substrate such as improved growth or altered metabolic or physiological activity in vivo. This aspect suggests that safety assessments conducted on the live microorganism in isolation might not be sufficient to enable a conclusion about its safety when paired with a substrate that alters physiology or might in effect alter the dose delivered in vivo. Implicitations of such an
**Consensus Statement**

**Table 3** Minimum criteria to appropriately use the terms ‘probiotic’, ‘prebiotic’ and ‘synbiotic’

| Substance                  | Safe for intended use | Identity characterized | Scientifically valid name | Strain designated | Micro-organism deposited in international culture collection | Mechanism of action linked to microbiota | Selective utilization of substrate | By resident micro-organism | By co-administered live micro-organism | Study in demonstrating both: | Health benefit | Selective utilization of substrate | Proper conditions of use |
|----------------------------|------------------------|-------------------------|---------------------------|-------------------|---------------------------------------------------------------|----------------------------------------|-----------------------------------|-------------------------------|----------------------------------------|--------------------------|------------------------|-----------------------------------|--------------------------|
| Probiotic                  | ☑                      | ☑                       | ☑                         | ☑                 | ☑                                                             | NA                                     | NA                                | NA                            | NA                                     | ☑                        | ☑                      | ☑                                 | ☑                        |
| Prebiotic                  | ☑                      | ☑                       | ☑                         | ☑                 | ☑                                                             | ☑                                      | ☑                                 | NA                            | NA                                     | ☑                        | ☑                      | ☑                                 | ☑                        |
| Synbiotic                  |                        |                         |                           |                   |                                                               |                                        |                                   |                               |                                        |                          |                        |                                   |                          |
| Complementary synbiotic    | ☑                      | ☑                       | ☑                         | ☑                 | ☑                                                             | ☑                                      | ☑                                 | NA                            | NA                                     | ☑                        | ☑                      | ☑                                 | ☑                        |
| Synergistic synbiotic      | ☑                      | ☑                       | ☑                         | ☑                 | ☑                                                             | ☑                                      | ☑                                 | ☑                             | ☑                                      | ☑                        | ☑                      | ☑                                 | ☑                        |

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. A prebiotic is a substrate that is selectively utilized by host microorganisms conferring a health benefit. Synbiotics are a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host. A complementary synbiotic is a mixture of a probiotic plus a prebiotic. A synergistic synbiotic is a synbiotic in which the substrate is designed to be selectively utilized by the co-administered microorganisms. A synbiotic must meet the evidence required for either complementary or synergistic synbiotics. All substances should be made available to the scientific community for validation of research findings. The intent of a synergistic synbiotic is for the substrate to support the growth and/or activity of the co-administered live microorganisms but selective utilization by the resident microbiota is not a disqualifier. The prebiotic component of a complementary synbiotic must be selectively utilized by the resident microbiota, but if it is also utilized by the co-administered probiotic, it is not a disqualifier. NA, not applicable; NR, not required.

**Implications of this consensus**

The panel recognizes the importance of developing a scientifically valid definition of the term synbiotic. The intention is to provide clarity for a diverse range of stakeholders, including consumers, regulators, health-care providers, researchers, industry and scientific organizations communicating about synbiotics. **TABLE 3** is designed to clearly lay out the criteria for synbiotics in comparison to probiotics and prebiotics. Within the commercial supply chain, many different industry sectors, including ingredient suppliers, end-product manufacturers and retailers are very interested in how synbiotics are defined. As synbiotic products are being used more frequently in clinical trials, it is incumbent upon scientists to clarify the appropriate use of this term as has been done for the terms ‘probiotic’ and ‘prebiotic’.12

Although the term ‘synbiotic’ might not be as well recognized as probiotics and prebiotics, it is nonetheless found on product labels, in popular press articles and in the scientific literature. The first mention of a synbiotic was in 1995 yet, according to PubMed searches, in 2019, 269 papers were published using the term. Consumer exposure is expected to increase. Thus, it is hoped that the definition herein is clear and widely accepted and will counter misuse of the term, including by scientists. **TABLE 3** provides the minimum criteria for the correct use of terms associated with synbiotics.

**The importance of context.** The panel urges stakeholders to carefully consider context for communications to consumers on the health benefits of synbiotics. The overall impression of any communication should lead consumers to understand the claim in a manner that is consistent with the evidence; any misleading use of the term constitutes misuse. Communication of the tested health benefit must accurately reflect what was reported in the clinical trial; results should not be extrapolated to health conditions, populations or synbiotics that have not been studied.

**Regulators.** Regulatory authorities are primarily focused on two issues: product safety and product labelling. These encompass both truthfulness and compliance with regulatory statutes. Even if the term synbiotic is not included in governmental guidelines or regulations, the use of our proposed scientific definition of the term will aid regulatory oversight of products labelled as ‘synbiotic’. Regulatory statutes will differ with regard to geographical regions, regulatory categories, types of allowable claims and premarket approval. Furthermore, different standards exist for manufacturing, efficacy and safety depending on geographical region and product category. The term synbiotic does not stipulate a regulatory category, so (simply stated), regulatory requirements for a synbiotic would need to meet those that apply to the category (for example, drug, food or supplement) of the marketed product.

Regulatory complications can result in regions that impose probiotic-specific regulations. For example, Canada11,12, Italy13, Argentina14, Chile15, Colombia16 and Brazil17 have requirements specific to probiotic foods or supplements. Furthermore, there is a proposal18 under consideration by Codex Alimentarius that could result in probiotic-specific global standards19. The Codex Alimentarius is a collection of standards, guidelines and codes of practice adopted under the auspices of the Food and Agricultural Organization of the United Nations and World Health Organization to protect consumer health and promote fair practices in food trade. Codex Alimentarius standards could affect probiotic products traded globally. Could product manufacturers potentially avoid these regulations by labelling a product...
as a synbiotic? Without the use of the term probiotic or prebiotic, relevant specific regulations would not be triggered. Perhaps this approach would not provide a marketing advantage, as consumer recognition and demand for synbiotic products is currently not as advanced as for probiotics and prebiotics. However, regions supporting probiotic-specific (or prebiotic-specific) regulations will need to address how the concept of synbiotics fits into those regulations. Our stipulation is that manufacturers of complementary synbiotics should meet current probiotic or prebiotic regulations.

One regulatory consequence of probiotic and prebiotic definitions is that the European Union has determined that labelling a food product as such amounts to an implied health claim. As health claims in the European Union must be approved, the use of ‘probiotic’ or ‘prebiotic’ on a food label is subject to a health claim approval process. Despite controversy surrounding this situation, we can expect that the European Union might adopt a similar position for the use of the term ‘synbiotic’ because it also requires evidence of a health benefit.

Scientists. Synbiotics present challenges for researchers, including deciphering mechanisms underlying the health benefit and proving that the microbiota are modulated via complementary or synergistic means. Unless appropriate experimental methods of verification are used, the product under assessment should not be referred to as ‘synbiotic’.

As for probiotics, prebiotics and synbiotics, it might be possible a priori to stratify study participants to enhance either the magnitude of the response or the number of responders to a given synbiotic treatment. The baseline composition of gut microbiota of study participants could be one useful stratification factor. This stratification might improve mechanistic understanding of observed effects and could be useful for characterizing responders and non-responders. Ultimately, this approach could enable better translation of clinical trial outcomes to those who are likely to benefit.

Scientists involved in the publication process (authors, editors, reviewers) should use the term synbiotic correctly and reject erroneous or unsupported use of the term. Even if a given treatment fails to demonstrate an effect (that is, acceptance of the null hypothesis) in a well-conducted study, such results still warrant publication.

Industry. The business community plays a vital part in translating the outcomes of fundamental and clinical research into commercial products that can benefit consumers. To the extent that industry funds research, it is essential that studies adhere to well-established guidelines to manage conflicts of interest and minimize bias. Further, industry bears the duty of responsible manufacture, quality control and marketing of synbiotic products. It is incumbent on industry to follow good manufacturing practices, engage in truthful labelling and product promotion as well as adhere to appropriate use of the term ‘synbiotics’.

Media. The media (TV, radio, newspapers, magazines, websites and social media) have an increasingly central role in communicating science. These efforts require commitment and skill to craft clear, simple messages that are true to the science. Too often, scientists or their institutions do not effectively translate complex research findings so that they can be understood by the lay public. At times, overextended or inflated representations of research findings can be communicated through official academic or journal press releases. Communicators are therefore encouraged to distinguish between association studies and those presenting causal evidence, to describe single studies in the context of the totality of evidence, to avoid overgeneralizing results (for example, from model organisms such as mice) and to note study limitations. This requirement is true for null studies as well as those suggesting benefits from the interventions being tested. In this context, the media should adopt the scientific definition of synbiotics herein.

Conclusions

This Consensus Statement provides a new definition for a ‘synbiotic’ based on review by a panel of experts. To summarize, a synbiotic is a mixture comprising live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host. Two categories of synbiotics are recognized. A complementary synbiotic is composed of a probiotic and a prebiotic that together confer one or more health benefits but do not require co-dependent function; the components must be used at doses that have been shown to be effective for the components alone. A synergistic synbiotic contains a substrate that is selectively utilized by the co-administered live microorganism(s). Synbiotic products are not confined to human applications but could also include companion animals and livestock. They might also be directed to specific subpopulations (age, sex, health status) of the target species. The definition can also be applied to intestinal or extra-intestinal microbial ecosystems. The hope is that, going forward, this updated definition will be utilized and that it will aid in advancing synbiotic research, improve stakeholder understanding and enable better communication to consumers.
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