

Chapter 16: Probiotics, Prebiotics, and "Psychobiotics"

Summary

Probiotic capsules, prebiotic sodas, and "mood" supplements fill store shelves and social media feeds. This chapter defines the products scientists actually mean (probiotics, prebiotics, synbiotics, and postbiotics), explains why the exact strain on the label matters, and shows how lightly supplements are regulated in the United States compared with medicines. It covers who should be careful with probiotics, including premature babies and people with weak immune systems. Then it follows the "psychobiotic" idea from a famous mouse study to a human trial that did not work, and teaches the tools you need to read probiotic trials yourself: systematic reviews, effect sizes, primary outcomes, publication bias, and replication.

Concepts Covered

1. Probiotic
2. Prebiotic
3. Synbiotic
4. Postbiotic
5. Psychobiotic
6. Lactobacillus
7. Bifidobacterium
8. Strain Specificity
9. Colony-Forming Unit
10. Dietary Supplement Regulation
11. Probiotic Safety
12. Systematic Review
13. Effect Size
14. Primary Outcome
15. Publication Bias
16. Replication Failure

Prerequisites

- [Chapter 3: Meet the Microbiome](#) (microbiome, dysbiosis, germ-free mice)
- [Chapter 6: Fiber, Fatty Acids, and the Blood-Brain Barrier](#) (how microbes ferment fiber)
- [Chapter 11: Anxiety, Depression, and the Gut](#) (meta-analysis, symptom questionnaires)
- [Chapter 13: Autism, ADHD, and the Gut](#) (open-label vs placebo-controlled trials, sample size)
- [Chapter 15: Food and Mood](#) (randomized controlled trials)

A capsule with a big promise



Probiotics are probably the gut-brain product you'll see advertised most, and many of the ads talk about mood, stress, or focus. This chapter gives you the vocabulary and the trial-reading skills to look past the label and ask what was actually tested, in whom, and what happened. Those same skills work on almost any supplement claim you'll ever meet.

16.1 "Calm in a Capsule"

Sam's older cousin Dev posts a lot about supplements. This week it's a bottle with a sunrise on the label and the words "Calm in a Capsule: the psychobiotic for stress, mood, and focus. 50 billion CFU!" Dev tags Sam in the comments: "Bro, this would fix your race nerves AND your stomach." (Sam and Dev are fictional.)

Sam has IBS with mixed bowel habits, and his symptoms flare before big tests and races. He's been learning gut-directed relaxation, and it helps. He's also learned to be suspicious of anything that promises to fix two problems at once. At lunch he shows the post to his best friend Riya, who has Crohn's disease. Riya shrugs. "I asked Dr. Alvarez about probiotics once. She said it depends on which one and what for, and that for Crohn's they're mostly still being studied." Sam looks at the bottle again. Which one? For what? The label says "psychobiotic," but what does that even mean, and who checked that this capsule does anything?

Those are the right questions. By the end of this chapter, you'll be able to read Dev's bottle the way a scientist would.

16.2 Seeds, Fertilizer, and the Garden in Your Gut

Picture your gut microbiome (the trillions of microbes living in your intestines, from [Chapter 3](#)) as a garden. There are two obvious ways to change a garden. You can plant new seeds, or you can add fertilizer that helps certain plants already growing there. You can also do both at once. Or, stranger, you could spread something made from plants that are no longer alive, like mulch, and still change how the garden grows.

Scientists have names for each of these approaches. The definitions below come from consensus statements written by panels of the International Scientific Association for Probiotics and Prebiotics (ISAPP), a scientific group that meets to agree on how these words should be used.

A **probiotic** is defined as "live microorganisms that, when given in adequate amounts, confer a health benefit on the host" ([ISAPP, 2014](#), keeping the wording used by the United Nations Food and Agriculture Organization and the World Health Organization). Three parts of that definition matter. The microbes must be **alive** when you take them. They must be given in a **big enough amount**. And they must have a **demonstrated health benefit**. A yogurt full of live bacteria is not automatically a probiotic in this scientific sense unless a benefit has been shown.

A **prebiotic** is "a substrate that is selectively utilized by host microorganisms conferring a health benefit" ([ISAPP, 2017](#)). In plain words, it is food for your microbes, but a picky kind of food: it feeds certain microbes more than others, and it has to produce a health benefit. Many prebiotics are types of fiber, which connects to the fermentation story in [Chapter 6](#). The 2017 statement says prebiotics are not limited to carbohydrates, and that a health benefit has to be shown before something earns the name.

A **synbiotic** is "a mixture of live microorganisms and substrate(s) selectively utilized by host microorganisms that confers a health benefit on the host" ([ISAPP, 2020](#)). The ISAPP panel described two kinds. A *complementary* synbiotic is simply a probiotic plus a prebiotic in the same product. A *synergistic* synbiotic is designed so the food part is chosen to feed the live microbes it comes with.

A **postbiotic** is "a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host" ([ISAPP, 2021](#)). "Inanimate" means no longer alive. Under this definition, a postbiotic must contain inactivated microbial cells or cell parts. A purified chemical made by microbes, all by itself, doesn't count.

Term	Garden comparison	What it is	Must show a health benefit?
Probiotic	Planting seeds	Live microbes in adequate amounts	Yes
Prebiotic	Fertilizer for certain plants	A substance gut microbes use selectively	Yes
Synbiotic	Seeds plus fertilizer	Live microbes plus a substance microbes use	Yes
Postbiotic	Mulch made from old plants	Inactivated microbes or their parts	Yes

Notice the last column. Every one of these scientific definitions requires a **health benefit**. That's the part marketing tends to skip. A product can contain live bacteria or fiber and still not meet the scientific definition, because nobody has shown it does anything for people.

The benefit is part of the definition



When I read "probiotic" on a label, I remind myself that scientists only use the word for live microbes with a proven benefit. So the real question is never "Does it contain bacteria?" but "Which benefit was shown, for which strain, in which people?"

16.3 The Usual Suspects: Lactobacillus and Bifidobacterium

If you turn a few probiotic bottles around, you'll see the same two names again and again. [The National Center for Complementary and Integrative Health](#) (NCCIH), part of the US National Institutes of Health, says the most common probiotic bacteria belong to these two groups. Yeasts such as *Saccharomyces boulardii* are also used.

Lactobacillus is a group of bacteria known for turning sugars into lactic acid. Lactic acid bacteria are used to make yogurt and other fermented foods, and some live naturally in the human body. There's a twist for anyone reading older labels and studies. In 2020, a team of microbiologists led by Zheng compared the full genomes of these bacteria and found that the old genus *Lactobacillus*, which then held 261 species, was really many different groups. They split it into 25 genera. Some famous probiotic species got new first names:

Lactobacillus rhamnosus, for example, is now *Lacticaseibacillus rhamnosus* (see the official [List of Prokaryotic names with Standing in Nomenclature](#) entry, which credits the 2020 Zheng paper). The informal word "lactobacilli" is still used for the whole family of former members. So if a 2011 paper and a 2025 bottle use different names, they may mean the same microbe.

Bifidobacterium is another large group of bacteria that live naturally in the human gut. Like lactobacilli, they ferment sugars and some fibers, which is one reason they show up so often in probiotic and synbiotic products.

Every strain is an individual

Here's the most important idea in this section. A species is not specific enough. Think about how people are named. "Smith" tells you a family, "Jordan Smith" narrows it down, but you need an address to find the one Jordan Smith you mean. Bacteria are named the same way: a **genus** (family name, like *Lacticaseibacillus*), a **species** (like *rhamnosus*), and a **strain** code (like GG or JB-1) that pins down one specific lineage grown in a lab.

Strain specificity is the finding that a probiotic's effects belong to a particular strain, used for a particular condition, so a result from one strain cannot be assumed to apply to another strain, even one from the same species. NCCIH puts it simply: if one kind of *Lactobacillus* helps prevent an illness, that doesn't mean another kind of *Lactobacillus*, or any *Bifidobacterium*, would do the same thing.

The best evidence for strain specificity comes from a [2018 systematic review](#) by McFarland, Evans, and Goldstein, which looked at 228 trials of probiotics with identifiable strains. They found that effects depended

on both the strain and the disease. For example, among *Lactobacillus* products tested for preventing diarrhea caused by antibiotics in adults, some specific strains and mixtures worked while other *Lactobacillus* strains did not. They also found that a single strain could help with one condition but not another. Their warning for scientists: reviews that lump different probiotics together can reach misleading conclusions.

Strain specificity matters for Dev's bottle. A label that says only "*Lactobacillus* blend" or "bifidobacteria" doesn't tell you which strains you're getting, so it's impossible to match the product to any study.

Hype Meter: "All probiotics are basically the same, so just grab any one"

Strong

Moderate

Preliminary

Hype

Verdict: Hype. A 2018 systematic review of 228 trials found that probiotic effects depend on both the specific strain and the specific condition, and NCCIH says a benefit from one strain doesn't carry over to others. Strains from the same species can behave differently, and a strain that helps one problem may not help another. **What would change the grade:** Large head-to-head trials showing that many different strains give the same benefit for the same condition. So far, the evidence points the other way.

16.4 Reading the Label: What "50 Billion CFU" Means

Dev's bottle brags about "50 billion CFU." That sounds impressive. What is it actually counting?

A **colony-forming unit** (CFU) is a count of how many microbes in a sample are alive and able to multiply. To measure it, scientists spread a diluted sample on a dish of nutrient gel and wait. Each living cell (or tiny clump of cells) that can grow forms a visible dot called a colony. Count the colonies, multiply by how much the sample was diluted, and you get CFU. Dead bacteria don't form colonies, so they don't count. That's why probiotic doses are given in CFU: the definition of a probiotic requires live microbes.

Three things about CFU trip people up.

1. **Bacteria die on the shelf.** An [ISAPP guide to probiotic labels](#), written by microbiologist Mary Ellen Sanders (updated in 2025), explains that most strains lose live cells during storage, some faster than others. A count printed "at time of manufacture" may be much higher than what's alive when you open the bottle months later. Guidance from FAO/WHO calls for listing the minimum live count at the **end of shelf life**.
2. **A big total can hide a small dose of the strain that matters.** In a product with many strains, one total CFU number doesn't tell you how much of each strain is inside. The bulk could be a cheaper strain rather than the one with evidence behind it.
3. **More is not automatically better.** The amount that matters is the amount shown to work in a study of that strain. A product with ten times more CFU of an untested strain isn't ten times better; it's untested at a higher number.

The same ISAPP guide describes a survey of supplements sold in Washington, DC: 45% didn't list strain designations, and only 35% could be linked to evidence of a health benefit for that strain at that dose.

What a careful label shows	What a weak label shows
Genus, species, and strain code for each microbe	Only "probiotic blend" or a genus name
CFU guaranteed at the end of shelf life	CFU "at time of manufacture" only
A dose matching a published study	A huge number with no study
Storage instructions	None

Match the strain, the dose, and the condition



A probiotic claim is only as good as three matches: the same strain that was studied, at about the same dose, for the same health problem. If any of the three is missing, the study doesn't really apply to the bottle in your hand.

16.5 Who Checks the Bottle? Dietary Supplement Regulation

Most people assume that anything sold in a pharmacy has been tested and approved by the government. For medicines, that's true. For supplements, it isn't.

Dietary supplement regulation is the set of US rules for products like vitamins, herbs, and most probiotics, which, unlike medicines, do not need FDA approval for safety or effectiveness before they are sold. In 1994, Congress passed the Dietary Supplement Health and Education Act (DSHEA), which defined "dietary supplement" and set out the FDA's role. According to the [FDA](#), under DSHEA:

- The FDA does **not** have the authority to approve dietary supplements before they are marketed.
- The companies that make and sell supplements are **responsible for** making sure their products are safe and correctly labeled before they go on sale.
- The FDA can take action against an unsafe or mislabeled product **after** it reaches the market.

NCCIH explains that the FDA might treat a probiotic product as a dietary supplement, a food ingredient, or a drug, depending on how it's meant to be used. Many probiotics are sold as supplements. If a company wants to market a probiotic as a drug to treat a disease, it must prove the product is safe and effective in clinical trials and get FDA approval first. That's the path the medicines in [Chapter 17](#) had to travel.

What can a supplement label say? NCCIH notes that supplement labels may make claims about how a product affects the structure or function of the body (such as "supports digestive health") without FDA approval. They aren't allowed to claim the product treats, cures, or prevents a disease. That's why many bottles carry a small legally required disclaimer, which the FDA quotes: "This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease." (Chapter 20 looks more closely at these "structure-function" claims and how advertising is policed.)

Put these facts together and Dev's bottle looks different. "Calm in a Capsule" is almost certainly a dietary supplement. No government agency checked that it reduces stress before it went on sale, and words like "psychobiotic" are marketing language, not an FDA category.

	New prescription drug	Dietary supplement (most probiotics)
FDA approval before sale?	Yes	No
Must prove it works first?	Yes, in clinical trials	No
Who is responsible for safety before sale?	Company, reviewed by FDA	Company
Can it claim to treat a disease?	Yes, for its approved use	No

16.6 "Natural" Doesn't Mean Risk-Free: Probiotic Safety

Probiotics are often described as completely harmless. For most healthy people, that's close to true, but "close" matters.

Probiotic safety refers to the risks of taking live microbes, which are low for most healthy people but higher for people who are very sick, have weakened immune systems, or were born very early, because the microbes can occasionally cause infections. NCCIH says probiotics have a long history of apparently safe use, especially in healthy people. But it also says few studies have looked at safety in detail, so there isn't solid information on how often side effects happen or how serious they are. The risk of harm is greater in people with severe illnesses or weakened immune systems, and NCCIH says doctors should weigh the risks carefully for high-risk people such as premature infants and seriously ill hospital patients.

Why would a "good" bacterium cause harm? A healthy gut lining and immune system keep microbes inside the gut, where they belong. In a very premature baby, whose gut and immune system are still developing, or in a person whose immune system is weakened by illness or treatment, live microbes from a capsule can occasionally cross into the bloodstream and cause an infection. Products can also be contaminated with organisms that aren't supposed to be there. In a [2015 report](#), the Centers for Disease Control and Prevention

described a baby born at 29 weeks who died of a rare fungal infection after receiving a probiotic powder; unopened bottles from the same batch grew the same fungus.

The clearest warning came in 2023. On October 26, 2023, the [FDA announced](#) that probiotic products used in hospitals for preterm infants, often to try to prevent a serious gut disease called necrotizing enterocolitis, had contributed to invasive disease, including **one infant death in 2023**, and had been associated with **more than two dozen other reported harmful events in the United States since 2018**. The FDA sent warning letters to two companies for illegally selling probiotics to treat or prevent disease in preterm infants, and it stated that it "has not approved any probiotic product for use as a drug or biological product in infants of any age."

There's a real scientific debate behind this. In 2020, the [American Gastroenterological Association \(AGA\) guideline on probiotics](#) conditionally suggested certain strains for preventing necrotizing enterocolitis in preterm, low-birth-weight babies. Three years later, the FDA warned about serious infections and said no probiotic is approved as a drug for infants. Both statements are real, and they point in different directions. That's why decisions about very sick babies belong to the hospital care team and the family together, not to a supplement label.

Hype Meter: "Probiotics are always safe because they're natural"

Strong

Moderate

Preliminary

Hype

Verdict: Hype. Probiotics have a long record of apparently safe use in healthy people, but NCCIH says risk is greater for people with severe illness or weakened immune systems, and few studies have measured side effects in detail. In 2023, the FDA reported that probiotics given to hospitalized preterm infants contributed to invasive disease, including a death. "Natural" describes where something comes from, not how safe it is for a particular person. **What would change the grade:** Nothing about the "always" part. Better safety studies could show more precisely who is at risk and who isn't.

What does the AGA 2020 guideline say about the gut conditions in this book? It recommends using probiotics for IBS, Crohn's disease, and ulcerative colitis only in clinical trials, not as routine treatment. It suggests specific strains for a few uses, such as preventing *C. difficile* infection in people taking antibiotics and a specific eight-strain mix for pouchitis (inflammation of a surgically made pouch after colon removal), and it suggests against probiotics for children with acute infectious diarrhea. That matches what Dr. Alvarez told Riya: for Crohn's, probiotics are still a research question.

For families

It's natural to want to do something when your child or sibling is sick, and a probiotic can feel like a safe, hopeful step. Before giving one, bring the actual bottle to the care team, especially if your child is on medicines that affect the immune system, is going through cancer treatment, or was born very early. Asking "Is there any reason this could be risky for my child?" is not an insult to the doctor; it's exactly the question they want you to ask. And if a teen in your family is skeptical of a product a relative keeps pushing, that skepticism is a sign of good thinking, not stubbornness.

16.7 Psychobiotics: From a Mouse Maze to a Human Trial

Now to the word on Dev's label. In 2013, three researchers in Cork, Ireland (at University College Cork and the nearby Teagasc Moorepark research centre), Timothy Dinan, Catherine Stanton, and John Cryan, published a paper titled "[Psychobiotics: a novel class of psychotropic](#)." A **psychobiotic**, in their original definition, is a live organism that, when taken in adequate amounts, produces a health benefit in patients with psychiatric illness. Later papers stretched the term to include other ways of changing the microbiome to help mental health, but the 2013 definition is the original. The same paper said that results from large placebo-controlled studies were still "awaited."

Two things follow. "Psychobiotic" is a **research term**, not an approved product category; no agency checks whether a product labeled "psychobiotic" helps anyone. And by the original definition, it would apply only to organisms shown to benefit people with psychiatric illness, which is a high bar.

The mouse study that launched a thousand headlines

Much of the excitement traces back to a [2011 study](#) in the journal *PNAS* by Javier Bravo and colleagues, also in Cork. They fed mice a specific strain, *Lactobacillus rhamnosus* JB-1, for several weeks. Compared with control mice, the treated mice showed less anxiety-like and depression-like behavior in standard lab tests, and lower levels of corticosterone (the mouse version of the stress hormone cortisol) after stress. The researchers also found changes in brain receptors for GABA, the brain's main "calming" chemical messenger, in several brain regions.

The most striking part was an experiment that tested cause. In mice whose vagus nerve had been cut (a vagotomy), the bacteria had **no effect** on behavior or brain receptors. That suggested the bacteria's signal traveled from the gut to the brain along the vagus nerve, the gut-brain nerve highway from [Chapter 2](#). It's a clever experiment, and it fit the gut-brain story perfectly.

Notice the type of evidence: **mice**, and an **experiment that tested cause**, but only in mice.

The human trial that didn't work

Six years later, much of the same research group took the natural next step and gave the same strain to people. In a [2017 study](#) in *Brain, Behavior, and Immunity*, Kelly and colleagues gave *L. rhamnosus* JB-1 or a placebo to 29 healthy men in an 8-week randomized, placebo-controlled crossover design (each man took the probiotic for 4 weeks and the placebo for 4 weeks, in random order, without knowing which was which). They measured mood, anxiety, stress, sleep quality, the stress hormone response to a lab stress test, inflammation, memory and attention, and brain waves on EEG.

The probiotic did no better than placebo on any of these. The paper's title asked, "Lost in translation?" The authors noted that the original mouse work used an especially anxious strain of mouse, while the human volunteers were healthy, and they called for studies in people with stress-related disorders.

This pair of studies is a textbook example of **replication failure**: when a later study tests the same idea and does not find the original result. A replication failure doesn't automatically mean the first study was wrong. Here, the second study changed several things at once (mice to humans, anxious animals to healthy people, and a small group of 29 men), so it can't say whether JB-1 would help people with anxiety. What it does show is that a strong mouse result didn't carry over to healthy men. That's common. As Chapter 20 explains, only about one in three highly cited animal studies were later tested successfully in human trials.

Don't let a mouse speak for you



I love the JB-1 mouse experiment, and it really does show that a gut microbe can change mouse behavior through the vagus nerve. But when the same strain was tested in healthy men, nothing happened. When an ad leans on a mouse study, the honest summary is "promising in mice, unproven in people."

16.8 What Do All the Trials Say? Reading the Evidence

One study can't settle a question, especially a small one. So how do scientists combine many trials? And why do different reviews of the same topic sometimes disagree?

Systematic reviews and meta-analyses

A **systematic review** is a study of studies that uses a written plan to search for every relevant study on a question, judge each one's quality, and summarize the results, so that the conclusion doesn't depend on which studies an author happened to pick. Think of the difference between asking three friends what they thought of a movie and reading every review in a big database using fixed rules. The "systematic" part is what makes it trustworthy: the search terms, the rules for including studies, and the quality checks are all written down in advance, often registered publicly.

Many systematic reviews then combine the numbers from the included trials into one overall estimate. That step is a meta-analysis, which you met in [Chapter 11](#). Not every systematic review includes a meta-analysis

(sometimes the studies are too different to combine), but most of the probiotic reviews in this chapter do both.

How big is the effect?

To compare trials that used different questionnaires, scientists convert results into an **effect size**: a number that describes how big a difference is between groups, often measured in standard deviations (a unit for how spread out people's scores are), so that results from different scales can be compared. A common version is called *d* or the standardized mean difference. An effect size of 0 means no difference. Bigger numbers mean bigger differences, whatever the sign. (In depression studies, a negative number usually means the treatment group's scores dropped more, which is good.)

Effect size answers a different question from "Was there an effect?" A huge study can detect a real but tiny effect that hardly matters to anyone, and a small study can produce a big-looking effect by luck. Researchers often describe an effect around 0.2 standard deviations as small. In a 2019 review, Liu and colleagues called an effect of 0.24 "small" and one of 0.73 "medium-to-large."

Different reviews, different answers

Here's what four recent reviews of probiotics for depression found. (Liu also pooled prebiotic trials, and Pan pooled a wider group of "microbiome-targeted" treatments that includes probiotics.) All are human studies, and all pool randomized controlled trials that compare a treatment group with a control group, so they are designed to test cause. But look how much they differ.

Review	Trials included	Main finding for probiotics and depression	Notes
Liu et al., 2019	34 controlled trials (probiotics and prebiotics)	Small effect, $d = 0.24$	Prebiotics showed no effect; bigger effect in clinical samples, and 0.73 in a preliminary analysis of people with a psychiatric diagnosis
Rahmannia et al., 2024	12 trials, 707 people	Improvement on one questionnaire (BDI), not on three others	Authors urge cautious interpretation
Asad et al., 2025	23 trials, 1,401 patients with a diagnosis (18 trials tested probiotics for depression)	Large effect, about 0.96, but results varied a lot	High heterogeneity (trials disagreed with each other)

Review	Trials included	Main finding for probiotics and depression	Notes
Pan et al., 2025	34 trials of "microbiome-targeted" treatments, including probiotics	Small effect, about 0.26	Benefit in Asian studies, not European ones; no benefit beyond 12 weeks

Why don't they agree? They included different trials, different people (healthy volunteers versus people with a diagnosis), different strains, and different lengths of treatment. Strain specificity alone means "probiotics" in one review might be completely different products from "probiotics" in another. When a review reports **high heterogeneity**, that's a warning that the trials inside it disagree so much that one average number may be misleading.

The trap of many outcomes

The Rahmannia 2024 review deserves a closer look because it's often summarized as "probiotics reduce depression (12 trials, 707 people)." Here's what the abstract actually reports for its four depression scales:

Depression scale	Who fills it out	Result
Beck Depression Inventory (BDI), 7 trials	The patient	Scores dropped more with probiotics (about 2.7 points)
Hamilton Depression Rating Scale (HAMD)	A clinician	No significant difference
Depression Anxiety Stress Scales (DASS)	The patient	No significant difference
Montgomery-Åsberg Depression Rating Scale (MADRS)	A clinician	No significant difference

One out of four scales showed a benefit. Is that a real effect that only the BDI picked up, or a chance result? The review can't tell, and its authors say the mixed results call for caution.

This is why good trials name a **primary outcome**: the one main measurement a study commits to in advance as the test of whether the treatment works, written down before the results are known. Other measurements are called secondary outcomes. Picking the primary outcome first matters because of a simple fact about chance. If a treatment does nothing, any single measurement still has a small chance of looking "significant" just by luck. Measure one thing and you'll rarely be fooled. Measure ten things and report whichever looked

best, and you'll be fooled often. A trial that names its primary outcome ahead of time can't quietly switch to whichever result looked best.

The missing studies: publication bias

There's one more trap, and it's sneaky because you can't see it in any single paper. **Publication bias** is the tendency for studies with exciting, positive results to be published more often (and faster) than studies that found nothing, so the published research makes a treatment look better than it really is.

The most famous demonstration comes from antidepressant medicines, not probiotics. In 2008, [Turner and colleagues](#) compared 74 antidepressant trials that companies had registered with the FDA against what was published in medical journals. Almost all the positive trials were published, but most of the negative or questionable ones were either never published (22 trials) or were published in a way that made the result sound positive (11 trials). Reading only the journals, 94% of trials looked positive. The FDA's full records showed about 51% were. Because the negative studies were missing, the published research made the drugs' effect look about 32% bigger overall than the full set of data did.

If publication bias can distort the evidence for heavily regulated medicines, it can affect probiotic research too, where many trials are small. Systematic reviews try to detect it with statistical checks, and trial registries (public lists where trials are recorded before they start) help reveal studies that disappeared. But a meta-analysis of the published trials can only be as honest as the trials that got published.

Hype Meter: "Probiotics treat depression and anxiety"

Strong

Moderate

Preliminary

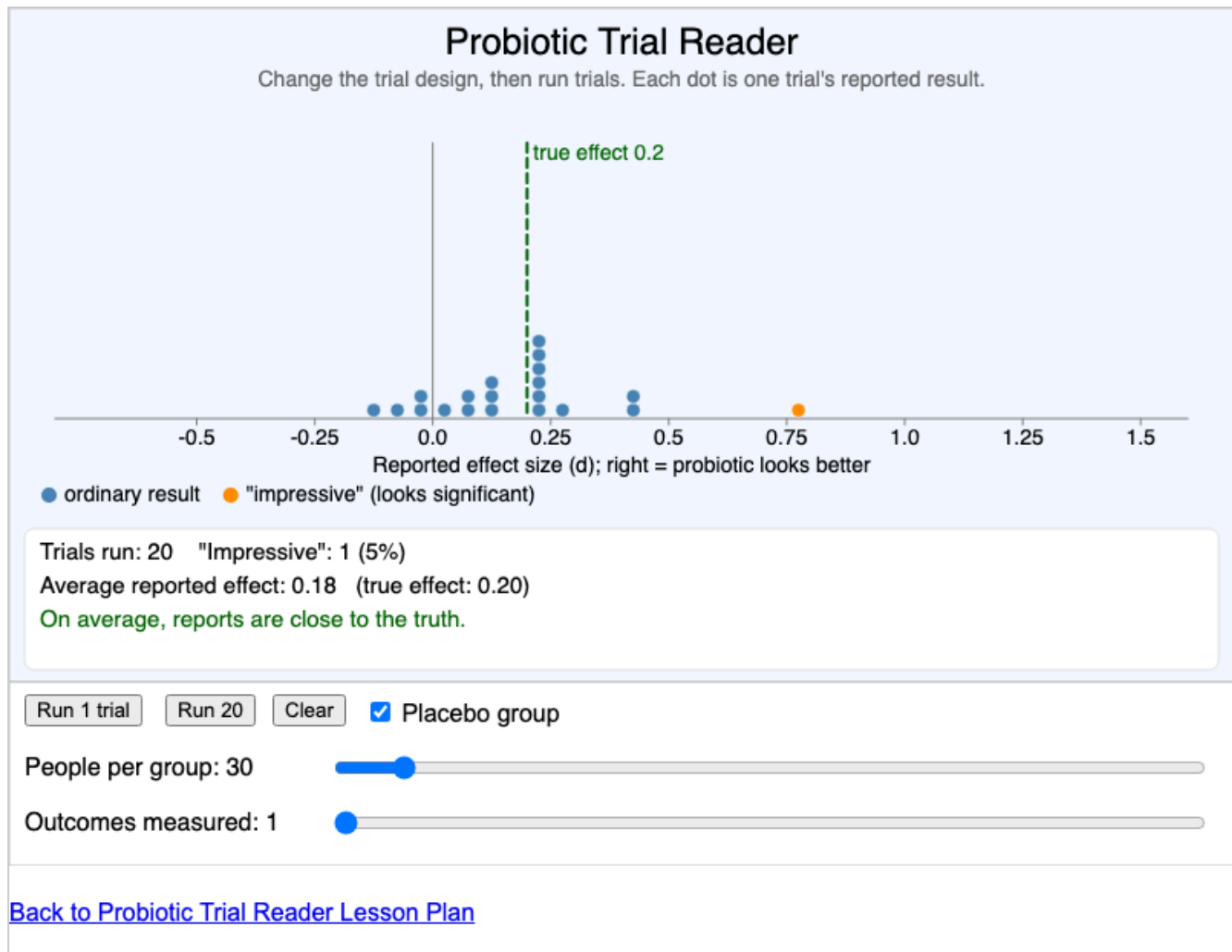
Hype

Verdict: Preliminary. Several meta-analyses of human randomized trials report some benefit, but the estimates range from small to large, the trials disagree a lot, and the results depend on the strain, the people, and the questionnaire. A 2024 review of 12 trials (707 people) found improvement on one depression scale but not on three others, and one of the best-designed add-on trials so far (Section 16.10) was a small pilot. No probiotic is approved to treat depression or anxiety. **What would change the grade:** Large, preregistered, placebo-controlled trials of a specific strain in people with a diagnosed condition, with one primary outcome, that are then repeated by independent teams.

16.9 Try It Yourself: The Probiotic Trial Reader

Why do small trials sometimes produce exciting results for treatments that do very little? You can see it happen. In the simulation below, a made-up probiotic has a small true effect, about 0.2 standard deviations, similar in size to the small pooled effects some reviews report. Every time you press a button, the sim runs pretend trials and plots the result each trial would report. You choose how many people are in each group, how many outcomes each trial measures (with the "best" one reported, like an ad would), and whether the trial has a placebo group.

Diagram: Probiotic Trial Reader



Interactive simulation: <https://aaryavvatts-lab.github.io/gut-brain-textbook/sims/ch16-trial-reader/main.html>

Open the Probiotic Trial Reader fullscreen



MicroSim specification: Probiotic Trial Reader



Type: microsim **sim-id:** ch16-trial-reader

Library: p5.js

Status: Implemented

Bloom Level: Evaluate

Bloom Verb: judge

Learning Objective: The learner will judge how trial size, number of outcomes measured, and the presence of a placebo group change how much confidence a reported probiotic result deserves.

Canvas: 440 px drawing area plus 120 px controls (iframe 562 px); responsive to about 380 px wide.

Controls: Run 1 trial, Run 20 (trials), Clear; Placebo group checkbox (default on); People per group slider (10 to 300, default 30); Outcomes measured slider (1 to 10, default 1).

Rules: True effect $d = 0.2$ (illustrative). For each trial and each outcome, the measured effect = true effect + random noise with standard error $\sqrt{2/n}$. The trial reports its best (largest) outcome. Without a placebo group, a placebo response of 0.4 is added (everyone improves) and noise uses $\sqrt{1/n}$. A result is flagged "impressive" if it is more than about 1.96 standard errors above zero. Results are drawn as a dot plot on an effect-size axis with lines at 0 and at the true effect.

Feedback: A panel shows trials run, the share flagged impressive, the average reported effect, and how that compares with the true effect.

Provenance: Section 16.8 (primary outcome, effect size, publication bias). All numbers are illustrative, not from a real trial.

Start with the defaults (30 people per group, 1 outcome, placebo group on) and press **Run 20** a few times. The dots scatter widely around the true effect line, and some land far to the right. Those are the trials that would make headlines, even though the true effect never changed. Now press **Clear** (do this every time you change a setting, so old dots don't mix in), slide **People per group** to 300, and run again. The dots crowd close to the true effect, and the average reported effect lands near 0.2.

Next, set people per group back to 30 and raise **Outcomes measured** to 10. Each trial now reports its best of ten outcomes, and the average reported effect jumps well above the truth, with many more "impressive" results. Finally, uncheck **Placebo group**. With no comparison group, the placebo response gets counted as if it were the probiotic's effect. Ask yourself which combination of settings looks most like a typical supplement ad, and which looks like a trial you'd trust.

What this model leaves out

- The true effect is fixed at a made-up 0.2. In reality, nobody knows the true effect, and it probably differs by strain, condition, and person.
- Real outcomes in one trial are related to each other (people who feel better on one scale often feel better on another), so the "best of many outcomes" boost is usually smaller than in the sim.
- Trial length isn't modeled. Real effects might grow, fade, or disappear over time (one 2025 review found no benefit beyond 12 weeks).
- The sim leaves out dropouts, people guessing their group, funding, and publication bias, all of which can shift real results.
- The "impressive" flag is a simplified version of statistical significance, which Chapter 20 explains properly.

16.10 How to Read a Gut-Brain Claim: A Probiotic Add-On Pilot Trial

Let's apply the six questions to one of the best-designed recent probiotic trials in people with depression. In 2023, [Nikolova and colleagues](#) at King's College London published a trial in *JAMA Psychiatry*. They enrolled adults aged 18 to 55 with major depressive disorder who were already taking an antidepressant but hadn't fully improved. For 8 weeks, half took a multistrain probiotic (8 billion CFU a day, a 14-strain commercial product called Bio-Kult Advanced) and half took a placebo, added to their usual medicine. Neither the participants nor the researchers knew who got which (double-blind). Of 49 people analyzed, 24 got the probiotic and 25 got placebo. Only 8% dropped out, people took 97% of their capsules, and there were no serious adverse reactions. Depression and anxiety scores improved more in the probiotic group on several scales, though not on one anxiety questionnaire (GAD-7).

How to read a gut-brain claim: the 2023 probiotic add-on pilot trial

Question	This study
Mouse or human?	Human: adults with diagnosed major depression already on antidepressants.
Correlation or cause?	Designed to test cause (randomized, placebo-controlled, double-blind), but it was a pilot trial whose main goals were feasibility: whether people would stick with it and tolerate it, plus rough effect estimates to plan a larger trial.
How many?	49 people analyzed (24 probiotic, 25 placebo). Too few to prove the probiotic works.
How long?	8 weeks. Nothing about long-term effects.
Who paid for it?	A UK Medical Research Council industrial PhD studentship with ADM Protexin, the probiotic's maker, as industry partner, plus a charitable donor. The paper says the funders had no role in design, analysis, or publication.
Is something being sold?	Yes. The probiotic is a commercial product, its maker co-funded the work, and the first author was also affiliated with the company.

The conclusion: this is a careful, honest small trial, and its authors described the results as "promising" and called for a definitive trial, not as proof. It supports running a bigger study. It does **not** show that this product, or probiotics in general, treats depression, and it says nothing about teens or about people not already on medicine. The company link doesn't make the results wrong; it's a fact a careful reader notes.

If you're going through this

If you live with IBS, IBD, anxiety, or depression, it's exhausting to be told by ads and relatives that a capsule will fix you, and it can feel like your fault when it doesn't. It isn't. Your treatment plan was built from much stronger evidence than a supplement label. If you're curious about a probiotic, bring the exact product to your doctor or dietitian and ask what's known about that strain for your condition, and never stop or swap a prescribed medicine for a supplement on your own.

At the Bedside: A Parent's Question in the NICU



Meet the patient (fictional)

Amara was born 10 weeks early and is 2 weeks old, growing slowly in the neonatal intensive care unit (NICU). Her mother, Grace, has been reading online parent groups, where several posts say probiotics "protect preemies' guts." Grace brings a bottle of a probiotic supplement from a store and asks the nurse whether she can mix some into Amara's milk.

What the doctor checks: The neonatologist (a doctor for newborns) listens to Grace's concerns and reviews Amara's history: how early she was born, her weight, how her feeding is going, any signs of infection, and whether she has a central line (a thin tube into a large vein). The doctor also looks at the bottle Grace brought: it's a dietary supplement, sold without FDA review, with a multi-strain "blend" and no strain codes.

Connecting the signals: Preterm babies are at risk of necrotizing enterocolitis, a serious inflammation of the gut, and researchers have studied whether certain probiotics lower that risk. But a premature baby's gut lining and immune system are still immature, so live microbes can occasionally get into the bloodstream and cause an infection. A product that hasn't been tested to drug standards might also contain organisms that aren't on the label.

Diagnosis: Prematurity with a family question about probiotic use. (There's no new disease; the "diagnosis" here is a benefit-risk decision.)

Why it happens: This chapter's probiotic safety section explains the core issue: probiotics are low-risk for most healthy people, but risk rises for people whose barriers and immune defenses aren't fully working. In October 2023, the FDA reported that probiotic products given to hospitalized preterm infants contributed to invasive disease, including one death, and said no probiotic is approved as a drug for infants.

The mind-body side: NICU parents often feel powerless, and giving a probiotic can feel like one thing they can do. The care team treats Grace's question as loving and reasonable, not foolish. They explain the risks, invite her to be part of decisions, and point her toward things that are within her control and supported by the team, such as skin-to-skin holding when Amara is stable and help with providing breast milk if she chooses. A NICU social worker or parent support group can help with the stress.

Treatment today: The team explains that hospital NICUs make their own policies about probiotics, weighing studies like those behind the 2020 AGA guideline against the 2023 FDA warning, and that no parent should add a store-bought supplement to a premature baby's feeds. The American Academy of Pediatrics, in a [2021 clinical report](#), said current evidence does not support giving probiotics routinely to all preterm infants, especially babies who weighed less than 1,000 grams at birth. Amara's care continues with standard NICU support: careful feeding, monitoring for infection and gut problems, and growth tracking.

What's new in research: A [2023 Cochrane review](#) by Sharif and colleagues pooled 60 randomized trials with 11,156 very preterm or very low birth weight babies. Probiotics may lower the risk of necrotizing enterocolitis (low-certainty evidence) and probably lower the risk of death slightly (moderate-certainty evidence). But most trials were small, the products differed, and for the most premature and smallest babies the review found little or no clear effect. Researchers continue to study specific, well-characterized strains made to strict

manufacturing standards. In its 2023 statement, the FDA said that for a probiotic to be lawfully marketed as a drug or biological product for infants, it would need FDA approval based on evidence of safety and effectiveness. **Evidence grade: Moderate for a benefit in very preterm babies, but not settled for routine use.** Many human trials point toward fewer cases of necrotizing enterocolitis, but certainty is low to moderate, results vary by strain and setting, serious infections have been documented, and no probiotic is approved as a drug for infants.

 Your turn: reason through a variation

Grace's nephew, Kofi, is 15 and getting chemotherapy for leukemia. A relative suggests a probiotic to help with his diarrhea. What should the family keep in mind?

Answer: Chemotherapy can weaken the immune system, which puts Kofi in the higher-risk group that NCCIH describes, where live microbes are more likely to cause infections. NCCIH also reports that a 2018 review of 12 studies found the evidence for probiotics preventing or treating chemotherapy-related diarrhea was inconclusive. So the possible benefit is uncertain and the risk is higher than for a healthy teen. The family should show the exact product to Kofi's oncology team before giving it, and follow their advice.

This is a fictional teaching case. It is not medical advice. If you or someone you know has symptoms like these, talk to a doctor.

Common Misconceptions

Myth: Probiotics are regulated like medicines, so the FDA has checked that they work.

Reality: Most probiotics in the US are sold as dietary supplements. Under a 1994 law, the FDA does not approve supplements before they're sold, and companies are responsible for their own safety and labels. Only a probiotic marketed to treat a disease must go through drug trials and FDA approval.

Myth: More CFUs means a better probiotic.

Reality: What matters is the specific strain, at the dose shown to work in a study, for the condition you care about. A huge CFU number of an untested strain is just untested at a higher amount, and counts printed "at time of manufacture" may overstate how many microbes are still alive.

Myth: If a probiotic worked in mice, it works in people.

Reality: The strain *L. rhamnosus* JB-1 reduced anxiety-like behavior in mice in 2011, but in a 2017 trial of 29 healthy men, it did nothing measurable for stress, mood, or thinking. Mouse results are a starting point, not proof.

Myth: "Psychobiotics" are an approved treatment for anxiety or depression.

Reality: "Psychobiotic" is a research term coined in 2013. It's not an approved product category, and no probiotic is FDA-approved to treat any mental health condition.

Your Gut Check

Test yourself. Try each one before you open the answer.

- ? 1. Claim Check: "Clinically proven psychobiotic! 50 billion CFU of our exclusive Lactobacillus blend for calm, focus, and mood." ✓**

Grade: Hype. "Psychobiotic" is a research term, not an approved category, and "clinically proven" means nothing unless the specific strains were tested in well-designed human trials. A "Lactobacillus blend" gives no strain codes, so you can't match it to any study, and strain specificity means results don't transfer between strains. A large CFU count doesn't make up for missing evidence. A careful version would say: "Some specific probiotic strains are being studied for mood, with mixed and preliminary results in human trials. This product's strains have not been tested for that."

- ? 2. Predict: Sam reads that a new probiotic strain reduced anxiety-like behavior in mice whose vagus nerves were intact, but not in mice whose vagus nerves were cut. He wonders what a trial of the same strain in healthy teens would find. What would you predict, and why? ✓**

The most likely result is a small effect or no measurable effect, though it can't be known without testing. The mouse experiment suggests the vagus nerve carries the signal in mice, but mouse findings often don't carry over to people, as with JB-1, which helped mice and then did nothing in healthy men. Healthy teens also have less anxiety to reduce than a specially anxious mouse strain. A good trial would be randomized and placebo-controlled with a primary outcome chosen in advance.

- ? 3. Explain: A meta-analysis of 12 probiotic trials found a significant improvement on the Beck Depression Inventory but not on three other depression scales. Explain why this result should be interpreted cautiously. ✓**

When you measure several outcomes, the chance that at least one looks significant by luck goes up, even if the treatment does nothing. Only one of four scales showed a benefit, and the two clinician-rated scales did not. Different trials also used different strains and people, so the result could reflect certain trials rather than probiotics in general. The authors themselves called for cautious interpretation.

- ? 4. Apply: Riya's grandmother wants to buy her a probiotic labeled "supports digestive health" to help her Crohn's disease. Using this chapter, what should Riya know before taking it? ✓**

The label is a structure-function claim that a supplement can make without FDA review; it doesn't mean the product treats Crohn's, and it isn't allowed to claim that. The AGA 2020 guideline recommends probiotics for Crohn's only within clinical trials. Riya also takes a biologic, which affects her immune system, so she should show the product to Dr. Alvarez before taking it. Her grandmother's care is real, and Riya can thank her while explaining that her doctor needs to check first.

5. Read the data. In a 2017 randomized, placebo-controlled crossover trial, Kelly and colleagues gave the probiotic strain *L. rhamnosus* JB-1 or a placebo to healthy men for 4 weeks each (8 weeks in total). Compare it with the earlier mouse study of the same strain (Bravo 2011):

Feature	Bravo et al., 2011	Kelly et al., 2017
Who	Mice (an anxious lab strain, per Kelly)	29 healthy men
Design	Probiotic vs control feeding; plus vagotomy experiment	Randomized, placebo-controlled crossover, 4 weeks per period (8 weeks total)
Stress hormone after stress	Lower with probiotic	No difference from placebo
Anxiety- or mood-related measures	Less anxiety- and depression-like behavior	No difference in mood, anxiety, stress, or sleep quality
Thinking and brain activity	GABA receptor changes in brain regions	No improvement in memory, attention, or EEG

? 5. What does this data show, and what can't it show? ✓

It shows that a strain with clear effects in mice had no measurable effect in a small, well-controlled trial of healthy men. That's a replication failure across species. It can't show that JB-1 is useless for everyone: the human study was small (29 people), included only healthy men, and didn't test people with anxiety or depression, women, or teens. It also can't tell us whether a different dose or longer treatment would matter. A helpful follow-up would be a larger placebo-controlled trial of JB-1 in people with a diagnosed stress-related or anxiety disorder, with a primary outcome named in advance.

Exercises

Remember

1. Give the ISAPP definition of a probiotic in your own words, and name the three conditions it includes.

✎ Answer ✓

A probiotic is a live microbe that gives a health benefit when taken in a large enough amount. The three conditions: the microbes are alive, they are given in an adequate amount, and a health benefit has been shown.

1. What does a colony-forming unit count, and why are probiotic doses given in CFU?



Answer



It counts the microbes in a sample that are alive and able to multiply, because each one forms a visible colony on a lab dish. Doses use CFU because the definition of a probiotic requires live microbes, and dead ones don't form colonies.

Understand

1. Explain the difference between a prebiotic and a postbiotic, using the garden comparison.



Answer



A prebiotic is like fertilizer: a substance that certain microbes already in the gut use selectively, producing a health benefit. A postbiotic is like mulch made from old plants: a preparation of inactivated (non-living) microbes or their parts that gives a health benefit.

1. Explain why a probiotic trial should name its primary outcome before the results are known.



Answer



If researchers measure many outcomes, some will look significant by chance even if the treatment does nothing. Naming one primary outcome in advance prevents them from reporting whichever result happened to look best, so the main test of the treatment is fair.

Apply

1. Find a probiotic product label (online or in a store, without buying it). Using the table in Section 16.4, list what the label tells you and what it leaves out, and decide whether you could match it to a published study.
2. Using the Probiotic Trial Reader, run 20 trials at 20, 60, and 300 people per group (1 outcome, placebo on). Record the share of "impressive" results and the average reported effect for each. Describe the pattern and explain how it relates to small supplement studies in ads.

Analyze

1. Compare the Bravo 2011 mouse study and the Kelly 2017 human trial using all six questions from the claim box. Which question best explains why the results differ?

2. The Liu 2019, Asad 2025, and Pan 2025 meta-analyses reached different effect sizes for probiotics and depression. Analyze at least three reasons, from this chapter, that reviews of "the same" question can disagree.

Evaluate

1. A friend argues: "The FDA warned about probiotics for preterm babies, but the AGA suggested some strains for them, so the experts are just confused." Write a paragraph judging this argument. What does the disagreement actually reflect, and how should families and hospitals handle it?
2. Evaluate the Nikolova 2023 pilot trial as evidence. Would you call its result Strong, Moderate, Preliminary, or Hype for the claim "probiotics help people with depression who are already on antidepressants"? Defend your grade using the claim box.

Create

1. Design a trial that could fairly test whether a specific probiotic strain reduces test anxiety in high school students. Name your strain choice, groups, blinding, length, primary outcome, sample size reasoning, and how you would prevent publication bias.
2. Rewrite Dev's "Calm in a Capsule" post (Section 16.1) as an honest product description that would earn a fair Hype Meter grade. Keep it under 80 words.

Key Takeaways

- A probiotic is a live microbe given in adequate amounts with a demonstrated health benefit; prebiotics feed certain gut microbes, synbiotics combine the two, and postbiotics are inactivated microbes or their parts. Every definition requires a proven benefit.
- Most probiotics belong to the Lactobacillus (now split into 25 genera) and Bifidobacterium groups, but effects are strain specific: results from one strain and one condition don't carry over to others.
- A CFU count measures live microbes. More CFU isn't automatically better; what matters is the tested strain, at the tested dose, for the tested condition, counted at the end of shelf life.
- In the US, most probiotics are dietary supplements, which don't need FDA approval before sale and can't claim to treat disease. "Psychobiotic" is a research term from 2013, not an approved category.
- Probiotics are low-risk for most healthy people but riskier for people who are very ill, immunocompromised, or born early; in 2023 the FDA warned that probiotics given to hospitalized preterm infants caused serious infections, including a death.
- The JB-1 strain calmed mice but did nothing in healthy men, a classic replication failure. Evidence that probiotics treat depression or anxiety in people is Preliminary.

- To read trials, look for systematic reviews, effect sizes, a primary outcome set in advance, and signs of publication bias, and be wary of small trials that measured many outcomes.

You can read the back of the bottle now!



You've learned to check the strain, the dose, the regulation, and the trials behind any probiotic claim. Next, in Chapter 17, we'll look at gut-brain treatments that did earn FDA approval, from stool-based medicines to nerve stimulators, and how they got there.

Quiz: Probiotics, Prebiotics, and "Psychobiotics"

Test your understanding of Chapter 16. Choose the best answer, then click **Show Answer** to check.

Question 1

According to the ISAPP scientific definition, which of these is required for a product to be called a probiotic?

- A. It must contain at least 50 billion colony-forming units.
- B. It must contain live microorganisms, in adequate amounts, with a shown health benefit.
- C. It must be approved by the FDA as a drug.
- D. It must contain fiber that feeds gut bacteria.

 **Show Answer**



The correct answer is **B**. The ISAPP (2014) definition is "live microorganisms that, when given in adequate amounts, confer a health benefit on the host." Option D describes a prebiotic, which is food for microbes rather than live microbes. No specific CFU number or FDA approval is part of the definition.

Concept Tested: Probiotic **Bloom's Level:** Remember

Question 2

A product contains heat-killed bacterial cells and their parts, and a health benefit has been shown. Under the ISAPP definitions, what is it?

- A. A probiotic
- B. A prebiotic
- C. A synbiotic
- D. A postbiotic

 Show Answer



The correct answer is **D**. A postbiotic is "a preparation of inanimate microorganisms and/or their components that confers a health benefit on the host." It can't be a probiotic, because probiotics must be alive. A synbiotic combines live microbes with a substance microbes use.

Concept Tested: Postbiotic **Bloom's Level:** Remember

Question 3

Under the 1994 Dietary Supplement Health and Education Act (DSHEA), which statement is true about probiotics sold as dietary supplements in the US?

- A. The FDA does not approve them for safety or effectiveness before they are sold.
- B. The FDA tests every bottle before it reaches stores.
- C. They must show benefit in two clinical trials before sale.
- D. They are allowed to claim they cure diseases if the company believes it.

 Show Answer



The correct answer is **A**. Under DSHEA, the FDA does not have the authority to approve dietary supplements before they are marketed; companies are responsible for safety and labeling, and the FDA can act after a product is on the market. Option D is wrong: supplements may make structure-function claims but cannot claim to treat, cure, or prevent a disease.

Concept Tested: Dietary Supplement Regulation **Bloom's Level:** Remember

Question 4

Why can't the results of a trial on one *Lactobacillus* strain be assumed to apply to a different *Lactobacillus* strain?

- A. Because only one *Lactobacillus* strain can survive in the human gut
- B. Because the FDA approves each strain separately before sale
- C. Because probiotic effects are strain specific and also depend on the condition being treated
- D. Because *Lactobacillus* strains all have the same effect, so testing a second one is unnecessary

? Show Answer



The correct answer is **C**. A 2018 review of 228 trials found that probiotic efficacy depends on both the strain and the disease, and NCCIH says one strain's benefit doesn't prove another works. Option B is wrong because most probiotics are supplements that the FDA doesn't approve before sale.

Concept Tested: Strain Specificity **Bloom's Level:** Understand

Question 5

A probiotic label lists "20 billion CFU at time of manufacture." Why might this overstate what you actually get?

- A. CFU counts dead bacteria as well as live ones.
- B. Many strains lose live cells during storage, so fewer may be alive by the time you take it.
- C. The FDA requires labels to round CFU numbers up.
- D. CFU measures the weight of the capsule, not the number of microbes.

? Show Answer



The correct answer is **B**. ISAPP's label guide explains that most strains lose live cells over their shelf life, so a count at manufacture can be much higher than at the end of shelf life. Option A is backwards: CFU counts only microbes alive enough to form colonies.

Concept Tested: Colony-Forming Unit **Bloom's Level:** Understand

Question 6

In a 2011 study, the strain *L. rhamnosus* JB-1 reduced anxiety-like behavior in mice, but in a 2017 trial of 29 healthy men it did nothing measurable. What does this pair of studies best illustrate?

- A. A replication failure across species, showing a mouse result may not carry over to people
- B. Proof that the mouse study was faked
- C. Proof that probiotics can never affect the brain
- D. Publication bias, because the human study was never published

 Show Answer



The correct answer is **A**. When a later study tests the same idea and doesn't find the original result, that's a replication failure. It doesn't prove fraud or that probiotics can never matter; the human study was small and used healthy men, not people with anxiety. Option D is wrong because the human study was published.

Concept Tested: Replication Failure **Bloom's Level:** Understand

Question 7

A meta-analysis of probiotic trials found improvement on one depression questionnaire but not on three others. A news story says, "Probiotics proven to reduce depression!" What is the best response?

- A. Accept it, because any significant result counts as proof.
- B. Reject probiotics completely, because three scales showed no difference.
- C. Ignore the questionnaires and look only at the number of participants.
- D. Be cautious: with several outcomes, one positive result could be chance, so the evidence is mixed.

 Show Answer



The correct answer is **D**. When many outcomes are measured, the chance that at least one looks significant by luck rises, which is why trials name a primary outcome in advance. The Rahmannia 2024 review's authors urged cautious interpretation. Option B overcorrects: mixed results mean uncertainty, not proof of no effect.

Concept Tested: Primary Outcome **Bloom's Level:** Apply

Question 8

Sixteen-year-old Malia is getting chemotherapy, and a relative wants her to start a store-bought probiotic. Based on the chapter, what is the most accurate advice?

- A. It is safe, because probiotics are natural.
- B. Her oncology team should review the exact product first, because people with weakened immune systems face higher risk from live microbes.
- C. She should take a double dose to make sure enough bacteria survive.
- D. Probiotics are only risky for adults over 65.

 Show Answer



The correct answer is **B**. NCCIH says the risk of harm from probiotics is greater in people with severe illness or weakened immune systems, which can include people on chemotherapy. Option A is the "natural means safe" myth, and the book never recommends doses.

Concept Tested: Probiotic Safety **Bloom's Level:** Apply

Question 9

In a 2008 study, published journal articles made about 94% of antidepressant trials look positive, but FDA records showed about 51% were positive. What explains the gap?

- A. Publication bias: negative trials were often unpublished or reported as if positive.
- B. The FDA made errors in judging the trials.
- C. The drugs became more effective after the trials ended.
- D. Journals only publish trials with more than 1,000 people.

 Show Answer



The correct answer is **A**. Turner and colleagues found that 22 negative or questionable trials were never published and 11 were published in a way that conveyed a positive result, which made the drugs' effect look about 32% bigger overall. That pattern is publication bias. Nothing in the study suggests FDA errors.

Concept Tested: Publication Bias **Bloom's Level:** Analyze

Question 10

Three meta-analyses of probiotics (and related treatments) for depression report effect sizes of about 0.24, 0.26, and 0.96. Which explanation from the chapter best accounts for the difference?

- A. One of the reviews must have made a math mistake.
- B. Effect sizes always triple when more trials are added.
- C. Larger effect sizes always come from the best-designed reviews.
- D. The reviews included different trials, people, strains, and lengths of treatment, and the trials disagreed a lot.



Show Answer



The correct answer is **D**. The reviews pooled different sets of trials: for example, Asad 2025 included only people with a diagnosis and reported high heterogeneity, while Liu 2019 also included people without a diagnosis (and found a bigger effect in clinical samples). Strain specificity means "probiotics" can mean different products in each review. Option C is wrong because a bigger effect size does not mean better design.

Concept Tested: Systematic Review **Bloom's Level:** Analyze
