


Little bugs for big depression

Clinical and metabolic response to probiotic administration in patients with major depressive disorder: A randomized, double-blind, placebo-controlled trial 



Introduction

Almost [20% of the population](#) is affected by major depressive disorder (MDD) at some point during their life. Not only is this depressing news, but a number of studies have shown a link between MDD and [biomarkers of inflammation](#), [oxidative stress](#), [insulin resistance](#), and other [medical comorbidities](#).

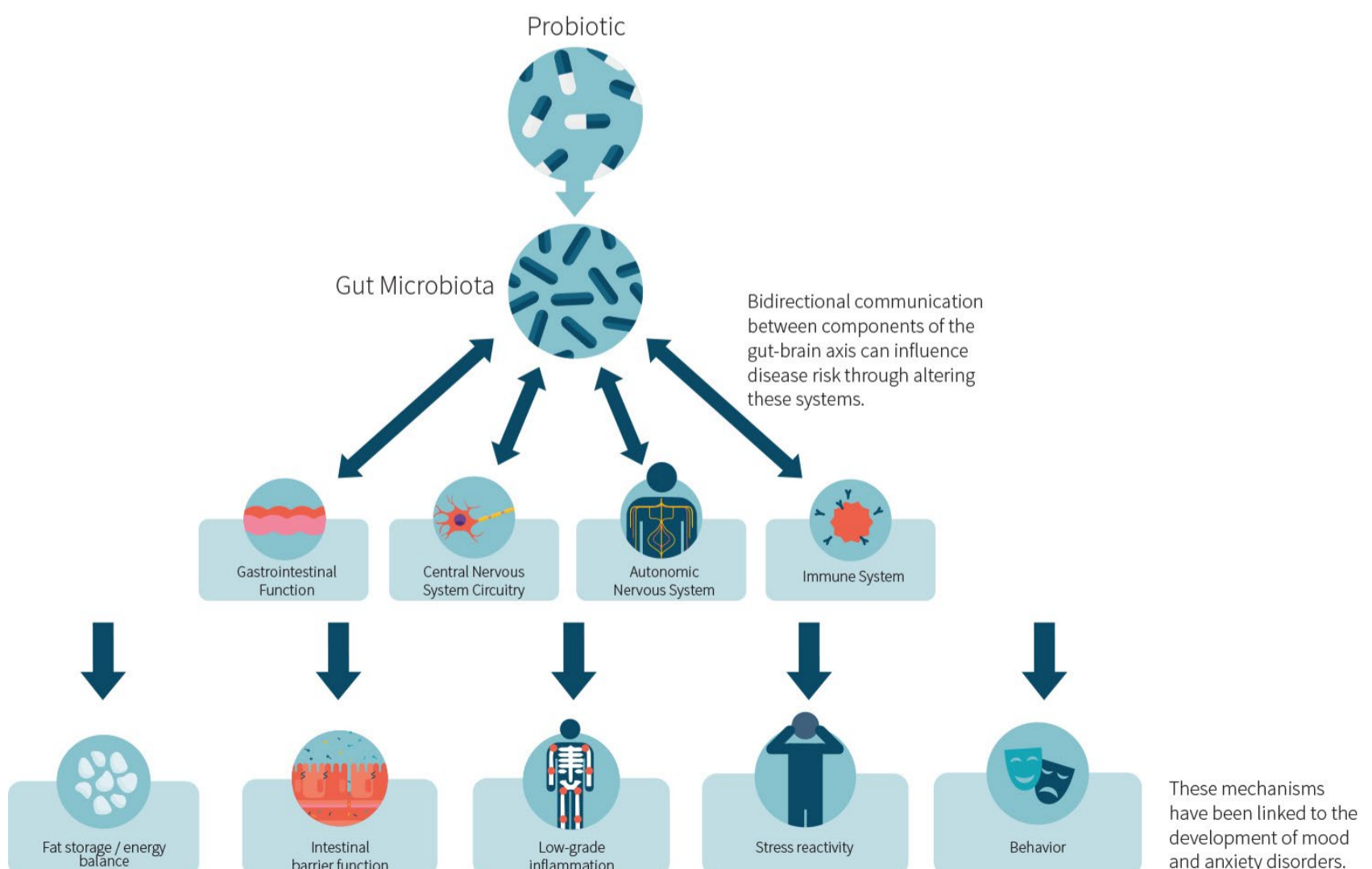
A number of emerging treatment options exist for depression, including the use of probiotics. Although probiotics are more often thought of as helpful for [IBS](#) or even [lowering cholesterol](#), it is possible they can also provide benefits for people with mood disorders like [depression](#). You may remember a previous article from ERD #8 discussing a [study](#) that showed the effect of probiotics on reducing the likelihood of future sad mood in people who were currently healthy. [Multiple other studies](#) have shown improvements in [mood](#) states,

as well as markers of [inflammation and oxidative stress](#), after probiotic supplementation in a [variety](#) of participant populations.

The reason that probiotics might have an effect on a person's mood relates to the [gut-brain axis](#), as shown in Figure 1. Communication between the [gut and brain](#) exists through a variety of neural, endocrine, and immune pathways that interact with intestinal microbiota. Supplementation with probiotics is [not always](#) effective, however, for improving mental health.

Despite a number of promising studies looking at the effects of probiotics on mood states, the effect of supplementation on depressive symptoms and metabolic biomarkers in patients specifically having MDD had not been assessed. Therefore, the aim of this new study was to determine the effects of a multi-strain probiotic supplement on symptoms of depression, markers of

Figure 1: Probiotics and the gut-brain axis



Adapted from : Foster and Neufeld. Trends Neurosci. 2013 May.

glucose control, lipid concentrations, biomarkers of inflammation, and oxidative stress in people with MDD.

Almost 20% of people may be affected by major depressive disorder (MDD) at some point in their lives. Probiotics represent a potential intervention that can improve symptoms of depression, but it's yet to be studied in people with MDD.

Who and what was studied?

This double-blind, placebo controlled trial recruited 40 people (34 women and 6 men) with MDD between the ages of 20-55 years. Participants were considered to have MDD based on [DSM-IV criteria](#) and a score of 15 or higher on the Hamilton Depression Rating Scale. Potential participants were excluded if they had been taking any dietary or probiotic supplements during the previous two months.

Participants were randomly assigned to consume either a probiotic supplement containing *Lactobacillus acidophilus* (2 x 10⁹ CFU/g), *Lactobacillus casei* (2 x 10⁹ CFU/g), and *Bifidobacterium bifidum* (2 x 10⁹ CFU/g), or placebo, for eight weeks. These are all species that

occur naturally on the human body and are thought to have probiotic effects. Participants were told not to change their physical activity routine or typical dietary intake throughout the study, not to consume any additional supplements, and not to take any medications that could affect the results.

The primary outcome of this study was the Beck Depression Inventory (BDI) score, a 21-item multiple-choice questionnaire that measures [depression](#). Additionally, blood samples were analyzed for fasting plasma glucose, lipid concentrations, serum high-sensitivity C-reactive protein (hs-CRP), and biomarkers of oxidative stress, including total antioxidant capacity and glutathione (GSH) levels. Markers of insulin metabolism including the homeostasis model of assessment of insulin resistance (HOMA-IR), homeostasis model of assessment of b-cell function (HOMA-B), and quantitative insulin sensitivity check index (QUICKI) were also measured.

Participants were provided a multi-strain probiotic supplement or placebo for eight weeks, and were tested for changes in depression using the Beck Depression Inventory. Blood markers for glucose tolerance, oxidative stress, and inflammation were also measured.

The DSM

DSM-IV refers to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition. This is a manual published by the [American Psychiatric Association](#) (APA) that includes all currently recognized mental health disorders, and is used by healthcare professionals to describe mental disorders. It has recently been [updated](#) to DSM-5, but this study was likely started before the latest version came out. DSM-5 contains several new depressive disorders, including disruptive mood dysregulation disorder and premenstrual dysphoric disorder. The [Hamilton Depression Rating Scale](#) is a widely used questionnaire to quantify levels of depression and evaluate recovery.

The DSM is widely used in the US, but globally the International Classification of Diseases (ICD) is more frequently used. The ICD is not limited to mental health, as it deals with human health as a whole. Controversy surrounding the DSM has been prevalent in recent years, especially with the DSM V, due to a variety of issues including the evidentiary basis of its classifications.

What were the findings?

The main findings are shown in Figure 2. At the end of the eight-week intervention, participants that received the probiotic supplement had a significantly decreased BDI total score (-5.7 vs. -1.5). Additionally, significant decreases were observed for changes in serum insulin levels, HOMA-IR (a measure of insulin resistance), and hs-CRP concentrations (a marker of systemic inflammation), while a significant increase in levels of the antioxidant glutathione (GSH) was found in the probiotic group.

Non-significant trends towards a decrease in HOMA-B and increase in QUICKI score (both relating to changes in insulin sensitivity and glucose control) were also observed after probiotic supplementation. No significant changes were found for fasting glucose, lipid profiles, or total antioxidant capacity. Additionally,

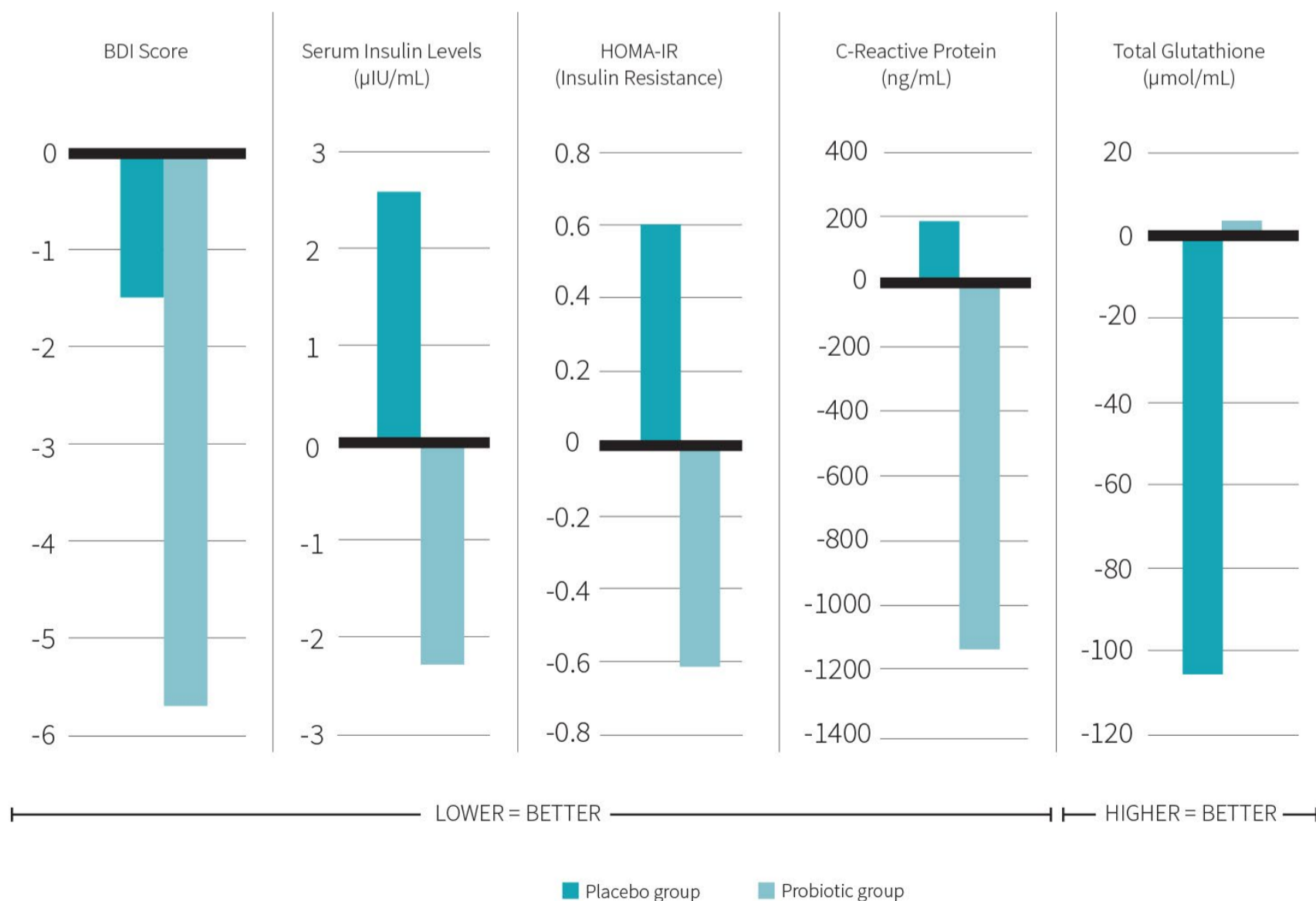
there were no differences between groups for dietary intake, as measured by a three-day food diary.

Probiotic supplementation for eight weeks by people with major depressive disorder had beneficial effects on depression, insulin, inflammation, and levels of glutathione, but had no effect on fasting glucose or lipid profiles, or total antioxidant capacity.

What does the study really tell us?

“The main findings were that probiotic supplementation improved the Beck Depression Inventory score and insulin function, and decreased oxidative stress in patients with Major Depressive Disorder.”

Figure 2: Changes in BDI and metabolic markers



This study adds to the growing literature on probiotic supplementation by being the first to show a benefit on depression for people with MDD. Due to the way the authors reported their results, it is difficult to tell exactly how great of a change occurred, but it appears to be clinically significant.

However, it is unknown if similar effects would occur in people already taking antidepressant medication. Also, this was a multi-species probiotic containing *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum*. It remains to be seen if the benefits were due to one particular species or if there was a synergistic effect among the three species. It is also unknown if other strains or species of probiotic can lead to similar improvements in depression in people with MDD.

The big picture

This is the first study to look at the effects of probiotic supplementation on symptoms of major depression, as well as biomarkers for inflammation and oxidative stress in people with MDD.

Previous [research](#) on participants with chronic fatigue syndrome reported a decrease in anxiety symptoms when taking a probiotic (*Lactobacillus casei* Shirota) but no significant effect on BDI score. A recent [study](#) in healthy participants found that a multi-strain probiotic led to decreased cognitive reactivity to a sad mood,

which could imply that the likelihood of future depression is reduced.

Other [studies](#) in healthy people reported improved mood in those whose mood was initially poor after they took a milk-based probiotic drink for three weeks, and in [healthy participants](#) taking a probiotic formulation

of *Lactobacillus helveticus* and *Bifidobacterium longum* for 30 days. In contrast, [14 weeks](#) of probiotic supplementation (*Lactobacillus rhamnosus* and *Bifidobacterium animalis*) in people with schizophrenia resulted in no changes in psychiatric symptoms, although they did report improvements in gastrointestinal function. Be careful not to lump results together - while both are related to mental health, MDD and schizophrenia are very different disorders.

Improvements in glucose tolerance observed in this study are in line with previous research. A recent [review](#) on the role of probiotics in glucose control in both humans and animals

reported that 19 out of 21 studies showed significant improvements in at least one parameter related to glucose homeostasis. One potential reason for the improved markers of glucose and insulin metabolism is the increase in [natural killer T-cells](#) in the liver and a reduction in inflammatory signaling. Additionally, [conjugated linoleic acid](#) is produced by some species of *Lactobacillus*, which might decrease inflammation and

“Be careful not to lump results together - while both are related to mental health, MDD and schizophrenia are very different disorders.”

block suppression of the glucose transporter GLUT4, allowing more glucose to be transported into cells and out of the bloodstream.

The decrease in inflammation that was observed with probiotic supplementation was also in line with previous research. Multiple other studies using a probiotic yogurt have also found decreased levels of hs-CRP in people who were [overweight](#), [pregnant](#), and people that had [rheumatoid arthritis](#). In contrast, one [study](#) in women with polycystic ovary syndrome found no effect on CRP levels. Potential reasons for a decrease in inflammation with probiotic supplementation include an increase in colonic [short-chain fatty acid production](#) as well as a decreased expression [inflammatory cytokines](#).

The reasons behind the changes in emotional function with probiotic supplementation are not fully understood. As seen in Figure 3, it appears that probiotic consumption may lead to an increase in plasma tryptophan levels, as well as decreased concentrations of serotonin and dopamine metabolites and GABA expression in the brain. However, many questions still remain. Additionally, some research suggests that probiotics may improve carbohydrate malabsorption, which is associated with early signs of depression.

The results of this study are in line with previous research showing beneficial effects of probiotics on mood, inflammation, and markers of blood glucose control.

Frequently asked questions

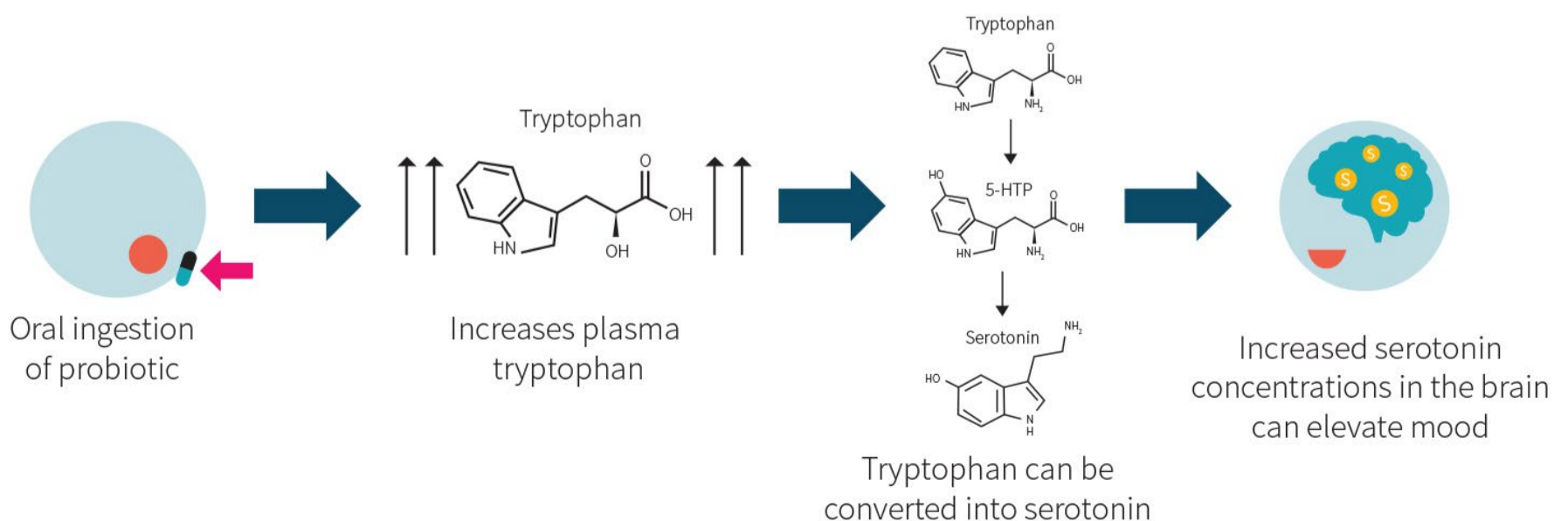
Would this supplementation have the same effect for men and women?

This is an important question when looking at any dietary, supplement, or exercise intervention. The study recruited both men and women, though it was predominantly (85%) made up of women and results were not included separately by gender. Other trials using probiotic supplements have found both [similar](#) and [differing](#) effects among men and women. It is difficult to say how this specific product (or most other ones) would compare between genders.

There was no effect on total antioxidant capacity in this study, but there was an increase in glutathione, which is an antioxidant. What is the difference between them?

The methodology for quantifying antioxidants can differ and lead to [different results](#). This study used the Ferric Reducing Ability of Plasma (FRAP) assay as a measure of total antioxidant capacity, which measures

Figure 3: Mechanisms of probiotic mood improvement



antioxidant potential in samples through the reduction of ferric iron (Fe^{3+}) to ferrous iron (Fe^{2+}). Glutathione, a known [antioxidant](#), was measured using a different [method](#). Also, glutathione is only one of the antioxidants in circulation, and it can change without having a major impact on total antioxidant capacity.

Is the evidence strong enough to suggest that people with major depressive disorder would benefit from probiotic supplementation?

The effects may vary across populations and with different probiotic strains, but the use of probiotic supplementation in depression appears to be possibly useful and not likely to be harmful. However, one should always consult with their physician as drug-supplement interactions are always possible.

What should I know?

In people with major depressive disorder, taking a probiotic containing *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum* for eight weeks led to decreased symptoms of depression as well as beneficial effects on markers of inflammation and glucose homeostasis. ◆

You know what they say: happy bacteria, happy ... okay so nothing rhymes with bacteria. Discuss anything about probiotics and depression (except for rhymes) at the [ERD Facebook forum](#).