REVIEW ARTICLE

Probiotics and Disease: A Comprehensive Summary—Part 3, Cardiometabolic Disease and Fatigue Syndromes

Christy B. Williamson, MS, CNS; Cathleen M. Burns, MS, RD, LDN; Crystal M. Gossard, MS, CNS; Jessica M. Pizano, MS, CNS; Keren E. Dolan, MS; Heather J. Finley, MS, RD, LD, CEDRD; Margaret G. Gasta, MS, RDN, CCN; Emily C. Parker, MS, RD; Elizabeth A. Lipski, PhD, CNS, CCN, BCHN, IFMCP

Abstract

This article series provides a literature review of the disease-specific probiotic strains, associated with cardiometabolic diseases and fatigue syndromes, studied in published clinical trials in humans and animals. This is not an exhaustive review. The table design allows for quick access to supportive data and will be helpful as a guide for both researchers and clinicians. The goal of the probiotics and disease series is to provide clinically useful tools. The first article (part 1) focused on mental health and neurological conditions and the second article (part 2) explored cultured and fermented foods that are commonly available in the United States. This third article (part 3) explores the relationship between bacterial strains and 2 of the most prevalent diseases we have in modern society: cardiometabolic disease and fatigue syndromes. Future articles will review conditions related to respiratory, ear, nose, and throat infections and infectious diseases; autoimmunity and dermatological conditions; cancer; and gastrointestinal and genitourinary, followed by an article focused on probiotic supplements. This literature review is specific to disease condition, probiotic classification, and individual strain.

Christy B. Williamson, MS, CNS; Cathleen M. Burns, MS, RD; Crystal M. Gossard, MS, CNS; Jessica M. Pizano, MS, CNS; Keren E. Dolan, MS; Heather J. Finley, MS, RD, LD, CEDRD; Margaret G. Gasta, MS, RDN, CCN; and Emily C. Parker, MS, RD, are doctoral students in the doctor of clinical nutrition program; Elizabeth A. Lipski, PhD, CNS, CCN, BCHN, IFMCP, is a professor. All are located at Maryland University of Integrative Health in Laurel, Maryland.

Corresponding author: Christy B. Williamson, MS, CNS
E-mail address: cwilliamson@muih.edu

The purpose of this summary is to provide nutritionists and other medical practitioners with a reference guide for recommending health-promoting commercially produced cultured and fermented food products to patients. Research was conducted via grocery stores trips, company Web site reviews, personal communication with food company personnel, along with PubMed and EBSCO Research Premier searches. The lists contained herein are not exhaustive; however, they represent items that are commonly accessible to US consumers.

There is considerable research on the gut microbiome and role of probiotics; however, this research has not been clearly connected with clinical practice. The authors undertook a review of current literature to explore which specific probiotics and probiotic strains have been utilized in clinical and laboratory studies. To make this clinically valuable, product names of probiotics and fermented foods have been included. Finished products vary between manufacturers; thus, the researchers included brand listing to provide transparency and to facilitate a functional probiotics guide for clinicians. Exclusions of products meeting our criteria do not imply that these products are not effective—we simply were not aware of them.

Methodology

This literature review originated from a group project that was part of the requirements for a course in the doctoral program in functional and clinical nutrition at Maryland University of Integrative Health (Laurel, MD, USA). The student researchers had approximately 2 months to review the literature and synthesize the paper. The authors agreed on format, templates, and execution. Each author researched and wrote sections reviewing probiotics in relation to various health conditions with literature searches conducted in PubMed, Biomed Central, EBSCO Research Premier, PloS One, Cochrane reviews, and topic-specific open-source journals.

The review of specific probiotic products in the professional marketplace and specific probiotics products was performed using Internet searches, primarily Shop Google, in addition to topic specific databases to search for specific probiotic species including the strains listed in the research. Novel strains were cross-referenced to determine whether the strain was available only for research purposes. If a probiotic combination was used in the research, formulas that closely matched the combination were included. Formulas that contain all or most of the specific probiotics and strains were also included. The food survey focused on bacterial strains in food and includes foods that are commercially produced and commonly available in the refrigerated sections of grocery stores in the United States. Information was gleaned from commercial Web sites and by visiting grocery stores (primarily in California).

Research Overview: Cardiometabolic Diseases

Currently, 29% of US adults suffer from cardiometabolic disease,[1] whereas in obese and overweight children, this number exceeds 60%.[2] This number is projected to reach 40.5% by 2030 for the adult population, generating awareness for the magnitude of the epidemic.[3] Genetic susceptibility as well as environmental factors are involved in the pathogenesis of cardiometabolic disease. Despite the growing evidence for this epigenetic disease model, there is an abundance of evidence for agonistic and antagonistic mechanisms of the microbiome on cardiometabolic health. Current animal studies and randomized controlled trials suggest that a multitude of bacterial strains exert an influence not only on the microbiome but have lasting benefits and consequences for the host. Currently, there is evidence to suggest a corollary between the microbiome and the following cardiometabolic diseases: obesity, insulin resistance, type 2 diabetes, nonalcoholic steatosis hepatitis, dyslipidemia, polycystic ovary syndrome, and gout.[4-14]

The microbiota influences nutrient use and weight changes by contributing to energy extraction. The microbiome operates in a mostly anaerobic environment,[15] resulting in fermentation of chyme and fecal material. Most ferments are derived from either saccharolytic or proteolytic fermentation.[16] Saccharolytic fermentation contributes to the daily energy requirement and results in the creation of short chain fatty acids including acetate, propionate, and butyrate. Diets rich in lipids are associated with a decrease of *Bifidobacterium*, known to produce butyrate, an anti-inflammatory, antineoplastic product promoting gut barrier integrity.[16] On the negative side, proteolytic fermentation produce amines and ammonia, which are toxic.[16]

The chronic low-grade inflammation associated with obesity can be attenuated by targeted probiotic strains.[17] Bienenstock et al[16] found that overweight subjects had a decrease in beneficial bacteria, an increase in pathogenic species, and overall less diversity of species than did controls. Manipulation of gut microbiota through the administration of probiotics can improve microbial diversity and epithelial barrier integrity, and it can optimize metabolic balance, promote weight loss, and decrease disease prevalence. Thus, developing innovative treatment approaches for cardiometabolic diseases are imperative not only for disease modulation, but also for public health.

Table 1. Cardiometabolic Disease

Cardiometabolic Disease	Strains	Overview	Professional and Commercial Products	Foods
Obesity, T2DM, and NAFLD				
Obesity, T2DM Mohamadshahi et al[18] (2014); Tonucci et al[19] (2015); Sáez-Lara et al[4] (2016)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12, *L salivarius* LS-33	Lowered HbA_{1c}, TC, and LDL-C.	ProSynbiotic (Standard Process) Strengtia (Apex Energetics) TruBiotics (Bayer)	*L acidophilus* LA-5 (Nancy's Organic cow's milk yogurt) *B lactis* BB-12 (Nancy's Organic cow's milk kefir)
Obesity Larsen et al[20] (2013); Sáez-Lara et al[4] (2016)		Increase in the ratios of *Bacteroides*, *Prevotellae*, and *Porphyromonas*. Subjects: 50 obese adolescents.	Aloe 10 000 & Probiotics, Berry Dophilus Extra Strength (NOW) GoLive Probiotic & Prebiotic Drink Mix Hyper-Implante (InterPlexus) Probiotic Supreme (DF Designs for Health) ProtoDophilus (Protocol For Life Balance) Ultimate Intestinal Shield (Phyto Therapy) UltraFlora Spectrum (Metagenics)	None
Obesity Kadooka et al[17,21] (2010, 2013); Sáez-Lara et al[4] (2016)	*L gasseri* SBT-2055, *L gasseri* LG-2055 (5^{1010} CFU)	Reduction in BMI, waist, abdominal VFA, and hip circumference and adiponectin levels; subjects: 87 subjects with high BMI and 210 adults with large VFA.	Isolated for research and not commercially available (prepared with lactic acid bacteria starter cultures); (*S thermophilus* and *L delbrueckii* sbsp *bulgaricus*) commonly used for conventional yogurt production and viable cells of LG2055.	None
Obesity Sharafedtinov et al[22] (2013)	*L plantarum* (TENSIA 1.5^{1011} CFU/g added to cheese milk before renneting)	Reduction in BMI and arterial BP value; subjects: 40 adults with obesity.	Isolated for research, from the GI of healthy Estonian children, and not commercially available.	None

Table 1. (continued)

Cardiometabolic Disease	Strains	Overview	Professional and Commercial Products	Foods
Obesity Zarrati et al[23,24,25] (2013a, 2013b, 2014); Sáez-Lara et al[4] (2016)	*L acidophilus* LA-5, *B lactis* BB-12, *L casei* DN-001 (108 CFU/g)	Changes in gene expression in PBMCs as well as BMI, fat percentage, and leptin levels; 75 subjects with high BMI.	ProSynbiotic (Standard Process) TruBiotics (Bayer) Strengtia (Apex Energetics)	*L acidophilus* LA-5 (Nancy's Organic cow's milk yogurt) *B lactis* BB-12 (Nancy's Organic cow's milk kefir); *L casei* DN001; None
Obesity Agerholm-Larsen et al[26] (2000); Sáez-Lara et al[4] (2016)	*E faecium*, 2 strains of *S thermophilus*	Reduction in body weight, systolic BP, LDL-C, and increase on fibrinogen levels in 70 overweight and obese subjects.	***E. faecium*:** Enterogenic Concentrate (Integrative Therapeutics) Nature's Secret Ultimate Probiotic (4 billion) Health-Bac 100 grams (North American Herb & Spice) ***S thermophilus*:** BIFIDO DIGEST 60C (F) (Protocol for Life)	*E faecium* (None) *S thermophilus* (lassi, kefir, all yogurts)
Obesity, NAFLD, T2DM Rajkumar et al[27] (2013); Sáez-Lara et al[4] (2016)	*Bifidobacteria*, *Lactobacilli*, *S thermophilus*	Improvement in lipid profile, insulin sensitivity, and decrease in CRP; 60 overweight subjects.	***S thermophilus*:** BIFIDO DIGEST 60C (F) (Protocol for Life) NOW Foods Probiotic (10 50 Billion)	Cultured dairy and dairy alternatives; fermented vegetables.
Obesity, T2DM Ivey et al[28,29] (2014, 2015); Sáez-Lara et al[4] (2016)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12	Reduction in fasting glucose concentration and increase in HOMA-IR; subjects: 156 overweight adults.	ProSynbiotic (Standard Process) TruBiotics (Bayer) Strengtia (Apex Energetics)	*L acidophilus* LA-5 (Nancy's Organic cow's milk yogurt) *B lactis* BB-12 (Nancy's Organic cow's milk kefir)
Obesity, NAFLD Yoo et al[30] (2013); Park et al[31] (2013)	*L curvatus* HY-7601, alone or in combination with *L plantarum* KY-1032	↓ Body weight gain; ↓ hepatic lipid droplet accumulation and adipocyte size; ↓ cholesterol in plasma and liver; ↓ gene expressions of fatty acid synthesis enzymes; ↓ proinflammatory cytokines (TNF-α, IL-6, IL-1β, and MCP); ↓ fatty acid oxidation-related genes (PGC1α, CPT1, CPT2, and ACOX1) in the liver.	Isolated for research purposes only.	None
Obesity, NAFLD Wang et al[32] (2015)	*L paracasei* CNCM I-4270, *L rhamnosus* I-3690, *B animalis* subsp *lactis* I-2494	↓ Body weight gain; ↓ macrophage infiltration into epididymal adipose tissue; ↓ hepatic steatosis; ↑ glucose-insulin; homeostasis (strain-specific) attenuation of obesity comorbidities; effects on MS-associated phylotypes of gut microbiota in mice.	Isolated for research purposes only.	None
Obesity, NAFLD, T2DM An et al[33] (2011)	LAB supplement (*B pseudocatenulatum* SPM-1204, *B longum* SPM-1205, *B longum* SPM-1207; 108-109 CFU)	↓ Body weight gain and fat accumulation; ↓ blood serum levels of total cholesterol, HDL-C, LDL-C, triglyceride, glucose, leptin; ↓ liver toxicity biomarkers (AST, ALT).	Isolated from stool for research purposes.	None
Obesity, T2DM Chen et al[34] (2012)	*B adolescentis*	↓ Body weight gain and visceral fat accumulation; ↑ insulin sensitivity.	Isolated from stool for research purposes.	None
Obesity, NAFLD Zhao et al[35] (2012)	*P pentosaceus* LP-28/ *L plantarum* SN-13T (as comparator)	↓ Body weight gain, visceral fat accumulation, and liver lipid contents (triglyceride and cholesterol); ↓ hepatic lipid droplet accumulation and adipocyte size; ↓ lipid metabolism-related genes (*CD36*, *SCD1*, *PPARγ*).	*P pentosaceus* LP-28 (isolated from longan fruit [*E longana*] for research purposes. *L plantarum* SN13T (plant derived and isolated for research purposes).	None
Obesity, T2DM, NAFLD Gauffin et al[36] (2012)	*B uniformis* CECT-7771	↓ Body weight gain, visceral fat accumulation and liver lipid contents (triglyceride and cholesterol); ↑ small adipocyte numbers; ↓ serum cholesterol, triglyceride, glucose, insulin, and leptin levels; ↑ oral tolerance to glucose; ↓ dietary fat absorption (reduced number of fat micelles in enterocytes); ↑ immune defence mechanisms;	Isolated from stools of healthy infants (mean age, 5.7 y; range, 1.0–10.8 y) for research purposes.	None
Obesity, NAFLD Everard et al[37] (2014)	*S boulardii*	↓ Body weight gain and fat mass; ↓ hepatic steatosis and total liver lipids content; ↓ decreases hepatic (50% decrease in CD11c macrophages level, F4/80, IL-1β and MCP-1mRNA); ↓ systemic inflammation (↓ plasma cytokine concentrations of IL-6, IL-4, IL-1β and TNF-α).	Designs for Health (FloraMyces) Digestive Probiotic for Travelers (NatureMade) Florastor (Biocodex) Strengtia (Apex Energetics)	None

Table 1. (continued)

Cardiometabolic Disease	Strains	Overview	Professional and Commercial Products	Foods
Obesity, NAFLD, T2DM Kim et al[38] (2013); Park et al[39] (2015); Ritze et al[40] (2014)	*L rhamnosus* GG	↓ Body weight gain and fat mass; ↑ insulin sensitivity; ↑ expression of genes related to glucose metabolism (GLUT4 mRNA in skeletal muscle); ↑ adiponectin production in adipose tissue; ↑ AMPK in skeletal muscle and adipose tissue; ↑ glucose tolerance; ↑ Insulin-stimulated Akt phosphorylation and GLUT4 translocation in skeletal muscle; ↓ endoplasmic reticulum (ER) stress in skeletal muscle; ↓ M1-like macrophage activation in white adipose tissues; ↓ liver inflammation and steatosis (protection from NAFLD development); ↓ duodenal IκB protein levels and restoration of the duodenal tight junction protein concentration; ↓ portal LPS; ↓ TNF-α, IL-8R, and IL-1β mRNA expression in the liver.	Advanced Multi-Billion Dophilus (Solgar) Advanced 40+ Acidophilus (Solgar) Digestive Health Probiotic, Kids Chewables & Packets (Culturelle) UltraFlora Baby (Metagenics) Walgreens Probiotic Lactobacillus GG	None
Obesity, T2DM, NAFLD Yadav et al[41] (2006)	*L lactis*	↓ HbA_{1C}; ↓ fasting blood glucose, insulin, free fatty acids and triglyceride.	Obtained from National Collection of Dairy Cultures for research purposes.	Activia yogurt (Redwood); Hill Farm goat milk kefir
Obesity, NAFLD Yin et al[42] (2010); Reichold et al[43] (2014)	*Bifidobacteria* L66-5, L75-4, M13-4, FS31-12; *B adolescentis*	↓ Liver triglyceride, total cholesterol and total lipid deposition (all 4 strains, but in strain-dependent manner, more pronounced for *B L66-5*); ↓ serum triglyceride and total cholesterol (all 4 strains, but in strain-dependent manner, more pronounced for *B L66-5* and *B FS31-12*); ↓ body weight gain (*B L66-5*); ↑ body weight gain (*B M13-4*); no changes in body weight gain L75-4 and FS31-12; ↓ liver inflammation and steatosis (protection from NASH development); ↓ formation of reactive oxygen species; ↓ activation of NF-κB; no effect on portal LPS, TLR-4, and Myd-88 mRNA expression in livers.	BL66-5, L75-4, M13-4, and FS31-12- isolated from healthy volunteers' fresh feces for research purposes. ***B adolescentis*:** Cultured in brain, heart under anaerobic conditions for research purposes.	None
Obesity, NAFLD Plaza-Diaz et al[44] (2014)	*L paracasei* CNCM I-4034, *B breve* CNCM I-4035, *L rhamnosus* CNCM (or mixture of 3 strains)	↓ Triacylglycerol liver content (for *L rhamnosus*, *B breve* or the mixture); ↓ neutral lipids liver content (for all 4 probiotic groups); ↓ serum LPS levels (for all 4 probiotic groups); ↓ serum TNF-α levels (for *B breve, L rhamnosus*, or the mixture); ↓ serum IL-6 levels (for *L paracasei*).	Isolated from feces of exclusively breast-fed infants for research purposes.	None
Obesity, T2DM, NAFLD Savcheniuk et al[45] (2014)	14 alive probiotic strains (*Lactobacillus, Lactococcus, Bifidobacterium, Propionibacterium, Acetobacter*)	↓ Body weight gain and visceral fat accumulation; ↓ liver lipid contents (protection from NAFLD development); ↓ serum cholesterol, triglyceride, glucose, insulin and leptin levels; ↑ insulin sensitivity (decreased HOMA-IR, increased adipocytokine.	***Propionibacterium*:** Securil, Nutricology ***Acetobacter*:** Not available	Various cultured and fermented foods.
Obesity Kobyliak et al[46] (2016)	*Bacteroidates*, (*Bacteroides*)↓, *Bacteroidates*, (*Prevotella*)↑, ↑*Bacillales*, (*Bacillus*)↑, *Lactobacillus*↓, *Clostridiales*, (*Clostridium*)↑, *Actinomycetales*↑, *Bifidobacteriales*↓, (*Bifidobacterium*)	The alteration of microbiota in gut in the conditions of obesity.	Broad spectrum probiotic providing *Bifidobacterium* and *Lactobacillus.*	None
T2DM Hartstra et al[47] (2014)	*Firmicutes*	Levels are increased in T2DM.	Phylum of bacteria (not available)	None
T2DM Hartstra et al[47] (2014)	*Bacteroidetes*	Levels are decreased in T2DM	Phylum of bacteria (not available)	None
T2DM Hartstra et al[47] (2014)	Intestinal bacterial species	Levels are increased in T2DM.	Not applicable	None
T2DM Hartstra et al[47] (2014)	*Roseburia*	Levels are decreased in T2DM.	Not available	None
T2DM Hartstra et al[47] (2014)	*E halii*	Levels are decreased in T2DM.	Not available	None
T2DM Hartstra et al[47] (2014)	*F prauznitzii*	Levels are decreased in T2DM.	Not available	None

Table 1. (continued)

Cardiometabolic Disease	Strains	Overview	Professional and Commercial Products	Foods
T2DM Hartstra et al[47] (2014)	*L gasseri*	Levels are increased in T2DM.	Not available	None
T2DM Bayat et al[48] (2016)	*C ficifolia*, Probiotic yogurt	Alone or in combination; ↓FBS & A_{1C} levels.	Not applicable	Yogurt (unspecified)
T2DM Hariri et al[49] (2015); Bayat et al[48] (2016)	*L plantarum* A-7	Decreased methylation process, SOD, and 8-OHDG; subjects: 40 patients with T2DM.	Provided in probiotic soy milk	None
T2DM Ejtahed et al[50,51] (2010, 2012); Sáez-Lara et al[4] (2016)	*L acidophilus* LA-5, *BB lactis* BB-12	Reduced fasting blood glucose and antioxidant status; TC and LDL-C improvement; subjects: 2 studies (60 patients with T2D 64 patients with T2D).	**Combination of *L acidophilus* LA-5, *B lactis* BB-12:** ProSynbiotic (Standard Process) TruBiotics (Bayer) Strengtia (Apex Energetics)	*L acidophilus* LA-5 (Nancy's Organic cow's milk yogurt) *B lactis* BB-12 (Nancy's Organic cow's milk kefir)
Dyslipidemia				
Shimizu et al[10] (2015); Taranto et al[52] (2000); Gilliland & Speck[53] (1977)	Fermented milk product, *L acidophilus*, *L reuteri*, *S thermophilus*, *L streptococcus*, *L thermophilus*, *L rhamnosus*	This meta-analysis shows that fermented milk products are effective in decreasing TC and LDL-C levels and probiotic preparations are effective in decreasing TC levels. Therefore, probiotic supplementation (fermented milk products and probiotic preparations) could be useful in the primary prevention of hypercholesterolemia and may lead to reductions in risk factors for CVD. *L acidophilus* deconjugates bile acids into free acids that are excreted more rapidly from the intestinal tract than are conjugated bile acids. Because free bile salts are excreted from the body, the synthesis of new bile acids from cholesterol can reduce the total cholesterol concentration in the body.	Strengtia (Apex Energetics)	Fermented milk products: lassi, kefir, yogurt (check ingredients list for specific stains).
Ettinger et al[54] (2014)	*L rhamnosus* GG GR-1, PL-60, NCIMB-30242; *L sakei* NR28; *Lactobacillus*/ *Bifidobacterium* multistrain; *L plantarum* PL-62, 299-V; *L reuteri* NCIMB-30242	Weight reduction, prevent ischemia in I/R injury attenuate heart failure, cardiac hypertrophy, reduced adipose tissue mass; weight reduction; reduce BMI in obese adults, reduce serum cholesterol; produce ACE-inhibitory peptides; reduce adipose tissue mass; reduce severity of ischemia in I/R injury lower serum cholesterol.	***Lactobacillus* GG:** Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar) ***L rhamnosus* GR-1:** Pro-B (Rephresh) Women's Fem Dophilus (Jarrow Formulas) UltraFlora Women's (Metagenics) Clinicians Flora Restore (Douglas Pharmaceuticals) ***L rhamnosus* NCIMB 30242:** Microbiome Plus+ (Gastrointestinal Probiotics) Natural Health Probiotic (Cardioviva) ***L plantarum* 299V:** Jarrow Formulas Ideal Bowel Support Probiotic Supplement (GoodBelly) Probiotic GX (Nature's Bounty) Probiata Digestion Support and Critical Care (Kyolic) Probiotic Balance (Sundown Naturals) Heart Healthy Probiotic Solutions (Dr Sinatra) Digestive Health Probiotic (Nature Made) Sibiotica (Apex Energetics) ***L reuteri* NCIMB 30242:** Cardioviva (UAS Labs)	*L plantarum* 299V (GoodBelly Probiotic Drinks) Other strains (None)
Cholesterol				
Aggarwal et al[55] (2013)	*L fermentum* KC4-B	Lactobacilli, hydrolyses the bile salts and hydroxyl steroid dehydrogenase, degrades the bile salts, interrupts the enterohepatic circulation of the bile acids; Lactobacilli inhibit hydroxy methyl glutarate CoA; *L fermentum* KC-4B reduced the cholesterol in medium by 14.8 mg.	Not available	None
Stroke				
Sun et al[11] (2016)	*C butyricum*	*C butyricum* is able to exert neuroprotective effects against I/R injury mice through antioxidant and antiapoptotic mechanisms, and reversing decrease of butyrate contents in the brain might be involved in its neuroprotection.	***C butyricum*:** AOR Probiotic-3 Miyarisan (630 Tablets)	Common in fermented milk and cheeses.

Table 1. (continued)

Cardiometabolic Disease	Strains	Overview	Professional and Commercial Products	Foods
Gout				
Li et al[12] (2014)	Strain DM9218 (analysis of this strain 16S rRNA sequences showed that DM-9218 has the highest similarity [99%] to *L plantarum* WCFS-1)	Showed high inhibitory activities to *E coli* and *S aureus*; DM9218-A is a promising candidate as an adjunctive treatment in patients with hyperuricemia, especially during the onset period of disease.	Colonized from Chinese sauerkrauts for research purposes (not commercially available).	None
NASH/NAFLD				
Vajro et al[56] (2011); Sáez-Lara et al[4] (2016)	*L rhamnosus* GG (1.2^{109} CFU/d)	Decreased ALT and PG-PS IgA antibodies; subjects: 20 obese children with NAFLD.	Walgreens Probiotic *Lactobacillus* GG Advanced Multi-Billion Dophilus (Solgar)	None
Aller et al[57] (2011); Sáez-Lara et al[4] (2016)	*L bulgaricus*, *S thermophilus* (5.0^{1011} CFU/d)	Decreased ALT and γ-GTP levels; subjects: 28 adults individuals with NAFLD.	Dr Ohhira's Probiotics Professional Formula Dr Ohhira's Probiotics Original Formula MegaFood (MegaFlora) VSL#3 (Sigma Tau Pharmaceuticals, Inc)	All Yogurt containing "Live and active cultures."
Nabavi et al[58] (2014); Sáez-Lara et al[4] (2016)	*L acidophilus* LA-5, *B breve* subsp *lactis* BB-12	Reduced serum levels of ALT, ASP, TC, and LDL-C; subjects: 72 patients with NAFLD.	ProSynbiotic (Standard Process) TruBiotics (Bayer) Strengtia (Apex Energetics) Sibiotica (Apex Energetics)	*L acidophilus* LA-5 (Nancy's Organic cow's milk yogurt) *B lactis* BB-12 (Nancy's Organic cow's milk kefir)
Alisi et al[59] (2014); Sáez-Lara et al[4] (2016)	*B thermophilus*, *L thermophilus*, *S thermophilus*	Improved fatty liver severity, decreased BMI, and increased GLP1/aGLP1; subjects: 44 obese children with NAFLD.	Found in most probiotic formulas.	Various cultured and fermented foods.
PCOS				
Guo et al[14] (2016)	Increasing of *Lactobacillus* and *Clostridium*, and decreasing of *Prevotella* (with fecal microbiota transplant)	After treating PCOS rats with *Lactobacillus* and FMT from healthy rats, estrous cycles were improved in all 8 rats in FMT group, and in 6 of the 8 rats in *Lactobacillus* transplantation group with decreasing androgen biosynthesis; microbiota interventions through *Lactobacillus* and FMT transplantation were beneficial in PCOS rats.	Not applicable	None
Tremellen et al[60] (2012)	*Bifidobacteria*, *Lactobacterium* (combined with prebiotic food source [inulin, fructose oligosaccharide])	Likely to improve intestinal barrier function, resulting in a reduction in transfer of LPS across the mucosal wall, reducing metabolic endotoxaemia. A probiotic mediated increase in colonocyte production of the satiety hormone GLP-1 will reduce energy intake, producing a drop in adipose tissue mass and a decrease in inflammation, with a resulting further improvement in gut mucosal barrier function. The net reduction in colonic mucosal permeability and resulting metabolic endotoxemia will lead to an improvement in insulin receptor function, a drop in serum insulin and a normalization of ovarian function.[60]	Flora8 (PromoPharma) Probiotic + Prebiotic Flora Renew (Family Flora) Sunbiotics Potent Probiotics With Organic Prebiotics Powder	Cultured dairy products with inulin or FOS as ingredients.

Abbreviations: T2DM, type 2 diabetes mellitus; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; PCOS, polycystic ovary syndrome; LAB, lactic acid bacterium; HbA_{1C}, hemoglobin A_{1C}; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; VFA, visceral fat area; BP, blood pressure; PBMC, peripheral blood mononuclear cell; HOMA-IR, homeostasis model assessment of insulin resistance; IL, interleukin; MCP, monocyte chemotactic protein; MS, multiple sclerosis; HDL-C, high-density lipoprotein cholesterol; AST, aspartate transaminase; ALT, alanine transaminase; IL-4, interleukin 4; ER, endoplasmic reticulum; LPS, lipopolysaccharide; NF-κB, nuclear factor κB; CVD, cardiovascular disease; I/R; ischemia-reperfusion; FMT, fecal microbiota transplant; GI, gastrointestinal; FOS, fructooligosaccharide.

Discussion: Cardiometabolic Disease

Probiotic strains of *Lactobacillus* and *Bifidobacterium* are marketed in products for human consumption because they alter the intestinal flora. These probiotic strains may be protective of various metabolic processes by shielding the colonocytes from microbial endotoxin release and reducing innate immune system activation through increased competition with bacteriocin-producing microbial families. Bacteriocins are proteinaceous toxins that bacteria produce to prevent the growth of bacterial strains that are closely related and may be beneficial in cardiometabolic diseases.[30]

In relation to cholesterol, it has been shown that probiotics inhibit cholesterol hepatic recirculation. Etjahed et al[61] found that *L acidophilus* LA-5 and *B lactis* BB-12 facilitated bile salt hydrolase to deconjugate bile salts resulting in a decrease of enterohepatic cholesterol circulation. This effect is 2-fold as cholesterol is the substrate for de novo synthesis of bile acids and was beneficial for those suffering from type 2 diabetes mellitus. An alternate mechanism for the decrease in cholesterol seen by probiotics is the bacterial fermentation product of short-chain fatty acids, an inhibitor of hepatic cholesterol synthesis. Last, hydroxymethylglutarate CoA, the enzymatic target of statin drugs, can also be modulated by *L fermentum* KC-4B, reducing the amount of cholesterol in a cultured medium.[55]

Research Overview: Fatigue Syndromes

Fatigue syndromes such as chronic fatigue syndrome (CFS), myalgic encephalomyelitis, systemic exertion intolerance disease, and fibromyalgia syndrome are intricately linked to gastrointestinal health. On average, approximately 60% of these patients also qualify for the clinical diagnosis of irritable bowel syndrome and 97% of CFS patients report neuropsychological disturbances.[62,63] Microbial translocation induces inflammatory markers such as lipopolysaccharides (LPS), LPS-binding protein, C-reactive protein, tumor necrosis factor α (TNF-α), interleukin 6 (IL-6), and soluble CD14 in those with CFS, which results in T-helper 2 dominance.[64-66] CFS patients also have dysbiotic flora with the relative ratios of *Firmicutes*, *Lactobacillus*, and *Escherichia coli* being considerably lower than in controls with approximately 2-fold the number of *Proteobacteria* (Enterobacteriaceae family). This imbalance can result in an overall decrease in anti-inflammatory bacterial species such as *Bifidobacteria*.[65] Furthermore, the overrepresented species found in the *Enterococcus* and *Streptococcus* families are capable of producing D-lactic acid, potentially resulting in chronic acidosis in CFS patients.[16] The overabundance of *Prevotella* suggests a strong reliance on carbohydrate intake within the population[67] and lends insight into why a lower carbohydrate diet often results in a decrease in clinical symptoms.

CFS is characterized by unexplained fatigue along with a minimum of 4 of the following symptoms: memory impairment, sore throat, tender lymph nodes, muscle or joint pain, headaches, unrefreshing sleep, and postexertional malaise.[64] CFS is also associated with an increase in anxiety and/or depression. The dysbiotic flora in these patients can partially explain the microbial-neuroendocrine relationship between certain species and the resultant change in hormones and neurotransmitters. *Lactobacillus* and *Bifidobacterium* species produce calming neurotransmitters such as acetylcholine and gamma-amino butyrate (GABA) respectively, whereas *Escherichia* species produce norepinephrine, serotonin, and dopamine and, in addition, *Streptococcus and Enterococcus* species produce serotonin.[67] Thus, in these patients, there is the potential for the overproduction or underproduction of serotonin, a lack, of both acetylcholine and GABA, and a decrease in norepinephrine and dopamine. Microbial production of tryptophan, tyrosine and phenylalanine can be altered owing to microbial dependence on a key pathway that humans lack called the *shikimate pathway*.[68] Furthermore, serotonin, melatonin, melanin, epinephrine, dopamine, thyroid hormone, folate, coenzyme Q_{10}, vitamin K, and vitamin E all depend on this pathway for metabolites.[68] This crucial pathway can be disrupted by the consumption of glyphosate, an herbicide found in Roundup Ready Crops and in the environment.[68] The metabolism of these nutrients and hormones are bacteria dependent and depending on the dietary intake of those with CFS, several critical biomolecules can be altered.

Table 2. Fatigue Syndromes

Fatigue Syndrome	Strains	Overview	Professional and Commercial Products	Foods
Groeger et al[64] (2013)	*B infantis* 35624	Reduce systemic proinflammatory biomarkers; 71% of CFS patients had decreased levels of CRP, TNF-α, and IL-6, when fed *B infantis* 35624. TNF-α and IL-6 control CRP on the transcription level.	***B infantis* 35624:** Align Probiotic Digestive Care (Procter & Gamble)	None
Choppa et al[69] (2012)	LAB, LAB-loaded alginate beads	"Immobility and PSF were found to increase considerably in FST rats (665 ± 22 s and 196 ± 6 s) as compared with the naïve (32 ± 7 s and 22 ± 2 s) at 20 days, establishing severe fatigue like behavior. FST control group exhibited significant ($P < .05$) hypertrophy of spleen, hypertrophy of thymus, and increased oxido-nitrosative stress in brain and tumor necrosis factor-α (TNF-α) levels in serum." Probiotic supplementation attenuated postswim fatigue time and reduced ($P < .05$) oxidonitrosative stress and TNF-α levels and restored the spleen and thymus to normal size.	***L acidophilus* beads:** Probiotic Acidophilus BioBeads (Natrol, Inc) Theralac Probiotic (Master Supplements) Strengtia (Apex Energetics) ***L acidophilus*:** Widely available in probiotic supplements.	Yogurt, kefir, (Nancy's Organic yogurts)

Table 2. (continued)

Fatigue Syndrome	Strains	Overview	Professional and Commercial Products	Foods
Rao et al[62] (2009)	*L casei* Shirota (Yakult Honsha, Tokyo, Japan)	Resulted in a significant rise in both *Lactobacillus* and *Bifidobacteria* as well as a significant decrease in anxiety symptoms ($P = .01$) in CFS patients.	Not available	Yakult
Rao et al[62] (2009)	*L plantarum* 299-V	Resulted in significant rise in fecal *Bifidobacteria* levels. "*Bifidobacteria* can boost plasma tryptophan levels and alter serotonin and dopamine turnover in areas of the brain associated with depression and anxiety."	Digestive Health Probiotic (Nature Made) Heart Healthy Probiotic Solutions (Dr Sinatra) Ideal Bowel Support, 10 Billion Organisms V-Capsules (Jarrow Formulas) Probiata Digestion Support and Critical Care (Kyolic) Plantadophilus- 3 Billion CFU (Transformation Enzymes) Probiotic Balance (Sundown Naturals) Probiotic GX (Nature's Bounty) Probiotic Supplement (GoodBelly) UltraFlora Intensive Care (Metagenics)	GoodBelly
Sullivan et al[66] (2009)	*L paracasei* sbsp *paracasei* F-19, *L acidophilus* NCFB-1748, *B lactis* BB-12 (together); *Lactobacillus* F-19, *L acidophilus* NCFB-1748, *B lactis* BB-12	Results in fatigue and quality of life improvements based on visual analogue scales and the SF-12 Health Survey after 2 wk.	***L paracasei* sbsp *paracasei* F19:** Gene-filus F19 (Siffra Farmaceutici) ***L acidophilus* NCFB 1748:** Not available (grown for research purposes). ***B lactis BB-12*:** Metabiotic (Procter & Gamble) TruBiotics (Bayer)	No commonly available foods in the United States.
Giloteaux[65] et al (2016); Quevrain[70] et al (2016)	*F prausnitzii*	Is significantly decreased in those with CFS and produces an anti-inflammatory protein capable of "inhibiting the NF-κB pathway in intestinal epithelial cells and to prevent colitis in an animal model."	Isolated for research purposes only.	None
Galland[67] (2014)	*B fragilis*	Associated with decreased anxiety in CFS patients. "Corrects excessive gut permeability, alters gut microbial composition, and ameliorates deficits in communication and stereotypic, anxiety-like, and sensorimotor behaviors in the maternal immune activation model."	Not applicable	*B fragilis* (None)
Giloteaux et al[65] (2016)	*P freudenreichii*	Bifidogenic substance that increases butyrate. Butyrate modulates hormone and cytokine secretion and activates anti-inflammatory processes.	Securil (Nutricology)	Bacterium found in Swiss cheese, produces substances that enhance growth of *Bifidobacteria*.
Galland[67] (2014)	*Lactobacillus* sp	"Some species of *Lactobacillus* are D-lactate producers and high-dose β-glucan (found in oats and barley) can increase intestinal permeability." Case report showing that a symbiotic: *B breve* Yakult and *L casei* Shirota as probiotics and galacto-oligosaccharide as a prebiotic resolved the acidosis in a man with short-bowel syndrome. Suggest a probiotic that is free of *Lactobacillus* and high-dose β-glucan.	***Lactobacillus* sp:** Widely available in dietary supplements. ***B breve* Yakult, *L casei* Shirota:** Not available.	Fermented dairy products. Fermented soy products. Fermented vegetables.

Abbreviations: CFS, chronic fatigue syndrome; CRP, C-reactive protein; TNF-α, tumor necrosis factor α; IL-6, interleukin 6; LAB, lactic acid bacterium.

Discussion: Fatigue Syndromes

The research reviewed previously indicates that certain probiotic species can be useful in the amelioration of CFS symptoms and quality of life. Key inflammatory substances such as tumor necrosis factor α (TNF-α) and IL-6 control C-reactive protein on the transcription level elucidating the role between dysbiotic flora that have the ability to alter these proinflammatory biomolecules and disease presentation. Groeger et al[64] found that supplementation with *Bifidobacterium infantis* 35624 for 6 to 8 weeks reduced these proinflammatory markers in 71% of those with CFS, resulting in a decrease of symptoms in 3 separate randomized, double-blind, placebo-controlled interventions. Quevrain[70] also found that *Faecalibacterium prausnitzii* can significantly inhibit the nuclear factor κB pathway in intestinal epithelial cells by producing a protein that results in a decrease in inflammatory markers. Choppa[69] found that probiotic supplementation with *Lactobacillus acidophilus* and *L acidophilus* loaded alginate beads reduced postswim fatigue time in CFS induced mice while decreasing ($P < .05$) oxidonitrosative stress, TNF-α levels, and restoring the diminished spleen and thymus to normal size.

Addressing more directly the neuroendocrine imbalances in CFS are 2 studies that show that supplementation with certain *Lactobacillus* species can reduce symptoms of anxiety as well as increase *Bifidobacteria* levels.[62,66] Galland[67] also showed that supplementation with *Bacteroides fragilis* decreased anxiety levels while improving excessive gut permeability, whereas Giloteaux[65] found that supplementation with the bifidogenic substance *Propionibacterium freudenreichii*

improved butyrate levels, which induces an anti-inflammatory cascade. Sullivan[66] found that a blend of *Lactobacillus paracasei* F19, *L acidophilus* NCFB 1748, and *B lactis* BB-12 improved fatigue and quality of life via the visual analogue scales and the SF-12 Health Survey in only 2 weeks. Caution is advised for those who have short-bowel syndrome and CFS as over supplementation with D-lactate producing *Lactobacilli* can result in D-lactic acidosis. Galland[67] presented a case report elucidating the mechanism of D-lactate overgrowth that was ameliorated by a symbiotic consisting of *Bifidobacterium breve* Yakult, *Lactobacillus casei* Shirota, and galacto-oligosaccharide with no concurrent change in diet. Overall, these studies suggest that direct modulation of the microbiome can reduce anxiety, improve quality of life, restore dysbiotic flora, and reduce inflammatory markers in those with CFS.

Nutritional Supplements Overview

Professional and commercial dietary supplements containing probiotics are widely available.[71] In 2002, it was estimated that more than 100 companies in the United States marketed probiotic supplements and nearly 2 million adults used them.[72] In 2012, probiotic or prebiotic use was the third most commonly used nonvitamin, nonmineral dietary supplement and global sales are projected to reach to $42 billion by the end of 2016.[73,74] Using probiotics for general health versus targeting a specific health concern is more complex as the properties of probiotic species are strain specific.[75] Unfortunately, there is a lack of consistency naming therapeutic strains in research and strains are often not listed on supplement labels. This makes it difficult to know if the ingredients in a product matches the ingredients used in the research and is a limitation of these tables. If the researched strain was not readily available on the label or marketing material, the brand, potentially containing the strain, was not included on the table.

The Joint Food and Agriculture Organization of the United Nations/World Health Organization Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics developed guidelines for evaluating probiotics in food.[76] A combination of phenotypic and genotypic tests must be performed to determine the strain; however, regulations on species identification is not in place and supplement companies are not required to list this information on labels. During this multiseries review, it was identified that 30 species were specifically isolated for research purposes and were unavailable and another 56 strains were not commercially available. Owing to the wide variety of formulations on the market, lack of knowledge, and poor labeling, it is difficult for practitioners and consumers to determine which brand contains specific strains researched to address a particular health concern.

This table is designed to be a resource to see what is available at-a-glance. The brands were chosen by searching the probiotic strain and/strain-species in Google, several supplement companies, Probiotics Advisor,[77] and the Clinical Guide to Probiotic Products.[78] Based on the results and to determine what was commercially available, the search was refined using Google Shopping. In some instances, the supplement company was called to determine if the formula contained a specific species.

Table 3. Supplemental Information on Cardiometabolic Diseases and Fatigue Syndromes

Disease	Supplement	Probiotic Strain(s)
Dyslipidemia	Advanced Multi-Billion Dophilus (Solgar)	*Lactobacillus* GG
Dyslipidemia	Digestive Health Probiotic (Nature Made)	*L plantarum* 299V
Dyslipidemia	Heart Healthy Probiotic Solutions (Dr Sinatra)	*L plantarum* 299V
Dyslipidemia	Jarrow Formulas Ideal Bowel Support	*L plantarum* 299V
Dyslipidemia	Pro-B (Rephresh)	*L rhamnosus* GR-1
Dyslipidemia	Probiata Digestion Support and Critical Care (Kyolic)	*L plantarum* 299V
Dyslipidemia	Probiotic Balance (Sundown Naturals)	*L plantarum* 299V
Dyslipidemia	Probiotic GX (Nature's Bounty)	*L plantarum* 299V
Dyslipidemia	Probiotic Supplement (GoodBelly)	*L plantarum* 299V
Dyslipidemia	UltraFlora Women's (Metagenics)	*L rhamnosus* GR-1
Dyslipidemia	Walgreens Probiotic Lactobacillus GG	*Lactobacillus* GG
Dyslipidemia	Women's Fem Dophilus (Jarrow Formulas)	*L rhamnosus* GR-1
Fatigue syndrome	Align Probiotic Digestive Care (Proctor & Gamble)	*B infantis* 35624
Fatigue syndrome	Digestive Health Probiotic (Nature Made)	*L plantarum* 299V
Fatigue syndrome	Gene-filus F19 (Siffra Farmaceutici)	*L paracasei* sbsp *paracasei* F19
Fatigue syndrome	Heart Healthy Probiotic Solutions (Dr Sinatra)	*L plantarum* 299V
Fatigue syndrome	Isolated for research purposes only	*F prausnitzii*
Fatigue syndrome	Jarrow Formulas Ideal Bowel Support (10 Billion) Organisms V-Capsules	*L plantarum* 299V
Fatigue syndrome	Not available	*L casei strain* Shirota (Yakult Honsha, Tokyo, Japan)
Fatigue syndrome	Not Available	*B fragilis*
Fatigue syndrome	Not available	*B breve* Yalult *L casei* Shirota
Fatigue syndrome	Probiata Digestion Support and Critical Care (Kyolic)	*L plantarum* 299V
Fatigue syndrome	Probiotic Acidophilus BioBeads (Natrol, Inc)	*L acidophilus*-loaded alginate beads
Fatigue syndrome	Probiotic Balance (Sundown Naturals)	*L plantarum* 299V
Fatigue syndrome	Probiotic GX (Nature's Bounty)	*L plantarum* 299V
Fatigue syndrome	Probiotic Supplement (GoodBelly)	*L plantarum* 299V
Fatigue syndrome	Securil (Nutricology)	*P freudenreichii*
Fatigue syndrome	Theralac Probiotic (Master Supplements)	*L acidophilus* alginate
Fatigue syndrome	TruBiotics (Bayer)	*B lactis* BB-12
Fatigue syndrome	Ultraflora Balance (Metagenics)	*L acidophilus* NCFB 1748
Fatigue syndrome	Widely available in dietary supplements	*Lactobacillus* species
Gout	Isolated and colonized from Chinese sauerkrauts for research purposes (not commercially available	Strain DM9218 (analysis of this strain 16S rRNA sequences showed that DM9218 has the highest similarity [99%] to Lactobacillus plantarum WCFS1)
NAFLD	BIFIDO DIGEST 60C (F) (Protocol for Life)	*S thermophilus*

Table 3. (continued)

Disease	Supplement	Probiotic Strain(s)
NAFLD	Isolated - cultured in brain, heart under anaerobic conditions for research purposes	*B adolescentis*
NAFLD	Isolated for research purposes only	*L curvatus* HY7601 alone or in combination with *L plantarum* KY103
NAFLD	Isolated from healthy volunteers' fresh feces for research purposes	Bifidobacteria L66-5, L75-4, M13-4, and FS31-12
NAFLD	NOW Foods Probiotic (10 50 Billion)	*S thermophilus*
NASH/NAFLD	Advanced Multi-Billion Dophilus (Solgar)	*L rhamnosus* GG (1.2^{109} CFU/d)
NASH/NAFLD	Dr Ohhira's Probiotics Original Formula	*L bulgaricus*, *S thermophilus* (5.0^{1011} CFU/d)
NASH/NAFLD	MegaFood (MegaFlora)	*L bulgaricus*, *S thermophilus* (5.0^{1011} CFU/d)
NASH/NAFLD	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B breve* subsp *lactis* BB-12
NASH/NAFLD	TruBiotics (Bayer)	*L acidophilus* LA-5, *B breve* subsp *lactis* BB-12
NASH/NAFLD	Walgreens Probiotic Lactobacillus GG	*L rhamnosus* GG (1.2^{109} CFU/d)
NASH/NAFLD	Widely available (found in most probiotic formulas)	*B thermophilus*, *L thermophilus*, *S thermophilus*
Obesity	BIFIDO DIGEST 60C (F) (Protocol for Life)	*S thermophilus*
Obesity	Enterogenic Concentrate (Integrative Therapeutics)	*E faecium*
Obesity	GoLive Probiotic & Prebiotic Drink Mix	*L salivarius* LS-33
Obesity	Health-Bac 100 grams (North American Herb & Spice)	*E faecium*
Obesity	Hyper-Implante (InterPlexus)	*L salivarius* LS-33
Obesity	Isolated - cultured in brain, heart under anaerobic conditions for research purposes	*B adolescentis*
Obesity	Isolated for research and not commercially available - prepared with lactic acid bacteria starter cultures (*Streptococcus thermophilus and Lactobacillus delbrueckii ssp. bulgaricus*) commonly used for conventional yogurt production and viable cells of LG2055	*L gasseri* SBT-2055, *L gasseri* LG-2055 (5^{1010} CFU)
Obesity	Isolated for research purposes only	*L curvatus* HY-7601 alone or in combination with *L plantarum* KY-1032
Obesity	Isolated for research, from the GI of health Estonian children, and not commercially available	*L plantarum* TENSIA (1.5^{1011} CFU/g added to cheese milk before renneting)
Obesity	Isolated from healthy volunteers' fresh feces for research purposes	*Bifidobacteria* L66-5, L75-4, M13-4, and FS31-12
Obesity/T2DM	Isolated from stool for research purposes.	*B adolescentis*
Obesity	Nature's Secret Ultimate Probiotic (4 billion)	*E faecium*
Obesity	Probiotic Supreme DF (Designs for Health)	*L salivarius* LS-33
Obesity	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12
Obesity	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B lactis* BB-12 *L casei* DN001 (108 CFU/g)
Obesity	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12
Obesity	TruBiotics (Bayer)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12
Obesity	TruBiotics (Bayer)	*L acidophilus* LA-5, *B lactis* BB-12, *L casei* DN001 (108 CFU/g)
Obesity	TruBiotics (Bayer)	*L acidophilus* LA-5, *B animalis* subsp *lactis* BB-12
Obesity	Ultimate Intestinal Shield (Phyto Therapy)	*L salivarius* LS-33

Table 3. (continued)

Disease	Supplement	Probiotic Strain(s)
Obesity	UltraFlora Spectrum (Metagenics)	*L salivarius* LS-33
Obesity/NAFLD	Florastor (Biocodex)	*S boulardii* (Biocodex)
Obesity/NAFLD	Strengtia (Apex Energetics)	*S boulardii*
Obesity/NAFLD	Designs for Health	*S boulardii*
Obesity/NAFLD	Isolated for research purposes (plant derived)	*L plantarum* SN13T as comparator
Obesity/NAFLD	Isolated from feces of exclusively breast (fed infants for research purposes)	*L paracasei* CNCM I-4034, *B breve* CNCM I-403, *L rhamnosus* (CNCM or mixture of 3 strains)
Obesity/NAFLD	Isolated from longan fruit (*Euphoria longana*) for research purposes	P pentosaceus LP28
Obesity/NAFLD	Isolated for research purposes only	*L paracasei* CNCM I-4270, *L rhamnosus* I-3690, *B animalis* subsp *lactis* I-2494
Obesity/NAFL/ T2DM	Advanced Multi-Billion Dophilus (Solgar)	*L rhamnosus* GG
Obesity/NAFLD/ T2DM	Isolated from stool for research purposes	Lactic acid bacterium supplement *(B pseudocatenulatum* SPM-1204, *B longum SPM-1205*, *B longum* SPM-1207 (108-109 CFU)
Obesity/NAFL/ T2DM	Walgreens Probiotic *Lactobacillus GG*	*L rhamnosus* GG
Obesity/T2DM/ NAFLD	Isolated and obtained from National Collection of Dairy Cultures for research purposes.	*L lactis*
Obesity/T2DM/ NAFLD	Isolated from stools of healthy infants (mean age, 5.7 y; range, 1.0–10.8 y) for research purposes	*B uniformis* CECT 7771
Obesity/T2DM/ NAFLD	Not available	*Acetobacter*
O Obesity/T2DM/ NAFLD	Securil (Nutricology)	*Propionibacterium*
PCOS	Flora8 (PromoPharma)	*Bifidobacteria* and *Lactobacterium* combined with prebiotic food source (inulin, fructose oligosaccharide)
PCOS	Probiotic + Prebiotic Flora Renew (Family Flora)	*Bifidobacteria* and *Lactobacterium* combined with prebiotic food source (inulin, fructose oligosaccharide)
PCOS	Sunbiotics Potent Probiotics with Organic Prebiotics Powder	*Bifidobacteria* and *Lactobacterium* combined with prebiotic food source (inulin, fructose oligosaccharide)
T2DM	BIFIDO DIGEST 60C (F) (Protocol for Life)	*S thermophilus*
T2DM	Not available	*Roseburia*
T2DM	Not available	*E halii*
T2DM	NOW Foods Probiotic (10 50 Billion)	*S thermophilus*
T2DM	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B animalis subsp lactis* BB-12
T2DM	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B animalis subsp lactis* BB-12
T2DM	TruBiotics (Bayer)	*L acidophilus* LA-5, *B animalis subsp lactis* BB-12
T2DM	TruBiotics (Bayer)	*L acidophilus* LA-5, *B animalis subsp lactis* BB-12
T2DM	Not available	*F prauznitzii*
T2DM	ProSynbiotic (Standard Process)	*L acidophilus* LA-5, *B lactis* BB-12 combination
T2DM	Provided in probiotic soy milk	*L plantarum* A7
T2DM	TruBiotics (Bayer)	*L acidophilus* LA-5, *B lactis* BB-12 combination

Abbreviations: NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; T2M, type 2 diabetes mellitus; PCOS, polycystic ovary syndrome.

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References

1. Beltrán-Sánchez H, Harhay MO, Harhay, MM, McElligott S. Prevalence and trends of metabolic syndrome in the adult U.S. population, 1999–2010. *J Am Coll Cardiol.* 2013;62(8):697-703.
2. Graf C, Ferrari N. Metabolic syndrome in children and adolescents. *Visc Med.* 2016;32(5):357-362.
3. Heidenreich P, Trogdon J, Khavjou O, et al. Forecasting the future of cardiovascular disease in the United States. *Circulation.* 2011;123:933-944.
4. Sáez-Lara et al (2016)
5. Ivey KL, Hodgson JM, Kerr DA, Lewis JR, Thompson PL, Prince RL. The effects of probiotic bacteria on glycaemic control in overweight men and women: A randomised controlled trial. *Eur J Clin Nutr*. 2014;68:447-452.
6. Ivey KL, Hodgson JM, Kerr DA, Thompson PL, Stojceski B, Prince RL. The effect of yoghurt and its probiotics on blood pressure and serum lipid profile: A randomised controlled trial. *Nutr Metab Cardiovasc Dis*. 2015;25(1):46-51.
7. Wang J, Tang H, Zhang C, et al. Modulation of gut microbiota during probiotic-mediated attenuation of metabolic syndrome in high fat diet-fed mice. *ISME J*. 2015;9(1):1-15.
8. Kobyliak N, Conte C, Cammarota G, et al. Probiotics in prevention and treatment of obesity: A critical view. *Nutrit Metab*.2016;13(1):1-13.
9. Hartstra AV, Bouter KEC, Bäckhed F, Nieuwdorp M. Insights into the role of the microbiome in obesity and type 2 diabetes. *Diabetes Care.* 2014;38(1):159-165.
10. Shimizu M, Hashiguchi M, Shiga T, Tamura H, Mochizuki M. Meta-analysis: Effects of probiotic supplementation on lipid profiles in normal to mildly hypercholesterolemic individuals. *PLoS ONE.* 2015;10(10):e0139795.
11. Sun J, Ling Z, Wang F, et al. Clostridium butyricum pretreatment attenuates cerebral ischemia/reperfusion injury in mice via anti-oxidation and anti-apoptosis. *Neurosci Lett*. 2016;613:30-35.
12. Li M, Yang D, Mei L, Yuan L, Xie A, Yuan J. Screening and characterization of purine nucleoside degrading lactic acid bacteria isolated from Chinese sauerkraut and evaluation of the serum uric acid lowering effect in hyperuricemic rats. *PLoS One*. 2014;9(9):e105577.
13. Sáez-Lara MJ, Robles-Sanchez C, Ruiz-Ojeda FJ, Plaza-Diaz J, Gil A. effects of probiotics and synbiotics on obesity, insulin resistance syndrome, type 2 diabetes and non-alcoholic fatty liver disease: A review of human clinical trials. *Internat J Mol Sci*. 2016;17(6):928.
14. Guo Y, Qi Y, Yang X, Zhao L, Wen S, Liu Y, Tang L. Association between polycystic ovary syndrome and gut microbiota. *PLoS One*. 2016;11(4):e0153196.
15. Claus S, Guillou H, Ellero-Simatos S. The gut microbiota: A major player in the toxicity of environmental pollutants? *NPJ Biofilm Microbiome*. 2016;16003:1-11.
16. Bienenstock J, Gibson G, Klaenhammer TR, Walker WA, Neish AS. New insights into probiotic mechanisms. *Gut Microbes.* 2013;4(2):94-100.
17. Kadooka Y, Sato M, Imaizumi K, et al. Regulation of abdominal adiposity by probiotics (*Lactobacillus gasseri* SBT2055) in adults with obese tendencies in a randomized controlled trial. *Eur J Clin Nutr.* 2010;64:636-643.
18. Mohamadshahi M, Veissi M, Haidari F, Javid AZ, Mohammadi F, Shirbeigi E. Effects of probiotic yogurt consumption on lipid profile in type 2 diabetic patients: A randomized controlled clinical trial. *J Res Med Sci*. 2014;19(6):531-536.
19. Tonucci LB, Olbrich Dos Santos KM, Licursi de Oliveira L, Rocha Ribeiro SM4, Duarte Martino HS. Clinical application of probiotics in type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled study. *Clin Nutr*. 2015. pii:S0261-5614(15)00331-3.
20. Larsen N, Vogensen FK, Gøbel RJ, et sl. Effect of Lactobacillus salivarius Ls-33 on fecal microbiota in obese adolescents. Clin Nutr. 2013;32:935-940.
21. Kadooka Y, Sato M, Imaizumi K, et al. Regulation of abdominal adiposity by probiotics (Lactobacillus gasseri SBT2055) in adults with obese tendencies in a randomized controlled trial. *Eur J Clin Nutr.* 2010;64:636-643.
22. Sharafedtinov KK, Plotnikova OA, Alexeeva RI, et al. Hypocaloric diet supplemented with probiotic cheese improves body mass index and blood pressure indices of obese hypertensive patients: A randomized double-blind placebo-controlled pilot study. *Nutr J*. 2013;12:138.
23. Zarrati M, Salehi E, Nourijelyani K, et al. Effects of probiotic yogurt on fat distribution and gene expression of proinflammatory factors in peripheral blood mononuclear cells in overweight and obese people with or without weight-loss diet. *J Am Coll Nutr*. 2014;33(6):417-425.
24. Zarrati M, Shidfar F, Nourijelyani K, et al. Lactobacillus acidophilus La5, Bifidobacterium BB12, and Lactobacillus casei DN001 modulate gene expression of subset specific transcription factors and cytokines in peripheral blood mononuclear cells of obese and overweight people. *Biofactors*. 2013;39(6):633-643.
25. Zarrati M, Salehi E, Mofid V, et al. Relationship between probiotic consumption and IL-10 and IL-17 secreted by PBMCs in overweight and obese people. *Iran J Allergy Asthma Immunol*. 2013;12(4):404-406.
26. Agerholm-Larsen L, Raben A, Haulrik N, et al. Effect of 8 week intake of probiotic milk products on risk factors for cardiovascular diseases. *Eur J Clin Nutr*. 2000;54:288-297.
27. Rajkumar H, Mahmood N, Kumar M, et al. Effect of probiotic (VSL#3) and Ω-3 on lipid profile, insulin sensitivity, inflammatory markers, and gut colonization in overweight adults: A randomized, controlled trial. *Mediat Inflamm*. 2014;2014:348959.
28. Ivey KL, Hodgson JM, Kerr DA, et al. The effects of probiotic bacteria on glycaemic control in overweight men and women: A randomised controlled trial. *Eur J Clin Nutr*. 2014;68:447-452.
29. Ivey KL, Hodgson JM, Kerr DA, Thompson PL, Stojceski B, Prince RL. The effect of yoghurt and its probiotics on blood pressure and serum lipid profile: A randomised controlled trial. *Nutr Metab Cardiovasc Dis*. 2015;25(1):46-51.
30. Yoo JY, Kim SS. Probiotics and prebiotics: Present status and future perspectives on metabolic disorders. *Nutrients*. 2016;8:173.
31. Park MK, Ngo V, Kwon YM, et al. Lactobacillus plantarum DK119 as a probiotic confers protection against influenza virus by modulating innate immunity. *PLoS ONE.* 2013;8(10):e75368.
32. Wang J, Tang H, Zhang C, et al. Modulation of gut microbiota during probiotic-mediated attenuation of metabolic syndrome in high fat diet-fed mice. *ISME J*. 2015;9(1):1-15.
33. An HM, Park SY, Lee DK et al. Antiobesity and lipid-lowering effects of *Bifidobacterium* spp. in high fat diet-induced obese rats. *Lipid Health Dis*. 2011;10:116.
34. Chen J, Wang R, Li XF, Wang RL. Bifidobacterium adolescentis supplementation ameliorates visceral fat accumulation and insulin sensitivity in an experimental model of the metabolic syndrome. *Br J Nutr*. 2012;107(10):1429-1434.
35. Guo Y, Qi Y, Yang X, Zhao L, Wen S, Liu Y, Tang L. Association between polycystic ovary syndrome and gut microbiota. PLoS One. 2016;11(4):e0153196.
36. Gauffin Cano P, Santacruz A, Moya Á, Sanz Y. Bacteroides uniformis CECT 7771 ameliorates metabolic and immunological dysfunction in mice with high-fat-diet induced obesity. *PLoS ONE.* 2012;7(7):e41079.
37. Everard A, Matamoros S, Geurts L, Delzenne NM, Cani PD. Saccharomyces boulardii administration changes gut microbiota and reduces hepatic steatosis, low-grade inflammation, and fat mass in obese and type 2 diabetic db/db mice. *mBio*. 2014;*5*(3):e01011-e01014.
38. Kim S, Park K, Kim B, Kim E, Hyun C. Lactobacillus rhamnosus GG improves insulin sensitivity and reduces adiposity in high-fat diet-fed mice through enhancement of adiponectin production. *Biochem Biophys Res Commun*. 2013;431:258-263.
39. Kim S, Park K, Kim B, Kim E, Hyun C. Lactobacillus rhamnosus GG improves insulin sensitivity and reduces adiposity in high-fat diet-fed mice through enhancement of adiponectin production. *Biochem Biophys Res Commun*. 2013;431:258-263.
40. Ritze Y, Bárdos G, Claus A, et al. Lactobacillus rhamnosus *GG* protects against non-alcoholic fatty liver disease in mice. *PLoS ONE*. 2014;*9*(1):e80169.
41. Yadav H, Jain S, Sinha P. Formation of oligosaccharides in skim milk fermented with mixed dahi cultures, Lactococcus lactis ssp diacetylactis and probiotic strains of lactobacilli. *J Dairy Res*. 2007;74(2):154-159.
42. Yin YN, Yu QF, Fu N, Liu XW, Lu FG. Effects of four Bifidobacteria on obesity in high-fat diet induced rats. *WJG*. 2010;16(27):3394-3401.
43. Reichold A, Brenner S, Spruss A, et al. Bifidobacterium adolescentis protects from the development of nonalcoholic steatohepatitis in a mouse model. *J Nutr Biochem*. 2014;25:118-125.
44. Plaza-Díaz J, Fernandez-Caballero JÁ, Chueca N, et al. Pyrosequencing analysis reveals changes in intestinal microbiota of healthy adults who received a daily dose of immunomodulatory probiotic strains. *Nutrients.* 2015;7:3999-4015.
45. Savcheniuk OA, Virchenko OV, Falalyeyeva TM, et al. The efficacy of probiotics for monosodium glutamate-induced obesity: Dietology concerns and opportunities for prevention. *EPMA J*. 2014;5(1):2.
46. Kobyliak N, Conte C, Cammarota G, Haley AP, et al. Probiotics in prevention and treatment of obesity: A critical view. *Nutri Metab*. 2016;13(1):1-13.
47. Kobyliak N, Conte C, Cammarota G, Haley AP, et al. Probiotics in prevention and treatment of obesity: A critical view. *Nutri Metab*. 2016;13(1):1-13.
48. Bayat A, Azizi-Soleiman F, Heidari-Beni M, et al. Effect of cucurbita ficifolia and probiotic yogurt consumption on blood glucose, lipid profile, and inflammatory marker in type 2 diabetes. *Internat J Prevent Med*. 2016;7:30.

49. Hariri M, Salehi R, Feizi A, Mirlohi M, Ghiasvand R, Habibi N. A randomized, double-blind, placebo-controlled, clinical trial on probiotic soy milk and soy milk: Effects on epigenetics and oxidative stress in patients with type II diabetes. *Gene Nutrit*. 2015;10(6):52.
50. Ejtahed HS, Mohtadi-Nia J, Homayouni-Rad A, et al. Effect of probiotic yogurt containing Lactobacillus acidophilus and Bifidobacterium lactis on lipid profile in individuals with type 2 diabetes mellitus. *J Dairy Sci*. 2011;94:3288-3294.
51. Ejtahed HS, Mohtadi-Nia J, Homayouni-Rad A, Niafar M, Asghari-Jafarabadi M, Mofid V. Probiotic yogurt improves antioxidant status in type 2 diabetic patients. *Nutrition*. 2012;28:539-543.
52. Taranto M, Medici M, Perdigon G, Ruiz H, Valdez G. Effect of Lactobacillus reuteri on the prevention of hypercholesterolemia in mice. *J Dairy Sci*. 2000;83:401-403.
53. Gilliland SE, Speck ML. Deconjugation of bile acids by intestinal lactobacilli. *Appl Environ Microbiol*. 1977;33:15-18.
54. Ettinger G, MacDonald K, Reid G, Burton JP. The influence of the human microbiome and probiotics on cardiovascular health. *Gut Microbes*. 2014;5(6):719-728.
55. Aggarwal J, Swami G, Kumar M. Probiotics and their effects on metabolic diseases: An update. *J Clin Diagnost Res*. 2013;7(1):173-177.
56. Vajro P, Mandato C, Licenziati M, Franzese A, Vitale D, Lenta S. Effects of Lactobacillus rhamnosus strain GG in pediatric obesity-related liver disease. *J Pediatr Gastroenterol Nutr*. 2011;52:740-743.
57. Aller R, De Luis DA, Izaola O, et al. Effect of a probiotic on liver aminotransferases in nonalcoholic fatty liver disease patients: A double blind randomized clinical trial. *Eur Rev Med Pharmacol Sci*. 2011;15(9):1090-1095.
58. Nabavi S, Rafraf M, Somi MH, Homayouni-Rad A, Asghari-Jafarabadi M. Effects of probiotic yogurt consumption on metabolic factors in individuals with nonalcoholic fatty liver disease. *J Dairy Sci*. 2014; 97:7386-7393.
59. Alisi A, Bedogni G, Baviera G, et al. Randomised clinical trial: The beneficial effects of VLS3 in obese children with non-alcoholic steatohepatitis. *Aliment Pharmacol Ther*. 2014;39:1276-1285.
60. Tremellen K, Pearce K. Dysbiosis of gut microbiota (DOGMA): A novel theory for the development of polycystic ovarian syndrome. *Med Hypoth*. 2016;*79*(1):104-112.Ejtahed HS, Mohtadi-Nia J, Homayouni-Rad A, et al. Effect of probiotic yogurt containing *Lactobacillus acidophilus* and *Bifidobacterium lactis* on lipid profile in individuals with type 2 diabetes mellitus. *J Dairy Sci*. 2011;94:3288-3294.
61. Rao AV, Bested AC, Beaulne TM, et al. A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. *Gut Pathog*. 2009;1(1):6.
62. Frémonta M, Coomansb D, Massartc S, De Meirleir K. High-throughput 16S rRNA gene sequencing reveals alterations of intestinal microbiota in myalgic encephalomyelitis/chronic fatigue syndrome patients. *Anaerobe*. 2013;22:50-56.
63. Groeger D, O'Mahony L, Murphy EF, et al. Bifidobacterium infantis 35624 modulates host inflammatory processes beyond the gut. *Gut Microbes*. 2013;4(4):325-339.
64. Giloteaux L, Goodrich J, Walters W, Levine S, Ley R, Hanson, M. Reduced diversity and altered composition of the gut microbiome in individuals with myalgic encephalomyelitis/chronic fatigue syndrome. *Microbiome*. 2016;4(1):30
65. Sullivan A, Nord CE, Evengard B. Effect of supplement with lactic-acid producing bacteria on fatigue and physical activity in patients with chronic fatigue syndrome. *Nutr J*. January 2009;8:4.
66. Galland L. The gut microbiome and the brain. *J Med Food*. 2014;17(12):1261-1272.
67. Samsel A, Seneff S. Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies. *Surg Neurol Internat*. 2015;6:45.
68. Choppa SK, Akuhad A, Kaur IP. Role of Lactobacillus acidophilus loaded floating beads in chronic fatigue syndrome: Behavioral and biochemical evidences. *India Neurogastroenterol Motil*. 2012;24(4):366-e170.
69. Quevrain E, Maubert MA, Michon C, et al. Identification of an anti-inflammatory protein from Faecalibacterium prausnitzii, a commensal bacterium deficient in Crohn's disease. *Gut*. 2016;65(3),415-425.
70. Sanders ME. Probiotics: definition, sources, selection, and uses. *Clin Infect Dis*. 2008;46(Suppl 2):S58-S60.
71. Sanders ME. Probiotics, strains matter. *Funct Foods Nutraceut Mag*. 2007;48:36-41.
72. Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002–2012. *Nat Health Stat Rep*. 2015;79:1.
73. Berkley Wellness. Probiotics pros and cons. http://www.berkeleywellness.com/supplements/other-supplements/article/probiotics-pros-and-cons. Published March 3, 2014. Accessed December 24, 2016.
74. Boyle RJ, Robins-Browne RM, Tang ML. Probiotic use in clinical practice: What are the risks? *Am J Clin Nutrit*. 2006;83(6):1256-1264.
75. Venugopalan V, Shriner KA, Wong-Beringer A. Regulatory oversight and safety of probiotic use. *Emerg Infect Dis*. 2010;16(11):1661-1665. Hawrelak J. https://www.probioticadvisor.com/. Published 2015. Accessed December 24, 2016.
76. Skokovic-Sunjic D. Clinical guide to probiotic products. http://usprobioticguide.com/. Published 2016. Accessed December 24, 2016.