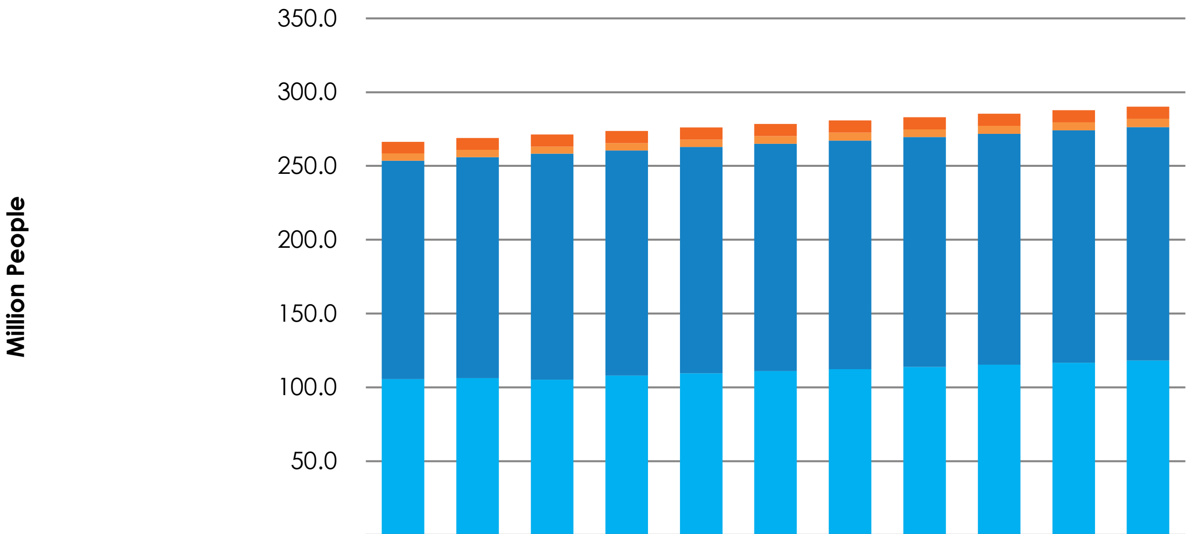
LABOR PRODUCTIVITY GAINS FROM THE USE OF PROBIOTICS BY SUFFERERS OF IRRITABLE BOWEL SYNDROME

The Burden and Social Consequences

Irritable Bowel Syndrome (IBS) is a gastrointestinal tract disorder that causes significant abdominal pain to sufferers and can significantly impact quality of life. Due to changes in bowel movement frequency and stool form, IBS leads to higher-than-expected absenteeism from work or school which in turn impacts productivity [156]. IBS puts a heavy burden on sufferers, and they can struggle to cope with its increasing prevalence, as well as the consequential increasing costs of managing the disease condition. IBS affects all Americans of all ages and backgrounds. Specifically, 13.0 million U.S. adults aged 18 and older have IBS, an event risk of 5.0% [157].

Chart 28. Target Population Size and Prevalence of Irritable Bowel Syndrome, United States, Adults Aged 18 and older, 2020-2030



	'20	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Employed Adults w/IBS	7.8	7.9	8.1	8.1	8.1	8.2	8.2	8.2	8.3	8.3	8.4
Non-working Adults with IBS	4.9	5.0	4.9	5.0	5.1	5.2	5.2	5.3	5.4	5.4	5.5
Healthy Employed Adults	147.9	149.7	153.0	152.4	153.3	154.1	154.9	155.8	156.6	157.4	158.2
Healthy Non-working Adults	105.7	106.2	105.2	108.1	109.5	110.9	112.4	113.8	115.3	116.7	118.2
All Adults Age 18 and Older	253.6	256.0	258.2	260.5	262.8	265.0	267.3	269.6	271.8	274.1	276.4

Source: Doshi et al 2014, Palsson et al. 2020, Source: U.S. Bureau of Labor Statistics, US Census, and Frost & Sullivan analysis

Table 66. Target Population Size and Prevalence of Irritable Bowel Syndrome, United States, Adults Aged 18 and older, 2020-2030

Year	Total Population, age 18 and older (million people)	Population of Labor Force (Employment) (million people)	Population, Diagnosed with IBS (million people)	Population of Labor Force (Employment), Diagnosed with IBS (million people)
2021	255.97	157.68	12.90	7.94
2022	258.24	161.14	13.01	8.12
2023	260.50	160.48	13.12	8.08
2024	262.77	161.38	13.23	8.12
2025	265.04	162.26	13.34	8.16
2026	267.31	163.14	13.45	8.21
2027	269.57	164.01	13.56	8.25
2028	271.84	164.87	13.67	8.29
2029	274.11	165.73	13.78	8.33
2030	276.38	166.57	13.89	8.37
Average ('22-'30)	267.31	163.29	13.45	8.21
CAGR	0.9%	0.6%	0.8%	0.6%

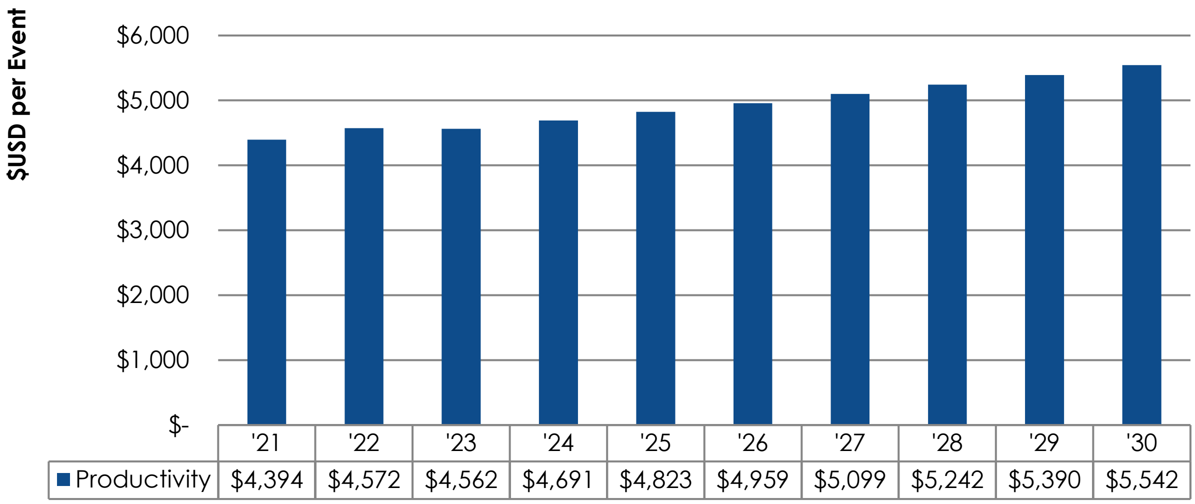
Source: Doshi et al 2014, Palsson et al. 2020, Source: U.S. Bureau of Labor Statistics, US Census, and Frost & Sullivan analysis

Measuring the degree of suffering of IBS patients requires the examination by medical professionals who uses a variety of similar questionnaires to assess self-reported pain and suffering and information regarding abdominal pain, distension, flatulence, and rumbling of the gut are common areas of investigation across the various types of IBS tests available [158]. Common IBS examination scores include the composite IBS symptom score (Total IBS-SSS), Abdominal Pain Severity - Numeric Rating Scale (APS-NRS), Visual Analogue Scale (VAS) for pain ratings, and self-reported Quality of Life (QoL) scores [159]. What is common across all of these scoring systems despite having different scoring ranges is that a higher score typically indicates a greater burden, so any percent reductions in scores can be standardized and compared across related studies using standardized weighted mean differences in severity of symptoms compared to a common baseline.

Researchers from the University of Pennsylvania found that individuals with IBS with constipation paid an additional $6,703 per year on average in additional medical costs compared to non-IBS people and an additional $1,363 per year in 2010 [156]. Productivity losses also add up. Sickness-attributed absenteeism is the phenomenon of missing work due to disability arising from any type of illness or injury which in turn leads to substantial costs to all stakeholders involved including workers who may lose wages, employers who are obligated to pay unproductive wages and even governments in terms of lost tax potential, higher social welfare, and health care costs [160]. In a 2015 survey of Americans who suffer from IBS conducted by Gfk Public Affairs & Corporate

Communications of 3,254 individuals, it was discovered that respondents missed approximately 1.5 days of work or school or month due to IBS-related reasons or an estimated 144 hours per year assuming full employment and an 8-hour work schedule [161].

Chart 29. Average Productivity Losses Caused by Irritable Bowel Syndrome Episode-attributed Absenteeism, $USD per Sufferer per year, United States, 2020-2030



Source: U.S. Bureau of Labor Statistics and Frost & Sullivan analysis

In 2022, 161.1 million people aged 18 and older are in the American workforce given an employment rate of 62.4% [162]. In 2022, the average American is expected to have worked 1,708 hours per year (which is equivalent to about nearly 33 hours per week per person) at an average hourly wage of $31.75 per hour [162]. Assuming that the demographic characteristics of IBS sufferers is representative of the American workforce except for the disease state, it is expected that the population of wage earners with IBS in 2022 was 8.12 million individuals aged 18 and older and the value of loss wages due to their IBS absenteeism was $37.1 billion in 2022 and is expected to be an annual average of $41.0 billion per year in productivity losses from 2022 to 2030. The per capita health care costs and productivity losses caused by irritable bowel syndrome episode-attributed absenteeism is shown in Table 67 and the derivation process for the annual value of loss wages due to IBS absenteeism is shown in Table 68.

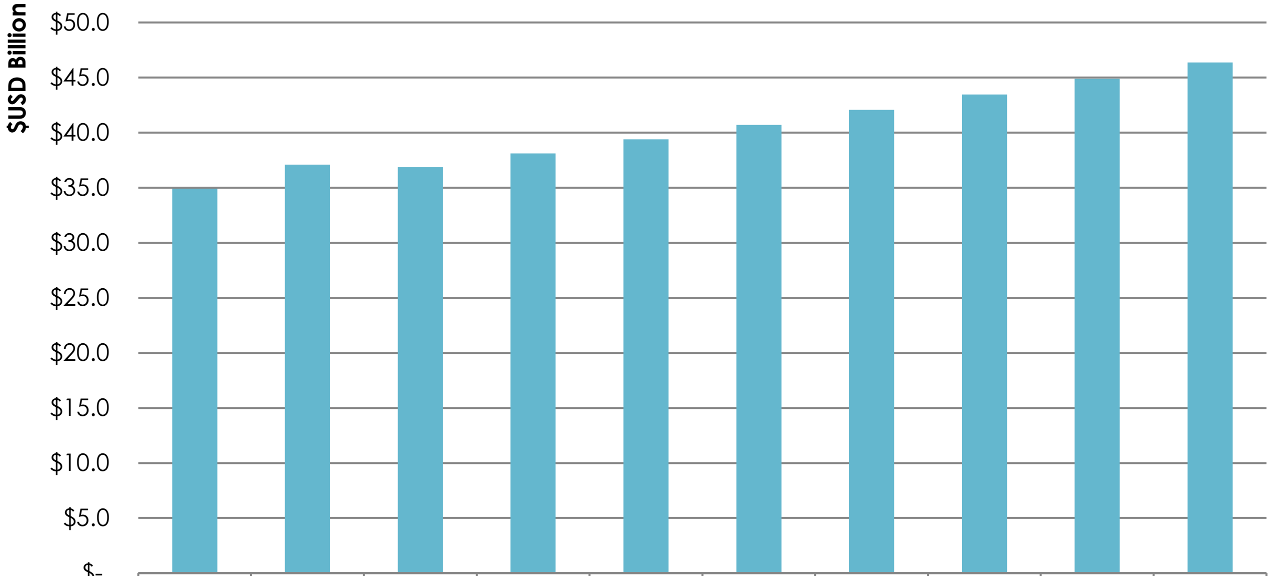
Table 67. Per Capita Health Care Costs and Productivity Losses Caused by Irritable Bowel Syndrome Episode-attributed Absenteeism, $USD per Sufferer per year, United States, 2020-2030

Year	IBS, Cost of Medical ($ per Event Case)	IBS, Cost of Pharma ($ per Event Case)	IBS, Cost per Event Case ($ per Event Case)	IBS, Loss in Productivity ($ per Event Case)	IBS, Population Lost Productive Time Due to IBS Event ($ billion)
2021	$8,513	$1,731	$14,564	$4,395	$34.91
2022	$8,703	$1,770	$14,889	$4,572	$37.11
2023	$8,897	$1,809	$15,221	$4,563	$36.87
2024	$9,096	$1,849	$15,561	$4,691	$38.10
2025	$9,299	$1,891	$15,908	$4,823	$39.38
2026	$9,506	$1,933	$16,263	$4,959	$40.70
2027	$9,718	$1,976	$16,626	$5,099	$42.05
2028	$9,935	$2,020	$16,998	$5,243	$43.45
2029	$10,157	$2,065	$17,377	$5,391	$44.90
2030	$10,384	$2,111	$17,765	$5,542	$46.38
Average ('22-'30)	$9,522	$1,936	$16,290	$4,987	$40.99
CAGR	2.2%	2.2%	2.2%	2.6%	3.2%
Cumulative ('22-'30)					$368.94

Source: U.S. Bureau of Labor Statistics and Frost & Sullivan analysis

Prevention of episodes that leads to absenteeism is critical in minimizing productivity losses. An IBS episode is partially preventable, or its seriousness can be significantly reduced, if the IBS sufferer adopts the use of certain regimens that is known to be effective. One area of growing interest is the role of certain key dietary supplements, especially the role that probiotic supplements, can play in lowering a person’s odds of experiencing a severe IBS episode. In this report, a review of the literature that looks at the use of probiotic supplements on the severity of an IBS-attributed episode experienced by sufferers will be undertaken in order to determine the size of the expected health benefit. Then, this expected health benefit will used as a key input in an economic analysis that aims to understand the value of absent time saved due to the relieve in suffering of the IBS workforce.

Chart 30. Total Population Productivity Losses Attributed to Irritable Bowel Syndrome, $USD Billion, United States, 2021-2030



	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Total	$34.91	$37.11	$36.87	$38.10	$39.38	$40.70	$42.05	$43.45	$44.90	$46.38

Source: Doshi et al 2014, Palsson et al. 2020, Source: U.S. Bureau of Labor Statistics, US Census, and Frost & Sullivan analysis

Table 68. Productivity Statistics of the American Workforce and the Derivation Process for the Annual Value of Loss Wages due to IBS Absenteeism, 2022

Metric	Measure
Population of labor force (Employment) - million people	161.14 M
Population of labor force (Employment) - % of population	62.4%
Average hourly earnings of all employees, total private - $/hour	$31.75 / hour
Average annual hours worked - hours per Year	1,708 / year
Total US wages - $ billion	$8,741 B
Estimated workforce of people with IBS - million people	8.12 M
Number of hours loss due to IBS-attributed absenteeism per IBS worker	144 hours
Total population productivity losses due to IBS, $USD billion	$37.1 B

Source: Doshi et al 2014, Palsson et al. 2020, Source: U.S. Bureau of Labor Statistics, US Census, and Frost & Sullivan analysis

Table 69. Irritable Bowel Syndrome Cost Summary Statistics for All U.S. Working Adults, Age 18 and over, 2021–2030

Metric	'21	CAGR ('21 - '30)	Average ('22 - '30)
Total workforce, million people	157.68 M	0.61%	163.29 M
Total workforce with IBS, million people	7.94 M	0.58%	8.21 M
Indirect cost of IBS, productivity losses, $USD per sufferer per year	$4,395	2.61%	$4,987
Total productivity losses due to IBS, $USD billion	$34.9 B	3.21%	$41.0 B
Price inflation rate, %	6.95%	--	2.23%

Source: Doshi et al 2014, Palsson et al. 2020, Source: U.S. Bureau of Labor Statistics, US Census, and Frost & Sullivan analysis

A significant amount of clinical research has already been published exploring the association between the use of probiotics by sufferers of IBS for productivity-debilitating symptom relief. In this update study, we examine the potential productivity gains that could be realized if workers with IBS were to regularly use probiotics as a means to reduce productivity-debilitating symptoms. Specifically, this report will examine evidence that demonstrates that the use of probiotics can bring relief to users which in turn can lead to reduced productivity losses associated with absenteeism.

The overarching research methodology used in this economic report is based on a health-to-wealth Cost-Benefit Analysis (CBA) model created in 2013 to address this topic [4]. This model was built to allow the comparison of dietary supplement users versus non-users in terms of any changes in disease-attributed risk which in turn would imply that associated disease treatment and management costs were different as well. Specifically, this CBA can be used to assess various use (and non-use) scenarios and to identify the potential savings or loss that can be realized in one scenario versus another. The determination of whether a given dietary supplement regimen is cost-effective is based on the risk level faced by the user's risk profile, the supplement's effectiveness at reducing the risk of the potential supplement user and the magnitude of the economic consequences (costs) that could be incurred if the potential user did not use the supplement and experienced a medical event [4].

This issue is similar to the basic methodology of most clinical studies; the treatment's effect on the outcome of a given event can be assessed when a treatment regimen is applied to one group versus a control group. From these types of analyses, risk—and possible risk reduction—can be calculated using a cost-benefit model which can be useful to key decision makers (including patients, health care professionals, governments, insurance companies, and employers) in determining if a given regimen is cost-effective.

To find the true effect size of treatment for a given dietary supplement, a rigorous search for clinical research studies and meta-analyses of clinical research studies for each of the seven interventions was conducted to deduce the expected efficacy of dietary supplementation on the incidence of disease events that required medical treatment and/or resulted in increased costs due to disease management and productivity losses. The aim is to collect a comprehensive set of studies that represented the totality of evidence of efficacy for a given dietary supplement's effects on the relative risk of a specific disease event.

Regarding cost estimate forecasts, expected compound annual growth rates (CAGR) were derived from a historic assessment of population growth rates and price inflation growth. Specifically, health care costs per person are expected to grow at an average annual growth rate of 2.2% from 2022 to 2030 based on the observed average price inflationary growth rate over the last 10 years. Given current inflation rates, we consider this expected growth rate to be conservative. Also, this growth rate was applied for all procedures for all conditions assessed in this study. Growth in the targeted population was expected to occur at the average annual growth rate of the population as a whole during the forecast period, and it was assumed that growth in disease incidence is equal to population growth based on a review of population growth and disease incidence trends. Dietary supplement retail prices were expected to grow at a compound annual growth rate of 2.2% per year, the same as price growth in general. The authors do not endorse the specific findings of any scientific study reviewed.

Probiotics

Literature Review

As defined by the International Scientific Association for Probiotics and Prebiotics (ISAPP), "Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host [163]." Also, "[l]ive microorganisms may be present in many foods and supplements, but only characterized strains with a scientifically demonstrated effect on health should be called probiotics." Gut microbiota must maintain homeostasis to prevent diseases from entering the body. The exact characterization, function, and interaction of microbiota with the host body are important research areas for the development of innovative therapeutic solutions and applications in other industries.

The microbiome refers to the genome of all microorganisms, including symbiotic (benefitting the host and microbiota) and pathogenic (promoting disease), living in humans, animals, and plants. Symbiotic and pathogenic microbiota coexists peacefully in a healthy body, but any disturbance to their coexistence will make the body vulnerable to disease, including in the gut. Microbiota use digestive enzymes to help break down compounds such as starch and fibers. Also, the microbiota can disintegrate indigestible fibers, creating short-chain fatty acids that influence muscle function and prevent chronic diseases, including some bowel disorders.

Live microorganisms may be present in many foods and supplements, however only characterized strains with demonstrated effect on health are termed to be probiotics. Probiotics are generally known by genus, species, and strains. Different strains of the same species have different health effects. The amount of dose administered or consumed is the key as higher doses may not necessarily have a greater health benefit. The dose level should ideally match with the efficacy studies that confer benefits. Probiotics have been researched for decades to prove health benefits, however not all benefits are delivered by just one product or strain.

Lactobacilli and bifodobacteria are the dominate probiotic genera from which most proprietary probiotic strains are based [164]. All other strains make up less than 10% of all probiotics in the marketplace [164]. Hence, the majority of the scientific research on probiotics has used some combination of lactobacilli and bifodobacteria strains in the experimental supplement formulations being tested for gastrointestinal health benefits, though the amount of each strain used in a given formulation and the strain mix used widely varies across studies.

Due to the wide variety of strains and product forms in the marketplace, there is no agreed upon recommended intake level for probiotics. Suggested intake levels depend on strain and target condition. Plus, probiotics are not necessary for use daily, but only when an individual's microbiota is imbalanced. According to the International Probiotics Association, daily doses of 5 to 10 billion colony forming units (CFUs) has been shown to be effective at reducing antibiotic-associated diarrhea (AAD) in children [165]. With respect to this study's systematic review, the typical (mode) dose size to help reduce severity of IBS-attributed pain is 10 billion CFUs per day of required use.

Overall, the breadth and depth of scientific research exploring the association between use of probiotics and the severity in IBS-attributed discomfort is significant. However, the literature is quite heterogeneous with respect to study design, types of effect sizes measured, dose size, strain types and mixes, and types of IBS. In 2016, Ford et al. conducted a meta-analysis of 43 RCTs and found that the RR of IBS symptoms persisting among probiotic users versus placebo was 0.79 (95% CI 0.70-0.89). This means that over 20% more people reported relief in the probiotic group compared to the placebo group [166]. In 2014, researchers found that quality of life of IBS sufferers improved significantly among probiotic users versus placebo (IBS-QoL 18 ± 3 points (P = 0.041) and 22 ± 4 points (P = 0.023) in the high and the low dose groups, respectively [167].

To infer the expected efficacy of using probiotics on reducing the severity of an IBS episode that motivates absenteeism, a literature review was conducted in December 2021 that focused on published studies that directly tested for and quantified the effect of Probiotic supplementation on the severity of IBS episodes reported by sufferers. The goal of this study was to collect a comprehensive sample of studies that represented the state of all scientific literature on Probiotic supplementation as it related to reducing self-reported gastrointestinal pain among individuals diagnosed with IBS. It was preferred that the selected studies were similar in study protocol in an attempt to control for likely differences in study protocol, though this is not always possible due to the nature of this body of research being highly heterogeneous with respect to types of probiotic strains used in the formulations. Specifically, of the various study methods found for probiotic supplementation, randomized controlled trials (RCT) were preferred because they are designed to directly test for a cause-and-effect relationship between treatment and outcome. Studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings.

One hundred forty-nine (149) studies were found in a PubMed search based on the use of "probiotic" or "supplement" and "irritable bowel syndrome" and "pain" as filtering keywords. The search was conducted between December 1, 2021, and May 31, 2022. After reviewing all studies' titles, abstracts, and full-texts, 19 RCTs consisting of 24 test arms were identified as being representative of the hypothesis being tested and these studies were used to deduce the estimated efficacy of using any probiotic supplement on reducing IBS-related gastrointestinal pain. Tables 70 and 71 provide a description of the selection of included studies in the final meta-analysis described below.

Table 70. Probiotics Literature Review: Description of the Qualified Studies

REF.	Author	Publication Year	Event definition	Product Description
168	Skrzydło-Radomańska B	2021	Total IBS-SSS	A mixture of Lactobacillus, Bifidobacterium, and Streptococcus thermophilus
169	Lewis ED	2020	Total IBS-SSS	L. paracasei
169	Lewis ED	2020	Total IBS-SSS	B. longum
170	Martoni CJ	2020	APS-NRS Score	L. acidophilus DDS-2
170	Martoni CJ	2020	APS-NRS Score	B. lactis UABla-13
170	Martoni CJ	2020	Total IBS-SSS	L. acidophilus DDS-2
170	Martoni CJ	2020	Total IBS-SSS	B. lactis UABla-13
171	Sadrin S	2020	VAS Composite	2-strain mixture of Lactobacillus acidophilus
172	Oh JH	2019	Abdominal pain (VAS)	mixture of lactobacilli probiotics
173	Preston K	2018	QoL Improvement	A combination of Lactobacillus acidophilus CL1285, Lactobacillus casei LBC80R and Lactobacillus rhamnosus CLR2
159	Lyra A	2016	Severity of pain	One capsule per day containing either 109 (low dose) or 1010 (high dose) CFU of L. acidophilus NCFM (ATCC 700396).
174	Stevenson C	2014	QoL Improvement	Two capsules of L. plantarum 299v
175	Lorenzo-Zúñiga V	2014	QoL Improvement	Combination of three strains of lactic acid bacteria: two Lactobacillus plantarum (CECT7484 and CECT7485) and one Pediococcus acidilactici (CECT7483)
175	Lorenzo-Zúñiga V	2014	QoL Improvement	Combination of three strains of lactic acid bacteria: two Lactobacillus plantarum (CECT7484 and CECT7485) and one Pediococcus acidilactici (CECT7483)
176	Yoon JS	2014	Abdominal pain	Patients were randomly assigned to two groups: either to receive multi-species probiotics (a mixture of Bifidobacterium longum, Bifidobacterium bifidum, Bifidobacterium lactis, Lactobacillus acidophilus, Lactobacillus rhamnosus, and Streptococcus thermophilus) twice a day for four weeks, or to receive a placebo twice a day for four weeks.
177	Ducrotté P	2012	Abdominal pain (VAS)	L. plantarum 299v
178	Ki Cha B	2012	VAS Composite	Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus rhamnosus, Bifidobacterium breve, Bifidobacterium lactis, Bifidobacterium longum, and Streptococcus thermophilus 1.0 1010 CFU) groups
179	Williams EA	2009	Total IBS-SSS	Lactobacillus acidophilus CUL60 (NCIMB 30157) and CUL21 (NCIMB 30156), Bifidobacterium lactis CUL34 (NCIMB 30172) and Bifidobacterium bifidum CUL20 (NCIMB 30153)
180	Sinn DH	2008	Abdominal pain	Lactobacillus acidophilus-SDC 2012, 2013
181	Kajander K	2008	Total IBS-SSS	Lactobacillus rhamnosus GG, L. rhamnosus Lc705, Propionibacterium freudenreichii ssp. shermanii JS and Bifidobacterium animalis ssp. Lactis Bb12
182	Whorwel, P	2006	Abdominal pain or discomfort	B. longum 35624
183	O'Mahony L	2005	VAS Composite	B. longum 35624

Note: All figures are rounded. Source: Frost & Sullivan

Table 71. Probiotics Literature Review: Description of the Qualified Studies (continued)

REF.	Author	Dose Size (CFU billion)	Study Duration (Days)	Sample Size	Treatment Group Size	Control Group Size
168	Skrzydło-Radomańska B	250	56	48	25	23
169	Lewis ED	10	56	165	84	81
169	Lewis ED	10	56	164	83	81
170	Martoni CJ	10	42	220	111	109
170	Martoni CJ	10	42	219	110	109
170	Martoni CJ	10	42	220	111	109
170	Martoni CJ	10	42	219	110	109
171	Sadrin S	10	56	80	40	40
172	Oh JH	10	28	50	26	24
173	Preston K	50	84	85	58	27
159	Lyra A	10	84	228	110	118
174	Stevenson C	5	70	81	54	27
175	Lorenzo-Zúñiga V	20	42	56	27	29
175	Lorenzo-Zúñiga V	200	42	57	28	29
176	Yoon JS	10	28	49	25	24
177	Ducrotté P	10	28	204	105	99
178	Ki Cha B	10	56	50	25	25
179	Williams EA	250	56	52	28	24
180	Sinn DH	10	28	40	20	20
181	Kajander K	6	140	86	43	43
182	Whorwell P	0.1	28	182	90	92
183	O'Mahony L	10	56	64	25	25

Note: Dose size as measured by CFU should not be used as an indication of strength of efficacy. Efficacy and CFU varies by strain type. All figures are rounded. Source: Frost & Sullivan

Clinical research in the probiotic for gastrointestinal health remains an active field of clinical research and a number of studies demonstrating probiotic supplement's efficacy has been published just within the last decade. A 12-week study consisting of 340 IBS adult volunteers in 2016 explored the efficacy of using Lactobacillus acidophilus on IBS symptoms and quality of life (QoL) [159]. The researchers found that IBS-SSS improved over a 12-week treatment in volunteers with moderate to severe abdominal pain at baseline (VAS > 35/100) [159]. Specifically, pain scores fell by 29.4 ± 17.9and 31.2 ± 21.9 in the placebo, active low-dose, and active high-dose groups versus the 20.8 ± 22.8 in the control group respectively (P value for placebo versus combined active doses = 0.046) [159].

In 2019, researchers in Vietnam invested whether use of a mixture of lactobacilli probiotics could improve abdominal symptoms in subjects with IBS [172]. Once a day, 50 subjects took either a placebo or a probiotic supplement based on a mixture of lactobacilli strains and abdominal pain visual analogue scale was assessed after 4 weeks of use [172]. The study found that use of lactobacilli-based probiotics significantly improved observed VAS scores in the probiotic group (p = 0.048) [172].

And in 2018, researchers reported that self-reported quality of life was improved among IBS users of probiotic supplements based on the strains Lactobacillus acidophilus CL1285, Lactobacillus casei LBC80R and Lactobacillus rhamnosus CLR2 [173]. Specifically, 113 subjects were randomized into two groups and given either a placebo or a probiotic supplement formulation using the aforementioned strains at a 50×109 CFU concentration daily for 12 weeks [173]. The key finding from this study was that quality of life was improved, especially when it came to stool frequency and consistency among the treatment group [173].

Researchers in 2020 reported the results of their double-blind RCT that included 336 subjects aged 18 to 70 which investigated the efficacy of two probiotic strains on both abdominal pain severity (APS-NRS) and total IBS-SSS score from baseline [170]. Subjects with IBS according to Rome IV criteria were either provided for 6 weeks a placebo, a supplement containing Lactobacillus acidophilus DDS-1 (1 × 1010 CFU/day) or a supplement containing Bifidobacterium animalis subsp. lactis UABla-12 (1 × 1010 CFU/day) [15]. APS-NRS was significantly improved in both probiotic groups vs. placebo in absolute terms (DDS-1: -2.59 ± 2.07, p = 0.001; UABla-12: -1.56 ± 1.83, p = 0.001) and improvement was observed in IBS Symptom Severity Scale (IBS-SSS) scores for L. acidophilus DDS-1 (-133.4 ± 95.19, p < 0.001) and B. lactis UABla-12 (-104.5 ± 96.08, p < 0.001) groups vs. placebo [170].

Also in 2020, scientists explored the effectiveness of two probiotic supplement formulations based on Lactobacillus paracasei HA-196 (L. paracasei) and Bifidobacterium longum R0175 (B. longum), respectively, on reducing physical and psychological symptoms of IBS [14]. Two hundred fifty-one adults were randomized to take one of the two different probiotic supplements or a placebo for 4-

and 8-week study durations [169]. The researchers found that use of L. paracasei-based probiotic supplements improved regularity in people with both IBS-constipation (IBS-C) and IBS-diarrhea (IBS-D) and both formulations significantly improved self-reported quality-of-life in emotional well-being baseline ($p < 0.05$) [169].

Another study published in 2020 aimed to show that a two-strain mixture of Lactobacillus acidophilus improved irritable bowel syndrome symptoms, as proxied by an abdominal pain score assessed with a 100-mm visual analogue scale (VAS) among users versus placebo users [171]. In this 8-week study, 80 subjects were randomized into either the control group or the treatment group who were provided two capsules containing either Lactobacillus acidophilus probiotics at a concentration of 5 × 109 cfu per capsule daily [171]. The scientists found that the abdominal pain score between the two groups were not significantly different but that the probiotic treatment group did have improvement in the visual analogue scale (VAS) score after 8 weeks [171].

In 2021, researchers released the results of an RCT study that explored the efficacy of multi-strain probiotic in adults with diarrhea-predominant irritable bowel syndrome (IBS-D) [168]. The multi-strain probiotic supplement contained a mixture of Lactobacillus, Bifidobacterium, and Streptococcus thermophilus strains and the study duration was 8 weeks [168]. Use of the multi-strain probiotic supplement significantly improved the IBS symptom severity (the change of total IBS-SSS score from baseline –165.8 ± 78.9 in the probiotic group versus –105.6 ± 60.2 in the placebo group, $p = 0.005$) and secondary end points also demonstrated that the severity of pain ($p = 0.015$) and the quality-of-life ($p = 0.016$) improved in the treatment group after eight weeks [168].

To deduce the effect of using probiotics on reducing the severity of an IBS episode that motivates absenteeism, a random-effects meta-analysis model was developed which is best model for deducing the true treatment effect from a set of clinical research citations that varies by sample size, methodologies and study protocols, and patient population dynamics [184, 185]. This approach allows for a systematic and objective approach to weighing each of the qualified reported effects sizes [184, 185].

Based on applying the random-effects meta-analysis model to the qualified set of clinical studies described above, it is expected that the weighted standard mean difference (WSMD) in the severity of reported IBS episodes by those using probiotic supplements, or the reported Cohen's d score, is 0.516 (95% CI: 0.200 – 0.833) after controlling for variance caused by study sample size, research protocols, and patient population differences within each study and among all studies. A Cohen's d effect size score is a way to standardize similar types of tests into one overarching expected effect size. All of the different types of quality-of-life scales used by the researchers in the eligible studies measured the mean difference in pain and/or quality of life scores before and after treatment and, independent of the scoring system used, it would be expected that the distribution of IBS severity would be different between the user group and the non-user group. It can be shown that an effect size of 0.516 means that approximately 65.3% of the treatment population are feeling similar levels of discomfort and pain as the participants in the control group and that 34.7% (95% CI: 15.2%-49.8%) of the treatment group is feeling equal to or better than the best feeling person in the control group [186]. Thus, 34.7% of probiotic supplement users with chronic IBS feel better and have an improved quality of life than the best-off person in the control group.

Given the nature of the disorder, the goal of managing IBS is to increase quality of life so that the individual can have a much more productive life. The topic of absenteeism caused by IBS is a good way to understand the direct economic impact of IBS as researchers first did in 2014 which estimated that the average number of days a worker with IBS is absent from work per month due to IBS-attributed symptoms was 1.5 days per month (or 144 hours per year) [161]. Since it is expected that 34.7% of the target population will experience improvements in symptoms, this portion of the population will be able to fully work and hence will not contribute to the average number of hours lost per year to absenteeism. In other words, a 34.7% reduction in absenteeism can be expected per user which is equivalent to a savings in 50.0 hours per year. Table 72 describes the empirical results of the included studies in the final systematic review and Table 73 reports the aggregated expected effect size of probiotics use on reducing the severity of an IBS episode.

Table 72. Probiotics Literature Review: Summary of Study Findings

REF.	Author	Standardized Mean Difference (Cohen's d, Improvement Effect Size)	95% Low	95% High
168	Skrzydło-Radomańska B	0.81	0.53	1.10
169	Lewis ED	0.06	-0.09	0.21
169	Lewis ED	-0.45	-0.60	-0.29
170	Martoni CJ	0.35	0.22	0.49
170	Martoni CJ	0.26	0.13	0.39
170	Martoni CJ	0.52	0.39	0.65
170	Martoni CJ	0.08	-0.05	0.21
171	Sadrin S	0.37	-0.23	0.21
172	Oh JH	3.70	1.29	1.85
173	Preston K	0.30	-0.17	0.26
159	Lyra A	0.14	0.01	0.27
174	Stevenson C	0.46	0.24	0.68
175	Lorenzo-Zúñiga V	1.56	1.30	1.82
175	Lorenzo-Zúñiga V	0.39	0.13	0.65
176	Yoon JS	0.39	0.11	0.67
177	Ducrotté P	0.05	0.01	0.28
178	Ki Cha B	1.46	1.18	1.73
179	Williams EA	3.42	3.14	3.69
180	Sinn DH	0.32	0.01	0.63
181	Kajander K	4.65	4.23	4.65
182	Whorwell P	1.36	1.40	1.32
183	O'Mahony L	0.44	0.38	0.50

Note: All figures are rounded. Source: Frost & Sullivan

Table 73. Expected Efficacy of Supplement Use Based on Literature Review, Probiotics

Metric	Measure
Standardized Weighted Mean Difference (weighted for intra-study variance) (WMD)	0.516 (95% CI: 0.200 – 0.833)
% Overlap of self-reported IBS discomfort distribution between the Treatment Group and Control Group, %	65.3% (95% CI: 50.2%-84.8%)
% of Treatment Group who feel better than the Control Group with respect to self-reported IBS discomfort, %	34.7% (95% CI: 15.2%-49.8%)
Number of Avoided Absentee Hours Lost due to IBS discomfort per Probiotic User, hours per user	50.2 hours
Population potential of number of Avoided Absentee Hours Lost due to IBS discomfort per Probiotic User, total population hours	650.58 M hours

Note: All figures are rounded. Source: Frost & Sullivan

Economic Implications

As already highlighted in the previous section, it is expected that the population of wage earners with IBS in 2022 was 8.12 million individuals aged 18 and older and the value of loss wages due to their IBS absenteeism was $37.1 billion in 2022 and is expected to be an annual average of $41.0 billion per year in productivity losses from 2022 to 2030. If 100% of the target population of IBS suffering wage earners used probiotic supplements consistently, the total potential savings in lost productivity due to avoiding 50.2 absentee hours per year per person would have been 650.6 million hours valued at $12.89 billion in 2022. From 2022 to 2030, the annual average in total potential saved wages will be $14.24 billion during the forecast period.

The daily cost of using probiotic supplements ought to be included in the final accounting in order to ensure that all cost components are considered in the final analysis. Based on the review of the best-selling retail probiotic supplement products currently sold through online sales channels, the median cost of a daily dose of probiotics is approximately $0.61 per day. Given this daily cost requirement, the median annual expected cost of probiotics dietary supplementation for all U.S. adults aged 18 and over would be $241.80 per person per year or $1.99 billion per year for the total target population of wage earners with IBS over the period 2022 to 2030. Table 74 provides a summary of the cost of dietary supplementation with probiotics of the entire target population.

Table 74. Probiotics Productivity Gains Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population*, 2022-2030

Metric	Measure
Median daily cost per person of Probiotic supplementation at protective daily intake levels, 2022	$0.61
Expected daily median cost per person of Probiotic supplementation at protective daily intake levels, 2022-2030	$0.66
Median annual cost per person of Probiotic supplementation at protective daily intake levels, 2022	$220.98
Expected annual median cost per person of Probiotic supplementation at protective daily intake levels, 2022-2030	$241.78
Total target population cost of Probiotic supplementation at protective daily intake levels, 2022	$1.79 B
Total target population cost of Probiotic supplementation at protective daily intake levels, 2022-2030	$1.99 B

Table 75 reports the economic implications of the systematic review finding of the beneficial use of Probiotic supplements to support cardiovascular health. Given the incurred cost of probiotics dietary supplementation, the net Productivity Gains expected from avoided absenteeism caused by severe IBS episodes would have been $11.10 billion in 2022 or $12.25 billion per year in net savings during the period 2022 to 2030. The above productivity gains results are the maximum savings potential that is obtainable if everyone in the target population (all adults aged 18 and older) had not used this product prior to the base year of analysis (e.g., 2022) and then 100% of the population adopted the probiotics regimen in the same year and gained all potential benefits. This assumption was made in order to calculate per capita net benefits which in turn can be used to calculate the net avoided productivity gains for the subset of the population yet to use probiotics. It follows that the calculation of avoided health care expenditures and net productivity gains yet to be realized is simply a proportional adjustment of the total potential avoided expenditures and net productivity gains.

Chart 31. Probiotics Productivity Gains Analysis: Labor Productivity Gains from the Use of Probiotic Supplements, 2022 Scenario Analysis

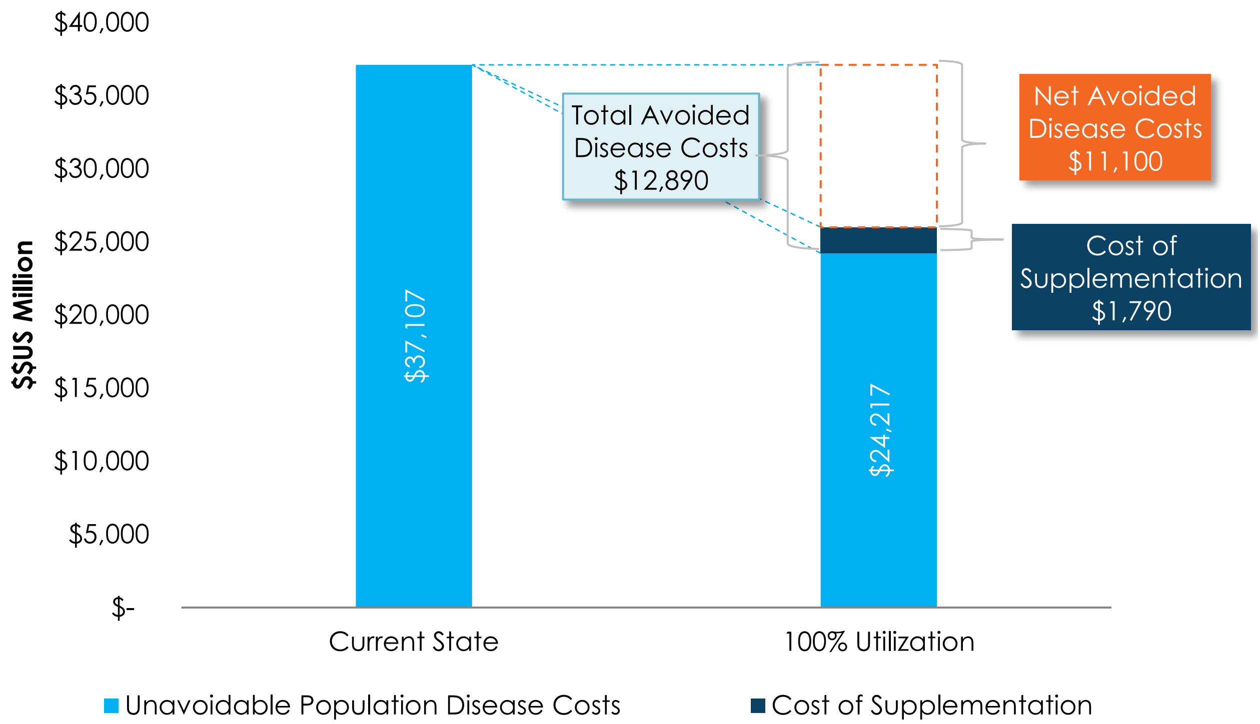
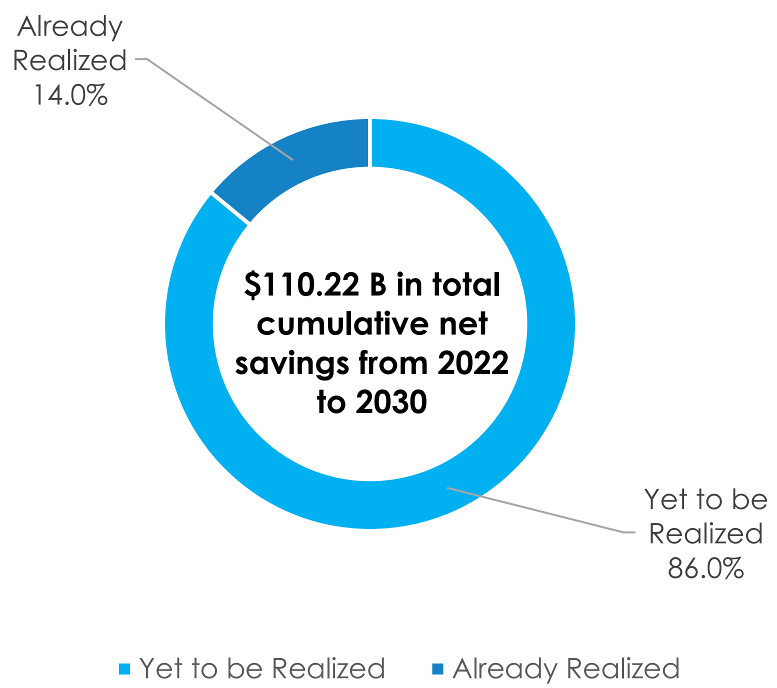


Table 75. Probiotics Productivity Gains Analysis: Summary Results—Avoided Productivity Losses due to Dietary Supplement Intervention, 2022-2030

Metric	Measure
Avoided loss wages from IBS-attributed absenteeism given Probiotic supplement intervention per year, 2022	$12.89 B
Average avoided loss wages from IBS-attributed absenteeism given Probiotic supplement intervention per year, 2022-2030	$14.24 B
Net loss wages from IBS-attributed absenteeism given Probiotic supplement intervention per year, 2022 (includes cost of supplementation)	$11.10 B
Net average avoided Loss Wages from IBS-attributed absenteeism given Probiotic supplement intervention per year, 2022-2030 (includes cost of supplementation)	$12.25 B
Net benefit cost ratio, $ Savings per one dollar spent on dietary supplement	$7.16
Cumulative Net Target Avoided Costs, 2022-2030 (NET BENEFITS) ($ billion)	$110.22 B

Today, the use of Probiotic supplements remains relatively low. According to the 2021 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, 14% of U.S. dietary supplement users aged 18 and over have used probiotics dietary supplements in the last 12 months [152]. Also, over 40% of US adults aged 18 and older are regular users of dietary supplements which implies that only 5.6% of the target population aged 18 and over reported using probiotics in the last months [152].

Chart 32. Probiotics Productivity Gains Analysis: Summary Results—Cumulative Net Productivity Gains Yet to be Realized due to Avoided Loss Wages through Probiotic Supplement Intervention, 2022-2030



Source: Council for Responsible Nutrition

Consequently, $9.54 billion of the $11.10 billion in net potential direct savings in 2022 from avoided loss wages because of probiotic supplement intervention will not be gained. If utilization rates go unchanged, an average productivity gains opportunity of $10.54 billion per year could be lost because of underutilization of probiotic dietary supplements. In conclusion, this case study's findings support the proposition that utilization of a probiotic supplement can help in lowering a person's odds of experiencing a severe IBS episode which in turn can lead to positive knock-on effects on the costs of labor productivity. Accordingly, adopting new regimens or routines that have been shown to help to minimize IBS-related episodes that a person might experience and pay for in terms of lost work hours ought to be considered.

Table 76. Probiotics Productivity Gains Analysis: Summary Results—Net Productivity Gains Yet to be Realized due to Avoided Productivity Losses through Dietary Supplement Intervention, 2022-2030

Metric	Measure
Net loss wages from IBS-attributed absenteeism given Probiotic supplement intervention yet to be realized per year, 2022	$9.54 B
Net average loss wages from IBS-attributed absenteeism given Probiotic supplement intervention yet to be realized per year, 2022-2030	$10.54 B
Cumulative net loss wages from IBS-attributed absenteeism yet to be realized, 2022-2030 (NET BENEFITS) ($ billion)	$94.83 B

Detailed Results

Table 77. Productivity Statistics of the American Workforce, 2022 – 2030

Year	Average Annual Hours Worked (Hours per Year)	Average Hourly Earnings of All Employees, Total Private ($/hour)
2021	1713.31	30.52
2022	1708.46	31.75
2023	1703.61	31.68
2024	1698.76	32.58
2025	1693.91	33.50
2026	1689.06	34.44
2027	1684.21	35.41
2028	1679.36	36.41
2029	1674.51	37.43
2030	1669.66	38.49
Average ('22-'30)	1689.06	34.63
CAGR	-0.3%	2.6%

Source: Frost & Sullivan

Table 78. Probiotics Productivity Gains Analysis: Detailed Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Year	Probiotics, Daily Cost of Supplementation ($ per day)	Probiotics, Annual Cost of Supplementation ($ per year)	Probiotics, Population Cost of Supplementation ($ billion)
2021	$0.59	$216.05	$1.716
2022	$0.61	$220.98	$1.793
2023	$0.62	$225.91	$1.825
2024	$0.63	$230.96	$1.876
2025	$0.65	$236.11	$1.928
2026	$0.66	$241.39	$1.981
2027	$0.68	$246.77	$2.035
2028	$0.69	$252.28	$2.091
2029	$0.71	$257.92	$2.148
2030	$0.72	$263.67	$2.207
Average ('22-'30)	$0.66	$241.78	$1.987
CAGR	2.2%	2.2%	2.8%
Cumulative ('22-'30)	--	--	$94.561

Source: Frost & Sullivan

Table 79. Probiotics Productivity Gains Analysis: Detailed Results—Avoided Productivity Losses due to Dietary Supplement Intervention, 2022-2030

Year	Probiotics & IBS, Total Target Avoided Loss Wages (BENEFITS) ($ billion)	Probiotics & IBS, Net Target Avoided Loss Wages (NET BENEFITS) ($ billion)	Probiotics & IBS, Benefit/Cost Ratio: $Value of Reduced Risk per $1 spent on Supplement ($/$1 supplement spend)
2021	$12.13	$10.41	$6.08
2022	$12.89	$11.10	$6.18
2023	$12.81	$10.98	$6.03
2024	$13.24	$11.36	$6.07
2025	$13.68	$11.75	$6.10
2026	$14.14	$12.16	$6.14
2027	$14.61	$12.57	$6.17
2028	$15.09	$13.00	$6.21
2029	$15.60	$13.45	$6.24
2030	$16.11	$13.91	$6.28
Average ('22-'30)	$14.24	$12.25	$6.16
CAGR	3.21%	3.27%	$0.00
Cumulative ('22-'30)	$128.16	$110.22	

Source: Frost & Sullivan

Table 80. Probiotics Productivity Gains Analysis: Detailed Results— Net Productivity Gains Yet to be Realized due to Avoided Productivity Losses through Dietary Supplement Intervention, 2022-2030

Year	Probiotics & IBS, Total Target Avoided Loss Wages Yet to be Realized (BENEFITS) ($ billion)	Probiotics & IBS, Net Target Avoided Loss Wages Yet to be Realized (NET BENEFITS) ($ billion)
2021	$10.43	$8.95
2022	$11.08	$9.54
2023	$11.01	$9.44
2024	$11.38	$9.77
2025	$11.76	$10.11
2026	$12.16	$10.45
2027	$12.56	$10.81
2028	$12.98	$11.18
2029	$13.41	$11.56
2030	$13.86	$11.96
Average ('22-'30)	$12.25	$10.54
CAGR	3.21%	3.27%
Cumulative ('22-'30)	$110.22	$94.83

Source: Frost & Sullivan

Council for Responsible Nutrition

The Science Behind the Supplements