THE ECONOMIC BENEFITS OF USING LUTEIN & ZEAXANTHIN TO SLOW AGE-RELATED MACULAR DEGENERATION

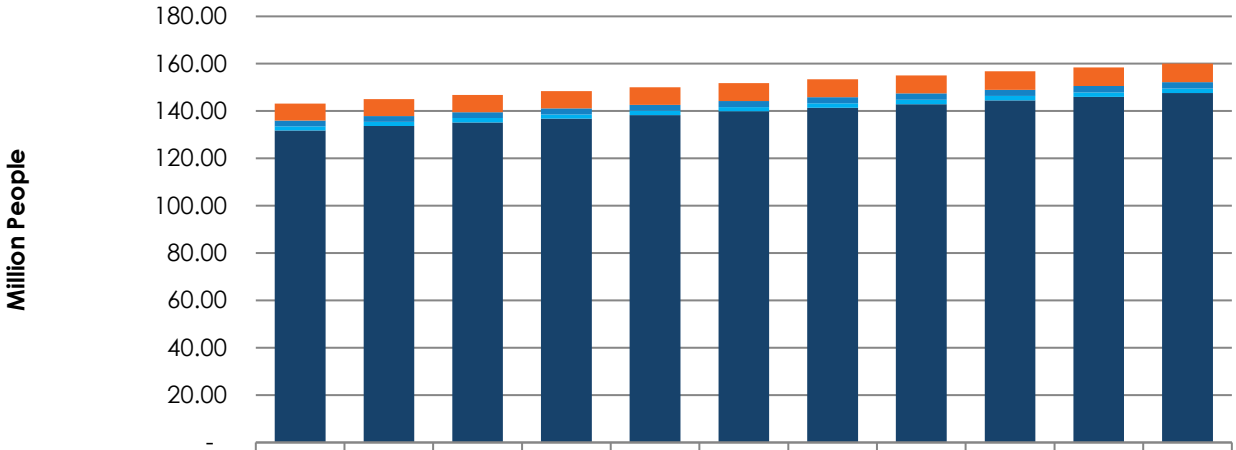
The Burden and Social Consequences

Age-related macular degeneration (AMD) is a progressive degenerative eye disease mostly inflicting many people over the age of 50. AMD is characterized by the degeneration of the central part of the retina known as the macula [53, 54]. AMD is diagnosed by comprehensive eye examination to obtain images of the retina which enable to detect the presence, number, and dimension of drusen (yellow deposits beneath the retina that represent the hallmark of AMD), and the eventual presence of newly formed and/or leaking blood vessels. AMD, which inhibits the ability to see objects directly ahead, can cause irreversible and progressive decline in an individual's independence and ability to perform daily activities, which often leads to significant emotional distress and significantly impacts quality of life [54].

According to the CDC, more than 4.2 million people aged 40 and older suffer from low vision or blindness, an event risk of 3.0**%** given a total population of 143.13 million Americans aged 44 and older [154, 56]. 7.17 million U.S. adults aged 44 and older had a large drusen and are at significant risk of developing AMD in the near future, a risk of transition of 24.7% and 1.77 million U.S. adults aged 44 and older suffer from AMD, an event risk of 1.1% [8]. Among those with AMD, sufferers typically suffer from a significant reduction in visual acuity (VA) or severe vision loss, which causes difficulty in daily activities, some emotional impact and some difficulty going outside the home without assistance and thus requiring long-term care.

Macular pigment optical density, or MPOD, is the quantitative measure of the amount of pigment in each eye's macula and it is expected to be a biomarker of interest in diagnosing and tracking AMD. The pigments, which are carotenoid-based and naturally include both lutein and zeaxanthin, are necessary for optimal optical performance. Macular pigments help to absorb harmful blue light that enters the eye and in turn could cause damage to the eye's photoreceptors [57]. In addition, the concentration of macular pigments in the eye has been tied to visual performance overall in terms of visual acuity, contrast and light sensitivity, and glare recovery caused by high intensity lighting that can cause sunspots and temporary visual impairment [57].

Chart 18. Target Population Size and Prevalence of Low Vision and Blindness, United States, Age 44 and older, 2020-2030



	'20	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
With Large Drusen	7.17	7.23	7.30	7.37	7.44	7.51	7.58	7.65	7.72	7.79	7.86
Other Cause LVB	2.38	2.43	2.46	2.49	2.52	2.55	2.58	2.61	2.64	2.67	2.70
Diagnosed AMD	1.77	1.78	1.80	1.82	1.83	1.85	1.87	1.89	1.90	1.92	1.94
Healthy Vision	131.81	133.67	135.21	136.76	138.30	139.85	141.39	142.94	144.48	146.02	147.57
All Adults	143.13	145.10	146.77	148.43	150.09	151.76	153.42	155.08	156.75	158.41	160.07

Source: Centers for Disease Control and Prevention, US Census, and Frost & Sullivan analysis

Table 44. Target Population Size and Prevalence of Low Vision and Blindness, United States, Age 44 and older, 2020-2030

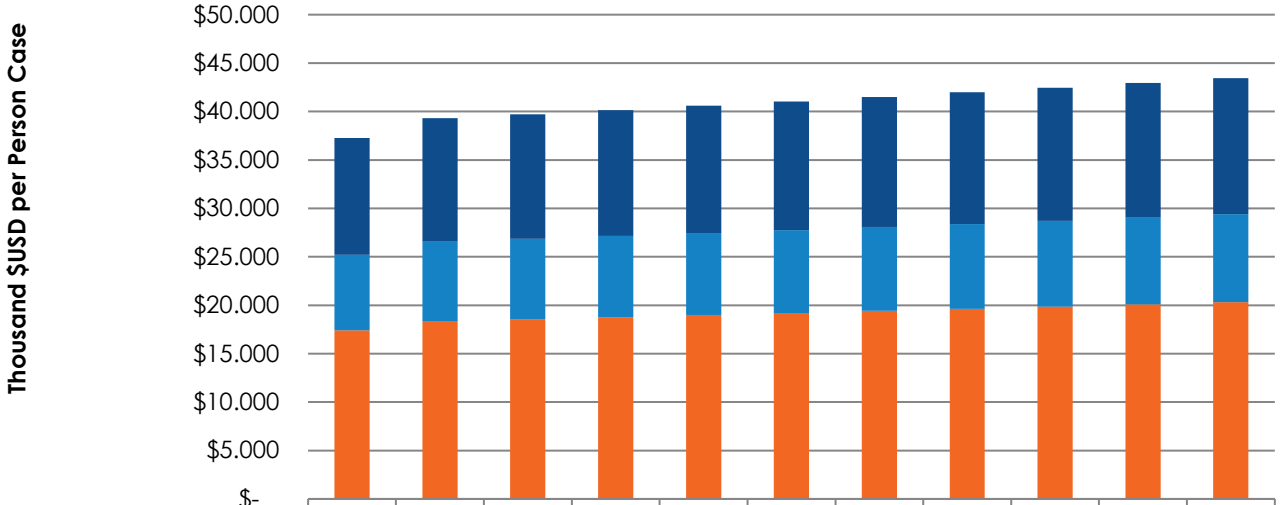
Year	Total Population, age 44 and older (million people)	Population, Diagnosed with Age-Related Macular Degeneration (million people)	Population, Diagnosed with Large Drusen (million people)	Population, Other Low Vision & Blind (million people)	Population, Healthy Vision (million people)
2021	145.10	1.78	7.23	2.43	133.67
2022	146.77	1.80	7.30	2.46	135.21
2023	148.43	1.82	7.37	2.49	136.76
2024	150.09	1.83	7.44	2.52	138.30
2025	151.76	1.85	7.51	2.55	139.85
2026	153.42	1.87	7.58	2.58	141.39
2027	155.08	1.89	7.65	2.61	142.94
2028	156.75	1.90	7.72	2.64	144.48
2029	158.41	1.92	7.79	2.67	146.02
2030	160.07	1.94	7.86	2.70	147.57
Average ('22-'30)	153.42	1.87	7.58	2.58	141.39
CAGR	1.1%	0.9%	0.9%	1.2%	1.1%

Source: Centers for Disease Control and Prevention, US Census, and Frost & Sullivan analysis

Visual acuity is nearly always assessed to verify how the AMD affects visual function and progression [59]. Visual acuity is measured on many scales such as Snellen, LogMAR, and Best Corrected Visual Acuity (BCVA). A common scale used by clinical researchers is the LogMAR which is an acronym that stands for "Logarithm of the Minimum Angle of Resolution" [58]. The range of the LogMAR is typically between "0" for near-perfect vision and 1.4 (or greater) for complete blindness in both eyes [58]. The LogMAR baseline for poorly corrected severe vision impairment is 0.6 or 6/24 vision which is characterized by some vision problems that make it difficult to recognize faces or objects across a room and a LogMAR baseline score of 1.0 is considered legally blind [58,60].

The relationship between MPOD levels and a change in visual acuity has been independently assessed by a number of researchers [61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88]. Puell MC et al. 2013 and Loughman et al. 2010 found that there is a statistically significant positive relationship between a change in MPOD and change in visual acuity [61, 62]. The expected change in population LogMAR given a change in average population MPOD levels from use of lutein & zeaxanthin is 0.026 LogMAR points [61, 62]. Note that the LogMAR score is inversely related to visual acuity; it is expected that given a positive 0.1 change in MPOD levels (measured in optical density units), LogMAR levels decrease by 0.03 basis points less than the placebo group [61, 62].

Chart 19. Average Healthcare Costs per Person with Low Vision and Blindness, Thousand $USD per case, United States, 2020-2030



	'20	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Productivity Losses	$12.1	$12.7	$12.9	$13.0	$13.1	$13.3	$13.4	$13.6	$13.7	$13.9	$14.1
Disease Management	$7.8	$8.2	$8.3	$8.4	$8.5	$8.6	$8.7	$8.8	$8.9	$9.0	$9.1
Medical	$17.4	$18.4	$18.6	$18.8	$19.0	$19.2	$19.4	$19.6	$19.9	$20.1	$20.3
Total	$37.3	$39.3	$39.7	$40.2	$40.6	$41.0	$41.5	$42.0	$42.5	$43.0	$43.5

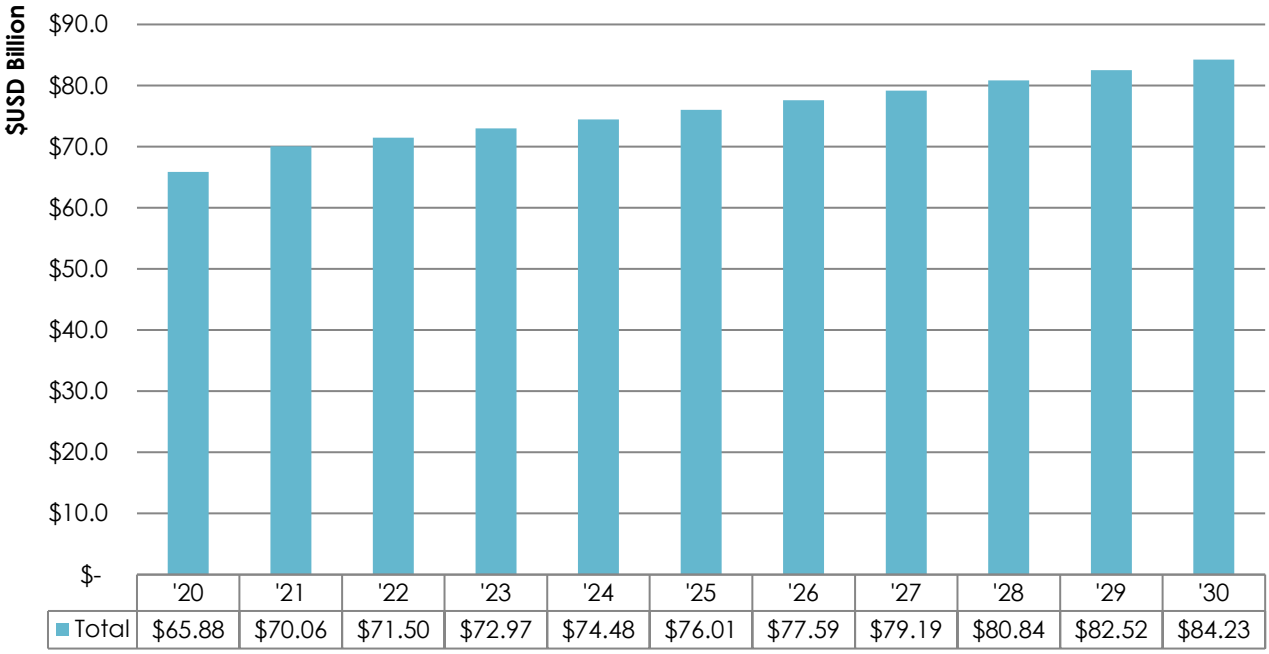
Source: Wittenborn et al 2013 and Frost & Sullivan analysis

Table 45. Healthcare Costs per Person with Low Vision and Blindness, Thousand $USD per case, United States, 2020-2030

Year	Low Vision & Blind, Direct Medical Costs ($ per Event Case)	Low Vision & Blind, Indirect Medical Costs ($ per Event Case)	Low Vision & Blind, Productivity Losses ($ per Event Case)	Low Vision & Blind, Cost per Event Case ($ per Event Case)	Low Vision & Blind, Total Cost ($ billion)
2021	$18,378	$8,199	$12,723	$39,301	$70.06
2022	$18,576	$8,288	$12,860	$39,723	$71.50
2023	$18,777	$8,378	$13,000	$40,155	$72.97
2024	$18,984	$8,470	$13,143	$40,596	$74.48
2025	$19,195	$8,564	$13,289	$41,048	$76.01
2026	$19,411	$8,660	$13,438	$41,509	$77.59
2027	$19,631	$8,759	$13,591	$41,981	$79.19
2028	$19,857	$8,859	$13,747	$42,463	$80.84
2029	$20,087	$8,962	$13,906	$42,955	$82.52
2030	$20,322	$9,067	$14,069	$43,458	$84.23
Average ('22-'30)	$19,427	$8,667	$13,449	$41,543	$77.70
CAGR	1.1%	1.1%	1.1%	1.1%	2.1%
Cumulative ('22-'30)					$699.33

Source: Wittenborn et al 2013 and Frost & Sullivan analysis

Chart 20. Total Population Healthcare Costs Attributed to Age-related Macular Degeneration, $USD Billion, United States, 2020-2030



	'20	'21	'22	'23	'24	'25	'26	'27	'28	'29	'30
Total	$65.88	$70.06	$71.50	$72.97	$74.48	$76.01	$77.59	$79.19	$80.84	$82.52	$84.23

Source: Wittenborn et al 2013, US Census and Frost & Sullivan analysis

Measuring the economic burden of low vision and blindness due to age-related macular degeneration bore by Americans includes a mix of both direct medical costs and indirect non-medical costs related to supporting the individual sufferer's quality of life. According to research by NORC at the University of Chicago, the total cost of vision loss and blindness in the US was $139 billion in 2013 of which $65 billion was attributed to direct medical costs and the remaining $74 billion indirect costs attributed disease burden management and loss productivity [89]. At the time, there were 3.8 million Americas suffering from low vision and blindness at 2013 [89]. Projecting this figure to today given recent trends in prices and population growth, it is expected that the per capita cost of managing the burden of low vision and blindness in the US was $39,310 per person in 2022. Table 46 provides a detailed description of the total and per case medical costs of low vision and blindness due to age-related macular degeneration in the United States.

Lutein and zeaxanthin are xanthophylls, carotenoids that are typically found in the human diet and are well known for their antioxidant properties. Also, lutein and zeaxanthin concentrate in the macula lutea, where they are a key component of the macular pigment, which suggests their important role in protecting eyes and eyesight [90, 10, and 91]. Specifically, recent evidence has found that lutein and zeaxanthin are believed to play roles in protecting the eye from oxidative damage caused by light interacting with other pigments in the retina [90, 10, and 91]. This case study explores the possible health effect and economic benefit that could be expected from the daily use

of dietary supplements with effective levels of lutein and zeaxanthin intake to inhibit the rate of visual acuity decline typically associated with age-related macular degeneration. This will be done by determining the potential cost savings that could be realized given the usage of lutein and zeaxanthin dietary supplements that are scientifically shown to reduce the occurrence of age-related visual acuity decline episodes among adults aged 44 and older. Specifically, this report will attempt to show that using lutein & zeaxanthin dietary supplements by subjects with low vision and blindness due to age-related macular degeneration can result in health care-related cost savings.

Table 46. Age-related Low Vision and Blindness Demographic Descriptive Statistics for All U.S. Adults Aged 44 and over, 2021–2030

Metric	'21	CAGR ('21 - '30)	Average ('22 - '30)
Total population, age 44 and older, million people	145.10 M	1.10%	153.42 M
Population with Age-Related Macular Degeneration (AMD), million people	1.78 M	0.93%	1.87 M
Population with Other Cause Low Vision and Blindness, million people	2.43 M	1.22%	2.58 M
Population with Large Drusen, million people	7.23 M	0.93%	7.58 M
Estimated LogMAR of individuals with Age-Related Macular Degeneration (AMD), Score	--	--	1.00
Estimated LogMAR of individuals with Other Cause Low Vision and Blindness, Score	--	--	0.67
Estimated LogMAR of individuals with Large Drusen, Score	--	--	0.33
Estimated LogMAR of individuals Healthy Vision, Score	--	--	0.00
Direct cost of Age-related Macular Degeneration, medical service utilization, $USD per Case	$18,378	1.12%	$19,427
Direct cost of Age-related Macular Degeneration, pharmaceutical utilization, $USD per Case	$8,199	1.12%	$8,667
Indirect cost of Age-related Macular Degeneration, disease management, $USD per Case	$12,723	1.12%	$13,449
Total cost of Age-related Macular Degeneration, $USD per Case	$39,301	1.12%	$41,543
Total target population cost of Age-related Macular Degeneration, $USD billion	$70.06	2.07%	$77.70
Price inflation rate, %	6.95%	--	2.23%

Source: Centers for Disease Control and Prevention, Wittenborn et al 2013, US Census and Frost & Sullivan analysis

Lutein & Zeaxanthin

Literature Review

Lutein and zeaxanthin are xanthophyllic carotenoids that are typically found in the human diet [10]. Rich sources of lutein and zeaxanthin are green vegetables, particularly dark green leafy vegetables such as spinach and kale, orange pepper, maize, and eggs [10]. Lutein and zeaxanthin are well known for their antioxidant properties that help protect cells against damage caused by dangerous, naturally occurring chemicals known as free radicals. Also, lutein and zeaxanthin are selectively concentrated in the macula lutea, where they are a key component of the macular pigment, which suggests their important role in protecting eyes and eyesight [10, 90]. Like all the carotenoids, lutein and zeaxanthin are not synthesized by the body; these nutrients must be consumed from the diet from lutein and zeaxanthin rich foods or through food supplementation [10].

The American Optometric Association (AOA) proposes that 10 mg per day of lutein and 2 mg per day of zeaxanthin benefits eye health based on results of recent clinical research [91]. This recommended dose, which is based on the observations from the US National Eye Institute sponsored Age-Related Eye Disease Study II (AREDS2), is assumed to be sufficient to derive the expected benefits and is also the quantity found in the majority of products currently in the market today [92,93].

Recent studies have revealed that increasing intake with lutein and/or zeaxanthin in AMD patients leads to an increase in macular pigment and improved visual acuity. For example, Liu et al. (2014) conducted a detailed meta-analysis of eight randomized controlled trials (RCTs) of AMD patients (n=1,176 patients) that explored the relationship between lutein and zeaxanthin intake and its effect on visual acuity [94]. The researchers found that the groups of users with mild AMD using 10 to 20 mg of lutein and/or 0.6 to 10 mg of zeaxanthin – the typical amount in the AREDS2 formulation which also includes vitamin E, copper, and zinc – versus users of a placebo had a baseline LogMAR levels of VA by a statistically significant 0.04 basis point less than the placebo group. This implies that there were significantly less transitions from mild to severe cases of AMD in the lutein & zeaxanthin groups compared to the placebo group [56].

In 2013, Frost & Sullivan conducted a similar assessment of the use of lutein & zeaxanthin on the incidence of both age-related macular degeneration and cataracts. In this case study, the analysis has been modified by specifically looking at how use of lutein & zeaxanthin supplements impacts MPOD levels which in turn impacts visual acuity and risk of age-related eye disorders.

Specifically, there are over 20 years of scientific publications indicating that higher lutein and zeaxanthin intake is associated with higher macular pigment optical density (MPOD). Based on a rigorous systematic review of the scientific literature, 59 studies were identified in a search exercise

(see research methodology) based on using key words related to use of lutein and zeaxanthin and a number of biomarkers that are typically used as proxies for measuring relative eye health, including "MPOD" and "visual acuity". Of this set of studies, 24 clinical studies were identified that tested the same hypothesis that use of lutein and zeaxanthin resulted in a change in MPOD levels between an observed treatment group and a placebo group. The objective of this meta-analysis was to identify the best set of studies that tested using similar study protocols for a direct causal relationship between intake of lutein and zeaxanthin and the MPOD levels. Studies were not selected on the basis of the magnitude, direction, or statistical significance of the reported findings. Table 47 provides a description of a selection of included studies in the final meta-analysis described below.

From this qualified set, the studies' findings were weighted using a random-effects meta-analysis process by sample size and inter-study variance and aggregated to determine an overall expected effect size of a lutein & zeaxanthin supplement intervention on relative MPOD levels [69]. Among the 24 qualified studies, the dose size ranges were 5 to 20 mg of lutein and 0 to 20 mg of zeaxanthin. The typical dose size was 10 mg of lutein and 2 mg of zeaxanthin. See Table 48 for the results of the meta-analysis.

Based on the results of the random-effects meta-analysis, the expected change in macular pigment optical density (MPOD) among users of lutein and zeaxanthin daily at supportive intake levels was a positive 0.088 optical density unit increase compared to the control group using a placebo. This expected 0.088 optical density unit increase is controls for both intra-study and inter-study variance through weights derived from relative study sample size and reported confidence intervals of each study's findings.

Table 47. Lutein & Zeaxanthin Literature Review: Description of the Qualified Studies

Ref.	Studies	Year	Dose Size of Lutein	Dose Size of Zeaxanthin	Sample Size	Disease State of Patient Population
95	Wilson L. et al.	2021	5 to 20 mg per day		215	Healthy Eyes and AMD
96	Arnold C et al.	2013	10	3	20	AMD
97	Bone, R.A et al.	2007	5.5	1.4	19	Healthy Eyes
98	Bone, R.A et al.	2010	5	20	100	Healthy Eyes
99	Bovier, E.R et al.	2015	8	20	102	Healthy Eyes
100	Connolly, E.E et al..	2011	5.9	1.2	44	Healthy Eyes
101	Curran-Celentano J et al.	2001	0.28 ± 0.13 micro mol/L	0.091 ± 0.044 micro mol/L	280	AMD
102	Dawczynski, J et al.	2013	10	1	172	AMD
103	García-Layana, A et al.	2013	12	0.6	44	AMD
104	Huang, Y.M et al.	2015	12.5	10	112	AMD
105	Johnson, E.J et al.	2008	12	0.5	57	Healthy Eyes
106	Kvansakul, J. et al.	2006	10	10	92	Healthy Eyes
107	Landrum, J et al.	2012	20	0	30	Healthy Eyes
108	Loughman, J et al.	2012	20	2	36	Healthy Eyes
109	Murray, I.J et al..	2013	10	0	72	AMD
110	Nolan JM et al.	2007	[A]	[B]	28	AMD
111	Nolan, J.M et al.	2011	12	1	121	Healthy Eyes
112	Nolan, J.M et al.	2016	10	2	105	Healthy Eyes
113	Richer, S et al.	2007	10	0	90	AMD
114	Trieschmann et al.	2007	12	2	130	AMD
115	van der Made SM et al.	2014	[C]	[C]	101	AMD
116	Weigert, G et al.	2011	15	0	126	AMD
117	Wolf-Schnurrbusch UE et al.	2015	10	1	79	AMD
118	Yao, Y et al.	2013	10	2	120	Healthy Eyes

[A] Entire study group Serum Lutein L (µ g/mL): 0.280 (Absolute Dietary L(mg/day)); 0.303* (Energy-Adjusted Dietary L); 0.299* (Nutrient Density of Dietary L); 1 (Serum L (µ g/mL))

[B] Entire study group Serum zeaxanthin (Z) (µ g/mL) :0.160* (Absolute Dietary L (mg/day)); 0.166* (Energy-Adjusted Dietary L); 0.146* (Nutrient Density of Dietary L); 0.462* (Serum L (µ g/mL)); 0.237* (Absolute Dietary Z (mg/day)); 0.260*(Energy-Adjusted Dietary Z); 0.259* (Nutrient Density of Dietary Z); 1 Serum Z (µ g/mL)

[C] 1-y daily consumption of a buttermilk drink containing 1.5 lutein-rich egg yolks

Table 48. Lutein & Zeaxanthin Literature Review: Systematic Review Results

Ref.	Studies	Weighted Mean Difference (Δ in MPOD)	CI 95% Min	CI 95% Max	Sample Size Weight	Std. VAR Weight	Average Weight
95	Wilson L et al.	0.040	0.020	0.070	9.37%	5.57%	7.47%
96	Arnold C et al.	0.270	0.230	0.310	0.96%	3.71%	2.34%
97	Bone, R.A et al.	0.030	-0.020	0.080	4.81%	2.97%	3.89%
98	Bone, R.A et al.	0.240	0.180	0.300	0.91%	2.47%	1.69%
99	Bovier, E.R et al.	0.110	0.020	0.200	4.90%	1.65%	3.28%
100	Connolly, E.E et al.	0.050	-0.060	0.160	2.12%	1.35%	1.73%
101	Curran-Celentano J et al.	0.210	0.050	0.350	13.46%	0.99%	7.22%
102	Dawczynski, J et al.	0.030	0.030	0.030	8.27%	0.15%	4.21%
103	García-Layana, A et al.	-0.100	-0.110	-0.090	2.12%	14.84%	8.48%
104	Huang, Y.M et al.	0.100	0.040	0.160	5.38%	2.47%	3.93%
105	Johnson, E.J et al.	0.120	-0.130	0.370	2.74%	0.59%	1.67%
106	Kvansakul, J. et al.	0.040	0.040	0.040	4.42%	0.15%	2.29%
107	Landrum, J et al.	0.050	-0.070	0.170	1.44%	1.24%	1.34%
108	Loughman, J et al.	0.060	-0.060	0.180	1.73%	1.24%	1.48%
109	Murray, I.J et al.	0.150	0.060	0.240	3.46%	1.65%	2.55%
110	Nolan JM et al.	0.208	0.136	0.303	1.35%	1.77%	1.56%
111	Nolan, J.M et al.	0.100	0.040	0.160	5.82%	2.47%	4.14%
112	Nolan, J.M et al.	0.120	0.090	0.150	5.05%	4.95%	5.00%
113	Richer, S et al.	0.120	-0.200	0.440	4.33%	0.46%	2.40%
114	Trieschmann et al.	0.070	0.060	0.080	6.25%	14.84%	10.54%
115	van der Made SM et al.	0.070	0.050	0.090	4.86%	7.42%	6.14%
116	Weigert, G et al.	0.080	0.070	0.090	6.06%	14.84%	10.45%
117	Wolf-Schnurrbusch UE et al.	0.120	0.121	0.119	3.80%	14.84%	9.32%
118	Yao, Y et al.	0.110	0.060	0.160	5.77%	2.97%	4.37%

	Weighted Mean Difference (Δ in MPOD)	CI 95% Min	CI 95% Max
Expected WMD - All People	**0.085**	**0.036**	**0.133**

Source: Frost & Sullivan analysis

As previously noted, the relationship between MPOD levels and a change in visual acuity had been independently assessed by a number of researchers including Puell et al. 2013 and Loughman et al. 2010 [61, 62]. Both researchers found that there is a statistically significant positive relationship between a change in MPOD and change in visual acuity. It is expected that given a positive 0.1 change in MPOD levels (measured in optical density units), LogMAR levels decrease by 0.03 basis point less than the placebo group. Because now that it is known that MPOD increases at a weighted average of 0.085 optical density units given the use of lutein zeaxanthin at supportive intake levels from the meta-analysis results, the expected change in population LogMAR given a change in average population MPOD levels from use of lutein & zeaxanthin can be deduced. Specifically, the basis point decrease in LogMAR given the use of lutein & zeaxanthin at supportive intake levels is 0.025 (95% CI: 0.011-0.039). Thus, there would be an increase in average visual acuity levels in the population leading to a lessening of dependency on medical services and other services required to maintain an acceptable quality of life for those inflicted with severe visual impairment or blindness. Note that the 2014 meta-analysis developed by Lui et al. (2014) deduced a 0.04 basis point impact on LogMAR from use of lutein & zeaxanthin, which looked at completely different set of clinical studies that explored the direct relationship between lutein and zeaxanthin use and observed visual acuity levels as opposed to the direct relationship between lutein and zeaxanthin use and MPOD levels explored in this case study [94].

By applying the information of the change in visual acuity given the use of lutein & zeaxanthin to current knowledge on the population prevalence of age-related macular degeneration and low vision people in general, the potential percent change in population prevalence of age-related macular degeneration given the use of lutein and zeaxanthin can be determined. As noted previously, there are 11.6 million Americans aged 44 and older that have some type of vision problem and based on the mix of vision disorder types it is expected that the baseline LogMAR of this target population is 0.574. Subtracting 0.025 LogMAR basis points from baseline LogMAR yields an estimate for the consequential LogMAR score the total target population of low vision Americans would have if 100% of this population had used a lutein & zeaxanthin supplement at daily supportive levels which is 0.549. This is equivalent to a 4.4% improvement in the target population's visual acuity. Assuming that the improvement is shared across the entire target population, we would expect to see up to 21,022 avoided transitions in 2022 to a more severe vision impairment state. The number of potentially avoidable prevalent cases of severe visual acuity decline transition episodes could surpass 22,414 cases in 2030 if all eligible users used lutein & zeaxanthin dietary supplements at daily supportive intake levels. Table 49 provides a description of the calculation steps used to derive the number of potentially avoidable transitions to more severe cases of vision loss and blindness.

Table 49. Steps to Derive Expected Change in Population Prevalence Given a Change in Visual Acuity, 2022

Step	Measure	AMD	Other ARED Low vision or blindness	Large Drusen	Healthy Eyes	Total	Notes
A	Current Population Prevalence, Age 44 and older, million people	1.80	2.46	7.30	133.14	144.70	--
B	% Current Population Prevalence, Age 44 and older, %	1.28%	1.75%	5.20%	91.77%	100.0%	--
C	Current Population Prevalence, % of total Vision Impaired	24.7%	33.7%	41.6%	--	100% of vision impaired population	--
D	LogMAR Baseline Level	1.00	0.60	0.30	0.00	0.574	
E	Reduction in LogMAR given use of lutein and zeaxanthin (from meta-analysis)	--	--	--	--	0.0251 (95% CI: 0.011 - 0.39)	--
F	Updated LogMAR Baseline Level given use of lutein and zeaxanthin	--	--	--	--	0.549	F = D - E
G	% Reduction in LogMAR Levels	--	--	--	--	95.6%*	G = F / D
H	Population Prevalence Given use of Lutein & Zeaxanthin, % of total Population	1.23%	1.68%	4.97%	92.13%	--	H = G x B
I	Implied Absolute Risk Reduction: Difference in Population Prevalence Given use of Lutein & Zeaxanthin, % of total Population	-0.06%	-0.08%	-0.23%	0.36%	--	*I* = H - B
J	Number of Avoided Transitions to More Severe Vision Impairment, people cases	1,089	2,027	17,906	--	21,022	J = -1**I*A

*Equals 100% minus 4.4% Visual Acuity Improvement. Source: Frost & Sullivan analysis

Economic Implications

As stated above, the expected number of avoided age-related vision loss transition events given the use of lutein & zeaxanthin dietary supplements at preventive intake levels was 21,022 potentially avoidable events in 2022 and an average of 21,718 avoided events per year from 2022 to 2030 given current population and disease risk growth expectations. Subsequently, the expected reduction in health care expenditures in 2022 attributed to avoided age-related vision loss transition events would have been $835.1 million in 2022 given an average age-related macular degeneration transition person case cost of $39,723 per year. Given current population growth, disease risk growth and price inflationary factors, the expected cost savings derived from avoided age-related vision loss transition events caused by the use of lutein & zeaxanthin at daily protective intake levels is $902.8 million per year in total savings from 2022 to 2030.

It is proper to include the cost of using lutein & zeaxanthin supplements daily in the final accounting in order to ensure all cost components are considered. Based on the review of the thirty best-selling retail products currently sold through online sales channels, the median cost of a daily dose of dietary supplements that contains one or more of the lutein & zeaxanthin is approximately $0.27 per day. Given this daily cost requirement, the median annual expected cost of lutein & zeaxanthin dietary supplementation for all U.S. adults aged 50 and over would be $104.96 per person per year or $796.2 million per year for the target population of people diagnosed with a large drusen over the period 2022 to 2030. Table 50 provides a summary of the cost of dietary supplementation with lutein & zeaxanthin of the entire target population.

Table 50. Lutein & Zeaxanthin Cost Savings Analysis: Summary Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Metric	Measure
Median daily cost per person of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022	$0.27
Expected daily median cost per person of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022-2030	$0.29
Median annual cost per person of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022	$100.30
Expected annual median cost per person of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022-2030	$104.96
Total target population cost of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022	$732.2 M
Total target population cost of Lutein & Zeaxanthin supplementation at protective daily intake levels, 2022-2030	$796.2 M

Note: M indicates million. Source: Frost & Sullivan analysis

Based the incurred cost of lutein & zeaxanthin dietary supplementation, the net cost savings expected from reduced health care-attributed expenditures in 2022 derived from avoided age-related vision loss transition events would have been $102.9 million in 2022, or $959.2 million in cumulative net savings during the period 2022 to 2030. Table 51 reports the economic implications of the systematic review finding of the beneficial use of lutein & zeaxanthin supplements to support age-related eye health.

Table 51. Lutein & Zeaxanthin Cost Savings Analysis: Summary Results—Avoided Healthcare Expenditures due to Dietary Supplement Intervention, 2022-2030

Metric	Measure
Avoided Age-related Macular Degeneration-attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention per year, 2022	$835.1 M
Average avoided Age-related Macular Degeneration-attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention per year, 2022-2030	$902.8 M
Net avoided Age-related Macular Degeneration-attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention per year, 2022 (includes cost of supplementation)	$102.9 M
Net average avoided Age-related Macular Degeneration-attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention per year, 2022-2030 (includes cost of supplementation)	$106.6 M
Net benefit cost ratio, $ Savings per one dollar spent on dietary supplement	$1.13
Cumulative net target avoided costs, 2022-2030 (NET BENEFITS) ($ million)	$959.2 M

Note: M indicates million. Source: Frost & Sullivan analysis

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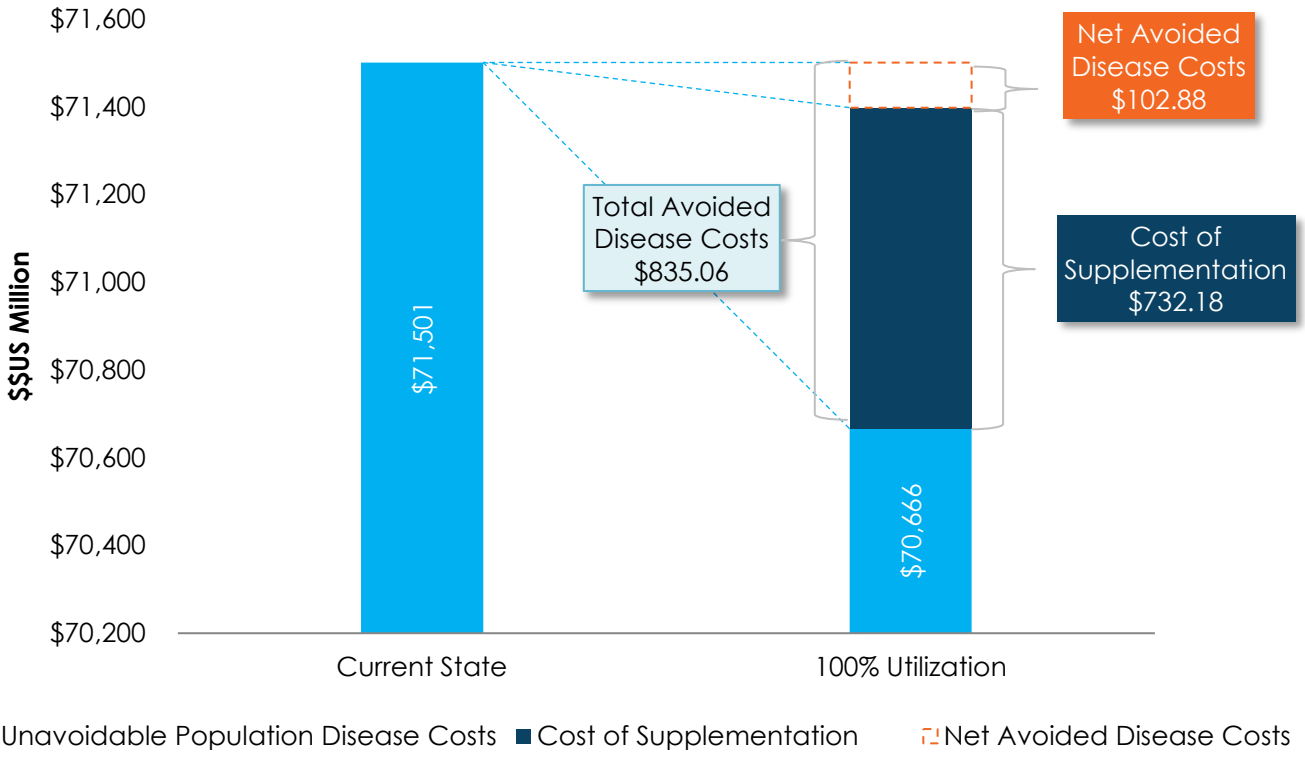
Chart 21. Lutein & Zeaxanthin Cost Savings Analysis: Healthcare Cost Savings from the Use of Health Supplement, 2022 Scenario Analysis



Note: M indicates million. Source: Frost & Sullivan analysis

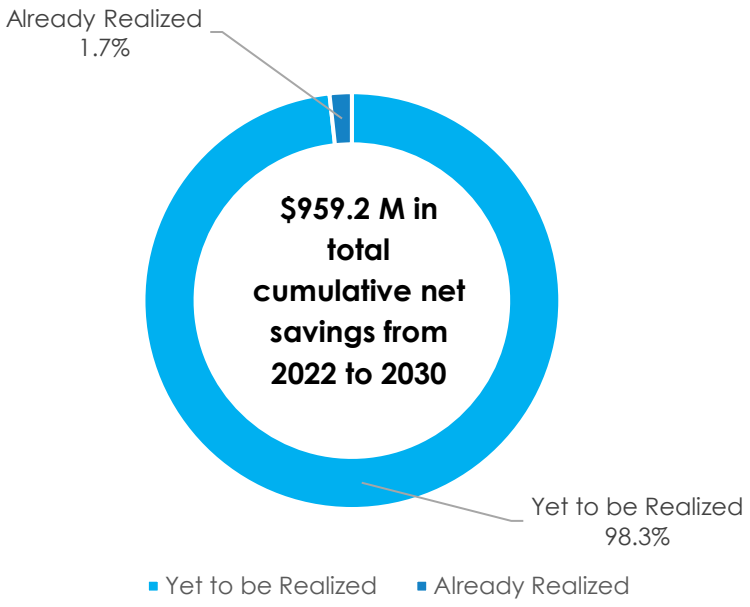
The above cost savings results are the maximum savings potential that is obtainable if everyone in the target population (all adults aged 44 and older) had not used this product prior to the base year of analysis (e.g., 2022) and then 100% of the population adopted the lutein & zeaxanthin regimen in 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 cost savings for the subset of the population yet to use lutein & zeaxanthin.

According to the 2021 Council for Responsible Nutrition Consumer Survey on Dietary Supplements conducted by Ipsos Public Affairs, over 40% of US adults aged 55 and older are regular users of dietary supplements and only 4.0% of supplement users aged 55 and over reported being regular users of lutein dietary supplements, or 1.7% of the total target population [152]. This implies that the remaining 98.3% of the target population has yet to realize the potential benefits of the supplements' regular use on eye health. Because avoided expenditures and net cost savings are a direct function of the total number of people in the target population using lutein & zeaxanthin dietary supplements, the calculation of avoided health care expenditures and net cost savings yet to be realized is simply a proportional adjustment of the total potential avoided expenditures and net cost savings. It should be noted that the target population of this case study includes individuals

younger than 55, so the use of these consumer research findings for deducing the proportion of the population yet to realize the benefits from using this supplement is likely underestimated since use of dietary supplements generally increases with age.

Despite this, it is expected that at least $101.1 million of the $102.9 million in net potential direct savings in 2022 from avoided age-related eye health events because of lutein & zeaxanthin dietary supplement intervention was not realized. This corresponds to an average of $104.7 million per year in net savings yet to be realized, or $942.7 million in cumulative savings from 2022 to 2030, due to underutilization of lutein & zeaxanthin dietary supplements. Thus, there are still significant cost savings potential from the increased use of lutein & zeaxanthin dietary supplements among the high-risk target population.

Chart 22. Lutein & Zeaxanthin Cost Savings Analysis: Summary Results—Cumulative Net Cost Savings Yet to be Realized due to Avoided Hospital Utilization Expenditures through Dietary Supplement Intervention, 2022-2030



Source: Council for Responsible Nutrition

Table 52. Lutein & Zeaxanthin Cost Savings Analysis: Summary Results—Net Cost Savings Yet to be Realized due to Avoided Healthcare Expenditures through Dietary Supplement Intervention, 2022-2030

Metric	Measure
Net avoided Age-related Macular Degeneration -attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention yet to be realized per year, 2022	$101.1 M
Net average avoided Age-Related Macular Degeneration-attributed healthcare expenditures given Lutein & Zeaxanthin supplement intervention yet to be realized per year, 2022-2030	$104.7 M
Cumulative net target avoided costs yet realized, 2022-2030 (NET BENEFITS) ($ million)	$942.7 M

Note: M indicates million. Source: Frost & Sullivan analysis

Detailed Results

Table 53. Lutein & Zeaxanthin Cost Savings Analysis: Detailed Results—Cost of Dietary Supplementation of the Target Population, 2022-2030

Year	Lutein & Zeaxanthin, Daily Cost of Supplementation ($ per day)	Lutein & Zeaxanthin, Annual Cost of Supplementation ($ per year)	Lutein & Zeaxanthin, Population Cost of Supplementation ($ billion)
2021	$0.27	$97.06	$0.702
2022	$0.27	$100.30	$0.732
2023	$0.28	$101.42	$0.747
2024	$0.28	$102.83	$0.765
2025	$0.28	$103.70	$0.779
2026	$0.29	$104.85	$0.795
2027	$0.29	$106.02	$0.811
2028	$0.29	$107.50	$0.830
2029	$0.30	$108.40	$0.845
2030	$0.30	$109.61	$0.862
Average ('22-'30)	$0.29	$104.96	$0.796
CAGR	1.4%	1.4%	2.3%
Cumulative ('22-'30)			$7.166

Source: Frost & Sullivan.

Table 54. Lutein & Zeaxanthin Cost Savings Analysis: Detailed Results—Avoided Healthcare Expenditures due to Dietary Supplement Intervention, 2022-2030

Year	Lutein & Zeaxanthin & Low Vision & Blind, Number of Avoided Transitions to More Severe Vision Impairment (# of Avoided Event Cases)	Lutein & Zeaxanthin & Low Vision & Blind, Total Target Avoided Costs (BENEFITS) ($ billion)	Lutein & Zeaxanthin & Low Vision & Blind, Net Target Avoided Costs (NET BENEFITS) ($ billion)	Lutein & Zeaxanthin, Benefit/Cost Ratio: $Value of Reduced Risk per $1 spent on Supplement ($/$1 supplement spend)
2021	20,849	$0.819	$0.118	$1.17
2022	21,022	$0.835	$0.103	$1.14
2023	21,196	$0.851	$0.104	$1.14
2024	21,369	$0.868	$0.102	$1.13
2025	21,543	$0.884	$0.106	$1.14
2026	21,717	$0.901	$0.107	$1.13
2027	21,891	$0.919	$0.108	$1.13
2028	22,065	$0.937	$0.107	$1.13
2029	22,240	$0.955	$0.111	$1.13
2030	22,414	$0.974	$0.112	$1.13
Average ('22-'30)	21,718	$0.903	$0.107	$1.13
CAGR	0.81%	1.94%	-0.50%	-0.36%
Cumulative ('22-'30)	195,458	$8.125	$0.959	

Source: Frost & Sullivan.

Table 55. Lutein & Zeaxanthin Cost Savings Analysis: Summary Results—Net Cost Savings Yet to be Realized due to Avoided Healthcare Expenditures through Dietary Supplement Intervention, 2022-2030

Year	Lutein & Zeaxanthin & Low Vision & Blind, Total Target Avoided Costs Yet to be Realized (BENEFITS) ($ billion)	Lutein & Zeaxanthin & Low Vision & Blind, Net Target Avoided Costs Yet to be Realized (NET BENEFITS) ($ billion)
2021	$0.805	$0.116
2022	$0.821	$0.101
2023	$0.836	$0.102
2024	$0.853	$0.101
2025	$0.869	$0.104
2026	$0.886	$0.105
2027	$0.903	$0.106
2028	$0.921	$0.105
2029	$0.939	$0.109
2030	$0.957	$0.110
Average ('22-'30)	$0.887	$0.105
CAGR	1.94%	-0.50%
Cumulative ('22-'30)	$7.99	$0.9427

Source: Frost & Sullivan.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