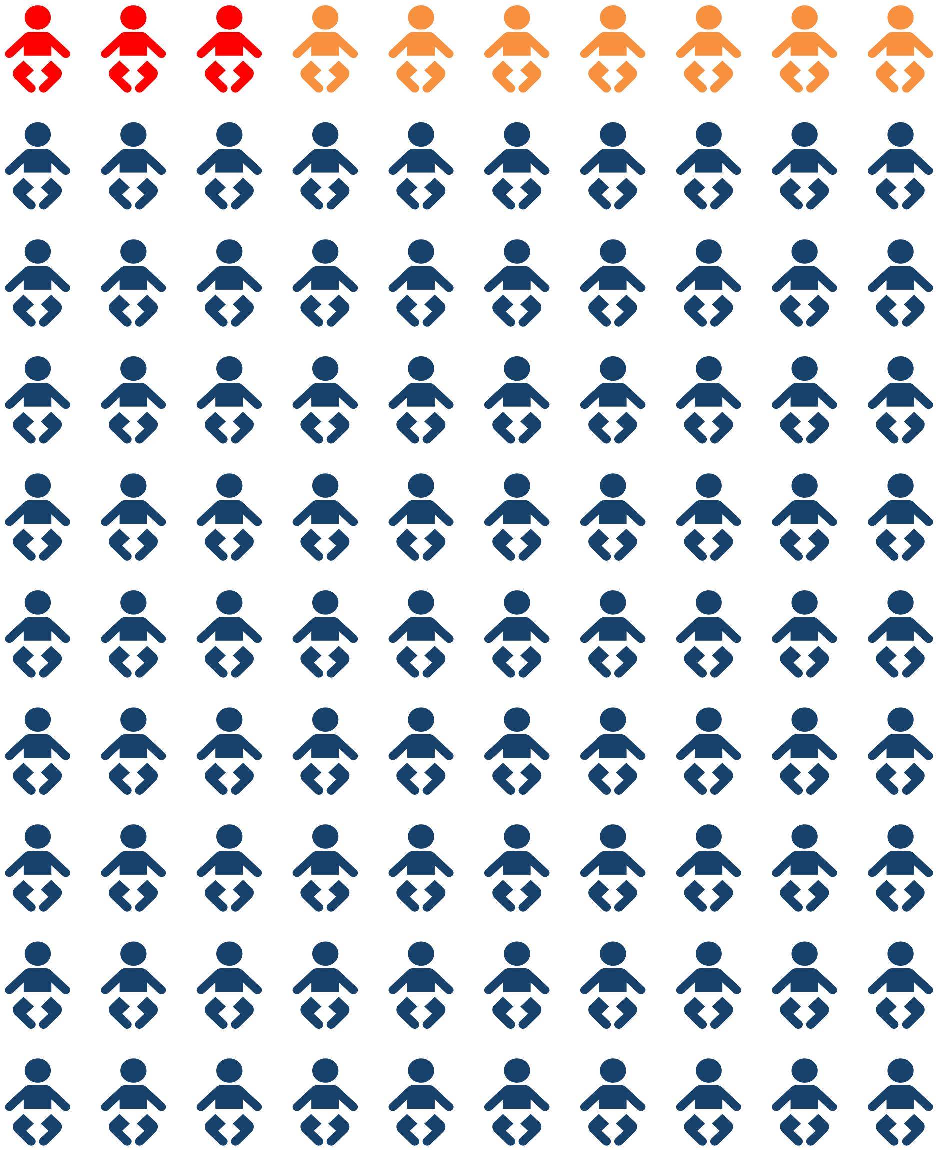

IN THE UNITED STATES:

10 OUT OF **100** BABIES ARE BORN PRETERM

3 OUT OF **100** BABIES ARE BORN EARLY PRETERM

Reducing the economic impact of preterm and early preterm birth in the United States by providing supplemental algal DHA to expectant mothers

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Executive Summary

Preterm birth (PTB, <37 weeks gestation), including early preterm birth (ePTB, <34 weeks gestation), is a leading cause of infant mortality in the United States, and is associated with increases in the incidence of several lifelong disabilities. The risk of death or disability increases dramatically the earlier the baby is born and is highest for those born early preterm. The U.S. preterm birth rate has been climbing steadily in recent years, and reached 10.5% in 2021, the highest rate since at least 2007. The ePTB rate was 2.8%, the highest since 2011. In total, 383,979 infants were born preterm in the U.S. in 2021, including 103,004 born early preterm. These rates are higher than rates in similarly developed nations such as Canada, the UK, and countries in western Europe where the PTB rates are ~6 – 8%. Furthermore, there is a pronounced racial and ethnic disparity in the rates of PTB and ePTB, with increased burden in Black and Hispanic women, as compared to White women. Indeed, the rate of PTB in Black mothers is more than 50% higher than in White mothers, whereas their rate of ePTB is more than double.

In addition to the human tragedy, there is a tremendous economic burden placed by PTB and especially by ePTB. Babies born too early incur high hospital costs in the first 6 months of life, due to time spent in the neonatal intensive care unit (NICU) and the increased incidence of a variety of serious and often life-threatening medical issues. Later in life, the incidence of cerebral palsy, intellectual disability, and other disorders are dramatically increased, leading to increased lifetime medical costs and decreased productivity. Our analysis estimates an average excess lifetime cost burden at over $44,000 per person born between 34 – 36 weeks gestation in 2021. For infants born at <34 weeks gestation, the cost is over $222,000 per person. The total population cost burden of PTB in the United States was $34.54 billion in 2021, with almost $23 billion of that attributed to ePTB.

Reducing the incidence of PTB is a national priority. While few tools are available, there is a well-demonstrated, easily implementable, and inexpensive nutritional solution that promises to dramatically reduce the risk of PTB and especially ePTB. Extensive data show that low dietary intake of omega-3 fatty acids, and particularly docosahexaenoic acid (DHA), increases the risk for PTB/ePTB. Furthermore, meta-analyses of clinical trials that include tens of thousands of participants conclude with high certainty that universal supplementation of pregnant women reduces the incidence of both PTB and ePTB, with the most recent analysis reporting reductions of 12% and 35%, respectively. Recent clinical trials in the U.S. conducted with DHA produced by algae demonstrate that for most women, 600 – 1,000 mg of algal DHA per day is highly effective at reducing PTB and ePTB. We estimate that universal supplementation at these levels would have prevented 45,000 preterm births in 2021, including over 35,000 early preterm births. Between 2023 – 2030, the number of preterm and early preterm births could be reduced by 317,000 and 253,000, respectively, and 25% of the reduction in ePTB would be in infants born to Black women.

We conducted an economic analysis to estimate the potential cost savings of supplementing all pregnant women with protective levels of algal DHA, to reduce the impact of PTB and ePTB. The cost of supplementing pregnant women with 1000mg of algal DHA per day for 24 weeks (the time clinically shown to be protective) would be $927 million. Considering both the efficacy and cost of DHA, we estimate that universal supplementation would have reduced net direct hospital costs associated with preterm birth by nearly 5.0 billion dollars in 2021, with the total net savings (including lifetime costs associated with PTB-associated comorbidities) being $7.39 billion. Between 2023 and 2030, the cumulative potential direct and indirect net savings is expected to be nearly $67 billion.

The high rates of PTB and ePTB in the U.S. is a crisis, and one that places disproportionate burden on certain minority communities. Compelling, high-quality data demonstrate unequivocally that universal DHA supplementation of pregnant women substantially reduces the rates of PTB and ePTB, and thus their associated lifetime disabilities. Supplementing pregnant women with algal DHA is relatively inexpensive, would prevent tens of thousands of preterm births, and would save tens of billions of dollars through the rest of this decade.

Introduction

Preterm birth (PTB) is a leading cause of infant mortality, accounting for over one third of infant deaths in the United States (1). Even for survivors, PTB dramatically increases the incidence of certain lifelong disabilities such as cerebral palsy, as well as other intellectual and developmental disabilities (1). The earlier an infant is born, the greater the risks (1). Any birth before 37 weeks is considered preterm, but infants are commonly categorized as late preterm (born between 34-36 weeks gestation) and early preterm (born before 34 weeks gestation) (2). The preterm birth rate in the US reached its highest point in at least 14 years in 2021. In 2022, the March of Dimes published their maternal health report card and rated the United States a D+ because of increasing rates of PTB and a widening racial health equity gap (3). Furthermore, infant mortality rates are higher in the US than almost all other industrialized countries, largely because of the high preterm birth rate (4).

Several factors can contribute to increased risk of PTB, including inadequate prenatal care, maternal age, diabetes, hypertension, obesity, and poor nutrition (5). Public health strategies to reduce preterm birth rates include those aimed at optimizing health prior to pregnancy and providing effective interventions to women most at risk of PTB (1). Unfortunately, interventions to prevent preterm birth are very limited. The only drug aimed at preventing recurrent preterm birth is being pulled off the market because the FDA determined that it is ineffective (6, 7).

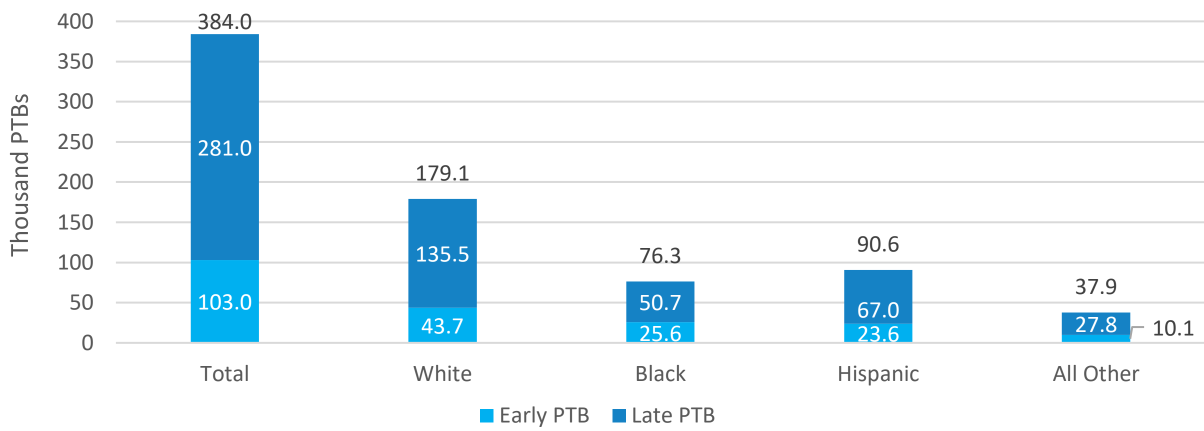
A 2018 Cochrane meta-analysis concluded there is high-quality evidence that dietary supplementation with omega-3 fatty acids, such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), during pregnancy is an effective intervention to reduce the risk of PTB and early preterm birth (ePTB), and that no further studies were needed to establish causality (8). These findings were more compelling for studies that utilized DHA alone or DHA predominant blends. A 2021 updated meta-analysis included 36 trials with 23,726 participants that investigated PTB, and 12 trials with 16,782 participants that explored ePTB. This analysis confirmed with high certainty that omega-3 supplementation during pregnancy reduces the incidence of both PTB and ePTB, with reductions of 12% and 35%, respectively (9).

In this study, we examine the potential immediate direct medical cost savings and lifetime indirect cost savings that could be realized if expectant mothers were to consume algal DHA supplements that have been shown to lower the incidence of PTB and ePTB. Specifically, this report will demonstrate that universal supplementation of algal DHA at protective levels by expectant mothers in the U.S. could reduce the direct and indirect medical costs associated with PTB by tens of billions of dollars through the rest of this decade.

Preterm Birth Rates in the United States

CDC data show that the rate of PTB has been increasing since 2014. Nearly 384 thousand infants were born preterm in 2021, representing 10.5% of all births, the highest rate since at least 2007 (2, 10). Over 103 thousand of these babies were born before the end of the 34th week of gestation, corresponding to an ePTB rate of 2.8%, the highest since 2011 (2). Furthermore, the rates of PTB and ePTB are disproportionately higher in certain minority populations (2). Most of the growth in PTB rates in recent years was driven by increasing PTB rates among Black Americans.[1] In 2021 almost 15% of infants born to Black mothers were premature, compared to 9.5% of infants born to White mothers (2). The rate of ePTB was more than double in Black women (4.95% of births) compared to White women (2.31%) (2). Rates of PTB and ePTB are also higher among Hispanic, Native American or Alaska Native, and Native Hawaiian or Pacific Islander women compared to White women, but lower than in Black women (2, 10). Rates of PTB and ePTB are similar between White and Asian women (2). For the purposes of this report, race/ethnicity cohorts are reported as White, Black, Hispanic, and all other. Chart 1 shows U.S. total preterm births and PTB rates by race/ethnicity cohorts and gestation duration in 2021.

Chart 1. Number of Preterm Births and Preterm Birth Rates by Gestation Duration and Race/Ethnicity, 2021



	Total	White	Black	Hispanic	All Other
Total PTB (%)	10.5%	9.5%	14.8%	10.2%	10.2%
Early PTB (%)	2.8%	2.3%	5.0%	2.7%	2.7%
Late PTB (%)	7.7%	7.2%	9.8%	7.6%	7.5%

Note: All figures are rounded to nearest significant digit. All other includes all other race/ethnicity cohorts that are not Hispanic, Black or White. Source: Osterman 2023, US Census and Frost & Sullivan analysis

[1] For the purposes of this study, the Black American cohort classification is synonymous with non-Hispanic Black Americans and the White American cohort classification is synonymous with non-Hispanic White Americans. Hispanic Americans includes all Americans of Hispanic descent, independent of race. The All-Other cohort includes all other people not classified as Hispanic, Black, or White.

Looking forward, we took a conservative forecasting approach and assumed that U.S. birth rates would continue to decline at similar rates as they have in the past decade (2, 10). Furthermore, since the PTB rate in 2021 (10.5%) was the highest it had been since 2007 and to avoid overestimating, we applied an average of PTB rates between 2016 to 2021 (10.1%) to forecast the number of PTB from 2022 to 2030 (2). Likewise, we applied an average ePTB rate of 2.76% for all years from 2022 to 2030 following the same logic. See Supplement Table 1 for projected birth rates including PTB and ePTB rates. Given these projections, it is conservatively estimated that over 2.6 million babies will be born preterm between 2023 and 2030, including 728,000 babies that will be born early preterm.

The Direct Costs of Preterm Birth

PTB and especially ePTB often result in high economic costs. For example, those born early often spend time in a hospital's neonatal intensive care unit (NICU) to monitor growth and development, as well as to treat serious preterm birth-attributed health conditions such as necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), respiratory distress syndrome (RDS), retinopathy of prematurity (ROP), and neonatal sepsis (11, 12). Some babies need NICU care for weeks or months until they can breathe on their own, eat by mouth, and maintain their body temperature and body weight. Costs associated with the first six months of medical care are referred herein as "direct costs".

Beam et al. 2020 conducted a detailed review of the excess health care expenditures associated with neonatal hospitalization related to PTBs in the first six months of life in a commercially insured population in the U.S. from 2008-2016 (13). The researchers found that from 2008-2016, the average first 6-month healthcare cost of infants with billing codes indicating preterm status (<37 weeks, n = 50,511) incurred medical expenditures of $76,153 versus a baseline cost of a full-term of only $6,370 per birth (13). After adjusting for recent price inflation, it is expected that the average six-month excess expenditure on health care costs per PTB for all infants born under 37 weeks and paid for by private insurers was $89,693 in excess of the normal cost of a full-term birth in 2021. This cost varies by gestation duration and increases for early preterm infants born before 34 weeks of gestation. Specifically, the average direct excess expenditure per late PTB (34-36 weeks) was only $23,629 per case, but this increases to $175,050 per ePTB (<34 weeks) because of the higher likelihood of suffering from a comorbidity and longer duration of hospitalization. The cost of care also varies by the type of insurance provider and the above estimates accounts for only those who were privately insured and not those who are insured by Medicaid. According to McLaurin 2019, the hospital cost of a PTB by Medicaid recipients was less than the cost of a PTB by patients with private insurance by a factor of 7 to 10 (14). And according to Meltzer et al. 2019, forty-nine percent (49%) of PTBs in the United States are paid for with Medicaid benefits (15).

Using the aforementioned findings, it is expected that the average direct excess health care expenditures in the first six months of life per PTB for all infants born under 37 weeks independent of payer (private insurance and Medicaid births combined) was $76,414 in 2021, after also adjusting for recent price inflation. For babies born in the 34th to 36th week of gestation (late PTB), the average direct excess health care expenditures associated with post-birth neonatal hospitalization was estimated at $20,131 and for children born under 34 weeks, the direct excess costs associated with post-birth neonatal hospitalization increases to $149,134 above the cost of a full-term birth.

When considering only the direct costs of a PTB-attributed neonatal hospitalization (first 6 months), the total population's direct cost burden was $21.02 billion in the year 2021 (Table 1). The total direct cost burden attributed to ePTBs was $15.36 billion in 2021, or nearly three-fourths (73.1%) of the total direct cost burden of managing the consequences of PTBs. This projects to $183.07 billion in cumulative direct excess healthcare expenditures related to future PTB cases from 2023 to 2030.

Table 1. Total Excess Direct Cost of Premature Births: Expected Direct Excess Health Care Cost of PTB-attributed Neonatal Hospitalization by Gestation Duration, $US Billion, United States, 2021-2030

Gestation Duration	2021, $US B	Average per Year, yrs. 2022-2030, $US B	Cumulative, yrs. 2023-2030, $US B
Total Under 37	21.02	22.57	183.07
34–36	5.66	5.95	48.12
Under 34	15.36	16.62	134.95

Note: All figures are rounded to nearest significant digit. Source: Frost & Sullivan analysis

The Indirect Costs of Preterm Birth

PTB and especially ePTB dramatically increase the incidence of certain lifelong disabilities such as cerebral palsy, as well as other intellectual and developmental disabilities (1, 16). These lifetime comorbidities can lead to a greater "indirect cost" burden on each individual sufferer and on society as a whole.

The most common comorbidity associated with PTB is asthma, but the most debilitating include cerebral palsy (CP), intellectual and developmental disabilities (IDD), and autism (16, 17). The CDC National Health Interview Survey (NHIS) and other sources report the incidence of these comorbidities by gestation length, and the risk of all four increase dramatically with decreasing gestation (1, 16-24). Table 2 reports the risk of developing key comorbidities over the lifetime, by gestational age.

Table 2. Risk of Comorbidities Over the Lifetime Associated with Preterm Birth by Gestation Duration, Diagnoses per 1,000 births

Gestation Duration	Cerebral Palsy	Autism	IDD	Asthma
Full Term	2.3	24.3	11.9	145.4
34–36	6.7	34.1	19.7	190.5
Under 34	34.8	39.5	36.3	256.0

Source: CDC's National Health Interview Survey (NHIS), Chen et al. 2021, Wu et al. 2011 and Frost & Sullivan analysis

The aforementioned increased risk of suffering from PTB-associated comorbidities adds a greater cost burden on each individual sufferer and on society as a whole. These indirect lifetime costs include excess medical costs for disease management and therapy as the child ages, assistive devices, long-term disability care, special education, lost future earnings of the sufferer and caretakers, and premature death (25). Based on a review of health economic articles exploring the lifetime costs of CP and adjusting to 2021 dollars, it is expected that the average lifetime costs of each CP case was $1.365 M in 2021 (25). Similarly, it is expected that the average lifetime costs of each IDD case were $1.503 M, and the average lifetime costs of each ASD case were $0.540 M in 2021 (25). It is expected that the average lifetime costs of each asthma case were $52,822 in 2021 (23, 24). See Supplement Table 2 for the components of the lifetime costs of the comorbidities associated with PTBs.

Of course, not every PTB results in a comorbidity that leads to excess lifetime disability costs. Thus, only a portion of premature infants are actually at risk of bearing these extra indirect costs. After controlling for the risk of developing each of the aforementioned comorbidities and controlling for possible double counting of disability costs among those people suffering from more than one comorbidity, it is expected that the average risk-adjusted indirect cost of lifetime disability associated with related comorbidities for any PTB was $37,555 in 2021 (See Table 3). For babies born in the 34th to 36th week of gestation, the average risk-adjusted indirect cost of lifetime disability was estimated at $24,400 in 2021 and for children born under 34 weeks the indirect lifetime disability costs increases to $73,442 given the increased risk of developing comorbidities with ePTB.

Adding together the expected direct and indirect costs, it is expected that the total direct and risk-adjusted indirect cost of any PTB was $113,969 in 2021. For babies born in the 34th to 36th week of gestation, the expected direct and indirect cost was estimated at $44,531 in 2021 and for infants born under 34 weeks the indirect lifetime disability costs increases to $222,576 given the increased risk of developing comorbidities with ePTB. Table 3 reports the total direct and risk-adjusted indirect lifetime cost of disability associated with PTB per birth by cost component.

Table 3. Expected Per Case Cost Burden (Direct + Indirect) of Premature Births: Direct Excess Health Care Cost of a PTB-attributed Neonatal Hospitalization (First 6 months) and Risk-adjusted Lifetime Cost of Disability Associated with Preterm Birth-attributed Comorbidities by Gestation Duration, $ per Event, United States, 2021

Cost Components	Total Under 37 weeks	34–36 Weeks	Under 34 weeks
Risk-adjusted Indirect Cost of Lifetime Disability	37,555	24,400	73,442
Direct Excess Health Care Cost of a PTB-attributed Neonatal Hospitalization (First 6 months)	76,414	20,131	149,134
Total Direct and Indirect Cost per PTB, 2021	113,969	44,531	222,576

Note: All figures are rounded to nearest significant digit. Source: Frost & Sullivan analysis

These individual costs can then be summed across the entire population. The expected overall population burden of PTBs, which includes both the direct excess healthcare expenditure attributed to PTB neonatal care (Table 1) and the risk-adjusted indirect cost of disability attributed to PTB-associated comorbidities was $34.54 billion in 2021. The overall burden of ePTBs was $22.93 billion, or 66% of the total cost burden. Given forecasted growth and inflation rates, the total direct + indirect cost is expected to grow from now to 2030 to a cumulative total of $310.42 billion. Table 4 reports the total direct and indirect cost burden of PTBs for the United States as a whole.

Table 4. Total Cost (Direct + Indirect) of Premature Births: Expected Direct Excess Health Care Cost of a PTB-attributed Neonatal Hospitalization and Risk-adjusted Lifetime Cost of Disability Associated with Comorbidities by Gestation Duration, $US Billion, United States, 2021-2030

Gestation Duration	2021, $US B	Average per Year, yrs. 2022-2030, $US B	Cumulative, yrs. 2023-2030, $US B
Total Under 37	34.54	38.45	310.42
34–36	11.61	12.84	103.76
Under 34	22.93	25.61	206.66

Note: All figures are rounded to nearest significant digit. Source: Frost & Sullivan analysis

Reducing Preterm Birth Risk with DHA Supplementation

Women who have adequate DHA levels and/or intakes prior to and early in pregnancy have lower preterm birth rates compared to women with low DHA levels and/or intakes (26-28). At a population level, preterm birth rates fall as omega-3 intakes increase up to a threshold of about 550 – 600mg omega-3 per day (29, 30). These fatty acids may help to prolong gestation by shifting metabolic pathways toward the production of anti-inflammatory mediators to reduce or prevent the inflammatory processes associated with the induction of labor (31-33). Although omega-3 fatty acids in general have been associated with reduced PTB risk, DHA appears to be responsible for most of the observed effect (8, 34).

Unfortunately, few foods are rich in DHA. DHA is produced by algae, and in the human diet is mainly found in fatty fish), and ~95% of pregnant women and women of child-bearing age in the United States have omega-3 intakes (DHA plus EPA) below recommended levels (35). A recently published study reported that women who consumed inadequate amounts of DHA from combined diet and supplements were more likely to have lower income, less education, and be Black or Hispanic (36).

A 2018 Cochrane meta-analysis of available clinical data concluded that there is high quality evidence that omega-3 intake (mostly via supplementation) during pregnancy is an effective strategy to reduce the risk of PTB and ePTB, and that no further studies comparing DHA or DHA+EPA to placebo were needed to establish causality (8). The researchers found that the relative risk of a PTB decreased by 11% and that the relative risk of an ePTB decreased by 42% among expectant mothers supplementing with omega-3 fatty acids (8). Importantly, these findings were driven largely by studies using doses of omega-3 fatty acids in the range of 600-1000mg per day and were more compelling for studies that utilized DHA alone or DHA predominant blends (8). The average length of supplementation among all included studies was 24 weeks (8).

Since then, additional clinical trials have been reported, including three large trials conducted in China, the United States, and Australia (26, 28, 37). An updated meta-analysis including the newer trials was published in 2022 (9). This publication included 36 trials with 23,726 participants that investigated PTB, and 12 trials with 16,782 participants that explored ePTB. This analysis confirmed with high certainty that omega-3 supplementation during pregnancy reduces the risk of both PTB and ePTB, with calculated reductions of 12%

and 35%, respectively (9). Table 5 reports the findings from the two meta-analyses, including predicted relative risk reductions with 95% confidence intervals.

Table 5. Expected Efficacy of DHA supplement Utilization on Preterm Birth Event Occurrence

Study [Ref]	Gestation Period	Trials	Participants (n)	Risk Ratio (95% CI)	Relative Risk Reduction (95% CI)
Middleton et al. 2018	Preterm Birth (<37w)	26	10,304	0.89 (0.81-0.97)	0.11 (0.19-0.03)
	Early Preterm Birth (<34w)	9	5,204	0.58 (0.44-0.77)	0.42 (0.56-0.23)
Best et al. 2022	Preterm Birth (<37w)	36	23,726	0.88 (0.81-0.95)	0.12 (0.19-0.05)
	Early Preterm Birth (<34w)	12	16,782	0.65 (0.46-0.92)	0.35 (0.54-0.08)

The number of possible PTBs that could be prevented if all expectant mothers were to consume DHA supplements at effective levels can be calculated by multiplying the observed event risk rate of a PTB for each segment of the population (as reported in Chart 1) by the expected risk ratios (relative risk) reported in the most recent meta-analysis (Table 5) (9). This establishes new event rate estimates that are conditioned on the use of DHA supplements. The difference between observed event rates and the conditional event rates is an estimate of the absolute risk reduction an individual user would capture if they supplemented with DHA. Taking the inverse of the calculated absolute risk reduction provides an estimate for total number of people within a target cohort who would have to supplement with DHA in order to realize one avoided PTB or ePTB and once the absolute risk reduction is determined, the total number of potentially avoided PTBs and ePTBs can be calculated. See Supplement Table 3 for a detailed description of the derivation of the number needed to treat metric used to estimate total potential avoided PTBs.

In 2021, the estimated total number of potentially avoidable PTBs given 100% utilization of DHA supplements at protective levels by all pregnant women would have been approximately 45 thousand births, of which over 35 thousand births would have been avoided ePTBs. The predicted cumulative number of potentially avoidable PTBs per year from now (2023) to 2030 is approximately 317 thousand avoided PTBs, of which nearly 253 thousand are ePTBs. The reductions in PTB and ePTB would be disproportionately greater in certain minority communities compared to in White women, given their higher rates of preterm birth. For example, it is predicted that over 68 thousand of the avoided PTBs (22%), including over 62,000 avoided ePTBs (25%), would be in Black women. Refer to Table 6 for the estimated number of potentially avoidable PTB and ePTBs (reported with 95% confidence intervals) given utilization of DHA supplements by the total population and selected race/ethnicity cohorts.

Table 6. Estimated Number of Potentially Avoidable Preterm Births Given Utilization of DHA Supplements by Expectant Mothers by Selected Race/Ethnicity Cohorts and Gestation Duration, Thousand Births, United States, 2021-2030

Race/ Ethnicity	Gestation Duration	2021, Thousand Births (95% CI)	Average per Year, yrs. 2022-2030, Thousand Births (95% CI)	Cumulative, yrs. 2023-2030, Thousand Births (95% CI)
Total	Total Under 37	45.28 (17.92-68.08)	40.57 (16.53-62.82)	317.40 (115.72-439.73)
	34–36	9.85 (8.76-15.25)	8.32 (8.08-14.07)	64.63 (56.55-98.5)
	Under 34	35.43 (7.83-52.83)	32.24 (7.22-48.75)	252.77 (50.55-341.24)
White(1)	Total Under 37	21.12 (8.37-31.79)	18.77 (7.63-28.99)	146.48 (53.4-202.94)
	34–36	6.1 (5.04-9.33)	5.19 (4.6-8.51)	40.28 (32.17-59.57)
	Under 34	15.02 (3.33-22.46)	13.58 (3.03-20.48)	106.20 (21.24-143.37)
Black(1)	Total Under 37	9.9 (3.91-14.86)	8.76 (3.56-13.52)	68.33 (24.91-94.67)
	34–36	1.08 (0.81-1.95)	0.78 (0.74-1.77)	5.88 (5.15-12.42)
	Under 34	8.82 (1.96-13.24)	7.98 (1.78-12.04)	62.45 (12.49-84.30)
Hispanic	Total Under 37	10.69 (4.23-16.08)	9.85 (4.04-15.36)	77.62 (28.3-107.54)
	34–36	2.56 (2.38-4.09)	2.32 (2.28-3.91)	18.22 (15.94-27.34)
	Under 34	8.12 (1.78-11.99)	7.53 (1.7-11.46)	59.40 (11.88-80.2)
All Other	Total Under 37	4.47 (1.74-6.6)	3.92 (1.59-6.05)	30.57 (11.14-42.35)
	34–36	1.01 (0.93-1.6)	0.88 (0.85-1.47)	6.83 (5.97-10.30)
	Under 34	3.46 (0.74-4.99)	3.04 (0.68-4.58)	23.74 (4.75-32.05)

Note: All figures are rounded to nearest significant digit. (1) Non-Hispanic. All other includes all other race/ethnicity cohorts that are not Hispanic, Black or White. Source: Frost & Sullivan analysis

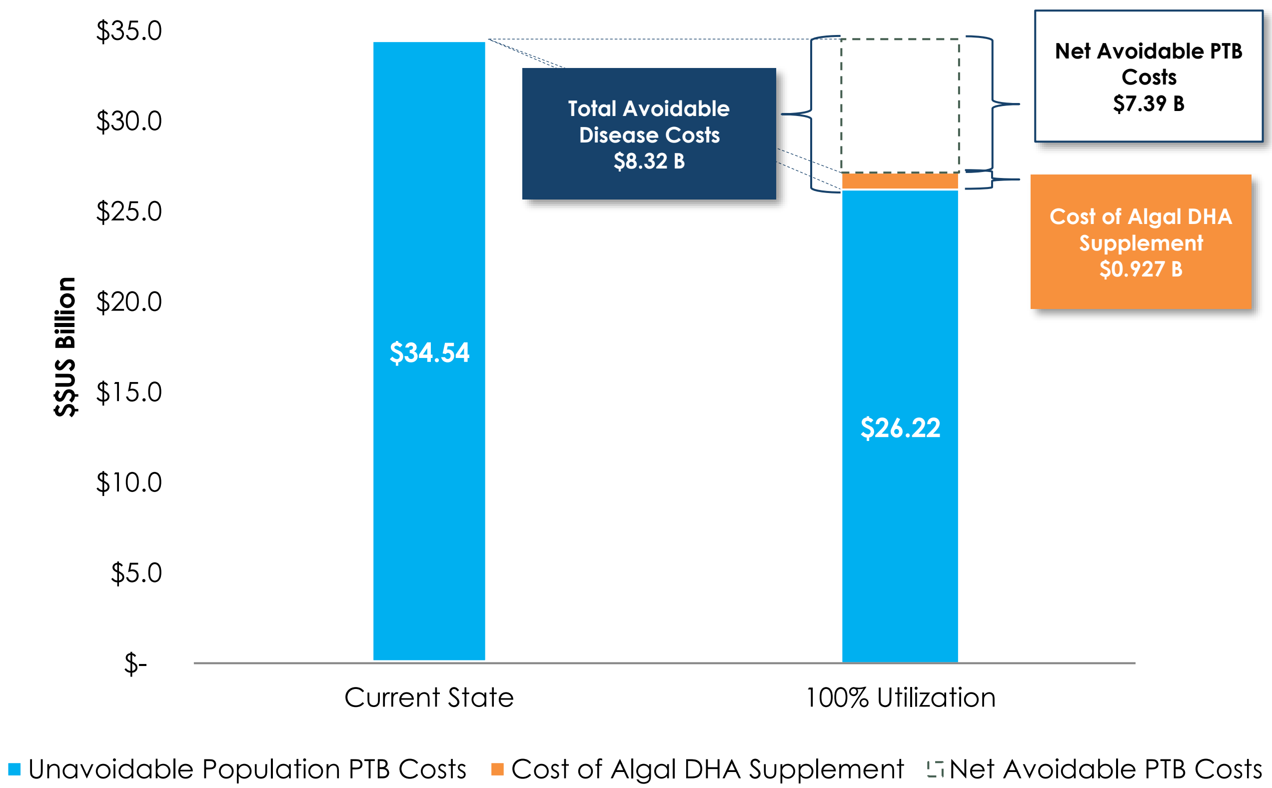
Economic Implications of Preterm Birth Prevention

The research methodology used in this economic report is based on a health-to-wealth Supplement Utilization Cost-Benefit Analysis (CBA) model developed in 2013 that allows 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 (38). After estimating the number of potentially avoidable PTBs given utilization of DHA supplements (see Table 6), the potential avoided healthcare and lifetime disability costs associated with these avoided PTBs can be calculated (38). First, the total avoided PTBs by gestation period and race/ethnicity from Table 6 was multiplied by the expected cost burden of each PTB as reported in Table 3 and then summed up to report total potential savings (Table 7). Then, the cost of DHA supplementation was subtracted from this total benefit since supplementation does have a small financial cost to each user and is considered the trade-off required to gain the absolute risk reduction (Table 8).

With respect to the basis of the expected cost of algal DHA supplementation, the average length of time of supplementation from the Cochrane review was 24 weeks (168 days) (8). The algal DHA dose chosen for this analysis was 1000 mg per day because it was at the upper end of the range identified as being the most impactful in the Cochrane review, and because a recent, large NIH-funded clinical trial demonstrated that 1,000mg of algal DHA was more effective than 200mg at reducing PTB and ePTB (28, 39). Choosing the highest, and thus the most expensive, dose is the most conservative case from an economics perspective. Prices for OTC algal DHA supplements were referenced on Oct. 12, 2022, from retailers including Amazon, Target, Walgreens, GNC and direct from manufacturers e-commerce platforms. Only algal-derived DHA supplements were included because the Cochrane review indicated that DHA or DHA predominant omega-3 blends had a greater impact on reducing ePTB than did mixed DHA/EPA blends (fish oils tend to have more EPA than DHA). In addition, algal DHA is more sustainable environmentally than that from fish. It was determined that the average price for 1,000 mg of algae-sourced DHA supplements was approximately $1.53 per daily dose in 2021. Given this daily cost requirement, the expected cost of a full 24-week DHA supplement regimen at 1,000 mg per day for an expectant mother would have been $257.37 per regimen per user in 2021. Furthermore, the total cost of supplying DHA supplements to all expectant mothers would have been approximately $927 million in 2021, and $1.03 billion per year from 2022 to 2030.

Chart 2 provides a summary of the total direct and indirect cost savings related to avoidable preterm births that could have been realized given 1,000 mg daily DHA supplementation per user in 2021. The total direct and indirect health care cost of PTB in 2021 was $34.54 billion (Table 4). The avoidable cost from DHA usage reducing PTB and ePTB was $8.32 billion (Table 7). Subtracting the population cost of DHA ($927 million), **the net avoided direct and indirect costs of PTB in 2021 would have been $7.39 billion (Table 8).**

Chart 2. Summary of the Benefits and Total Direct and Indirect Cost Drivers Related to Avoidable Preterm Births, 1,000 mg Daily DHA supplementation per User, $USD Billion, United States, 2021



Source: Frost & Sullivan

More specifically, the potential direct and indirect healthcare cost savings from avoidable PTBs given 100% utilization of omega-3 DHA by all expectant mothers at 1,000 mg per day serving would have been $8.32 billion in 2021 of which $7.89 billion of these savings is associated with the highly expensive ePTBs (Table 7). In other words, **95% of potential healthcare cost savings related to avoided preterm births would have been directly associated with preventing early PTBs.** Moving forward, the average direct and indirect healthcare cost savings from avoidable PTBs is expected to be $9.29 billion per year from 2022 to 2030 of which $8.83 billion of these savings is associated with ePTBs. It is expected that cumulatively $75.02 billion in total potential direct and indirect healthcare cost savings from avoidable PTBs would be realized between 2023 to 2030, given 100% utilization of 1,000 mg of algal DHA by expectant mothers. See Table 7 for the full economic results reporting the total potential direct and indirect health care cost savings from avoidable PTBs given 100% utilization of DHA supplements.

Table 7. Total Potential Direct and Indirect Health Care Cost Savings from Avoidable Preterm Births Given 100% Utilization of 1,000 mg Algal DHA supplements by Expectant Mothers by Selected Race/Ethnicity Cohorts and Gestation Duration, $US billion, United States, 2021-2030

Gestation Duration	2021, $US B (95% CI)	Average per Year, yrs. 22-30, $US B (95% CI)	Cumulative, yrs. 23-30, $US B (95% CI)
Total Under 37	8.32 (1.85-18.96)	9.29 (2.16-22.11)	75.02 (17.43-178.45)
34–36	0.44 (0.28-1.32)	0.47 (0.33-1.54)	3.77 (2.68-12.49)
Under 34	7.89 (1.57-17.64)	8.83 (1.83-20.56)	71.26 (14.75-165.97)

Note: All figures are rounded to nearest significant digit. Source: Frost & Sullivan analysis

As previously stated, the cost of algal DHA supplementation ought to be accounted for when determining net cost savings available to users. In 2021, the **net** potential direct and indirect healthcare cost savings from avoidable PTBs given 100% utilization of omega-3 DHA by all expectant mothers at a 1,000 mg per day serving would have been $7.39 billion in total net savings, and the net annual average cost savings from avoidable PTBs from 2022 to 2030 is expected to be $8.26 billion per year (Table 8). **Cumulatively, $66.64 billion in total net potential direct healthcare cost savings from avoidable PTBs given 100% utilization of 1,000 mg of omega-3 DHA is expected through 2030.** Twenty-eight percent (28%) of the total potential health care cost savings from avoidable preterm births had all expectant mothers utilized algal DHA supplements at preventive intake levels of 1,000 mg per day would have been among Black Americans in 2021 ($2.10 billion in total net savings). See Table 8 which reports the net potential direct and indirect health care cost savings from avoidable PTBs given the cost of 100% utilization of DHA supplements by expectant mothers by selected race/ethnicity cohorts at 1,000 mg dose.

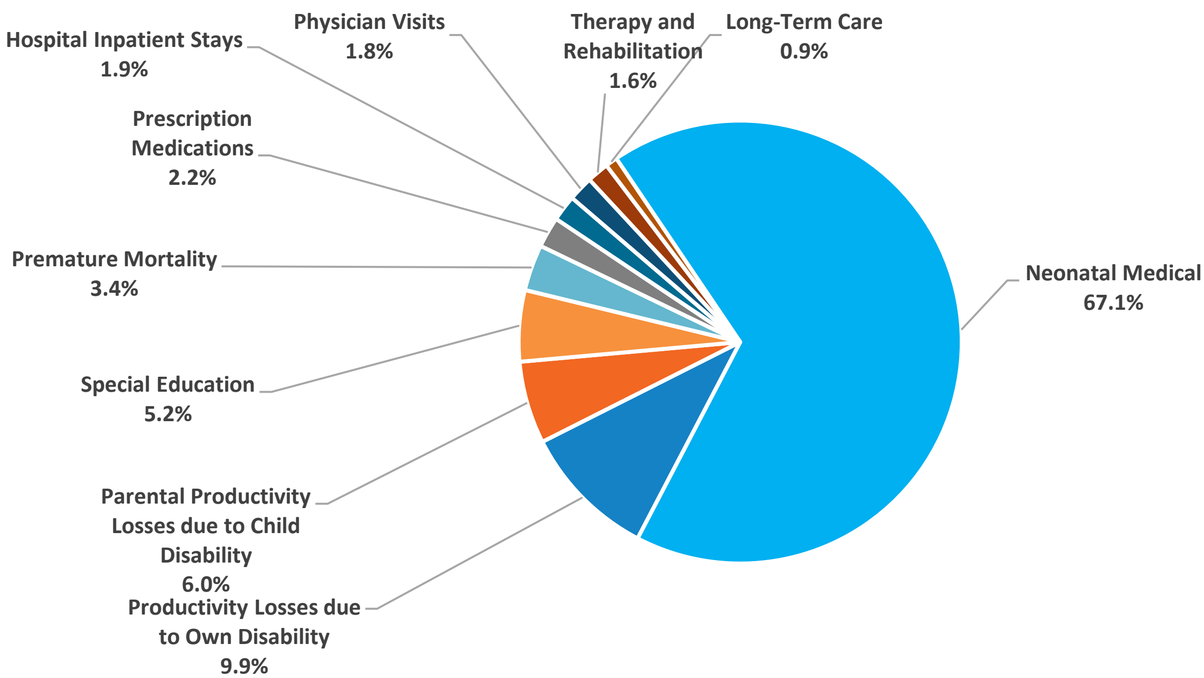
Table 8. Net Potential Direct and Indirect Health Care Cost Savings from Avoidable Preterm Births Given 100% Expectant Mother Utilization of DHA supplements, 1,000 mg dose, $US billion, United States, 2021-2030

Race/ Ethnicity	2021, $US B (95% CI)	Average per Year, yrs. 22-30, $US B (95% CI)	Cumulative, yrs. 23-30, $US B (95% CI)
Total	7.39 (0.85-17.29)	8.26 (0.99-20.16)	66.64 (8.01-162.58)
White(1)	3.08 (0.31-7.32)	3.42 (0.35-8.44)	27.51 (2.84-67.93)
Black(1)	2.10 (0.32-4.85)	2.34 (0.37-5.59)	18.87 (3.02-45.09)
Hispanic	1.59 (0.17-3.76)	1.83 (0.21-4.55)	14.80 (1.68-36.8)
All Other	0.63 (0.05-1.36)	0.68 (0.06-1.58)	5.46 (0.47-12.76)

Note: All figures are rounded to nearest significant digit. (1) Non-Hispanic. All other includes all other race/ethnicity cohorts that are not Hispanic, Black or White. Source: Frost & Sullivan analysis

Importantly, sixty-seven percent (67%) of potential healthcare cost savings will be in the form of avoided excess direct neonatal healthcare costs that occur during the child's first 6 months. In other words, the net potential direct healthcare cost savings directly attributed to excess neonatal hospitalization would have been approximately $4.96 billion dollars out of $7.39 billion in total net savings in 2021. The reason why the potential cost avoidance is so heavily weighted toward avoided excess hospitalization is because most of the avoided PTBs are ePTBs, the costliest type in terms of direct excess cost burden. Lifetime productivity losses related to possible comorbidities, both the losses of the sufferer and the caregiving parent, are the next largest cost components (15.9%) that could be avoided if all expectant mothers were to have used omega-3 DHA at PTB preventive intake levels. The remainder of the potential cost savings is in the form of avoided possible costs associated with direct and indirect medical costs related to comorbidities. Avoided expenditure on special education accounted for 5% of potential healthcare cost savings in 2021. See Chart 3 for the share of total potential health direct and indirect care cost savings from avoidable PTBs had mother utilized algal DHA supplements (1,000 mg) by cost type in 2021.

Chart 3. Share of Net Potential Health Direct and Indirect Care Cost Savings from Avoidable PTBs had Mother Utilized Algal DHA Supplements (1,000 mg) by Cost Type, %, United States, 2021



Note: All figures are rounded to nearest significant digit. Source: Frost & Sullivan analysis

Conclusion

The social burden of PTBs in the United States is immense and is at emergency levels (2, 3). PTB/ePTB is a leading cause of infant mortality in the United States, and among survivors is associated with increases in the incidence of several lifelong disabilities. The risk of death or disability increases dramatically the earlier the baby is born and is highest for those born early preterm. Furthermore, certain racial and ethnic groups bear an oversized incidence and burden of PTB and ePTB.

This study found that universal supplementation with effective levels of algal DHA to all expectant mothers in the US would result in a potential decrease of 317 thousand PTBs including 253 thousand ePTBs from now to 2030. This would result in a net potential average cost savings of $8.26 billion per year over the next seven years, culminating in a total potential net direct and indirect cost savings of $66.64 billion to the US healthcare system and society through 2030. These findings can inform government policy makers as well as non-government organizations focused on improvements in prenatal health outcomes in the US. Strategies that target increasing access to algal DHA supplements in all expectant mothers, but especially in those at higher risk of PTB and ePTB, would be highly impactful. Universal algal DHA supplementation to all pregnant mothers is a cost-effective strategy to save healthcare dollars, but more importantly it can save lives and improve long-term health outcomes for pregnant women and their children.

References

1. Shapiro-Mendoza CK, Barfield WD, Henderson Z, et al. CDC Grand Rounds: Public Health Strategies to Prevent Preterm Birth. *MMWR Morb Mortal Wkly Rep*. 2016;65:826–830. Available at http://dx.doi.org/10.15585/mmwr.mm6532a4external icon
2. Osterman MJK, Hamilton BE, Martin JA, et al. Births: final data for 2021. *National Vital Statistics Reports.* 2023;72(1):1-53.
3. March of Dimes. 2022 March of Dimes Report Card. November 2022. Available at https://www.marchofdimes.org/sites/default/files/2022-11/2022-MarchofDimes-ReportCard-UnitedStates.pdf
4. MacDorman MF, Mathews TJ, Mohangoo AD, et al. International comparisons of infant mortality and related factors: United States and Europe, 2010. *National Vital Statistics Reports.* 2014;63(5):1-7.
5. Bronstein JM, Wingate MS, Brisendine AE. Why is the U.S. preterm birth rate so much higher than the rates in Canada, Great Britain, and Western Europe? *Int J Health Serv.* 2018;48(4):622-40.
6. Center for Drug Evaluation and Research (CDER), Food and Drug Administration (FDA). Briefing materials supporting CDER's proposal to withdraw approval of Makena. Docket No. FDA-2020-N-2029. Available at: https://www.fda.gov/media/162246/download
7. U.S Food & Drug Administration. "FDA Commissioner and Chief Scientist Announce Decision to Withdraw Approval of Makena." Available at: https://www.fda.gov/news-events/press-announcements/fda-commissioner-and-chief-scientist-announce-decision-withdraw-approval-makena
8. Middleton P, Gomersall JC, Gould JF, et al. Omega-3 fatty acid addition during pregnancy. *Cochrane Database Syst Rev.* 2018;11(11):CD003402.
9. Best KP, Gibson RA, Makrides M. ISSFAL statement number 7 - Omega-3 fatty acids during pregnancy to reduce preterm birth. *Prostaglandins Leukot Essent Fatty Acids.* 2022;186:102495.
10. Hamilton BE, Martin JA, Osterman MJK. Births: Provisional Data for 2021. *National Vital Statistics Reports.* May 2022;20(1):1-11. Available at https://www.cdc.gov/nchs/data/vsrr/vsrr020.pdf
11. Moster D, Lie RT, Markestad T. Long-term medical and social consequences of preterm birth. *N Engl J Med.* 2008;359(3):262-73.
12. Centers for Disease Control. "Preterm Birth | Maternal and Infant Health | Reproductive Health | CDC." Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. Available at https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pretermbirth.htm
13. Beam AL, Fried I, Palmer N, et al. Estimates of healthcare spending for preterm and low-birthweight infants in a commercially insured population: 2008- 2016. 2020. *J Perinatol.* 2020;40(7):1091-99.
14. McLaurin KK, Wade SW, Kong AM, et al. Characteristics and health care utilization of otherwise healthy commercially and Medicaid-insured preterm and full-term infants in the US. *Pediatric Health Med Ther.* 2019;10:21-31.
15. Meltzer R, Markus AR. An Analysis of Payment Mix Patterns of Preterm Births in a Post-Affordable Care Act Insurance Market: Implications for the Medicaid Program. *Women's Health Issues*. 2020;30(4):248–259.
16. Pravia CL, Benny M. Long-term consequences of prematurity. *Cleve Clin J Med.* 2020;87(12):759-67.
17. Chen R, Sjölander A, Johansson S, et al. Impact of gestational age on risk of cerebral palsy: unravelling the role of neonatal morbidity. *International Journal of Epidemiology.* 2021;50(6):1852-63.
18. National Health Interview Survey (NHIS). National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). Available at https://www.cdc.gov/nchs/nhis/index.htm
19. Wu YW, Xing G, Fuentes-Afflick E, et al. Racial, ethnic, and socioeconomic disparities in the prevalence of cerebral palsy. *Pediatrics.* 2011;127(3), e674–e681.
20. McIntyre S, Goldsmith S, Webb A, et al. Global prevalence of cerebral palsy: a systematic analysis. *Dev Med Child Neurol.* 2022;64(12):1494-1506.
21. Centers for Disease Control and Prevention. Facts about intellectual disability. May 10, 2022. Available at https://www.cdc.gov/ncbddd/developmentaldisabilities/facts-about-intellectual-disability.html
22. Lord C, Elsabbagh M, Baird G, et al. Autism spectrum disorder. *Lancet.* 2018;392(10146):508-520.
23. Nurmagambetov T, Kuwahara R, Garbe P. The Economic Burden of Asthma in the United States, 2008-2013. *Ann Am Thorac Soc.* 2018;15(3):348-356.

24. Belova A, Fann N, Haskell J, et al. Estimating lifetime cost of illness. an application to asthma. *Annals of the American Thoracic Society.* 2020;17(12):1558–1569.
25. Honeycutt AA, Grosse SD, Dunlap LJ, et al. "Economic costs of mental retardation, cerebral palsy, hearing loss, and vision impairment." In Altman BM, Barnartt SN, Hendershot GE, et al. Using survey data to study disability: Results from the National Health Survey on Disability. Emerald Group Publishing Limited. 2003;3:207-28. Available at https://doi.org/10.1016/S1479-3547%2803%2903011-2
26. Olsen SF, Halldorsson TI, Li M, et al. Examining the effect of fish oil supplementation in Chinese pregnant women on gestation duration and risk of preterm delivery. *J Nutr.* 2019;149(11):1942–51.
27. Simmonds LA, Sullivan TR, Skubisz M, et al. Omega-3 fatty acid supplementation in pregnancy-baseline omega-3 status and early preterm birth: exploratory analysis of a randomised controlled trial. *BJOG.* 2020;127(8):975-981.
28. Carlson SE, Gajewski BJ, Valentine CJ, et al. Higher dose docosahexaenoic acid supplementation during pregnancy and early preterm birth: A randomised, double-blind, adaptive-design superiority trial. *EClinicalMedicine.* 2021;36:100905.
29. Ciesieleski TH, Bartlett J, Williams SM. Omega-3 polyunsaturated fatty acid intake norms and preterm birth rate: a cross sectional analysis of 184 countries. *BMJ Open*. 2019;9:e027249.
30. Ciesieleski TH, Williams SM. Low omega-3 intake is associated with high rates of depression and preterm birth on the country level. *Sci Rep.* 2020;10(1):19749.
31. Wang L, Fu Z, Deng W, Zhu S, Zhang C, Zhang W. Maternal fish and shellfish consumption and preterm birth: a retrospective study in urban china. Br J Nutr. 2021;Sep 24:1-9.
32. Massaro M, Habib A, Lubrano L, et al. The omega-3 fatty acid docosahexaenoate attenuates endothelial cyclooxygenase-2 induction through both NADP(H) oxidase and PKCε inhibition. *PNAS.* 2006;103(41):15184-9.
33. Araujo P, Belghit I, Aarsaether N, et al. The effect of omega-3 and omega-6 polyunsaturated fatty acids on the production of cyclooxygenase and lipoxygenase metabolites by human umbilical vein endothelial cells. *Nutrients.* 2019;11:966.
34. Lauterbach R. EPA + DHA in Prevention of Early Preterm Birth - Do We Know How to Apply it? *EBioMedicine.* 2018;35:16-17.
35. Zhang Z, Fulgoni VL, Kris-Etherton PM, et al. Dietary Intakes of EPA and DHA Omega-3 Fatty Acids among US Childbearing-Age and Pregnant Women: An Analysis of NHANES 2001-2014. *Nutrients.* 2018;10(4):416.
36. Christifano DN, Crawford SA, Lee G, et al. Utility of a 7-question online screener for DHA intake. *Prostaglandins Leukot Essent Fatty Acids.* 2022:177:102399.
37. Makrides M, Best K, Yelland L, et al. A randomized trial of prenatal n-3 fatty acid supplementation and preterm delivery. *NEJM*. 2019;381:1035-45.
38. Shanahan CJ, de Lorimier R. From Science to Finance—A Tool for Deriving Economic Implications from the Results of Dietary Supplement Clinical Studies. *J Dietary Supplements.* 2016;13(1):16-34.
39. Carlson SE, Gajewski BJ, Valentine CJ, et al. Early and late preterm birth rates in participants adherent to randomly assigned high dose docosahexaenoic acid (DHA) supplementation in pregnancy. *Clin Nutr.* 2023;42:235-43.

Supplementary 1

Supplementary Tables

Supplement Table 1. Current and Projected U.S. Births by Race/Ethnicity Cohorts and Gestation Duration, 2021-2030

Race/Ethnicity	Gestation Duration	2021, Thousand Births (% of Total Births)	Average per Year, yrs. 2022-2030, Thousand Births	Cumulative, yrs. 2023-2030, Thousand Births
Total	All Births	3664 (100)	3,337	26,109
	Total Under 37	384 (10.5)	340	2,652
	34–36	281 (7.7)	247	1,924
	Under 34	103 (2.8)	93	728
White(1)	All Births	1888 (51.5)	1,646	12,734
	Total Under 37	179 (4.9)	152	1,168
	34–36	135 (3.7)	114	877
	Under 34	44 (1.2)	38	290
Black(1)	All Births	518 (14.1)	508	4,043
	Total Under 37	76 (2.1)	72	575
	34–36	51 (1.4)	48	377
	Under 34	26 (0.7)	25	198
Hispanic	All Births	886 (24.2)	839	6,630
	Total Under 37	91 (2.5)	83	650
	34–36	67 (1.8)	61	479
	Under 34	24 (0.7)	22	170
All Other	All Births	373 (10.2)	345	2,702
	Total Under 37	38 (1)	33	260
	34–36	28 (0.8)	24	191
	Under 34	10 (0.3)	9	69

Note: All figures are rounded to nearest significant digit. (1) Non-Hispanic. All other includes all other race/ethnicity cohorts that are not Hispanic, Black or White. Source: Osterman 2023, US Census and Frost & Sullivan analysis

Supplement Table 2. Per Case Cost Burden of Premature Births: Expected Risk-adjusted Lifetime Cost of Disability Associated with Preterm Birth-attributed Comorbidities, % Share of Total Event Cost and $ per Event, United States, 2021

Cost Components	CP	IDD	Autism	Asthma
Physician Visits	4.6%	1.6%	0.0%	22.4%
Prescription Medications	0.5%	0.3%	0.0%	41.3%
Hospital Inpatient Stays	2.4%	6.4%	12.2%	3.1%
Assistive Devices	0.4%	0.2%	0.0%	0.0%
Therapy and Rehabilitation	2.0%	6.0%	11.4%	0.0%
Long-Term Care	0.4%	4.2%	5.3%	0.0%
Total Direct Medical Costs	**10.3%**	**18.6%**	**28.9%**	**66.8%**
Home Modifications and Transport	0.3%	0.1%	0.0%	0.0%
Special Education	7.1%	23.2%	28.0%	0.0%
Total Direct non-Medical Costs	**7.4%**	**23.3%**	**28.0%**	**0.0%**
Parental Productivity Losses due to Child Disability	22.5%	16.9%	27.4%	4.1%
Productivity Losses due to Own Disability	46.6%	34.9%	15.7%	3.8%
Premature Mortality	13.3%	6.3%	0.0%	25.3%
Total Productivity Losses	**82.3%**	**58.1%**	**43.1%**	**33.2%**
Total Lifetime Costs per Case	**100.0%**	**100.0%**	**100.0%**	**100.0%**
Expected Indirect Lifetime Cost per Confirmed Case, 2021 dollars	$1.365 M (95% CI $0.383 M-$2.494 M)	$1.503 M (95% CI $0.121 M-$1.733 M)	$0.540 M (95% CI $0.422 M-$2.746 M)	$52,822 (95% CI $42,055-$54,420)

Note: All figures are rounded to nearest significant digit. Source: Honeycutt et al. 2009, Nurmagambetov 2018, Belova 2019, Frost & Sullivan Analysis

Supplement Table 3. Expected Efficacy of 100% Utilization Omega-3 DHA Utilization by Expectant Mothers on a Preterm Birth Event Occurrence Given Risk of PTB by Selected Race/Ethnicity Cohorts and Gestation Period, United States, 2021-2030

Race/Ethnicity	Gestation Duration	Event Risk of PTB, % of Total Births born Preterm in 2021	Event Risk of PTB Given Use of DHA, % (95% CI)	Absolute Risk Reduction of PTB Given Use of DHA, % (95% CI)	Number of Expectant Mothers Needing to Supplement with DHA to Avoid One PTB or EPB, Users per Avoided PTB/EPB (95% CI)
Total	Total Under 37	10.5	9.2 (8.2-9.6)	1.3 (0.5-1.9)	80 (52-198)
	Under 34	2.8	1.8 (1.3-2.5)	1 (0.2-1.5)	102 (67-454)
White(1)	Total Under 37	9.5	8.4 (7.4-8.7)	1.1 (0.5-1.7)	88 (57-218)
	Under 34	2.3	1.5 (1-2.1)	0.8 (0.2-1.2)	123 (81-548)
Black(1)	Total Under 37	14.7	13.0 (11.5-13.5)	1.9 (0.8-3)	51 (34-128)
	Under 34	5.0	3.2 (2.3-4.5)	1.7 (0.4-2.6)	58 (38-255)
Hispanic	Total Under 37	10.2	9.0 (7.9-9.3)	1.2 (0.5-1.9)	81 (54-204)
	Under 34	2.7	1.7 (1.2-2.4)	0.9 (0.2-1.4)	107 (72-486)
All Other	Total Under 37	10.2	8.9 (7.8-9.1)	1.2 (0.5-1.8)	82 (55-208)
	Under 34	2.7	1.8 (1.2-2.4)	0.9 (0.2-1.4)	106 (72-488)

Note: All figures are rounded to nearest significant digit. (1) Non-Hispanic. All other includes all other race/ethnicity cohorts that are not Hispanic, Black or White. Source: Best et al 2022 and Frost & Sullivan analysis

Note on Research Methodology

As noted previously, the methodology used in this economic report is based on a health-to-wealth Supplement Utilization Cost-Benefit Analysis (CBA) model developed in 2013 that allows 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 (38). Using this model, it can be determined whether a given dietary supplement regimen is cost-effective 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 (38).

The definition of total benefits in this study is the total direct and indirect cost savings that would result if all expectant mothers had not supplemented with DHA supplements at protective levels prior to the base year of analysis (e.g., 2021) and then 100% of the target population adopted the DHA regimen in the same year and gained all potential benefits. This assumption was made in order to calculate per capita net benefits given DHA supplement utilization which in turn can be used to calculate the net avoided cost savings for the subset of the population yet to use DHA supplements.

The difference between the potential healthcare cost savings and the cost of DHA supplementation gives us the total net potential benefits to society if all eligible expectant mothers were to use DHA supplements. Accordingly, if the potential net cost savings are positive, the DHA supplement regimen would be considered a cost-effective means of reducing overall PTB-related individual lifetime costs and total social health care costs. This cost-benefit analysis approach assumes that in the supplementation scenario, the entire population of the target cohort of expectant mothers were supplemented at protective intake levels, and this was compared to zero utilization at protective levels in that population segment. Hence, the calculated net savings are actually the maximum potential net savings theoretically achievable. That said, DHA intakes among pregnant women in the U.S. are very low (60 – 75mg per day), so we believe that these estimates of net savings are reasonable (35).