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A Public Health Approach of Cataract Prevention Through Nutrition

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Abstract

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Results: There are enough evidence supporting the use of multivitamins decreases the risk of cataract. Higher intakes of antioxidants and vitamins has shown a protective association with the incidence or progression of cataract.

Conclusion: Developing healthy dietary and lifestyle patterns may help to protects against cataract. A moderately strong recommendation to consume foods that are rich in antioxidants (lutein, zeaxanthin, vitamin E and vitamin C), Vitamin A, Vitamin B or multivitamin are suggested.

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Cataract, Reactive Oxygen Species (ROS), Oxidative Stress, Free Radicals, Antioxidants, Posterior sub-capsular (PSC) Cataract

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A PUBLIC HEALTH APPROACH OF CATARACT PREVENTION THROUGH NUTRITION

by

AKANKSHA

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Keyword: Cataract, Reactive Oxygen Species (ROS), Oxidative Stress, Free Radicals, Antioxidants, Posterior sub-capsular (PSC) Cataract, Public Health

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INTRODUCTION

Cataract is the vision changing eye condition in which a normal crystalline lens becomes cloudy or loses its transparency. The crystalline lens is mostly made up of water soluble proteins called crystalline and water, the precise arrangement of which makes the lens transparent. This material is uniquely capable of transmitting light and focusing it on the retina to form clear vision.

Anatomy of crystalline lens

The crystalline lens is the transparent, avascular structure which focuses objects at various distances by changing its shape. Lens capsule, lens epithelium and lens fibers are the three main parts of crystalline lens.

Lens capsule is the outermost layer which surrounds the lens and it consists of type 4 collagen and sulfated glycosaminoglycan (GAGs) which make the capsule very transparent, and allow it to change the shape of lens during accommodation. Different growth factors are found in the capsule which allows migration and differentiation of the cells inside the lens. The lens capsule also facilitates metabolic waste in and out of the lens.[1]

The lens epithelium lies between the lens capsule and the lens fibers and is made up of simple cuboidal cells that are thought to be the primary source of metabolic activity in the lens. Na+/K+-ATPase pumps located in the lens epithelium help maintain appropriate lens osmotic balance through proper transportation which maintains lens transparency. The epithelium generates lens fibers which are responsible for proper growth and lens development throughout life.[2]

Lens fibers are thin, long and transparent cells which are tightly packed and form a larger portion of the lens. Lens transparency can be maintained by the continuous proliferation of the lens epithelium and their differentiation into lens fibers. Fiber cells continuously move from the periphery to the center of the lens as lens grows throughout life.[3]

Cataract is caused due to chemical changes within the protein material of the lens which causes a disruption in the transmission of light to the retina, preventing a clear image forming on the retina. Cataracts might be congenital, hereditary or age-related. The most common type of cataract is age-related cataract, which can be categorized as nuclear, cortical, or posterior

subcapsular (PSC), depending upon their location. Nuclear cataract is the gradual clouding of nucleus (center) of the lens and is most common in advancing age. Cortical cataract is the clouding of lens cortex that resembles like spokes of a wheel extending from outside to center of the lens and is most common in diabetic patient. PSC is an opacification of posterior surface under the capsule of lens and is mostly affect diabetics or long-term steroid users.[4] Nuclear cataracts and PSC commonly affect the central visual axis and hence affect central vision the most. The symptoms of cataract are hazy vision, difficulty with glare, halos, monocular diplopia, reduced color vision and contrast sensitivity.

Mechanism of cataract formation

The exact etiology of age-related cataract is not known. It can be formed due to various genetic or environmental factors. As age increases it also increases the risk for developing cataract. Cataract can be caused by various factors including aggregation and modifications of lens proteins due to various chemical reactions leading to oxidative damage to the lens. Some of the important mechanisms leading to cataract formation are:

Photochemical generation of reactive oxygen species (ROS) causing oxidative stress

Exposure to Ultra-violet (UV) radiation or smoking can lead to the generation of ROS, such as superoxide and singlet oxygen, hydrogen peroxide and hydroxyl radical, which causes damage to the deoxyribonucleic acid (DNA) found in the epithelial cell of the lens, which can lead to cataract formation.[5]

Polyol pathway

In diabetes, high concentrations of glucose can diffuse into the lens through aqueous humor. There is an enzyme called aldose reductase which converts excess glucose to sorbitol. These sugar alcohols (polyols – sorbitol) accumulate inside the lens. This accumulation of polyols inside the lens can cause diffusion of water and sodium from the aqueous humor to the crystalline lens. This can lead to the lens swelling and electrolyte imbalances resulting in the disruption of lens fiber leading to cataract formation.[6]

Denaturation and aggregation of lens proteins- The lens consists of proteins called α, β, and γ-crystalline which constantly undergo age related changes and can be denatured in the presence of oxidative or osmotic stress. As age increases, this crystalline becomes modified and aggregated causing the lens to lose its transparency which leads to cataract formation causing the light to scatter rather than focusing on to the retina.[7]

Hyperglycemia leading to the formation of advanced glycation end products (AGEs) - Type 2 diabetes can cause glycation of protein or lipid due to excess of sugar which are known as AGEs. This progressive accumulation of AGEs in the diabetic patients can cause oxidative stress leading to cataract formation.[8]

Decrease activity of Na+/K+ pump- As age increases there is a decrease in activity of the Na+/K+ pump which may lead to over hydration, protein loss, or increased Na+ and Ca+ and decreased K+ content inside the lens. The decrease in pump activity may cause oxidative damage to the fiber cell leading to osmotic swelling of lens fibers causing cataract.[5]

Abnormalities of gene and/or chromosomal expression within the lens can also lead to cataract formation, even at birth or early In life.

PREVALENCE

Cataract is the most common cause of vision loss in people over age 40 and is the principal cause of blindness responsible for economic and public health burden worldwide. Cataract blindness has become a global epidemic, accounting for 33% of blindness worldwide. According to the World Health Organization, cataracts in adults over 50 years of age are responsible for causing 47.8% of global blindness.[9] In the United States, age-related cataract has been reported in 42% of people between the age group of 52 and 64 years, 60% of people between the age group of 65 and 74 years, and 91% of people between the age group of 75 and 85 years.[10] Although cataract is the leading cause of blindness in the world, the impact of cataract is higher in developing countries due to the problems of access to effective treatment, growing population, illiteracy and low income. The proportion of blindness due to cataract among all eye diseases

ranges from 5% in developed countries to 50% or more in poor and/or remote regions. Cataract has been recorded to be the most significant cause of bilateral blindness in India. In India, cataract is the principal cause of blindness, accounting for 62.6% of blindness.[11]

Several studies revealed that many environmental and nutritional factors may play an important role in cataract incidence and progression. Oxidative stress is considered a major contributor to normal aging and results in many age-related diseases including cataract formation and its progression.[12,13] Oxidative stress is defined as the imbalance between damaging free oxygen radicals and the systems protective mechanisms (e.g. antioxidants). Free radicals are atoms or groups of atoms with an unpaired number of electrons and can be formed when oxygen interacts with certain molecules. Once formed these highly reactive radicals can start a chain reaction. Free radicals are a by-product of normal cell function that react quickly with other compounds and cause cellular damage. Antioxidants bind to free radicals and neutralize them. The number of free radicals may exceed the naturally occurring antioxidants due to various factors.[4] There are different factors which may cause an oxidative stress ultimately leading to cataract formation. Some of the risk factors which can be controlled by changing a life style are diabetes, excessive exposure to sunlight, excessive alcohol consumption, smoking and Improper diet.

Diabetes

A study was conducted by Li et al. to investigate the association between type 2 diabetes and the risk of cataract.[14] The study found that the risk of cataract in type 2 diabetic patients was higher than that in non-diabetics (OR = 1.97, 95% CI: 1.45-2.67, $P < 0.001$). Among different types of cataracts, the risk of PSC (OR = 1.55, 95% CI: 1.27-1.90, $P < 0.001$) and cortical cataract (OR = 1.68, 95% CI: 1.47-1.91, $P < 0.001$) was significantly associated with diabetes. However the study did not find any significant association between nuclear cataract and diabetes (OR = 1.36, 95% CI: 0.97-1.90, $P = 0.070$).[14] Diabetes causes progressive accumulation of AGEs which can cause oxidative stress leading to the cataract formation.[8] Megha Saraswat et al. showed that nutrients like ginger, cumin, cinnamon, black pepper and green tea may inhibit AGE formation to lens proteins up to 40– 90 %.[15]

Hypertension

Hypertension can increase the risk of developing cataract by causing inflammatory alteration of lens proteins. A meta-analysis conducted by Xiaoning Yu et.al. found that the risk of developing cataract with hypertension was significantly increased among different cohort studies (RR 1.08; 95% CI: 1.05–1.12) and case-control (OR 1.28; 95% CI: 1.12–1.45). PSC was more significantly associated with hypertension.[16] In one of the population-based prospective cohort studies, hypertension was significantly associated with a 12% increased risk of cataract extraction (RR, 1.12; 95% CI, 0.99–1.26).[17] Maintaining blood pressure by eating a diet rich in fruits, vegetables, low-fat dairy products may reduce the risk of developing cataract.[18]

Exposure to sunlight

Exposure to ultraviolet radiation, infrared radiation, and Ionizing radiation (such as X-rays and microwaves) can lead to cataract formation. When we are exposed to sunlight, many more reactive oxygen species like singlet oxygen, superoxide, and hydrogen peroxide are formed. Lens epithelium contains specific enzymes like superoxide dismutase that can destroy these destructive oxygen species by inactivating them. UVR exposure can inactivate superoxide dismutase causing oxidative stress inside the lens from ROS formation leading to cataract formation.[5] Antioxidants like glutathione, ascorbic acid (vitamin C) and alpha tocopherol (vitamin E) are present in the lens to detoxify this potentially dangerous reactive oxygen species. Exposure to UV radiation can cause depletion of glutathione oxidation reduction cycle which is also found in the lens epithelium resulting in oxidative damage and cataract formation.[19] Prevention of ocular exposure to UV radiation may reduce the risk of early cataract and retinal damage. UV radiation can be blocked by wearing large-framed wraparound sunglasses and different styles of hats like broad-brimmed hats, bucket hats and Legionnaires.[20, 21]

Excessive alcohol consumption

A meta-analysis conducted by Gong et al. to evaluate the association between different amounts of alcohol consumption and the risk of age-related cataract.[22] Study found that heavy alcohol consumption (daily intake of 20g of alcohol) was associated with an increased risk of age-related cataract (OR, 1.26; 95% confidence interval, 1.06 to 1.50), whereas the associations between

moderate alcohol consumption (daily consumption of less than 20g of alcohol) and age-related cataract was not significant (OR, 0.88; 95% confidence interval, 0.74 to 1.05).[22] The risk of developing cataract in heavy drinkers may be due to conversion of alcohol to acetaldehyde, which can react with lens protein leading to aggregation or denaturation of lens protein.[23] The findings on the association between cataract and alcohol consumption are inconsistent. Wei Wang et al performed a meta-analysis study to see overall increased risk of cataract due to alcohol intake. They did not find any correlation between alcohol use and cataract.[24]

Cigarette Smoking

Tobacco smoke contains carbon monoxide, nicotine, and other free radicals which can cause oxidative stress inside the lens. A meta-analysis of cohort and case-control studies was conducted to summarize the risk of developing age-related cataract due to smoking.[25] The study found a significant association between age-related cataract and smoking. Among different types of cataract, they found a strong association between nuclear cataract and smoking.[25]

Diet

Diet plays a very important role in maintaining eye health. Foods rich with vitamins, minerals and antioxidant such as those found in fruit and vegetables, help protect against oxidative damage and may decrease the development and progression of cataract. A high level of sugar in the blood and food with high level of fat and cholesterol may contribute to cataract formation. A case-control study was conducted in Athens, Greece, to assess the association between diet and risk of cataract including total of 314 cases of cataract and 314 frequency-matched controls of both sexes, aged 45-85 years.[26] All participants were interviewed using a food-frequency questionnaire, covering consumption of about 120 food items. They found a protective association between cataract risk and intake of carotene (OR = 0.56, $p < 0.001$), vitamins C (OR = 0.50, $p < 0.001$) and vitamins E (OR = 0.50, $p < 0.001$), while consumption of meat was positively associated with cataract (OR = 1.46, $p = 0.001$). The study concluded that diets rich in fruits, vegetables, fish, and pulses (legumes) may protect against cataract.[26] A meta-analysis was conducted to find the association of dietary carbohydrate intake and dietary glycemic index, and risk of age-related cataract.[27] The study found that higher dietary intake of carbohydrate (OR =

1.18, 95% CI: 1.01–1.38) as well as foods with a higher glycemic index (OR= 1.15, 95% CI: 1.00–1.32) were associated with increased risk of cataract. Higher carbohydrate intake was associated with increased risk of cortical cataract (OR: 1.37, 95% CI: 0.99–1.90), whereas, a higher glycemic index was associated with increased risk of nuclear cataract (OR: 1.23, 95% CI: 1.03–1.46).[27]

PURPOSE

Cataract is the major cause of blindness worldwide which accounts for almost half of global blindness. Increasing incidence of cataract with increasing age is a major public health concern. We have shown that there is growing evidence of exposure to UV light, cigarette smoking, and improper diet may contribute to the development of cataract. In recent years, nutrition and concern for a healthy diet has become an important public health issue. With an increase in the lifespan of elderly people, there is an increased risk of developing cataracts. Can changing eating habits and eating healthy nutritious food reduce this risk? Nutritious diets can be accessible to everyone. The purpose of this paper is to conduct a literature review related to preventing cataract through nutrition either in the form of consuming nutrient dense foods or supplements and making some public health recommendations. In this review paper, we address the following questions with respect to preventing cataract through nutrition:

1. Can eating healthy reduce the risk of cataract formation?
2. Whether nutrient dense foods or supplements are better?

METHODOLOGY

Searching Strategy and inclusion criteria:

The online databases OVID MEDLINE and WEB OF SCIENCE were used for electronic search. To build a well-designed question for this review PICO framework has been used. The following keywords were used based on PICO (Population, Intervention, Control and Outcome):

Population: “older people”

Interventions: “Nutrition”, “diet”, “antioxidants”, “multivitamin”

Control: comparator like people who didn't eat healthy food

Outcome: Cataract

Inclusion and exclusion criteria:

The eligible studies included were: (1) Meta-analyses (2) randomized control trials, case control or prospective cohort studies (3) Studies with human subject (5) Studies published in English from 2006 to current (6) Studies with people 45 or older.

Exclusion criteria for this review were the following: (1) letters, reviews, case reports, conference abstracts, editorials, and expert opinions; (2) studies in languages other than English; (3) animal studies.

Quality of studies included in this review were ranked using the American Optometric Association clinical guidelines as A, B, C, D in the reference list. Studies were graded depending upon strength of evidence and clinical recommendation.

Table 1: Studies grading strategy

Grade	Type of study	Strength of the evidence
A	Randomized clinical trials (RCT) with more than 50 subjects; Systematic reviews; meta-analyses of RCT	well-designed, convincing, with clear reason to make recommendations

B	Randomized clinical trials with less than 50 subjects; Meta-analysis of observational study, Cohort studies (retrospective or prospective);	weaker designs, quality of evidence is not as strong
C	Nonrandomized trials; Case control studies (retrospective or prospective)	strong design, uncertainty about conclusions or ambiguous
D	Cross sectional studies; case reports/series Reviews; position papers; expert opinion; or reasoning from principal	Lack of evidence to support or refutes the conclusion. Unclear balance between benefit and harm

http://www.aoa.org/Documents/EBO/EyeCareOfThePatientWithDiabetesMellitus%20CPG3.pdf

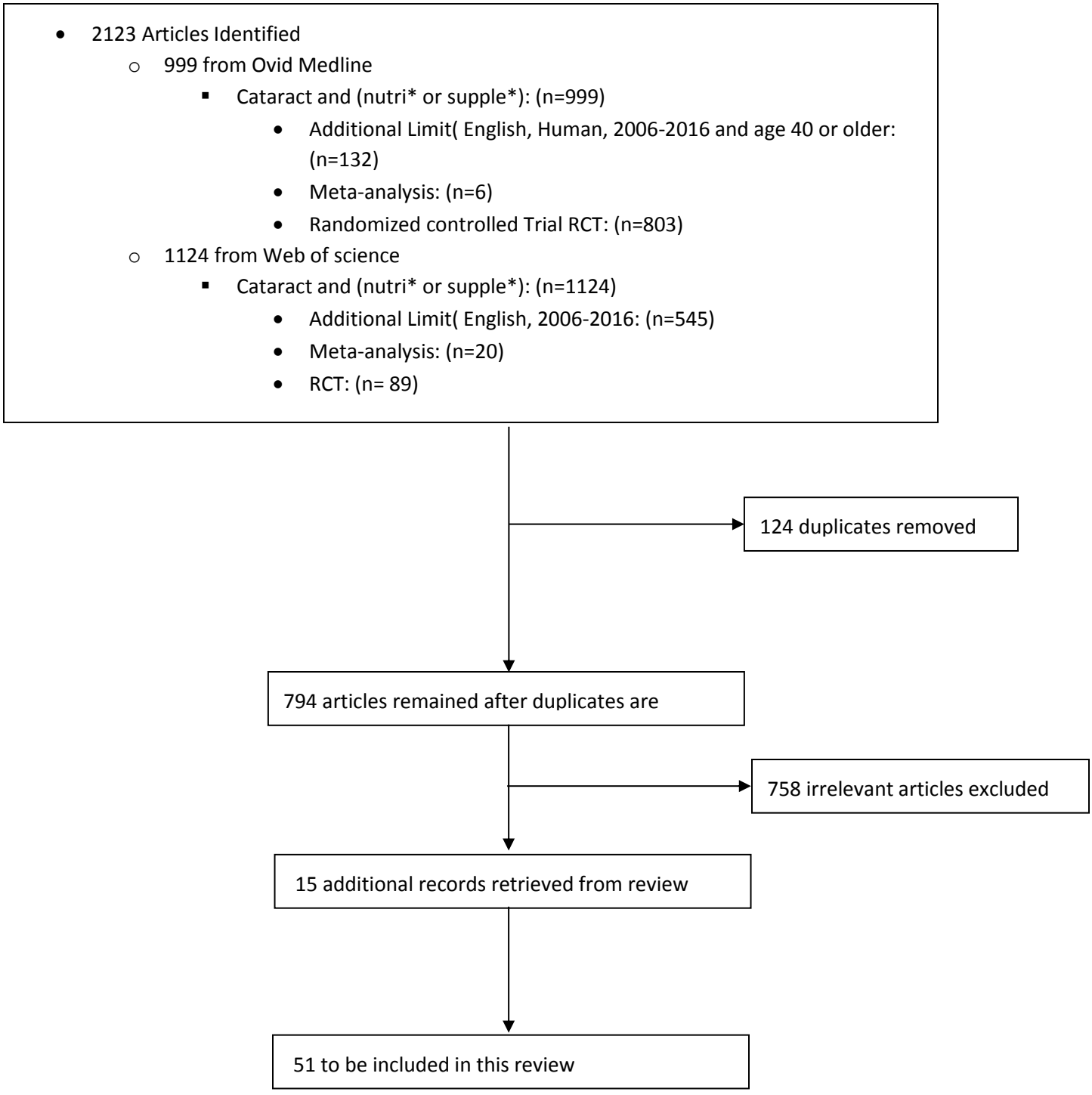

Figure 1: Flow Diagram of study Inclusion

RESULTS AND ANALYSIS

Our search strategy identified a total of 999 articles from Ovid Medline and 1124 from the Web of Science. After restricting the search to English language, human studies, studies published from 2006-current and studies with people 45 or older, 677 articles had been identified through these databases. A total of 26 meta-analysis and 892 randomized controlled trials were identified. Total number of articles after duplicates removed was 794. 720 of these 794 articles were subsequently excluded because of irrelevant topic. 30 were excluded after abstract review. 44 articles were considered relevant for this review. Out of 44 articles 8 articles were not found in full text. And 15 articles were retrieved manually from review paper. So 51 articles were included in the review. This review focuses on the studies which categorize different types of nutrients and see whether it alone or in combination works better to delay incidence and progression of cataract. Whether it works better in supplement form or nutrients from food. Studies excluded- those with different topic, outcome was not cataract, no full text available, uncertain about their conclusion, book chapter, an initial paper without result, not available in English or involved treatment other than nutrition like medication.

Table 2: Meta-analysis studies showing effectiveness of nutrition on cataract incidence and prevention.

Pooled estimates of odds ratios are reported in parentheses next to the nutrients. Odds ratios less than 1 are protective. Asterisks (*) indicate whether the 95% confidence interval does not overlap 1. Grading's of the studies are indicated in parenthesis in Authors column (A= Asterisks (*), B= (**), C= (***), D= (****)

Authors	Title	Studies	Participants	Study type	Nutrient(s)	Support/No support
Yu-Hong Cui, et al.[13] (***)	Association of blood antioxidants and vitamins with risk of age-related cataract: a meta-analysis of observational studies	13	18,999	2 case-control, 3 cohort, 8 cross-sectional	vitamin E (0.75*), α carotene (0.72*), lutein (0.75*), zeaxanthin (0.70*), Vitamins A (0.69*), vitamin C (0.67*0, β-Carotene (0.90), lycopene (0.86)and β-cryptoxanthin (0.83)	Supports inverse association between lutein (OR- 0.75; 95% CI: 0.65, 0.87), zeaxanthin (OR- 0.70; 95% CI: 0.60, 0.82), vitamin E (OR- 0.75; 95% CI: 0.58, 0.96) and α-carotene (OR- 0.72; 95% CI: 0.59, 0.88) and risk of cataract. Inverse association between Vitamins A (OR- 0.69; 95% CI: 0.58, 0.83) and vitamin C (OR- 0.67; 95% CI: 0.57, 0.78) and risk of cataract in Asian populations but not in Western populations
Xiao-Hong Liu, et al.[28] (***)	Association between Lutein and Zeaxanthin Status and the Risk of Cataract: A Meta-Analysis	8	12,080	7 cross-sectional, 1 cohort	Lutein (0.73*), zeaxanthin (0.63*)	Supports inverse association between lutein (RR-0.73; 95% CI: 0.59, 0.87), zeaxanthin (RR-0.63;95% CI: 0.49, 0.77) and nuclear cataract
Wang, Aimi, Han, Jing et al.[29] (**)	Association of vitamin A and [beta]-carotene with risk for age-related cataract: A meta-analysis	48	27572	30 prospective, 10 cross-sectional, 6 case-control, 2 RCT	β-carotene (0.93*), vitamin A (0.83*)	Supports inverse association between β-carotene(RR- 0.937; 95% CI: 0.880-0.997) and vitamin A (RR- 0.831; 95% CI: 0.757-0.913) and cataract formation

Yufei Zhang, et al.[30] (**)	Vitamin E and risk of age-related cataract: a meta-analysis	32	249,446	13 case-control, 8 cohort,5 RCT, 6 Cross sectional	Dietary vitamin E (0·73*), supplemental vitamin E (0·86*)	Supports inverse association between Dietary vitamin E intake (RR- 0·73*; 95 % CI: 0·58- 0·92), dietary and supplemental vitamin E intake (RR-0·73; 95% CI: 0·58, 0·92), high serum tocopherol levels (RR-0·77; 95% CI: 0·66-0·91), with the risk of cataract. No significant association between supplemental vitamin E intake (RR-0·92; 95% CI: 0·78-1·07) and risk of cataract
Li-Quan Zhao, et al.[31] (**)	The Effect of Multivitamin/Mineral Supplements on Age-Related Cataracts: A Systematic Review and Meta-Analysis	14	50828	12 cohort, 2 RCT	multivitamin/mineral supplements (0.73*)	Supports inverse association between multivitamin/minerals and risk of nuclear cataract (RR-0.73*; 95% CI: 0.64–0.82), Cortical (RR- 0.81*; 95% CI: 0.68–0.94), Other cataracts (RR-0.66*; 95% CI: 0.39–0.93), no-significant association with PSC (RR-0.96; 95% CI: 0.72–1.20)
Lin Wei et al.[32] (**)	Association of vitamin C with the risk of age-related cataract: a meta-analysis	30	16 205	14 prospective, 8 case-control, 7 cross sectional, 1 RCT	vitamin C (0.81*)	Supports inverse association between higher vitamin C intake (RR-0.814; 95% CI: 0.707–0.938) and serum ascorbate (RR-0.704; 95% CI: 0.564–0.879) and risk of cataract
Guoqiang Huang et al.[33] (**)	Association between vegetables consumption and the risk of age-related cataract: a meta-analysis	9	112,447	5 cohort, 3 case-control, 1 cross-sectional	Compared highest vs. lowest vegetables	Supports Inverse associations between higher vegetable consumption (RR-0.723; 95% CI: 0.594-0.879) and risk of

					consumption (0.72*)	cataract. Significant association in America (RR- 0.872; 95% CI: 0.791-0.960) and Europe (RR-0.507; 95% CI: 0.416-0.619)
Ma, Le; Hao et al.[34] (**)	A dose-response meta-analysis of dietary lutein and zeaxanthin intake in relation to risk of age-related cataract	6	41,999	6 prospective cohort	dietary lutein and zeaxanthin intake (0.75*)	Supports inverse association between high dietary intake of lutein and zeaxanthin and Nuclear cataract (RR-0.75*; 95 % CI: 0.65- 0.85), non-significant association for Cortical cataract (RR- 0.85; 95% CI: 0.53- 1.17) and PSC (RR-0.77; 95% CI: 0.40- 1.13)
Han Wu et al.[27] (**)	Association Between Dietary Carbohydrate Intake and Dietary Glycemic Index and Risk of Age-Related Cataract: A Meta-Analysis	7	11,944	1 case- control, 6 cohort	Dietary carbohydrate (1.18*), Dietary glycemic index (1.15*)	Direct association between higher carbohydrate (OR-1.18*; 95% CI: 1.01–1.38),food with higher glycemic index intake (OR-1.15*; (95% CI: 1.00–1.32) and risk of cataract

OR= Odd Ratio, CI= Confidence interval, RR=Relative risk, RCT= Randomized controlled trial

Table 3: Clinical studies supporting the effectiveness of nutrition on cataract prevention.

Grading's of the studies are indicated in parenthesis in Authors column: (A= Asterisks (*), B= (**), C= (***), D= (****)

Author	Title	Study design	# participant/ Duration	Nutrients evaluated	Study result
Christen WG et al. [35](*)	Effects of multivitamin supplement on cataract and age-related macular degeneration in a randomized trial of male physicians	Randomized, double-blind, placebo-controlled trial	14 641 subjects Follow-up: 11.2 yrs.	Vitamin E, vitamin C, beta-carotene	9 % reduction of cataract in multivitamin group compare to placebo (872 vs.945 cases HR, 0.91; 95% CI: 0.83–0.99; P = 0.04). 13% reduction of nuclear cataract (800 vs. 900 cases; HR, 0.87; 95% CI: 0.79–0.96; P = 0.005). No significant reduction in cortical cataract (356 vs. 387 cases; HR, 0.90; 95% CI: 0.78–1.04; P = 0.17) and PSC (247 vs. 248 cases; HR, 0.98; 95% CI: 0.82–1.17; P = 0.85)
Maraini G et al.[36] (*)	A randomized, double-masked, placebo-controlled clinical trial of multivitamin supplementation for age-related lens opacities. Clinical trial of nutritional supplements and age-related cataract report no. 3	Randomized, Double-blind, Placebo-Controlled trial	1020 subjects Follow-up=9 yrs.	Centrum (broad spectrum of vitamins and minerals)	Inverse association between multivitamin/mineral intake and incidence of cataract (HR, 0.82; 95% CI: 0.68–0.98; P = 0.03) compare to placebo
Glasr TS et al. [37] (***)	The Association of Dietary Lutein plus Zeaxanthin and B Vitamins with Cataracts in the Age-Related Eye Disease Study: AREDS Report No. 37	Clinical, cross-sectional and prospective cohort study	3115 subjects Follow-up= 9.6 yrs.	Dietary Vitamin B2, B12, B6	Inverse association between high dietary intake of Vitamin B2 (OR- 0.62; 95% CI: 0.43–0.90; P = 0.01), B6 (OR- 0.67; 95% CI: 0.45–0.99), B12 (OR- 0.62; 95% CI: 0.43–0.88; P = 0.01) and incidence of moderate nuclear cataract.
Ravilla D et al. [38](***)	Inverse Association of Vitamin C with Cataract in Older People in India	Population-based cross-sectional study	5638 subjects	Vitamin C, lutein, zeaxanthin, retinol, β-carotene,α-tocopherol	Inverse association between vitamin C (OR- 0.61; 95% CI: 0.51–0.74), and risk of cataract

OR= Odd ratio, CI= Confidence interval, HR= Hazard ratio

Table 4: Clinical studies not supporting the effectiveness of nutrition on cataract prevention.

Grading's of the studies are indicated in parenthesis in Authors column: (A= Asterisks (*), B= (**), C= (***), D= (****)

Author	Title	Study design	#participants/Duration	Nutrients evaluated	Study result
Christen WG et al. [39] (*)	Vitamin E and Age-Related Cataract in a Randomized Trial of Women	Randomized, double-blind, placebo-controlled trial	39,876 subjects Follow-up= 9.7 yrs.	vitamin E (α-tocopherol)	No significant difference between vitamin E (1159) and placebo groups (1217) in the incidence of cataract (RR- 0.96; 95% CI,: 0.88–1.04)
Zheng Selin J et al. [40] (**)	High-Dose Supplements of Vitamins C and E, Low-Dose Multivitamins, and the Risk of Age-related Cataract: A Population-based Prospective Cohort Study of Men	Population-based Prospective Cohort Study of Men	31,120 subjects Follow-up= 9 yrs.	Vitamin C, vitamin E supplements	Risk of cataract with higher vitamin C supplement=21% high (HR, 1.36, 95% CI: 1.02-1.81), Risk of cataract with higher Vitamin E=59% high (HR, 1.59, 95% CI: 1.12- 2.26). Intake of vitamin C and the risk of cataract stronger among (>65 years) (HR,1.92, 95% CI: 1.41- 2.60) and corticosteroid users (HR, 2.11, 95% CI: 1.48-3.02)
William G. Christen et al. [41] (*)	Age-related Cataract in a Randomized Trial of Vitamins E and C in Men	Randomized, double-blind, placebo-controlled trial	11545 subjects Follow-up=8 yrs.	Vitamin E and vitamin C supplements	No significant harm or benefits of vitamin E (579) and placebo group (595) placebo group (HR, 0.99; 95% CI: 0.88- 1.11) and also for

					vitamin C (593) and placebo group (581), (HR, 1.02; CI: 0.91- 1.14)
Kassoff, A et al. [42] (*)	A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss: AREDS report no. 9	Randomized, placebo-controlled trial	4757 subjects Follow-up= 6.3 yrs.	vitamin C, vitamin E,	Non-significant effect of the antioxidant formulation on the incidence or progression of cataract (OR- 0.97, P-0.55) over placebo
William G. Christena et al. [43] (*)	Folic Acid, Vitamin B6, and Vitamin B12 in Combination and Age-Related Cataract in a Randomized Trial of Women	Randomized, double-blind, placebo-controlled trial	5442 subjects Follow-up= 7.3 yrs.	Folic acid, Vitamin B6, Vitamin B12 supplement	60% Increased risk of PSC in treatment (63) v/s placebo group (39); (HR, 1.60 95% CI: 1.07–2.39)

OR= Odd ratio, CI= Confidence interval, HR= Hazard ratio

Vitamin C and risk of cataract

Vitamin C is a water soluble antioxidant vitamin which is found in aqueous compartments of cell membranes in the lens and functions as an antioxidant to protect lens from photo-oxidative destruction, inhibiting cataract formation.[32]

Three meta-analysis[13,31,32] one cross-sectional and two RCTs[35,36,38] found strong inverse association between vitamin C and risk of cataract , whereas one population-based Prospective Cohort Study and two RCT did not find any protective role of vitamin C in combination with other vitamins in cataract prevention.[40,41,42]

Three meta-analysis of mostly prospective cohort and case-control studies and only one RCT investigated the association between dietary vitamin C and risk of cataract. These three studies supported the inverse association between vitamin C intake and risk of cataract ranges from (OR: 0.6-0.9).[13,31 ,32] Out of three, only one of these studies investigated alone on vitamin C[32], while the other two used vitamin C in combination with other nutrients. Since these meta-analyses mostly included prospective cohort studies and only one RCT, the strength of evidence was not very strong.

Yu-Hong Cui, et al. conducted a meta-analysis of an observational studies including thirteen studies with a total 18,999 participants, found that the high blood level of lutein, zeaxanthin, vitamin E and α-carotene were significantly associated with reduced risk of cataract.[13] This study also found that vitamins A and vitamin C were inversely associated with age-related cataract in Asian populations but not in Western populations. The reason could be, since most of the studies included in this meta-analysis are case control and cross sectional which may overestimate the effect size of the association making the relation between exposure and outcome unclear and also since there were no RCT included, it makes this meta-analysis less conclusive.[13] Li-Quan Zhao, et al. conducted a meta-analysis including fourteen studies with a total 50,828 participants found significant beneficial effect of multivitamin/mineral supplements in decreasing the risk of age-related cataract in well-nourished Western populations.[31] Several high quality cohort and RCT were included. The study systematically reviewed and assessed the association between multivitamin/mineral supplements with different types of cataract. Although prospective cohort studies provided the most consistent and strong evidence, only two RCTs were involved. The results of a meta-analysis of RTCs are known to be more precise and

convincing than the results of a meta-analysis of observational data. Included studies used different cataract assessments and supplement durations and all studies were conducted in relatively well-nourished populations in the United States and other developed Western countries except one RCT which was conducted in China where they got same results.[31] Another meta-analysis conducted by Lin Wei et al. including thirty studies for vitamin C intake and ten studies for serum ascorbate including total of 16,205 participants with 23,510 cataract cases found that higher vitamin C intake and higher serum ascorbate might be inversely associated with risk of cataract formation.[32] The major strength of this study was the large number of participants which provided more precise estimation. The limitations of this study included involvement of case control studies that showed overstated association due to factors such as lack of dose–response analysis which was a result of limited data in the reported articles and small number of included studies because of which the result of vitamin C intake and age-related cataract risk were only applicable for American population.[32]

One cross-sectional and two RCT investigated the role of vitamin C in combination with other vitamins in cataract prevention. The studies found strong inverse association between vitamin C and risk of cataract.[35,36,38] Christen WG et al. conducted a randomized, double-blind, placebo-controlled trial on male physicians of age ≥50 years.[35] The purpose of the study was to investigate that long-term daily use of multivitamin supplements affects the incidence of cataract. A total of 14,641 subjects were participated and followed-up for 11.2 years. Multivitamins like vitamin E (400 IU synthetic α-tocopherol) on every other day, vitamin C (500 mg synthetic ascorbic acid) daily, and beta-carotene (50 mg lurotin) on every other day was randomly given to the subjects. The study indicated that long-term daily use of multivitamin can modestly and significantly decreased the risk of cataract, but there were no significant benefit or risk of daily multivitamin use on AMD. Study showed that multivitamin/mineral supplements have a role in the prevention of nuclear cataracts and may have a role in the prevention of cortical cataracts. Study randomization were evenly distributed between the two treatment groups- the multivitamin and placebo groups and also their random misclassification was reduced by the use of medical records to confirm the participant reports. One of the limitations of this study was the fact that it conducted on well-nourished male physicians, and their findings may not apply to women or to less well-nourished populations.[35]

Another randomized, double-masked, placebo-controlled clinical trial was conducted by Maraini G et al. to examine the effect of multivitamin/mineral supplementation for age-related cataract.[36] A total of 1020 subjects of age between 55 to 75 years were examined and followed up for 9 years. Centrum (popular multivitamin and mineral supplement) 1 tablet daily was randomly given to the subjects. The study found that intake of multivitamin/mineral reduces the incidence of cataract. Randomization to assign treatment was based on subject's age (≤65, >65) and their baseline lens status (no cataract, early cataract).[36] Ravilla D et al. conducted a population-based cross-sectional study to examine the association between vitamin C and cataract.[38] A total of 5638 subjects aged ≥60 years were examined. Their plasma level of vitamin C and other nutrients were measured. The study showed strong inverse association between vitamin C and cataract for highest compare to lowest quartile. A weaker inverse association was found between lutein, zeaxanthin, retinol and the risk of cataract, but they did not find any inverses association between β-carotene or α-tocopherol and risk of cataract. Their effect size was clinically relevant including larger population which provides a strong evidence of vitamin C intake and risk of cataract among low- or middle-income country.[38]

One population-based prospective cohort study and two RCT did not find any protective role of vitamin C in combination with other vitamins in cataract prevention.[40, 41, 42] Zheng Selin J et al. conducted a population-based prospective cohort study to examine the associations of high-dose supplements of vitamins C and E and low-dose multivitamins with the risk of age-related cataract.[40] A total of 31,120 subjects aged 45-79 years were examined and followed-up for 9 years. Their dietary Intakes of vitamin C and vitamin E from diet and supplement use were assessed using food frequency questionnaire. Long term vitamin C supplement showed 21% increased risk of cataract, whereas Vitamin E showed 59% increased risk of cataract compared with non–supplement use. Multivitamin use in addition to vitamin E and vitamin C did not show any significant association with the risk of having cataract. Intake of vitamin C and the risk of cataract was stronger among older men (>65 years) and corticosteroid users, which could be associated to their age and the increased oxidative stress as most of the subjects were >65 years and were long term user of corticosteroid. Antioxidants could not neutralize the oxidative stress in these subjects. Another factor could be that these subjects also consumed vitamin E and C in its supplement form.[40]

William G. Christen et al conducted a randomized, double-masked, placebo-controlled trial on male physician of aged ≥50 years with no cataract at baseline to investigate whether the vitamin E and vitamin C supplements affects the incidence of cataract.[41] A total of 11545 subjects participated and followed-up for 8 years. 400 IU of vitamin E on every other day, and 500 mg of vitamin C daily verses placebo was randomly given to the subjects. The study did not find any beneficial or harmful effect of vitamin E and C verses placebo on cataract progression. No cataract at baseline could be a good reason for delaying a cataract progression, whereas at the same time the use of vitamin E supplement and excess doses of vitamin E and C could be bad in terms of cataract prevention. The duration of follow-up time should be considered important, as cataracts develop over many years and may require even longer periods of treatment to see the effect.[41]

Another randomized, placebo-controlled trial was conducted by Kassoff, A et al. to evaluate the effect of a high-dose combination of antioxidants on the incidence and progression of age-related cataract.[42] A total of 4757 participants were examined and followed-up for 6.3 years. A formulation/combination of antioxidants containing vitamin C (500 mg); vitamin E (400 IU); and beta carotene (15 mg) were randomly given to the participants. The study did not find any significant effect of the antioxidant formulation on the incidence or progression of age-related cataract over placebo. The reason could be associated to the short duration of follow-up time or the use of other medication for age-related macular degeneration during trial that slows down the effect of antioxidant formulation.[42]

On review of all the studies above, it is observed that a follow-up time duration should be considered important for the studies that does not show any beneficial or harmful effect of antioxidants or vitamins on the risk of cataract progression. Cataract progression can be slow and can take many years to develop, it can require longer periods of treatment to see the effect.

Based on the strength of the evidence of the above studies that showed protective role of Vitamin C towards Cataract, it is considered to be moderately helpful for cataract prevention. Additionally since most of the above studies investigated vitamin C in combination with other nutrients, effectiveness of vitamin C alone remains debatable. Foods rich in vitamin C are recommended on daily regular basis, however vitamin C supplement should be used with caution as one of the population-based prospective cohort study showed 21% increased risk of cataract with higher intake of vitamin C supplement.[40]

Table below shows some list of fruits and vegetables heavy with vitamin C.

Table 5: Foods rich in vitamin C:

Food	**Serving**	**(mg)**
Orange juice	¾ cup (6 ounces)	62-93
Grapefruit juice	¾ cup (6 ounces)	62-70
Kiwifruit, gold	1 fruit (86 g)	91
Orange	1 medium	70

Vitamin E and risk of cataract

Vitamin E is a lipid soluble antioxidant vitamin which is found in the lens fibers and membranes that may reduce photo peroxidation of lipids inside the lens and stabilizing the cell membranes and thus may inhibit cataract formation.[30,38] Three meta-analysis[13, 30, 31], one cross-sectional and two RCT [35,36,38] found strong inverse association between vitamin E and risk of cataract. Whereas one population-based Prospective Cohort study and three RCT did not find any protective role of vitamin E in combination with other vitamins in cataract prevention.[39,40,41,42]

Three meta-analysis of mostly prospective cohort, case control and cross sectional with five RCT investigated the association between dietary and supplemental vitamin E and risk of cataract. Three studies supported the inverse association between vitamin E intake and risk of cataract ranges from (OR: 0.7-0.9).[13,30,31] The strength of evidence is stronger with more RCT and larger number of participants. Out of three only one study investigated the effect of vitamin E alone on cataract prevention and provided highest order of the strength of evidence because of involving more RCT.[30] Yufei Zhang, et al. conducted a meta-analysis including thirty-two studies with 249,446 participants and found that those taking higher quintile of Vitamin E had 17% reduced risk of age-related cataract compared to those taking lower quintile.[30] Dietary vitamin E intake, dietary and supplemental vitamin E intake and high serum tocopherol levels were significantly associated with decreased risk of cataract. These studies however did not show a significant decrease in cataract with vitamin E supplement use. Since the prospective design of most of the observational studies met all the criteria of this meta-analysis, it provides the highest order of the strength of evidence than case–control and cross-sectional studies.[30]

One cross-sectional and two RCT investigated the role of vitamin E in combination with other vitamins in cataract prevention. The studies found strong inverse association between vitamin E and risk of cataract.[35, 36, 38] whereas another four RCT did not find any protective role of vitamin E in combination with other vitamins in cataract prevention.[39,40,41 ,42]

Christen WG et al. conducted a double-mask randomized controlled trial on female health professionals of aged ≥45 years named as Women's Health Study (WHS).[39] The purpose of the study was to investigate the occurrence of age-related cataract in a large trial of vitamin E use. A total of 39,876 subjects were participated and followed-up for 10 years. 600 IU natural-source vitamin E was randomly given to the subjects on every other day. The study did not find any significant difference between vitamin E and placebo groups in the incidence of cataract, which implies that vitamin E supplementation has low impact on cataract progression in early stages in compare to advance stages, and since the subjects did not have cataract at the baseline, it didn't show any benefits.[39]

Based on the weight of the evidence of the following studies vitamin E is moderately helpful for cataract prevention when used in the combination with other nutrients. The strength of evidence is stronger with more RCT and larger number of participants. Therefore foods rich in vitamin E are recommended on regular basis, however, one of the population-based prospective cohort study showed direct association between higher intake of Vitamin E and risk of cataract and found 59% increased risk of cataract with higher intake of vitamin E supplement.[40] It is therefore advised that vitamin E supplement should be used with caution.

Table below shows some list of fruits and vegetables heavy with vitamin E.

Table 6: Foods rich in Vitamin E:

Food	**Serving**	**(mg)**
Blackberries, raw	½ cup	0.8
Avocado (California)	1 fruit	2.7
Peanuts	1 ounce	2.4
Pecans	1 ounce	0.4

Lutein, Zeaxanthin and risk of cataract

Antioxidants like lutein and zeaxanthin are found in the lens and macula. Approximately 74% of lutein and zeaxanthin are found in lens epithelium and. It can prevent cataract formation by preventing oxidative stress and lipid peroxidation in the epithelial cells.[34,44]

Five meta-analysis[13,28,29,31,34], two RCT and one population-based cross-sectional study[35,36,38] supported the inverse association between lutein and zeaxanthin intake and risk of cataract. No RCT were found regarding ineffectiveness or adverse effect of lutein and zeaxanthin.

Five meta-analysis of mostly prospective cohort, case control and cross sectional with four RCT investigated the association between dietary lutein and zeaxanthin in combination with other nutrients and risk of cataract. Studies supported the inverse association between lutein and zeaxanthin intake and risk of cataract ranges from (OR: 0.7-0.93).[13,28,29,31,34] Out of five only two studies investigated alone using lutein and zeaxanthin and found inverse association with risk of cataract[28,34]

Xiao-Hong Liu, et al. conducted a meta-analysis including eight studies with 12,080 participants of seven cross-sectional and one cohort studies to investigate on higher intake of lutein and zeaxanthin and risk of cataract. The study supported the inverse association between lutein and zeaxanthin and nuclear cataract.[28] One of the limitation of this study was to include only observational studies and not RCT which could confound the result and might fail to give exact statistical data. Also very few studies evaluated the relationship between lutein and zeaxanthin status and the risk of cortical cataract or posterior sub capsular cataract; thus, this study was unlikely to detect significant effect of lutein and zeaxanthin on opacities in these regions.[28]

Another dose-response meta-analysis of dietary lutein and zeaxanthin intake in relation to risk of age-related cataract was conducted including six studies with 41,999 participants found that dietary intake of lutein and zeaxanthin is associated with a reduced risk of cataract, strongly for nuclear cataract and weaker association for cortical or PSC.[34] This could be due to the fact that different types of cataract are related to different risk factor. The study showed that every 300 [mu] g/d increment in dietary lutein and zeaxanthin intake was associated with a 3 % reduction in the risk of nuclear cataract. One of the limitations of this study was that only a small number of studies were included in this meta-analysis which might fail to give exact statistical data and also as dietary data were self-reported in all included studies it might have weakened the strength of the association.[34]

Wang, Aimi, Han, Jing et al conducted a meta-analysis to investigate the effect of intake of lutein and zeaxanthin with the combination of vitamin A on the risk of cataract. The meta-analysis included thirteen studies for serum level of β-carotene(lutein and zeaxanthin), seventeen studies of intake of β-carotene seven studies for serum level of vitamin A and eleven studies related to intake of vitamin A intake including total of 27,572 participants, found an inverse association between higher intake of vitamin A, β-carotene and cataract.[29] Strength of this meta-analysis was large number of participants with more precise estimation of the relationship between β-carotene or vitamin A and cataract and most of the studies were prospective which are less likely to have bias. The limitation of this study was involvement of many case control studies which might show overstated association due to different factor, lack of dose–response analysis because of limited data in the reported articles and limited articles about subtypes of cataract and β-carotene or vitamin A intake.[29]

Two RCT and one population-based cross-sectional study investigated the role of lutein and zeaxanthin in combination with other vitamins in cataract prevention. The studies found strong inverse association between lutein and zeaxanthin and risk of cataract.[35, 36, 38] the effect size of three studies were clinically relevant including larger population which provides a strong strength of evidence to use lutein and zeaxanthin in combination with other nutrients to prevent from cataract. Based on the strength of evidence of the above studies, dietary intake of lutein and zeaxanthin in the form of natural food or supplements are recommended on the regular basis.

Table below shows some list of fruits and vegetables heavy with Lutein and Zeaxanthin.

Table 7: Foods rich in Lutein + Zeaxanthin:

Food	**Serving**	**(mg)**
Spinach, frozen, cooked	1 cup	29.8
Kale, frozen, cooked	1 cup	25.6
Pumpkin, cooked	1 cup	2.5
Broccoli, frozen, cooked	1 cup	2.0

Vitamin A and risk of cataract

Three meta-analysis[13,29,31] one RCT and one population-based cross-sectional study[36, 38] found strong inverse association between Vitamin A and risk of cataract.

Three meta-analysis of mostly prospective cohort, case control and cross sectional with four RCT investigated the association between dietary vitamin A and risk of cataract. Studies supported the inverse association between vitamin A intake and risk of cataract ranges from (OR: 0.6-0.8).[13,29,31] One of these three meta-analysis found that vitamins A and vitamin C were inversely associated with age-related cataract in Asian populations but not in Western populations.[13] Since most of the studies included in this meta-analysis are case control and cross sectional they may overestimate the effect size of the association making the relation between exposure and outcome unclear. There were no RCT included in the review which makes this meta-analysis less conclusive.[13]

One RCT and one population-based cross-sectional study investigated the role of vitamin A in combination with other vitamins in cataract prevention. The studies found strong inverse association between Vitamin A and risk of cataract[36, 38] A population-based cross-sectional study by Ravilla D et al. found a weaker inverse association between lutein, zeaxanthin, vitamin A and the risk of cataract.[38] The effect size of this study was clinically relevant including larger population which provides a strong evidence that vitamin A has very little or no effects on cataract prevention. Since no studies were found investigating vitamin A alone on cataract prevention, vitamin A is mildly recommended on regular basis as it might have some beneficial effect when combining with other nutrients.

Table below shows some list of fruits and vegetables heavy with vitamin A.

Table 8: Foods rich in vitamin A:

Food	**Serving**	**(IU)**
Whole milk	1 cup (8 fl oz)	395
Sweet potato (canned, mashed)	½ cup	11,091
Kale (cooked)	½ cup	8,854
Carrot (raw, chopped)	½ cup	10,692

Vitamin B complex and risk of cataract

Vitamins B12 and B6 act as enzymatic cofactors which maintains metabolic pathway that eliminates the excess of plasma homocysteine and thus reducing oxidative stress by maintaining the cellular response and may inhibit cataract formation. Riboflavin maintains healthy blood cells, facilitate healthy metabolism, preventing free radical formation inhibiting cataract. Thiamine helps to maintain protein and fat metabolism which positively influence muscle and nerve signaling and thus preventing cataract.[36,45,37]

One meta-analysis[31],one RCT and one cross-sectional prospective cohort study[36,37] found strong inverse association between Vitamin B and risk of cataract. Whereas, one RCT found increased risk of cataract with vitamin B intake.[43]

One meta-analysis with twelve prospective cohort studies and two RCT investigated the association between multivitamin including vitamin B and risk of cataract. Studies supported the inverse association between multivitamin intake and risk of cataract ranging from (OR- 0.6-0.7).[31]

One RCT and one cross-sectional and prospective cohort study investigated the role of vitamin B in combination with other vitamins in cataract prevention. The studies found strong inverse association between Vitamin B and risk of cataract.[36,37] Glasr TS et al. conducted a cross-sectional and prospective cohort study to examine the association between dietary intake of lutein/zeaxanthin and B vitamins in cataract prevalence and incidence.[37] A total of 3115 subjects were followed-up for 9.6 years. The study found that high dietary intake of riboflavin are 22% less likely to cause mild and 38% less likely to cause moderate nuclear cataract and also 20 % less likely to cause mild cortical cataract with significant effect size. High dietary intake of vitamin B6 causes 33% reduction of moderate nuclear cataract and higher intake of vitamin B12 causes reduced risk of both mild and nuclear cataract. Vitamin B12 were also associated with 23% less likely to cause mild cortical cataract. The study found a protective effect of supplementation of riboflavin and vitamin B6 on the occurrence of nuclear and cortical cataract. The study included large number of participants with each types of cataract with the long duration of follow-up (almost 10 years) which supported a strong evidence of role of Vitamin B in slowing down cataract progression.[37]

Whereas, one RCT conducted by Christen found that daily supplementation of combination of folic acid (2.5 mg every day), vitamin B6 (50 mg every day), and vitamin B12 (1 mg every day) had significant

increased risk of PSC among women at high risk of cardiovascular disease.[43] When vitamin B used in combination with other vitamins it showed an inverse association with the risk of cataract. [31,36] Based on the strength of evidence of the above studies vitamin B intake are recommended starting early in life and in appropriate amount.

Table below shows the list of foods rich in vitamin B complex.

Table 9: Foods rich in vitamin B

Food	**Serving**	**(mg)**
Wheat germ breakfast cereal (toasted, plain)	1 cup	1.88
Pecans	1 ounce	0.19
Long-grain, brown rice (cooked)	1 cup	0.19
Green peas (cooked, boiled	½ cup	0.2
Milk (nonfat)	1 cup (8 ounces)	0.45
Egg (cooked, hard-boiled)	1 large	0.26
Almonds	1 ounce	0.29

Some of the RCT's have strong strength of evidence of multivitamin use for cataract prevention. These studies showed strong inverse association between multivitamin intake and the risk of cataract formation. Many of the previous studies did not find any protective association of these nutrients when taken alone, whereas studies did find strong evidence of inverse association between combination of these nutrients as multivitamins and risk of cataract. [31,35,36,38]

As most of the previous studies used natural food in combination with supplements, the present study does not have substantial evidence that natural food is better over supplements or vice versa. However, two RCT included in this review showed increased risk of cataract with supplement use.[40,43] After evaluation of all the prior studies, the current study supports the idea of intake of nutritious diet starting from early in life and in the appropriate amount.

LIMITATIONS

The public health perspective from the above studies suggests that dietary intake of antioxidants (like vitamin E, C, lutein, zeaxanthin), vitamin A, vitamin B or multivitamins reduces the risk of cataract. Higher intakes of antioxidants and vitamins has shown a protective association with the incidence or progression of cataract.[37, 38] Many of the meta-analysis studies included in this review showed the inverse association between these nutrients and the risk of cataract, but these studies do not get much strength of evidence as most of the meta-analysis included in this review included observational study rather than RCT. A meta-analysis of observational studies is weaker strength of evidence compare to a meta-analysis of RCT.

In this review we did not include animal studies, non-English publications, articles with no full text available and also other search engines.

CONCLUSION

Nutrition plays an important role in maintaining eye's health. Good nutritional habits and a balanced diet is key to maintain healthy vision. Developing healthy dietary and lifestyle patterns may help to protects against cataract. Nutrients are best consumed through natural sources such as fruits and vegetables.[46, 47] however in absence of natural sources, supplements can be used. Studies have shown that supplements can be as effective as natural sourced food in preventing cataract formation, however majority of these studies were done by combining natural source food with supplements and although there is enough information and evidence about nutrients preventing cataract, further research should be done using supplements or dietary food separately not in combination to see their effectiveness on incidence or prevention of cataract. Studies need to be performed on different population with high or low socioeconomic status.

RECOMMENDATION

The above literature review motivates several recommendations with respect to diet and nutrition. The strength of the recommendations was based on the strength of the evidence. Our recommendations have a moderate strength because most of the research in this field has been observational prospective and case control studies or randomized control study showed equal proportion of benefit or no effects.

Based on the above studies we give a moderately strong recommendation to consume foods that are rich in antioxidants (lutein, zeaxanthin, vitamin E and vitamin C), vitamin A, vitamin B or multivitamin.[13,28 ,29,30,31,32,33,35,37,38]

Foods higher in fibers which contains low glycemic index and carbohydrates, including dark green or bright colored fruits and vegetables such as spinach, carrot, green pepper, pineapple, papaya, tomatoes, celery and oranges should be consumed in some form or other on a daily basis.[27,47,48] However, there is a barrier of accessibility and financial issues with some of these fruits and vegetables that are seasonal or too expensive.[49] A potential resolution is by consuming these fruits and vegetables when they are in season by growing them in the garden. In poorer rural areas where people are primarily earn their living by farming, they could plant a little additional to set aside for the family rather than selling everything they produce. In urban areas perhaps people could either grow small gardens or have window boxes for fruits. The local community should set aside space for community gardens.

A weak recommendation would be to use supplements.[40 ,43] There is variability in the quality of vitamins and it is more cost effective compare to foods and unless there are local reviews of the available vitamins, this option should be considered with caution.[50] We recommend to consult physician before start taking any supplements on regular basis as use of supplement could lead to the level greater than Recommended Daily Allowances (RDAs) which body might does not need that amount and eventually can cause some side-effects, particularly for the fat-soluble vitamins A, D, E, and K. Supplements will not be as good as fresh fruits and vegetables and hence should be chosen only as an alternative to fresh food in the off season months.

Wear sunglasses and hats before heading out of home, to the market, to the park, or anywhere outside in a bright or cloudy day. Wearing wide-brimmed hats with fabric blocks about 99 percent of UV

radiation to provide optimal protection of eyes from harmful UV radiation. Wearing large framed, close fitting, wraparound sunglasses blocks 100 % of UV rays.[20, 21]

Lack of health awareness and financial issues are some of the barriers that prevent average people from using sunglasses and hats outside their home or work.[51] we recommend their use through awareness and health promotion campaigns as well as developing programs to distribute cheap sunglasses and hats to those that cannot afford them. Working with local and state government bodies to help spread these campaigns to a larger audience may eventually decrease the number of cataract patients each year.

For regular updates on ongoing research related to cataracts and nutrition can be found on the following website: http://lpi.oregonstate.edu/mic/disease-index

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