Supplements for Aging

HOW TO RECEIVE CREDIT

- Read the enclosed course.
- Complete the questions at the end of the course.
- Return your completed Evaluation to NetCE by mail or fax, or complete online at www.NetCE.com. (If you are a physician or Florida nurse please return the included Answer Sheet/Evaluation.) Your postmark or facsimile date will be used as your completion date.
- Receive your Certificate(s) of Completion by mail, fax, or email.

Faculty

Chelsey McIntyre, PharmD, is a clinical pharmacist who specializes in drug information, literature analysis, and medical writing. She earned her Bachelor of Science degree in Genetics from the University of California, Davis. She then went on to complete her PharmD at Creighton University, followed by a clinical residency at the Children's Hospital of Philadelphia (CHOP). Dr. McIntyre held the position of Drug Information and Policy Development Pharmacist at CHOP until her move to Washington state in 2017, after which she spent the next six years as a clinical editor for Natural Medicines, a clinical reference database focused on natural products and alternative therapies. She continues to create rigorous professional analysis and patient education materials for various publications while also practicing as a hospital pharmacist. Her professional interests include provider and patient education, as well as the application of evidence-based research to patient care.

Faculty Disclosure

Contributing faculty, Chelsey McIntyre, PharmD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Division Planners

John M. Leonard, MD
Mary Franks, MSN, APRN, FNP-C
Randall L. Allen, PharmD

Senior Director of Development and Academic Affairs

Sarah Campbell

Division Planners/Director Disclosure

The division planners and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This course is designed for healthcare professionals whose older patients are taking or are interested in supplements.

Accreditations & Approvals

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This activity was planned by and for the healthcare team, and learners will receive 5 Interprofessional Continuing Education (IPCE) credits for learning and change.

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AACN Synergy CERP Category A.

NetCE designates this activity for 5 hours ACPE credit(s). ACPE Universal Activity Numbers: JA4008164-0000-24-017-H04-P and JA4008164-0000-24-017-H04-T.

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Special Approval

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Disclosure Statement

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Course Objective

The purpose of this course is to provide healthcare professionals in all practice settings the knowledge necessary to increase their understanding of the supplements that may be used by their older adult patients.

Learning Objectives

Upon completion of this course, you should be able to:

1. List the dietary supplements most commonly used for age-related changes.
2. Explain the safety concerns associated with the use of natural products in older adults.
3. Discuss the risks and benefits of common vitamins and minerals in older adults.
4. Review the evidence for the use of dietary supplements for age-related changes in physical health.
5. Describe the proposed and actual effects of dietary supplements for dementia.

Pharmacy Technician Learning Objectives

Upon completion of this course, you should be able to:

1. Outline dietary supplements most commonly used by older adults, including potential safety concerns.
2. Review supplements used to address dementia and age-related physical changes.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

As the population ages, maintaining both physical and cognitive health becomes increasingly important. In recent years, the use of dietary supplements, including vitamins, minerals, fibers, and proteins, has gained significant attention for their potential to improve various aspects of health. Older adults may turn to these supplements to address age-related deficiencies, enhancing physical vitality, and supporting cognitive function. This course is designed to provide a comprehensive review of the role of supplements in promoting well-being among older adults.

SUPPLEMENT USE IN OLDER ADULTS

Older adults, defined as those at least 65 years of age, are a rapidly growing portion of the United States population that is expected to make up 20% of the country's total population by 2030 [1]. As life expectancy and overall quality of life continues to improve for this age group, many older adults have shown an increased interest in taking an active role in their health, often seeking out alternative and complementary options for both prevention and treatment.

The term "complementary therapy" covers a wide range of modalities, from breathing exercises and yoga, to healing touch and massage, to herbs and vitamins. For many Americans, the most commonly utilized complementary therapy is dietary supplements, a category that includes herbal products, vitamins, minerals, fibers, probiotics, fish oil, and many more.

In fact, as of 2017, 70% of older adults reported using at least one dietary supplement. A full 54% reported taking two supplements and 29% reported taking four or more supplements. The most frequently used supplements were multivitamins, Vitamin D, calcium, and omega-3s. At least 9% also reported using an herbal/botanical product, a number that is likely to have increased since the time of this survey [2].

Most older adults reported using these products to improve overall health. Other commonly cited reasons included bone health, nutritional supplementation, heart health and cholesterol, and eye health. Women, who reported using supplements more often than men, were more likely to use supplements for musculoskeletal health. Not surprisingly, most of this use was not related to recommendations from healthcare professionals, although the use of calcium, vitamin D, iron, and fiber products, specifically, was more likely to be associated with a recommendation from a healthcare professional [2].

PHYSIOLOGICAL CHANGES IN OLDER AGE

There are many physiological changes that occur as the body ages. These changes affect almost every organ system and can alter the way that the body responds to activity, food, and medications.

Some of the most striking changes occur in the musculoskeletal system. These changes often manifest as a reduced tolerance for physical activity, changes in overall mobility, and an increase in various forms of pain. As the body ages, it naturally loses muscle and water content and increases fat stores. It also loses bone mass and experiences a reduction in joint lubrication [3].

Most older adults are also aware of changes to their cardiovascular system. As the body ages, cardiac output decreases, along with resting and maximal heart rate. Conversely, systemic vascular resistance increases, which leads to increased blood pressure. The cardiovascular system in general has a reduced response to stress and a reduction in baroreceptor activity. Many older adults also have high levels of cholesterol. These changes increase the risk for various adverse cardiovascular outcomes, as well as an increased likelihood for cardiovascular adverse effects from medications and natural products [3].

Another commonly recognized change occurs in the nervous system. As the central nervous system ages, portions of the brain, such as the hippocampus and the frontal and temporal lobes, shrink in size, which reduces the capacity for short-term memory

and executive function. Sleep patterns also change, commonly resulting in insomnia. Older adults also undergo a reduction in neuroreceptors and an increase in receptor sensitivity. This can increase sensitivity to medications and natural products that affect the nervous system, such as those with anticholinergic or sedating activity [3].

Reduced production of hormones, specifically estrogen in women and testosterone in men, can cause a myriad of changes to the body. Older adults also often experience a reduction in taste perception [3].

Many of the other changes that occur with aging are more likely to alter the body's response to foods and medications, without necessarily causing noticeable changes in physical function [3; 4; 5]:

- The liver undergoes a reduction in volume and blood flow, reducing the functional capacity to metabolize chemicals.
- The large intestine becomes less motile, which may impact the absorption of various nutrients and chemicals.
- The kidneys undergo a gradual reduction in overall mass and blood flow, which reduces the glomerular filtration rate (GFR). These changes can reduce the clearance of medications and other chemicals that are normally eliminated by the kidneys.
- Thinning skin can increase the absorption of chemicals that are applied topically, whether absorption is intended or not.

SAFETY CONCERNS WITH NATURAL PRODUCTS

As mentioned, various physiologic changes place older adults at an increased risk for adverse reactions to medications and natural products. The most predictable effects occur in relation to reduced kidney and/or liver function. However, reduced body water and increased body fat can also significantly alter the distribution and storage of chemicals in the body, which can increase sensitivity to the chemical and alter the likelihood for adverse effects.

In fact, medication-related adverse effects occur up to seven times more frequently in older adults when compared with younger adults. As many natural products are physiologically active and are cleared by the kidney and/or liver, this increased risk applies to natural products as well [6].

BEERS CRITERIA

Many healthcare professionals are familiar with the Beers Criteria, a list of drugs and drug classes that an expert panel, led by the American Geriatrics Society (AGS), considers to be potentially inappropriate for use in older adults. These include medications that are potentially harmful in all older adults, as well as those considered to be of concern in older adults with specific conditions or who are taking specific medications. In essence, this list identifies medications and medication classes for which potential harm is thought to outweigh expected benefit [7].

Although this list does not specifically include natural products, healthcare professionals should keep in mind that many supplements have pharmacological effects, some of which fall into classes listed on the Beers Criteria.

For example, sedative medications are a concern in older adults and should be used with caution. Many natural products are known to have clinically significant sedative effects and should thus be used with caution. Some common examples include kava, hops, passionflower, and valerian [8]. Anticholinergic medications are also considered to be of high concern in older adults. Some natural products, including bitter yam, European barberry, muira puama, and scopolia, have potent anticholinergic effects [9].

Various supplements also have anti-inflammatory activity, which may introduce many of the risks associated with nonsteroidal anti-inflammatory drugs (NSAIDs). Similarly, many supplements can increase the risk of bleeding and should be used with caution in this population.

DRUG INTERACTIONS

Older adults are often prescribed multiple medications, which increases their risk of drug-drug and drug-supplement interactions. In fact, in the 2017 survey discussed earlier, older adults that reported taking at least three prescription drugs were more likely to also take dietary supplements, further increasing the risk for interactions [2].

Many of the same principles apply to drug-drug interactions and drug-supplement interactions:

- Many supplements are metabolized by the same enzymes that metabolize drugs, including the cytochrome P450 (CYP) enzyme family. Drugs that inhibit or induce these enzymes can alter the effects of natural products.
- Some supplements can cause significant inhibition of drug metabolizing enzymes, which can increase or decrease the effects and adverse effects of prescribed medications.
- Drug transporters, such as P-glycoprotein and the organic anion transporter (OAT) family, also transport the chemicals contained in supplements.
- Because supplements can have significant physiological effects, taking a supplement and drug with similar activity can cause additive effects. Examples of this type of interaction include additive reductions in blood glucose or blood pressure, additive antiplatelet activity, and additive photosensitization.

However, it is important to understand that there is much greater uncertainty and risk associated with drug-supplement interactions. This is due to two major factors. The first is the low quantity and quality of evidence available for drug-supplement interactions. Because there are no regulations requiring the evaluation of possible interactions with supplements, very few human studies are available. Thus, most of the proposed interactions are based on extrapolation from case reports, proposed physiological effects, and laboratory research. And more importantly, many possible interactions remain completely unknown.

The second factor is the variability of contents in natural products. Natural products do not necessarily contain reliable quantities of each ingredient, as is expected with medications. Some of this variability is due to inaccurate labelling and poor quality assurance by manufacturers. But in the case of herbs and botanicals, this variability is completely natural. Growing conditions, seasonal weather variations, harvesting practices, and extraction methods can all alter the chemical composition of herbal products. This makes it difficult to predict the likelihood for effects and interactions.

CONDITION INTERACTIONS

As with medications, natural products also carry a risk for condition interactions, particularly conditions that are more prevalent in older adults. Many of the physiological changes discussed previously can alter the effects of medications and natural products in the body.

Liver Disease

As mentioned, natural products are metabolized by many of the same enzymes involved in drug metabolism. Patients with liver disease may require lower doses, and natural products that have been associated with hepatoxicity should be avoided completely. These include some relatively well-known supplements, such as green tea extract, kava, garcinia, ephedra, turmeric, red yeast rice, and black cohosh [10].

Kidney Disease

Similarly, many natural products are excreted by the kidneys and should thus be used with caution in patients with kidney disease. Natural products that have been associated with nephrotoxicity should be avoided completely, including cannabis, colloidal silver, horse chestnut, saffron, and yohimbine [11].

Anticoagulation

Certain natural products have demonstrated clinically relevant antiplatelet or anticoagulant effects. In patients requiring the use of antiplatelet or anticoagulant medications, these products should be avoided. Some examples include garlic, ginseng, ginkgo, high doses of vitamin E or fish oil, and many others [12].

PRODUCT QUALITY

Variable Quality

As mentioned, the actual contents of supplements can vary, either due to inaccurate labelling or poor quality assurance by the manufacturer. To ensure the selection of a high-quality product, look for third-party quality certification stamps, such as those from United States Pharmacopeia (USP) or NSF.

USP

The USP is typically considered the standard for verifying the quality of dietary supplements. In addition to inspecting manufacturing facilities for compliance with Good Manufacturing Practices (GMP) at least two times in a three-year period, USP will also conduct random off-the-shelf analyses of verified products to ensure that the contents of the product match those listed on the label. This random testing holds manufacturers to a high standard. The USP verification stamp can be found on a product's label.

NSF

NSF is also a strong source of dietary supplement quality verification. However, general NSF certification does not always imply the same quality standards as USP verification. For a manufacturer to list NSF certification on their website, they must pass an NSF inspection of GMP compliance every six months. However, NSF does not conduct off-the-shelf analyses of products unless the manufacturer is enrolled in the "Contents Tested and Certified" or "Certified for Sport" programs. Under these programs, products are subject to random off-the-shelf testing. These products can carry the NSF seal of approval on the label. The seal will typically state "NSF: Contents Certified" or "NSF: Certified SPORT."

NUTRITIONAL SUPPLEMENTS

The class of dietary supplements most commonly used by older adults is micronutrients, which includes vitamins and minerals. There are a number of reasons that these products may be used, including for the improvement of overall health and bone health and for supplementation of the diet.

MULTIVITAMINS

Formulations

About 40% of all older adults that take dietary supplements report using a multivitamin [2]. Many people consider multivitamins to be a quick and easy well-rounded supplement to the diet. These products contain 20 to 30 different micronutrients. However, each multivitamin product contains different ingredients and different ingredient quantities.

All dietary supplement labels are required to provide the % daily value (DV) for each nutrient included in the product. This DV derives from the Dietary Reference Intakes established by the Institute of Medicine [13; 14; 15]. This can act as a helpful way to determine whether the product contains too much or too little of a specific micronutrient. In some cases, products will contain only a small portion of the dietary requirement (1% to 20%). In other cases, they may contain much more than is recommended in the daily diet (more than 1,000%). There is no legal limit on the amount of any micronutrient that can be included in a dietary supplement.

Although older adults may be using a wide range of specific multivitamin products, some of the best-selling multivitamins on the market are specifically targeted to older men and women, with formulas that claim to specifically address nutrient concerns related to age and biological sex. These best sellers (e.g., Centrum Silver) can be used as an example of the multivitamin composition that many older adults are likely to be taking. As with other multivitamins, these products contain more than 25 individual ingredients, with percent of DVs ranging from 17% to 1,042%.

Safety

The safety of taking doses that are much higher than the DV depends on the specific nutrient in question. Fat-soluble vitamins, which are stored in the body, can cause toxicity over time. These include vitamins A, D, E, and K. Water-soluble vitamins are typically eliminated by the kidneys when quantities exceed physiological needs. Thus, toxicity is much less likely when these vitamins are taken in large quantities.

In addition to developing DVs for each nutrient, the Institute of Medicine also developed tolerable upper intake levels (ULs) to help guide patients and healthcare professionals in preventing toxicity and adverse effects. Some ULs are based on the risk for long-term toxicity, as is the case for vitamin D [13]. Other ULs, such as that of vitamin C, are based on the risk for temporary adverse effects, including gastrointestinal upset [15].

It is important to keep in mind that many patients who take multivitamins also take individual vitamin or mineral supplements. For example, it is not uncommon for patients to take a multivitamin along with a vitamin D/calcium supplement. Healthcare professionals should be aware of these duplicate therapies so that they can prevent a total intake of doses above the UL.

One simple way to avoid consuming too much of any one micronutrient is to first attempt to obtain all of these nutrients from foods in the diet. If a patient is concerned about adequate intake, encourage them to consider how much of each nutrient is obtained from both food and drinks and to identify ways to boost dietary intake. If the patient is already taking a multivitamin or other supplements, remind them to also consider the quantity of each nutrient found in these products.

Another consideration that is not often addressed with multivitamins is the potential for reduced or enhanced absorption of various micronutrients in the presence of other micronutrients. For example, vitamin C (ascorbic acid) can increase the absorption of chromium and iron [16; 17]. The presence of vitamin D increases the absorption of calcium in the intestine [18]. Iron and zinc can interfere with each other's absorption when taken on an empty stomach [19; 20]. Thus, it can be difficult to predict the actual benefits and risks with these products, particularly in patients with specific nutritional needs or medical conditions.

Many multivitamin tablets and capsules are large, which may increase the risk of choking in some patients, particularly older adults. From 2006 to 2015, about 20% of the reports submitted to the U.S. Food and Drug Administration (FDA) Center for Food Safety and Applied Nutrition Adverse Event Reporting System (CAERS) concerning dietary supplements involved choking or other swallowing problems. About 73% of these reports involved multivitamin supplements, and most of the adverse reports occurred in older adult patients [22]. Clinicians should ensure that older patients with swallowing difficulties are not placing themselves at risk for choking with the use of multivitamins.

Benefits

Despite the widespread use of multivitamin products, the evidence to-date, which includes many large randomized controlled trials, does not support their use. The U.S. Preventive Services Task Force (USPSTF) currently states that there is insufficient evidence to recommend the use of multivitamins for the prevention of cardiovascular disease (CVD) or cancer [21]. Research evaluating these products for reducing overall mortality has shown no benefit.

Considering this lack of benefit in the context of high product costs and variable quality, consider steering patients away from taking multivitamins or relying on them for adequate nutrition.

INDIVIDUAL MICRONUTRIENTS

Unlike multivitamins, there is supportive evidence for the use of various individual micronutrients in older adults. Although the recommended daily intake for the majority of nutrients is the same for older adults as for younger adults, there are some important exceptions.

Vitamin B12 (Cyanocobalamin)

The recommended daily intake for vitamin B12 is the same for all adults, regardless of age. However, as humans age, their ability to absorb vitamin B12 from the intestinal tract decreases. Additionally, many older adults take medications that have the potential to further reduce the absorption of vitamin B12. Some examples of these medications include metformin and proton pump inhibitors (PPIs), such as pantoprazole and omeprazole [22; 23]. Due to this reduced absorption, it is recommended that older adults consume fortified foods, such as breakfast cereal. However, some may also require vitamin B12 supplements to meet their needs [24].

Vitamin B6 (Pyridoxine)

It is recommended that older adults obtain more vitamin B6 from the diet than younger adults. Prior to 51 years of age, all adults are recommended to consume 1.3 mcg per day. Beginning at 51 years of age, the recommendation for women increases to 1.5 mcg; for men, it increases to 1.7 mcg [24]. This recommendation is related to an increased rate of vitamin B6 deficiency in older adults, which is thought to be due to reduced absorption and increased catabolism [25]. As with vitamin B12, vitamin B6 can be obtained from fortified foods. Supplements can be considered if dietary intake is inadequate.

Calcium and Vitamin D

One of the most popular combination supplements available on the market is calcium-vitamin D. Although calcium and vitamin D have distinctive effects, they are often discussed, and provided, in combination for bone health. While calcium is the nutrient that directly builds and maintains bone, vitamin D is crucial to the appropriate absorption of calcium from the intestine. Thus, adequate vitamin D intake is an important component of adequate calcium intake and bone health.

Due to age-related bone loss, the recommended daily intake for both calcium and vitamin D increases with age. And due to hormonal changes associated with menopause, the recommended intake for calcium increases faster for women than for men [13].

The recommended vitamin D intake is [13]:

- 1 to 70 years of age: 600 IU (15 mcg)
- 71 years of age and older: 800 IU (20 mcg)

The recommended intake of calcium is [13]:

- Women:
  - 19 to 50 years of age: 1,000 mg
  - 51 years of age and older: 1,200 mg
- Men:
  - 19 to 69 years of age: 1,000 mg
  - 70 years of age and older: 1,200 mg

Many older adults take calcium-vitamin D supplements to improve bone health and ensure adequate intake of both nutrients. However, this may not always be necessary or even appropriate. Whenever possible, experts recommend obtaining these nutrients from the diet. In fact, due to a lack of strongly supportive evidence, guidelines have not recommended the routine use of calcium and vitamin D supplements in many older adults [26; 27]. For the prevention of fractures in community-dwelling, postmenopausal adults, the USPSTF found insufficient evidence to assess the balance of benefits and harms when calcium and vitamin D are supplemented in doses of at least 1,000 mg daily and 400 IU daily, respectively. The USPSTF also recommends against daily supplementation with lower doses of calcium and/or vitamin D. For the primary prevention of fractures in men and premenopausal women, the current evidence is insufficient to assess the balance of the benefits and harms of vitamin D and calcium supplementation, alone or combined.

The Bone Health and Osteoporosis Foundation (BHOF) recommends a diet with adequate total calcium intake based on the recommended daily intake, incorporating calcium supplements if intake is insufficient. They also recommend maintenance of serum vitamin D sufficiency (a 25-hydroxyvitamin D level of 30–50 ng/mL), with the use of supplemental vitamin D as needed to achieve sufficient vitamin D levels.

In 2024, the Endocrine Society published a new evidence-based guideline for using vitamin D supplementation in select patient populations [118]. The Endocrine Society Panel advises against routine use of vitamin D supplements in most healthy adults younger than 75 years of age and recommends against testing for vitamin D blood levels in the general population. The Panel does suggest empiric vitamin D supplementation for the following groups [118]:

- Children 1 to 18 years of age, to prevent rickets and potentially lower the risk of respiratory infections
- Adults older than 75 years of age, because of its potential to lower the risk of mortality
- Pregnant individuals, because of its potential to lower the risk of pre-eclampsia, intrauterine mortality, preterm birth, and other neonatal complications
- Adults with prediabetes who are at high risk for progression to type 2 diabetes

The Panel advises that empiric vitamin D supplementation may include daily intake of fortified foods, vitamin formulations that contain vitamin D, and/or daily intake of a vitamin D supplement [118]. For nonpregnant older adults for whom vitamin D is indicated, the panel suggests supplementation via daily administration of vitamin D, approximating the age-adjusted dosage specified by the Institute of Medicine (600 IU for persons 1 to 70 years of age; 800 IU for those older than 70 years of age) rather than intermittent use of higher doses [13; 118].

There has also been interest in the use of vitamin D supplements for reducing fall risk. However, high-quality research on this topic has yielded negative results. The USPSTF actually recommends against vitamin D supplementation to prevent falls in community-dwelling older adults [28].

Potassium

There is no recommendation for increased intake of potassium in older adults. However, the 2017 American Heart Association (AHA)/American College of Cardiology (ACC) Guidelines recommend increased intake of potassium in patients with elevated blood pressure or hypertension [112]. This recommendation should be considered with caution in older adults, who may have reduced kidney function or be taking medications that reduce potassium excretion. In fact, the guideline specifies that potassium supplementation should be obtained through the intake of potassium-rich foods as opposed to potassium supplements. This reduces the risk of excessive potassium intake or hyperkalemia.

Magnesium

Magnesium is an important nutrient for bone health. Magnesium deficiency can increase the formation and activity of osteoclasts, which resorb bone. Increased bone resorption causes release of magnesium and calcium from the bone, which can increase magnesium levels in times of deficiency. However, no large prospective studies have been conducted to evaluate the benefits of magnesium supplementation for the prevention of osteoporosis.

Regardless, it is important for patients to ensure adequate intake of magnesium from the diet. The daily recommended intake for magnesium is 320 mg for all adults 31 years and older [24]. Many foods are rich in magnesium and will allow most patients to attain this intake level.

However, some older adults may be at increased risk for magnesium deficiency due to the use of certain medications. The most important culprits are diuretics and PPIs. For diuretics, loop diuretics are the greatest cause for concern. This risk increases when taken with other magnesium-depleting drugs like PPIs. For patients taking PPIs long-term, the FDA recommends checking serum magnesium levels at baseline and annually thereafter. Although some patients may need to discontinue the PPI permanently, others with hypomagnesemia can take a PPI and magnesium supplement concurrently [29].

OTHER NUTRITIONAL SUPPLEMENTS

Protein

Due to the loss of muscle mass that occurs with age, protein consumption becomes particularly important for older adults. However, research shows that many older adults do not consume enough protein to keep up with the daily requirements, and that protein consumption actually decreases with age. The recommended daily intake of protein for all adults 18 years of age and older is 0.8 grams/kg [24].

However, the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) recommends a higher protein intake for women older than 50 years of age. This recommendation calls for 1–1.2 grams/kg, as postmenopausal women experience an even greater loss in muscle mass [30].

As with other nutrients, patients should be counseled to obtain adequate protein intake from a well-rounded diet whenever possible. Although protein supplements may be appropriate for some patients, most patients are able to obtain adequate protein by making healthy changes to their diet. Common protein supplements, including whey, pea, and soy protein, will be discussed later in this course.

Fibers

Fiber is an important component of the diet. It is recommended that older women consume 25 grams daily and that older men consume 28 grams daily [24]. These intakes are actually less than those recommended for adults younger than 51 years of age. However, research shows that, as with protein, many older adults are not obtaining enough fiber from the diet.

The FDA has an established definition for what can be called a dietary fiber on a product label. This definition essentially states that the fiber must be a naturally occurring, nondigestible carbohydrate obtained from plants that has beneficial effects in the body. Fiber can be either water-soluble or water-insoluble. Water-soluble fibers, such as oats, beta-glucans, and barley, help to lower both blood glucose and cholesterol levels. Water-insoluble fibers, such as wheat bran and rice bran, help the body digest food and improve bowel health [31].

Most people will be able to meet their dietary fiber needs by increasing their intake of certain foods, such as oatmeal, whole wheat cereals, and grains. However, some patients may wish to take a fiber supplement as well. Most of the popular fiber supplements on the market contain blond psyllium (*Plantago ovata*), which is a water-soluble fiber that has shown benefits for constipation, coronary heart disease, hyperlipidemia, and diabetes. In these studies, patients typically consumed 10–20 grams of supplemental psyllium daily [32].

NATURAL PRODUCTS FOR PHYSICAL CHANGES

Almost all systems of the body are affected by age. Some changes can be directly tied to specific events, such as menopause, whereas other changes simply happen slowly over time. This section will explore some of the natural products most commonly used to counteract the physical changes that occur with age.

MUSCULOSKELETAL HEALTH

As mentioned, one of the best ways to improve musculoskeletal health in older age is to ensure adequate dietary intake of calcium, vitamin D, and protein. However, for those who would like to improve their overall physical performance and ability to recover from exercise, other natural products may be considered.

Physical Activity

First and foremost, it is important to ensure that patients are getting adequate physical activity for their age. This can be key to combatting the increased weight gain that is seen after menopause. In addition, it can help to reverse age-related muscle loss (sarcopenia) and even slow bone loss in all older adults.

The Centers for Disease Control and Prevention (CDC) recommends that all adults older than 65 years of age [33]:

- Obtain at least 150 minutes of moderate-intensity activity per week, such as brisk walking. Alternatively, this can be replaced with 75 minutes of vigorous-intensity activity, such as hiking, jogging, or running.
- Participate in muscle-strengthening exercises at least two days per week
- Participate in activities that improve balance at least three days per week

Muscle-strengthening exercises can include a wide range of options and are not solely limited to weightlifting. Patients can also consider the use of resistance bands; exercises that use their own body weight for resistance, such as push-ups, sit-ups, and certain forms of yoga and Pilates; and even heavy gardening [33]. Balance exercises are more specific and involve activities such as walking backwards, standing on one leg, or using a wobble board [33].

If a patient has had only limited physical activity and is interested in initiating a new exercise program, encourage them to seek guidance from a physical therapist. To avoid injury, patients should also be evaluated before initiating a new exercise program involving compressive or contractile stressors (such as running or weightlifting).

Supplements for Physical Performance

Some older adults may struggle to complete these recommendations due to fatigue or reduced muscle mass. Others may wish to exceed these recommendations but feel that they do not have adequate strength or energy to do so.

Protein Supplements

Protein was briefly discussed in the last section, within the context of ensuring adequate protein intake throughout the day. For a small number of older adults who cannot obtain adequate protein from the diet, protein supplements may be considered. There is also increasing interest in the use of protein supplements to improve physical performance and exercise endurance.

There are many protein supplement products on the market. The majority of these products use whey protein, which is derived from milk [34]. Other products use pea protein or soy protein. All three of these are considered complete proteins, meaning they contain all essential amino acids, which are amino acids that cannot be made by the body and must be obtained from the diet. Collagen is also becoming popular as a protein supplement. It is important to note that all collagen protein products are derived from animals and that collagen is not a complete protein [35]. Older adults should not rely on collagen protein supplements as a primary source of protein in the diet.

It is not clear if the form of protein used affects outcomes. Some small studies in young athletes suggests that whey, soy, beef, chicken, and dairy protein are similarly beneficial for improving muscle strength [36]. However, there is no researching comparing protein sources in older adults, so it is unclear if different protein formulations can be interchanged.

Some research suggests that taking 35 grams of whey protein three times weekly, either before or after resistance training, can modestly increase muscle mass, muscle strength, and functional capacity [37; 38]. However, it is unclear if these benefits are clinically significant. Additionally, it is unclear if there are any benefits to muscle mass in people who are not regularly exercising [39].

There is very little, inconclusive research available for using soy protein to improve physical performance in older adults. To date, pea protein and collagen have not been studied for this purpose.

Branched-Chain Amino Acids (BCAAs)

Although branched-chain amino acids (BCAAs) are not protein supplements, they are comprised of amino acids, the building blocks of protein. BCAA products typically contain leucine, isoleucine, and valine, which are all essential amino acids.

Research on the use of BCAAs in older adults has mostly been limited to those who are relatively malnourished or are known to have inadequate dietary protein intake. The small studies that are available have overall shown no benefit for muscle strength or physical function [40; 41].

Creatine

Most research shows that taking creatine while taking part in a resistance training program can increase upper and/or lower body muscle strength in older adults. Research also suggests that creatine improves total muscle mass in older adults [42; 43]. In the available research, most participants took a loading dose of up to 20 grams daily for up to 7 days, followed by a maintenance dose of 2.25–10 grams daily for up to 12 weeks. The benefits of creatine at larger doses or for longer than 12 weeks is unknown.

Some case reports have suggested that taking creatine can worsen kidney dysfunction in some people. Additionally, creatine has been reported to cause water retention and edema in some adults [44]. In most clinical studies, participants did not experience these adverse effects. However, because older adults are more likely to have reduced kidney function, as well as cardiovascular dysfunction, recommend that patients monitor their fluid intake and output when initiating creatine supplementation.

Hydroxymethylbutyrate (HMB)

Hydroxymethylbutyrate (HMB), a metabolite of the amino acid leucine, is a naturally occurring molecule that is thought to be involved in protein synthesis. This has led to some interest in its use for performance enhancement.

Studies in older adults suggest that it might increase muscle mass or minimize the loss of muscle mass, particularly in those adults who have already experienced a loss of muscle mass [45; 46; 47]. However, it does not seem to improve muscle mass or overall exercise tolerance when used in conjunction with exercise [48; 49].

Beta-Alanine

Beta-alanine, a beta-amino acid, is naturally found in the diet. Over the years, it has become a popular supplement for improving exercise performance.

MULTI-NUTRIENT SUPPLEMENTATION FOR AMD

Nutrient	Dose
Original AREDS	
Vitamin C	500 mg
Vitamin E	400 IU
Beta-Carotene	15 mg
Zinc (zinc oxide)	80 mg
Copper (cupric oxide)	2 mg
AREDS2	
Vitamin C	500 mg
Vitamin E	400 IU
Lutein/zeaxanthin	10 mg/2 mg
Zinc (zinc oxide)	80 mg OR 25 mg
Copper (cupric oxide)	2 mg

Source: [55] *Table 1*

The available research in older adults does show that taking beta-alanine 2.4–3.2 grams daily for 4 to 12 weeks improves exercise capacity and reduces fatigue by a small amount. However, it does not improve strength or exercise performance [50; 51; 52]. Beta-alanine is generally well-tolerated, but some people experience a dose-dependent feeling of pins and needles, as well as skin flushing [53; 54].

EYE HEALTH

One of the leading causes of vision impairment in adults older than 55 years of age is age-related macular degeneration (AMD). Although it does not cause complete blindness, this condition blurs a person's central vision. This can significantly limit the ability to complete activities of daily living by making it harder to see faces, read, drive, or do close-up tasks like cooking or repairs [55].

The most common form of AMD, dry AMD, occurs in three stages—early, intermediate, and late. People with early and intermediate AMD typically do not experience symptoms. However, those with late AMD tend to notice a blurry area in their field of vision, which may get bigger over time.

One of the recommended preventive measures for AMD is a multinutrient supplement. Extensive research, referred to as the Age-Related Eye Disease Studies (AREDS), has been conducted on the use of very specific nutrient formulations to limit the progression of AMD. The American Academy of Ophthalmology Guideline recommends one of these formulations, AREDS2, for all patients who have progressed to intermediate or advanced AMD in at least one eye [55].

EVIDENCE-BASED PRACTICE RECOMMENDATION

According to the American Academy of Ophthalmology, antioxidant vitamin and mineral supplementation as per the Age-Related Eye Disease Study (AREDS2) should be considered in patients with intermediate or advanced AMD. There is no evidence to support the use of these supplements for patients who have less than intermediate AMD and no evidence of any prophylactic value for family members without signs of AMD.

(https://www.aaojournal.org/article/S0161-6420(19)32091-3/pdf. Last accessed May 29, 2024.)

Level of Evidence: Expert Opinion/Consensus Statement

Because there is still some confusion regarding the appropriate product to recommend for patients with AMD, it can be helpful to review the formulations that have been studied (***Table 1***) [55]. Both formulations contain the same quantities of vitamin C, vitamin E, and copper. However, they differ in relation to the type of carotenoid provided. Carotenoids are dietary precursors to vitamin A that are converted to vitamin A in the body. The Original AREDS formulation provided beta-carotene, whereas the AREDS2 formulation provides a mixture of two carotenoids, lutein and zeaxanthin.

One of the primary reasons that beta-carotene was removed from the AREDS2 formulation was safety concerns. Multiple studies have shown that heavy smokers who take beta-carotene supplements have an increased risk of lung cancer and an increased rate of mortality. In fact, these known risks led the USPSTF to recommend against the use of beta-carotene supplements [21].

The quantity of zinc in these products also differs. In AREDS2 studies, two different doses of zinc were evaluated. Importantly, only the higher dose of zinc was found to be beneficial, suggesting that only products containing 80 mg of zinc should be used. Research also suggests that taking zinc alone, or taking the other ingredients found in AREDS2 without zinc, results in reduced benefits for patients with advanced AMD. Thus, patients should be counseled to take the specific combination product studied in AREDS2 providing 80 mg zinc [55].

CARDIOVASCULAR HEALTH

Another common area of concern for older adults is cardiovascular health. As discussed, many older adults experience elevated blood pressure and cholesterol. Additionally, there is interest in using supplements to assist in maintaining optimal cardiac function and health for as long as possible.

As noted, multivitamins are incredibly popular with older adults, and one of the stated reasons for use is cardiovascular health. However, the USPSTF has concluded that there is insufficient evidence to assess the balance of benefits and harms with the use of multivitamin supplements for the prevention of CVD or cancer in community-dwelling adults [21]. Similarly, the USPSTF has found that there is insufficient evidence to assess the balance of benefits and harms for the use of single or paired nutrient supplements for these purposes [21]. In general, multivitamins and vitamin/mineral supplements should not be recommended for cardiovascular health.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force recommends against the use of beta carotene or vitamin E supplements for the prevention of cardiovascular disease or cancer.

(https://jamanetwork.com/journals/jama/fullarticle/2793446. Last accessed May 29, 2024.)

Level of Evidence: D (Evidence is insufficient to assess the balance of benefits and harms)

Omega-3 Fatty Acids

Some of the supplements most frequently used by older adults are omega-3 fatty acid supplements. These supplements typically contain fish oil, which is high in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Many fish contain large amounts of omega-3 fatty acids, and fish oil supplements can be derived from various fish, ranging from anchovy to mackerel to sturgeon. Fish oil supplements can vary significantly in contents and quality, with EPA content ranging from 18% to 51% and DHA content ranging from 12% to 32% [113].

Omega-3 fatty acids are generally considered "healthy fats" and are found in high concentrations in the human brain, retina, and spermatozoa. The reason that these are popular for cardiovascular health ties in to multiple purported and confirmed benefits. However, research has identified significant differences between the benefits of fish oil supplements and fish oil obtained from dietary intake of fish.

Prescription vs. Supplemental Fish Oil

Two prescription fish oil products have been approved by the FDA. The first product, with the original brand name Lovaza, provides omega-3 acid ethyl esters. It was approved for triglyceride levels greater than 500 mg/dL in patients who do not have adequate reduction in triglycerides after lifestyle and dietary modifications. For this purpose, the medication is taken as 4 grams daily. The other product, with the original brand name Vascepa, provides icosapent ethyl, which is a derivative of EPA. Similar to the omega-3-acid ethyl esters, this product is approved for the treatment of hypertriglyceridemia at a dose of 4 grams daily. For both products, the daily dose is obtained by taking four capsules [114].

It is important to note that the contents of these prescription products have been purified and standardized and that each capsule contains the exact amount of each omega-3 fatty acid stated on the label. In general, fish oil supplements have not been purified and also may not be standardized.

Another important note to consider is that the quantity of omega-3 fatty acids found in prescription products is significantly higher than that found in supplements. Although some fish oil supplements may have some benefit for reducing triglycerides, these forms of fish oil are generally considered inadequate in comparison to prescription products because doses of up to 12 capsules, as opposed to four capsules of the prescription preparation, may be needed to produce the same effect [56].

Cardiovascular Disease (CVD)

Clinical and observational research has found that routinely eating fatty fish, such as salmon or mackerel, as part of the diet may reduce the risk of developing heart disease and all-cause mortality in adults without a history of CVD [57; 58]. In fact, the AHA recommends one to two weekly servings of non-fried fish in place of less healthy sources of protein and fat to reduce the risk of CVD [59]. However, the use of fish oil supplements for the primary prevention of heart disease does not seem to be beneficial. In addition, neither increased dietary intake of fish oil nor fish oil supplements are associated with a benefit in patients who already have CVD [57; 58].

The best evidence to date shows that fish oil supplements, which are typically taken in doses of 1 gram daily, are not beneficial for primary or secondary prevention of CVD. Additionally, prescription fish oil products in higher doses of 4 grams daily do not seem to be beneficial for the prevention of CVD. Although the benefits of consuming fish oil as part of the diet might offer only modest benefits for the primary or secondary prevention of CVD, people should continue to eat fish and other foods that provide omega-3 fatty acids, as these foods make up part of a healthy diet. In fact, in 2019, the FDA determined that it would allow a qualified health claim stating that foods containing EPA and DHA may reduce the risk of CVD. However, the FDA states that this claim is based on supportive, rather than conclusive, evidence [60].

Hypertension

There is some promising research on using fish oil supplements for blood pressure reduction, although most research suggests that this benefit may only occur in patients with very elevated blood pressure as opposed to those with mild hypertension. A meta-analysis of clinical research shows that, overall, fish oil reduces systolic blood pressure by about 3–5.5 mm Hg and diastolic blood pressure by 2–3.5 mm Hg in patients with hypertension. It is not clear whether the hypotensive effect of fish oil is dose-dependent [61; 62].

Interestingly, some studies have suggested that different antihypertensive medications can alter the effect of fish oil on blood pressure. Some clinical evidence shows that adding fish oil 5 grams daily for six weeks does not provide additive blood pressure reduction in patients being treated with ACE inhibitors. However, other clinical research shows that fish oil provides additive reduction of systolic and diastolic blood pressure in hypertensive patients taking beta-blockers or diuretics [63].

If patients are interested in taking fish oil to reduce blood pressure, remind them that fish oil supplements have not been shown to provide any benefit for preventing CVD. Also, counsel patients that supplements containing only DHA or EPA, the omega-3 fatty acids in fish oil, have not been shown to provide the same benefits as fish oil for either blood pressure or CVD. Finally, the doses used in studies of fish oil supplements for hypertension are very high and can be difficult to obtain. This is similar to the need to take 12 capsules of supplemental fish oil versus 4 capsules of prescription fish oil for the treatment of hypertriglyceridemia.

Safety Concerns

Older adults may be at risk for some specific potential side effects from fish oil products. One commonly discussed adverse effect of omega-3 fatty acids is a potential increased risk for bleeding. This concern is due to some older research which suggested that doses greater than 3 grams per day can inhibit blood coagulation and potentially increase bleeding risk [64]. The most rigorous research to date shows that short-term doses of fish oil 10 grams daily and long-term doses of 1.5 grams daily for up to one year do not increase the risk of bleeding or affect coagulation parameters in chronically ill patients [64]. However, the doses studied for hypertension and hypertriglyceridemia exceed 1.5 grams daily; use caution when recommending fish oil supplements for older adults.

More recently, large randomized controlled trials have identified a possible increased risk for atrial fibrillation in people taking prescription fish oil. One large clinical study, called the STRENGTH trial, found that taking prescription fish oil 4 grams daily for up to six years was associated with an increased risk for atrial fibrillation, with a number needed to harm of 114 when compared with a corn oil control [65]. Also, meta-analyses show that taking omega-3 fatty acid supplements increases the incidence rate ratio for atrial fibrillation by up to 37% when compared with placebo. This incidence rate seems to increase with doses of more than 1 gram daily [66; 67]. Thus, fish oil supplements should be used with caution in older adults at risk for atrial fibrillation.

Other adverse effects of fish oil are milder in nature and are typically limited to the gastrointestinal tract. Some patients experience fishy hiccups and a fishy breath odor and/or aftertaste. If patients experience diarrhea, heartburn, bloating, discomfort, or indigestion, they should be encouraged to start at a lower dose and increase slowly, and to take their supplements with meals.

Some fish may contain unsafe levels of certain toxins, including dioxins, mercury, and polychlorinated biphenyls (PCBs). PCBs are found in fish living in polluted waters and in some farmed fish, such as salmon. Freshwater fish frequently contain high levels of these chemicals, which may be carcinogenic [68]. Dioxins may be found in high concentrations in the feed given to farmed fish. Farmed salmon, the most common store-bought salmon in North America, is more likely to contain high concentrations of dioxin than wild-caught salmon [69]. Thus, fish should be consumed in moderation.

For patients who would like to take a fish oil supplement, make sure to only recommend products with appropriate quality certifications, including USP-Verified and NSF: Contents Certified. These supplements have been verified to reliably contain what is stated on the label and to be free of unsafe levels of contaminants, such as pesticides and heavy metals.

JOINT HEALTH

Joint health is another common concern that comes with aging. While some people may already have osteoarthritis, others are interested in taking supplements to prevent the development or slow the progression of the condition.

Glucosamine and Chondroitin

The most popular supplements for joint health are glucosamine and chondroitin, often taken together in a combination product. Glucosamine is an amino sugar that occurs naturally in humans. It is necessary for the synthesis of glycoproteins, glycolipids, and glycosaminoglycans. These compounds are found in tendons, ligaments, cartilage, synovial fluid, mucous membranes, blood vessels, heart valves, and structures of the eye. There are multiple forms of glucosamine available on the market [70]. Glucosamine sulfate is the most common form. This form must be created semi-synthetically in a lab. Glucosamine hydrochloride is the second most common form. This salt occurs naturally and can be obtained from shellfish, fungi, or corn via a simple extraction process. *N*-acetyl glucosamine, the acetylated derivative of glucosamine, is the least common form found in supplements [71].

Chondroitin sulfate is a glycosaminoglycan found naturally in the body, particularly in connective tissues. It is a very large molecule; the species or tissue of origin, as well as the extraction method used, can affect its final size [72].

Extensive research has been conducted on the use of glucosamine for the management of osteoarthritis. Thus far, the best evidence is for glucosamine sulfate. Glucosamine hydrochloride has not shown any real benefit in clinical research.

Glucosamine

Most research has focused on the use of oral glucosamine sulfate for the management of knee osteoarthritis. Meta-analyses of the available research show that taking glucosamine sulfate 1,500 mg daily for up to three years modestly improves pain and function when compared with placebo [73]. Individual studies have shown a 28% to 41% pain reduction and 21% to 46% improvement in function [74]. Small studies comparing glucosamine sulfate with NSAIDs, such as ibuprofen 400 mg three times daily or piroxicam 20 mg daily, suggest that these treatments provide similar benefit. However, NSAIDs appear to relieve symptoms within two weeks, whereas glucosamine sulfate can take four to eight weeks [75].

The benefits of glucosamine sulfate seem to vary depending on the product used. To date, the most consistently positive evidence for glucosamine sulfate has been seen with Dona, a specific, pharmaceutical-grade, crystalline glucosamine sulfate product. This formulation of glucosamine sulfate has demonstrated high bioavailability resulting in high plasma concentrations, although the clinical relevance of this is unclear [76]. Experts currently disagree as to whether the benefit seen with this product is due to bias introduced by industry funding or due to a higher quality product.

Chondroitin Sulfate

Chondroitin sulfate, when taken alone, has demonstrated modest benefit for reducing pain and improving function in some patients with knee osteoarthritis. Meta-analyses of the available research show that taking chondroitin sulfate 800–2,000 mg in single or divided doses daily for at least three months can modestly reduce pain and disability when compared with placebo [77]. Other clinical research in adults with knee or hip osteoarthritis shows that taking chondroitin sulfate daily at a dose of at least 800 mg for two years might modestly reduce joint degeneration and narrowing when compared with placebo or celecoxib [78; 79].

Glucosamine Sulfate and Chondroitin Sulfate Combinations

Although most evidence evaluating glucosamine sulfate or chondroitin sulfate alone suggests modest benefit for knee osteoarthritis, research on the use of combination products is less conclusive. Some long-term studies in patients with osteoarthritis show that taking this combination modestly reduces joint space narrowing when compared with a control group [71; 80]. But not all research is positive. Some individual clinical studies, as well as meta-analyses of the available research, have not shown a reduction in pain in patients taking chondroitin sulfate in combination with either glucosamine hydrochloride or glucosamine sulfate [81].

The place of glucosamine and chondroitin in clinical practice is unclear. In fact, clinical guidelines provide conflicting recommendations [71; 82]. The American College of Rheumatology (ACR) strongly recommends against the use of any glucosamine or chondroitin products for any form of osteoarthritis. Conversely, the European Society of Clinical and Economic Aspects of Osteoarthritis (ESCEO) strongly recommends for the use of pharmaceutical-grade glucosamine sulfate or chondroitin sulfate products in patients with osteoarthritis. The ESCEO also provides a weak recommendation against the use of glucosamine and chondroitin in combination.

These conflicting recommendations are related to differing interpretations of the previously discussed evidence. The ACR has determined that the positive benefits identified in industry-funded studies indicates the introduction of industry bias [82]. The ESCEO, on the other hand, has determined that the positive benefits identified in industry-funded studies is due to the higher quality and bioavailability of the products used [71].

If a patient would like to use these products, be sure to recommend one that carries a third-party quality certification to minimize concerns related to product quality and potency.

Safety

Both glucosamine and chondroitin are relatively safe for most adults. The most commonly reported adverse effects are minor gastrointestinal disturbances, such as abdominal pain, bloating, constipation, diarrhea, and heartburn.

Some case reports have suggested that glucosamine and/or chondroitin may interact with warfarin, causing an elevation in international normalized ratio (INR). Although the likelihood of this risk is unclear, use caution in patients taking warfarin and monitor INR closely.

Collagen

Another supplement that has gained popularity for osteoarthritis and joint health is collagen. Collagen is a hard, insoluble protein that occurs naturally in the human body and is found in the bones, cartilage, muscles, skin, and tendons. It is a structural protein, meaning that it is crucial to the shape and structure of cells and tissues in the body [83].

Some supplements contain intact collagen, often either collagen type I, II, or III. However, much more often, collagen supplements contain hydrolyzed collagen, or collagen peptides, that are derived from these intact forms of collagen. This is also sometimes referred to on labels as collagen hydrolysate.

Benefits

Collagen types I and II have been evaluated for use in knee osteoarthritis, with small studies suggesting the potential for modest benefit with certain formulations. However, the most extensive research has been conducted with collagen peptides [84; 85].

Some clinical studies in adults with knee osteoarthritis suggest that collagen peptides 5–10 grams, taken for three to six months, may modestly reduce pain. However, any improvements appear to be small, and not all research has yielded positive findings. One clinical study shows that taking oral collagen peptides reduces pain by at least 30% in 42% more patients when compared with placebo. However, there was no improvement when the Western Ontario and McMaster Universities (WOMAC)

scale was used [84]. In another study, taking collagen peptides reduced pain by about two points on a 100-point scale, compared with a 0.9-point reduction in those taking glucosamine sulfate 1,500 mg. There was no reduction in the use of ibuprofen in these patients [85].

Although some research suggests the potential for modest benefit, it is not clear that collagen peptides can improve pain to a clinically meaningful degree. Patients should not rely on collagen peptides for the management of knee osteoarthritis, although it may be considered as an adjunct therapy in patients with more severe disease.

Safety

Overall, collagen appears to be safe for adults when taken by mouth at doses evaluated in clinical research. There are very limited reports of adverse effects with collagen products. Some minor gastrointestinal upset has been reported rarely with the use of collagen peptides.

NATURAL PRODUCTS FOR COGNITIVE CHANGES

One of the major concerns that comes with age is a decline in cognitive function, which can present as either cognitive impairment or dementia. Because there are no approved or confirmed preventive strategies for reducing the risk of age-related cognitive impairment or dementia, many people consider the use of supplements. Similarly, some people use supplements to slow the advancement of cognitive impairment and/or dementia.

It should be noted that many studies of supplements for the improvement of cognitive function in older adults are small and may be of low quality. For example, some studies do not use a placebo control, and the majority of these products have not been compared to prescription drugs for dementia. Although this does not invalidate all of the available research, the results should be interpreted with caution.

WHAT IS A MEDITERRANEAN-LIKE DIET?

A Mediterranean-like diet emphasizes foods such as olive oil, fruits, vegetables, legumes, and whole grains. This is intended to provide a high ratio of monounsaturated-to-saturated fat. The diet also emphasizes fish and reduces overall meat intake, while allowing for moderate-to-modest amounts of red wine and dairy. In general, the diet avoids highly processed foods, refined grains, and sugars.

Source: Author *Table 2*

LIFESTYLE INTERVENTIONS

First, it is worth noting that lifestyle changes are the most commonly recommended preventive measures for mild cognitive decline or dementia. The World Health Organization (WHO) recommends that all adults, with or without cognitive impairment, get adequate physical activity (as discussed) to reduce the risk of cognitive impairment. The organization also recommends that all adults consume a Mediterranean-like diet in order to slow cognitive decline (***Table 2***) [86]. However, it should be noted that the research identifying a benefit for age-related cognitive impairment involved strict adherence to the Mediterranean diet; people who had only moderate adherence did not experience a benefit [87; 88].

In general, regular consumption of fruits, vegetables, and fish is most consistently associated with a reduced risk of dementia. This has led to interest in the use of fish oil to prevent cognitive decline. However, the observational research that has been conducted to date has not found an association between risk of mild cognitive impairment or dementia and the use of fish oil supplements [89; 90; 91].

The WHO also recommends weight loss for people who are overweight or obese, as well as reducing alcohol consumption. Both of these changes can have multiple downstream health benefits, but there is also some early evidence suggesting that they can reduce cognitive decline [86].

Finally, the WHO recommends social participation and social support, which "are strongly connected to good health and well-being throughout life and social inclusion should be supported over the life-course" [86]. However, it is important to note that there is no evidence showing a direct association between social participation and cognitive function. For now, encourage social support and participation due to the many other benefits it can offer, including to mental health [86].

NUTRIENT SUPPLEMENTS

Vitamin E

Vitamin E is one of the most popular vitamin supplements for dementia and cognitive impairment. In fact, there is some evidence to show that taking vitamin E can modestly slow cognitive function decline in patients with Alzheimer disease. However, it does not seem to prevent the onset of Alzheimer disease or prevent cognitive decline in general. Thus, the WHO recommends against the use of vitamin E for prevention [86].

Additionally, there are concerns about the safety of vitamin E in older adults. Most of the studies showing benefit for Alzheimer disease used a dose of 2,000 IU daily. Some research in middle-aged and older patients with chronic diseases suggests that vitamin E in doses above 400 IU daily may increase the risk of adverse outcomes and mortality [115]. On the other hand, these doses appear to be safe in otherwise healthy adults. It is not entirely clear which population is safe to use large supplemental doses of vitamin E, but it should be used with caution in older adults, particularly those with multiple comorbidities.

Idebenone

Another nutrient-like supplement that is sometimes touted for cognitive function is idebenone. This is a synthetic analogue of coenzyme Q10. Some older studies have shown that taking 90–120 mg three times daily for six months slows the decline of cognitive function in adults with Alzheimer disease [92]. However, there is no available research in adults with mild cognitive impairment or other forms of dementia.

Idebenone seems to be well tolerated by most adults although it can cause some gastrointestinal side effects such as nausea and vomiting, abdominal pain, and loose stools.

HERBAL SUPPLEMENTS

Ginkgo

Ginkgo (*Ginkgo biloba*) is one of the most popular herbal supplements for dementia and cognitive impairment. The leaves of this plant have a long history of use in traditional Chinese medicine, and there is some evidence to support their use in people who already have dementia. Research in people with Alzheimer disease, vascular dementia, or mixed dementia shows that taking ginkgo 240 mg daily for about six months modestly improves cognition and activities of daily living when compared with placebo. A lower dose of 120 mg daily does not seem to offer the same benefit [93; 94; 95; 96].

It is important to note that the product used in these studies was a specific ginkgo supplement—Egb 761. This supplement differs from other ginkgo products because it has been standardized to contain 22% to 27% flavone glycosides and 5% to 7% terpene lactones, which includes ginkgolides A, B, and C. Other ginkgo supplements may not be standardized to these same chemicals, and thus they may have different (or lower) activity [97].

As with vitamin E, ginkgo has not shown benefit for the prevention of dementia in those with normal cognitive function or in those with mild cognitive impairment. It also does not seem to prevent disease progression in people with Alzheimer disease. Thus, the WHO guidelines do not recommend ginkgo for the prevention of MCI or dementia [86].

Ginkgo is considered generally safe for most adults. There have been some rare reports of arrhythmia in patients who take ginkgo supplements. It is unclear if this relationship is coincidental or causative, but there have been enough reports to lead Health Canada and the WHO to release warnings about the use of these products [86; 98].

There is also significant interest in the use of ginkgo supplements for tinnitus, another issue that becomes more common with age. In fact, tinnitus can even contribute to cognitive impairment and lack of social participation. Unfortunately, clinical studies show that taking ginkgo leaf extract does not improve symptoms of tinnitus [99; 100]. It should not be recommended for this purpose.

Huperzine A

Huperzine A is a chemical that is isolated from a type of moss, called the Chinese club moss (*Huperzia serrata*). Because it is derived from moss, this chemical is sometimes sold as a supplement, either as a single ingredient or in combination with other ingredients. There are multiple reasons that this chemical is of interest for dementia and mild cognitive impairment, including its antioxidant and anti-apoptotic effects, as well as its possible activity against beta-amyloid.

Clinical research in adults with Alzheimer disease shows that taking huperzine A 200–800 mg in divided doses daily for two to nine months improves cognitive function on the Mini-Mental State Exam (MMSE) when compared with placebo [101; 102]. It should be noted that most research has been conducted in China, where this chemical is an approved drug. One clinical study conducted in the United States shows that taking 400 mg twice daily improves performance on the MMSE and the Alzheimer Disease Assessment Scale – Cognitive Subscale (ADAS-Cog) when compared with placebo. A lower dose of 200 mg twice daily was not consistently beneficial [103].

Huperzine can cause cholinergic side effects such as dizziness, sweating, insomnia, nausea, vomiting, and diarrhea. However, it is generally well tolerated by most adults.

Bacopa

Another herbal supplement that is sometimes touted for cognitive health in older adults is bacopa (*Bacopa monnieri*). This plant is found in India and has been used for centuries in Ayurvedic medicine. There is interest in its use for dementia and cognitive impairment because it has demonstrated cholinergic activity in laboratory studies. However, only one small study has evaluated bacopa in adults with Alzheimer disease or mild cognitive impairment. This study showed that taking bacopa 300 mg daily for 12 months did not offer any benefits when compared with donepezil or baseline [104].

Bacopa has been reported to cause increased stool frequency, nausea, and abdominal cramps in 16% to 30% of patients in clinical studies [116]. Considering that it has not shown benefit for cognitive function in older adults, steer patient away from bacopa supplements.

ENDOGENOUS SUBSTANCES

Alpha-L-Carnitine

Alpha-L-carnitine is an ester of L-carnitine, which is an amino acid derivative that is found naturally in the body. It is made in the brain, liver, and kidneys, and the body can convert it to and from L-carnitine as needed. Alpha-L-carnitine is structurally similar to acetylcholine, which has led to interest in its use for dementia and mild cognitive impairment. Small clinical studies show that taking 1.5–2 grams daily for three months can improve some measures of cognitive function in older adults with mild cognitive impairment [105; 106]. Similarly, small clinical studies show that taking 1.5–3 grams daily for three to 12 months can slow the rate of Alzheimer disease progression and improve some measures of cognitive function [107].

Alpha-L-carnitine is generally well tolerated by most adults, although it can cause headache, insomnia, and agitation in some people. Let patients know that it can also cause the breath, urine, and sweat to have a fishy odor, which is not harmful [108].

Phosphatidylserine

Phosphatidylserine is a phospholipid that is naturally made by the human body. It is a component of the cell membrane and is found in high quantities in the brain. Thus, there is interest in its use for improving cognitive function in all age groups.

To date, the best evidence for the use of phosphatidylserine is for the improvement of cognitive function in adults with age-related mild cognitive impairment or Alzheimer disease. This research shows that taking phosphatidylserine, usually as 300 mg daily in divided doses, for six weeks to six months improves attention, verbal fluency, and memory. However, it should be noted that these studies were very small, and some did not use blinding or a placebo control group. Additionally, the studies are old and may not be representative of current standards of care [109; 110].

As for preventing the development of Alzheimer disease or mild cognitive impairment, clinical research has not shown a benefit. Also, there is currently no research on the use of phosphatidylserine in other types of dementia. However, phosphatidylserine is generally safe to use, with the most common adverse effects being flatulence and nausea. This may be a reasonable option for patients interested in taking a supplement.

Citicoline

Citicoline is a chemical that occurs during the synthesis of choline from phosphatidylcholine in the body. Some small clinical studies in older adults with MCI have shown that taking citicoline 500–2,000 mg daily for up to three months moderately improves memory scores when compared with placebo [111]. The research in patients with Alzheimer disease is relatively limited, and there is no available research in patients with other forms of dementia. Citicoline is well tolerated by most adults.

Alpha-GPC

Alpha-GPC is another chemical that is related to choline, except that this chemical is naturally produced by the body from choline. It is a precursor to acetylcholine, a neurotransmitter. There has been some research on the use of this supplement in patients with vascular dementia and Alzheimer disease that shows modest benefit, but these studies are small and should not be relied upon [117]. The most common adverse effects with alpha-GPC are diarrhea, heartburn, nausea, and vomiting.

CONCLUSION

Aging causes a number of changes to the body that affect physical function, cognitive function, and overall quality of life. Older adults frequently report using supplements, often for the purpose of improving overall health, but also for the purposes of improving musculoskeletal health, nutrition, cardiovascular health, and more. It is important for healthcare professionals to be aware that supplements can interact with drugs and medical conditions, and that some supplements carry serious health risks for certain patients. However, some supplements may be a reasonable option for older patients who are looking to improve their health and quality of life and can be safely recommended.

Implicit Bias in Health Care

The role of implicit biases on healthcare outcomes has become a concern, as there is some evidence that implicit biases contribute to health disparities, professionals' attitudes toward and interactions with patients, quality of care, diagnoses, and treatment decisions. This may produce differences in help-seeking, diagnoses, and ultimately treatments and interventions. Implicit biases may also unwittingly produce professional behaviors, attitudes, and interactions that reduce patients' trust and comfort with their provider, leading to earlier termination of visits and/or reduced adherence and follow-up. Disadvantaged groups are marginalized in the healthcare system and vulnerable on multiple levels; health professionals' implicit biases can further exacerbate these existing disadvantages.

Interventions or strategies designed to reduce implicit bias may be categorized as change-based or control-based. Change-based interventions focus on reducing or changing cognitive associations underlying implicit biases. These interventions might include challenging stereotypes. Conversely, control-based interventions involve reducing the effects of the implicit bias on the individual's behaviors. These strategies include increasing awareness of biased thoughts and responses. The two types of interventions are not mutually exclusive and may be used synergistically.

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