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Plant-based nutrition for healthcare professionals: implementing diet as a primary modality in the prevention and treatment of chronic disease

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Abstract

Cardiovascular disease remains the world's leading cause of death. Yet, we have known for decades that the vast majority of atherosclerosis and its subsequent morbidity and mortality are influenced predominantly by diet. This paper will describe a health-promoting whole food, plant-based diet; delineate macro- and micro-nutrition, emphasizing specific geriatric concerns; and offer guidance to physicians and other healthcare practitioners to support patients in successfully utilizing nutrition to improve their health.

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1 Introduction

Today, many early deaths in the United States are preventable and nutrition-related. According to an analysis of risk factors over the period 1990–2010, the leading cause of early death and disability in the United States is diet.[1] The authors note: "The most important dietary risks in the United States are diets low in fruits, low in nuts and seeds, high in sodium, high in processed meats, low in vegetables, and high in trans fats." Geoffrey Rose proposes[2] that at every office visit, there is an obligation to ask, "Why did this patient get this disease at this time?" He adds, "It is an integral part of good doctoring to ask not only, what is the diagnosis, and what is the treatment? but also, why did this happen, and could it have been prevented?" This approach relates to the sage advice of Hippocrates,[3] the "physician must not only be prepared to do what is right himself, but also to make the patient, the attendants, and the externals cooperate.[3]"

Substantive dietary intervention requires significant efforts by both patients and healthcare providers. For this reason, potential bias may hinder compliance or even create the appearance of conflicting advice.[4–6] When nutrition practices are discussed with patients, physicians typically spend an average of five minutes on the topic, which may not provide enough time and detail for success.[7] Unfortunately, pharmacological and procedural interventions are more common than dietary interventions. Diet is often viewed as more difficult to implement as it is an intrinsic part of culture, family, and self-identity. Recommending a diet that is widely divergent from either the patient's or attendant physician's personal choice may be likened to social discordance surrounding smoking in the 1930s through early 1950s. At that time, the majority of physicians smoked but nonetheless were increasingly responsible for beginning office visits with advice discouraging smoking.[8,9]

With accumulating scientific evidence supporting its health advantages, whole food, plant-based diets are steadily on the rise.[10] Moving from the standard "meat and potatoes" diet to one that features whole plants often requires restructuring and the development of new skills. With practice and the accumulation of nutrition knowledge and a repertoire of recipes, this lifestyle becomes progressively easier.

A whole food, plant-based diet consists of vegetables, fruits, legumes, whole grains, nuts, seeds, herbs, and spices, which can be consumed in infinite combinations (Table 1). In accordance with the United States Department of Agriculture, American Heart Association, and American Institute for Cancer Research, half of the plate should consist of vegetables and fruits in order to ensure adequate intake of fiber, potassium, magnesium, folate, iron, and vitamins A and C, nutrients that tend to be low in the standard Western diet.[11]

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Table 1. Food groups and recommended servings per day.

Food group	Recommended servings per day
Vegetables, all types including starchy vegetables	Ad libitum, with a variety of colors represented
Fruits, all types	2–4 servings (1 serving = 1 medium piece of 1/2 cup)
Whole grains (e.g., brown rice, quinoa, oats)	6–11 servings (1 serving = 1/2 cup cooked or 1 slice whole grain bread)
Legumes (beans, lentils, peas, soy foods)	2–3 servings (1 serving = 1/2 cup cooked)
Leafy green vegetables (e.g., broccoli, cabbage, lettuce)	At least 2–3 servings (1 serving = 1 cup raw or 1/2 cup cooked)
Nuts (e.g., almonds, pecans, walnuts)	1–2 ounces
Seeds (e.g., chia, flax, hemp seeds)	1–3 tablespoons
Fortified plant milks (e.g., almond, soy, rice)	Optional, 2–3 cups
Fresh herbs and spices	Optional, ad libitum

Plant-based diets are associated with lowering overall mortality and ischemic heart disease mortality;[12,13] reducing medication needs;[14–16] supporting sustainable weight management;[17–21] reducing incidence and severity of high-risk conditions, such as obesity[22] and obesity-related inflammatory markers,[23] hyperglycemia,[24,25] hypertension,[26–28] and hyperlipidemia;[29] and even reversing advanced cardiovascular disease and type 2 diabetes.[25,30,31]

These advantages are likely the result of both the consistent consumption of innate health-promoting compounds found in whole plant foods and the reduction of exposure to harmful substances found in animal products and highly processed foods. Meat (including processed, red, and white assortments), fish, dairy, and eggs contain health-damaging saturated fats, heme iron, N-glycolylneuraminic acid (Neu5Gc), carnitine, and chemical contaminants formed when flesh is cooked, such as polycyclic aromatic hydrocarbons, heterocyclic amines, and advanced glycation end products. Highly processed foods encompass a class of commercially produced items made with adulterants including oils, salts, sugars, and other food additives.[32–52] These aforementioned constituents in animal products and processed foods contribute to inflammation, oxidation, and carcinogenesis, promoting disease and, therefore, are better omitted from the diet.

Plant foods exclusively contain two critical nutrients: fiber and phytonutrients. Fiber, found in multiple varieties in all intact plant foods, proffers powerful protection of the gastrointestinal, cardiovascular, and immune systems, while phytonutrients, a vast class of thousands of compounds including glucosinolates, carotenoids, and flavonoids, work synergistically to reduce inflammation and oxidation, providing protection from disease initiation and progression.[53–60]

Interestingly, longevity, aging, and healthspan investigations provide cellular, mechanistic evidence that support dietary intervention in the prevention and treatment of cardiovascular disease.[61] A plant-based diet is a practical way of implementing dietary restriction and may positively impact a variety of metabolic pathways that are under pharmacologic investigation given their potential health benefits in humans. They include inhibition of the growth hormone (GH) and insulin-like growth factor 1 (IGF-1) axis, mammalian target of rapamycin (mTOR) pathway, and inflammation and activation of sirtuins and adenosine monophosphate kinase (AMPK).[62–67] Additionally, protein (essential amino acid) restriction, traditionally seen as a limitation of a vegetarian or vegan diet, may confer similar benefits to those seen in dietary restriction experiments in a wide range of organisms, from yeast to primates.[68–72] While reduced levels of dietary amino acids, such as methionine and leucine were once seen as limitations for plant-sourced proteins, it is now recognized as potentially beneficial.

2 Geriatric nutrition

Several issues to consider with respect to nutrition in the elderly include altered appetite, caloric, and nutrient needs as well as dentition and dexterity. Although seniors typically require fewer calories because of the natural reduction in muscle mass (sarcopenia) and decreased physical activity, these matters leave concern for malnutrition.[73–75] Although there is variance in approach depending upon current weight status (see Box 1), the goal is nutrient adequacy, while avoiding malnutrition, both under- and over-nutrition. Special nutritional needs, including increased protein needs, vitamin B12 absorption, vitamins and minerals for bone health, long-chain omega-3 fatty acids, and more will be discussed in detail below (See Table 2 for Food Sources of Notable Nutrients).

3 Meeting energy needs

Geriatric patients who struggle to consume enough calories should increase their intake of more calorically dense plant-based foods. Examples appropriate for those with poor

Box 1. Overweight and underweight.

For overweight patients, recommend shifting diet up the Food Triangle (Figure 1) to focus on higher fiber leafy greens, starchy vegetables, and legumes and to limit nuts, seeds, and avocado during weight loss period.

For underweight patients, increase nuts, seeds, avocados and eat together with lower fiber starchy vegetables and fruits (e.g., green smoothies, nut and seed butter spreads, sauces, and dressings).

Table 2. Sources of notable nutrients.

Nutrient	Food sources
Protein	Legumes (beans, lentils, peas, peanuts), nuts, seeds, soy foods (tempeh, tofu)
Omega-3 fats	Seeds (chia, flax, hemp), leafy green vegetables, microalgae, soybeans and soy foods, walnuts, wheat germ, supplement
Fiber	Vegetables, fruits (especially berries, papayas, pears, dried fruits), avocados, legumes (beans, lentils, peas), nuts, seeds, whole grains
Calcium	Low-oxalate leafy greens (bok choy, broccoli, cabbage, collard, dandelion, le, watercress), calcium-set tofu, almonds, almond butter, fortified plant milks, sesame seeds, tahini, figs, blackstrap molasses
Iodine	Sea vegetables (e.g., arame, dulse, nori, wa me), iodized salt, supplement if necessary
Iron	Legumes (beans, lentils, peas, peanuts), leafy greens, soybeans and soy foods, quinoa, potatoes, dried fruit, dark chocolate, tahini, seeds (pumpkin, sesame, sunflower), sea vegetables (dulse, nori)
Zinc	Legumes (beans, lentils, peas, peanuts), soy foods, nuts, seeds, oats
Choline	Legumes (beans, lentils, peas, peanuts), bananas, broccoli, oats, oranges, quinoa, soy foods
Folate	Leafy green vegetables, almonds, asparagus, avocado, beets, enriched grains (breads, pasta, rice), oranges, quinoa, nutritional yeast
Vitamin B12	Fortified foods (nutritional yeast, plant milks), supplement
Vitamin C	Fruits (especially berries, citrus, cantaloupe, kiwifruit, mango, papaya, pineapple), leafy green vegetables, potatoes, peas, bell peppers, chili peppers, tomatoes
Vitamin D	Sun, fortified milks, supplement if deficient
Vitamin K	Leafy green vegetables, sea vegetables, asparagus, avocado, broccoli, Brussels sprouts, cauliflower, lentils, peas, natto (a traditional Japanese food made from fermented soybeans)

dentition or appetite include green smoothies (blended vegetables, fruits, nuts, and seeds), nut and seed butters, bean spreads (e.g., hummus), soups and purees, cooked cereals (whole grains), and nut- and seed-based sauces (Table 3). Food preparation can be simplified by stocking frozen produce (e.g., vegetable or bean burgers, and whole grains); canned legumes and tomatoes, jarred nut and seed butters, sauces (e.g., salsa, marinara), dried legumes, whole grains, and whole grain pastas, and boxed vegetable broths and soups; fortified plant milks, seeds (especially flax, hemp, and chia), tofu, tempeh, and jars of minced garlic and ginger. Further, user-friendly kitchen tools such as a high-powered blender, microwave, rice cooker, electric pressure cooker, and automatic jar opener can improve access to healthful foods.

Table 3. Calorie density.

Food group	Calories per 100 g
Non-starchy vegetables (e.g., broccoli, carrots, beets, okra)	16–49
Fruits (e.g., berries, apples, bananas, tomatoes)	18–89
Starchy vegetables (e.g., potatoes, squash, corn)	17–94
Whole grains (e.g., rice, oats, quinoa)	71–120
Legumes (e.g., beans, lentils, peas)	116–164
Foods made with flour (e.g., bread, bagels, pasta)	149–280
Dried fruits (e.g., dates, prunes, raisins)	240–299
Sugars (e.g., table sugar, maple syrup, agave, corn syrup)	260–399
Nuts and Seeds (e.g., walnuts, cashews, flax seeds)	486–654
Oils (e.g., olive, coconut, canola)	884–892

4 Nutrient adequacy

A common concern when considering any diet, including an entirely plant-based one, is nutrient adequacy. The Academy of Nutrition and Dietetics states in their position paper:[10] "*Vegetarian diets, including vegan, diets are healthful, nutritionally adequate, and may provide health benefits for the prevention and treatment of certain diseases. These diets are appropriate for all stages of the life cycle, including pregnancy, lactation, infancy, childhood, adolescence, older adulthood, and for athletes*." Even calorie-restricted plant-based diets intended for weight loss, have been found to be consistent with dietary guidelines.[76]

5 Plant-based macro-nutrition

The ideal ratio of intake of macronutrients is highly debated. However, it appears that despite nearly a century of macronutrient-centered grouping of food, the quality of the overall diet is likely responsible for health outcomes rather than the more simplistic ratio of macronutrients.

Accordingly, evidence supporting the health and weight management benefits of a whole food, plant-centered plate is abundant.[12,77–79] Much of the benefit may relate to dietary restriction of specific macronutrients (e.g., essential amino acids) and is likely more important than energy restriction alone.[80–83] Dietary restriction has demonstrated improvement in neoplasia, cardiovascular disease, and glucoregulatory impairment in long term primate studies.[84]

Dietary restriction without malnutrition appears to overlap with known cultural loci for centenarian eating patterns such as is demonstrated in the Okinawan diet.[85–87] For example, the Okinawan region of Japan has one of the longest-lived populations in the world, with a high number of centenarians, and a low risk of age-related diseases.[88–90] Their traditional diet is low in calories, very low in fat (especially low in saturated fat), and nutrient-dense, consisting primarily of orange-yellow root vegetables (particularly sweet potatoes), leafy green vegetables, soy foods, and medicinal plants. As their dietary patterns shift away from the traditional plant-centered Okinawan diet and towards a Western one, their life expectancy is declining.[91] Smaller studies suggest coronary artery disease and type 2 diabetes may benefit from a very low-fat diet, but there appears to be more to this benefit than dietary fat percentages alone.[14,30,31] For example, the Mediterranean and certain raw food diets consisting of upwards of 35% of calories from fat show consistent positive health advantages.[92–94]

Recognizing that the traditional categories of protein, carbohydrate and fat may not have enough specificity (i.e., essential versus nonessential amino acids, saturated/trans versus mono/polyunsaturated fats, complex carbohydrates versus simple sugars) to prescribe healthful eating patterns, the Food Triangle (Figure 1) was proposed as an improved way of visualizing and educating people using whole food language.[49,95] The Food Triangle not only addresses energy density, but also conveniently segregates foods based on other nutritional components important to health span and longevity. Bringing the office visit language back to one that is whole-food centered may be helpful and mitigate the confusion and obfuscation that has become the hallmark of food advertising and labeling. However, given the current macronutrient focus, they will be discussed below.

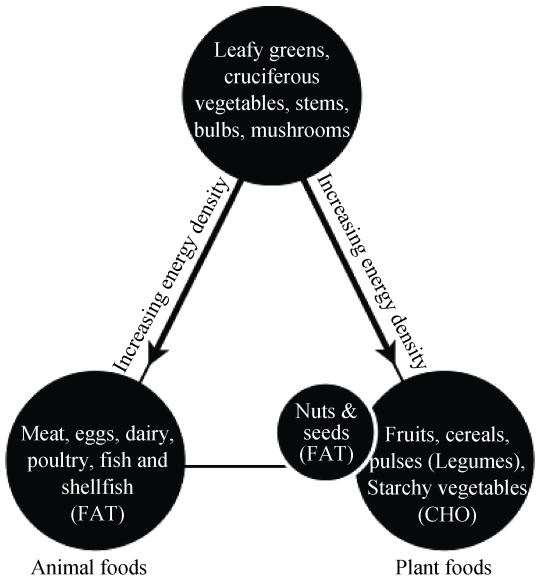

Figure 1. The Food Triangle. The Food Triangle organizes whole food using an energy density paradigm. This organization of energy density permits individuals to address their micronutrient requirements (the apex of the triangle) without driving chronic overnutrition (the bottom vertices of the triangle). These apex foods become the nutritional foundation of daily meals, rather than the more energy dense alternatives. They also provide a rich source of phytonutrients and can be eaten in nearly unlimited quantities. It further places emphasis on foods that are increasingly important for a healthy gut microbiota. Highly refined oils, sugars, and flours are not listed, as they are not whole foods and should be consumed in limited quantities. This image was reproduced with permission from Liebert Publishing.

6 Carbohydrates

The Institute of Medicine (IOM)'s adequate intake (AI) of carbohydrates[96] is 130 g per day for everyone (except during pregnancy and lactation) after the age of one year. Optimal sources of carbohydrates, such as vegetables, fruits, whole grains, and legumes, are high in fiber and other nutrients. Refined carbohydrates from sugars, flours, and other processed foods can lead to malnourishment and promote illness.[97]

Certain foods, for example, whole food tubers like sweet potatoes or cassava, are typically labeled as carbohydrates based on primary energy source. They are traditionally viewed as high in energy and low in protein. However, the opposite is true and these foods are in fact rich sources of protein and low in energy.[98,99] Nitrogen balance is positively maintained even when rice is used as 100 percent replacement for chicken.[100] These results may appear discordant with traditional macronutrient-centered food education, but reinforces the fact that that nutritional requirements can be healthfully met using whole food plant-based sources.

7 Protein

The IOM's AI of protein[96] for adults is based on the recommended 0.8 g/kg per day (about 46 g per day for women and 56 g per day for men). Some research suggests increasing this recommendation to 1.0–1.2 g/kg per day after the age of 65 to reduce the risk for sarcopenia and osteoporosis[101,102] and possibly the risk of cancer and overall mortality.[69] While food marketing and education typically focus on protein from animal sources, all essential amino acids originate with bacterial or plant synthesis and can be obtained from plant sources.[103] Overall, protein is readily

available throughout the plant kingdom. Plant-sourced foods that are particularly rich in protein include legumes, nuts, seeds, soy foods, whole grains, and leafy green vegetables. They tend to have lower levels of essential amino acids as compared to animal-based foods, but this difference may be an advantage.[70]

8 Dietary fatty acids

Compared to other nutrient recommendations, the dietary fat acceptable macronutrient distribution range (AMDR) is wide, ranging from 20% to 35% of total calories for adults after 19 years of age.[96] This range is intended to provide enough fat calories as energy while decreasing risk of chronic disease. However, there are more specific guidelines when it comes to the different types of fatty acids, as although they may be isocaloric, they are not isometabolic and hence impart unique influences on health.

Polyunsaturated fatty acids—namely omega-3 and omega-6—are the only essential fats in the diet. Omega-3 fats are found in their shorter chain form as alpha linolenic acid (ALA) and are used as energy and also converted by the body to the longer chain eicosapentaenoic acid (EPA) and then docosahexaenoic acid (DHA).[104] ALA can be found in flaxseeds, hemp seeds, chia seeds, leafy green vegetables (both terrestrial and marine), soybeans and soy products, walnuts, and wheat germ, as well as in their respective oils. A direct plant source of EPA and DHA is microalgal oil, through which fish acquire them.[105–110] Plant sources are superior because they do not contain the contaminants that fish contain, including heavy metals, such as mercury, lead, and cadmium, industrial pollutants like dichlorodiphenyltrichloroethane, polychlorinated biphenyls, and dioxin, and possibly even radioactive isotopes.[111–114] The AI for ALA is 1.1 g per day for adult females and 1.6 g per day for men. Conversion of ALA to EPA and DHA is limited in humans.[115,116] Serum and adipose levels of EPA and DHA have been found to be significantly lower in vegetarians and vegans when compared to omnivores, although there is no evidence of any adverse health or cognitive effects.[117,118] Vegetarians, vegans, and those with reduced conversion ability, such as the elderly, may benefit from doubling the recommended dose of ALA (2.2 g for females and 3.2 g for males per day) and adding a microalgal supplement.[107,119]

As omega-6 fats (linoleic acid), are available ubiquitously in the food supply in the seeds of most plants, they are not a nutrient of concern. In fact, Western diets tend to be excessive in omega-6 fats due to their prevalence in processed foods, which are also low in omega-3 fats. The resultant elevated omega-6/omega-3 ratio has been associated with inflammation and increased chronic disease risk.[120,121] This adverse ratio can be attenuated by ensuring adequate omega-3 intake and minimizing the consumption of highly processed foods.

Mono-unsaturated fats are not essential, but impart either a neutral or slightly beneficial effect on serum cholesterol levels, depending on which nutrient they are replacing. When swapped for saturated or trans fats or refined carbohydrates, monounsaturated fats may lower low density lipoprotein cholesterol (LDL-C) and raise high density lipoprotein cholesterol (HDL-C) cholesterol.[33] These fatty acids are found in olives, avocados, macadamia nuts, hazelnuts, pecans, peanuts, and their respective oils, as well as in canola, sunflower, and safflower oils.

Saturated fats are not essential in the diet and can promote cardiovascular disease.[33,122,123] They are found primarily in animal products, but are available in some plant foods, mostly in tropical fats and oils, such as palm and coconut, and also in other high-fat foods, including avocados, olives, nuts, and seeds. The American Heart Association recommends limiting saturated fat to less than 5 to 6 percent of total calories (about 14 g total on a 2000 calorie per day diet).[124] While recent headlines may cast doubt on the adverse impact of saturated fat, the preponderance of the evidence supports its reduction.[123,125] Underlying mechanisms, metabolic ward studies, and wider observational studies of the last century are still supportive of the reduction of saturated fat.[126–128]

Trans fatty acids (TFAs) are lab-made via hydrogenation and are found in processed, fried, and fast foods. Although they were originally developed to be a healthy alternative to butter and lard, TFAs were found to increase cardiovascular disease risk.[33] In November 2013, the United States Food and Drug Administration (FDA) issued a notice that TFAs were no longer considered safe; the FDA is now trying to eliminate artificially produced TFAs (small amounts are found naturally in some meat and dairy products) from the food supply. Note that a nutritional label can state a food product contains "0 g trans fats" even if it contains up to 0.5 g per serving. Thus, advise patients to focus on the ingredient list on food products and avoid anything with the words "hydrogenated" or "partially hydrogenated."

Dietary cholesterol is a sterol found only in animal products. Although cholesterol is necessary for the production of hormones, vitamin D, and bile acids, the liver produces adequate quantities of cholesterol and exogenous intake is unnecessary. Dietary cholesterol's impact on plasma cholesterol is less significant than saturated fat's, and absorption may be highly individualized, but it nonetheless, may have a significant impact on some individuals and impact

may only manifest when individual plasma lipid concentrations are low.[129–132] Saturated fat may potentiate dietary cholesterol absorption and endogenous synthesis.[133,134]

Phytosterols, another class of fats, are plant-based sterols found in all plant foods (especially wheat germ, nuts, seeds, whole grains, legumes, and unrefined plant oils), which are similar to cholesterol. Phytosterols reduce cholesterol absorption in the gut, thereby optimizing lipid profiles. Together with viscous fibers, soy proteins, and almonds, phytosterols have been found to be as effective as statins in lowering LDL-C.[15,60,135,136]

Overall, some dietary fat is necessary to meet the essential fatty acid requirements. Whole food sources of fat (e.g., nuts, seeds, avocados) should be prioritized over processed fats (e.g., oils). Oils provide excess energy (more than 2000 calories per cup) with minimal nutrition including zero fiber.

While nearly a century of macronutrient-centric education has created widespread familiarity with these terms, it may also add a layer of complexity and confusion in chasing mythical macronutrient ratios that seem yet unresolved. Organizing food into isoenergetic macronutrient categories may create a false equivalency of non isometabolic food (e.g., refined sugar versus legumes). This false equivalency may contribute to apparent contradiction in dietary studies and create unnecessary complexity in patient messaging; for example, "choose low glycemic, complex carbohydrates" instead of simple messaging, "eat carrots." "Eat towards the right side of the Food Triangle" is a simple food-centric instruction that naturally restricts specific deleterious nutrients (e.g., saturated/trans fatty acids, refined sugars, while increasing beneficial nutrients (e.g., dietary fiber, vitamins, minerals, phytonutrients).

9 Plant-based micronutrition

While much of the focus on food centers on the macronutrient content, or energy density, there are many benefits to a whole food, plant-based diet that fall outside of these energy categories. A proper diet should be varied as it is not likely that every micronutrient (e.g., vitamins, minerals, and phytonutrients) is ingested each day. One of the advantages of a fruit- and vegetable-rich diet is the large variety of micronutrient exposure. Beyond the basic vitamin and mineral dietary reference intakes, there are a host of other phytonutrients that may play a significant, but yet not fully understood, role in health. For example, a class of plant-derived compounds, poly-phenols, offers a wide range of antioxidant and other cellular regulatory properties.[137–140] These flavonoids, stilbenes, and curcuminoids have a positive impact on cardiovascular disease, cancer, and neurodegeneration.[141–144] These nutrients are often enzymatic cofactors and may have both additive and synergistic pleiotropic effects that reduce risk of chronic disease.[145–150]

Outside of the emerging science of exotic phytonutrients, fruits and vegetables provide an abundant source of vitamins and minerals. While the vast majority of micronutrients on an exclusively plant-based diet are plentiful, a few need particular attention (of note, there are many micronutrient dietary needs that may be an issue in an omnivorous diet that should be addressed in the elderly population.) Some micronutrient levels may be optimized by adding more vegetables and fruits to the diet and other may require supplementation. The key to success is centered on appropriate periodic testing and avoiding excessive supplementation as has been seen with vitamins A and E.[151,152] We will address notable micronutrients and some suggestions on testing.

10 Vitamin B12

Cobalamin, commonly referred to as vitamin B12, is the only nutrient not directly available from plants. B12 is synthesized by microorganisms, bacteria, fungi, and algae, but not by animals or plants. Animal-sourced B12 results from its natural concentration in flesh, organs and byproducts (e.g., eggs and dairy) after they ingest these microorganisms along with their food. Vitamin B12 deficiency poses an adverse threat of potentially irreversible neurological disorders, gastrointestinal problems, and megaloblastic anemia. B12 deficiency, however, is not unique to vegans who do not supplement. In fact, deficiency is prevalent in the elderly population, due to inadequate intake or absorption. The body can store vitamin B12 for approximately three to five years, or even up to ten years, but without repletion or an ability to absorb, deficiency ensues.[153–156] Often, symptoms are either subclinical or subtle and nonspecific. Due to this lag time and because serum tests for B12 levels (including serum cobalamin, serum methylmalonic acid, and Schilling test) can be skewed by other variables, irreversible damage may occur before a deficiency is caught.

In a plant-based diet, vitamin B12 can be found in fortified plant milks, cereals, and nutritional yeast. Since absorption varies greatly depending on the dose and the individual, it is recommended to supplement with greater than the Recommended Daily Allowance (RDA) to ensure adequate intake.[157] The daily RDA for adults is 2.4 μg and weekly is 16.8 μg, which can be accomplished by a 50 μg dose twice a day, 150 μg once a day, or 2500 μg once a week.[157,158] The standard treatment for B12 deficiency is parenterally administered cyanocobalamin.[159–162] No tolerable upper

limit for B12 has been established and high doses are considered safe, but periodic testing and dosage adjustment is recommended.[163] Since accurate diagnosis of B12 deficiency is challenging, symptoms are nonspecific, prevalence is common, and treatment is safe and effective, it is recommended that vegans and even all adults over the age of 60 years supplement to avoid deficiency.[164]

11 Vitamin D

Vitamin D, or calciferol, is also known as the "sunshine vitamin" since it is the only nutrient that is acquired from the sun. Although vitamin D is considered a fat-soluble vitamin, it is actually a prohormone produced in the skin upon exposure to ultraviolet B (UVB) sun radiation and then activated by the liver and kidneys.

Despite the fact that bodies evolved to absorb vitamin D via the sun, there appears to be a worldwide epidemic of deficiency. In the geriatric population, deficiency has been associated with an increased risk for cognitive impairment, secondary hyperparathyroidism and its resultant osteoporosis, falls, and fracture risks, certain cancers, type 2 diabetes, cardiovascular disease, and autoimmune disease.[165–171]

Aging significantly decreases the capacity of the skin to produce vitamin D, particularly with limited exposure to UVB rays.[10,168,170]

Furthermore, vitamin D is not widely available from the food supply. Sources of preformed vitamin D include fish liver oil, oily fish, liver, and in smaller doses, meat and egg yolk. Vitamin D from sunshine and animal sources is in the form of cholecalciferol, or vitamin D3. An additional form called ergocalciferol, or vitamin D2, is found in plant sources, mostly in UVB-irradiated mushrooms. However, there is a more recently discovered plant-derived version of D3 made by lichen. Dietary supplements may contain either D2 or D3, both of which can be effective at raising blood levels.

Some physicians test for serum levels of vitamin D with the 25-hydroxyvitamin D test. As vitamin D is fat-soluble and excess levels can result in toxicity, it is preferable to monitor vitamin D levels in order to avoid deficiency. The Institute of Medicine concluded that adequate serum 25-hydroxyvitamin D levels of at least 20 ng/mL (50 nmol/L) meet the needs of about 97.5% of the population and is considered adequate for bone and overall health in healthy individuals.[172]

If patients have suboptimal levels, emphasizing food sources (especially fortified plant milks) as well as sun therapy may prove effective as a first line of treatment. Supplementation may be reasonable if levels remain low.

12 Vitamin K

Vitamin K is necessary for blood coagulation, cardiovascular health, and bone strength. Although vitamin K1, phylloquinone, is abundantly available in leafy green vegetables, there is increasing evidence that vitamin K2, menaquinone, is also necessary. Produced by microorganisms as well as converted from K1 by intestinal bacteria in small amounts, supplementing with a direct source of K2 may be beneficial.[173–177]

13 Calcium

Calcium is the most abundant mineral in the human body, with 99 percent stored in the bones and teeth and the remaining one percent circulating in the blood and tissues. Calcium is a nutrient of concern for the general population with respect to bone mineral optimization over the lifespan. However, because bone metabolism is multi-factorial and complex, it is important to emphasize ample sources of calcium as well as vitamins K and B12, fluoride, magnesium, phosphorus, and potassium; to maintain serum vitamin D levels; and to ensure regular resistance exercise.

To maximize absorption, frequent consumption of calcium sources spread throughout meals is recommended; prioritize low oxalate leafy greens such as bok choy, broccoli, napa cabbage, collard greens, dandelion greens, kale, turnip greens, and watercress; be wary of excessive intakes of sodium, protein, caffeine, and phosphorus (as from sodas); and ensure normal serum vitamin D levels.[178]

14 Iron

Although iron is one of the most abundant metals, iron deficiency remains one of the most common and widespread nutritional deficiencies, with prevalence increasing with age.[179,180] Iron-deficiency anemia is no more common in vegetarians than in non-vegetarians and vegetarian diets typically include the same or higher amounts of iron than non-vegetarian diets.[181–183]

Plant-sourced iron is non-heme, which is susceptible to compounds that both inhibit (e.g., phytates and polyphenolics) and enhance (e.g., vitamin C and organic acids) its absorption. However, individuals adapt absorption of non-heme iron more effectively than heme iron and are able to adapt to low iron intakes over time.[10,184,185]

There is a wide array of iron-rich food choices in the plant kingdom. Leafy greens and legumes are excellent sources of iron and myriad other nutrients, so it is advantageous to include these foods often. Other good choices in-

clude soy products, dark chocolate, blackstrap molasses, tahini, pumpkin seeds, sunflower seeds, raisins, prunes, and cashews. In order to enhance absorption, consume iron-rich foods in combination with foods high in vitamin C- and organic acid-rich foods. This combination improves solubility, thereby facilitating absorption. Examples include a green smoothie with leafy greens (iron) and fruit (vitamin C), salad greens (iron) with tomatoes (vitamin C), or a bean-based chili (iron) with tomato sauce (vitamin C).

15 Iodine

Dietary plant sources of iodine, a trace mineral, are unreliable due to varying soil qualities. Available options include iodized salt and sea vegetables. One half teaspoon of iodized salt provides the daily recommended 150 μg dose.[186] Importantly, iodine levels in sea vegetables fluctuate dramatically, with some (especially dulse and nori) containing safe amounts and others (such as kelp) harboring toxic doses.[187] Hijiki, also spelled hiziki, should be avoided due to its excessive arsenic levels.[188] However, for those avoiding iodized salt (e.g., patients with hypertension or people opting for gourmet, non-iodized salts) and also not regularly consuming sea vegetables, iodine deficiency and the risk for thyroid issues are a concern. A pre-existing iodine deficiency, a selenium deficiency, or high intake of goitrogens (antinutrients found in cruciferous vegetables, soy products, flaxseeds, millet, peanuts, peaches, pears, pine nuts, spinach, sweet potatoes, and strawberries) can interfere with iodine absorption. There is no need to avoid goitrogenic foods as long as iodine intake is sufficient. If a patient does not enjoy sea vegetables or is minimizing intake of salt, an iodine supplement may be warranted.[189,190]

16 Selenium

Selenium is an essential trace mineral that plays a role in thyroid hormone regulation, reproduction, and DNA synthesis and also exerts powerful antioxidant, antiviral, and anti-inflammatory effects.[191] Brazil nuts are an especially rich source of selenium in the plant kingdom. Just one ounce (approximately 6 to 8 nuts) provides 777 percent of the RDA. When accessible, one Brazil nut a day is an ideal way of meeting selenium recommendations. In a randomized crossover trial involving 15 men and women, a single dose (20 g) of Brazil nuts (about 4 nuts) reduced LDL-C by about 22 mg/dL and increased HDL-C by nearly 20 mg/dL 30 days later.[192] Other plant sources include whole grains, legumes, vegetables, seeds, and other nuts.

17 Zinc

Zinc supports immune function and wound healing; synthesis of protein and DNA; and growth and development throughout pregnancy, childhood, and adolescence.[193] Zinc status in vegetarians is similar, or somewhat lower, than that of non-vegetarians because of the decreased bioavailability of zinc in plant foods due to their phytate content. However, there do not appear to be adverse health consequences of these lower levels, suggesting increased efficiency of absorption with adaptation to long-term vegetarian diets.[194] Zinc deficiency may be difficult to detect in blood tests but can show up clinically as delayed wound healing, growth retardation, hair loss, diminished immunity, suppressed appetite, hair loss, taste abnormalities, or skin or eye lesions. Advise patients to include legumes, cashews and other nuts, seeds, soy foods, and whole grains. Preparation methods such as soaking, sprouting, leavening, and fermenting will help improve absorption.

18 Note on supplements in general

Because the supplement industry is not regulated by the FDA, it is buyer beware in the supplement market.[195] Thus, aim to find reputed companies. A few organizations, such as Consumer Lab, NSF International, and U.S. Pharmacopeia, act as independent third parties and offer seals of approval after testing products for potency and contaminants. They do not, however, test for safety or efficacy.

19 Conclusions

A plant-based diet is beneficial throughout the lifespan, and may be particularly useful in the elderly population. Evidence from prospective cohort studies suggests that a diet rich in vegetables, fruits, whole grains, legumes, nuts, seeds, herbs, and spices is associated with a significantly lower risk of cardiovascular disease; the protective effects of these foods are likely mediated through multiple beneficial nutrients. A plant-based diet can meet energy and satiety needs and is ideal for the elderly population as it involves simple food preparation, easily digested balanced meals, and, if required, may be easily blended into a flavorful and nutritious liquid diet.

Making a significant change in diet and lifestyle can be difficult at any age, especially when the new diet may not at first appear equally familiar, convenient and enjoyable to the Western diet. A survey of human populations in both time and culture, however, reveals that normal has a wide range of what might be considered palatable. Wilbur O.

Atwater, a leading 19th century nutritionist, wrote: "*In our practice of eating, we are apt to be influenced too much by taste [and] the dictates of the palate; we are prone to let natural instinct be overruled by acquired appetite. We need to observe our diet and regulate appetite by reason. In doing this we may be greatly aided by the knowledge of what our food contains and how it serves its purpose in nutrition.*"[196] This is still true today, despite knowing more about food than any time in human history.

This brings us back to a critical person in the dietary transformation, the attendant physician. As was clear in the very successful campaign to adjust the social habits surrounding smoking, a highly addictive activity that most physicians practiced at that time, each of us providing nutritional advice must look at our own diet.

Ultimately the dietary change needed in society requires the leadership of all healthcare professionals. A whole food, plant-based diet pattern can be easily achieved and is at least one solution to the tremendous socioeconomic burden that nutritionally-induced, non-communicable chronic diseases places on all of humanity.

References

1 Murray CJ, Abraham J, Ali MK, *et al.* The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. *JAMA* 2013; 310: 591–606.

2 Rose G. Sick individuals and sick populations. *Int J Epidemiol* 2001; 30: 427–432.

3 Adams F. *The genuine works of Hippocrates*. Sydenham society, 1849.

4 Connor R, Cialdella-Kam L, Harris SR. A Survey of Medical Students' Use of Nutrition Resources and Perceived Competency in Providing Basic Nutrition Education. *J Biomed Educ* 2015; 2015: 1–7.

5 Mishra S, Xu J, Agarwal U, *et al.* A multicenter randomized controlled trial of a plant-based nutrition program to reduce body weight and cardiovascular risk in the corporate setting: the GEICO study. *Eur J Clin Nutr* 2013; 67: 718–724.

6 Kent L, Morton D, Rankin P, *et al.* The effect of a low-fat, plant-based lifestyle intervention (CHIP) on serum HDL levels and the implications for metabolic syndrome status–a cohort study. *Nutr Metab* (*Lond*) 2013; 10: 1.

7 Glanz K. Review of nutritional attitudes and counseling practices of primary care physicians. *Am J Clin Nutr* 1997; 65: 2016S–2019S.

8 Scott RB. Some medical aspects of tobacco-smoking. *Br Med J* 1952; 1: 671.

9 Garland LH. The smoking physician. *CA Cancer J Clin* 1959; 9: 60–61.

10 Melina V, Craig W, Levin S. Position of the Academy of Nutrition and Dietetics: Vegetarian Diets. *J Acad Nutr Diet* 2016; 116: 1970–1980.

11 Committee DGA. Scientific report of the 2015 dietary guidelines advisory committee. USDA and US Department of Health and Human Services: Washington, D.C., USA, 2015.

12 Orlich MJ, Singh PN, Sabaté J, *et al.* Vegetarian dietary patterns and mortality in Adventist Health Study 2. *JAMA Intern Med* 2013; 173: 1230–1238.

13 Crowe FL, Appleby PN, Travis RC, *et al.* Risk of hospitalization or death from ischemic heart disease among British vegetarians and nonvegetarians: results from the EPIC-Oxford cohort study. *Am J Clin Nutr* 2013; 97: 597–603.

14 Barnard ND, Cohen J, Jenkins DJ, *et al.* A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. *Am J Clin Nutr* 2009; 89: 1588S–1596S.

15 Jenkins DJ, Kendall CW, Marchie A, *et al.* Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants. *Am J Clin Nutr* 2005; 81: 380–387.

16 Ornish D. Statins and the soul of medicine. *Am J Cardiol* 2002; 89: 1286–1290.

17 Huang RY, Huang CC, Hu FB, *et al.* Vegetarian diets and weight reduction: A meta-analysis of randomized controlled trials. *J Gen Intern Med* 2016; 31: 109–116.

18 Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. *J Acad Nutr Diet* 2015; 115: 954–969.

19 Newby P, Tucker KL, Wolk A. Risk of overweight and obesity among semivegetarian, lactovegetarian, and vegan women. *Am J Clin Nutr* 2005; 81: 1267–1274.

20 Spencer E, Appleby P, Davey G, *et al.* Diet and body mass index in 38000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans. *Int J Obesity* 2003; 27: 728–734.

21 Rosell M, Appleby P, Spencer E, *et al.* Weight gain over 5 years in 21966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. *Int J Obesity* 2006; 30: 1389–1396.

22 Tonstad S, Butler T, Yan R, *et al.* Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care* 2009; 32: 791–796.

23 Eichelmann F, Schwingshackl L, Fedirko V, *et al.* Effect of plant-based diets on obesity-related inflammatory profiles: a systematic review and meta-analysis of intervention trials. *Obes Rev* 2016; 17: 1067–1079.

24 Barnard ND, Cohen J, Jenkins DJ, *et al.* A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. *Diabetes Care* 2006; 29: 1777–1783.

25 Yokoyama Y, Barnard ND, Levin SM, *et al.* Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. *Cardiovasc Diagn Ther* 2014; 4: 373–382.

26 Appleby PN, Davey GK, Key TJ. Hypertension and blood pressure among meat eaters, fish eaters, vegetarians and ve-

gans in EPIC–Oxford. *Public Health Nutr* 2002; 5: 645–654.
27 Pettersen BJ, Anousheh R, Fan J, *et al.* Vegetarian diets and blood pressure among white subjects: results from the Adventist Health Study-2 (AHS-2). *Public Health Nutr* 2012; 15: 1909–1916.
28 Berkow SE, Barnard ND. Blood pressure regulation and vegetarian diets. *Nutr Rev* 2005; 63: 1–8.
29 Wang F, Zheng J, Yang B, *et al.* Effects of vegetarian diets on blood lipids: a systematic review and meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2015; 4: e002408.
30 Ornish D, Scherwitz LW, Billings JH, *et al.* Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998; 280: 2001–2007.
31 Esselstyn Jr CB, Gendy G, Doyle J, *et al.* A way to reverse CAD? *J Fam Pract* 2014; 63: 356–364.
32 Fritsche S, Steinhart H. Occurrence of hormonally active compounds in food: a review. *Eur Food Res Technol* 1999; 209: 153–179.
33 Vannice G, Rasmussen H. Position of the academy of nutrition and dietetics: dietary fatty acids for healthy adults. *J Acad Nutr Diet* 2014; 114: 136–153.
34 Hopkins PN. Effects of dietary cholesterol on serum cholesterol: a meta-analysis and review. *Am J Clin Nutr* 1992; 55: 1060–1070.
35 Howell WH, McNamara DJ, Tosca MA, *et al.* Plasma lipid and lipoprotein responses to dietary fat and cholesterol: a meta-analysis. *Am J Clin Nutr* 1997; 65: 1747–1764.
36 Spence JD, Jenkins DJ, Davignon J. Dietary cholesterol and egg yolks: not for patients at risk of vascular disease. *Can J Cardiol* 2010; 26: e336–e339.
37 Allen NE, Appleby PN, Davey GK, *et al.* The associations of diet with serum insulin-like growth factor I and its main binding proteins in 292 women meat-eaters, vegetarians, and vegans. *Cancer Epidemiol Biomarkers Prev* 2002; 11: 1441–1448.
38 NIH. Dietary Supplement Fact Sheet: Iron, 2006. https://ods.od.nih.gov/factsheets/Iron-HealthProfessional/ (Accessed October 25, 2017).
39 Jomova K, Valko M. Advances in metal-induced oxidative stress and human disease. *Toxicology* 2011; 283: 65–87.
40 Bastide NM, Pierre FH, Corpet DE. Heme iron from meat and risk of colorectal cancer: a meta-analysis and a review of the mechanisms involved. *Cancer Prev Res* 2011; 4: 177–184.
41 Ahluwalia N, Genoux A, Ferrieres J, *et al.* Iron status is associated with carotid atherosclerotic plaques in middle-aged adults. *J Nutr* 2010; 140: 812–816.
42 Hunt JR. Bioavailability of iron, zinc, and other trace minerals from vegetarian diets. *Am J Clin Nutr* 2003; 78: 633S–639S.
43 Straif K, Baan R, Grosse Y, *et al.* Carcinogenicity of polycyclic aromatic hydrocarbons. *Lancet Oncol* 2005; 6: 931–932.
44 Layton DW, Bogen KT, Knize MG, *et al.* Cancer risk of heterocyclic amines in cooked foods: an analysis and implications for research. *Carcinogenesis* 1995; 16: 39–52.
45 Uribarri J, Woodruff S, Goodman S, *et al.* Advanced glycation end products in foods and a practical guide to their reduction in the diet. *J Am Diet Assoc* 2010; 110: 911–916.
46 Koeth RA, Wang Z, Levison BS, *et al.* Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat Med* 2013; 19: 576–585.
47 Hedlund M, Padler-Karavani V, Varki NM, *et al.* Evidence for a human-specific mechanism for diet and antibody-mediated inflammation in carcinoma progression. *Proc Natl Acad* 2008; 105: 18936–18941.
48 Taylor RE, Gregg CJ, Padler-Karavani V, *et al.* Novel mechanism for the generation of human xeno-autoantibodies against the nonhuman sialic acid N-glycolylneuraminic acid. *J Exp Med* 2010; 207: 1637–1646.
49 Cronise RJ, Sinclair DA, Bremer AA. Oxidative priority, meal frequency, and the energy economy of food and activity: implications for longevity, obesity, and cardiometabolic disease. *Metab Syndr Relat Disord* 2017; 15: 6–17.
50 Johnson RK, Appel LJ, Brands M, *et al.* Dietary sugars intake and cardiovascular health a scientific statement from the american heart association. *Circulation* 2009; 120: 1011–1020.
51 Cook NR, Cutler JA, Obarzanek E, *et al.* Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ* 2007; 334: 885.
52 Monteiro CA. Nutrition and health. The issue is not food, nor nutrients, so much as processing. *Public Health Nutr* 2009; 12: 729–731.
53 Clemens R, Kranz S, Mobley AR, *et al.* Filling America's fiber intake gap: summary of a roundtable to probe realistic solutions with a focus on grain-based foods. *J Nutr* 2012; 142: 1390S–1401S.
54 Anderson JW, Baird P, Davis RH, *et al.* Health benefits of dietary fiber. *Nutr Rev* 2009; 67: 188–205.
55 Liu RH. Health benefits of fruit and vegetables are from additive and synergistic combinations of phytochemicals. *Am J Clin Nutr* 2003; 78: 517S–520S.
56 Jacobs DR, Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. *Am J Clin Nutr* 2003; 78: 508S–513S.
57 Bellik Y, Boukraâ L, Alzahrani HA, *et al.* Molecular mechanism underlying anti-inflammatory and anti-allergic activities of phytochemicals: an update. *Molecules* 2012; 18: 322–353.
58 Schmitz H, Chevaux K. Defining the role of dietary phytochemicals in modulating human immune function. In *Nutrition and Immunology*; Humana Press: New York, NY, USA, 2000; 107–119.
59 Liu RH. Potential synergy of phytochemicals in cancer prevention: mechanism of action. *J Nutr* 2004; 134: 3479S–3485S.
60 Fraga CG. *Plant phenolics and human health: biochemistry,*

nutrition and pharmacology. John Wiley & Sons: Hoboken, USA, 2009; 1–487.
61 North BJ, Sinclair DA. The intersection between aging and cardiovascular disease. *Circul Res* 2012; 110: 1097–1108.
62 Longo VD, Antebi A, Bartke A, *et al.* Interventions to slow aging in humans: are we ready? *Aging Cell* 2015; 14: 497–510.
63 Hubbard BP, Sinclair DA. Small molecule SIRT1 activators for the treatment of aging and age-related diseases. *Trends Pharmacol Sci* 2014; 35: 146–154.
64 Mercken EM, Carboneau BA, Krzysik-Walker SM, *et al.* Of mice and men: the benefits of caloric restriction, exercise, and mimetics. *Ageing Res Rev* 2012; 11: 390–398.
65 Longo VD, Panda S. Fasting, circadian rhythms, and time-restricted feeding in healthy lifespan. *Cell Metab* 2016; 23: 1048–1059.
66 Choi IY, Lee C, Longo VD. Nutrition and fasting mimicking diets in the prevention and treatment of autoimmune diseases and immunosenescence. *Mol Cell Endocrinol*. Published Online First: Jan 28, 2017; DOI: 10.1016/j.mce.2017.01.042.
67 Wei M, Brandhorst S, Shelehchi M, *et al.* Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. *Sci Transl Med*. Published Online First: Feb 15, 2017. DOI: 10.1126/scitranslmed.aai8700.
68 Lee BC, Kaya A, Gladyshev VN. Methionine restriction and life-span control. *Ann N Y Acad Sci* 2016; 1363: 116–124.
69 Levine ME, Suarez JA, Brandhorst S, *et al.* Low protein intake is associated with a major reduction in IGF-1, cancer, and overall mortality in the 65 and younger but not older population. *Cell Metab* 2014; 19: 407–417.
70 McCarty MF, Barroso-Aranda J, Contreras F. The low-methionine content of vegan diets may make methionine restriction feasible as a life extension strategy. *Med Hypotheses* 2009; 72: 125–128.
71 McIsaac RS, Lewis KN, Gibney PA, *et al.* From yeast to human: exploring the comparative biology of methionine restriction in extending eukaryotic life span. *Ann N Y Acad Sci* 2016; 1363: 155–170.
72 Mattison JA, Colman RJ, Beasley TM, *et al.* Caloric restriction improves health and survival of rhesus monkeys. *Nat Commun* 2017; 8: 14063.
73 Morley JE, Argiles JM, Evans WJ, *et al.* Nutritional recommendations for the management of sarcopenia. *J Am Med Dir Assoc* 2010; 11: 391–396.
74 Brownie S. Why are elderly individuals at risk of nutritional deficiency? *Int J Nurs Pract* 2006; 12: 110–118.
75 Razak PA, Richard KJ, Thankachan RP, *et al.* Geriatric oral health: a review article. *J Int Oral Health* 2014; 6: 110.
76 Farmer B, Larson BT, Fulgoni VL, *et al.* A vegetarian dietary pattern as a nutrient-dense approach to weight management: an analysis of the national health and nutrition examination survey 1999–2004. *J Acad Nutr Diet* 2011; 111: 819–827.
77 Hever J. Plant-Based Diets: A Physician's Guide. *Perm J* 2016; 20: 93–101.
78 Hu FB. Plant-based foods and prevention of cardiovascular disease: an overview. *Am J Clin Nutr* 2003; 78: 544S–551S.
79 Barnard ND, Bush AI, Ceccarelli A, *et al.* Dietary and lifestyle guidelines for the prevention of Alzheimer's disease. *Neurobiol Aging* 2014; 35: S74–S78.
80 Fontana L, Partridge L. Promoting health and longevity through diet: from model organisms to humans. *Cell* 2015; 161: 106–118.
81 Solon-Biet SM, Mitchell SJ, Coogan SC, *et al.* Dietary protein to carbohydrate ratio and caloric restriction: comparing metabolic outcomes in mice. *Cell Rep* 2015; 11: 1529–1534.
82 Solon-Biet SM, McMahon AC, Ballard JWO, *et al.* The ratio of macronutrients, not caloric intake, dictates cardiometabolic health, aging, and longevity in ad libitum-fed mice. *Cell Metab* 2014; 19: 418–430.
83 Fontana L, Partridge L, Longo VD. Dietary restriction, growth factors and aging: from yeast to humans. *Science* (*New York, NY*) 2010; 328: 321.
84 Colman RJ, Anderson RM, Johnson SC, *et al.* Caloric restriction delays disease onset and mortality in rhesus monkeys. *Science* 2009; 325: 201–204.
85 Lee C, Longo V. Dietary restriction with and without caloric restriction for healthy aging. *F1000 Res* 2016; 5.
86 Omodei D, Fontana L. Calorie restriction and prevention of age–associated chronic disease. *FEBS Lett* 2011; 585: 1537–1542.
87 Willcox BJ, Willcox DC, Todoriki H, *et al.* Caloric restriction, the traditional Okinawan diet, and healthy aging. *Ann N Y Acad Sci* 2007; 1114: 434–455.
88 Willcox DC, Willcox BJ, Todoriki H, *et al.* The Okinawan diet: health implications of a low-calorie, nutrient-dense, antioxidant-rich dietary pattern low in glycemic load. *J Am Coll Nutr* 2009; 28 (suppl 4): 500S–516S.
89 Willcox DC, Scapagnini G, Willcox BJ. Healthy aging diets other than the Mediterranean: a focus on the Okinawan diet. *Mech Ageing Dev* 2014; 136: 148–162.
90 Willcox BJ, Willcox DC. Caloric restriction, caloric restriction mimetics, and healthy aging in Okinawa: controversies and clinical implications. *Curr Opin Clin Nutr Metab Care* 2014; 17: 51–58.
91 Todoriki H, Willcox DC, Willcox BJ. The effects of post-war dietary change on longevity and health in Okinawa. *The Okinawan Journal of American Studies* 2004; 2004: 52–61.
92 Sofi F, Abbate R, Gensini GF, *et al.* Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. *Am J Clin Nutr* 2010; 92: 1189–1196.
93 Willett WC, Sacks F, Trichopoulou A, *et al.* Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr* 1995; 61: 1402S–1406S.
94 Davis B, Vesanto M, Berry R. *Becoming Raw*. Book Publishing Company: Canada , 2010.
95 Cronise RJ, Sinclair DA, Bremer AA. The "metabolic winter" hypothesis: a cause of the current epidemics of obesity and cardiometabolic disease. *Metab Syndr Relat Disord* 2014; 12: 355–361.

96 United States Department of Agriculture. Dietary Reference Intakes: Macronutrients, 2005. https://www.nal.usda.gov/ sites/default/files/fnic_uploads//macronutrients.pdf (Accessed September 29, 2016).
97 Willett WC, Koplan JP, Nugent R, *et al.* Prevention of chronic disease by means of diet and lifestyle changes. In *Source Disease Control Priorities in Developing Countries*, 2nd Edition; Jamison DT, Breman JG, Measham AR, *et al*, Eds.; World Bank : Washington (DC), USA, 2006.
98 van der Zaag D, Woolfe JA. The potato in the human diet. *Potato Res* 1988; 31: 173–173.
99 Woolfe JA. *Sweet potato: an untapped food resource*. Cambridge University Press: Cambridge, UK; 1992.
100 Lee CJ, Howe JM, Carlson K, *et al.* Nitrogen retention of young men fed rice with or without supplementary chicken. *Am J Clin Nutr* 1971; 24: 318–323.
101 Beasley JM, Shikany JM, Thomson CA. The role of dietary protein intake in the prevention of sarcopenia of aging. *Nutr Clin Pract* 2013; 28: 684–690.
102 Gaffney-Stomberg E, Insogna KL, Rodriguez NR, *et al.* Increasing dietary protein requirements in elderly people for optimal muscle and bone health. *J Am Geriatr Soc* 2009; 57: 1073–1079.
103 Young VR, Pellett PL. Plant proteins in relation to human protein and amino acid nutrition. *Am J Clin Nutr* 1994; 59: 1203S–1212S.
104 Goyens PL, Spilker ME, Zock PL, *et al.* Conversion of α-linolenic acid in humans is influenced by the absolute amounts of α-linolenic acid and linoleic acid in the diet and not by their ratio. *Am J Clin Nutr* 2006; 84: 44–53.
105 Ryan L, Symington AM. Algal-oil supplements are a viable alternative to fish-oil supplements in terms of docosahexaenoic acid (22: 6n-3; DHA). *J Funct Foods* 2015; 19: 852–858.
106 Lane K, Derbyshire E, Li W, *et al.* Bioavailability and potential uses of vegetarian sources of omega-3 fatty acids: a review of the literature. *Crit Rev Food Sci Nutr* 2014; 54: 572–579.
107 Sarter B, Kelsey KS, Schwartz TA, *et al.* Blood docosahexaenoic acid and eicosapentaenoic acid in vegans: Associations with age and gender and effects of an algal-derived omega-3 fatty acid supplement. *Clin Nutr* 2015; 34: 212–218.
108 Innis SM. Dietary (n-3) fatty acids and brain development. *J Nutr* 2007; 137: 855–859.
109 Farzaneh-Far R, Lin J, Epel ES, *et al.* Association of marine omega-3 fatty acid levels with telomeric aging in patients with coronary heart disease. *JAMA* 2010; 303: 250–257.
110 Bourre JM. Dietary omega-3 fatty acids and psychiatry: mood, behaviour, stress, depression, dementia and aging. *Age Nutr* 2005; 16: 70.
111 Domingo JL. Nutrients and chemical pollutants in fish and shellfish. Balancing health benefits and risks of regular fish consumption. *Crit Rev Food Sci Nutr* 2016; 56: 979–988.
112 FDA. Environmental chemical contaminants and pesticides. *Fish and Fishery Products Hazards and Controls Guidance,* 3rd edition; US Food & Drug Administration Center for Food Safety & Applied Nutrition: Rockville, USA, 2001.
113 Fisher NS, Beaugelin-Seiller K, Hinton TG, *et al.* Evaluation of radiation doses and associated risk from the Fukushima nuclear accident to marine biota and human consumers of seafood. *Proc Natl Acad* 2013; 110: 10670–10675.
114 Wada T, Nemoto Y, Shimamura S, *et al.* Effects of the nuclear disaster on marine products in Fukushima. *J Environ Radioact* 2013; 124: 246–254.
115 Muskiet FA, Fokkema MR, Schaafsma A, *et al.* Is docosahexaenoic acid (DHA) essential? Lessons from DHA status regulation, our ancient diet, epidemiology and randomized controlled trials. *J Nutr* 2004; 134: 183–186.
116 Burdge GC, Wootton SA. Conversion of α-linolenic acid to eicosapentaenoic, docosapentaenoic and docosahexaenoic acids in young women. *Br J Nutr* 2002; 88: 411–420.
117 Rosell MS, Lloyd-Wright Z, Appleby PN, *et al.* Long-chain n–3 polyunsaturated fatty acids in plasma in British meat-eating, vegetarian, and vegan men. *Am J Clin Nutr* 2005; 82: 327–334.
118 Sanders TA. DHA status of vegetarians. *Prostaglandins Leukot Essent Fatty Acids* 2009; 81: 137–141.
119 Saunders AV, Davis BC, Garg ML. Omega-3 polyunsaturated fatty acids and vegetarian diets. *Med J Aust* 2012; 9: 22.
120 Simopoulos AP. The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. *Exp Biol Med* 2008; 233: 674–688.
121 Simopoulos A. Evolutionary aspects of diet, the omega-6/omega-3 ratio and genetic variation: nutritional implications for chronic diseases. *Biomed Pharmacother* 2006; 60: 502–507.
122 Hooper L, Summerbell CD, Thompson R, *et al.* Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database Syst Rev* 2012; 5: CD002137.
123 Zong G, Li Y, Wanders AJ, *et al.* Intake of individual saturated fatty acids and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies. *BMJ* 2016; 355: i5796.
124 Lichtenstein AH, Appel LJ, Brands M, *et al.* Diet and lifestyle recommendations revision 2006. A scientific statement from the American Heart Association nutrition committee. *Circulation* 2006; 114: 82–96.
125 Stamler J. Diet-heart: a problematic revisit. *Am J Clin Nutr* 2010; 91: 497–499.
126 Hruby A, Hu FB. Saturated fat and heart disease: The latest evidence. *Lipid Technol* 2016; 28: 7–12.
127 Anderson CA, Appel LJ. Dietary modification and CVD prevention: a matter of fat. *JAMA* 2006; 295: 693–695.
128 Jackson R, Ni Mhurchu C. Chewing the saturated fat: we still shouldn't. *NZ Med J* 2015; 128: 2010–2019.
129 Wilson MD, Rudel LL. Review of cholesterol absorption with emphasis on dietary and biliary cholesterol. *J Lipid Res* 1994; 35: 943–955.
130 Griffin JD, Lichtenstein AH. Dietary cholesterol and plasma lipoprotein profiles: randomized controlled trials. *Curr Nutr*

Rep 2013; 2: 274–282.
131 Weggemans RM, Zock PL, Katan MB. Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: a meta-analysis. *Am J Clin Nutr* 2001; 73: 885–891.
132 Mistry P, Miller N, Laker M, *et al.* Individual variation in the effects of dietary cholesterol on plasma lipoproteins and cellular cholesterol homeostasis in man: studies of low density lipoprotein receptor activity and 3-hydroxy-3-methylglutaryl coenzyme A reductase activity in blood mononuclear cells. *J Clin Invest* 1981; 67: 493.
133 Dietschy JM. Dietary fatty acids and the regulation of plasma low density lipoprotein cholesterol concentrations. *J Nutr* 1998; 128: 444S–448S.
134 David Spence J. Dietary cholesterol and egg yolk should be avoided by patients at risk of vascular disease. *J Transl Int Med* 2016; 4: 20–24.
135 Jenkins DJ, Kendall CW, Marchie A, *et al.* Effects of a dietary portfolio of cholesterol-lowering foods vs lovastatin on serum lipids and C-reactive protein. *JAMA* 2003; 290: 502–510.
136 John S, Sorokin AV, Thompson PD. Phytosterols and vascular disease. *Curr Opin Lipidol* 2007; 18: 35–40.
137 Williamson G, Manach C. Bioavailability and bioefficacy of polyphenols in humans. II. Review of 93 intervention studies. *Am J Clin Nutr* 2005; 81: 243S–255S.
138 Podsędek A. Natural antioxidants and antioxidant capacity of Brassica vegetables: A review. *LWT-Food Sci Technol* 2007; 40: 1–11.
139 Bravo L. Polyphenols: chemistry, dietary sources, metabolism, and nutritional significance. *Nutr Rev* 1998; 56: 317–333.
140 Ignat I, Volf I, Popa VI. A critical review of methods for characterisation of polyphenolic compounds in fruits and vegetables. *Food Chem* 2011; 126: 1821–1835.
141 Thangapazham RL, Sharma A, Maheshwari RK. Multiple molecular targets in cancer chemoprevention by curcumin. *AAPS J* 2006; 8: E443–E449.
142 Anderson JJ, Anthony MS, Cline JM, *et al.* Health potential of soy isoflavones for menopausal women. *Public Health Nutr* 1999; 2: 489–504.
143 Kris-Etherton P, Lefevre M, Beecher G, *et al.* Bioactive compounds in nutrition and health-research methodologies for establishing biological function: the antioxidant and anti-inflammatory effects of flavonoids on atherosclerosis. *Annu Rev Nutr* 2004; 24: 511–538.
144 Mandel S, Weinreb O, Amit T, *et al.* Cell signaling pathways in the neuroprotective actions of the green tea polyphenol (–)-epigallocatechin–3–gallate: implications for neurodegenerative diseases. *J Neurochem* 2004; 88: 1555–1569.
145 Davinelli S, Sapere N, Zella D, *et al.* Pleiotropic protective effects of phytochemicals in Alzheimer's disease. *Oxid Med Cell Longev* 2012; 2012: 386527.
146 Araújo JR, Gonçalves P, Martel F. Chemopreventive effect of dietary polyphenols in colorectal cancer cell lines. *Nutr Res* 2011; 31: 77–87.
147 Leifert WR, Abeywardena MY. Grape seed and red wine polyphenol extracts inhibit cellular cholesterol uptake, cell proliferation, and 5-lipoxygenase activity. *Nutr Res* 2008; 28: 842–850.
148 Kishimoto Y, Tani M, Kondo K. Pleiotropic preventive effects of dietary polyphenols in cardiovascular diseases. *Eur J Clin Nutr* 2013; 67: 532–535.
149 Kim HS, Quon MJ, Kim JA. New insights into the mechanisms of polyphenols beyond antioxidant properties; lessons from the green tea polyphenol, epigallocatechin 3-gallate. *Redox Biol* 2014; 2: 187–195.
150 Weseler AR, Bast A. Pleiotropic-acting nutrients require integrative investigational approaches: the example of flavonoids. *J Agric Food Chem* 2012; 60: 8941–8946.
151 Duffield-Lillico AJ, Begg CB. Reflections on the landmark studies of β-carotene supplementation. Oxford University Press: Oxford , USA; 2004.
152 Miller ER, Pastor-Barriuso R, Dalal D, *et al.* Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. *Ann Intern Med* 2005; 142: 37–46.
153 Wong C. Vitamin B12 deficiency in the elderly: is it worth screening. *Hong Kong Med J* 2015; 21: 155–164.
154 Liu KW, Dai LK, Jean W. Metformin-related vitamin B12 deficiency. *Age Ageing* 2006; 35: 200–201.
155 Johnson LE. Vitamin B12, 2016. http://www.merckmanuals.com/professional/nutritional-disorders/vitamin-deficiency,-dependency,-and-toxicity/vitamin-b-12 (Accessed September 29, 2016).
156 Dali-Youcef N, Andrès E. An update on cobalamin deficiency in adults. *QJM* 2009; 102: 17–28.
157 Carmel R. How I treat cobalamin (vitamin B12) deficiency. *Blood* 2008; 112: 2214–2221.
158 Allen LH. How common is vitamin B-12 deficiency? *Am J Clin Nutr* 2009; 89: 693S–696S.
159 Ulrich CM. Folate and cancer prevention: a closer look at a complex picture. *Am J Clin Nutr* 2007; 86: 271–273.
160 Wien TN, Pike E, Wisløff T, *et al.* Cancer risk with folic acid supplements: a systematic review and meta-analysis. *BMJ Open* 2012; 2: e000653.
161 Fife J, Raniga S, Hider P, *et al.* Folic acid supplementation and colorectal cancer risk: a meta analysis. *Colorectal Dis* 2011; 13: 132–137.
162 Figueiredo JC, Grau MV, Haile RW, *et al.* Folic acid and risk of prostate cancer: results from a randomized clinical trial. *J Natl Cancer Inst* 2009; 101: 432–435.
163 IOM. *Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B6, folate, vitamin B12, pantothenic acid, biotin, and choline*. National Academies Press: Washington, USA; 1998.
164 Wolters M, Ströhle A, Hahn A. Cobalamin: a critical vitamin in the elderly. *Prev Med* 2004; 39: 1256–1266.
165 Llewellyn DJ, Lang IA, Langa KM, *et al.* Vitamin D and cognitive impairment in the elderly US population. *J Gerontol A Biol Sci Med Sci* 2010; 66: 59–65.

166 Holick MF. The vitamin D epidemic and its health consequences. *J Nutr* 2005; 135: 2739S–2748S.
167 Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocr Rev* 2001; 22: 477–501.
168 Mosekilde L. Vitamin D and the elderly. *Clin Endocrinol* (*Oxf*) 2005; 62: 265–281.
169 Holick MF. Sunlight and vitamin D for bone health and prevention of autoimmune diseases, cancers, and cardiovascular disease. *Am J Clin Nutr* 2004; 80: S1678–S1688.
170 Wacker M, Holick MF. Sunlight and vitamin D: a global perspective for health. *Dermatoendocrinol* 2013; 5: 51–108.
171 Holick MF. Evolution and function of vitamin D. *Recent Results Cancer Res* 2003; 164: 3-28.
172 Ross AC, Manson JE, Abrams SA, *et al.* The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab* 2011; 96: 53–58.
173 Beulens JW, Booth SL, van den Heuvel EG, *et al.* The role of menaquinones (vitamin K 2) in human health. *Br J Nutr* 2013; 110: 1357–1368.
174 Knapen M, Drummen N, Smit E, *et al.* Three-year low-dose menaquinone-7 supplementation helps decrease bone loss in healthy postmenopausal women. *Osteoporos Int* 2013; 24: 2499–2507.
175 Geleijnse JM, Vermeer C, Grobbee DE, *et al.* Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. *J Nutr* 2004; 134: 3100–3105.
176 Beulens JW, Bots ML, Atsma F, *et al.* High dietary menaquinone intake is associated with reduced coronary calcification. *Atherosclerosis* 2009; 203: 489–493.
177 Beulens JW, Grobbee DE, Sluijs I, *et al.* Dietary phylloquinone and menaquinones intakes and risk of type 2 diabetes. *Diabetes Care* 2010; 33: 1699–1705.
178 Mangels AR. Bone nutrients for vegetarians. *Am J Clin Nutr* 2014; 100 (Suppl1): S469–S475.
179 Coban E, Timuragaoglu A, Meriç M. Iron deficiency anemia in the elderly: prevalence and endoscopic evaluation of the gastrointestinal tract in outpatients. *Acta Haematol* 2003; 110: 25–28.
180 Guralnik JM, Eisenstaedt RS, Ferrucci L, *et al.* Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood* 2004; 104: 2263–2268.
181 Mangels R, Messina V, Messina M. The dietitian's guide to vegetarian diets, 3rd Edition; Jones & Bartlett Publishers: Sudbury, USA, 2011; 359.
182 Craig WJ. Nutrition Concerns and Health Effects of Vegetarian Diets. *Nutr Clin Pract* 2010; 25: 613–620.
183 Rizzo NS, Jaceldo-Siegl K, Sabate J, *et al.* Nutrient profiles of vegetarian and nonvegetarian dietary patterns. *J Acad Nutr Diet* 2013; 113: 1610–1619.
184 Hunt JR, Roughead ZK. Adaptation of iron absorption in men consuming diets with high or low iron bioavailability. *Am J Clin Nutr* 2000; 71: 94–102.
185 Hunt JR, Roughead ZK. Nonheme-iron absorption, fecal ferritin excretion, and blood indexes of iron status in women consuming controlled lactoovovegetarian diets for 8 wk. *Am J Clin Nutr* 1999; 69: 944–952.
186 Trumbo P, Yates AA, Schlicker S, *et al.* Dietary reference intakes: vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. *J Am Diet Assoc* 2001; 101: 294–301.
187 Lee K, Bradley R, Dwyer J, *et al.* Too much versus too little: the implications of current iodine intake in the United States. *Nutr Rev* 1999; 57: 177–181.
188 Rose M, Lewis J, Langford N, *et al.* Arsenic in seaweed—forms, concentration and dietary exposure. *Food Chem Toxicol* 2007; 45: 1263–1267.
189 Davis B, Melina V. *Becoming Vegan*; Book Publishing Company: Summertown, USA, 2014.
190 Leung AM, LaMar A, He X, *et al.* Iodine status and thyroid function of Boston-area vegetarians and vegans. *J Clin Endocrinol Metab* 2011; 96: E1303–E1307.
191 Wrobel JK, Power R, Toborek M. Biological activity of selenium: Revisited. *IUBMB Life* 2016; 68: 97–105.
192 Colpo E, Vilanova CDdA, Brenner Reetz LG, *et al.* A single consumption of high amounts of the Brazil nuts improves lipid profile of healthy volunteers. *J Nutr Metab* 2013; 2013: 653185.
193 Das M, Das R. Need of education and awareness towards zinc supplementation: a review. *Int J Nutr Metab* 2012; 4: 45–50.
194 Foster M, Samman S. Chapter Three-Vegetarian Diets Across the Lifecycle: Impact on Zinc Intake and Status. *Adv Food Nutr Res* 2015; 74: 93–131.
195 Denham BE. Dietary supplements—regulatory issues and implications for public health. *JAMA* 2011; 306: 428–429.
196 Atwater WO. Food and Diet. Government Printing Office: Washington D.C., USA 1895; 386.

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