

RHYTHMOS



April 2016 • Volume 11 • No 2 (42)

ISSN: 1792-7919

e-ISSN: 1792-7927

URL: www.rhythmios.gr / <http://rhythmios.info.tm> / <http://www.evangelismos.dom.gr>

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EDITORIAL

You Are What You Eat, Hence Curtail Saturated and Trans Fats, Free Sugars and Salt

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Rhythmios 2016;11(2):28-38

Abstract

The new Dietary Guidelines for Americans 2015-2020 focus on healthy eating patterns and exercise. They recommend 3 different healthy eating patterns: the Healthy US Style, the Healthy Mediterranean Style, and the Healthy Vegetarian Style eating pattern, accommodating a variety of cultural and individual preferences, but sharing many common food based features. A healthy eating pattern includes a variety of vegetables, fruits, grains, low-fat dairy products, protein foods, and oils. Specific recommendations have been made for particular dietary components to reduce: saturated fat (< 10% of calories); sodium (< 2.3 g/day); and added sugars (< 10% of calories). Interestingly, these guidelines do not make a recommendation for a quantitative limit for dietary cholesterol indicating the lack of adequate evidence for such recommendation. However, they state that there is evidence showing that eating patterns that include lower intake of dietary cholesterol (~100 - 300 mg/d) are associated with reduced risk of cardiovascular disease, and risk of obesity. Finally the new

guidelines emphasize the importance of physical activity and exercise to promote health.

Key Words: diet; healthy eating pattern; saturated fat; unsaturated fat; trans fats; added sugars; salt, alcohol; caffeine; exercise; physical activity

Abbreviations: ACC = American College of Cardiology, ACS = American Cancer Society, AHA = American Heart Association, CVD = cardiovascular disease, FDA = Food and Drug Administration. HDL = high density lipoprotein, LDL = low density lipoprotein, NAFL = nonalcoholic fatty liver, NAFLD = nonalcoholic fatty liver disease, NASH = nonalcoholic steatohepatitis, WHO = World Health Organization

INTRODUCTION

The new Dietary Guidelines for Americans 2015-2020 focus on healthy eating patterns and exercise.¹ They recommend a healthy dietary pattern high in vegetables, fruit, whole grains, seafood, legumes, and nuts; moderate in low- and non-fat dairy products; lower in red and processed meat; and low in sugar-sweetened foods and beverages and refined grains. The Guidelines recommend 3 different healthy eating patterns: the Healthy US Style, the Healthy Mediterranean Style, and the Healthy Vegetarian Style eating pattern, accommodating a variety of cultural and individual preferences, but sharing many common food based features. Specific recommendations have been made for particular dietary components: < 10%

of calories from saturated fat; < 2.3 g of sodium/day; and < 10% of calories from added sugars. Interestingly, these guidelines do not make a recommendation for a quantitative limit for dietary cholesterol indicating the lack of adequate evidence for such recommendation. However, they state that there is evidence showing that eating patterns that include lower intake of dietary cholesterol are associated with reduced risk of cardiovascular disease (CVD), and that these eating patterns are associated with reduced risk of obesity. Nevertheless, the food-based eating patterns that are recommended in the dietary guidelines contain ~100 - 300 mg of cholesterol per day. Finally the new guidelines emphasize the importance of physical activity and exercise to promote health.

The guidelines for the first time recommend limiting consumption of *added sugars* to <10% of calories per day. Previous guidelines only recommended cutting back on calories from such sugars.² However, they do not limit sugar consumed from natural products (such as fruits and dairy) because they contain other nutrients needed for healthy diets, but only added sugars (those put in foods during preparation or processing or at the dining table). Similar recommendation has been made by the World Health Organization (WHO);³ however, the American Heart Association (AHA) has been stricter in recommending to limit added sugars to <100 calories per day for women and 150 calories per day for men, or about 5% of daily caloric consumption, considering soft drinks and other sugar-sweetened beverages as the primary source of added sugars, all contributing to obesity and several metabolic abnormalities and other health ailments, as well as deficiency of essential nutrients.⁴

Key Recommendations for Healthy Eating Patterns¹ (<http://health.gov/dietaryguidelines/2015/guidelines/>) (Table 1)

- Consume a *healthy eating pattern* that regards all foods and beverages within an appropriate calorie level. A healthy eating pattern includes: a variety of vegetables from all subgroups (dark green, red and orange), legumes (beans and peas), starchy, and other; fruits, especially whole fruits; grains, at least half of which are whole grains; fat-free or low-fat dairy products, including milk, yogurt, cheese, and/or fortified soy beverages; a variety of protein foods, including seafood, lean meats and poultry, eggs, legumes, nuts, seeds, and soy products; and finally, oils

- A *healthy eating pattern* limits: Saturated fats and trans fats, added sugars, and sodium

- Quantitative Key Recommendations: Consume <10% of calories per day from added sugars; Consume <10% of calories per day from saturated fats; Consume <2.3 g per day of sodium; If alcohol is consumed, it should be consumed in moderation—up to 1 drink per day for women and up to 2 drinks per day for men.

- Additionally, individuals of all ages should ***meet the Physical Activity Guidelines*** (<http://health.gov/paguidelines/pdf/paguide.pdf>) to help promote health and reduce the risk of chronic disease, aiming to achieve and maintain a healthy body weight.⁵ The relationship between diet and physical activity contributes to calorie balance and managing body weight.

These guidelines are in line with the latest 2013 AHA/ACC Guideline on lifestyle management to reduce cardiovascular risk, published in July 2014.⁶ They emphasize healthy eating patterns combined in synergism with physical activity and exercise (Table 2). The WHO recommendations both for primary and secondary prevention of CVD are also in keeping with the healthy diet and physical activity life style pattern (http://www.who.int/cardiovascular_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf) (Table 3). Finally, the American Cancer Society (ACS) publishes Nutrition and Physical Activity Guidelines as recommendations for individual choices to reduce cancer risk; the latest 2012 ACS guidelines are consistent with the guidelines from the American Heart Association (AHA) and the American Diabetes Association for the prevention of coronary heart disease and diabetes, as well as for general health promotion.⁷

Table 1. Dietary Guidelines 2015-2020: Key Recommendations¹

1. *Follow a healthy eating pattern across the lifespan:* to help achieve and maintain a healthy body weight, support nutrient adequacy, and reduce the risk of chronic disease.
2. *Focus on variety, nutrient density, & amount:* to meet nutrient needs within calorie limits, choose a variety of nutrient-dense foods across & within all food groups in recommended amounts
3. *Limit calories from added sugars and saturated fats and reduce sodium intake.*
4. *Shift to healthier food and beverage choices.* Choose nutrient-dense foods and beverages across and within all food groups in place of less healthy choices.
5. *Support healthy eating patterns for all:* from home to school to work to communities.
6. *Quantitative Key Recommendations:*
 - Consume <10% of calories per day from added sugars
 - Consume <10% of calories per day from saturated fats
 - Consume <2,300 mg per day of sodium
 - If alcohol is consumed, it should be in moderation—up to 1 drink per day for women and up to 2 drinks per day for men
7. *Meet the Physical Activity Guidelines* to help promote health and reduce the risk of chronic disease by achieving and maintaining a *healthy body weight*

Meats and Poultry

Red meat includes beef, pork, lamb, veal, goat, and non-bird game (e.g., venison, bison, and elk). Poultry, or white meat, includes chicken, turkey, duck, geese, guineas,

and game birds (e.g., quail and pheasant). Meats and poultry vary in fat content and include both fresh and processed forms. Lean meats and poultry contain <10 g of fat, ≤4.5 g of saturated fats, and <95 mg of cholesterol per 100 g and per labeled serving size (e.g., 95% lean ground beef, pork tenderloin, and skinless chicken or turkey breast). Processed meats and processed poultry (e.g., sausages, luncheon meats, bacon, and beef jerky) are products preserved by smoking, curing, salting, and/or the addition of chemical preservatives.

Strong evidence from mostly prospective cohort studies but also randomized controlled trials has shown that lower intake of meats as well as processed meats and processed poultry are associated with reduced risk of CVD;^{1, 8-11} some studies have focused on the preservatives used in processed meats as the notable difference.¹⁰ Moderate evidence indicates that these eating patterns are associated with reduced risk of obesity, type 2 diabetes, and some types of cancer in adults.^{9, 12-14} Some evidence has identified lean meats and lean poultry in healthy eating patterns, contributing important nutrients within limits for sodium, calories from saturated fats and added sugars, and total calories when consumed in recommended amounts in healthy eating pattern. For those who eat animal products, the recommendation for the protein foods subgroup of meats, poultry, and eggs can be met by consuming a variety of *lean meats*, *lean poultry*, and *eggs*. Choices within these eating patterns may include processed meats and processed poultry, as long as the resulting eating pattern is within limits for sodium, calories from saturated fats and added sugars, and total calories.

Oils

Oils are fats that contain a high percentage of monounsaturated and polyunsaturated fats and are liquid at room temperature.¹ Although they are not a food group, oils are emphasized as part of healthy eating patterns because they are the major source of *essential fatty acids* and *vitamin E*. Commonly consumed oils extracted from plants include canola, corn, olive, peanut, safflower, soybean, and sunflower oils. Oils also are naturally present in nuts, seeds, seafood, olives, and avocados. The fat in some tropical plants, such as coconut oil, palm kernel oil, and palm oil, are not included in the oils category because they do not resemble other oils in their composition; they contain a higher percentage of saturated fats than other oils. Oils are part of healthy eating patterns, but because they are a concentrated source of calories, the amount consumed should be within the recommended restrictions for total fats without exceeding calorie limits. Oils should replace solid fats rather than being added to the diet.

Specific mention has been made in the literature regarding *olive oil* consisting of monounsaturated fats;

epidemiological studies suggest that adherence to Mediterranean diet, which is rich in virgin olive oil, decreases CVD risk;^{15, 16} additionally, in countries where the populations followed a typical Mediterranean diet, such as Spain, Greece and Italy, where virgin olive oil is the principal source of fat, cancer incidence rates were lower than in northern European countries.¹⁵

Table 2. 2013 AHA/ACC Lifestyle Management Guideline: Key Recommendations⁶

1) Consume and adapt to relevant calorie requirements*/preferences/medical conditions (e.g. diabetes) a dietary pattern that includes vegetables, fruits (especially whole fruits), and whole grains; low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils, and nuts

- limit intake of sweets, sugar-sweetened beverages, and red meats
- reduce percent of calories (to 5-6%) from saturated fat.
- reduce percent of calories from trans fat

2) Lower sodium intake

- Consume ≤2.4 g of sodium/d
- Further reduction of sodium intake to 1.5 g/d can result in even greater reduction in BP
- Even without achieving these goals, reducing sodium intake by at least 1 g/d lowers BP

3) Engage in aerobic physical activity to reduce LDL/non-HDL cholesterol and/or lower BP: 3–4 sessions per week (~40 min per session) involving moderate- to vigorous-intensity physical activity

ACC = American College of Cardiology; AHA = American Heart Association; BP = blood pressure; LDL = low density lipoprotein

* N.B.: carbohydrates & protein contain 4 calories/g; fats contain 9 calories/g, and; alcohol has 7 calories/g

Saturated Fats, Trans Fats, and Cholesterol

Saturated Fats

Saturated fats are quite heterogeneous in nature and based on their structure, can be sub-classified into short chain (≤6 carbon atoms), medium chain (8–10 carbons), and long chain fats (≥12 carbon chains), whereas mono- and polyunsaturated fats are all long chain fats. Fats with a higher amount of polyunsaturated and monounsaturated fatty acids are usually liquid at room temperature and are referred to as “oils.” Fats with a higher amount of saturated fatty acids are usually solid at room temperature and are referred to as “solid fats.” A plethora of studies have shown the deleterious effects of saturated fats in contrast to the beneficial actions of unsaturated fats,¹⁷⁻¹⁹ but most of them comparing the effects of saturated to unsaturated fats have focused on fats that contained a large proportion of their fatty acids as long chain fatty acids.

Intake of saturated fats should be limited to <10% of calories per day by replacing them with unsaturated fats.

Table 3. WHO Recommendations for Primary and Secondary Prevention of CVD *

Primary Prevention	Secondary Prevention **
Smoking Cessation	Smoking Cessation
<ul style="list-style-type: none"> • All nonsmokers should be encouraged not to start smoking • All smokers should be strongly encouraged to quit smoking and supported in their efforts to do so • Those who use other forms of tobacco should be advised to stop 	<ul style="list-style-type: none"> • All individuals with established CHD/CeVD should be strongly encouraged to stop smoking & supported in their efforts to do so • Cessation of other forms of tobacco use is recommended
<ul style="list-style-type: none"> • Nicotine replacement therapy and/or nortriptyline or amfebutamone (bupropion) should be offered to motivated smokers who fail to quit with counselling 	<ul style="list-style-type: none"> • Nicotine replacement therapy should be offered to individuals who continue to smoke ≥ 10 cigarettes/day, who are likely to be markedly nicotine dependent. Use of antidepressants for smoking cessation is not recommended for patients with CHD / CeVD • Non-smoking people with CHD / CeVD should be advised to avoid exposure to second-hand smoke
Dietary Changes	Dietary Changes
<p>All individuals should be strongly encouraged to reduce total <i>fat</i> (~30% of calories) and saturated fat (<10% of calories) intake</p> <ul style="list-style-type: none"> • trans fatty acids intake should be reduced as much as possible or eliminated • most dietary fat should be polyunsaturated (up to 10% of calories) or monounsaturated (10–15% of calories) 	<p>All individuals with CHD/CeVD should follow a pattern of diet likely to reduce the risk of recurrent CVD</p> <ul style="list-style-type: none"> • Reduce total fat to <30% of calories; • saturated fat to <10% of calories; • trans fats should be reduced as much as possible or eliminated; • most dietary fat should be polyunsaturated (up to 10% of calories) or monounsaturated (10–15% of calories)
<p>All individuals should be encouraged to eat at least 400 g a day of a range of <i>fruits and vegetables</i> as well as whole <i>grains and pulses</i></p>	<p>All individuals should be encouraged to eat, at least 400 g a day, of a range <i>fruits and vegetables</i>, as well as whole <i>grains and pulses</i></p>
<p>All individuals should be strongly encouraged to reduce daily <i>salt</i> intake by at least one third and, if possible, to <5 g or <90 mmol per day</p>	<p>All individuals should be strongly encouraged to reduce daily <i>salt</i> intake by at least one-third and, if possible, to <5 g or <90 mmol per day</p>
Physical Activity	Physical Activity
<p>All individuals should be strongly encouraged to take at least 30 minutes of moderate physical activity (e.g. brisk walking) a day, through leisure time, daily tasks and work-related physical activity</p>	<p>Regular light to moderate intensity physical exercise is recommended for all subjects recovering from major CHD events (including coronary revascularization)</p> <ul style="list-style-type: none"> • Supervised programs of exercise should, where feasible, be offered to all subjects recovering from major CHD / CeVD events
Weight Control	Weight Control
<p>All individuals who are overweight or obese should be encouraged to lose weight through a combination of a reduced-energy diet (dietary advice) and increased physical activity</p>	<p>In patients with CVD who are overweight or obese, weight loss should be advised through the combination of a reduced energy diet and increased physical activity</p>
Alcohol Intake †	Alcohol Intake †
<p>Individuals who take >3 units of alcohol per day should be advised to reduce alcohol consumption</p>	<p>Individuals who take > 3 units of alcohol per day should be advised to reduce alcohol consumption</p>

* http://www.who.int/cardiovascular_diseases/guidelines/PocketGL.ENGLISH.AFR-D-E.rev1.pdf

CHD = coronary heart disease; CeVD = cerebrovascular disease;
WHO = World Health Organization

** Intensive life style advice should be given simultaneously with drug treatment

† One unit (drink) = half pint (~237 ml) of beer/lager (5 % alcohol), 100 ml of wine (10 % alcohol), spirits 25 ml (40% alcohol)

The human body uses some saturated fats for physiological and structural functions, but it makes more than enough to meet those needs.¹ Individuals of ≥ 2 years of age therefore have no dietary requirement for saturated fats.

Strong and consistent evidence shows that replacing saturated fats with unsaturated fats, poly- or mono-unsaturated fats, is associated with reduced blood levels of total cholesterol and of low-density lipoprotein (LDL)-cholesterol and a reduced risk of CVD morbidity and mortality.^{1, 18, 20, 21} On the other hand, there is evidence that replacing saturated fats with carbohydrates reduces blood levels of total and LDL-cholesterol, but increases blood levels of triglycerides and reduces high-density lipoprotein (HDL)-cholesterol. Replacing total fat or saturated fats with carbohydrates is not associated with reduced risk of CVD.^{18, 22} Hence, saturated fats in the diet should be replaced with polyunsaturated and monounsaturated fats, and not with carbohydrates.

Finally, some studies suggest discrimination between long chain saturated fats, which have been shown to result in higher total cholesterol and LDL-cholesterol concentrations compared to unsaturated fats, and medium chain saturated fats. There is some evidence that medium chain triglyceride consumption may confer some benefits^{23, 24} or may lead to comparable effects on CVD risk factors as an equal amount of olive oil, an oil consisting of mono-unsaturated fats, which is considered to have beneficial health effects.²⁵

Trans Fats

Individuals should limit intake of trans fats to as low as possible by limiting foods that contain synthetic sources of trans fats, such as partially hydrogenated oils in margarine, and by limiting other solid fats. A number of studies have observed an association between increased intake of trans fats and increased risk of CVD.^{21, 26, 27} This increased risk is due, in part, to its LDL cholesterol-raising effect.

Trans fats occur naturally in some foods and also are produced in a process called hydrogenation.²⁸ Hydrogenation is used by food manufacturers to make products containing unsaturated fatty acids solid at room temperature (i.e., more saturated) and therefore more resistant to becoming spoiled or rancid. Partial hydrogenation means that some, but not all, unsaturated fatty acids are converted to saturated fatty acids; some of the unsaturated fatty acids are changed from a cis to trans configuration. Trans fatty acids produced this way are referred to as “artificial” or “industrially produced” trans fatty acids. Artificial trans fatty acids are found in the

partially hydrogenated oils used in some margarines, snack foods, and prepared desserts as a replacement for saturated fatty acids. They constitute *the worst type of dietary fats*. Although food manufacturers and restaurants have reduced the amounts of artificial trans fats in many foods in recent years, these fats can still be found in some processed foods, such as some desserts, microwave popcorn, frozen pizza, margarines, and coffee creamers.

Foods rich in trans fats increase serum LDL cholesterol and reduce HDL cholesterol.²⁸ Trans fats are pro-inflammatory, and are linked to heart disease, stroke, diabetes, and other chronic conditions. They contribute to insulin resistance, increasing the risk of type 2 diabetes. They can be harmful in even small amounts; for every 2% of calories from trans fat consumed daily, the risk of heart disease may rise by 23%.²⁶

Margarines and margarine-like vegetable oil spreads are composed of one or more oils or solid fats designed to replace butter with its high content in saturated fats. These products may be sold in sticks, tubs, bottles, or sprays, and generally contain less saturated fats than butter. However, they vary in their total and type of fat and calorie content. It is important to read the nutrition facts label to identify the calorie and saturated and trans fats content of the spread and choose foods with no trans fats and lower amounts of saturated fats.¹ A recent report associating higher consumption of margarine with diabetes after BMI adjustment is worrisome.²⁹

Naturally occurring trans fats, known as “natural” or “ruminant” trans fats, are produced by ruminant animals. Natural trans fats are present in small quantities in dairy products and meats, and consuming fat-free or low-fat dairy products and lean meats and poultry will reduce the intake of natural trans fats from these foods. Because natural trans fats are present in dairy products and meats in only small quantities and these foods can be important sources of nutrients, these foods do not need to be eliminated from the diet.

Dietary Cholesterol

The body uses cholesterol for physiological and structural functions but makes more than enough for these purposes. Therefore, people do not need to obtain cholesterol through foods. The recommendation from the 2010 Dietary Guidelines to limit consumption of dietary cholesterol to 300 mg/d is not included in the 2015 version,¹ but this change does not suggest that dietary cholesterol is no longer important to consider when adopting healthy eating patterns.²⁰ Individuals should eat as little dietary cholesterol as possible while consuming a healthy eating pattern. In general, foods that are higher in dietary cholesterol, such as fatty meats (e.g. sausages) and

high-fat dairy products (e.g. butter), are also higher in saturated fats.

Strong evidence from mostly prospective cohort studies but also randomized controlled trials has shown that eating patterns that include lower intake of dietary cholesterol are associated with reduced risk of CVD, and moderate evidence indicates that these eating patterns are associated with reduced risk of obesity. Dietary cholesterol is found only in animal foods such as egg yolk, dairy products, shellfish, meats, and poultry. A few foods, notably egg yolks and some shellfish, are higher in dietary cholesterol but not saturated fats. Eggs and shellfish can be consumed along with a variety of other choices within and across the subgroup recommendations of the protein foods group. Healthy eating patterns dictate that dietary cholesterol should be limited to a range of 100 to 300 mg/d.²⁰

With regard to *eggs*, those who still believe that dietary cholesterol is harmful, maintain their position that egg consumption should be limited.³⁰ Contrariwise, those who have long resisted this notion (i.e. the egg industry), assert that the new guidelines have finally removed dietary cholesterol and egg restrictions, claiming that eggs have little effect on CVD risk.³¹ The new guidelines include eggs in the healthy eating pattern as a source of protein among a variety of protein foods (along with lean or low-fat meats and poultry), and also as healthy foods (when prepared with little or no added solid fats, sugars, refined starches, and sodium) in a nutrient-dense form.¹ They allow 2-3 eggs for weekly consumption, as long as they are cooked to the recommended safe minimum internal temperature to destroy harmful microbes (cooked until yolk and white are firm), unless pasteurized. Indeed, egg white is classed as a valuable source of high-quality protein. Eggs are also a source of valuable nutrients (e.g. they provide the most choline; also a source of the xanthophylls, lutein and zeaxanthin). However, egg yolks are higher in dietary cholesterol, but fortunately not so in saturated fats. The opponents to egg consumption maintain that dietary cholesterol should be limited to <200-300 mg/day; a single large egg yolk contains 215-275 mg of cholesterol (more than a day's worth of cholesterol).³⁰ Particularly in diabetics, consumption of one egg a day doubled their risk compared with <one egg a week.³² Dietary cholesterol increases the susceptibility of LDL to oxidation, increases postprandial lipemia and potentiates the adverse effects of dietary saturated fat, hence, the argument is that patients at risk of CVD should limit their intake of cholesterol.^{30, 33}

Added Sugars

Added sugars include syrups and other caloric sweeteners. When sugars are added to foods and beverages to sweeten them, they add calories without contributing

essential nutrients.²⁰ Consumption of added sugars can make it difficult for individuals to meet their nutrient needs while staying within calorie limits. Naturally occurring sugars, such as those in fruit or milk, are not added sugars. Specific examples of added sugars include brown sugar, corn sweetener, corn syrup, dextrose, fructose, glucose, high fructose corn syrup, honey, invert sugar, lactose, malt syrup, maltose, molasses, raw sugar, sucrose, trehalose, and turbinado sugar.

Healthy eating patterns limit added sugars to <10% of calories per day.¹ This recommendation is a target to help the public achieve a healthy eating pattern, to meet nutrient and food group needs through nutrient-dense food and beverage choices and stay within calorie limits. When added sugars in foods & beverages exceed 10% of calories, a healthy eating pattern may be difficult to achieve.

Although the evidence for added sugars and health outcomes is still developing, the recommendation to limit calories from added sugars is consistent with research examining eating patterns and health. Strong evidence from prospective cohort studies but also randomized controlled trials has shown that eating patterns that include lower intake of sources of added sugars are associated with reduced risk of CVD in adults, and moderate evidence indicates that these eating patterns are associated with reduced risk of obesity, type 2 diabetes, and some types of cancer in adults.^{1, 22} As described earlier, eating patterns consist of multiple, interacting food components, and the relationships to health exist for the overall eating pattern, not necessarily to an isolated aspect of the diet. Moderate evidence indicates a relationship between added sugars and dental caries in children and adults.³

Added sugars provide sweetness that can help improve the palatability of foods, help with preservation, and/or contribute to functional attributes such as viscosity, texture, body, color, and browning capability. The two main sources of added sugars in the U.S. are sugar-sweetened beverages^{34, 35} and snacks and sweets. Many foods high in calories from added sugars provide few or no essential nutrients or dietary fiber and, therefore, may contribute to excess calorie intake without contributing to diet quality; intake of these foods should be limited to help achieve healthy eating patterns within calorie limits. There is room to include limited amounts of added sugars in eating patterns, including to improve the palatability of some nutrient-dense foods, such as fruits and vegetables that are naturally tart. Healthy eating patterns can accommodate other nutrient-dense foods with small amounts of added sugars, such as whole-grain breakfast cereals or fat-free yogurt, as long as calories from added sugars do not exceed 10% per day.

It should be noted that replacing added sugars with *high-intensity sweeteners* may reduce calorie intake in the short-term, yet questions remain about their effectiveness as a long-term weight management strategy. High-intensity sweeteners that have been approved by the U.S. Food and Drug Administration (FDA) include saccharin, aspartame, acesulfame potassium (Ace-K), and sucralose. Based on the available evidence, these high-intensity sweeteners have been determined to be safe for the general population.^{36, 37} The FDA has determined that the estimated daily intake of these high-intensity sweeteners would not exceed the acceptable daily intake, even for high consumers of each substance. However, recently, some concern has arisen regarding consumption of diet sodas related to reports of their association with increased blood pressure and other adverse metabolic effects;^{38, 39} one suggested mechanism may relate to alterations to the intestinal microbiota conferred by these non-caloric artificial sweeteners (sweetener-induced dysbiosis) and linked to host susceptibility to metabolic disease and glucose intolerance.⁴⁰

A cross-sectional study evaluating 9317 participants found that *ultra-processed foods* contribute almost 60% of calories and 90% of added sugars consumed in the USA.⁴¹ Ultraprocessed foods comprise industrial formulations of several ingredients which, besides salt, sugar, oils and fats, include food substances not used in culinary preparations, such as flavours, colours, sweeteners, emulsifiers and other additives. As mentioned, added sugars have been linked to increased risk of obesity, hypertension, inflammation, abdominal fat, and hyperlipidemia independent of obesity, all these factors being associated with CVD and type 2 diabetes;^{2, 22, 42} some investigators have suggested sugar-induced generation of reactive oxygen species as a mechanism of sugar-induced CVD.⁴³ Some studies even suggest that sugar intake may be linked with a higher risk for certain cancers, independent of obesity.⁴⁴

One component of the list of sugars, *honey*, deserves separate mention. Many agree that refined sugar should be completely eliminated from a healthy diet, but some believe that the natural sugars found in fruit, raw honey and other natural sweeteners may be fine in moderation. Opponents believe that sugar, whether refined or unrefined, behaves in very similar ways in the body by adversely affecting metabolism. Indeed, honey mainly consists of sugars (mostly fructose) and water, but it also contains several vitamins (B complex and vitamin C) and minerals (calcium, copper, iron, magnesium, manganese, phosphorus, potassium and zinc).⁴⁵ Honey has been used for its healing, nutritional and therapeutic properties since ancient times. Antibacterial potential when applied topically, as well as anti-inflammatory and antioxidant

capacities when ingested have been advocated, which may be useful for the prevention of chronic inflammatory process like atherosclerosis, diabetes mellitus and CVD, but the evidence is limited.⁴⁵⁻⁴⁷ According to small studies, some biochemical indices (lipids) may be favorably affected by honey in diabetics, but others (glycated hemoglobin) may not.^{48, 49} Contrariwise, other investigators have ascribed to fructose a potential role in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and CVD;⁵⁰ thus, whether honey intake is rid of this harmful potential remains dubious.

Sodium

The scientific consensus from expert bodies is that currently the average sodium intake is too high and should be reduced.⁵¹ Healthy eating patterns limit sodium to <2.3 g per day for adults and children ages ≥ 14 years.^{1, 20} Sodium is an essential nutrient and is needed by the body in relatively small quantities, provided that substantial sweating does not occur. Sodium is primarily consumed as salt (sodium chloride). The recommendation to limit sodium intake to <2.3 g per day is based on evidence showing a linear dose- response relationship between increased sodium intake and increased blood pressure in adults.⁵² In addition, moderate evidence, not as consistent as the evidence on blood pressure, suggests an association between increased sodium intake and increased risk of CVD in adults. Calorie intake is highly associated with sodium intake, i.e., the more foods and beverages people consume, the more sodium they tend to consume.

Adults with prehypertension and hypertension would particularly benefit from blood pressure lowering. For these individuals, further reduction to 1.5 g per day can result in even greater blood pressure reduction. Because of the linear dose-response relationship between sodium intake and blood pressure, every incremental decrease in sodium intake that moves toward recommended limits is encouraged. Even without reaching the limits for sodium intake, strong evidence indicates that reductions in sodium intake can lower blood pressure among people with prehypertension and hypertension.

Alcohol

Dietary Guidelines do not recommend that individuals who do not drink alcohol start drinking for any reason.¹ If alcohol is consumed, it should be in moderation—up to 1 drink per day for women and up to 2 drinks per day for men—and only by adults of legal drinking age. There are also many circumstances in which individuals should not drink, such as during pregnancy.

Caffeine

Caffeine is not a nutrient; it is a dietary component that functions in the body as a stimulant. Caffeine occurs

naturally in plants (e.g., coffee beans, tea leaves, cocoa beans, kola nuts). It is also added to foods and beverages (e.g., caffeinated soda, energy drinks). If caffeine is added to a food, it must be included in the listing of ingredients on the food label. Most intake of caffeine comes from coffee, tea, and soda. Caffeinated beverages vary widely in their caffeine content. Much of the available evidence on caffeine focuses on coffee intake. Moderate coffee consumption, three to five 8-oz (~237 ml) cups/day or providing up to 400 mg/day of caffeine, can be incorporated into healthy eating patterns.¹

Strong and consistent evidence shows that, in healthy adults, moderate coffee consumption is not associated with an increased risk of major chronic diseases (e.g., cancer) or premature death, especially from CVD. However, individuals who do not consume caffeinated coffee or other caffeinated beverages are not encouraged to incorporate them into their eating pattern. Limited and mixed evidence is available from randomized controlled trials examining the relationship between those energy drinks which have high caffeine content and cardiovascular risk factors and other health outcomes. In addition, caffeinated beverages, such as some sodas or energy drinks, may include calories from added sugars, and although coffee itself has minimal calories, coffee beverages often contain added calories from cream, whole or 2% milk, creamer, and added sugars, which should be limited. The same considerations apply to calories added to tea or other similar beverages. Nevertheless, moderate consumption of flavonoid-rich tea (green or black) appears to confer cardiovascular protection.⁵³

Those who choose to drink alcohol should be cautious about mixing caffeine and alcohol together or consuming them at the same time. In addition, women who are capable of becoming pregnant or trying to, or are pregnant, & those who are breastfeeding should consult their health care providers for advice concerning caffeine consumption.

Other Nutrients

Of the underconsumed nutrients, calcium, potassium, dietary fiber, and vitamin D are considered nutrients of public health concern because low intakes are associated with health concerns.¹ For young children, women capable of becoming pregnant, and women who are pregnant, low intake of iron also is of public health concern. Regarding vitamin D, this vitamin is unique in that skin exposure to sunlight enables the body to make vitamin D. Besides sun exposure, other strategies to achieve higher levels of intake of dietary vitamin D include consuming seafood with higher amounts of vitamin D, such as salmon, herring, mackerel, and tuna, and more foods fortified with vitamin D (milk, soy beverage or soymilk, yogurt, orange juice, and breakfast cereals). In some cases, taking a vitamin D

supplement may be appropriate, especially when sunshine exposure is limited due to climate or the use of sunscreen (vitamin D recommended daily allowance for males and females ages >70 years is 800 IU). For higher intakes of dietary fiber resort to vegetables, fruits, and whole grains; for potassium to vegetables, fruits, and dairy; and for calcium to dairy products. With regards to iron, foods containing iron include lean meats, poultry, and seafood; additional iron sources include legumes (beans and peas) and dark-green vegetables, as well as foods enriched or fortified with iron, such as many breads and ready-to-eat cereals. Absorption of iron from non-heme sources is enhanced by consuming them along with vitamin C-rich foods. Women who are pregnant are advised to take an iron supplement when recommended by their physician. Finally, although not discussed in these guidelines, vitamin B12 deficiency is more common than initially thought, more prevalent in its subclinical form, and as the human body does not manufacture this vitamin but gets it from animal products (meat, fish, dairy products, and eggs) or fortified cereals, one should be cognizant of its consequences and on the look-out for its detection, especially in older people.⁵⁴

Processed Foods

Foods are classified into 4 groups: ‘unprocessed or minimally processed foods’ (such as fresh, dry or frozen fruits or vegetables, grains, legumes, meat, fish and milk); ‘processed culinary ingredients’ (including table sugar, oils, fats, salt, and other substances extracted from foods or from nature, and used in kitchens to make culinary preparations); ‘processed foods’ (foods manufactured with the addition of salt or sugar or other substances of culinary use to unprocessed or minimally processed foods, such as canned food and simple breads and cheese) and ‘ultra-processed foods’ (formulations of several ingredients which, besides salt, sugar, oils and fats, include food substances not used in culinary preparations, in particular, flavours, colours, sweeteners, emulsifiers and other additives used to imitate sensorial qualities of unprocessed or minimally processed foods and their culinary preparations or to disguise undesirable qualities of final product).¹

Several studies have shown that a high consumption of processed red meat is related to increased overall and cause-specific mortality.^{8, 55} Studies have also linked processed meat consumption with risk of chronic diseases such as CVD, diabetes mellitus or some types of cancer.^{9, 13, 14, 55} Ultra-processed foods are also contributing to higher consumption of added sugars and salt.^{1, 41}

Importance of Calorie Balance Within Healthy Eating Patterns

Managing calorie intake is fundamental to achieving and maintaining calorie balance—the balance between the

calories taken in from foods and the calories expended from metabolic processes and physical activity.¹ The best way to determine whether an eating pattern is at an appropriate number of calories is to monitor body weight and adjust calorie intake and expenditure in physical activity based on changes in weight over time.

All foods and many beverages contain calories, and the total number of calories varies depending on the macronutrients in a food. On average, carbohydrates and protein contain 4 calories per gram, fats contain 9 calories per gram, and alcohol has 7 calories per gram. The total number of calories a person needs each day varies depending on a number of factors, including the person’s age, gender, height, weight, and level of physical activity. In addition, a need to lose, maintain, or gain weight and other factors affect how many calories should be consumed. All persons are encouraged to achieve and/or maintain a healthy body weight. Children and adolescents are encouraged to maintain calorie balance to support normal growth and development without promoting excess weight gain. Children and adolescents who are overweight or obese should change their eating and physical activity behaviors to maintain or reduce their rate of weight gain while linear growth occurs, so that they can reduce body mass index (BMI) percentile toward a healthy range.

Before becoming pregnant, women are encouraged to achieve and maintain a healthy weight, and women who are pregnant are encouraged to gain weight within gestational weight gain guidelines. Adults who are obese should change their eating and physical activity behaviors to prevent additional weight gain and/or promote weight loss.

Adults who are overweight should not gain additional weight, and those with one or more CVD risk factors should change their eating and physical activity behaviors to lose weight. To lose weight, most people need to reduce the number of calories they get from foods and beverages and increase their physical activity. Eating patterns that contain 1,200 - 1,500 calories each day can help most women lose weight safely, and eating patterns that contain 1,500 - 1,800 calories each day are suitable for most men for weight loss. In adults who are overweight or obese, if reduction in total calorie intake is achieved, a variety of eating patterns can produce weight loss, particularly in the first 6 months to 2 years; however, more research is needed on the health implications of consuming these eating patterns long-term. Older adults, >65 years, who are overweight or obese are encouraged to prevent additional weight gain. Among older adults who are obese, particularly those with CVD risk factors, intentional weight loss can be beneficial and result in improved quality of life and reduced risk of chronic diseases and associated disabilities.

Prospective cohort studies have shown significant inverse associations of nut consumption with total and cause-specific mortality.^{56, 57} Nutrients in *nuts*, such as unsaturated fatty acids, high quality protein, fiber, vitamins (e.g., folate, niacin, & vitamin E), minerals (e.g., potassium, calcium, and magnesium), and phytochemicals (e.g., carotenoids, flavonoids, and phytosterols), may confer cardioprotective, anticarcinogenic, antiinflammatory, and antioxidant properties. It should be noted that the protective effect of a Mediterranean diet against CVD might be partially ascribed to intake of nuts, as one component of the diet was the availability of an average of 30 g of nuts per day.⁵⁸ A plausible concern that frequent nut consumption might result in weight gain has not panned out in these studies, rather increased nut consumption was associated with reduced waist circumference, less weight gain, and a decreased risk of obesity.⁵⁶

Nonalcoholic fatty liver disease (NAFLD), either in the form of nonalcoholic fatty liver (NAFL) or nonalcoholic steatohepatitis (NASH), is associated with metabolic risk factors such as obesity, diabetes, and dyslipidemia.⁵⁹ It is generally agreed that patients with simple steatosis have very slow, if any, histological progression, while patients with NASH can exhibit histological progression to cirrhotic-stage disease. With regards to long term outcomes of these patients, the contemporary view is that patients with NAFLD have increased overall mortality compared to matched control populations, the most common cause of death in patients with NAFLD, NAFL and NASH is CVD, and patients with NASH (but not NAFL) have an increased liver-related mortality rate. Of course, the management of patients with NAFLD should target the associated metabolic co-morbidities (obesity, hyperlipidemia, insulin resistance and type 2 diabetes), and in this regard the dietary guidelines with caloric restrictions and balance via adoption of healthy eating patterns, herein reviewed, play a most important role.

The main intervention to combat this condition relates to life style modification, with the crucial recommendation emphasizing weight loss as a most important means to reduce hepatic steatosis, achieved either by hypocaloric diet alone or in conjunction with increased physical activity; while loss of at least 3-5% of body weight appears necessary to improve steatosis, a greater degree of weight loss (up to 10%) may be needed to improve necroinflammation. Others suggest that food intake pattern with increased meal frequency (snacking) in addition to caloric excess and weight gain may contribute to the occurrence of hepatic steatosis and abdominal obesity; hypercaloric snacking of fat and sugar may also reduce hepatic insulin sensitivity.⁶⁰ Therefore, reducing snacking behavior and encouraging consuming 3 meals per day

might have favorable metabolic consequences in the long term and might reduce the prevalence of NAFLD. Furthermore, patients with NAFLD should not consume heavy amounts of alcohol. As patients with NAFLD without steatohepatitis have excellent prognosis from a liver standpoint, treatments aimed at improving liver disease should be limited to those with NASH. Finally, there is evidence that overeating saturated fats promotes hepatic and visceral fat storage, whereas excess energy from polyunsaturated fats may instead promote lean tissue in healthy humans.⁶¹

Practical tips

- A healthy diet is generally low in fat, and specifically low in saturated and trans fat; low in added sugars; low in sodium; high in fiber; low in cholesterol; rich in vitamins and minerals; calorie balanced
- Limit sweetened soda drinks as a major source of added sugars;³⁵ choose beverages with no added sugars, such as water, or beverages low in added sugars, or low-fat or fat-free milk or 100% fruit or vegetable juice
- Limit sweets and snacks; in addition to providing excess calories, increased meal frequency with snacking may lead to abdominal obesity and nonalcoholic fatty liver disease⁶⁰
- Poly- or mono-unsaturated fats are well known for their beneficial health effects
- Medium- chained, compared to long-chained, fatty acids may confer some health benefits
- Avoid deleterious trans fats, which are produced from industrial hydrogenation of vegetable oils, commercial cooking (heating and frying of oils at high temperatures, e.g. at fast food stores) and manufacturing of processed foods²⁸
- Prefer whole grain vs refined carbohydrates which may be nutritionally superior
- Flavonoids, a group of plant metabolites found in tea, dark chocolate, and a variety of fruits and vegetables, are thought to provide health benefits through cell signalling pathways and antioxidant effects

PERSPECTIVE

The benefits of healthy eating patterns are multiple and culminate into a significant reduction of CVD and/or total mortality, as evidenced by various reports of adherence to Mediterranean diet^{16, 58, 62, 63} and other healthy diets recommended by the Guidelines.⁶⁴⁻⁶⁶ A favorable association of reduced low-grade inflammation with a Mediterranean eating pattern, with a particular emphasis on the associated dietary polyphenols, has been proposed by recent studies.^{67, 68} Finally, combining healthy eating patterns with physical activity contributes to calorie balance and maintains healthy body weight, essential components in primary and secondary prevention of CVD and cancer.^{6, 7, 69, 70}

In a concerted effort, it is important that authorities and food industry implement the *nutrition facts label* to all foods as an indispensable tool for patients to use in making food purchase decisions to help reduce consumption of harmful nutrients and select healthy ones; health care providers should advocate for its use with their patients. Importantly, regarding the latest recommendation of the guidelines, in addition to various types of fats and other ingredients, the content of added sugars should be on the nutrition facts label, which will be helpful in making informed and healthy food choices (http://www.acc.org/latest-in-cardiology/articles/2016/03/07/07/01/the-dietary-guidelines-for-americans-2015-2020?w_nav=TI)

Admittedly, additional research is needed on several issues related to diet, such as relative effects of different types of fats and carbohydrates, and different types of fiber (naturally occurring and supplemental or refined) on lipids, inflammation, microbiome, and other newer potential CVD risk factors; effects of diet and/or dietary cholesterol on LDL- and HDL-cholesterol; effects of minerals in combination (other than sodium) on blood pressure; effects of dietary carbohydrate on plasma triglycerides; effect of diet and/or sodium reduction in patients with diabetes, heart failure, chronic kidney disease, CVD, & methods of assessment and cost-effective strategies for implementing these life-style and dietary recommendations.⁶

REFERENCES

1. USDHHS. 2015-2020 Dietary Guidelines for Americans. US Department of Health and Human Services. 2015:1-189.
2. Mitka M. New Dietary Guidelines place added sugars in the crosshairs. *JAMA* 2016 Mar 23:[Epub ahead of print].
3. WHO. Guideline: Sugars intake for adults and children. Geneva: World Health Organization. 2015.
4. 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.
5. Haskell WL, Lee IM, Pate RR, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;116:1081-1093.
6. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;63:2960-84.
7. Kushi LH, Doyle C, McCullough M, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 2012;62:30-67.
8. Abete I, Romaguera D, Vieira AR, Lopez de Munain A, Norat T. Association between total, processed, red and white meat consumption and all-cause, CVD and IHD mortality: a meta-analysis of cohort studies. *Br J Nutr* 2014;112:762-775.
9. Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. *Circulation* 2010;121:2271-2283.
10. Micha R, Michas G, Lajous M, Mozaffarian D. Processing of meats and cardiovascular risk: time to focus on preservatives. *BMC Med* 2013;11:136.
11. Rohrmann S, Overvad K, Bueno-de-Mesquita HB, et al. Meat consumption and mortality--results from the European Prospective Investigation into Cancer and Nutrition. *BMC Med* 2013;11:63.
12. Rouhani MH, Salehi-Abargouei A, Surkan PJ, Azadbakht L. Is there a relationship between red or processed meat intake and obesity? A systematic review and meta-analysis of observational studies. *Obes Rev* 2014;15:740-748.
13. Choi Y, Song S, Song Y, Lee JE. Consumption of red and processed meat and esophageal cancer risk: meta-analysis. *World J Gastroenterol* 2013;19:1020-1029.
14. Feskens EJ, Sluik D, van Woudenberg GJ. Meat consumption, diabetes, and its complications. *Curr Diab Rep* 2013;13:298-306.
15. Perez-Jimenez F, Alvarez de Cienfuegos G, Badimon L, et al. International conference on the healthy effect of virgin olive oil. *Eur J Clin Invest* 2005;35:421-424.
16. Trichopoulou A, Bamia C, Trichopoulos D. Anatomy of health effects of Mediterranean diet: Greek EPIC prospective cohort study. *BMJ* 2009;338:b2337.
17. Erkkila A, de Mello VD, Riserus U, Laaksonen DE. Dietary fatty acids and cardiovascular disease: an epidemiological approach. *Prog Lipid Res* 2008;47:172-187.
18. Hooper L, Martin N, Abdelhamid A, Davey Smith G. Reduction in saturated fat intake for cardiovascular disease. *Cochrane Database Syst Rev* 2015;6:Cd011737.
19. Ley SH, Sun Q, Willett WC, et al. Associations between red meat intake and biomarkers of inflammation and glucose metabolism in women. *Am J Clin Nutr* 2014;99:352-360.
20. DeSalvo KB, Olson R, Casavale KO. Dietary Guidelines for Americans. *Jama* 2016;315:457-458.
21. Michas G, Micha R, Zampelas A. Dietary fats and cardiovascular disease: putting together the pieces of a complicated puzzle. *Atherosclerosis* 2014;234:320-328.
22. DiNicolantonio JJ, Lucan SC, O'Keefe JH. The Evidence for Saturated Fat and for Sugar Related to Coronary Heart Disease. *Prog Cardiovasc Dis* 2015.
23. Liao KM, Lee YY, Chen CK, Rasool AH. An open-label pilot study to assess the efficacy and safety of virgin coconut oil in reducing visceral adiposity. *ISRN Pharmacol* 2011;2011:949686.
24. Nagao K, Yanagita T. Medium-chain fatty acids: functional lipids for the prevention and treatment of the metabolic syndrome. *Pharmacol Res* 2010;61:208-212.
25. St-Onge MP, Bosarge A, Goree LL, Darnell B. Medium chain triglyceride oil consumption as part of a weight loss diet does not lead to an adverse metabolic profile when compared to olive oil. *J Am Coll Nutr* 2008;27:547-552.
26. Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. *N Engl J Med* 2006;354:1601-1613.
27. de Souza RJ, Mente A, Maroleanu A, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies. *Bmj* 2015;351:h3978.
28. Manolis AS. Health hazards from trans fatty acids: Ban of artificial trans fats long overdue. *Hosp Chronicles* 2010;5:1-3.
29. Buijsse B, Boeing H, Drogan D, et al. Consumption of fatty foods and incident type 2 diabetes in populations from eight European countries. *Eur J Clin Nutr* 2015;69:455-461.
30. Spence JD, Jenkins DJ, Davignon J. Dietary cholesterol and egg yolks: not for patients at risk of vascular disease. *Can J Cardiol* 2010;26:e336-339.

31. McNamara DJ. The Fifty Year Rehabilitation of the Egg. *Nutrients* 2015;7:8716-8722.
32. Qureshi AI, Suri FK, Ahmed S, et al. Regular egg consumption does not increase the risk of stroke and cardiovascular diseases. *Med Sci Monit* 2007;13:Cr1-8.
33. Spence JD, Jenkins DJ, Davignon J. Egg yolk consumption and carotid plaque. *Atherosclerosis* 2012;224:469-473.
34. Park S, Xu F, Town M, Blanck HM. Prevalence of sugar-sweetened beverage intake among adults - 23 States and the District of Columbia, 2013. *MMWR Morb Mortal Wkly Rep* 2016;65:169-174.
35. Johnson RK. Reducing intake of sugar-sweetened beverages is vital to improving our Nation's health. *Circulation* 2016;133:347-349.
36. Riobo Servan P, Sierra Poyatos R, Soldo Rodriguez J. Low and no calorie sweeteners; myths and realities. *Nutr Hosp* 2014;30 Suppl 2e:49-55.
37. de Koning L, Malik VS, Kellogg MD, et al. Sweetened beverage consumption, incident coronary heart disease, and biomarkers of risk in men. *Circulation* 2012;125:1735-1741, s1731.
38. Souza Bda S, Cunha DB, Pereira RA, Sichieri R. Soft drink consumption, mainly diet ones, is associated with increased blood pressure in adolescents. *J Hypertens* 2016;34:221-225.
39. Pepino MY. Metabolic effects of non-nutritive sweeteners. *Physiol Behav* 2015;152:450-455.
40. Suez J, Korem T, Zeevi D, et al. Artificial sweeteners induce glucose intolerance by altering the gut microbiota. *Nature* 2014;514:181-186.
41. Martinez Steele E, Baraldi LG, Louzada ML, et al. Ultra-processed foods and added sugars in the US diet: evidence from a nationally representative cross-sectional study. *BMJ Open* 2016;6:e009892.
42. Ma J, McKeown NM, Hwang SJ, et al. Sugar-sweetened beverage consumption is associated with change of visceral adipose tissue over 6 years of follow-Up. *Circulation* 2016;133:370-377.
43. Prasad K, Dhar I. Oxidative stress as a mechanism of added sugar-induced cardiovascular disease. *Int J Angiol* 2014;23:217-226.
44. Tasevska N, Jiao L, Cross AJ, et al. Sugars in diet and risk of cancer in the NIH-AARP Diet and Health Study. *Int J Cancer* 2012;130:159-169.
45. Vallianou NG, Gounari P, Skourtis A, Panagos J, Kazazis C. Honey and its anti-Inflammatory, anti-bacterial and anti-oxidant properties. *Gen Med (Los Angel)* 2014;2:1-5.
46. Ajibola A, Chamunorwa JP, Erlwanger KH. Nutraceutical values of natural honey and its contribution to human health and wealth. *Nutr Metab (Lond)* 2012;9:61.
47. Al-Waili NS. Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose. *J Med Food* 2004;7:100-107.
48. Bahrami M, Ataie-Jafari A, Hosseini S, et al. Effects of natural honey consumption in diabetic patients: an 8-week randomized clinical trial. *Int J Food Sci Nutr* 2009;60:618-626.
49. Abdulrhman MM, El-Hefnawy MH, Aly RH, et al. Metabolic effects of honey in type 1 diabetes mellitus: a randomized crossover pilot study. *J Med Food* 2013;16:66-72.
50. Johnson RJ, Segal MS, Sautin Y, et al. Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. *Am J Clin Nutr* 2007;86:899-906.
51. Jackson SL, King SM, Zhao L, Cogswell ME. Prevalence of Excess Sodium Intake in the United States - NHANES, 2009-2012. *MMWR Morb Mortal Wkly Rep* 2016;64:1393-1397.
52. Manolis AS, Sakellaris N, Pyrros I. Salt controversy stirred by "PURE" but settled by "NUTRICODE". *Hosp Chronicles* 2014;9:232-235.
53. Manolis AS. Moderate intake of flavonoid-rich tea, green or black, confers cardiovascular protection. *Hosp Chronicles* 2015;10:3-6.
54. Manolis AS, Manolis TA, Poulidakis E, Melita H. Beware of the ailments of vitamin B12 deficiency. *Hosp Chronicles* 2013;8:51-57.
55. Rohrmann S, Linseisen J. Processed meat: the real villain? *Proc Nutr Soc* 2015:1-9.
56. Bao Y, Han J, Hu FB, et al. Association of nut consumption with total and cause-specific mortality. *N Engl J Med* 2013;369:2001-2011.
57. Eslamparast T, Sharafkhan M, Poustchi H, et al. Nut consumption and total and cause-specific mortality: results from the Golestan Cohort Study. *Int J Epidemiol* 2016 Mar 5: [Epub ahead of print].
58. Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. *N Engl J Med* 2013;368:1279-1290.
59. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. *Gastroenterology* 2012;142:1592-1609.
60. Koopman KE, Caan MW, Nederveen AJ, et al. Hypercaloric diets with increased meal frequency, but not meal size, increase intrahepatic triglycerides: a randomized controlled trial. *Hepatology* 2014;60:545-553.
61. Rosqvist F, Iggman D, Kullberg J, et al. Overfeeding polyunsaturated and saturated fat causes distinct effects on liver and visceral fat accumulation in humans. *Diabetes* 2014;63:2356-2368.
62. Trichopoulou A, Bamia C, Trichopoulos D. Mediterranean diet and survival among patients with coronary heart disease in Greece. *Arch Intern Med* 2005;165:929-935.
63. Trichopoulou A, Orfanos P, Norat T, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. *Bmj* 2005;330:991.
64. Martinez-Gonzalez MA, Sanchez-Tainta A, Corella D, et al. A provegetarian food pattern and reduction in total mortality in the Prevencion con Dieta Mediterranea (PREDIMED) study. *Am J Clin Nutr* 2014;100 Suppl 1:320s-328s.
65. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr* 2016:0.
66. Harmon BE, Boushey CJ, Shvetsov YB, et al. Associations of key diet-quality indexes with mortality in the Multiethnic Cohort: the Dietary Patterns Methods Project. *Am J Clin Nutr* 2015;101:587-97.
67. Bonaccio M, Pounis G, Cerletti C, et al. Mediterranean diet, dietary polyphenols and low-grade inflammation: results from the moli-sani study. *Br J Clin Pharmacol* 2016.
68. Casas R, Sacanella E, Estruch R. The immune protective effect of the Mediterranean diet against chronic low-grade inflammatory diseases. *Endocr Metab Immune Disord Drug Targets* 2014;14:245-254.
69. Vanhees L, Geladas N, Hansen D, et al. Importance of characteristics and modalities of physical activity and exercise in the management of cardiovascular health in individuals with cardiovascular risk factors: recommendations from the EACPR. Part II. *Eur J Prev Cardiol* 2012;19:1005-1033.
70. Vanhees L, De Sutter J, Gelada SN, et al. Importance of characteristics and modalities of physical activity and exercise in defining the benefits to cardiovascular health within the general population: recommendations from the EACPR (Part I). *Eur J Prev Cardiol* 2012;19:670-686.