Healthy dietary patterns for preventing cardiometabolic disease: the role of plant-based foods and animal products

Kristina S. Petersen¹, Michael R. Flock², Chesney K. Richter³, Ratna Mukherjea⁴, Joanne L. Slavin⁵, Penny M. Kris-Etherton¹

¹Department of Nutritional Sciences, The Pennsylvania State University, University Park, Pennsylvania, USA
²Clinical & Translational Sciences Institute, University of Pittsburgh, Pittsburgh Pennsylvania, USA
³Department of Nutritional Sciences, University of Arizona, Tucson, Arizona, USA
⁴DuPont Nutrition & Health, St. Louis, Missouri, USA
⁵Department of Food Science and Nutrition, University of Minnesota, St. Paul, Minnesota, USA

Kristina S. Petersen PhD, APD (corresponding author)
Department of Nutritional Sciences
The Pennsylvania State University
320 Chandlee Lab
University Park, PA 16802
814-863-8622
kup63@psu.edu

Funding and financial disclosures

There are no funding and financial disclosures to report.

Conflict of interest disclosures
KSP, MF, CR, JS and PMKE have no conflicts of interest to report. RM is employed by DuPont Nutrition & Health, a food ingredient company.
ABSTRACT

Diets rich in plant foods are increasingly recommended to lower risk of cardiometabolic diseases because of strong evidence that fruits, vegetables, legumes, whole grains, nuts, and seeds are protective. Although some animal products such as unprocessed lean red meat, poultry, eggs, and dairy products are recommended in dietary patterns to prevent cardiometabolic diseases, many health professionals advocate for exclusively plant-based dietary patterns. The aim of this paper is to review recent evidence about the relative contributions of plant-based foods and animal products to a healthy dietary pattern. Secondary aims are to discuss current consumption patterns and adherence to dietary recommendations. Epidemiological evidence suggests that higher intake of plant-based foods is associated with lower risk of cardiometabolic disease, whereas a higher meat intake increases risk of cardiometabolic disease and replacement of small quantities of animal protein with plant protein is associated with lower risk. Randomized controlled studies show that nutrient dense diets containing animal protein, including some unprocessed lean meats, improve cardiovascular disease risk factors. Therefore, it is likely that consumption of animal products, at recommended levels, in the context of a dietary pattern that meets recommendations for fruits, vegetables, whole grains, nuts, seeds, and legumes, and does not exceed recommendations for added sugar, sodium, and saturated fat may not increase cardiometabolic risk. Currently, adherence to these recommendations is suboptimal. Therefore, rather than debating the merits of healthy dietary patterns that are exclusively plant-based or that include animal sources in recommended amounts, the focus should be on improving eating patterns to align with dietary guidelines. Registered Dietitian/Nutritionists have the requisite nutrition expertise to facilitate change at the individual and population level to promote adherence to healthy dietary patterns. Importantly, advocacy activities are
urgently needed to create a healthier food environment, and all health professionals including Registered Dietitian/Nutritionists must play a role.

Keywords: plant-based diets; cardiometabolic; cardiovascular disease; diabetes; animal protein
INTRODUCTION

Poor dietary practices are a leading risk factor for illness, disability and death worldwide and in the U.S. (1, 2). As such, defining dietary patterns that improve health and reduce chronic disease is of major scientific and public health importance. However, equally important, but often forgotten, is identifying healthful dietary patterns that can be followed by the general population. There is significant evidence showing that dietary recommendations are not being met in many countries and that consumption of “empty calories” (i.e., foods high in solid fats and added sugars) is increasing globally (3). In many countries, including the U.S., dietary guidelines are moving away from nutrient-based recommendations in favor of dietary pattern based recommendations. Recommended dietary patterns are rich in plant-based foods such as fruits, vegetables, legumes, whole grains, nuts, seeds, soy products and vegetable oils (4-7). They also include moderate amounts of fat-free or low-fat dairy. Many countries also recommend a variety of protein foods, including seafood, lean meats, poultry, eggs, legumes, nuts, seeds, and soy products. There is strong evidence that fruits, non-starchy vegetables, whole grains, nuts, seeds, and legumes have beneficial health effects and higher consumption is associated with a lower risk of cardiometabolic disease (8-13). Consequently, many organizations now recommend a diet that emphasizes plant foods (14, 15). There is ongoing active scientific debate, however, about the health effects of some animal products such as unprocessed red meat, poultry, eggs and dairy products (16). The purpose of this article is to review recent evidence on the relative contributions of plant-based foods and animal products to a healthy dietary pattern. Secondary aims are to discuss these findings in the context of current consumption patterns and adherence to dietary recommendations. The important role for Registered Dietitian/Nutritionists (RDNs) in helping individuals and the population adhere to current dietary guidelines will be described briefly.
Epidemiological evidence for the association between consumption of plant-based foods, animal products and cardiometabolic disease

A significant body of epidemiological evidence has shown that dietary patterns that are high in plant foods including fruits, vegetables, nuts, seeds, whole grains, legumes, and soy products are associated with lower risk of mortality, cardiovascular disease (CVD) and type 2 diabetes (17-19). In addition, a number of observational studies have shown that vegetarians are at lower risk of numerous chronic conditions, compared to those who consume a dietary pattern high in meat products (20). A recent study showed that higher plant protein intake was associated with a lower risk of all-cause mortality and CVD mortality (21). A 3% increase in plant protein intake was associated with a 10% reduction (95% confidence interval (95% CI) 0.86-0.95) in all-cause mortality and a 12% (95% CI 0.80-0.97) lower risk of CVD mortality. Conversely, a 10% increase in animal protein intake was associated with an 8% increase in the risk of CVD mortality (95% CI 1.01-1.16) and a non-significant 2% increase in risk of all-cause mortality (95% CI 0.98-1.05). A limitation of these analyses is that the dietary replacement for plant and animal protein was not considered. Implicit to this is that animal protein could have increased while plant protein could have decreased and vice versa. There are many other replacement scenarios, as well, which call for further research to be conducted. Further subgroup analysis demonstrated that higher animal protein intake only increased the risk of CVD mortality in people with an unhealthy lifestyle, which was defined as smoking for greater than five pack years (equal to one pack per day for 5 years), high alcohol consumption (>14g/day in women and >28g/day in men), BMI >27.5kg/m², or less than 150 minutes/wk of physical activity. In contrast, higher plant protein intake was only associated with a reduced risk of all-cause mortality and cardiovascular mortality in people with an unhealthy lifestyle. In those who had a healthy lifestyle, intake of plant or animal
protein was not associated with all-cause mortality or CVD mortality, after adjustment for potential confounders. Since the majority of people in high-income countries have an unhealthy lifestyle, based on BMI and physical inactivity alone (22, 23), the results of this study suggest that replacing animal protein with plant protein may reduce mortality risk. In a prospective cohort study of U.S. health professionals, Song et al. (21) demonstrated that replacing 3% of energy from animal protein sources, including unprocessed red meat, poultry, fish, eggs and dairy with plant protein was associated with a 6-19% reduction in the risk of all-cause mortality; similar risk reductions were observed for CVD mortality. This suggests that substituting a small percentage of animal protein with plant protein may reduce the risk of all-cause and cardiovascular death in high-income countries (24).

Higher animal protein intake has also been associated with increased risk of type 2 diabetes such that per 5% increase in animal protein consumption the risk of type 2 diabetes increases by 15% (95% CI 1.00-1.33) (25). In this study, intake of plant protein was not associated with the development of type 2 diabetes after adjustment for standard risk factors and consumption of energy, fiber, and saturated fat, monounsaturated fat (MUFA), polyunsaturated fat (PUFA), trans fat intake, and animal protein. A recent meta-analysis of prospective cohort studies also showed increased risk of type 2 diabetes with higher total protein intake (relative risk (RR) 1.09; 95% CI 1.06-1.13) and animal protein intake (RR 1.19; 95% CI 1.11-1.28), while there was no association for plant protein intake (RR 0.95; 95% CI 0.89-1.02) (25). Since plant-based foods contain many cardioprotective vitamins, minerals, nutrients and bioactives, in addition to protein, which is not an under-consumed nutrient in high-income countries, diets rich in plant-based foods should be evaluated in terms of their overall nutritional quality. Similarly, the overall quality of diets high in animal products should be considered since many animal products are rich in nutrients and also do not increase the risk
of cardiometabolic disease. In fact, similar to plant-based foods, some of the components of animal sources are protective (16).

Epidemiological evidence shows that red and processed meat are associated with increased risk of CVD and type 2 diabetes (21, 26, 27), whereas, poultry, eggs, fish and dairy do not increase CVD risk or CVD mortality (21, 26, 28-31). In fact, fish and dairy consumption have been associated with lower risk of CVD and CVD death (29-31). No association has been found between intake of fish and type 2 diabetes, but dairy intake may be protective against type 2 diabetes (32, 33). However, there is some evidence to suggest that eggs may increase the risk of type 2 diabetes, especially in U.S. populations (34, 35). At present, evidence suggests that red meat consumption is strongly associated with greater risk of cardiometabolic disease. Therefore, when considering the cardiometabolic effect of consuming a dietary pattern containing animal products, it is important to recognize that the associated risk may depend on the type of animal product consumed.

The evidence showing an adverse association between animal protein and a number of major chronic diseases is derived from observational studies and therefore is subject to confounding. Thus, it is unclear whether a causative relationship exists. It has been hypothesized that the association between meat consumption and higher risk of cardiometabolic diseases may be due to meat consumption being a marker of an overall less healthy diet and lifestyle, rather than meat consumption per se. In the European Prospective Investigation into Cancer and Nutrition (EPIC) – Oxford cohort, it was observed that meat eaters had the highest consumption of energy, protein, fat, saturated fat and lowest intake of fiber and PUFA when compared with fish eaters, vegetarians and vegans (36). This study suggests that meat consumers have poorer overall diet quality, which was observed in a Finnish cohort whereby greater meat consumption was associated with lower overall diet quality after adjustment for age, energy intake, physical activity, smoking, and education.
In this cohort, there was a direct relationship between higher consumption of meat, and higher physical inactivity, BMI, waist circumference and percentage body weight. The relationship between red and processed meat, and BMI persisted after adjustment for age, physical activity, education, smoking, intake of nuts and seeds, fruits, oil, coffee, whole grains, and potatoes. Recently, it was shown in French adults that greater plant protein intake was independently associated with greater dietary diversity and higher nutrient adequacy (38). In this study, the difference between animal protein intake in the highest and lowest quartile of nutrient adequacy was 7% of total energy intake, indicating that relatively small reductions in animal protein intake in favor of plant protein improves nutritional adequacy. In summary, the epidemiological evidence showing higher meat consumption is associated with mortality and chronic disease development may be confounded by other diet and lifestyle factors but modestly reducing meat consumption and including more plant-based foods will improve overall dietary quality and may reduce diet-related diseases.

**DIETARY PATTERNS CONTAINING ANIMAL PRODUCTS AND PLANT-BASED FOODS**

The results of epidemiological research are likely influenced by confounding, therefore to establish the cardiometabolic effects of diets containing plant-based foods and animal products well controlled clinical trials provide the highest evidence. The Dietary Approaches to Stop Hypertension (DASH) Diet is a nutrient-dense dietary pattern that emphasizes consumption of fruits, vegetables, whole grains, and low-fat dairy products, and limits consumption of red meat, sweets, and snacks (39). While this diet limits red meat consumption (0.5 servings/d of red meat), approximately two thirds of total protein intake is obtained from animal products (principally from 2.7 servings/d of dairy). In the original controlled feeding study, the DASH diet reduced blood pressure to a greater extent than the control diet (-5.5/3.0 mmHg), after 8 weeks in subjects with pre- and stage 1- hypertension.
The control diet had a macronutrient profile similar to the average American diet and included 0.5 servings/d of dairy and 1.5 servings/d of red meat. Interestingly, the DASH diet also reduced blood pressure more than a high fruit and vegetable diet (-2.7/1.9 mmHg), which also had a macronutrient profile similar to the average American diet but included 8.5 servings/d of fruits and vegetables, 0.3 servings/d of dairy and 1.8 servings/d of red meat.

These results show that the including low-fat dairy as part of a diet that is rich in fruits and vegetables and low in saturated fat improves blood pressure more than an average American diet rich in fruit and vegetables.

Subsequently, Appel and colleagues investigated the blood pressure and lipid effects of three healthful dietary patterns (all low in saturated fat) differing in protein, carbohydrate and unsaturated fat content (OmniHeart Study) (41). The high carbohydrate diet (58% of total energy) was based on the DASH diet, whereas the high protein diet and the high unsaturated fat diets replaced 10% of the calories from carbohydrates with protein or unsaturated fat, respectively. The high protein diet included 50% of total protein from plant sources. All the diets were high in fruits, vegetables and grains, and contained approximately 1 serving/d of red meat. It should be noted that the high carbohydrate diet included 4.6 servings/d of desserts and sweets compared to 2.5 and 1.7 servings/d in the protein and unsaturated fat diets, respectively. In this study, the high protein and unsaturated fat diet lowered blood pressure, total cholesterol, non-HDL cholesterol and triglycerides more than the high carbohydrate diet (42). Although all test diets lowered 10-year coronary heart disease (CHD) risk, the estimated 10-year CHD risk was reduced to a greater extent by the high protein and unsaturated fat diets compared with the high carbohydrate diet. These controlled feeding studies show that nutrient-dense high-quality diets that include animal products can improve risk factors for CVD, thereby reducing the overall risk of CVD.
The DASH diet has also been tested in free-living populations. In the PREMIER study, individuals with pre- and stage 1- hypertension were provided with education and counseling to implement key components of the DASH diet, in addition goals were set for weight loss, physical activity and alcohol consumption (43). This was compared to a group that just had goals for weight loss, physical activity and alcohol consumption, and an advice only control group. Subjects received weekly group sessions for the first 8 weeks, followed by biweekly sessions until the 6-month time point, and then monthly sessions were held for the final 12 months. After 18 months, intake of fruits (+1.8 servings/d), vegetables (+1.1 servings/d) and dairy products (+0.3 servings/d) were increased from baseline in the DASH group, but not to amounts recommended in the original DASH diet (9-12 servings/d of fruits and vegetables; 2-3 servings/d of dairy) and achieved in the controlled feeding study (44). Compared to subjects in the group that just had goals for weight reduction, increasing physical activity and reducing alcohol consumption, there was no additional blood pressure lowering effect for those who were in the group that also implemented key components of the DASH diet (45). Compared to the advice only control group, systolic and diastolic blood pressures were reduced by 4.3 mmHg (95% CI -5.9 to -2.8 mmHg) and 2.6 mmHg (95% CI -3.7 to -1.5 mmHg), respectively in subjects in the DASH group. Similar reductions of 3.7 mmHg (95% CI -5.3 to -2.1 mmHg) and 1.7 mmHg (95% CI -2.8 to -0.6 mmHg) for systolic and diastolic blood pressure, respectively, were observed in the group that had lifestyle goals. This study showed that it was challenging for free-living individuals to implement a dietary pattern consistent with the DASH recommendations, which has been shown in a number of other free-living populations as well (46). Nonetheless, there were positive steps made towards adherence with a DASH diet.

In America, beef is commonly consumed and there was some concern that the restriction placed on red meat in the DASH diet may hamper compliance in the U.S. In the Beef In an
Optimal Lean Diet (BOLD) study, a DASH diet with 28 g/d, 113 g/d or 153 g/d of lean beef lowered total and LDL-cholesterol, compared to a control healthy American diet, with no difference between the diets after 5 weeks (47). Apolipoprotein profile was also improved after consumption of the lean beef containing diets compared with the healthy American diet. The BOLD study included normotensive and pre-hypertensive subjects, and after consumption of the diet containing 153 g/day of lean beef systolic blood pressure was lower (-4.2 mmHg) than after the other three diets (48). In addition, augmentation index, a measure of arterial stiffness, was lower after the diet containing 113 g/d of lean beef compared with the other diets. These results suggest that that inclusion of lean beef as part of a healthy dietary pattern can reduce CVD risk factors. However, it is important to note that these effects were achieved under controlled feeding conditions and might be more difficult to achieve in a free-living setting. Additionally, the diets that included lean beef were also designed to limit saturated fat intake (6% of total energy) and “empty calorie” foods, while providing large quantities of fruits and vegetables (~8 cups/d) and grains (5.3-5.6 oz/d). The diet that provided 153 g/d of lean beef also included 4.2 oz/d of legumes, nuts, seeds and vegetable protein, and 4.7 cups of low fat dairy products. Therefore, these diets contained many nutrient dense foods in addition to the lean beef, and this combination, together with the lower saturated fat content of the diets likely explains the observed lipid-lowering effects. It remains unclear though whether a free-living population would be able to follow this dietary pattern long term.

Two trials conducted in free-living populations have also shown that DASH diets, which include lean red meat (beef or pork) improve blood pressure. Sayer et al. observed that blood pressure was lowered to a similar extent with a DASH diet that included 55% of total protein from lean pork compared to a DASH diet that included the same amount of protein from lean chicken and fish after 6 weeks, in healthy men and women with hypertension (49). Similarly,
a DASH diet containing lean red meat (six 100 g-servings/week) was more effective at lowering blood pressure in post-menopausal women after 14 weeks than a healthy reference diet (50). However, it should be noted that the healthy reference diet in this study included less than 2 servings/week of red meat, less fruits and vegetables, and more fats and oils, refined carbohydrates and sodium than the DASH group. Therefore, it is likely that the blood pressure lowering observed in this study by Nowson et al. was due to the higher fruit and vegetable consumption and lower sodium intake in the DASH group compared with the reference diet.

CURRENT POPULATION CONSUMPTION AND ADHERENCE TO DIETARY GUIDELINES

Epidemiological research shows that higher meat consumption is associated with lower consumption of nutrient-dense foods particularly fruits, vegetables, legumes, nuts, seeds, and soy products. Although data from controlled feeding studies show that when lean red meat is consumed as part of a dietary pattern that meets food-based dietary recommendations and limits saturated fat, sodium, and added sugar, risk factors for CVD are improved. Therefore, rather than focusing on the contribution of single foods or dietary components in isolation the totality of the diet should be considered. Ultimately, there are multiple dietary patterns that are healthful and individuals should choose the one they can follow long-term. In the 2015-2020 Dietary Guidelines for Americans, three dietary patterns are included, the healthy U.S. style diet, the healthy Mediterranean style eating pattern, and the healthy vegetarian eating pattern (4). Each of these dietary patterns meets nutrient requirements, although the foods recommended in each differ, albeit slightly. Identifying dietary patterns that are associated with better cardiometabolic health is not the challenge; rather, improving population adherence to healthful dietary patterns is the obstacle.
Current data show that population consumption patterns markedly diverge from recommendations for cardiometabolic disease prevention (51). In the U.S., consumption of vegetables, fruits, dairy products, legumes, whole grains and seafood is far lower than recommended. Also, intakes of meats, poultry, eggs, refined grains, solid fats, added sugar, and sodium are much higher than recommended. In quantitative terms, average intake of fruits and vegetables is 115 g/d and 183 g/d, respectively (52), whereas 300 g/d of fruits and 400 g/d of vegetables is recommended (4). Similarly intakes of nuts and seeds (~12 g/d) and whole grains (21 g/d) are well below recommended levels of ~20 g/d (5 oz/wk) and 125 g/d, respectively (4, 52). In comparison, American’s consume approximately 47 g/d of unprocessed red meat and 31 g/d of processed meat, whereas evidence shows that the lowest risk of cardiometabolic disease is observed when red meat consumption is less than 100 g/wk (14 g/d), and processed meat should not be consumed (4, 52). Further, 90% of individuals in the U.S. consume discretionary foods on a daily basis, and among consumers average intake of discretionary food items is approximately 500 kcal/d or one quarter of total energy intake (53). This demonstrates that to improve overall adherence to the dietary guidelines and diet quality there needs to be a shift in consumption patterns to include more nutrient-dense foods and less “empty calorie” foods, which are high in calories, added sugar, refined carbohydrates and solid fats. In total, the diet is high in energy-dense nutrient-poor foods, and low in fruits, vegetables, whole grains, legumes, nuts, and seeds.

The Dietary Guidelines Advisory Committee (2015) identified the following nutrients as being under-consumed in the U.S., vitamin A, vitamin D, vitamin E, vitamin C, folate, calcium, magnesium, fiber, and potassium (54). For adolescent and premenopausal women, iron is also an under-consumed nutrient. Plant-based foods are good sources of many of these shortfall nutrients, although dairy products and lean meat are high in calcium and iron,
respectively. This further indicates that consumption of fruits, vegetables, nuts, seeds and whole grains needs to increase, and replace nutrient-poor food choices.

**ACHIEVING HEALTHFUL DIETARY PATTERNS**

Many factors influence what foods an individual chooses to consume and their overall dietary patterns. Thus, to achieve meaningful changes in population dietary habits there needs to be intervention at the individual level but also health system changes and strong public policy are required (16). A recent meta-analysis showed that a 10% price decrease (i.e., a subsidy) on healthy foods increased consumption by 12% (95% CI 10-15%), and a 10% price increase (i.e. a tax) in the cost of unhealthy foods reduced consumption by 6% (95% CI 4-8%) (55). Afshin et al. (55) also showed that reducing the price of fruits and vegetables by 10% increased consumption by 14% (95% CI 11-17%). The American Heart Association cites Level 1 A evidence for economic incentives that lower the cost of more healthy foods and beverages, and Level 2 B evidence for increasing the price of unhealthy foods (56). Additionally, cost-effectiveness modeling based on the Australian population showed taxes and subsidies on foods and beverages are effective ways to improve population health and reduce health care expenditures (57). Other ways to improve population dietary intake are: media and education strategies; mandated nutritional labeling and front-of-pack labeling; interventions targeted at schools and workplaces; increased availability of healthy foods and reduced prevalence of food deserts; regulation of food marketing and advertising to children; regulation of food industry endorsement and sponsorship of children’s sporting and leisure activities (56). Many of these strategies target the food industry to encourage reformulation and development of healthier products; thus, the role of the food industry must be considered in public health efforts to improve diet quality (58).
An example of how the food industry can influence population intake is the change in *trans* fat levels in food products in response to the FDA mandating labeling of trans fat on the Nutrition Facts panel (59). In 2006, the FDA introduced this mandate and since this time there has been a reduction in the *trans* fat content of the food supply (60, 61). In 2013, the FDA further determined that partially hydrogenated vegetable oils were no longer “generally recognized as safe” (62), which means that food manufacturers will no longer be able to use partially hydrogenated vegetable oil in their products, further reducing *trans* fat levels in the food supply. The UK salt reduction program is another example of how product reformulation by the food industry can influence population intake and health outcomes. The UK salt reduction program had many components but notably the food industry was engaged and specific salt targets were set for product categories with clear timeframes for the targets to be achieved (63). The initiative was voluntary with the threat of legislation, and companies that achieved the targets were praised, and those that did not were publicly named and shamed. In the UK, salt intake was reduced from 9.5 g/day in 2001 to 8.6 g/day in 2008, and by a further 0.5g (6%) to 8.1 g/day in 2011 (63, 64). It has been estimated that as a result of this salt reduction program there are 9,000 fewer cardiovascular deaths per year in the UK (63).

**THE ROLE OF RDNs IN IMPROVING POPULATION LEVEL DIETARY INTAKE**

There is evidence of marked benefits to the food supply and the diet the population consumes as a result of policy interventions. RDNs can work to improve the overall food environment by advocating for stronger public health policies while also influencing dietary consumption patterns at the individual level. At an individual level, RDNs help patients and clients follow a dietary pattern that suits their specific needs and meets nutrient requirements. This individualized dietary prescription may also include education about recipe modification and cooking methods to achieve recommended intakes of foods and nutrients based on specific
needs. There is also a role for RDNs in influencing population health by advocating for health food environments, which may involve communicating with legislators, elected officials and others who influence policy and legislation (65). Further, when new policies or guidelines are introduced, RDNs can help to communicate the changes to individuals and the general public. RDNs can also work to translate research findings into practice. A recent systematic review aiming to determine how nutrition related evidence for the prevention and treatment of CVD is translated into practice showed that there are little data on how dietary knowledge is being translated to users (66). This is likely due to limited reporting of methods used to translate nutrition knowledge into practice rather than lack of translation altogether. However, detailed and accurate reporting of the effectiveness of the different methods used to translate nutrition knowledge into practice is needed to facilitate successful, timely translation of research findings. Since RDNs work in many settings including health care, the community, food service, industry, and research they are uniquely positioned to facilitate the translation of evidence-based nutrition research into clinical practice and population-based strategies to achieve sustainable improvements in dietary consumption patterns (67).

**CONCLUSION**

Epidemiological evidence suggests that plant-based diets are associated with lower risk of cardiometabolic disease and that individuals with higher meat intakes are at greater risk of CVD; however, it is unclear whether this relationship is indicative of a causative effect or due to other diet and lifestyle factors that differ between high and low meat consumers. These studies, however, show that small increases in plant-based foods reduce CVD risk. Data from randomized controlled trials with hard endpoints are not available, but well-controlled studies of intermediate outcomes have shown that nutrient dense diets, which contain animal protein, including some unprocessed lean meat do not have adverse effects and may improve risk factors for CVD. Therefore, it is likely that consumption of animal products (excluding
processed red meats) at recommended levels in the context of a dietary pattern that meets recommendations for fruits, vegetables, whole grains, nuts, seeds, and legumes, and does not exceed recommendations for added sugar, sodium and, saturated fat may not adversely affect, and in fact, may benefit cardiometabolic risk. However, population adherence to these recommendations is markedly suboptimal. Therefore, improving intake patterns to align with dietary guidelines should be the focus of our efforts rather than engaging in debates about whether diets for cardiometabolic disease prevention should be exclusively plant-based or include animal foods in recommended amounts. This will require that RDNs intervene at both the individual and population level, and also advocate for public policy that will effectively create healthier food environments.

Acknowledgements

None

Author contributions

All authors contributed to writing the paper. KSP was responsible for advancing an early draft of the paper. MRF prepared an early draft of the paper. All other authors contributed sections to the paper. KSP and PMK finalized the paper for submission.

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