THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Food Consumption and its Impact on Cardiovascular Disease: Importance of Solutions Focused on the Globalized Food System

A Report From the Workshop Convened by the World Heart Federation

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ABSTRACT

Major scholars in the field, on the basis of a 3-day consensus, created an in-depth review of current knowledge on the role of diet in cardiovascular disease (CVD), the changing global food system and global dietary patterns, and potential policy solutions. Evidence from different countries and age/race/ethnicity/socioeconomic groups suggesting the health effects studies of foods, macronutrients, and dietary patterns on CVD appear to be far more consistent though regional knowledge gaps are highlighted. Large gaps in knowledge about the association of macronutrients to CVD in low- and middle-income countries particularly linked with dietary patterns are reviewed. Our understanding of foods and macronutrients in relationship to CVD is broadly clear; however, major gaps exist both in dietary pattern research and ways to change diets and food systems. On the basis of the current evidence, the traditional Mediterranean-type diet, including plant foods and emphasis on plant protein sources provides a well-tested healthy dietary pattern to reduce CVD. (J Am Coll Cardiol 2015;66:1590–614) © 2015 by the American College of Cardiology Foundation.

There is much controversy surrounding the optimal diet for cardiovascular health. Data relating diet to cardiovascular diseases (CVDs) has predominantly been generated from high-income countries (HIC), but >80% of CVD deaths occur in low- and middle-income countries (LMIC). Relatively sparse data on diet and CVD exist from these countries though new data sources are rapidly emerging (1,2). Noncommunicable diseases are forecasted to increase substantially in LMIC because of lifestyle transitions associated with increasing urbanization, economic development, and globalization. The Global Burden of Disease study cites diet as a major factor behind the rise in hypertension, diabetes, obesity, and other CVD components (3). There are an estimated >500 million obese (4,5) and close to 2 billion overweight or obese individuals worldwide (6). Furthermore, unhealthy dietary patterns have negative environmental impacts, notably on climate change.

Poor quality diets are high in refined grains and added sugars, salt, unhealthy fats, and animal-source foods; and low in whole grains, fruits, vegetables, legumes, fish, and nuts. They are often high in processed food products—typically packaged and often ready to consume—and light on whole foods and freshly prepared dishes. These unhealthy diets are facilitated by modern food environments, a problem that is likely to become more widespread as food environments in LMIC shift to resemble those of HIC (5,7,8).

In this paper, we summarize the evidence relating food to CVD, and the powerful forces that underpin the creation of modern food environments—what we call the global food system—to emphasize the importance of identifying systemic solutions to diet-related health outcomes. We do this in the context of increasing global attention to the importance of improving food systems by the international development and nutrition community (9–11). Although the "food system" may seem remote to a clinician sitting in an office seeing a patient, its impact on the individuals they are trying to treat are very real. This paper is on the basis of a World Heart Federation international workshop to review the state of knowledge on this topic. This review of diet, dietary patterns, and CVD is not on the basis of new systematic reviews or meta-analyses but represents a careful review of many published meta-analyses, seminal primary studies, and recent research by the scholars who participated in the Consensus conference.

This paper presents: 1) an overview of the development of the modern, globalized food system and its implications for the food supply; 2) a consensus on the evidence relating various macronutrients and foods to CVD and its related comorbidities; and 3) an outline of how changes to the global food system can address current diet-related public health problems, and simultaneously have beneficial impacts on climate change.

THE CHANGING FOOD SYSTEM AND FOOD SUPPLY AND IMPLICATIONS FOR DIETS AND THE ENVIRONMENT

THE DEVELOPMENT OF THE MODERN, GLOBALIZED FOOD SYSTEM.
Food systems were once dominated by local production for local markets, with relatively little processing before foods reached the household (Online Appendix, Box 1) (12). In contrast, the modern
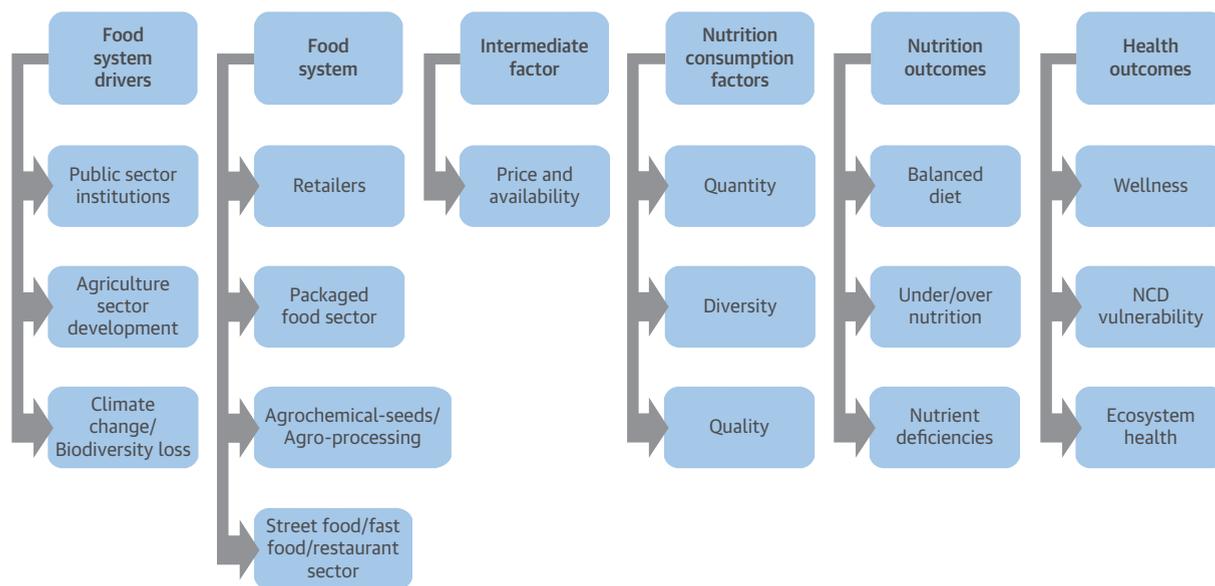
ABBREVIATIONS AND ACRONYMS

CHD = coronary heart disease

CI = confidence interval

CVD = cardiovascular disease

GI = glycemic index

GL = glycemic load

HDL-C = high-density lipoprotein cholesterol

HIC = high-income countries

LDL-C = low-density lipoprotein cholesterol

LMIC = low- and middle-income countries

MI = myocardial infarction

OR = odds ratio

RCT = randomized controlled trial

RR = relative risk

SSB = sugar-sweetened beverage

T2DM = type 2 diabetes mellitus

FIGURE 1   Food System Impact on Nutrition-Related NCDs

Source: revised version of Nugent, 2011 "Bringing Agriculture to the Table" Chicago Council on Global Affairs. NCD = noncommunicable disease.

food system is characterized by a global web of interactions between multiple actors from farm to fork, geared toward maximizing efficiency to reduce costs and increase production (**Figure 1**). The major actors who control this system have changed dramatically in HIC and LMIC, as described subsequently (13).
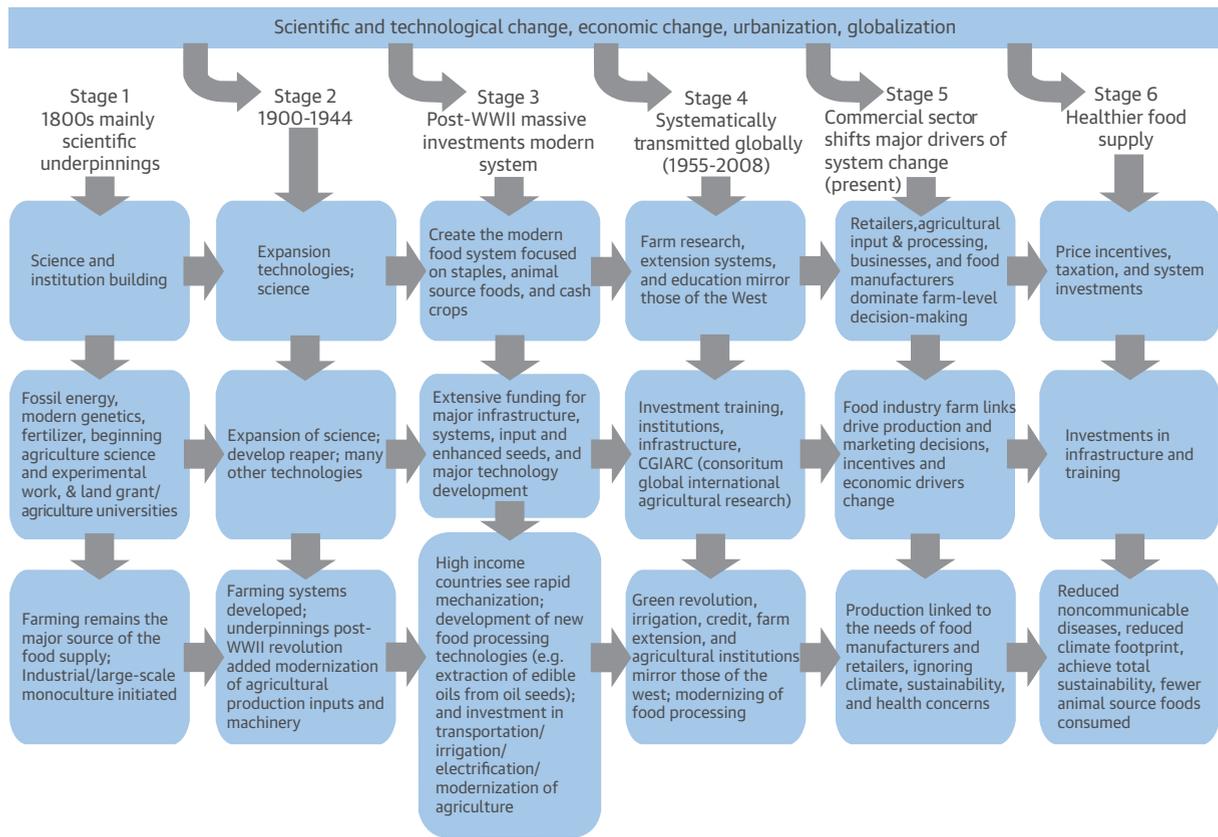
The shift to a global food system started in the United States and other high-income industrialized countries, and was driven initially by government investment and intervention in markets, infrastructure and research intended to raise farm-sector productivity. Building on actions taken in the late 19th century (14), policies on agricultural research and supporting on-farm production introduced in the period from 1930 to 1960 in the United States (14) and Europe focused on few major crops, particularly grains (e.g., wheat, corn, rice), oilseeds (e.g., soybeans), livestock (e.g., pigs, poultry, cattle), and critical cash crops, especially sugar cane and other sources of sugar (15-18). State intervention in most LMIC took a different form, such as policies to subsidize food, taxes on agricultural products, and systems to control the supply and marketing of key commodities (19-22). The 1960s also saw the start of significant agricultural transformation in LMIC, with the "Green Revolution," which focused on increasing productivity of corn, rice, and wheat.

These investments and changes in production systems were designed to make calories from staples (e.g., wheat, corn, rice) cheaply available, in order to simultaneously address hunger in LMIC and national food insecurity in HIC (23). In addition to vastly increasing the calorie supply, the ensuing productivity boom also provided the basis of cheap feed for livestock and cheap inputs for processed foods, in turn creating incentives for the growth of manufacturers of processed foods (24). This coincided with huge technological innovations in food processing, (24-28), the rise of mass marketing to persuade consumers to eat more, supermarket retailing, and fast food (29,30). As a result of these changes, the transformation of raw commodities into food and the distribution of consumable food items beyond the farm gate has become far more important (31). Today, integration and control of our farm-to-fork food supply by major agribusinesses, food manufacturers, retailers, and food service companies is more the rule than the exception (13). Meanwhile, production of less processed foods such as coarse grains (e.g., millet, sorghum), roots, tubers, and legumes has declined (32,33) whereas animal source food production has grown dramatically (34).

Figure 2 sets out the stages of change involved in leading to this modern food system. This model has spread unevenly to most LMIC (35-37). Many countries retain various forms of state intervention in agriculture and food systems (18,38-41), but policies to liberalize trade and private sector investment have

FIGURE 2 Stages of Global Agricultural System Development

Source: © (copyright) Barry M. Popkin, 2015.

revolutionized the entire sector in many regions (13,42). Retailing has been transformed in LMIC through the growth of supermarkets (18,38-41). Although this process originated with companies in industrialized countries looking for growth in foreign markets, companies based in LMIC are now also investing back into HIC.

DIETARY IMPACTS. The way people eat has changed greatly across the globe; moreover, the pace of change in LMIC is quickening. Snacking and snack foods have grown in frequency and number (43-48); eating frequency has increased; away-from-home eating in restaurants, in fast food outlets, and from take-out meals is increasing dramatically in LMIC; both at home and away-from-home eating increasingly involves fried and processed food (47,49); and the overall proportion of highly processed food in diets has grown (50,51).

These changes in the global food system coupled with these food behavior shifts have enabled some critical changes to the global food supply, all with dietary implications. First is the shift to refined

carbohydrates—refined grains and added sugars. Rapidly increasing production of starchy staples combined with processing technologies mean that refined flour is increasingly dominant in diets. White bread, for example, once rarely consumed in Latin America, became widespread after the introduction of high-yield wheat varieties. In Asia, white rice became dominant as a staple over legumes and coarse grains, with a more recent trend being rapidly rising consumption of instant noodles as a staple (52,53). Since 1964, average total carbohydrate intake in the United States has increased from about 375 g/day to 500 g/day (from 2 to 6 kg/year of ready-to-eat cereals), but the percent of carbohydrate that is fiber has not substantially changed over this time, reflecting increased refined carbohydrates and sugar-sweetened beverages (SSBs) is high in HIC (54). In the period from 1985 to 2005 extensive added sugar intake occurred across HIC (55) but more recently large increases have occurred in LMIC, particularly in consumption of SSBs and processed foods (56-59). Today in the

United States packaged and processed food supply, over 75% of foods, have some form of added sugar (60). With urbanization there is some evidence to show that refined carbohydrate consumption is increasing, whereas consumption of traditional grains (i.e., millet, maize) is decreasing in LMIC (61,62).

A second key change has been the increasing intake of vegetable oils, including processed vegetable oils, and a decline in consumption of animal fats (2,63). This was initially driven by rising production of soybeans in the United States, later in Argentina and Brazil, and then palm oil in East Asia. Oilseeds are now among the most widely traded crops, and are also processed to create margarines and vegetable shortenings and into partially hydrogenated fats and bleached deodorized oils for use in processed foods (Online Appendix, Box 2). Between 1958 and 1996, a major global shift occurred in the amount and types of available fats, with soybean, palm, and rapeseed/canola oils replacing butter, tallow, and lard. From 1958 to 1962, soybean, palm, and rapeseed/canola oils represented 20% of the 29 million metric tons of fat produced globally per year, whereas butter, lard, and tallow represented 37%. By 1996 to 2001, these oils accounted for 52% of the 103 million metric tons of fat produced globally per year, whereas butter, lard, and tallow contributed 20% (64). This has implications for consumption of fatty acids. Palm oil (deodorized) has become an increasing source of saturated fatty acids; and partially hydrogenated fats are the main source of trans fatty acids. Between 1990 and 2010, global saturated fat, dietary cholesterol, and trans fat intakes remained stable (trans fats going down in HIC and up in LMIC), whereas n-6, seafood n-3, and plant n-3 fat intakes each increased (65). Vegetable oil consumption remains 2 times higher in HIC than in LMIC. However, trans fat consumption is very high in many LMIC although decreasing markedly in HIC. In India, for example, vanaspati, a vegetable ghee used in bakery products, fried snacks, and foods sold by street vendors, is a leading source of trans fats, as is bakery shortening. In 75 countries representing 61.8% of the world's adult population, global saturated fat consumption was ∼9% of energy; though considerable variation existed across countries (range 2% to 28%). Country-specific omega 6 consumption ranged from ∼1% to 13% (global mean: 6%) of energy; trans fat consumption ranged from ∼0.2% to 6.5% (global mean: 1%) of energy; dietary cholesterol consumption ranged from ∼97 to 440 mg (global mean: 228 mg) per day; seafood n-3 ranged trans fat from ∼35 to 3,886 mg (global mean: 163 mg) per day; and plant n-3 ranged from <∼100 to 5,542 mg (global mean: 1,371 mg) per day (65).

A third key change has been the increasing global consumption of meat, which has been made economically feasible by subsidized production of crops for animal feed—most importantly corn and soybeans (soybean oil is a byproduct of soymeal production for animals) (66-69). At very low levels of intake animal food consumption may not induce harm, providing high-quality protein and iron, whereas excess animal food intake in HIC may be linked to adverse health outcomes, particularly from processed meats (70). Meat consumption has increased considerably worldwide, and there is substantially greater production of meat in HIC than in LMIC (71). North and South America, Europe, and Australia/New Zealand have the highest meat intake, whereas Asia and Africa have the lowest (72,73). Processed meats (which refers to post-butchering modifications of foods such as curing, smoking, or addition of sodium nitrate), account for 35.8% of all meat consumed in HIC (unpublished data from the PURE [Prospective Urban and Rural Epidemiological] study) (71).

Dietary consumption patterns of other protein sources have been mixed. Between 1973 and 1997, dairy consumption per capita (kilograms) increased in LMIC by ∼48% and is projected to almost double (93% increase) by 2020. On average, fish consumption is 2 to 3 times higher in HIC than LMIC (74), although with marked heterogeneity within income categories. China has the highest per-capita consumption of fish in the world, followed by Oceania, North America, and Europe (74). Globally, although there has been little or no increase in sea fish consumption *per capita* since the 1960s, catches per year have risen exponentially (75) and freshwater fish intake has increased during this time (71). Eggs are similarly consumed in higher quantities (2 to 6 times per week) in HIC relative to LMIC, with a 14% decline in consumption in HIC observed between 1980 and 2000, and no change was observed in LMIC (76). The consumption of legumes declined in the United States from 1960 and into the 1980s, with reduced consumption patterns observed globally (8). Relatively, HIC such as Canada, the United States, and Western Europe, tend to consume the lowest quantities of legumes per capita in the world, whereas LMIC within Africa and India consume the greatest quantities of legumes, along with certain South American countries where beef is uncommon, such as Colombia and Peru (77-79). Globally, pulse consumption has decreased since 1961, from ∼9.5 kg/person/year in 1961 to 6.5 kg/person/year in 2006. In LMIC countries pulses contributed ∼4% of energy to the diets, and just 1% of energy to diets of HIC (80).

Total production of tree nuts in 2012 was 3.5 million metric tons, a 5.5% increase from 2011. World consumption of tree nuts in 2011 exceeded 3 million metric tons (81).

A fourth key change is the marked growth of purchases of all packaged foods and beverages (all categories of processing). This process is accelerating across all LMIC markets (13,82,83). For example, 58% of calories consumed by Mexicans come from packaged foods and beverages, which is similar throughout the Americas (83) and even within the United States (66%) (65,84). The proportion for China is 28.5% and rising rapidly (36,82,83). The component of snack foods that is "ultra-processed" (i.e., ready to eat) varies depending on the method of measurement but is increasing wherever it is studied at all income levels (50,85,86). The shift to ultra-processed foods has not just affected the food available for consumption but also the way food is consumed (87). The way people eat has changed greatly across the globe and the pace of change is quickening. Snacking and snack foods have grown in frequency and number (43-48); eating frequency has increased; away-from-home eating in restaurants, in fast food outlets, and from take-out meals is increasing dramatically in LMIC; both at home and away-from-home eating increasingly involve fried and processed food (47); and the overall proportion of highly processed food in diets has grown (50,51).

A fifth trend noted previously in relation to the added sugar change is the shift in the way LMIC are experiencing a marked increase in added sugar in beverages. In the 1985 to 2005 period extensive added sugar intake occurred across HIC (55) but more recently large increases have occurred in LMIC, particularly in consumption of SSBs and ultra-processed foods (56-59). Today in the U.S. packaged and processed food supply, >75% of foods have some form of added sugar (60).

In addition, fruit and vegetable intake has remained inadequate. Fruit and vegetable consumption is substantially higher in HIC compared with LMIC (88). Analysis of 52 LMIC countries taking part in the World Health Survey (2002 to 2003) (89) found that low fruit and vegetable consumption (i.e., <5 fruits and vegetables per day) prevalence ranged from 36.6% (Ghana) to 99.2% (Pakistan) for men and from 38.0% (Ghana) to 99.3% (Pakistan) for women. Overall, 77.6% of men and 78.4% of women consumed less than the minimum recommended 5 daily servings of fruits and vegetables. In the United States, 32.6% of adults consumed fruit 2 or more times per day and 27.2% ate vegetables 3 or more times per day (90). In 2012, 40.6% of Canadians 12 years of age and older,

reported consuming fruits and vegetables 5 or more times per day (91).

Although all of these changes across LMIC display great heterogeneity (92), the global food system has clearly reached all corners of the LMIC urban and rural sector and major shifts in diets appear to be accelerating.

IMPLICATIONS FOR ENVIRONMENTAL IMPACTS. The modern food system is a major force in a range of serious environmental problems, including climate change (as a leading source of greenhouse gas emissions, including carbon dioxide, methane, and nitrous oxide), the loss of biodiversity, the strain on freshwater resources, and the release of persistent toxins, excess nitrates and phosphates (from fertilizer and concentrated livestock operations, causing widespread problems of eutrophication), and animal pharmaceutical residues into waterways (12,93-95).

The major causes are beef and other large animals for greenhouse gas and the metabolic losses associated with shifting the product of nearly one-third of the world's arable land to concentrated animals, which effectively magnifies the resource budgets and pollution loads of industrial monocultures (34). The expansion of low-input agriculture and extensive ranching are also major factors in deforestation, which bear heavily on both climate change (as carbon is released from vegetation and soils and sequestration capacity diminishes) and biodiversity loss.

In addition to being a major force in many environmental problems, world agriculture is also extremely vulnerable to climate change, biodiversity loss, declining freshwater availability, and the inevitable limits of nonrenewable resources (e.g., fossil energy, high-grade phosphorous) although vulnerability is highly uneven on a world scale (96). Many of the world's poorest-regions are poised to be most adversely affected by rising average temperatures, aridity, and water stress, as well as through increasingly severe extreme weather events such as drought or flooding; in fact some believe this is already occurring (97-99).

It is also noteworthy that the Food and Agriculture Organization of the United Nations estimates that one-third of all food produced for human consumption globally is wasted before it is consumed, which has both social and environmental costs that have been precisely measured in the United States (100-102). Waste affects the entire food system from production to post-harvest (including inside the home) (102). Hall et al.'s (101) estimate of home food waste of about 1,400 kcal/capita for the United States adds up to 25% to 45% waste of total food for some HIC.

MACRONUTRIENTS, FOODS, AND CVD RISK FACTORS

CARBOHYDRATES. Refined carbohydrates. *CVD Risk Factors.* U.S. ecological evidence demonstrates an association of refined carbohydrate (such as corn syrup) with type 2 diabetes mellitus (T2DM) and obesity (54). Robust data from systematic reviews and high-quality randomized controlled trials (RCTs) support a harmful effect of highly refined, high–glycemic load (GL) carbohydrates. A meta-analysis of observational studies indicated that high-glycemic index (GI) foods are associated with T2DM (103). Proof-of-concept studies have used alpha-glucosidase inhibitors, such as acarbose, to lower the GI of the foods consumed; for example, in the STOP-NIDDM (Study to Prevent Non-Insulin-Dependent Diabetes Mellitus) trial, acarbose reduced progression to T2DM by 25% compared with placebo (104). T2DM risk in individuals with the highest GL and lowest cereal fiber is 2.5-fold that of those with the lowest GL and highest cereal fiber diet (105). A large Danish prospective cohort study of the impact of replacing saturated fats with high-GI carbohydrates found that when high-GI carbohydrates replace saturated fat, myocardial infarction (MI) risk increases 33% (106). A meta-analysis of 10 prospective cohort studies (n = 296,849) (107) found increased GL associated with a 27% increased coronary heart disease (CHD) and MI risk (108). In controlled-feeding studies, replacing saturated fat with carbohydrates lowers low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) and increases triglycerides (109). Dietary interventions that raise HDL-C may not necessarily translate into CVD risk reduction, as serum HDL-C has recently been called into question regarding its role in the causal pathway of CVD (110). However, in a 5-week controlled-feeding trial of 163 generally healthy but overweight adults, low compared with high-GI diets did not improve insulin sensitivity, lipid levels, or systolic blood pressure in the context of a healthy, DASH (Dietary Approaches to Stop Hypertension)-like dietary pattern, and a low compared with high-GI diet increased LDL-C when the carbohydrate content of the diet was high (109). This study suggests that the adverse effect on CHD risk may not be mediated by short-term effects on classical risk factors, but that post-prandial hyperglycemia and hyperinsulinemia or hyperlipidemia may play a mediating role; further work is needed to clarify the effect of the GI on LDL-C and related lipid risk factors.

LMIC. Highly refined carbohydrates include polished white rice, cornstarch, and white wheat flour with reduced fiber content. Carbohydrate refinement is common in HIC and increasing in LMIC (111,112). Traditional diets in LMIC, once rich in whole grains and dietary fiber, now include highly refined carbohydrates, such as polished white rice and refined flours. In East Asian countries, white rice consumption is associated with a 55% higher T2DM risk (111,112). In the cross-sectional CURES 57 (Chennai Urban Rural Epidemiology Study 57) study, higher refined grain intake was associated with higher waist circumference, systolic and diastolic blood pressure, fasting glucose, triglycerides, and insulin resistance and lower HDL-C levels (61). Replacing white with brown rice (50 g/day) reduced T2DM risk by 16% (113), and substituting beans for white rice reduced the odds of metabolic syndrome by 35% (108). However, a 16-week randomized trial of replacing white with brown rice in middle-aged Chinese men and women with or at high risk for T2DM only improved HDL-C and reduced diastolic blood pressure in the brown rice group. Data from the international PURE study (138,926 individuals in 628 communities in 17 countries) suggest a need to consider the context and availability of specific foods before making food choice recommendations (114). Increasing whole grain and cereal fiber consumption whereas decreasing total and high-GI carbohydrate are helpful strategies to prevent T2DM and CVD in the general population (115). Furthermore, low-GI diets improve glycemic control and serum lipids in RCTs of participants with T2DM with major implications for CHD risk reduction in this vulnerable segment of the population whose numbers are increasing rapidly globally (116–119).

Sugar-sweetened beverages. *SSB and Cardiovascular Risk Factors.* SSB consumption accounts for up to 50% of added sugar in the American diet (120,121). The epidemiological relationships between SSB consumption, overweight, obesity, hypertension, and T2DM are strong (122). In a meta-analysis of prospective studies of SSB and hypertension, CHD, and stroke, the relative risk (RR) for a 1-serving increase in SSB/day was 1.17 (95% confidence interval [CI]: 1.10 to 1.24) for CHD and 1.08 (95% CI: 1.04 to 1.12) for incident hypertension, but no clear effect was seen for total stroke (RR: 1.06; 95% CI: 0.97 to 1.15) (123). A meta-analysis of 7 cohort studies and 5 RCTs found SSBs increased weight by 0.12 kg/serving/year (95% CI: 0.10 to 0.14) in adults (124). A World Health Organization systematic review reported similar positive associations (125). In a pooled analysis of NHS (Nurses' Health Study) and HPFS (Health Professionals Follow-up Study) data, a 1 SSB serving/day increment is associated with a 1 kg weight gain over a

4-year period (126), possibly due to incomplete compensation for this energy at other meals. After adjusting for important potential confounders, including body mass index, ≥1/day versus <1 SSB/month increased T2DM by 39% (127). A meta-analysis of 310,819 participants and 15,043 cases of T2DM reported a 26% increased T2DM risk among those consuming 1 to 2 SSB servings/day compared with nonconsumers (128). A meta-analysis of 4 cohort studies reported a linear association between SSB and hypertension risk (RR) of 1.08 (95% CI: 1.04 to 1.12) per serving per day (129). The Framingham Offspring Study reported a 22% higher incidence of hypertension among those consuming ≥1 SSB serving/day compared with nonconsumers (130). A potential explanation of the SSB-T2DM association is the high content of rapidly absorbed sugar from corn syrup, which increases blood glucose and insulin and de novo lipogenesis—which may contribute to pancreatic beta cell dysfunction and eventually T2DM (131). In the NHANES III (National Health and Nutrition Examination Survey III) study, with 831 CVD deaths during 163,039 person-years of follow-up, consumption of ≥7 SSB servings/week was associated with a 29% increased CVD mortality risk compared with <1 serving/week (120), with no increased risk up to 6 drinks/week. Few studies have investigated the association between SSBs and CVD events. Those that have, report increased CHD and stroke risk with SSB consumption. A 2015 meta-analysis reported an RR for incident CHD of 1.17 (95% CI: 1.10 to 1.24) per serving per day increase in SSB consumption (129). Both the HPFS and the NHS find an approximate 20% increased CHD risk in the highest category of SSB consumption compared with the lowest category (132,133); and, after adjusting for dietary and nondietary cardiovascular risk factors, a 16% increased stroke risk (134). Similarly, 2 Swedish prospective cohort studies in women and men reported a RR of 1.19 (95% CI: 1.04 to 1.36) for stroke among those consuming ≥2 SSB servings/day (135).

LMIC. Facing health concerns, the beverage industry is shifting from full-calorie carbonated soft drinks to lower-calorie carbonated soft drinks, coffees, and teas. According to the NHANES study, between 1999 and 2006 the average U.S. full-calorie carbonated soft drink intake decreased, whereas intake of diet carbonated soft drinks, low-calorie fruit drinks, and other sweetened beverages increased (122). These products will gradually enter the markets in China, Brazil, and other LMIC. However, there are practically no data on the effects of SSBs on health outcomes from LMIC (136,137).

FATS AND OILS. CVD risk factors. Vegetable oils that are primarily comprised of mono- (e.g., olive oil) and polyunsaturated fatty acids appear to reduce CHD risk, and sources of the n-3 polyunsaturated fat alpha-linolenic acid, such as rapeseed or canola oil, are cardioprotective. Replacing saturated fat with monounsaturated or polyunsaturated fat reduces LDL-C and preserves HDL-C (109). Further, canola oil, as part of a low-GI diet, improves glycemic control and blood lipids in T2DM (138). Trans fatty acids increase CHD risk compared with other macronutrients, with strong evidence of adverse effects of small amounts of trans fats on lipids (109,139) and CVD risk (140,141).

Though total fat (142), and specifically saturated fats, have generally been considered to be deleterious to insulin sensitivity (143), in large cohort studies, saturated fat is not associated with development of T2DM, after adjustment for body mass index, total dietary fiber, or magnesium intake (144–149). Macronutrient exchange generally does not influence markers of glucose homeostasis, though in 2 relatively large trials, replacing saturated fat with either monounsaturated fat or carbohydrate improved indices of glucose homeostasis (150,151). Associations have been seen between major food sources of saturated fat, such as red and processed meat, and development of T2DM (152,153), though dairy products, notably fermented dairy, may be protective (154,155).

CVD. Saturated fats have not been consistently associated with CVD in meta-analyses of cohort studies (odds ratio [OR]: 1.07; 95% CI: 0.96 to 1.19) of higher compared with lower intakes (156). However, in most of these studies the association of high saturated fat intake largely represents replacing highly refined carbohydrates. Replacing saturated fat with highly refined carbohydrate is not associated with lower CHD risk, whereas replacing saturated fat with polyunsaturated fat reduces CHD risk (157,158). This benefit of polyunsaturated fat includes the primary n-6 polyunsaturated fatty acid, linoleic acid (158,159). Replacing saturated fat with high-GI carbohydrate increases MI risk by 33%, whereas replacing with low- and medium-GI carbohydrates appears neutral (106). Emerging evidence suggests that the effect of a saturated fat on CHD may depend on the type of fatty acid and the specific food source (i.e., dairy vs. meat) (160,161). Consumption of nonhydrogenated vegetable oils appears to be superior to consumption of animal fats (162). Consumption of plant oils in a Mediterranean diet reduced CVD in 2 RCTs. The Lyon Diet Heart Study found regular consumption of alpha-linolenic acid (canola oil) significantly reduced

cardiac deaths and nonfatal CHD (163), whereas the PREDIMED (Prevención con Dieta Mediterránea) RCT found that a Mediterranean diet (50 g/day extra virgin olive oil) reduced CVD events by 30% over a 5-year period (164).

Palm oil is the dominant fat globally and is relatively high in saturated fat. On the basis of controlled-feeding studies examining changes in blood lipids, replacing palm oil with unsaturated fatty acids would be expected to lower CHD risk (109), but palm oil would be preferred to partially hydrogenated oils high in trans fatty acids. Few studies have directly compared palm oil with other oils for CHD risk. One large case-control study in Costa Rica found that soybean oil consumption was associated with lower acute MI risk compared with palm oil consumption (165).

Summary of fats and oils. Compared with saturated fat, vegetable oils rich in polyunsaturated fats reduce the TC:HDL-C (total cholesterol:HDL-C) ratio and CHD incidence; inclusion of n-3 fatty acids (alpha-linolenic acid) with the vegetable oils is important for CHD prevention. The effect of replacing saturated fat with carbohydrate on CHD risk appears to depend on the quality of the carbohydrate. Prospective studies consistently indicate adverse effects of trans fats on CHD. Effects of monounsaturated fat from plant sources require further study; extra virgin olive oil appears to reduce CVD.

PROTEIN SOURCES. Meats. *Nutrients and CVD Risk Factors.* Meat is rich in protein, iron, zinc, and B vitamins, but can also contain significant amounts of cholesterol and saturated fatty acids, which raise LDL-C and lower triglyceride (157). A high red meat intake (rich in heme iron), increases endogenous formation of *N-nitroso* compounds in the gastrointestinal tract that are associated with increased epithelial proliferation, oxidative stress, and iron-induced hypoxia signaling (166-168).

In a meta-analysis of 17 cohort studies (16 from Western countries), consumption of red and processed meat increased T2DM and CHD risk, but few included studies examined unprocessed red meat (169). Intake of red or processed meat was not associated with stroke, but only 3 studies evaluated these relationships (169). In more recent analyses, red meats, particularly processed red meats, were associated with increased CVD, CHD, stroke, and cancer mortality, whereas poultry was not (170-172). Potential mechanisms linking unprocessed red meat with CVD include saturated fat, cholesterol, iron, phosphatidylcholine, and carnitine; and cooking methods (e.g., barbecuing), that increase heterocyclic amine content and *N-nitroso* compounds, also implicated in colorectal cancer (167). The evidence suggests that processed meat consumption increases CHD risk, whereas unprocessed meat consumption has a small or no association with CHD, mainly when compared with refined starch and sugar. Both unprocessed and processed red meats are associated with greater CVD risk compared with poultry, fish, or vegetable protein sources. Both types of meat are associated with higher T2DM risk, although gram for gram the effect size is notably larger for processed meats.

LMIC. Data relating meat consumption to CVD risk in LMIC is limited. A recent pooled analysis of data from 296,721 individuals from Asian countries (i.e., Bangladesh, mainland China, Japan, Korea, and Taiwan) found no association between red meat and poultry consumption and CVD, cancer mortality, or all-cause mortality (173). Red meat intake is generally much lower in these areas than in HIC however, and current consumption does not likely reflect long-term patterns.

Dairy. *CVD Risk Factors.* The consumption of dairy products has been associated with weight loss in small studies (174), but the overall published data does not confirm an important effect on body weight. However, increased low-fat dairy consumption is associated with lower LDL-C, triglycerides, plasma insulin, insulin resistance, waist circumference, body mass index, possibly blood pressure; and reduced diabetes risk (174-182). In a large meta-analysis of cohort studies (13,000 incident cases), and the EPIC InterAct (European Prospective Investigation into Cancer and Nutrition) case-cohort study (12,000 incident cases), fermented dairy (i.e., yogurt, cheese, and thick fermented milk), but not total dairy, was inversely associated with T2DM (155,183). In a meta-analysis of prospective cohort studies, milk consumption was inversely associated with total CVD in a small subset of studies with few cases, but using a larger body of data with more specific endpoints, milk was not associated with CHD or stroke (173). In a prospective cohort study of 53,387 Japanese men and women, higher dairy calcium (173 mg/day vs. none) reduced risk for hemorrhagic stroke, ischemic stroke, and stroke mortality by ~50% over a 10-year follow-up (184). Collectively, these studies do not suggest a strong or consistent relationship between consumption of dairy products and T2DM and CVD risk.

LMIC. Data on dairy consumption and CVD in LMIC are limited. In a prospective cohort of 2,091 middle-aged Chinese men and women monitored for 6 years, individuals who reported consuming >1 dairy serving/day were 35% less likely to develop

T2DM (RR: 0.65; 95% CI: 0.49 to 0.85) than nonconsumers (185).

Egg. *CVD Risk Factors.* Eggs are a relatively inexpensive and low-calorie source of protein, folate, and B vitamins (186). Eggs are also a source of dietary cholesterol (a medium egg contains approximately 225 mg of cholesterol) (187). A meta-analysis showed that eggs increase TC, HDL-C, and TC:HDL-C (188), but 5 RCTs subsequently reported that egg consumption did not significantly alter these parameters (189-191) or endothelial function (192,193). No RCT has tested the effect of egg consumption on CVD events. In a meta-analysis (194) of 16 prospective cohort studies (90,735 participants) (191), egg consumption was not associated with overall CVD or CHD, stroke, or CHD or stroke mortality; but was associated with T2DM. Overall, consumption of eggs in moderation (1 egg/day) is likely neutral for CVD. However, relative to other protein-rich foods that lower LDL cholesterol, such as whole grains and nuts, eggs would likely increase CVD risk.

LMIC. Unpublished data from 3 large international studies, PURE (Prospective Urban and Rural Epidemiological Study), ONTARGET (Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial), and INTERHEART (a global study of risk factors for acute myocardial infarction), with collectively 200,000 individuals and 22,000 CVD events from regions including China, India, and Africa, show that moderate egg consumption appears to be neutral or protective against CVD. However, significant variations exist across regions, with a benefit of daily egg consumption in China but possible harm in South Asia.

Fish. *CVD Risk Factors.* Fish are a source of protein, vitamin D, multiple B vitamins, essential amino acids, and trace elements; and the long-chain omega-3 (n-3) fatty acids docosahexaenoic acid and eicosapentaenoic acid (195,196), though amounts vary over 10-fold across seafood species. Fatty fish, such as salmon, sardines, trout, white tuna, anchovies, and herring, have the highest concentrations. In clinical trials and meta-analyses of these trials the long-chain omega-3 polyunsaturated fatty acids in fish reduced multiple CVD risk factors, including vascular resistance, blood pressure, inflammation, serum lipids, and endothelial function (197).

Some prospective cohort studies find an inverse association between fish intake and CVD mortality, whereas others do not (198). Available evidence suggests cardiovascular benefits with fish consumption in secondary prevention, but the evidence is inconsistent regarding primary prevention. Possible explanations include differences in the amounts and types of fish consumed, cooking methods, and background fish consumption. Fifteen of the 16 cohort studies (with 1 exception) (199) were conducted in North America and European countries, where deep-frying fish is common. The DART-1 (Diet and Reinfarction) trials, a secondary prevention trial and DART-2, in men with stable angina, are the only randomized trial of fish intake and CVD outcomes. They arrive at opposite conclusions. In the DART-1 trial, fish lowered all-cause mortality and trended toward reducing CVD events after 2 years (194). In the DART-2 trial oily fish did not affect all-cause mortality or CVD events after 3 to 9 years, and increased sudden cardiac death, largely confined to the subgroup given fish oil capsules (200). Differential behavioral change or CVD stage may explain the discrepancy (201). Follow-up of the DART-1 trial at 5 years also showed increased rates of CVD in the fish/fish oil group that did not persist through the 10-year assessment (202). We know of no primary prevention trial on fish intake and CVD outcomes, but a meta-analysis of fish oil supplement RCTs is neutral (203).

Low-Income Countries and HIC. Most of the data indicating that fish is protective comes from studies in HIC (204-208). Unpublished data from 3 large international studies (PURE, ONTARGET, and INTERHEART) reflect considerable heterogeneity in the association between fish intake and CVD outcomes. In the PURE study fish intake was inversely associated with CVD outcomes in South America, China, North America, and Europe (RR: 0.76 to 0.84) but positively associated in South Asia (RR: 1.97). However, no associations between fish consumption and CVD outcomes were observed in a high-risk secondary population in the ONTARGET study. The INTERHEART study found fish intake beneficial in North America and Europe (RR: 0.73; 95% CI: 0.62 to 0.87) but harmful in the Middle East (RR: 1.59; 95% CI: 1.32 to 1.93). More work is needed in China and India to understand the effects of regional types and preparation methods of fish.

Nuts. *CVD Risk Factors.* In clinical trials nuts improve serum lipids (209-211). In observational studies, nuts lower CHD (196,212,213) and hypertension risk (213); but not stroke (207,213). In 1 meta-analysis of prospective cohorts, nuts were not associated with T2DM (214), but in another, they were protective (207). Despite their high energy density, nuts do not contribute to weight gain, changes in waist circumference, or obesity, perhaps due to their satiating effects and increased fecal energy losses (215,216).

In observational studies (133,217-220) and RCTs (164,221-223), a Mediterranean diet including nuts lowers CVD risk. However, no RCTs have assessed the effects of nut consumption alone on CVD events. Taken together, the published data from observational studies and clinical trials support nuts for lowering CVD risk.

LMIC. Unpublished data from the PURE cohort indicate that nut consumption is very low in LMIC (60% of individuals consume ≤1 nut serving/week). No associations between nut consumption and CVD outcomes are seen at this low level.

Legumes. *CVD Risk Factors.* In observational studies and RCTs consumption of legumes improves CVD risk factors, such as waist circumference, cholesterol, blood pressure, C-reactive protein, glucose; and is protective against T2DM (224-231). A meta-analysis of 26 RCTs (1,037 participants) found that 130 g legumes/day (~1 serving) reduced LDL-C by 0.17 mmol/l (95% CI: -0.25 to -0.09) (228). Legumes also reduce systolic blood pressure (by 2 mm Hg) and lowered mean arterial pressure (231) in a meta-analysis of 8 RCTs. A legume-rich diet reduced HbA1c (-0.3%; 95% CI: -1.4% to -0.1%) in an RCT in participants with diabetes (226).

CVD. In a meta-analysis of 5 observational studies, 100 g of legumes 4 times/week is inversely associated with CHD (RR: 0.86; 95% CI: 0.78 to 0.94) (232). However, that study and another meta-analysis of 8 prospective cohort studies found no association between legumes and diabetes (207) or stroke (232,233). A large prospective study of 2 cohorts of U.S. health professionals found a 45% increased risk of ischemic stroke per daily serving of legumes (RR: 1.45; 95% CI: 1.06 to 2.00) (234). This suggests that although legumes are valuable to reduce CHD risk, more research is required to understand their impact on total stroke risk.

LMIC. In a cohort of Chinese men and women, soy (the primary legume consumed in China) was negatively correlated with TC and LDL-C (235). A population-based cross-sectional study in India found that women consuming legumes once/day were less likely to develop T2DM (OR: 0.55; 95% CI: 0.34 to 0.88; n = 99,574). A similar but nonsignificant trend was observed in men (OR: 0.70; 95% CI: 0.39 to 1.26; n = 56,742) (236). In a prospective cohort study of middle-aged Shanghai women, a ~50 g/day increase in legume consumption over 4.6 years reduced T2DM risk by 38% (RR: 0.62; 95% CI: 0.51 to 0.74) (237). A prospective cohort study of 64,915 Chinese women 40 to 70 years of age (n = 62 cases; follow-up 2 years) found that individuals consuming ≥11.2 g/day of soy

protein were less likely to develop CHD (RR: 0.25; 95% CI: 0.10 to 0.63) than were those consuming ≤4.5 g/day (238).

Summary of major protein sources. Reducing red meats, especially processed meats, and increasing fish, nuts, legumes, and possibly fermented dairy products are likely beneficial. Sustainability issues discussed in this paper must also be addressed specifically in relation to meat, fish, and dairy foods (12,34,239-241).

FRUITS AND VEGETABLES. CVD risk factors. In the DASH RCT, higher intake of fruits and vegetables, either as part of a typical Western diet or the DASH eating plan, reduced blood pressure, TC, LDL-C, and HDL-C without affecting triglycerides (242). A meta-analysis of 3 prospective cohorts (3,415 cases) found high adherence to the DASH eating reduced T2DM risk by 27% (243). A strong evidence base from observational studies indicates that high consumption of vegetables and fruits reduces CHD and stroke (196).

CVD in HIC and LMIC. Large global studies and systematic reviews of prospective cohorts generally support a protective role of fruits and vegetables against CVD (244-246). In the global INTERSTROKE study (3,000 stroke cases and 3,000 control cases), compared with fewer than 1 serving per day, 1 serving of fruit was protective against stroke (OR: 0.61; 95% CI: 0.50 to 0.73), but the benefits were not clear with higher consumption of up to 3 servings/day of vegetables was not (OR: 0.91; 95% CI: 0.75 to 1.10) (244). A meta-analysis of 20 prospective cohort studies (16,981 stroke events) found that fruit and vegetable consumption was associated with decreased stroke risk (RR: 0.79; 95% CI: 0.75 to 0.84 for highest vs. lowest categories), as were fruits (RR: 0.77; 95% CI: 0.71 to 0.84) and vegetables (RR: 0.86; 95% CI: 0.79 to 0.93) separately (245). In unpublished INTERHEART study data a 1-serving/day increase in fruit decreased MI risk by 12% (RR: 0.88; 95% CI: 0.84 to 0.92); a 1-serving/day increase in vegetables decreased MI risk by 5% (RR: 0.95; 95% CI: 0.92 to 0.97). Large meta-analyses of observational studies support a ~5% to 10% reduction in CVD mortality per serving per day (246), and a protective association of green leafy vegetables with T2DM (RR per 0.2 servings/day: 0.87; 95% CI: 0.81 to 0.93) (247). The beneficial effects of fruits and vegetables appear consistent across regions of the world. A major issue has been the lack of success in encouraging increased fruit and vegetable consumption by the citizens of western nations (248).

Overall summary. Increased refined grains, starches, and added sugar (i.e., carbohydrates of lower quality) have paralleled the rise in obesity and T2DM. Collectively, the data support emphasizing low-GI whole grains, legumes, and nuts, fruits, and vegetables and minimizing high-GI refined grains and foods with added sugars, including SSBs (**Table 1**).

DIETARY SODIUM. Sodium is an essential nutrient required for normal physiological function (249-251). Increasing sodium intake well beyond physiological requirements increases blood pressure (241-243) and CVD mortality (95-97). In LMIC sodium sources include table salt and salt additives and spices; whereas processed foods are the primary source in HIC. Sodium consumption has declined slightly in LMIC as refrigeration has replaced salted-preserved foods. Short-term RCTs have reported reductions in blood pressure with reduced sodium intake to <1.5 g/day. Population recommendations for low sodium intake (252-254) (<2.0 g/day) have been achieved in short-term feeding clinical trials (254), but not sustained in longer-term clinical trials (>6 months) (255-257). No RCTs have determined whether low sodium intake reduces CVD events or deaths compared with moderate intake (249). Meta-analyses of CVD event trials did not report a significant reduction in CVD with lower sodium intake, but the included trials were underpowered to detect moderate risk reductions (258). Prospective cohort studies suggest a *J*-shaped association between sodium intake and CVD events, consistent across methods of sodium estimation (259-265). In a recent Cochrane Review (266) of 23 epidemiological studies (n = 274,683), the lowest risk of CVD events and deaths occurs at an intake between 2.7 and 5.0 g/day. PURE study findings (263) are consistent with this evidence, with sodium excretion both >6 g/day and <3 g/day being associated with higher mortality and CVD events compared to 4.00 to 5.99 g/day, despite an overall positive association between sodium excretion and blood pressure (251,263). The increased risk of CVD events with higher sodium intake (>5 g/day) was most prominent in those with hypertension (263). However, methodological issues make studies of sodium intake particularly challenging (267). Additional large appropriately designed observational studies and RCTs are needed to provide further evidence on optimal sodium intake for preventing CVD events (249,268-270).

ALCOHOL. Consumption patterns. Greater amounts of alcohol are consumed *per capita* by adults in HIC (9.6 l/year) than in LMIC (4.1 l/year), or low-income countries (3.1 l/year), although this may be an underestimate in LMIC and low-income countries due to the use of homemade or unsafe alcohol products (e.g., industrial or medical) (271). In the PURE study, 31% of participants identified as current drinkers, with considerable variation across income regions (13% to 80%). In all regions, men were more likely to be current drinkers than were women (272).

CVD risk factors. In a meta-analysis of randomized controlled intervention studies of 2 to 8 weeks' duration (273), moderate alcohol consumption (up to 1 drink or 15 g/day in women; or up to 2 drinks or 30 g/day in men) compared with no alcohol: raised HDL-C, Apo-A1, and adiponectin, and reduced LDL-C and fibrinogen. Total cholesterol, triglycerides, and lipoprotein (a) were not significantly affected. Results stratified by beverage type (wine/beer/spirits) were similar to the pooled analyses. The changes in lipid and hemostatic risk factors align with lower cardiovascular risk.

CVD. The EPIC (European Prospective Investigation on Cancer and Nutrition) study monitored 380,395 participants for 13 years (4,187 CVD deaths) (274). Female never-drinkers were at increased risk of CVD death (RR: 1.31; 95% CI: 1.13 to 1.53) compared with moderate drinkers (0.1 to 4.9 g/day); but the association was not significant for male never-drinkers (RR: 1.20; 95% CI: 0.89 to 1.62). In a dose-response meta-analysis of 24 prospective cohort studies (275), the association of drinking with CHD was *J*-shaped: nondrinkers were at slightly increased risk; in men the greatest protection was at 31 g/day with a trend for increased risk beginning at 63 g/day; for women, the greatest protection was at 11 g/day with a trend for increased risk beginning at 14 g/day. In a meta-analysis of 27 prospective studies of alcohol and stroke, no association was found between light or moderate alcohol use and stroke, but heavy alcohol use (>45 g/day) was shown to increase total stroke risk (RR: 1.20; 95% CI: 1.01 to 1.43), particularly hemorrhagic stroke (RR: 1.29 ; 95% CI: 0.98 to 1.71) (275). Patterns of alcohol consumption may be a particularly important determinant of the magnitude of the association—in a meta-analysis of 10 prospective cohort and 4 case-control studies, irregular "binge" drinking (>60 g of pure alcohol or ≥5 drinks per occasion at least monthly) increased CHD risk by 45% (RR: 1.45; 95% CI: 1.24 to 1.70) (276). In summary, small and inconsistent cardiovascular benefit is seen in moderate drinkers, but a strong increase in CVD and stroke risk is seen with regular heavy alcohol consumption and binge drinking.

LMIC. In HIC/upper middle income countries in the PURE study (272), current drinking was protective against MI, but not in low-income countries/LMIC (p = 0.02 for interaction); a similar trend was seen for

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Diet, Cardiovascular Disease, and the Food System

TABLE 1 Summary of Evidence of Associations Between Major Foods and Cardiovascular Disease

Food	HIC			LMIC			Sustainability
	Definitely Known	Suggested	Strength of Evidence	Definitely	Suggested	Strength of Evidence	
Refined carbohydrates (solid foods)	Refined, high-glycemic carbohydrates are associated with T2DM and CHD.	Refined, high-glycemic carbohydrates adversely affect the lipid profile.	High (SRMA of both RCT and prospective cohorts).	None.	Refined, high-glycemic index carbohydrates are associated with T2DM, markers of central adiposity, blood pressure, insulin, and lipids.	Moderate (cross-sectional, RCT).	Moderate.
Sugar-sweetened beverages	Excessive sugar-sweetened beverage consumption is associated with CVD mortality, stroke, obesity, hypertension, and T2DM.	None.	High (SRMA of both RCT and prospective cohorts).	None.	None.	Absent.	Low.
Saturated fats	None.	Replacement of saturated fats with unsaturated plant fats or low-glycemic carbohydrates reduces the risk of cardiovascular disease, and reduces LDL-C, without adversely affecting HDL-C.	High (SRMA of both RCT and prospective cohorts).	None.	None.	None.	Low; higher saturated fat from palm oil is unsustainable.
Trans fatty acids	Replacement of trans fatty acids with unsaturated plant fats or low-glycemic carbohydrates reduces the risk of CVD, and reduces LDL-C, without adversely affecting HDL-C.	None.	High (SRMA of both RCT and prospective cohorts).	None.	None.	None.	Low.
Unsaturated fatty acids (MUFA, PUFA)	Diets higher in unsaturated plant fats (monounsaturated and polyunsaturated fats from plants and fish) reduce risk of CVD, and improve the lipid profile.	None.	High (SRMA of both RCT and prospective cohorts).	None.	None.	None.	Low.
Red and processed meat	Red and processed meats are associated with CHD and T2DM.	Red and processed meats are associated with stroke.	Moderate (SRMA of prospective cohorts).	None.	No association between red meat consumption and CVD in LMIC.	Low (1 pooled analysis).	Very high; meat production is harmful to the environment.
Dairy	None.	Higher low-fat and fermented dairy products are inversely associated with CVD, blood pressure, and improved serum lipids.	Moderate (SRMA of both RCT and prospective cohorts).	None.	Consuming dairy is associated with reduced risk of T2DM.	Low (single prospective cohort).	Very high; cow's milk production is harmful to the environment and resource-intensive.
Eggs	None.	Consuming <7 eggs per week does not increase risk of CVD, nor do they affect the lipid profile.	Low (SRMA of prospective cohorts, SRMA of RCTs on lipids).	None.	Moderate egg consumption appears protective against CVD.	Low (unpublished case-control data from 3 large international studies).	Moderate.

Continued on the next page

TABLE 1 Continued

Food	HIC			LMIC			Sustainability
	Definitely Known	Suggested	Strength of Evidence	Definitely	Suggested	Strength of Evidence	
Fish	None.	Long chain omega-3 fats from fish reduce multiple CVD risk factors.	Low (SRMA of prospective cohorts, large RCTs that conflict).	None.	There is considerable heterogeneity in the association between fish and CVD outcomes.	Low (unpublished case-control data from 3 large international studies).	Sustainability of fish is challenging.
Nuts	Many varieties of nuts show beneficial effects on LDL-C, the LDL-C:HDL-C ratio, TC, and triglycerides; and nuts reduce CHD risk and hypertension, but not stroke.	Nuts may reduce risk of T2DM.	High (SRMA of both RCT and prospective cohorts).	None.	Nuts are not associated with CVD outcomes.	Weak (single observational study).	Sustainable alternative protein source to meat.
Legumes	Legumes show beneficial effects on LDL-C, the LDL-C:HDL-C ratio, TC, and triglycerides; and legumes reduce CHD risk and hypertension, but not stroke.	Legumes reduce CHD risk, but not stroke risk.	High (SRMA of both RCT and prospective cohorts).	None.	Legume consumption reduces risk of CHD and T2DM.	Weak (small number of prospective cohort studies, cross-sectional association).	Sustainable alternative protein source to meat.
Fruits and vegetables	Diets high in fruits and vegetables reduce blood pressure, TC, LDL-C, and HDL-C and protect against CVD.	None.	High (SRMA of both RCT and prospective cohorts).	None.	Protective role of fruits and vegetables against CVD.	Weak (small number of prospective studies).	Sustainable source of carbohydrate energy and micronutrients.
Sodium	None.	Lower sodium diets reduce blood pressure, but the association between lower sodium and CVD is unclear.	Low (conflicting observational and RCT data).	None.	Excessive or low-sodium diets are associated with CVD.	Low (single multicountry study).	Low.
Alcohol	Compared with nonalcoholic beverages, alcoholic beverages raise HDL-C.	Compared with not drinking, moderate drinking (up to 5 g alcohol/day) may reduce risk of CVD; but higher intakes (>30 g/day and above) increase risk of hemorrhagic stroke and cancers.	Low (SRMA of both RCT and prospective cohorts)	None.	Alcohol does not reduce risk of MI in LMIC.	Low (single multicountry study).	Low.
DASH dietary pattern	Following a DASH dietary pattern lowers blood pressure and serum lipid risk factors for CVD.	Higher DASH diet scores are associated with reduced all-cause mortality, CVD, and cancer mortality.	Moderate (RCT data, prospective cohorts, but no long-term event trials).	None.	None.	None.	Low if only plant based; moderate when uses low-fat dairy as key aspect.
Dietary portfolio	Following the dietary portfolio approach lowers blood pressure and serum lipid risk factors for CVD.	None.	Moderate (strong RCT data, but no event trials).	None.	None.	None.	Focus on plant foods enhances sustainability.
Mediterranean diet	Following a Mediterranean diet is associated with reduced CVD, blood pressure, and serum lipid risk factors for CVD.	None.	High (SRMA of both RCT and prospective cohorts).	None.	None.	None.	Low.

CHD = coronary heart disease; CVD = cardiovascular disease; DASH = Dietary Approaches to Stop Hypertension; HDL-C = high-density lipoprotein cholesterol; HIC = high-income countries; MUFA = mono-unsaturated fats; LDL-C = low-density lipoprotein cholesterol; LMIC = low- and middle-income countries; MI = myocardial infarction; PUFA = polyunsaturated fats; RCT = randomized controlled trial; SRMA = systematic review/meta-analysis; T2DM = type 2 diabetes mellitus; TC = total cholesterol.

stroke, but the between-region difference was not significant (p = 0.15 for interaction). In low-income countries and LMIC, heavy episodic drinking pattern and higher intakes of alcohol were associated with a composite outcome of mortality, MI, stroke, cancer, injury, and hospitalization. Current drinking was associated with an increased risk of alcohol-related cancers.

Summary of alcohol. The CVD risk benefits of moderate alcohol consumption (up to 5 g/day) compared with abstinence are small but consistent within individual study populations. Higher levels of consumption increase CVD risk, beginning at 30 g/day in women and 45 g/day in men. Therefore, recommendations for moderate alcohol consumption for CVD prevention in people who already drink must consider individual preferences, population-specific responses, and risk of comorbid conditions, such as addiction and cancers. It is not recommended that nondrinkers take up drinking.

DIETARY PATTERNS. Dietary pattern analysis assesses overall diet quality and is easier to translate into dietary recommendations than recommendations for single foods or nutrients (277). The U.S. Dietary Guidelines Advisory Committee modeled 3 dietary patterns—the Healthy U.S.-Type Pattern, the Healthy Mediterranean-Style Pattern, and the Healthy Vegetarian Pattern—for healthfulness and nutritional adequacy. All 3 include components of a dietary pattern associated with health benefits (277). The DASH diet emphasizes fruits, vegetables, whole grains, low-fat dairy products, and discourages sugar-sweetened foods and beverages, red meat, and added fats (254). The DASH diet was associated with lower systolic blood pressure, diastolic blood pressure, and cholesterol. However, the DASH trials were short and not designed to evaluate the impact of this diet on CVD clinical events. Further improvements in cardiovascular risk factors were seen when part of the carbohydrate in DASH was replaced with either monounsaturated fat or protein (278). In prospective cohort studies, a higher adherence to a DASH dietary pattern is associated with reduced stroke, as well as all-cause, CVD, and cancer mortality (279,280). The Portfolio Diet (281), which includes 30 g/day of nuts, 20 g/day of viscous fiber (i.e., oats, barley, legumes), 80 g/day of vegetable protein (soy, beans, chickpeas, lentils), and 2 g/day of plant sterols (plant sterol margarine) from plant foods, lowers LDL-C by up to 30% within 4 weeks, similar to statins (281). Reductions of 13% to 23% are maintained when this diet was extended to 12 months (282,283). However, no RCT has evaluated the impact of this diet on CVD clinical events. Strong evidence from prospective

cohort studies and randomized trials shows reduced CHD with the consumption of a higher-fat Mediterranean diet (196). In the PREDIMED randomized trial a plant-based diet high in nuts or extra virgin olive oil, vegetables, fruits, legumes, fish, and poultry but low in red meats, sweets, and whole-fat dairy was superior to the control group assigned to a low-fat Western diet in preventing CVD (164). It bears mention that low-fat diets have not been particularly effective for long-term CVD risk reduction, partly due to the difficulty sustaining such a diet in the long term (284,285). Online Table 1 translates the essence of the Mediterranean diet to other regions and cultures, suggesting replacement foods that maintain the major food groups in particular regions. Randomized trials of CVD outcomes are needed in different regions of the world.
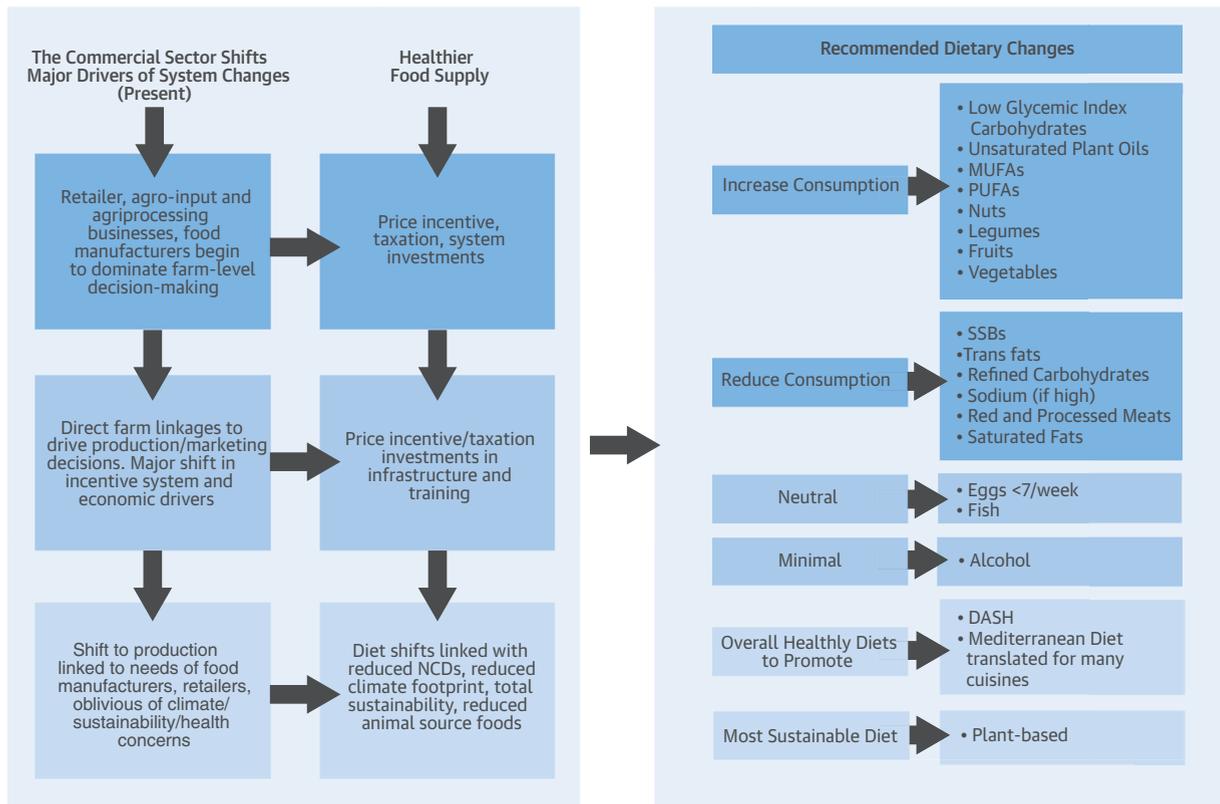
The **Central Illustration** provides a summary of the key diet changes needed and some of the options for changing our food system to attain this goal is summarized in the next section.

HEALTHIER FOOD SYSTEMS

If more people made healthier choices, the food systems would have greater incentives to produce healthier items. At the same time, a healthier food supply enables individuals to make healthier choices. Developing food systems that underpin healthier dietary patterns on the basis of our consensus noted previously involves improving the food supply by producing more heart-healthy foods and fewer foods associated with CVD (**Central Illustration**). It extends beyond merely growing and raising these foods to ensuring they reach people everywhere in a still healthy form in a way that is accessible and acceptable, including groups of lower socioeconomic status. Changing food systems thus extends beyond agricultural production to what happens between farm and fork (31). This is challenging in the modern global food system given the often extensive distance between production and consumption; multiple and complex transformations in ingredients and foods between farm and fork; and a multitude of other forces discouraging diversity and freshness. Producing more poultry, for example, may be seen as a way to enhance the quality of the food supply because it is healthier relative to red meat, but much chicken is transformed into fast food and other calorie-rich, ultra-processed, heavily advertised presentations (286). Additional public health impacts of industrial poultry production are also well reported, such as food-borne disease (e.g., *E. coli*, *Salmonella*, *Listeria*), antimicrobial residues, and avian flu (287). Clearly families and individuals also play a major role in selecting the quality

CENTRAL ILLUSTRATION Diet, Cardiovascular Disease, and the Food System: Recommendations for Global Food System Changes Needed to Create a Sustainable Healthy Diet

Anand, S.S. et al. J Am Coll Cardiol. 2015; 66(14):1590–614.

This figure summarizes the relationship between the major components of diet as well as overall dietary patterns that will lead to reduced risk of cardiovascular disease. This summarizes how the global food system contributes to dietary patterns that greatly increase the risks for the population to experience ill health. Although many perceive food consumption as an individual choice driven by the desires of consumers for tasty food, linked with rising incomes and urbanization, we have shown that the food system and all the stakeholders within it should play a major role. DASH = Dietary Approaches to Stop Hypertension; MUFA = mono-unsaturated fats; NCD = noncommunicable disease; PUFA = polyunsaturated fats; SSB = sugar-sweetened beverage.

of their diet, particularly in HIC and among middle- and higher-income LMIC, but our focus herein is on the broader environmental factors affecting this system.

There are also huge political, economic, and environmental challenges to changing the food system, not the least of which is the capacity of governments to implement change (288). Yet change is possible. It can start with a wider understanding of how the modern food system shapes dietary patterns and eating behaviors, as supported by education that makes clear the interrelationship between food systems, food environments, diets and adverse public health and environmental outcomes, and the potential for better diets to lead to major improvements in

public health and environmental sustainability. The pace and effectiveness of improvements will largely depend on political will, encouraged and reinforced by the work of civil society, with health-related professionals having important contributions to make and dietary guidelines sensitive to these issues having a major role to play.

IDENTIFYING FOOD SYSTEM SOLUTIONS. The task may be daunting, but there are many ways to move toward healthier food systems. There is no one solution but a multitude of both top-down and bottom-up starting points. Many changes need not be drastic and costly, and small modifications can improve nutritional intakes and overall diet quality (Online Appendix).

The first "top-down" step is to undertake rigorous analytical work at the global level in order to identify the main levers for change for each of the food groups and provide a framework more conducive to the success of bottom-up approaches (289). The bottom-up approach starts with engaging communities in finding their own solutions to food system–related problems with an emphasis on overall dietary patterns (277,290–292).

Experience indicates actions by the following key actors have potential to improve food systems, many of which can simultaneously have health and environmental benefits:

- **Governments** can review policies in various sectors which influence food systems for coherence with dietary objectives and realign policies so they "do no harm" (293–296); explore fiscal incentives from farm to fork to realign food and agricultural systems; and set a coherent framework of standards and regulations for large transnational food companies to disincentivize the production, sale, and marketing of foods high in refined carbohydrates and low in heart-healthy elements, including clear standards for promotional marketing (297,298). Continued efforts are needed to develop a systems-oriented, mutually reinforcing approach to reduce excessive consumption of SSBs (299).
- **Communities** can identify community-based solutions to poor food access, such as through engaging local/small/family farmers and/or innovative community-oriented production and marketing of whole grains, fruits, vegetables, legumes, and nuts in low-income communities, and developing local food policy councils (300).
- **Farmers and food producers** can leverage the potential of traditional/indigenous crops as part of biodiverse food systems, and support urban food production. Low-input, biodiverse farming systems are more sustainable than high-input monocultures and tend to be more productive per land area, making greater use of ecological space.
- **Agricultural and rural development agencies and programs** can, where whole grains, fruits, vegetables, legumes, and nuts are in short supply in LMIC, invest in transportation, distribution networks, procurement logistics, and price information systems to remove supply bottlenecks.
- **Investors in agriculture and food research and development** can shift investments and research toward the production, distribution, and consumption of healthier, more diverse sources of nutrients and agricultural programs; make national

and international investments in food research aligned with a healthy food supply; and invest in pre- and post-harvest systems to reduce food waste and focusing on recycling in home food waste (101,301).

- **Food processors and manufacturers of all scales** can ensure food processing does not strip fiber and positive nutrients from foods; direct research and marketing to enhance the desirability of nutritious foods to consumers.
- **Educational institutions** can improve curricula and build capacity among nutrition and public health students and professionals to identify and implement multisectorial food systems solutions to unhealthy diets.

In addition, middle-income countries and HIC have introduced measures to improve food environments—mainly introduced in the context of obesity—including (302):

- Taxation of SSBs and unessential foods (junk foods in general) in Mexico. A number of other LMIC are considering these taxes, and several European countries have introduced taxes on different food groups.
- Front-of-pack labels on packaged food products considered healthy (303) or unhealthy (304). Several Latin American countries have regulated front-of-pack labels, including Ecuador's traffic light label (implemented in 2014), and Chile's warning label (being implemented over the next 4 years). Several Asian countries are developing a healthier choices option.
- Mandatory school food standards are the most widely implemented action, in around 11 middle-income countries and 15 HIC. However the direction of the mandate must be appropriate.
- Effective marketing controls of unhealthy foods and beverages have not been widely implemented. Chile's new program is the most extensive (implemented over the 2015 to 2019 period). Mexico, South Korea, the United Kingdom, and Ireland present rare exceptions, but the regulations have loopholes and do not comprehensively restrict marketing. Efforts to restrict marketing in other countries through regulation have been met with strong opposition from the food and advertising industries. A critical issue is to go beyond marketing focused at children's TV to all TV viewed during key hours or full time and also to consider all other media. A second issue is linking marketing controls with the front-of-pack labeling efforts so either only healthy foods are marketed or all unhealthy foods are not allowed to be marketed.

- Encouraging food processers to produce vegetable protein-rich foods as meat and dairy alternatives with subsidies/tax incentives.

Although the evidence base for these policy options is growing more and more rigorous, evaluation of these actions is needed, though econometric evaluations of the Mexican 10% SSB tax and 8% junk food taxes are underway using longitudinal nationally representative scanned food purchase data at the household level. A critical need is much more evaluation of all these options, including to assessments of how they feed back to affect the food system (302,305). Nutrition labels, for example, have been shown to have a clear impact on reformulation (303,306).

CONCLUSIONS

This paper has provided a state-of-the-art review of the link between specific macronutrients and foods and CVD and summarized how the global food system contributes to dietary patterns that greatly increase the risks for the population to experience ill health. Although many perceive food consumption as an individual choice driven by the desires of consumers for tasty food, linked with rising incomes and urbanization, we have shown that the food system and all the stakeholders within it should play a major role (307).

Short-term controlled-feeding studies with CVD risk factors as outcomes; long-term prospective cohort studies with CHD, stroke, and T2DM as outcomes; and a limited number of RCTs with CVD as the outcome collectively show that multiple aspects of diet substantially influence CVD risk. However, similar data are needed from LMIC as dietary patterns differ in various regions of the world and the context in which foods are accessed differs markedly.

On the basis of the current evidence, the optimal dietary pattern to reduce CVD is one that emphasizes whole grains, fruits and vegetables, legumes, nuts, fish, poultry, and moderate dairy and heart-healthy vegetable oil intake; this pattern will likely reduce the CVD risk by about one-third. This healthy dietary pattern needs also to be low in refined grains, added sugars, trans fats, SSBs, and red and processed meats. The traditional Mediterranean-type diet provides a well-tested prototype for this healthy dietary pattern. Given that we now understand the components of this diet sufficiently, it may be possible to translate this pattern to other regions, with appropriate similar food replacements on the basis of food availability and preferences (Online Table 1). Despite significant advances in our understanding of optimal dietary

patterns to prevent CVD, additional research including large cohort studies and RCTs of dietary patterns are needed in different regions of the world to address existing knowledge gaps. This includes evaluation of the impact of specific fruits and vegetables, types of dairy foods, type and amount of carbohydrate, optimal cooking oils, region-specific dietary patterns, and cooking methods. Finally, we acknowledge that although this paper is focused on CVD, dietary choices and recommendations should also be made with consideration of the environmental implications of food choice (i.e., the environmental impact of poultry, livestock/cattle production, and diminishing wild fish stocks) and the role of diet in other disease processes. Human health must be linked to environmental health—the basis of the new Sustainable Development Goals (241). Additionally, modifications to our recommendations may provide improved protection against cancer or neurodegenerative or autoimmune diseases.

Policy actions and interventions that improve food supplies and dietary patterns have social, cultural, and environmental benefits. There are many opportunities to increase access to healthy food that are also likely to have significant environmental benefits. Health providers throughout the world can lead by advocating for action in the food system, as well as in food environments and behavior change communication. So too can other professionals, civil society and public interest organizations, influential writers and journalists, and organizations of chefs and gastronomes. A synergistic systems approach is essential. The challenge to create and sustain what is healthy and change what is unhealthy is compelling because improving the nourishment that goes into our bodies can have wide-ranging benefits in improving the health of societies and environments. A second major challenge is to identify and implement effective food systems and solutions and evaluate the national and local level policy actions underway to improve our diets.

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KEY WORDS cardiovascular disease, climate change, diet, food consumption, food system, low- and middle-income countries

APPENDIX For expanded supporting information, a supplemental table, and additional references, please see the online version of this article.