Health Economic Evaluation Modeling Shows Potential Health Care Cost Savings with Increased Conformance with Healthy Dietary Patterns among Adults in the United States

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ABSTRACT

Background Many American adults have one or more chronic diseases related to a poor diet, resulting in significant direct and indirect economic impacts. The 2015-2020 Dietary Guidelines for Americans (DGA) recognized that dietary patterns may be more relevant for predicting health outcomes compared with individual diet elements and recommended three healthy patterns based on evidence of favorable associations with many chronic disease risk factors and outcomes. Health economic assessments provide a model to estimate the potential influence on costs associated with changes in chronic disease risk resulting from improved diet quality in the US adult population.

Objective To estimate the impact on health care costs associated with increased conformance with the three healthy patterns recommended in the 2015-2020 DGA, including the Healthy US-Style, the Healthy Mediterranean-Style, and the Healthy Vegetarian eating patterns.

Methods Recent moderate- to high-quality meta-analyses of health outcomes associated with increased conformance with the Healthy US-Style eating pattern as measured by the Healthy Eating Index (HEI) or the Healthy Mediterranean-Style eating pattern measured by a Mediterranean diet score (MED) were identified. Given the lack of quantification of the association between an increased conformance with a vegetarian pattern and health outcomes, the analysis was limited to studies that evaluated Healthy US-style and Healthy Mediterranean-style eating patterns. The 2013-2014 What We Eat in America data provided estimates of conformance with these two eating patterns using the HEI-2015 and the 9-point MED among the US adult population. Risk estimates quantifying the association between eating patterns and health outcomes were combined with the eating pattern score increase under two conformance scenarios: increasing the average HEI-2015 and MED by 20% and increasing the average HEI-2015 and MED to achieve 80% of complete conformance. The resulting change in risk was combined with published data on annual health care and indirect costs, inflated to 2017 US dollars to estimate cost. To address double counting, costs were adjusted to minimize potential overlap of comorbidities.

Results Overall modeled cost savings were \$16.7 billion (range=\$6.7 billion to \$25.4 billion) to \$31.5 billion (range=\$23.9 billion to \$38.9 billion) based on a 20% increase in the MED and HEI-2015, respectively, resulting from reductions in cardiovascular disease, cancer, and type 2 diabetes for both patterns and including Alzheimer's disease and hip fractures for the MED. In the case that diet quality of US adults were to improve to achieve 80% of the maximum MED and HEI-2015, cost savings were estimated at \$88.2 billion (range=\$35.7 billion to \$133 billion) and \$55.1 billion (range=\$41.8 billion to \$68.2 billion), respectively.

Conclusions This is the first study quantifying savings from all health outcomes identified to be associated with the HEI and the MED to assess conformance with two eating patterns recommended as part of the 2015-2020 DGA. Findings from this study suggest that increasing conformance with healthy eating patterns among US adults could reduce costs, with billions of dollars in potential savings.
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ACCORDING TO THE SCIENTIFIC REPORT OF THE 2015 Dietary Guidelines Advisory Committee (DGAC), approximately half of American adults have one or more chronic diseases related to a poor quality dietary pattern and lack of physical activity.[1] Whereas previous Dietary Guidelines for Americans (DGA)[2,3] have focused on the association between individual nutrients or foods and health outcomes, the most recent 2015-2020 DGA[4] recognized that dietary patterns may be more relevant for predicting health outcomes given that individual diet elements are not consumed in isolation and there are potential synergistic effects on health outcomes. The DGAC noted that healthy eating patterns are consistent with higher intakes of vegetables, fruits, whole grains, low- or nonfat dairy, seafood, legumes, and nuts, moderate intakes of alcohol, and lower intakes of red and processed meats, sugar-sweetened foods and drinks, and refined grains. The DGAC concluded that there is strong and consistent evidence that such dietary patterns are associated with clinically meaningful influence on cardiovascular risk factors and moderate evidence that they are associated with favorable outcomes related to healthy body weight, risk of obesity, and the risk of developing type 2 diabetes. The 2015 DGAC also concluded that there is moderate evidence of an inverse association between healthy dietary patterns and risk of colon/rectal cancer and postmenopausal breast cancer.

Although health economic assessments have been applied to pharmaceutical and public health interventions for decades, only in recent years have they also been applied to changes in dietary consumption. Some studies focus on increased intake of a specific food or nutrient,[5-10] whereas others focus on decreased incidence of specific diseases, such as cardiovascular or dental diseases.[11,12] Studies on economic analyses and dietary patterns have been largely limited to the Mediterranean diet and heart disease[13,14] with one recent analysis estimating potential cardiovascular-related savings to range from $1 billion to $62.8 billion with adoption of the Mediterranean diet in the United States.[14]

The objective of the current study was to quantify the net annual change in costs, in terms of direct medical costs (ie, encounters, procedures, and prescription medications) and indirect costs (ie, mortality and lost productivity), associated with increased conformance among adults in the United States with the following three healthy eating patterns cited by the DGAC and recommended in the 2015-2020 DGA: the Healthy US-Style, the Healthy Mediterranean-Style, and the Healthy Vegetarian eating patterns. This is the first study modeling the potential health care costs and savings from all chronic health outcomes associated with conformance to healthy eating patterns recommended as part of the 2015-2020 DGA among the US adult population.

RESEARCH SNAPSHOT

Research Question: What is the potential net annual impact on direct and indirect costs associated with increased conformance among adults in the United States to healthy eating patterns recommended as part of the 2015-2020 Dietary Guidelines for Americans?

Key Findings: In this health economic evaluation, modeled increases in conformance with the Healthy US-Style and Healthy Mediterranean-Style eating patterns as measured by the Healthy Eating Index and the Mediterranean diet score, respectively, resulted in cost savings of more than $15 billion associated with the potential reduced risk of adverse chronic health outcomes including heart disease, cancer, type 2 diabetes, hip fractures, and Alzheimer's disease in the US adult population.

METHODS

Overview

The model used in the current health economics evaluation quantifies changes in US health care costs associated with increased conformance with the three healthy eating patterns outlined in the 2015-2020 DGA (Figure 1). Data inputs included relative risk (RR) estimates of the association between conformance with each eating pattern and health outcome, direct and indirect costs associated with health outcomes identified in the RR estimates, and conformance with each eating pattern among the US adult population. Conformance with eating patterns in the scientific literature is largely based on either *a priori* indexes derived from an individuals' reported consumption of specific dietary components or *a posteriori*-derived scores using factor or principal component analyses.[1] The Healthy Eating Index (HEI),[15] which was designed to operationalize adherence to the DGA, was used as the *a priori* index to measure conformance with the Healthy US-Style eating pattern, whereas conformance with a Healthy Mediterranean-Style eating pattern can be measured through a variety of Mediterranean diet scores (MED).[16-18] Due to the need to assign a numerical conformance score to the US adult population's dietary intake within the current model, *a posteriori* indices were excluded. Complete (100%) conformance by the US adult population with any of the healthy eating patterns is unrealistic. Therefore, the decision to model net changes in costs assuming two scenarios of a theoretical increase in conformance to each healthy eating pattern was made to provide a range of potential cost changes by pattern. In the first scenario (Scenario 1), the average conformance score was increased by 20% and in the second scenario (Scenario 2) the average conformance score was increased to achieve 80% of complete conformance. The two scenarios therefore reflect a modest and realistic population-level shift in conformance with eating patterns that could be realized within 1 to several years as well as a more extreme population-level shift resulting in a targeted goal of high compliance with dietary guidelines, respectively. This study was exempt from international review board approval because it is a secondary analysis of public data.

Dietary Patterns and Health Outcomes

Identification of Health Outcomes. *The 2015 DGAC report outlines the evidence-based development process for defining the Healthy US-Style, Healthy Mediterranean-Style, and Healthy Vegetarian eating patterns, noting that there is more than one way to achieve a healthy diet.[1] A review of the literature published subsequent to the 2015 DGAC's review through February 2018 further identified health outcomes associated with these three eating patterns. The following search terms were used: ((((Diet* pattern*) OR ("Healthy Eating Index") OR ("Diet, Mediterranean"[Mesh] OR Mediterranean [tiab]) OR (vegetarian* OR "Diet, Vegetarian"[Mesh])) AND (meta-analysis or*

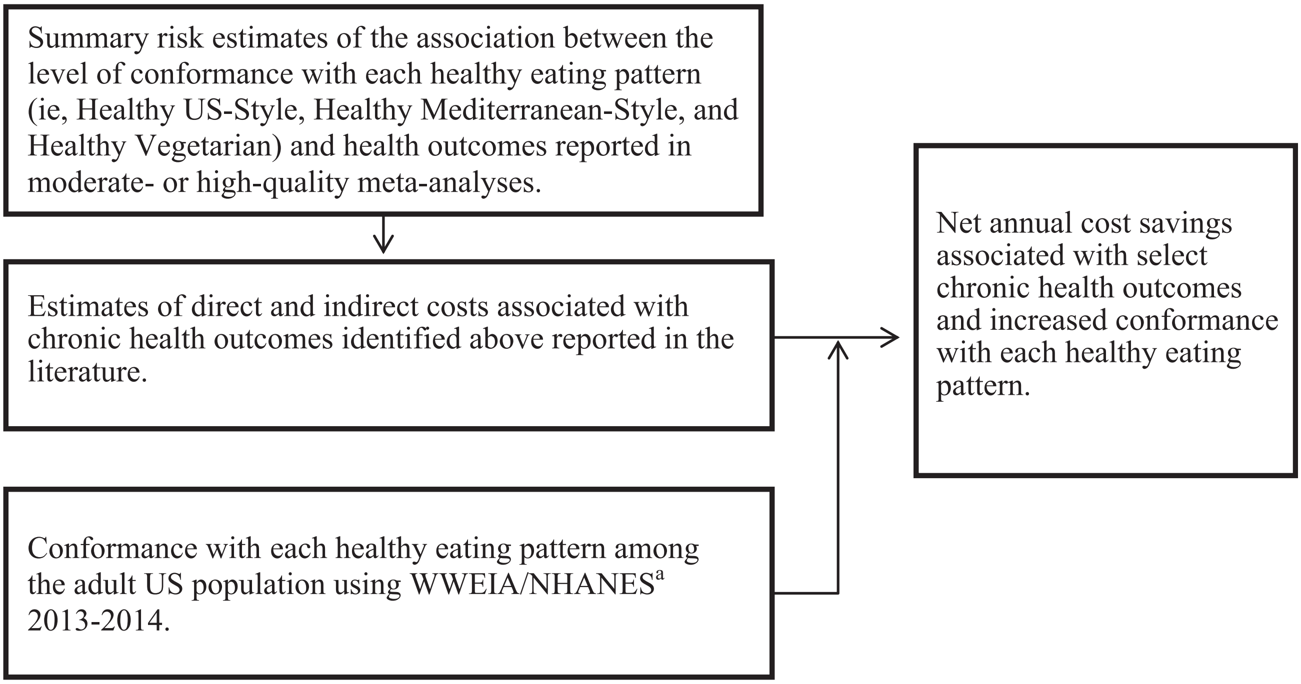

Figure 1. Overview of data inputs and model to estimate net annual cost savings associated with increased conformance with the three healthy eating patterns recommended in the Dietary Guidelines for Americans 2015-2020 among adults in the United States. [a]WWEIA/NHANES=What We Eat in America/National Health and Nutrition Examination Survey.

meta-analyses)) with limits only for human studies published in English.

The aim of the literature search was to identify moderate- to high-quality studies for each dietary pattern and outcome rather than to conduct a formal assessment of the evidence. Identified articles were independently screened by two authors (C. G. S. and J. K. M.) to determine whether they met the following inclusion criteria: meta-analysis of prospective cohort studies published subsequent to the 2015 DGAC's review of the dietary pattern literature (ie, 2014 and onward), conducted in a cohort of healthy adults (aged $\geq$18 years) at risk for chronic disease, and provided quantitative measures of the association (beneficial or adverse) between increased conformance to any of the three eating patterns identified by the 2015-2020 DGA and health outcomes.[19] Studies based on 1 data point in the meta-analysis were excluded along with studies with end points limited to intermediate markers of disease. No *a priori* selection of health outcomes was included in the search protocol; all outcomes, including adverse or favorable, were selected for inclusion in the review.

Following the exclusion of studies that were based on posterior scoring of dietary patterns, did not contain a disease end point, did not present quantitative results, or were older with recent updates available, 22 meta-analyses remained (Figure 2). The 22 meta-analyses that met the inclusion criteria were further evaluated using the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) checklist[20] to assess quality of reporting with MOOSE scores calculated by summing each of the 35 MOOSE criteria met by a given study and dividing by the total number of points possible (ie, 35 points). All studies were of moderate or high quality, defined as a MOOSE score >60%. In the case that more than one meta-analysis was available for a given health outcome, additional criteria were applied to determine which to select for the model. First, given the uncertainty inherent in combining risk estimates from individual studies based on the highest and lowest quantiles of conformance, a dose−response analysis was preferential when both dose−response and high vs low comparisons were available. Second, in the case that only high vs low comparisons were available, the most recent meta-analysis with the largest number of cohort studies was selected. Of the 22 studies that met all inclusion criteria, all showed similar significant beneficial effects of increased conformance with the dietary pattern and health outcomes of interest. Fifteen were either earlier publications from the same group of researchers with updates available, included fewer individual cohort studies in the summary risk estimates, or were high vs low comparisons of risk of a health outcome when a dose−response analysis for the same health outcome was available. A summary of the seven studies (2 studies with HEI[21,22] and 5 studies with MED[23-27]) included in the current model is provided in Table 1. It is important to note that based on the inclusion criteria, no studies on the association between conformance with a vegetarian dietary pattern and health outcomes were identified. Among the studies that evaluated the health effects of vegetarian diets,[28-30] the definition of conformance was based largely on what was not consumed, and therefore the comparison in these studies was between self-identified vegetarians and a control group of nonvegetarians, making it difficult to know what dietary components were consumed and therefore directly associated with any observed health outcomes. Further, the definition of vegetarian varied greatly, with some identified as "pure," "semi," "pesco," and "vegan." Therefore, there was no quantification of the association between an increased conformance with a vegetarian pattern and health outcomes that could be used in the model and as such, the current quantitative analysis is limited to studies that

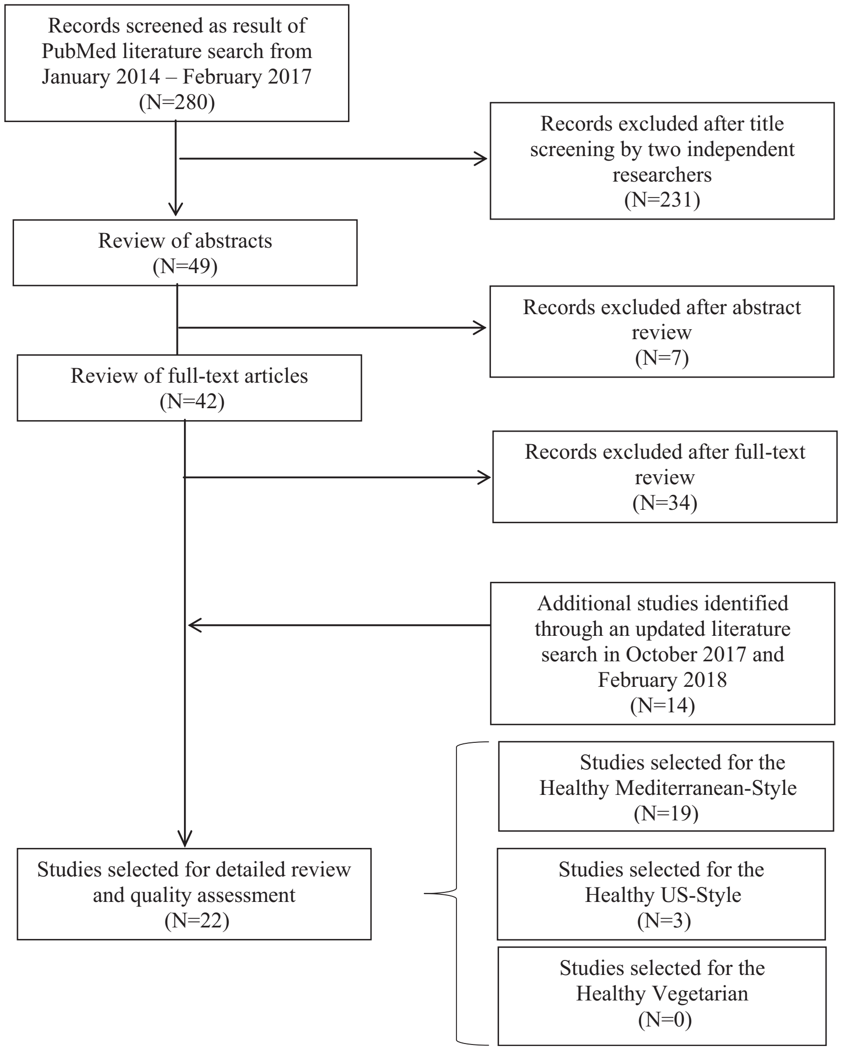

Figure 2. Study selection flow chart for review of published meta-analyses measuring the association between healthy eating patterns and chronic health outcomes.

evaluated Healthy US-Style and Healthy Mediterranean-Style eating patterns as measured by the HEI and the MED, respectively.

Overall, 10 health outcomes associated with the HEI and/or MED were included in the current study (Table 2). Health outcomes associated with the HEI were limited to total cardiovascular disease, cancer (all sites), and type 2 diabetes. Health outcomes associated with the MED include cardiovascular disease, coronary heart disease, stroke, cancer (all sites), breast cancer, colorectal cancer, prostate cancer, type 2 diabetes, Alzheimer's disease, and hip fractures.

HEI. Three recent meta-analyses were identified in the literature search that provided quantitative estimates of the association between HEI and both heart disease and cancer.[21,22,31] Heart disease end points in the three studies were limited to total cardiovascular disease. The risk estimate from Onvani and colleagues[21] associated with US cohorts and specific to total cardiovascular disease mortality was selected for inclusion in the current analysis (RR 0.83, 95% CI 0.79 to 0.86). Our search did not identify any published meta-analyses that quantified the association between the HEI and other heart disease end points such as coronary heart disease or stroke. Therefore, the HEI analysis for heart disease is limited to total cardiovascular disease. Cancer end points in two of the meta-analyses were limited to total cancer (all sites) outcomes,[21,31] whereas a 2018 study by Schwingshackl and colleagues[22] included specific sites of cancer such as breast, colorectum, and prostate. The Onvani and colleagues[21] meta-analysis of cancer mortality met the inclusion criteria, and associations with US cohorts were used in the current analysis (ie, RR 0.78, 95% CI 0.76 to 0.81). Given the lack of more than 1 data point to quantify the association between HEI and site-specific cancer outcomes, the current analysis is limited to total cancer (all sites). A summary measure of the association between the HEI and type 2 diabetes based on three prospective cohort studies (4 data points) among the US population was also included in the analysis (RR 0.87, 95% CI 0.82 to 0.93).[22]

MED. The associations between the Mediterranean diet and heart disease end points included in the current model were

Table 1. Summary of published meta-analyses measuring the association between conformance with the Healthy US-Style and the Healthy Mediterranean-Style eating patterns and health outcomes included in the health economic evaluation

Health outcome	Reference MOOSE[a] score	Characteristics of cohort studies included in meta-analysis	Description of search strategy used in the meta-analysis	Dietary pattern index	Comparator for the summary risk estimate
Cardiovascular disease	Onvani and colleagues[21] MOOSE=81%	• N=7 cohort studies (United States) • 741,389 participants • Age 18+ y at entry • 6.2−22 y of follow-up	• PubMed, Web of Science, Google Scholar through December 14, 2015; keywords included "Healthy Eating Index" • No language or publication restrictions; reference lists were reviewed for further relevant studies	• HEI[b] • HEI-2005 • HEI-2010	• High vs low conformance
	Rosato and colleagues[23] MOOSE=89%	• N=8 studies (United States=4, Europe=4) • 701,441 participants • Age ≥20 y at entry	• Medline; search terms were "Cardiovascular Diseases AND Mediterranean AND Diet" • No language or publication restrictions; reference lists were reviewed for further relevant studies	• MED[c]	• High vs low conformance
Coronary heart disease	Rosato and colleagues[23] MOOSE=89%	• N=5 studies (United States=3, Europe=2) • Age ≥20 y at entry	• Medline; search terms were "Cardiovascular Diseases AND Mediterranean AND Diet" • No language or publication restrictions; reference lists were reviewed for further relevant studies	• MED	• High vs low conformance
Stroke	Rosato and colleagues[23] MOOSE=89%	• N=5 cohort studies (United States=1, Europe=3, Asia=1) • 159,511 participants • Age ≥20 y at entry	• Medline; search terms were "Cardiovascular Diseases AND Mediterranean AND Diet" • No language or publication restrictions; reference lists were reviewed for further relevant studies	• MED	• High vs low conformance

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RESEARCH

Table 1. Summary of published meta-analyses measuring the association between conformance with the Healthy US-Style and the Healthy Mediterranean-Style eating patterns and health outcomes included in the health economic evaluation (*continued*)

Health outcome	Reference MOOSE[a] score	Characteristics of cohort studies included in meta-analysis	Description of search strategy used in the meta-analysis	Dietary pattern index	Comparator for the summary risk estimate
Type 2 diabetes mellitus	Schwingshackl and colleagues[22] MOOSE=86%	• N=3 cohort studies (United States=3) • 262,184 participants	• PubMed, Embase, and Scopus through May 15, 2017; keywords relating to healthy eating, Dietary Approaches to Stop Hypertension, diet, cancer, and mortality were searched • No language or publication restrictions; reference lists were reviewed for further relevant studies	• HEI • HEI-2005 • HEI-2010	• High vs low conformance
	Schwingshackl and colleagues[25] MOOSE=89%	• N=6 cohort studies (United States=3, Europe=3) • 103,247 participants • Age ≥20 y at entry	• Medline, Embase, Scopus, and Cochrane Trial Register through April 2, 2014; keywords included “MED” and “diabetes” • Reference lists were reviewed for further relevant studies • For studies published in duplicate, the most recent article with the longest follow-up period was used	• MED	• Continuous; 2-unit increase in conformance score
Alzheimer’s disease	Wu and Sun[26] MOOSE=89%	• N=4 cohort studies (United States=2, Europe=2) • 5,118 participants • Age ≥58 y at entry	• PubMed and Embase through August 13, 2016; keywords included “MED,” “dementia,” “Alzheimer’s disease,” and “cognitive” • No language restrictions; reference lists were reviewed for further relevant studies • For studies published in duplicate, the most comprehensive version was used	• MED	• Continuous; 1-unit increase in conformance score

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Table 1. Summary of published meta-analyses measuring the association between conformance with the Healthy US-Style and the Healthy Mediterranean-Style eating patterns and health outcomes included in the health economic evaluation (*continued*)

Health outcome	Reference MOOSE[a] score	Characteristics of cohort studies included in meta-analysis	Description of search strategy used in the meta-analysis	Dietary pattern index	Comparator for the summary risk estimate
Hip fractures	Malmir and colleagues[27] MOOSE=86%	• N=4 (3 cohort studies and 1 case-control) (United States=1, Europe=2, Asia=1) • 350,142 participants • Age ≥35 y at entry	• PubMed, Scopus, Institute for Scientific Information Web of Science, and Google Scholar through June 2016; keywords included "MED" and "fracture" • No language restrictions; reference lists were reviewed for further relevant studies	• MED	• Continuous; 1-unit increase in conformance score
Total cancer mortality; breast, colorectal, and prostate cancer incidence	Onvani and colleagues[21] MOOSE=81%	• N=7 cohort studies (United States) • 741,389 participants • Age ≥18 y at entry • 6.2–22 y of follow-up	• PubMed, Web of Science, Google Scholar through December 14, 2015; keywords included "Healthy Eating Index" • No language or publication restrictions; reference lists were reviewed for further relevant studies	• HEI • HEI-2005 • HEI-2010	• High vs low conformance
	Schwingshackl and colleagues[24] MOOSE=86%	• Total cancer: n=14 cohort studies • Breast: n=7 cohort studies • Colorectal: n • Prostate: n=6 (cohort=3; case control=3) • Age 29+ y at entry	• PubMed and Scopus through August 25, 2017; keywords included "MED," "cancer," and "cohort" • No language restrictions; reference lists were reviewed for further relevant studies	• MED	• High vs low conformance

[a]MOOSE=Meta-analyses of Observational Studies in Epidemiology.
[b]HEI=Healthy Eating Index used to assess conformanace with a Healthy US-Style eating pattern.
[c]MED=Mediterranean diet score used to assess conformation with a Healthy Mediterranean-Style eating pattern.

Table 2. Published summary risk estimates for health outcomes associated with increased conformance with healthy dietary patterns as measured by the Healthy Eating Index (HEI) and the Mediterranean diet score (MED) included in the health economic evaluation

	HEI				MED			
Health outcome	**% Change in risk (95% CI)**	**Comparator[a]**	**Comparator difference (point increase)**	**Source**	**% Change in risk (95% CI)**	**Comparator[a]**	**Comparator difference (point increase)**	**Source**
Cardiovascular disease	−17 (−14 to −21)	High vs low	48	Onvani and colleagues[21]	−16 (−8 to −23)	High vs low	6	Rosato and colleagues[23]
Coronary heart disease	—[c]	—	—		−21 (−11 to −30)	High vs low	6	Rosato and colleagues[23]
Stroke	—	—	—		−23 (−10 to −33)	High vs low	6	Rosato and colleagues[23]
Cancer (all sites)	−22 (−19 to −24)	High vs low	48	Onvani and colleagues[21]	−14 (−9 to −19)	High vs low	6	Schwingshackl and colleagues[24]
Breast cancer	—	—	—		−6 (−1 to −10)	High vs low	6	Schwingshackl and colleagues[24]
Colorectal cancer	—	—	—		−14 (−8 to −20)	High vs low	6	Schwingshackl and colleagues[24]
Prostate cancer	—	—	—		−4 (0 to −8)	High vs low	6	Schwingshackl and colleagues[24]
Type 2 diabetes	−13 (−7 to −18)	High vs low	34	Schwingshackl and colleagues[22]	−7 (−2 to −11)	2-pt increase	NA[b]	Schwingshackl and colleagues[25]
Alzheimer's disease	—	—	—		−8 (−1 to −14)	1-pt increase	NA	Wu and colleagues[26]
Hip fractures	—	—	—		−5 (−2 to −8)	1-pt increase	NA	Malmir and colleagues[27]

[a]For those risk estimates that correspond to a high vs low conformance comparison, the empirical change in dietary pattern conformance level was calculated based on reported HEI and MED (ie, based midpoint of reported ranges and/or reported medians of extreme categories) within the individual cohort studies included in the selected meta-analyses.
[b]NA=not applicable.
[c]—=no data available on the association between the Healthy Eating Index and health outcome.

based on a meta-analysis that summarized the effect of the MED on unspecified cardiovascular disease, coronary heart disease/myocardial infarction, and stroke (unspecified, ischemic, and hemorrhagic) incidence and mortality.[23] The objective of the current study was to evaluate potential savings in health care costs among the US healthy adult population, so the risk estimate associated with the non-Mediterranean cohorts in the most recent meta-analysis[23] was selected for inclusion in the analysis (ie, RR 0.84, 95% CI 0.77 to 0.92). In the same meta-analysis, MED was inversely associated with incidence of coronary heart disease/myocardial infarction when comparing individuals in the highest conformance quantile to those in the lowest conformance quantile restricted to non-Mediterranean populations only (RR 0.79, 95% CI 0.70 to 0.89) with no heterogeneity. A high MED was associated with a 23% reduction in stroke risk among five cohort studies (RR 0.77, 95% CI 0.67 to 0.90) when compared to low conformance.[23]

Four recent meta-analyses reported on the association between the MED and type 2 diabetes[25,32-34] and all showed a statistically significant reduction in risk when comparing individuals in the highest conformance quantile to those in the lowest conformance quantile with reduction of type 2 diabetes risk ranging from 13% to 23%. In a meta-analysis by Schwingshackl and colleagues,[25] the authors reported a dose–response association between MED and type 2 diabetes. This analysis, based on 6 data points, showed that for every 2-unit increase in MED (on a 0- to 9-point scale), there was a 7% reduction in type 2 diabetes (RR 0.93, 95% CI 0.89 to 0.98). Given the preference for a dose–response analysis, the 7% reduction per 2-unit increase in MED from the meta-analysis by Schwingshackl and colleagues[25] was selected for inclusion in the current analysis.

Three meta-analyses quantified the association between MED and cognitive disorders with disease end points including mild cognitive impairment, Alzheimer's disease, and dementia.[26,35,36] The most recent meta-analysis by Wu and Sun[26] reported a significant inverse association between MED and mild cognitive impairment but when analyzed as a dose–response linear relationship, the association was no longer observed (RR 0.97, 95% CI 0.78 to 1.17).[26] In contrast, Alzheimer's disease was inversely associated with MED in both high vs low comparisons as well as on a continuous scale.[26] For every 1-unit increase in the MED, there was an 8% reduction in Alzheimer's disease risk (RR 0.92, 95% CI 0.86 to 0.99).

Bone health outcomes were limited to hip fractures as a health outcome. Two recent meta-analyses[27,37] reported a statistically significant association between MED and risk of hip fractures. Given the inclusion of cross-sectional and case-control studies in one of the studies, the meta-analysis by Malmir and colleagues[27] reporting a significant inverse linear relationship between a 1-point increase in the MED and risk of hip fracture (RR 0.95, 95% CI 0.92 to 0.98) was selected for the current analysis.

The association between the MED and cancer focused on the most recent meta-analysis by Schwingshackl and colleagues[24] along with a review and analysis by Bloomfield and colleagues[38] and a meta-analysis focused on breast cancer by van den Brandt and colleagues.[39] Based on these three meta-analyses, greater conformance with a Mediterranean-style eating pattern was consistently found to be inversely associated with total cancer as well as site-specific cancers, including colorectal, breast, and prostate.

Risk Measures

RR measures on the associations between healthy dietary patterns as measured by the HEI or MED and health outcomes were extracted from the identified meta-analyses (Table 2). Risk estimates were not consistently expressed across studies, although the majority compared high vs low conformance based on quartiles or quintiles of the HEI or MED, whereas a limited number of studies reported RR per unit increase in conformance score (eg, 1.0-point increase in MED). When both types of comparisons were presented within a study, the dose–response RR was preferentially selected for extraction.

Costs Associated with Health Outcomes

Annual direct medical costs as well as indirect costs for the selected health outcomes are based on costs reported by the American Heart Association (2012-2013),[40] the American Diabetes Association (2012),[41,42] the National Cancer Institute (2010),[43,44] and case reports in the published literature for Alzheimer's disease[45,46] and hip fractures[47,48] and represent both a health care payer's and societal perspective. All costs were updated to end of year 2017 US dollars[49] (Table 3).

An important challenge in estimating net change in cost is that chronic health outcomes such as heart disease and type 2 diabetes have similar risk factors, which likely play a role in mediation or interaction along the proposed causal pathways. For example, type 2 diabetes is an established risk factor for heart disease. As shown in Table 3, to address these issues of potential double-counting, costs for one health outcome that may include the cost of comorbidities and/or risk factors of another health outcome were adjusted to reflect this overlap to the extent the data allowed. For type 2 diabetes, the proportion of costs attributed to cardiovascular complications was applied to estimate the net costs for type 2 diabetes alone.[41,51] A 2017 study noted that noncancer causes of death are highest in patients with breast, colorectal, and prostate cancer, with heart disease being the primary cause of death in many of these patients.[54] Therefore, when estimating the costs for the last year of life for breast, colorectal, and prostate cancer, the proportion of these cancer patients that die from other causes was used to adjust the net annual costs for cancer.

Conformance with Eating Patterns

Estimates of conformance with the healthy US-Style and Mediterranean-Style eating patterns as measured by the HEI and MED, respectively, among adults in the United States were based on food consumption records collected in the What We Eat in America (WWEIA) component of the National Health and Nutrition Examination Survey (NHANES) conducted during 2013 to 2014,[55] reported nutrient intakes by individuals, and the Food Patterns Equivalents Database (FPED) 2013-2014[56] developed by the US Department of Agriculture that translates each food into food components. Individual component scores used to score both dietary patterns were developed using detailed dietary recall records that collected information on all foods and beverages consumed by respondents during the previous 24-hour time period (midnight to midnight). The NHANES datasets provide nationally representative nutrition

Table 3. Estimated annual direct and indirect health care costs ($ billions) for selected health outcomes based on published studies and included in the health economic evaluation

Health outcome	Direct Costs[a]	Indirect Costs[a]	Total Costs[a]	Assumptions and adjustments
		($ billions)		
Cardiovascular disease	211.1	140.6	351.7	Annual average cost from 2012-2013; includes heart disease, stroke, hypertensive disease, and other circulatory conditions[40]
Coronary heart disease	109.8	112.3	222.1	Annual average cost from 2012-2013; includes coronary heart disease, heart failure, part of hypertension, cardiac dysrhythmias, rheumatic heart disease, cardiomyopathy, pulmonary heart disease, and other or ill-defined heart disease[40]
Stroke	19.9	17.8	37.7	Annual average cost from 2012-2013[40]
Type 2 diabetes	169.8	86.4	256.1	Annual average cost from 2012 for total expenditures and indirect costs for diabetes ($245 billion)[41] and assuming 96% of diabetes cases are type 2 diabetes based on a cited prevalence of 1.25 million type 1 diabetes cases out of total prevalence of 29.1 million Americans with diabetes in 2012.[42] The proportion of total costs allocated to direct and indirect costs was based on estimates from Dall and colleagues[50]
Type 2 diabetes[b]	137.2	50.1	187.3	19.2% of direct medical costs[51] and 42% of indirect costs[41] of type 2 diabetes were estimated to be associated with cardiovascular disease and therefore, subtracted from the total costs for type 2 diabetes estimated above
Cancer (all sites)	151.7	—[c]	151.7	Modeled estimates of annual medical costs in 2010 using SEER[d] and SEER-Medicare data[43]
Breast cancer	5.9	—	5.9	Modeled estimates of annual medical costs per case for stages of treatment for adults aged $<$65 y and $\geq$65 y associated with site-specific cancer in 2010 using SEER and SEER-Medicare data.[43] Combined estimate for the total adult US population estimated by combining cost data for all age and treatment categories weighted according to the prevalence of adults in each category[43] and the total prevalence of site specific cancer in 2014 adjusted to reflect the 2016 US adult population[44]
Colorectal cancer	14.0	—	14.0	
Prostate cancer	4.5	—	4.5	

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Table 3. Estimated annual direct and indirect health care costs ($ billions) for selected health outcomes based on published studies and included in the health economic evaluation (*continued*)

Health outcome	Direct Costs[a]	Indirect Costs[a]	Total Costs[a]	Assumptions and adjustments
		($ billions)		
Alzheimer's disease	45.6	—	45.6	Based on 2 case-control studies (2007-2011) comparing direct medical costs for patients with Alzheimer's disease compared with matched controls among beneficiaries of Medicare Advantage[52] and traditional Medicare plans.[46] Incremental costs for first year postdiagnosis were weighted and combined with costs for subsequent years based on the reported statistic that 9% of Alzheimer's disease patients are diagnosed in a given year with a total prevalence of 5.3 million[53]
Hip fractures	—	—	17.2	Costs of osteoporotic hip fractures among privately insured young adults (aged 18-64 y) and Medicare-insured elderly adults were compared with matched controls with osteoporosis and no fractures.[48] Direct medical costs were calculated; indirect costs (lost work productivity) were available for a subset of working patients (2006 dollars). The number of hip fractures annually in the United States was estimated to be approximately 341,000 (based on patients visiting emergency departments)[47]

[a]Costs presented are based on costs reported in cited sources and inflated to end of year 2017 dollars.
[b]Adjusted for costs of cardiovascular disease complications.
[c]—=no data available on the association between the Healthy Eating Index and health outcome.
[d]SEER=Surveillance, Epidemiology, and End Results.

and health data to estimate nutrition and health status measures in the United States. The study population for this analysis was limited to men and women aged 18 years and older who provided a reliable dietary recall meeting the minimum criteria as determined by the National Center for Health Statistics on Day 1 of the data collection (n=5,356).[55] All analyses to calculate the HEI-2015 and MED were conducted using STATA/SE software (version 12.1).[57]

HEI

The original HEI was developed in 1995,[58] followed by the 2005,[59] 2010,[60] and 2015[15] versions reflecting changes in the DGAs. The most recent HEI-2015 was selected as the basis for determining the US adult population's conformance with the Healthy US-Style pattern.[15] The HEI-2015 was designed to measure conformance with the 2015-2020 DGA[4] and includes 13 components with maximum component scores ranging from 5 for total fruits (including 100% fruit juice), whole fruits (all forms except juice), total vegetables, greens and beans, total protein foods, and seafood and plant proteins to 10 for dairy, fatty acids (ratio of poly- and monounsaturated fatty acids [PUFAs+MUFAs] to saturated fatty acids), refined grains, sodium, added sugars, and saturated fats. The HEI-2015 also includes new recommendations to limit the amount of added sugar to <10% of total energy intake and allocates legumes to four components: total protein foods, seafood and plant proteins, total vegetables, and greens and beans. HEI-2015 standards are expressed either as a percent of total energy or per 1,000 kcal, with the exception of the fatty acid component where the standard is expressed as the ratio of PUFA+MUFA to saturated fatty acids. The maximum sum of the 13 components is 100 points with points allocated from zero to a maximum of 5 or 10 based on intakes reported between the minimum and maximum standards for each component.

Mean HEI-2015 scores were calculated using FPED component intakes as reported in the FPED and the population ratio method.[61] The mean HEI-2015 score among the US adult population was 59.3 (Figure 3A). Therefore, under Scenario 1, the increase in conformance score that would be required for the US adult population to achieve a 20% increase of the mean would be 11.9 points for a total score of 71.2, whereas under Scenario 2, a 20.7-point increase would be required to reach a score of 80.0 (ie, 80% conformance) (Figure 3A).

MED

The traditional Mediterranean diet was first characterized by Ancel Keys in the 1960s as a dietary pattern high in vegetables, legumes, fruits and nuts, unrefined grains, and low-fat dairy; a moderately high intake of fish; low to moderate intakes of meat and poultry; and a moderate intake of alcohol, largely through wine consumption and when consumed with food.[62,63] Further, high intakes of MUFA+PUFA with a low intake of saturated fats are also key components of this diet. This dietary pattern was first assigned a score by Trichopoulou and colleageus[16] indicating the degree of conformance with the traditional Metiterranean-style eating pattern and numerous variations have been published and used in epidemiologic analyses since.[17,18,64] In the current review of the literature, the majority of the cohorts included in meta-analyses with pertinent health outcomes were scored using the index first constructed by Trichopoulou and colleagues.[16,64] Therefore, the scoring method derived and further modified by Trichopoulou and colleagues[64] was the basis for determining the distribution of the MED when applied to the dietary intake of the US adult population. The scoring method includes nine components resulting in a discrete total score ranging from 0 to 9 that was assigned to each individual in WWEIA/NHANES.

The WWEIA/NHANES data release does not translate each food into components of the MED. Therefore, for this study, the FPED was adapted to align with the MED components. For each WWEIA/NHANES respondent, the FPED 2013-2014 was used to identify the intakes of vegetable, legume, fruit and nut, cereal, fish, meat and poultry, and dairy components of the MED, reported in ounce or cup equivalents. Alcohol and fat intakes were obtained from Day 1 total nutrient intake data. A value of 0 or 1 was assigned to each of nine components with the weighted, sex-specific median as the cutoff. For components presumed to be beneficial (vegetables, legumes, fruits and nuts, cereals, fish, and the ratio of MUFA to saturated fats), participants whose consumption was greater than or equal to the median were assigned a value of 1. For components indicated to be consumed in moderation (meat and poultry and dairy products), participants whose consumption was less than the median were assigned a value of 1. For alcohol, a value of 1 was assigned to men who consumed between 10 and 50 g/day and to women who consumed between 5 and 25 g/day. The highest median intakes were estimated for cereals (6.9 and 5.3 oz-equivalents for US adult men and women, respectively), whereas the lowest median intakes were estimated for legumes and fish at 0 c- and oz-equivalents, respectively. Both the fruit and nuts and vegetable components were estimated to have median intakes <1 c-equivalent, whereas dairy intake was close to 1 c-equivalents (1.4 and 1.1 c-equivalents for US adult men and women, respectively). Meat and poultry intakes were higher among men (4.3 oz-equivalents) compared with women (2.7 oz-equivalents). The ratio of MUFA to saturated fats was close to 1 for both men and women in the US adult population. The average MED among the US adult population was 3.5 with a slightly higher score among men (3.6) compared with women (3.4) (Figure 3B). Therefore, under Scenario 1, the increase in conformance score required to achieve a 20% increase over the mean MED was 0.7 points for a total score of 4.2, whereas under Scenario 2, an increase of 3.7 points was required to reach a score of 7.2 (ie, 80% conformance).

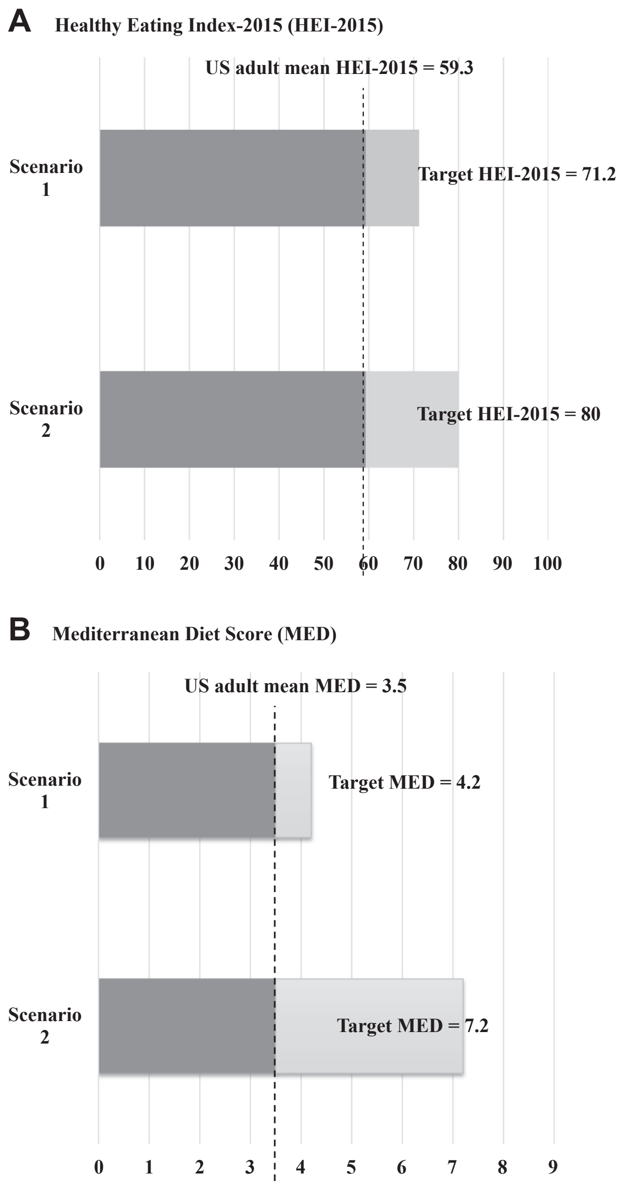

Figure 3. Mean conformance with the Healthy US-Style and Healthy Mediterranean-Style eating pattern measured by the A) Healthy Eating Index-2015 (HEI-2015) and the B) Mediterranean Diet Score (MED) among adults in the United States and modeled increase to achieve target conformance score in Scenario 1 (average conformance score increased 20%) and 2 (average conformance score increased to achieve 80% of complete conformance) models.

Model Structure

Summary RR estimates and corresponding lower and upper 95% CIs quantifying the association between increased conformance with the select dietary pattern and health outcomes were combined with the increase in the dietary pattern score required to achieve either a 20% increase of the average conformance score (Scenario 1) or 80% of complete conformance (Scenario 2). The resulting change in risk was used to estimate the influence on costs. The lower and upper 95% CIs on the summary RR estimates were included to provide a potential range of net change in costs associated with each health outcome. Annual costs were reduced proportionally to reflect the change in risk of each health outcome and the corresponding change in cost estimated using the equation below:

$$\Delta Cost_i = \left[\frac{RR_{i,adj} - 1}{\Delta DP_{cited}} \; x \; \Delta DP_{US\ adults} \; x \; (I_i + D_i)\right]$$

Where:

i = index for selected health outcome (eg, type 2 diabetes),
$RR_{i,adj}$ = adjusted RR for health outcome (i),
ΔDP_{cited} = change in dietary pattern score associated with the RR for health outcome (i),
$\Delta DP_{US\ adults}$ = change in dietary pattern score necessary to reach goal.
I_i = annual indirect costs associated with health outcome (i), and
D_i = annual direct health care costs associated with health outcome (i).

A summary of the select health outcomes along with the corresponding published RR per change in dietary pattern score is provided in Table 2. For those RRs that correspond to a high vs low conformance comparison, the empirical change in the MED was calculated assuming a difference of 6 MED points given that the majority of high vs low RRs within the cohort studies included in the selected meta-analyses were based on a 6- to 9-point (midpoint=7.5) vs 0- to 3-point (midpoint=1.5), respectively, comparison. For the HEI, a difference of 34 points and 48 points were assumed for type 2 diabetes and heart disease/cancer end points, respectively, based on reported scores for the high and low quantile groups in the individual cohort studies used in the selected meta-analyses.

Changes in costs per health outcome were then summed to estimate the total annual net change in costs associated with each dietary pattern.

$$\Delta Total\ Cost_{dp} = \sum_{i=1}^{n} \Delta Cost_i$$

Where:

i = index for selected health outcome (eg, type 2 diabetes),
n = number of health outcomes included for each dietary pattern, and
$\Delta Cost_i$ = annual change in costs associated with health outcome i.

When RRs for both cardiovascular disease and heart disease or stroke were selected, the summed total reflects the costs associated with heart disease and stroke rather than with total cardiovascular disease. The lower and upper 95% CI cost estimates for all health outcomes were also summed, but note that this lower-upper (L-U) range no longer reflects a 95% CI but rather a broad range of the potential change in costs associated with all health outcomes within a dietary pattern.

RESULTS

Healthy US-Style Eating Pattern

Under Scenario 1, an annual cost savings of $31.5 billion (L-U range=$23.9 billion to $38.9 billion) was estimated based on a 20% increased conformance as measured by the HEI-2015 among the US adult population, with approximately half of these savings resulting from a reduction in costs associated with cardiovascular disease alone (Table 4). Additional cost savings resulting from cancer and type 2 diabetes end points contributed to the total. A large portion of these savings were from a reduction in direct costs; however, cancer costs were limited to direct costs only, and therefore indirect costs of cancer are not reflected in this analysis. In the case that the US adult population was to reach a target of 80% of the total HEI-2015 (Scenario 2), annual cost savings associated with the individual health outcomes were approximately two times higher than for Scenario 1. Overall cost savings was $55.1 billion (L-U range=$41.8 billion to $68.2 billion).

Healthy Mediterranean-Style Eating Pattern

Total annual cost savings associated with a 20% increased conformance as measured by the MED was $16.7 billion (L-U range=$6.7 billion to $25.4 billion) with coronary heart disease contributing the most to overall annual costs savings ($5.4 billion; L-U range=$2.9 billion to $7.8 billion) followed by type 2 diabetes ($4.6 billion; L-U range=$1.3 billion to $7.2 billion when adjusted for overlapping risk factors with coronary heart disease), whereas Alzheimer's disease and stroke contributed $2.6 billion (L-U range=$0.3 billion to $4.5 billion) and $1.0 billion (L-U range=$0.4 billion to $1.5 billion), respectively (Table 5). Cost savings from site-specific cancer outcomes were a smaller proportion relative to heart disease cost savings with <$1 billion from breast, colorectal, and prostate cancer combined; however, it is not possible to directly compare with heart disease and type 2 diabetes outcomes due to the lack of data on indirect costs for cancer outcomes. Total cost savings associated with increased conformance measured by the MED were slightly lower when limiting to the three cancer sites (ie, breast, prostate, and colorectal) included in the analysis ($14.5 billion; L-U range=$5.2 billion to $22.4 billion). Total cost savings associated with a shift to 80% of the total MED (ie, 7.2) were estimated to be $88.2 billion (L-U range=$35.7 billion to $133 billion [including all cancer sites]) when combining all health outcomes together after adjusting for comorbidities.

DISCUSSION

There has been significant research and discussion of dietary patterns both as part of public health policy and dietary guidance as well as hypotheses for causal pathways leading to reduction in chronic disease outcomes. This is the first study to estimate net changes in costs based on a detailed review of the epidemiologic evidence of beneficial and adverse associations between the Healthy US-Style or Healthy Mediterranean-Style diet patterns and chronic health outcomes. This study illustrates the significant potential economic influence associated with greater conformance to these two dietary patterns included in the current 2015-2020 DGA recommendations. Based on WWEIA/NHANES 2013-2014, the average conformance score among US adults was 59.3 out of 100 when their

Table 4. Net annual cost savings ($ billions) associated with increasing conformance with a Healthy US-Style eating pattern among US adults

	Annual Cost Savings ($ billions)					
	Scenario 1[a]			Scenario 2[b]		
Health outcome	Direct (L-U range)[c]	Indirect (L-U range)	Total (L-U range)	Direct (L-U range)	Indirect (L-U range)	Total (L-U range)
	←relative risk (95% CI)→					
Cardiovascular disease	8.9 (7.3-10.9)	5.9 (4.9-7.3)	14.8 (12.2-18.2)	15.5 (12.8-19.2)	10.3 (8.5-12.8)	25.8 (21.3-31.9)
Cancer (all sites)[d]	8.2 (7.1-9.0)	—	8.2 (7.1-9.0)	14.4 (12.5-15.7)	—	14.4 (12.5-15.7)
Type 2 diabetes	6.2 (3.3-8.6)	2.3 (1.2-3.1)	8.5 (4.6-11.7)	10.9 (5.9-15.1)	4 (2.1-5.5)	14.9 (8.0-20.6)
Total (including all cancer sites)	23.3 (17.7-28.5)	8.2 (6.1-10.4)	31.5 (23.9-38.9)	40.8 (31.2-50.0)	14.3 (10.6-18.3)	55.1 (41.8-68.2)

[a]In Scenario 1, average conformance score as measured by the Healthy Eating Index-2015 increased 20%.
[b]In Scenario 2, average conformance score as measured by the Healthy Eating Index-2015 increased to achieve 80% of complete conformance.
[c]L-U range=Lower and upper range of costs based on the 95% CI of the relative risk associated with each health outcome.
[d]Limited to direct costs only.

diet is operationalized to the HEI-2015 and a 3.5 out of 9 on the MED. Both of these scores reflect generally suboptimal eating patterns and allow room for significant improvement in conformance levels to two dietary patterns shown in numerous epidemiologic studies to have beneficial health effects.

An annual net cost savings of more than $15 billion from reductions in heart disease and cancer cases could be realized when, on average, conformance with either the HEI-2015 or MED among all US adults increased by 20%. Total annual cost for heart disease was reported to be $199.6 billion in

Table 5. Net annual cost savings ($ billions) associated with increasing conformance with a Healthy Mediterranean-Style eating pattern among US adults

	Annual Cost Savings ($ billions)					
	Scenario 1[a]			Scenario 2[b]		
Health outcome	Direct (L-U range)[c]	Indirect (L-U range)	Total (L-U range)	Direct (L-U range)	Indirect (L-U range)	Total (L-U range)
	←relative risk (95% CI)→					
Cardiovascular disease	3.9 (2.0-5.7)	2.6 (1.3-3.8)	6.6 (3.3-9.4)	20.8 (10.4-29.9)	13.9 (6.9-19.9)	34.7 (17.4-49.9)
Coronary heart disease	2.7 (1.4-3.8)	2.8 (1.4-3.9)	5.4 (2.9-7.8)	14.2 (7.4-20.3)	14.5 (7.6-20.8)	28.8 (15.1-41.1)
Stroke	0.5 (0.2-0.8)	0.48 (0.2-0.7)	1.0 (0.4-1.5)	2.82 (1.2-4.1)	2.5 (1.1-3.6)	5.3 (2.3-7.7)
Cancer (all sites)[d]	2.5 (1.6-3.4)	—	2.5 (1.6-3.4)	13.1 (8.4-17.8)	—	13.1 (8.4-17.8)
Breast cancer[d]	0.04 (0-0.07)	—	0.04 (0-0.07)	0.2 (0-0.4)	—	0.2 (0-0.4)
Colorectal cancer[d]	0.2 (0.1-0.3)	—	0.2 (0.1-0.3)	1.2 (0.7-1.7)	—	1.2 (0.7-1.7)
Prostate cancer[d]	0.02 (0-0.04)	—	0.02 (0-0.04)	0.1 (0-0.2)	—	0.1 (0-0.2)
Type 2 diabetes	3.4 (1.0-5.3)	1.2 (0.4-1.9)	4.6 (1.3-7.2)	17.8 (5.1-27.9)	6.5 (1.9-10.2)	24.3 (6.9-38.1)
Alzheimer's disease	2.6 (0.3-4.5)	—	2.6 (0.3-4.5)	13.5 (1.7-23.6)	—	13.5 (1.7-23.6)
Hip fractures[e]	—	—	0.6 (0.2-1.0)	–	—	3.2 (1.3-5.1)
Total (including all cancer sites)	11.7 (4.5-17.8)	4.5 (2.0-6.5)	16.7 (6.7-25.4)	61.4 (23.8-93.7)	23.5 (10.6-34.6)	88.2 (35.7-133)
Total (limited to 3 cancer sites)	9.5 (3.0-14.8)	—	14.5 (5.2-22.4)	49.8 (16.1-78.2)	—	76.6 (28.0-118)

[a]In Scenario 1, average conformance score as measured by a 9-point Mediterranean diet score increased 20%.
[b]In Scenario 2, average conformance score as measured by a 9-point Mediterranean diet score increased to achieve 80% of complete conformance.
[c]L-U range=lower and upper range of costs based on the 95% CI of the relative risk associated with each health outcome.
[d]Limited to direct costs only.
[e]Cost data do not allow for distinction between direct and indirect costs.

2012-2013 ($222 billion when inflated to end-of-year 2017 dollars), whereas cancer costs were $124.6 billion in 2010 ($151.7 billion when inflated to end-of-year 2017 dollars). Therefore, an annual cost savings of at least $15 billion translates to approximately 4% of total annual costs associated with heart disease and cancer that could be saved with increased conformance with healthy eating patterns. This increase in conformance with the HEI is not unrealistic with time; analysis of previous NHANES populations reported a 20% increase in the mean HEI-2010 total score for the US population from 49.1 in 1999 to 2000 to 59.0 in 2011 to 2012.[65] Further, a 20% increase of the current HEI-2015 score from the 2013-2014 NHANES consumption data results in an increase from 59.3 to approximately 71.2. This is approaching the target of 74 cited as the HEI-2010 score that would reflect achievement of the nutrition objectives of Healthy People 2020.[66] However, such a change would require a similar or even slightly more rapid increase in the HEI score over the next 8 years compared with what was observed between 1999 to 2000 and 2011 to 2012 and it is possible that a continued linear increase may not be realistic as individuals get closer to 100% conformance of the various components. Wilson and colleagues[66] estimates that based on the recent trajectory, the HEI-2010 would reach a mean total score of 65.4 in 2019 to 2020, or an approximate 11% above current estimates and therefore falling short of both goals set forth in Scenario 1 and 2. Achievement of 80% of the HEI-2015 by the average adult in the United States would require a further 22% increase of the 2019 to 2020 predicted score; thus, although this scenario may be an unrealistic goal, the potential reduction in health care costs illustrates the high-end influence of near-perfect conformance. Based on 2013-2014 WWEIA/NHANES data, the adult US population has reached the maximum HEI-2015 score for protein foods, although substantial shortfalls remain among the whole grains, total fruits, and dairy HEI components where the mean score for each component was 28%, 52%, and 59% of the total 10 possible points for that component (data not shown). A small shift in increased consumption of these dietary components could have a large influence on overall HEI-2015 score.

The increase in the MED may be more difficult to achieve given American-style diets that favor higher meat intakes and fewer nuts and fruits and vegetables along with comparable intakes of saturated and unsaturated fats. However, a 20% increase in the MED of 3.5 among US adults is equivalent to a shift, on average, of 0.7 on the MED scale and would translate to an individual moving above the median intake in just one of the beneficial food categories or replacing saturated fat with MUFA, for example. More than 25% of the US adult population already has achieved a score >4.2 given that the 75th percentile of the MED distribution is 5.0. Achievement of 80% of the MED or 7.2 is a far-reaching goal considering that <1% of the US adult population is currently at or above a 7.0 on the MED. Components of the MED that could be significantly improved include both legume and fish intake where the median intake was 0 c- and oz-equivalents, respectively (data not shown).

Previous studies have reviewed or evaluated the cost effectiveness[67,68] and potential health care savings[13,14] associated with a Mediterranean-style diet. The health outcomes included in these reviews and analyses were limited to heart disease end points and only one considered health care costs in the United States.[14] The 2015 analysis by Abdullah and colleagues[14] estimated health care cost savings associated with a reduced risk of cardiovascular disease in the US population assuming varying levels of adoption of the Mediterranean diet to range from $1 billion to $62.8 billion. The lower end of this range was based on the assumption that 5% of the population would adopt a Mediterranean-style diet and a 10% reduction in cardiovascular disease incidence, whereas the upper end assumed 50% adoption rate with a 60% reduction in cardiovascular disease incidence. It is difficult to compare with the analysis by Abdullah and colleagues[14] given methodologic differences, including the use of WWEIA/NHANES data to model shifts in the US population's MED, reliance on published meta-analysis of prospective cohort studies to estimate cardiovascular disease risk reduction in adult cohorts, and cost data that include all direct and indirect costs according to the American Heart Association's most recent statistics in the current analysis. However, even with these methodologic differences, the modeled cost savings based on increased conformance with a Mediterranean-style diet under Scenario 1 (ie, a 20% increase in MED) among the US adult population fell within the range reported by Abdullah and colleagues[14] and support the conclusion in both analyses that there is a significant potential for a reduction in health-related costs associated with following a Mediterranean-style diet.

Although the current model follows an approach similar to other published health economic analyses, there are inherent limitations in these approaches. The use of observational data to measure the association between dietary patterns and health outcomes will include the potential for residual confounding in the estimates of the RR. For this reason, the lower and upper limits of the 95% CIs surrounding the summary RR estimate were included to capture the uncertainty present in observational studies and provide a range of potential changes in costs. Further, the methods used to operationalize the measure of diet quality used for the HEI and the MED varies among the individual studies included in the meta-analyses with many of the HEI scores developed to operationalize different sets of DGA recommendations,[60,69] whereas the MED varies with respect to how and which components of the Mediterranean diet are included.[16-18,64] These differences in scoring across the individual studies will result in potential misclassification of the level of conformance and thus may serve to attenuate the combined summary RR estimates used in the current model. However, this approach is largely used throughout the literature and even with multiple varying indexes, including within each meta-analysis, the majority of summary RR estimates included in the current model showed little to moderate heterogeneity among the studies included.

The current model assumes a linear relationship between each dietary pattern and risk of disease where an increase in conformance (ie, a healthier diet) will proportionally reduce risk, which in turn will have a linear effect on the net change in health care costs. In the case that there is a nonlinear, threshold association between increased conformance and health outcomes, the model will fail to accurately predict the resulting changes in health care costs, resulting in either an over- or underestimate of the true change depending where on the dose-response curve the current population falls and what change is needed to observe a change in risk. Further, given that the majority of the risk estimates that are translated to cost savings in the current model are based on comparisons of high vs low conformance, this adds uncertainty as to the true difference in conformance scores associated with the change in risk due to misclassification bias. It is conceivable that a high conformer in one study population could be classified as a low conformer in another study population. The translation to costs was calculated based on the difference between the reported scores within the high and low categories used for comparisons in the individual cohort studies. Although there remains inherent uncertainty given that typically only the range of scores in each score category is provided or not all studies provide sufficient information to confirm what cohorts were included in each summary RR, the use of all available data to estimate the difference will provide the most realistic estimate of the change in score that is associated with each summary RR based on a high vs low comparison. When this calculated difference is larger or smaller than the true difference, estimated cost savings would be underestimated or overestimated, respectively. A review of the majority of the high and low conformance scores from the underlying cohorts included in the analyses used in the current model indicates the low and high conformance scores associated with reduction in disease risk are largely similar among the cohorts, and therefore reduces some of the uncertainty in the high vs low comparison summary RR.

The model inputs are largely mean point estimates. Health care costs as well as consumption data are often right-skewed; thus, using the higher mean value instead of the median, for example, could overestimate costs and the shift required for a 20% increase in conformance score in Scenario 1 while underestimating the shift required to meet the 80% score in Scenario 2. Further, indirect and direct costs were not available for all health outcomes leading to potential underestimation of the true cost savings. For example, conditions such as Alzheimer's disease have significant burden on caregivers that was not included in the current model.

Costs included in the current model are derived from annual reported costs of a disease, which reflects a distribution of disease duration. When possible, the distribution of costs by duration of disease was estimated. For example, in the case of Alzheimer's disease, incremental costs for first year post-diagnosis were known and could be weighted and combined with costs for subsequent years based on the reported statistic that 9% of patients with Alzheimer's disease are diagnosed in a given year.[53] For cancer costs, annual mean net costs of care were published for the initial, continuing, and last year of treatment for cancer in patients aged <65 and ≥65 years. The annualized costs for the total US adult population were calculated using a weighted average of the cost data for each site-specific cancer (ie, breast, colorectal, and prostate) based on the proportion of individuals in each age group and stage of treatment. Improving diet quality may result in unmeasured benefits among undiagnosed or preclinical populations. For example, there are reported substantial costs associated with cases of prediabetes[50]; benefits before a formal diabetes diagnosis are not included in the current model.

The time basis of the current model is 1 year (ie, annual costs); however, actual benefits of changes in dietary patterns are likely to accrue in small increments over time. The current model assumes that the increased conformance with each of the dietary patterns results in the estimated risk reductions; that is, the full benefit, on an annual basis. Countervailing factors suggest that this may not result in an overestimate of cost savings. Because this model is limited to clinically diagnosed diseases, it likely underestimates costs for some outcomes. Improving dietary quality may result in unmeasured benefits among undiagnosed or preclinical populations.

The modeled increase in the US adult population's conformance was applied to the total HEI or MED and therefore assumed that all dietary components within each dietary pattern contribute proportionally to the reduced risk of adverse health outcomes. However, research has shown this to not be true. For example, in a meta-analysis[24] that evaluated the association between both the overall MED as well as the individual dietary components with overall cancer risk, there was a statistically significant inverse association of fruit, vegetable, whole grain, and moderate alcohol intake with overall cancer risk. In contrast, for cereals, dairy, fish, legumes, nuts, meat, and olive oil intakes, statistically significant associations were not found. In a similar analysis, dietary components of the MED, including fruits, legumes, olive oil, and vegetables were individually associated with a reduced risk of cardiovascular disease while dairy intake was associated with an increased risk.[70] It is important to note that in evaluation of the MED, dairy products are typically included as a detrimental component originating from the fact that most of the dairy consumption in Greece was of the high-fat variety, and in particular saturated fat (eg, cheese and full-fat yogurt).[64] However, several recent meta-analyses as well as a systematic review of the evidence on dairy and health outcomes independent of a dietary pattern have reported significant protective associations between both high- and low-fat dairy as well as cheese and yogurt intake, in particular with cardiovascular outcomes.[71-74]

Economic costs associated with adhering to an improved diet, in terms of grocery and preparation costs, implementation costs, or macro-level policy implications of shifts in demand for component foods were not considered in the current evaluation. The current evaluation is theoretical and intended to illustrate the potential economic influence on direct and indirect health-related costs of an increase in the US population's conformance to the 2015-2020 DGA recommendations. The net annual cost savings modeled in this study would only be realized when interventions aimed at increasing diet quality according to the HEI or MED are successful, and in the case that the observed associations between each dietary pattern and the associated health outcomes are accurate.

CONCLUSIONS

Results from the current study support the benefits of following a healthy dietary pattern similar to those recommended in the 2015-2020 DGA based on potential cost savings. One analysis shows that a modest, realistic shift in conformance with a healthy US-style and Mediterranean-style dietary pattern as measured by the HEI-2015 and MED, respectively, at the population level can result in substantial economic benefit, whereas the second analysis models the full potential in cost savings in the case that all US adults were highly conformant with these recommended patterns of healthful diets.

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STATEMENT OF POTENTIAL CONFLICT OF INTEREST

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