# Review





# Diet Quality as Assessed by the Healthy Eating Index, Alternate Healthy Eating Index, Dietary Approaches to Stop Hypertension Score, and Health Outcomes: An Updated Systematic **Review and Meta-Analysis of Cohort Studies**



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#### **ARTICLE INFORMATION**

Article history:

Submitted 20 March 2017 Accepted 16 August 2017 Available online 27 October 2017

#### **Keywords:**

Alternate Healthy Eating Index Dietary Approaches to Stop Hypertension (DASH) diet Health status Healthy Eating Index

Meta-analysis

#### Supplementary materials:

Figures 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, and 15 and Tables 3, 4, 5, 6, 7, and 8 are available at www. jandonline.org

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#### ABSTRACT

Background Diets of the highest quality have been associated with a significantly lower risk of noncommunicable diseases.

**Objective** It was the aim of this study to update a previous systematic review investigating the associations of diet quality as assessed by the Healthy Eating Index (HEI), Alternate Healthy Eating Index (AHEI), and Dietary Approaches to Stop Hypertension (DASH) score and multiple health outcomes. As an additional topic, the associations of these diet quality indices with all-cause mortality and cancer mortality among cancer survivors were also investigated.

Design A literature search for prospective cohort studies that were published up to May 15, 2017 was performed using the electronic databases PubMed, Scopus, and Embase. Summary risk ratios (RRs) and 95% CIs were estimated using a random effects model for high vs low adherence categories.

Results The updated review process showed 34 new reports (total number of reports evaluated=68; including 1,670,179 participants). Diets of the highest quality, as assessed by the HEI, AHEI, and DASH score, resulted in a significant risk reduction for all-cause mortality (RR 0.78, 95% CI 0.77 to 0.80;  $I^2$ =59%; n=13), cardiovascular disease (incidence or mortality) (RR 0.78, 95% CI 0.76 to 0.80;  $l^2$ =49%; n=28), cancer (incidence or mortality) (RR 0.84, 95% CI 0.82 to 0.87; *I*<sup>2</sup>=66%; n=31), type 2 diabetes (RR 0.82, 95% CI 0.78 to 0.85;  $l^2 = 72\%$ ; n=10), and neurodegenerative diseases (RR 0.85, 95% CI 0.74 to 0.98;  $I^2$ =51%; n=5). Among cancer survivors, the association between diets for the highest quality resulted in a significant reduction in all-cause mortality (RR 0.88, 95% CI 0.81 to  $0.95; l^2 = 38\%; n = 7$ ) and cancer mortality (RR 0.90, 95% CI 0.83 to 0.98;  $l^2 = 0\%; n = 7$ ).

**Conclusions** In the updated meta-analyses, diets that score highly on the HEI, AHEI, and DASH were associated with a significant reduction in the risk of all-cause mortality, cardiovascular disease, cancer, type 2 diabetes, and neurodegenerative disease by 22%, 22%, 16%, 18%, and 15%, respectively. Moreover, high-quality diets were inversely associated with overall mortality and cancer mortality among cancer survivors. J Acad Nutr Diet. 2018;118:74-100

N FEBRUARY 2015, A SYSTEMATIC REVIEW AND METAanalysis of prospective cohort studies investigating the associations between diet quality, as assessed by the Healthy Eating Index (HEI), Alternate Healthy Eating Index (AHEI), and Dietary Approaches to Stop Hypertension (DASH) score, and the risk of all-cause mortality, cardiovascular disease mortality or events, cancer mortality or incidence, type 2 diabetes, and neurodegenerative diseases was published.<sup>1</sup> Diets of the highest quality were associated with a lower risk of all-cause mortality, cardiovascular disease,

cancer, and type 2 diabetes.<sup>1</sup> However, due to the large number of studies that have been published since the release of the previous meta-analysis, it seems important to update the original analysis.

According to the National Cancer Institute, the number of cancer survivors is growing rapidly, with an estimated number of 26.1 million by 2040 compared to 15.5 million in 2016.<sup>2</sup> Due to the urgent need to establish evidence-based nutrition recommendations for cancer survivors, it was decided not only to re-execute the original search, but to

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include associations between diet quality and risk of mortality in cancer survivors as an additional research question.

Therefore, the aim of this study was to update the previous systematic review and meta-analysis conducted in prospective cohort studies that investigated the association of diet quality as assessed by the HEI, AHEI, and DASH score and health status (risk of all-cause mortality, cardiovascular disease mortality or incidence, cancer mortality or incidence, type 2 diabetes, and neurodegenerative disease). The second objective of this study was to summarize the evidence of diet quality as assessed by the HEI, AHEI, and DASH score and the risk of all-cause mortality and cancer mortality among cancer survivors.

### **METHODS**

The systematic review protocol of the previous meta-analysis is registered in PROSPERO International Prospective Register of Systematic Reviews (crd.york.ac.uk/prospero/index.asp Identifier: CRD42013006561). The protocol has meanwhile been adapted to the updated version of this systematic review.

### **Data Sources and Searches**

A literature search was performed to identify studies published from May 2014 up to May 15, 2017 using the electronic databases PubMed, Embase, and Scopus. For PubMed, the following search terms were used: *healthy* [All Fields] AND (*eating* [medical subject heading {MeSH} Terms] OR *eating* [All Fields]) AND (*abstracting and indexing as topic* [MeSH Terms] OR (*abstracting* [All Fields] AND *indexing* [All Fields] AND *topic* [All Fields]) OR *abstracting and indexing as topic* [All Fields] OR *index* [All Fields]) OR (*dash* [All Fields] AND (*diet* [MeSH Terms] OR *diet* [All Fields]).

The literature search investigating the association of diet quality indices and all-cause mortality and cancer mortality among cancer survivors was based on a recently published meta-analysis<sup>3</sup> using Scopus as an additional database and was updated to include studies published up to May 15, 2017. The following search terms were used for PubMed: (healthy [All Fields] AND (eating [MeSH Terms] OR eating [All Fields]) AND (abstracting and indexing as topic [MeSH Terms] OR (abstracting [All Fields] AND indexing [All Fields] AND topic [All Fields]) OR abstracting and indexing as topic [All Fields] OR index [All Fields]) OR (dash [All Fields] AND (diet [MeSH Terms] OR diet [All Fields]) AND (cancer [All Fields]) AND (survivors [All Fields] OR survivor [All Fields] OR recurrence [All Fields] OR mortality [All Fields]) AND (prospective [All Fields] OR cohort [All Fields] OR longitudinal [All Fields] OR follow up [All Fields]).

Both search strategies had no language restrictions. Moreover, the reference lists from retrieved articles were checked to search for further relevant studies. Literature searches were conducted by one author (L.S.), with questions or uncertainties resolved by discussion with another author.

### **Study Selection**

Prospective cohort studies were included in the metaanalysis if they met all of the following criteria: evaluated the association of diet quality as assessed by the HEI, and/or AHEI, and/or DASH score on all-cause mortality, and/or cardiovascular disease mortality or incidence, and/or cancer

### **RESEARCH SNAPSHOT**

**Research Question:** Does diet quality, measured in term of the Healthy Eating Index, the Alternate Healthy Eating Index, and the Dietary Approaches to Stop Hypertension score, influence health status?

**Key Findings:** In this updated systematic review and metaanalysis of 68 reports including 1,670,179 participants, diets that score highly were associated with a significant reduction in the risk of all-cause mortality (22%), cardiovascular disease (22%), cancer (16%), type 2 diabetes (18%), and neurodegenerative disease (15%). High-quality diets were also associated with a significant reduction in the risk of overall mortality (12%) and cancer mortality (10%) among cancer survivors.

mortality or incidence, and/or type 2 diabetes, and/or neurodegenerative disease; presented risk ratios (RRs) and/or hazard ratios (HRs) with corresponding 95% CI. In addition, the meta-analysis was expanded to include cancer survivors from cohort studies investigating the association of diet quality as assessed by the HEI, and/or AHEI, and/or DASH score and all-cause mortality and/or cancer mortality among cancer survivors. Detailed description of study selection is reported in the previous version,<sup>1</sup> the same study selection strategy was used for the additional research questions of the updated systematic review.

### Data Extraction and Quality Assessment

The following data were extracted from each study as reported in the previous version<sup>1</sup>: the first author's last name, year of publication, study origin, cohort name, outcome parameter, sample size, study length (follow up in years), age at entry, sex, diet quality score, adjustment factors, study quality score, and risk estimates (most adjusted HR or RR or highest vs lowest category) with their corresponding 95% CIs. The Newcastle-Ottawa Quality Assessment Scale<sup>4</sup> was used to assess study quality. Data extraction and quality assessment were performed by one author and checked by another (B.B.) for accuracy.

### HEI, AHEI, and DASH Components and Scoring

A detailed description of the  $\text{HEI}^{5-10}$  (HEI-2005<sup>11-23</sup> and HEI-2010<sup>24-37</sup>), AHEI<sup>5,12,15,38-51</sup> (AHEI-2010<sup>11,20,23,25-33,35,36,52-59</sup>), and DASH score<sup>9,12,20,21,25-36,40,44-47,54-57,59-72</sup> and its different updates and modifications are reported in the previous version of the systematic review.<sup>1,11</sup>

### **Statistical Analysis**

The meta-analysis was performed by combining the multivariable adjusted RRs, HR, or ORs of the highest compared with the lowest quantiles of HEI, AHEI, and DASH scores conformance category based on random-effects model using the DerSimonian-Laird method.<sup>73</sup> Because outcomes were not very rare and heterogeneity modeling was deemed important, the random-effects model was used. To evaluate the weighting of each study, the standard error for the logarithm HR/RR/OR of each study was calculated and regarded as the estimated variance of the logarithm HR/RR/OR, using an inverse variance method.<sup>73</sup> Meta-analysis was based on the assumption that all measures are RRs.

Studies were grouped according to the different clinical outcomes (ie, all-cause mortality, cardiovascular disease mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative diseases, and all-cause mortality and cancer mortality among cancer survivors). As described previously, subgroup analyses were performed for the HEI, AHEI, and for the DASH score, and by comparing the HEI vs HEI-2005 vs HEI-2010, and the AHEI vs AHEI-2010. Additional subgroup analyses included US studies, longerterm follow-up studies, high-quality studies, stratified analysis by sex, and comparing incidence and mortality outcomes for cardiovascular disease and cancer. Heterogeneity, funnel plots, and test for small study effects were performed as reported in the previous version.<sup>1</sup> The *heterogi* command in STATA was used to calculate the CIs for the heterogeneity estimates.<sup>74</sup> All analyses were conducted using the Review Manager by the Cochrane Collaboration (version 5.3)<sup>75</sup> and STATA.<sup>76</sup>

### RESULTS

### Literature Search and Study Characteristics

The detailed steps of the updated meta-analysis article search and selection process are given as an adapted PRISMA



**Figure 1.** Updated flow chart for the article selection process for a meta-analysis of the associations of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, and Dietary Approaches to Stop Hypertension score and health outcomes. <sup>a</sup>CVD=cardiovascular disease. <sup>b</sup>T2D=type 2 diabetes.

Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Anic and colleagues, 2016 <sup>26</sup>	US <sup>e</sup>	National Institutes of Health, American Association of Retired Persons Diet and Health Study cohort	Lung cancer	460,770 10.5	50-71	Both	n HEI <sup>f</sup> (2010) AHEI <sup>g</sup> (2010) DASH <sup>h</sup> score	Age, sex, race/ethnicity, education, BMI, physical activity, energy intake, smoking status, cigarettes per day, time since quitting smoking, regular use of cigars/pipes	Lung cancer HEI (2010) HR 0.83 (0.77-0.89) AHEI (2010) HR 0.86 (0.80-0.92) DASH score HR 0.84 (0.78-0.90)	8
Boggs and colleagues, 2015 <sup>68</sup>	US	Black Women's Health Study	All-cause mortality	37,001 16	30-69	φi	DASH score	Age, each DASH component, energy intake, education, marital status, physical activity, television watching, smoking status, alcohol consumption	All-cause mortality DASH score HR 0.75 (0.63-0.89)	9
Cespedes and colleagues, 2016 <sup>27</sup>	US	WHI <sup>i</sup> -Dietary Modification Trial and WHI- Observational Study	T2D <sup>k</sup>	101,504 15	50-79	Ŷ	HEI (2010) AHEI (2010) DASH score	Age, race/ethnicity, education, physical activity during recreational activities, use of postmenopausal HT <sup>I</sup> , family history of diabetes, smoking status, study arm, energy intake, BMI <sup>m</sup>	T2D HEI (2010) HR 0.83 (0.78-0.89) AHEI (2010) HR 0.78 (0.73-0.83) DASH score HR 0.74 (0.69-0.80)	8
Del Gobbo and colleagues, 2015 <sup>45</sup>	US	Cardiovascular Health Study	Heart failure incidence	4,490 21.5	≥65	Both	n AHEI DASH score	Age, sex, race/ethnicity, enrollment source, education, income, physical activity, walking pace, smoking status, alcohol consumption, BMI, diabetes status, history of coronary heart disease, prevalent treated hypertension	AHEI HR 0.90 (0.74-1.09) DASH score HR 1.05 (0.88-1.26)	7

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Djousse and colleagues, 2014 <sup>46</sup>	US	Physicians' Health Study	All-cause mortality CVD <sup>n</sup> mortality Cancer mortality	19,619 20	≥40	đ°	AHEI DASH score	NA <sup>p</sup>	All-cause mortality AHEI HR 0.59 (0.52-0.68) DASH score HR 0.81 (0.71-0.93) CVD mortality AHEI HR 0.62 (0.48-0.80) DASH score HR 0.90 (0.70-1.17) Cancer mortality AHEI HR 0.68 (0.54-0.86) DASH score HR 0.93 (0.74-1.18)	Quality assessment not possible because only abstract was available
Dugue and colleagues, 2016 <sup>53</sup>	Australia	Melbourne Collaborative Cohort Study	Urothelial cell carcinoma incidence	41,514 21.3	27-76	Both	n AHEI (2010)	Sex, country of birth, smoking status, alcohol consumption, BMI; physical activity, education, socioeconomic status	Urothelial cell carcinoma incidence AHEI (2010) HR 1.02 (0.73-1.43)	9

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Fung and colleagues, 2014 <sup>54</sup>	US	Nurses' Health Study	All-cause mortality Colorectal cancer mortality	1,201 colorectal cancer survivors 11.2	61-72	Ŷ	AHEI (2010) DASH score	Age, physical activity, BMI, weight change, cancer grade, chemotherapy, smoking status, energy intake, colon or rectal cancer stage of disease, date of colorectal cancer diagnosis	All-cause mortality AHEI (2010) HR 0.71 (0.52-0.98) DASH score HR 0.98 (0.71-1.35) Colorectal cancer mortality AHEI (2010) HR 0.72 (0.43-1.21) DASH score HR 0.87 (0.52-1.45)	8
George and colleagues, 2011 <sup>17</sup>	US	Health, Eating, Activity, and Lifestyle Study	All-cause mortality Breast cancer mortality	670 breast cancer survivors 6	≥18	Ŷ	HEI (2005)	Energy intake, physical activity, race/ethnicity, stage, tamoxifen use, BMI	HEI (2005) All-cause mortality HR 0.40 (0.17-0.94) Breast cancer mortality HR 0.12 (0.02-0.99)	8
George and colleagues, 2014 <sup>16</sup>	US	WHI-Dietary Modification Trial and WHI- Observational Study	All-cause mortality Breast cancer mortality	2,317 breast cancer survivors 9.6	50-79	Ŷ	HEI (2005)	Age at screening visit, WHI component, race/ethnicity, income, education, stage of disease, estrogen receptor status, progesterone receptor status, time since diagnosis, energy intake, physical activity, alcohol consumption, use of postmenopausal HT	HEI (2005) All-cause mortality HR 0.74 (0.55-0.99) Breast cancer mortality HR 0.91 (0.60-1.40)	8

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
George and colleagues, 2014 <sup>28</sup>	US	WHI-Observational Study	All-cause mortality CVD mortality Cancer mortality	63,805 12.9	50-79	Ŷ	HEI (2010) AHEI (2010) DASH score	Age, energy intake, race/ ethnicity, education, marital status, smoking status, physical activity, use of postmenopausal HT, BMI, alcohol consumption (except for AHEI), diabetes status	All-cause mortality HEI (2010) HR 0.76 (0.70-0.83) AHEI (2010) HR 0.82 (0.76-0.90) DASH score HR 0.76 (0.70-0.83) CVD mortality HEI (2010) HR 0.78 (0.65-0.93) AHEI (2010) HR 0.81 (0.68-0.96) DASH score HR 0.76 (0.65-0.90) Cancer mortality HEI (2010) HR 0.77 (0.68-0.89) AHEI (2010) HR 0.77 (0.68-0.89) AHEI (2010) HR 0.93 (0.81-1.06) DASH score HR 0.80 (0.70-0.91)	8

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	_Sex	Diet quality _index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
George and colleagues, 2015 <sup>29</sup>	US	WHI-Observational Study	Endometrial cancer incidence	84,415 13.3	50-79	Ŷ	HEI (2010) AHEI (2010) DASH score	Age, energy intake, race/ ethnicity, education, physica activity during recreational activities, diabetes status, use of postmenopausal HT, oral contraceptive use, age at first birth, participant in observational study, participant in HT trial, participant in dietary modification trial, alcohol consumption (except for AHEI (2010), BMI	Endometrial cancer incidence I HEI (2010) HR 1.11 (0.93-1.33) AHEI (2010) HR 0.98 (0.82-1.17) DASH score HR 1.00 (0.84-1.19)	8
Haridass, 2015 <sup>55</sup>	US	California Teacher Study	Invasive breast cancer incidence	94,404 16	22-104	Ŷ	AHEI (2010) DASH score	Menopausal status, family history of breast cancer, race/ethnicity, age at menarche, smoking status, socioeconomic status, physical activity, BMI, daily vitamin use, energy intake	Invasive breast cancer incidence AHEI (2010) HR 0.87 (0.79-0.97) DASH score HR 0.88 (0.79-0.97)	8
Haring and colleagues, 2016 <sup>30</sup>	US	WHI-Memory Study	Mild cognitive impairment o probable dementia incidence	6,425 r 9	65-79	Ŷ	HEI (2010) AHEI (2010) DASH score	Age, race/ethnicity, education, WHI Hormone Trial randomization assignment, baseline Modified Mini- Mental State Examination score, smoking status, physical activity, diabetes status, hypertension status, BMI, income, depression, history of CVD, energy intake	Mild cognitive impairment or probable dementia incidence HEI (2010) HR 1.12 (0.87-1.44) AHEI (2010) HR 0.82 (0.64-1.07) DASH score HR 0.93 (0.81-1.22)	7

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Diet quality	Adjustment	RRª/HR <sup>b</sup> (95% Cl), multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Harmon and colleagues, 2015 <sup>31</sup>	US	Multi-ethnic Cohort	All-cause mortality CVD mortality Cancer mortality	215,782 13-18	45-75	Both HEI (2010) AHEI (2010) DASH score	Age, BMI, diabetes status, energy intake, race/ethnicity, education, marital status, smoking status, alcohol consumption (except for AHEI (2010)), use of postmenopausal HT (only for \$), physical activity	All-cause mortality HEI (2010) dHR 0.75 (0.71-0.79) 9HR 0.79 (0.75-0.83) AHEI (2010) dHR 0.78 (0.74-0.82) 9HR 0.78 (0.74-0.82) 9HR 0.78 (0.74-0.82) DASH score dHR 0.81 (0.77-0.85) 9HR 0.80 (0.75-0.84) CVD-mortality HEI (2010) dHR 0.74 (0.69-0.81) 9HR 0.77 (0.71-0.84) AHEI (2010) dHR 0.79 (0.72-0.86) 9HR 0.79 (0.72-0.86) 9HR 0.79 (0.72-0.86) 9HR 0.76 (0.69-0.83) DASH score dHR 0.83 (0.76-0.91) 9HR 0.78 (0.71-0.85) Cancer mortality HEI (2010) dHR 0.76 (0.70-0.83) 9HR 0.89 (0.81-0.98) AHEI (2010) dHR 0.83 (0.76-0.90) 9HR 0.85 (0.77-0.93) DASH score dHR 0.78 (0.71-0.85) 9HR 0.86 (0.78-0.95)	9
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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	_Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
lzano and colleagues, 2013 <sup>56</sup>	US	Nurses' Health Study	Breast cancer mortality Non-breast cancer mortality	4,103 breast cancer survivors 9.33	30-55	Ŷ	AHEI (2010) DASH score	Age at diagnosis, energy intake BMI, BMI change, age at first birth, parity, oral contraceptive use, menopausal status, use of postmenopausal HT, smoking status, stage of disease, radiation treatment, chemotherapy and HT, physical activity	, Breast cancer mortality t AHEI (2010) RR 1.07 (0.77-1.49) DASH score RR 0.85 (0.61-1.19) Non-breast cancer mortality AHEI (2010) RR 0.57 (0.42-0.77) DASH score RR 0.72 (0.53-0.99)	8
Jacobs and colleagues, 2015 <sup>32</sup>	US	Multi-ethnic Cohort	T2D	89,185 NA	45-75	Both	n HEI (2010) AHEI (2010) DASH score	Physical activity, smoking status, education, energy intake, BMI	T2D HEI (2010) dHR 0.93 (0.85-1.01) PHR 0.92 (0.84-1.01) AHEI (2010) dHR 0.88 (0.81-0.96) PHR 0.88 (0.80-0.97) DASH score dHR 0.79 (0.73-0.87) PHR 0.77 (0.70-0.84)	9
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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% Cl), multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>6</sup>
Jacobs and colleagues, 2016 <sup>33</sup>	US	Multi-ethnic Cohort	All-cause mortality Colorectal cancer mortality	4,204 colorecta cancer r survivors 6	I 45-75	Both	HEI (2010) AHEI (2010) DASH score	Age at diagnosis, race/ethnicity, stage at diagnosis, energy intake, smoking status, pack- years of smoking, physical activity, education, radiation treatment, chemotherapy, nonsteroidal anti- inflammatory drug use, family history of colorectal cancer, comorbidities	All-cause mortality HEI (2010) dHR 0.91 (0.76-1.09) QHR 0.89 (0.72-1.09) AHEI (2010) dHR 1.08 (0.90-1.28) QHR 0.83 (0.67-1.03) DASH score dHR 1.06 (0.87-1.28) QHR 0.97 (0.77-1.22) Colorectal cancer mortality HEI (2010) dHR 0.85 (0.66-1.08) QHR 0.76 (0.58-1.01) AHEI (2010) dHR 1.07 (0.84-1.36) QHR 0.81 (0.61-1.07) DASH score dHR 1.05 (0.81-1.37) QHR 0.88 (0.64-1.19)	8
Larsson and colleagues, 2016 <sup>70</sup>	Sweden	Cohort of Swedish Men and Swedish Mammography cohort	Ischemic stroke incidence Intracerebral hemorrhages incidence Subarachnoid hemorrhages incidence	74,404 11.9	45-83	Both	m <sup>9</sup> DASH score	Education, family history of myocardial infarction before 60 years of age, smoking status, pack-years of smoking, aspirin use, walking/bicycling, physical activity, BMI, history of hypertension, hypercholesterolemia, diabetes, and atrial fibrillation, energy intake, alcohol consumption	mDASH score Ischemic stroke incidence RR 0.86 (0.78-0.94) Intracerebral hemorrhages incidence RR 0.81 (0.63-1.05) Subarachnoid hemorrhages incidence RR 0.95 (0.60-1.50)	8

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), _multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Larsson and colleagues, 2017 <sup>69</sup>	Sweden	Cohort of Swedish Men and Swedish Mammography cohort	Extrahepatic biliary tract cancer incidence, Gallbladder cancer incidence, Intrahepatic biliary tract cancer incidence	76,014 13.3	45-83	Both	mDASH score	Age, sex, education, smoking status, pack-years of smoking, diabetes status, BMI, energy intake	mDASH score Extrahepatic biliary tract cancer incidence HR 0.41 (0.26-0.64) Gallbladder cancer incidence HR 0.36 (0.20-0.64) Intrahepatic biliary tract cancer incidence HR 0.36 (0.11-1.21)	8
Lassale and colleagues, 2016 <sup>34</sup>	Europe	European Prospective Investigation into Cancer and Nutrition	All-cause mortality CVD mortality Cancer mortality	451,256 12.8	25-70	Both	HEI (2010) DASH score	Dietary score, age, BMI, physica activity, smoking status, education	All-cause mortality HEI (2010) HR 0.82 (0.78-0.86) DASH score HR 0.82 (0.78-0.86) CVD mortality HEI (2010) HR 0.82 (0.75-0.90) DASH score HR 0.77 (0.70-0.84) Cancer mortality HEI (2010) HR 0.87 (0.81-0.92) DASH score HR 0.87 (0.81-0.93)	8

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Mertens and colleagues, 2017 <sup>57</sup>	United Kingdom	Caerphilly Prospective Study	Cardiovascular disease	1,867 12	45-59	ð	AHEI (2010) DASH score	Age, smoking, social class, physical activity, energy intake, usual alcohol consumption	Cardiovascular disease AHEI (2010) HR 0.82 (0.66-1.01) DASH score HR 0.81 (0.66-0.99)	7
Morris and colleagues, 2015 <sup>71</sup>	US	Rush Memory and Aging Project	Alzheimer's disease incidence	923 4.5	58-98	Both	a DASH score	Age, sex, education, apolipoprotein ε4-allele, participation in cognitively stimulating activities, physical activity, energy intake, cardiovascular conditions	Alzheimer's disease incidence DASH score HR 0.60 (0.37-0.96)	6
Neelakantan and colleagues, 2016 <sup>58</sup>	I China	Singapore Chinese Health Study	Acute myocardial infarction	2,194 NA	45-75	Both	1 AHEI (2010)	Age, sex, dialect group, year of interview, year blood was collected, age at interview, energy intake, education, smoking status, physical activity, BMI, history of diabetes, history of hypertension, low- and high density lipoprotein cholesterol, triglycerides, high-sensitivity C-reactive protein, glycated hemoglobin, Creatinine, systolic blood pressure	Acute myocardial infarction AHEI (2010) OR <sup>®</sup> 0.64 (0.48-0.86)	7
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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Diet quality Sex_index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Newcastle Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Otto and colleagues, 2015 <sup>47</sup>	US	Multi-Ethnic Study of Atherosclerosis	T2D	5,160 10	45-84	Both AHEI DASH score	Age, sex, race/ethnicity, education, field center, smoking, energy intake, physical activity, dietary supplement, BMI, baseline waist circumference	T2D AHEI HR 0.81 (0.65-1.00) DASH score HR 1.02 (0.79-1.30)	7
Park and colleagues, 2016 <sup>9</sup>	US	Third National Health and Nutrition Examination Survey	All-cause mortality CVD mortality Cancer mortality	2,103 18.6	30-90	Both HEI DASH score	Age, sex, race/ethnicity, education, income, smoking status, alcohol consumption, physical activity, energy intake	All-cause mortality HEI HR 0.59 (0.45-0.77) DASH score HR 0.88 (0.71-1.09) CVD mortality HEI HR 0.55 (0.33-0.92) DASH score HR 0.52 (0.35-0.77) Cancer mortality HEI HR 0.53 (0.29-0.97) DASH score HR 0.85 (0.57-1.27)	6
Park and colleagues, 2017 <sup>35</sup>	US	Multiethnic Cohort Study	Colorectal cancer	· 190,949 16	45-75	Both HEI (2010) AHEI (2010) DASH score	Age, sex, ethnicity, family history of colorectal cancer, history of colorectal polyp, BMI, smoking, multivitamin use, nonsteroidal anti- inflammatory drugs, physica activity, menopausal status, menopausal hormone therapy use, energy intake, alcohol	Colorectal cancer HEI (2010) &HR 0.69 (0.59-0.80) &HR 0.82 (0.70-0.96) AHEI (2010) & &HR 0.75 (0.65-0.85) &PHR 0.90 (0.78-1.04) DASH score &HR 0.75 (0.66-0.86) &PHR 0.86 (0.75-1.00)	9

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Diet quality Sex_index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Pelser and colleagues, 2014 <sup>18</sup>	US	National Institutes of Health- American Association of Retired Persons Diet and Health study cohort	All-cause mortality Colorectal cancer specific mortality	4,213 colorecta cancer r survivors 5	al 50-71	Both HEI (2005)	Lag time, sex, education, family history of colon cancer, cancer stage, first course of treatment, BMI, physical activity, alcohol consumption, smoking status	HEI (2005) All-cause mortality RR 0.95 (0.78-1.16) Colorectal cancer-specific mortality RR 0.99 (0.77-1.27)	8
Shahar and colleagues, 2009 <sup>10</sup>	US	Health, Aging, and Body Composition study	All-cause mortality	298 9	70-82	Both HEI	Age, race/ethnicity, sex, enrollment source, smoking status, marital status, weight energy intake, subjective health evaluation, cognitive function score	All-cause mortality HEI , HR 1.9 (0.7-5.2)	5
Smyth and colleagues, 2015 <sup>48</sup>	Worldwide	ONTARGET <sup>6</sup> and TRANSCEND <sup>†</sup> studies	Cognitive decline	27,860 3	≥55	Both mAHEI	Age, education, sex, trial enrollment source, treatment allocation, geographical region, baseline Mini-Mental State Examination score, systolic blood pressure, history of stroke/transient ischemic attack, diabetes status, myocardial infarction, microalbuminuria, serum creatinine, statin therapy, b-blocker therapy, antithrombotic use, smoking status, BMI, physical activity, depression	Cognitive decline t mAHEI HR 0.76 (0.66-0.86)	6

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at _entry, y	Sex	Diet quality _index/score	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Thomson and colleagues, 2014 <sup>19</sup>	US	WHI-Observational Study and WHI-Clinical Trials	All-cause mortality Cancer mortality	636 ovarian cancer survivors 11	50-79	Ŷ	HEI (2005)	Age at diagnosis, stage at diagnosis, race/ethnicity, diabetes status, physical activity, energy intake, waist circumference, family history of ovarian cancer, clinical trial arms	HEI (2005) All-cause mortality HR 0.73 (0.55-0.97) Cancer mortality HR 0.75 (0.55-1.01)	8
Vargas and colleagues, 2016 <sup>36</sup>	US	WHI-Observational Study	Colorectal cancer incidence	r 78,273 12.4	50-79	Ŷ	HEI (2010) AHEI (2010) DASH score	Age, race/ethnicity, physical activity, education, smoking status, use of postmenopausal HT	Colorectal cancer inciden HEI (2010) HR 0.73 (0.59-0.90) AHEI (2010) HR 0.86 (0.70-1.07) DASH score HR 0.78 (0.62-0.97)	ce 8
Xie and colleagues, 2014 <sup>20</sup>	US	Nurses' Health Study	Epithelial ovarian cancer incidence	a 82,948 24	30-55	Ŷ	HEI (2005) AHEI (2010)	Age, energy intake, family history of ovarian cancer, tubal ligation, BMI, parity, number of additional pregnancies, oral contraceptive use, pack- years of smoking, menopausal status, use of postmenopausal HT (type and duration), age at menarche, hysterectomy, unilateral oophorectomy, lactose intake, caffeine intake, physical activity	Epithelial ovarian cancer incidence HEI (2005) HR 0.85 (0.65-1.12) AHEI (2010) HR 1.03 (0.80-1.34)	8
									(c	ontinued on next page)

Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Diet qua Sex_index/so	ality core	Adjustment	RRª/HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Yu and colleagues, 2014 <sup>59</sup>	China	Shanghai Men's Health Study and Shanghai Women's Health Study	All-cause I mortality CVD mortality Cancer mortality	రే61,239 \$73,216 రే6.5 9 \$12	40-74	Both mAHEI ( mDASH	(2010) score	Age, education, income, smoking status, alcohol consumption (except for mAHEI (2010)), multivitamin use, physical activity, BMI, waist-to-hip ratio, history of CVD, diabetes or hypertension, menopausal status and use of postmenopausal HT (only fo women), energy intake	All-cause mortality mAHEI (2010) dHR 0.68 (0.61-0.76) 9HR 0.80 (0.73-0.87) mDASH score dHR 0.76 (0.69-0.85) 9HR 0.84 (0.76-0.91) CVD mortality mAHEI (2010) dHR 0.56 (0.46-0.68) 9HR 0.73 (0.62-0.87) mDASH score dHR 0.60 (0.49-0.73) 9HR 0.79 (0.67-0.92) Cancer mortality mAHEI (2010) dHR 0.87 (0.74-1.02) 9HR 0.92 (0.80-1.06) mDASH score dHR 0.88 (0.75-1.04) 9HR 0.90 (0.78-1.03)	8

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Author(s), year	Country	Cohort	Outcome	Population, n Follow up, y	Age at entry, y	Sex	Diet quality index/score	Adjustment	RR <sup>a</sup> /HR <sup>b</sup> (95% CI), multivariate adjusted <sup>c</sup>	Newcastle Ottawa Quality Assessment Scale <sup>4</sup> (maximum 9) <sup>d</sup>
Yu and colleagues, 2015 <sup>37</sup>	US	Southern Community Cohort Study	All-cause mortality CVD mortality Cancer mortality	84,735 6.2	40-79	Both	n HEI (2010)	Race/ethnicity, enrollment source, education, income, marital status, medical insurance, smoking status, BMI, physical activity, sitting time, energy intake, menopausal status and use of postmenopausal HT (only for women), baseline disease status	HEI (2010) All-cause mortality HR 0.80 (0.73-0.86) CVD mortality HR 0.81 (0.70-0.94) Cancer mortality HR 0.81 (0.69-0.95)	9

#### <sup>a</sup>RR=risk ratio. <sup>b</sup>HR=hazard ratio.

<sup>c</sup>In case of multiple HR/RR values, the order in which data are given correspond to the respective order of outcomes listed in the "Outcomes" column.

<sup>d</sup>Higher scores indicate higher-quality studies.

<sup>f</sup>HEI=Healthy Eating Index.

<sup>9</sup>AHEI=Alternate Healthy Eating Index. <sup>h</sup>DASH=Dietary Approaches to Stop Hypertension. <sup>i</sup>♀=women. <sup>j</sup>WHI=Women's Health Initiative. <sup>k</sup>T2D=type 2 diabetes. <sup>I</sup>HT=hormone therapy. <sup>m</sup>BMI=body mass index.

<sup>n</sup>CVD=cardiovascular disease. °ð=men.

PNA=no data available.

<sup>r</sup>OR=odds ratio.

<sup>s</sup>ONTARGET=Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint.

<sup>t</sup>TRANSCEND=Telmisartan Randomized Assessment Study in ACE Intolerant Subjects with Cardiovascular Disease.

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(Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram (Figure 1).<sup>77</sup>

Taken together, 34 additional reports were identified that were not included in the previous meta-analysis.<sup>9,10,16-20,</sup> 26-37,45-48,53-59,68-71

General study characteristics are summarized in Table 1. Sample size varied between 298 and 460,770, with a followup time ranging from 3 to 24 years. Overall, 68 reports, 5-72 including 1,670,179 participants, were included in the updated meta-analysis. According to the different clinical outcomes, all-cause mortality w reports,<sup>6,9,10,25,28,31,34,37,46,49,52,59,68</sup> was evaluated in 13 cardiovascular disease mortality or incidence in 28 reports,<sup>6-9,11,21,25,28,31,34</sup>, 37,41,45,46,49,50,52,57-64,66,70,72 cancer mortality or incidence in reports, 6-9,11,13-15,20,22-26,28,29,31,34-38,41,46,49,52,53,55,59,67, 31 type 2 diabetes in 10 reports, 11,12,27,32,40,42,44,47,51,65 neurodegenerative diseases in 5 reports,<sup>30,39,43,48,71</sup> all-cause mortality among cancer survivors in 7 reports, 16-19,33,54,56 and cancer mortality among cancer survivors in 7 reports.<sup>16-19,33,54,56</sup>

### **Main Outcomes**

Using a random-effects model, the highest association of diet quality as assessed by the HEI, AHEI, or DASH score was found to be associated with a reduced risk of all-cause mortality (RR 0.78, 95% CI 0.77 to 0.80;  $l^2$ =59%, 95% CI 39% to 72%; n=13) (Figure 2), cardiovascular disease (incidence or mortality) (RR 0.78, 95% CI 0.76 to 0.80;  $I^2$ =49%, 95% CI 31% to 64%; n=28) (Figure 3; available online at www.jandonline.org), cancer (incidence or mortality) (RR 0.84, 95% CI 0.82 to 0.87;  $I^2 = 66\%$ , 95% CI 56% to 73%; n=31) (Figure 4; available online at www. jandonline.org), type 2 diabetes (RR 0.82, 95% CI 0.78 to 0.85; *I*<sup>2</sup>=72%, 95% CI 58% to 82%; n=10) (Figure 5; available online at www.jandonline.org), and neurodegenerative diseases (RR 0.85, 95% CI 0.74 to 0.98;  $I^2=51\%$ , 95% CI 0% to 78%; n=5) (Figure 6). Among cancer survivors, the association between diets for the highest quality resulted in a significant reduction in all-cause mortality (RR 0.88, 95% CI 0.81 to 0.95;  $l^2=38\%$ , 95% CI 0%, 67%; n=7) (Figure 7) and cancer mortality (RR 0.90, 95% CI 0.83 to 0.98;  $I^2 = 0\%$ , 95% CI, 0% to 55%; n=7; fixed effect model) (Figure 8; available online at www.jandonline.org). The corresponding enumerative data are summarized in Table 2.

### Subgroup and Sensitivity Analysis

Subgroup analysis showed an inverse association between diets that scored highly on the HEI, AHEI, and DASH and risk of colorectal, esophageal, lung, gallbladder, pancreatic, prostate, head/neck, as well as hepatocellular carcinoma (Figure 9; available online at www.jandonline.org). Subgroup analysis suggested that all diets that scored highly on the included dietary indexes (HEI, AHEI, and DASH score) were associated with a reduced risk of all-cause mortality, cardiovascular disease (CVD), cancer, and type 2 diabetes. However, the subgroup analysis for risk of neurodegenerative disease indicated that only diets that scored highly on AHEI were associated with reduced risk (RR 0.77, 95% CI 0.68 to 0.88;  $I^2=0\%$ ). Furthermore, the subgroup analysis for risk of all-cause mortality and cancer mortality or incidence indicated that diets that scored highly on the original version of the HEI were not significantly associated with reduced risk of all-cause mortality (RR 0.75, 95% CI 0.53 to 1.07;  $l^2$ =67%) and cancer (RR 0.87, 95% CI 0.76 to 1.00;  $l^2$ =89%), and diets that scored highly on the more recent diet quality indices (HEI-2005 and HEI-2010) were inversely associated with all-cause mortality (RR 0.78, 95% CI 0.77 to 0.80;  $l^2$ =37%) and cancer risk (RR 0.82, 95% CI 0.77 to 0.88;  $l^2$ =67%). Moreover, the original version of the AHEI was not significantly associated with reduced risk of cancer (RR 0.87, 95% CI 0.75 to 1.01;  $l^2$ =73%), and diets that scored highly on the more recent AHEI-2010 (RR 0.87, 95% CI 0.85 to 0.90;  $l^2$ =49%) were inversely associated with cancer risk.

Among cancer survivors, only diets that scored highly on HEI were inversely related to risk of all-cause mortality (RR 0.85, 95% CI 0.75 to 0.96;  $l^2$ =26%) and cancer mortality (RR 0.84, 95% CI 0.73 to 0.97;  $l^2$ =18%).

As in the previous version of the meta-analysis, additional subgroup analyses were performed for US studies, long-term studies ( $\geq$ 8 years of follow up), high-quality cohort studies (Newcastle Ottawa score  $\geq$ 7 points), and comparing men and women. Including only US studies confirmed the results of the primary analysis (Table 3; available at www.jandonline. org). Subgroup analyses taking into account longer-term follow up (Table 4; available at www.jandonline.org) and high-quality studies (Table 5; available at www.jandonline. org) confirmed the results of the main analysis, except for neurodegenerative disease risk, showing no significant associations. No significant differences comparing men and women were observed in the subgroup analysis, except for all-cause mortality and cancer mortality among cancer survivors, showing a significant inverse association only for women (Tables 6 and 7; available at www.jandonline.org).

Because for CVD and cancer, mortality and incidence rates were combined, sensitivity analyses were performed comparing mortality vs incidence (CVD incidence RR 0.79, 95% CI 0.75 to 0.83, cancer incidence RR 0.84, 95% CI 0.82 to 0.86, CVD mortality RR 0.79, 95% CI 0.75 to 0.80, and cancer mortality RR 0.85, 95% CI 0.83 to 0.87). No differences between mortality and incidence analyses were observed. In addition, a fixed-effects sensitivity analysis confirmed all results of the main analysis (Table 8; available at www. jandonline.org).

### **Publication Bias**

Egger linear regression tests (performed with at least 10 studies) provided no evidence of small study effects for risk of all-cause mortality (P=0.78), CVD (P=0.16), overall cancer mortality or incidence risk (P=0.13), and risk of type 2 diabetes (P=0.94), following comparison of the highest vs lowest quantiles of HEI, AHEI, and DASH scores. However, a potential risk of bias for all-cause mortality (P=0.01) and cancer mortality (P=0.03) among cancer survivors was observed.

Funnel plots were only generated when  $\geq$ 10 studies were available for a comparison. The funnel plots for risk of allcause mortality (Figure 10; available at www.jandonline. org), cardiovascular disease mortality or incidence (Figure 11; available at www.jandonline.org), indicate little asymmetry, whereas the funnels plots for cancer mortality or incidence (Figure 12; available at www.jandonline.org), for risk of type 2 diabetes (Figure 13; available at www. jandonline.org), as well as all-cause mortality (Figure 14; available at www.jandonline.org), and cancer mortality

		Risk Ratio	Risk Ratio	
Study or Subgroup	Weight	IV, Random, 95% CI	IV, Random, 95% CI	
HEI <sup>a</sup>				
George and colleagues 2014b <sup>28</sup> b	2.8%	0.76 [0.70, 0.83]		
Harmon and colleagues 2015 M <sup>31</sup>	4.3%	0.75 [0.71, 0.79]		
Harmon and colleagues 2015 W <sup>31</sup>	4.5%	0.79 [0.75, 0.83]		
Kappeler and colleagues 2013 <sup>6</sup>	0.7%	0.77 [0.63, 0.94]		
Lassale and colleagues 2016 <sup>34</sup>	4.6%	0.82 [0.78, 0.86]	-	
Park and colleagues 2016 <sup>9</sup>	0.4%	0.59 [0.45, 0.77]		
Reedy and colleagues 2014 M <sup>25</sup>	6.2%	0.78 [0.76, 0.80]	+	
Reedy and colleagues 2014 W <sup>25</sup>	5.3%	0.77 [0.74, 0.80]	-	
Shahar and colleagues 2009 <sup>10</sup>	0.0%	1.90 [0.70, 5.16]		→
Yu and colleagues 2015 <sup>37</sup>	2.5%	0.80 [0.73, 0.88]		
Subtotal (95% CI)	31.3%	0.78 [0.76, 0.80]	♦	
Heterogeneity: $Tau^2 = 0.00$ ; Chi <sup>2</sup> =	14.27. df	= 9 (P = 0.11); l <sup>2</sup> = 37%		
Test for overall effect: Z = 19.18 (P	< 0.0000	1)		
d		,		
Akbaraly and colleagues 2011	0.6%	0.76 [0.61, 0.95]		
Djousse and colleagues 2014 <sup>40</sup>	1.6%	0.59 [0.52, 0.67]		
George and colleagues 2014b <sup>20</sup>	3.1%	0.82 [0.76, 0.88]		
Harmon and colleagues 2015 M <sup>31</sup>	4.4%	0.78 [0.74, 0.82]		
Harmon and colleagues $2015 \text{ W}^{31}$	4.4%	0.78 [0.74, 0.82]		
Mursu and colleagues 2013 <sup>32</sup>	3.8%	0.82 [0.77, 0.87]	-	
Reedy and colleagues 2014 M <sup>23</sup>	6.2%	0.76 [0.74, 0.78]	-	
Reedy and colleagues $2014_{50}$ W <sup>25</sup>	6.2%	0.76 [0.74, 0.78]	-	
Yu and colleagues 2014 M <sup>39</sup>	1.9%	0.68 [0.61, 0.76]		
Yu and colleagues 2014 W <sup>39</sup>	2.5%	0.80 [0.73, 0.88]		
Subtotal (95% CI)	34.7%	0.76 [0.74, 0.79]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	31.06, df	= 9 (P = 0.0003); l² = 71%		
Test for overall effect: Z = 15.14 (P	< 0.0000	1)		
DASH score				
Boggs and colleagues 2015 <sup>68</sup>	0.9%	0.75 [0.63, 0.89]		
Djousse and colleagues 2014	1.5%	0.81 [0.71, 0.92]		
George and colleagues 2014 b <sup>28</sup>	2.8%	0.76 [0.70, 0.83]		
Harmon and colleagues 2015 M <sup>31</sup>	4.6%	0.81 [0.77, 0.85]	-	
Harmon and colleagues $2015 \text{ W}^{31}$	3.7%	0.80 [0.75, 0.85]		
Lassale and colleagues 2016 <sup>34</sup>	4.6%	0.82 [0.78, 0.86]	-	
Park and colleagues 2016 <sup>9</sup>	0.6%	0.88 [0.71, 1.09]		
Reedy and colleagues 2014 M <sup>25</sup>	5.5%	0.83 [0.80, 0.86]	-	
Reedy and colleagues 2014 W <sup>25</sup>	5.3%	0.78 [0.75, 0.81]	÷	
Yu and colleagues 2014 M <sup>59</sup>	2.3%	0.76 [0.69, 0.84]		
Yu and colleagues 2014 W <sup>59</sup> Subtotal (95% CI)	2.2% <b>34.0%</b>	0.84 [0.76, 0.93] <b>0.80 [0.79, 0.82]</b>	•	
Heterogeneity: $Tau^2 = 0.00$ Chi <sup>2</sup> =	10.99 df	$= 10 (P = 0.36) \cdot l^2 = 9\%$	·	
Test for overall effect: $Z = 21.01$ (P	< 0.0000	1)		
Total (95% CI)	100.0%	0.78 [0.77, 0.80]	•	
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	72.83, df	= 30 (P < 0.0001); l² <sup>t</sup> = 59%		-
Test for overall effect: Z = 27.14 (P	< 0.0000	1)	U.D U./ I I.D Z	
Test for subgroup differences: Chi <sup>2</sup>	= 7.58. dt	$f = 2 (P = 0.02),  ^2 = 73.6\%$	IEUUUEU IISK IIIUIEASEU IISK	

**Figure 2.** Forest plot showing pooled relative risks (RRs) with 95% Cl for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for all-cause mortality. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup>/<sup>2</sup>=inconsistency.

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Table 2. Relative risk (with 95% CIs) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular disease mortality or incidence, cancer mortality or incidence, cancer types, type 2 diabetes, neurodegenerative disease, as well as all-cause mortality and cancer mortality among cancer survivors

_					<i>I</i> <sup>2</sup> , % <sup>a</sup>	2h	Test for subgroup
Outcome	No. of reports	Index/score	Relative risk	95% Cl	(95% Cl)	H	difference (P value)
All-cause mortality	13	All indexes combined	0.78	0.77-0.80	59 (39-72)	2.43	
	8	HEI <sup>c</sup>	0.78	0.76-0.80	37	1.58	0.02
	7	AHEI <sup>d</sup>	0.76	0.74-0.79	71	3.44	
	8	DASH <sup>e</sup> score	0.80	0.79-0.82	9	1.09	
Cardiovascular disease mortality or incidence	28	All indexes combined	0.78	0.76-0.80	49 (31-64)	1.96	
	11	HEI	0.79	0.77-0.82	16	1.19	0.02
	13	AHEI	0.75	0.72-0.77	39	1.64	
	18	DASH score	0.80	0.77-0.84	49	1.96	
Cancer mortality or incidence	31	All indexes combined	0.84	0.82-0.87	66 (56-73)	2.94	
	21	HEI	0.83	0.79-0.87	73	3.70	0.03
	18	AHEI	0.88	0.85-0.91	54	2.17	
	15	DASH score	0.82	0.80-0.86	48	1.92	
Breast cancer	2	All indexes combined	0.94	0.81-1.08	86	1	<0.001
Colorectal cancer	4	All indexes combined	0.77	0.73-0.81	0	1	
Esophageal cancer	1	HEI	0.66	0.46-0.94	43	1.75	
Gastric cancer	1	HEI	0.90	0.72-1.12	0	1	
Pancreatic cancer	1	HEI	0.85	0.74-0.98	NA <sup>f</sup>	NA	
Prostate cancer	1	All indexes combined	0.93	0.89-0.97	NA	NA	
Head and neck cancer	1	HEI	0.61	0.40-0.94	75	4	
Hepatocellular carcinoma	1	HEI	0.72	0.53-0.98	NA	NA	
Lung cancer	1	All indexes combined	0.84	0.81-0.87	NA	NA	
Urothelial cell carcinoma	1	AHEI	1.02	0.73-1.43	NA	NA	
Gallbladder cancer	1	DASH score	0.36	0.20-0.65	NA	NA	
Ovarian cancer	1	All indexes combined	1.03	0.80-1.33	NA	NA	

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(continued on next page)

**Table 2.** Relative risk (with 95% Cls) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular disease mortality or incidence, cancer mortality or incidence, cancer types, type 2 diabetes, neurodegenerative disease, as well as all-cause mortality and cancer mortality among cancer survivors (*continued*)

Outcome	No. of reports	Index/score	Relative risk	95% CI	l <sup>2</sup> , % <sup>a</sup> (95% Cl)	H <sup>2b</sup>	Test for subgroup difference (P value)
Endometrial cancer	1	All indexes combined	1.03	0.93-1.14	NA	NA	
Type 2 diabetes	10	All indexes combined	0.82	0.78-0.85	72 (58-82)	3.57	
	3	HEI	0.87	0.82-0.93	61	2.56	0.13
	9	AHEI	0.80	0.74-0.86	76	4.16	
	7	DASH score	0.80	0.74-0.86	61	2.56	
Neurodegenerative diseases	5	All indexes combined	0.85	0.74-0.98	51 (0-78)	2.04	
	3	HEI	0.97	0.68-1.39	55	2.22	0.51
	2	AHEI	0.77	0.68-0.88	0	1	
	2	DASH score	0.80	0.53-1.20	66	2.94	
All-cause mortality among cancer survivors	7	All indexes combined	0.88	0.81-0.95	38 (0-67)	1.61	
	5	HEI	0.85	0.75-0.96	26	1.35	0.49
	3	AHEI	0.85	0.70-1.03	65	2.85	
	3	DASH score	0.94	0.82-1.08	27	1.37	
Cancer mortality among cancer survivors	7	All indexes combined	0.90	0.83-0.98	0 (0-55)	1	
	5	HEI	0.84	0.73-0.97	18	1.22	0.51
	3	AHEI	0.95	0.79-1.13	20	1.25	
	3	DASH score	0.93	0.79-1.10	0	1	

 $^{a}l^{2}$ =inconsistency, percentage of variation across studies due to heterogeneity.

<sup>b</sup>H<sup>2</sup>=total variability.

<sup>c</sup>HEI=Healthy Eating Index.

<sup>d</sup>AHEI=Alternate Healthy Eating Index. <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 6.** Forest plot showing pooled relative risks (RRs) with 95% CI for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for neurodegenerative disease. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup> $l^2$ =inconsistency.

(Figure 15; available at www.jandonline.org) among cancer survivors indicate moderate symmetry.

### DISCUSSION

In this updated systematic review and meta-analysis of prospective cohort studies investigating the pooled estimates from studies assessing diet quality using the HEI, AHEI, and DASH score on all-cause mortality, cardiovascular disease mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality among cancer survivors, findings were pooled from 68 reports, including more than 1.6 million participants.

In general, the main results suggest that diets of the highest quality, as assessed by the HEI, AHEI, and DASH score, were associated with a significant reduction in the risk of allcause mortality, cardiovascular disease, cancer, type 2 diabetes, and neurodegenerative disease by 22%, 22%, 16%, 18%, and 15%, respectively. Moreover, adherence to high-quality diet was inversely associated with overall mortality among cancer survivors by 12%.

The original systematic review and meta-analysis was, to the best of the authors' knowledge, the first approach to investigate the pooled estimates from studies assessing diet quality via these indices.<sup>1</sup> In congruence with the updated version, the original results emphasized the importance of dietary pattern analysis for studying the association between diet and health status. It could be shown that high-quality diets were associated with reduced risk of all-cause mortality as well as onset of disease. The present report represents a substantial update of the original, adding important evidence for a beneficial effect of diets of the highest quality, as assessed by the HEI, AHEI, and DASH score for additional types of neurodegenerative diseases, as well as additional types of cancer both not yet available in 2014 (gallbladder, lung, endometrial), and all-cause and cancer mortality among cancer survivors. This is a target group for nutritional recommendations gaining importance due to improved screening methods, early diagnosis, and enhanced treatment approaches.<sup>2</sup> The inverse association between the included diet quality indices and all-cause mortality in cancer survivors is in line with a previous meta-analysis of cohort studies, showing an inverse association between high diet quality indices or a prudent/health dietary pattern and reduced risk of overall mortality.<sup>3</sup>

Subgroup analyses revealed that the positive influence of adhering to the diet quality indices depends on their chronological development. Inverse associations of high adherence to HEI or AHEI with respect to cancer (incidence or mortality) could only be observed for later versions of both indices, that is, the 2005 and 2010 versions of the HEI and the 2010 version of the AHEI. Assessment of the overall quality of diet via *a priori* approaches instead of single nutrients is a comparatively new approach.<sup>78</sup> The indices used for the present systematic review represent *a priori* defined indices based on already existing national recommendations or data derived from prospective cohort studies for a healthy life-style.<sup>1</sup> The HEI and AHEI are continuously updated and improved by implementing new study data. Therefore, there is a time-dependent evolution of the corresponding indices



Heterogeneity: Tau<sup>2</sup> = 0.01; Chi<sup>2</sup> = 21.10, df = 13 (P = 0.07);  $l^{2}f = 38\%$ Test for overall effect: Z = 3.15 (P = 0.002)

Test for subgroup differences: Chi<sup>2</sup> = 1.44, df = 2 (P = 0.49), l<sup>2</sup> = 0% **Figure 7.** Forest plot showing pooled relative risks (RRs) with 95% CI for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for all-cause mortality among cancer survivors. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup> $l^2$ =inconsistency.

as well, for example, the original version of the HEI did not differentiate between refined and unrefined grains,<sup>79</sup> thereby limiting its sensitivity in the evaluation of the interactions between high adherence and onset and progression of type 2 diabetes, CVD, and cancer.<sup>7,8</sup> Likewise, there were differences in the scoring of the AHEI, with additional factors being included in its latest version to incorporate more recent scientific evidence on the relationship between diet and health.<sup>11</sup>

In another subgroup analysis, the impact of scoring highly on one of the diet quality indices with respect to different types of cancer was investigated. It has to be noted that for a number of tumor localizations, data could only be extracted from single epidemiological observations (pancreatic, prostate, hepatocellular, lung, urothelial cell, gallbladder, ovarian, and endometrial carcinoma). However, the inverse associations of high adherence to diet quality indices on the pathogenesis of colorectal cancer were covered by more than one cohort. Regarding colorectal and head and neck cancer, similar results were provided by a systematic review investigating 55 different diet quality scores.<sup>80</sup> In addition, the authors reported for several studies an inverse association between high-quality diets and risk of breast cancer, which could not be observed in present meta-analysis.<sup>80</sup> These discrepancies might be explained by the implementation of different dietary scores by Potter and colleagues, for example, the Mediterranean diet. Data on this *a priori* pattern were synthesized in an earlier meta-analysis finding that the highest adherence to a Mediterranean diet category was associated with a reduced risk of breast cancer by combining cohort and case-control studies.<sup>81,82</sup>

0.7

1

reduced risk increased risk

0.5

1.5 2

Despite the various differences between the diet quality indices used in the present study, a commonality is that they assess intake of desirable food groups such as fruits, vegetables, whole grains, nuts, and legumes.<sup>83-90</sup> At the same time, potentially detrimental food groups are appropriately taken

into account as well.<sup>83,90-92</sup> Taken together, this might help explain the results of the systematic synthesis of all available data on diet quality indices at hand.

#### Strengths and Limitations

Although the number of epidemiological studies is substantially higher compared to the original systematic review, there remains a considerable statistical heterogeneity with respect to all-cause mortality, cancer incidence/mortality, CVD incidence/mortality, type 2 diabetes, and incidence of neurodegenerative diseases. Basically, the limitations of the former analysis still apply for the updated version (heterogeneous scoring systems, risk estimates, population/sex/age and sample size, follow up, development stage of included indices). In addition, gray literature published outside regular academic distribution channels was not searched or inquired via contacting study authors. Publication bias is another important threat to the validity of meta-analysis. Due to the large number of studies, it was possible to test publication bias for all-cause mortality, CVD mortality or incidence, cancer mortality or incidence, and type 2 diabetes, whereas for all other outcomes the size of the meta-analyses were too small.<sup>93</sup> However, because all included studies were published post 2000, publication bias is less of a risk.<sup>94</sup>

However, the study has been strengthened by including additional forms of neurodegenerative diseases, additional types and localizations of cancer, and by enrolling cohorts of cancer survivors. The latter enhances the informative value of the data at hand with regard to secondary preventive measures. This led to a consecutive increase in power of the analyses (68 reports including 1,670,179 participants as compared to 34 reports including 1,020,642 participants in the original analysis). Regardless of the persisting limitations, present data provide good-quality evidence that the consumption of high-quality diets as assessed by the HEI, AHEI, and DASH score is associated with beneficial health effects, stressing the importance of the underlying dietary recommendations.

#### CONCLUSIONS

In the updated meta-analyses diets that score highly on the HEI, AHEI, and DASH were associated with a significant reduction in the risk of all-cause mortality, cardiovascular disease, cancer, type 2 diabetes, and neurodegenerative disease by 22%, 22%, 16%, 18%, and 15%, respectively. In addition, high-quality diets were inversely associated with overall mortality and cancer mortality among cancer survivors. This stresses the importance of lifestyle adaptations in primary as well as secondary prevention of non-communicable diseases.

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#### AUTHOR INFORMATION

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#### STATEMENT OF POTENTIAL CONFLICT OF INTEREST

No potential conflict of interest was reported by the authors.

#### **FUNDING/SUPPORT**

There is no funding to disclose.

#### ACKNOWLEDGEMENTS

L. Schwingshackl, B. Bogensberger, and G. Hoffmann collected the data. L. Schwingshackl and G. Hoffmann wrote the first draft with contributions from B. Bogensberger. All authors reviewed and commented on subsequent drafts of the manuscript.

		Risk Ratio	Risk Ratio
Study or Subgroup	Weight	IV, Random, 95% CI	IV, Random, 95% CI
HEI <sup>a</sup>			
Agnoli and colleagues 2011 <sup>21</sup>	0.4%	0.89 [0.60, 1.32]	
Chiuve and colleagues 2012 <sup>11</sup>	2.7%	0.79 [0.71, 0.88]	-
George and colleagues 2014 <sup>28</sup>	1.4%	0.78 [0.65, 0.94]	
Harmon and colleagues 2015 M <sup>31</sup>	3.7%	0.74 [0.69, 0.79]	-
Harmon and colleagues 2015 W <sup>31°</sup>	3.4%	0.77 [0.71, 0.84]	-
Kappeler and colleagues 2013 <sup>6</sup>	0.8%	0.85 [0.65, 1.11]	
Lassale and colleagues 2016 <sup>34</sup>	3.2%	0.82 [0.75, 0.90]	-
McCullough and colleagues 2000 M <sup>7</sup>	1.4%	0.72 [0.60, 0.86]	
McCullough and colleagues 2000 W <sup>8</sup>	1.5%	0.86 [0.72, 1.03]	
Park and colleagues 2016 <sup>9</sup>	0.2%	0.55 [0.33, 0.92]	
Reedy and colleagues 2014 M <sup>25</sup>	4.0%	0.85 [0.80, 0.90]	-
Reedy and colleagues $2014 \text{ W}^{25}$	3.5%	0 79 [0 73 0 85]	-
Yu and colleagues $2015^{37}$	1.9%	0.81 [0.70, 0.94]	
Subtotal (95% CI)	28.1%	0.79 [0.77, 0.82]	•
Heterogeneity: $Tau^2 = 0.00$ : $Chi^2 = 14$	36 df = 12	$(P = 0.28)$ : $l^2 = 16\%$	,
Test for overall effect: $7 = 13.17$ (P < (	00001	(1 0.20), 1 1070	
d			
AHEI			
Akbarahy and colleagues 2011 <sup>49</sup>	0.3%	0 58 [0 37 0 91]	
Relin and colleagues 2011 <sup>50</sup>	3.0%	0.30 [0.37, 0.31]	-
Chiwa and colleagues 2012 <sup>11</sup>	3.0%	0.77 [0.70, 0.85]	-
children and colleagues 2012	3.0%	0.76 [0.71, 0.61]	
del Gobbo and colleagues 2015	1.3%	0.90 [0.74, 1.09]	
Djousse and colleagues 2014	0.8%	0.62 [0.48, 0.80]	
George and colleagues 2014	1.5%	0.81 [0.68, 0.96]	-
Harmon and colleagues 2015 M <sup>31</sup>	3.5%	0.79 [0.73, 0.85]	
Harmon and colleagues 2015 W <sup>31</sup>	3.0%	0.76 [0.69, 0.84]	-
McCullough and colleagues 2002 M	1.1%	0.61 [0.49, 0.76]	
McCullough and colleagues 2002 W	1.4%	0.72 [0.60, 0.86]	
Mertens and colleagues 2017	1.1%	0.82 [0.66, 1.02]	
Mursu and colleagues 2013 <sup>52</sup>	3.1%	0.79 [0.72, 0.87]	-
Neelakantan and colleagues 2016	0.7%	0.64 [0.48, 0.85]	
Reedy and colleagues 2014 M <sup>25</sup>	4.1%	0.74 [0.70, 0.78]	-
Reedy and colleagues 2014 W <sup>23</sup>	3.7%	0.72 [0.67, 0.77]	-
Yu and colleagues 2014 M <sup>59</sup>	1.3%	0.56 [0.46, 0.68]	<u> </u>
Yu and colleagues 2014 W <sup>39</sup>	1.7%	0.73 [0.62, 0.86]	<u> </u>
Subtotal (95% CI)	35.2%	0.75 [0.72, 0.77]	•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 26.	28, df = 16	(P = 0.05); l <sup>2</sup> = 39%	
Test for overall effect: Z = 14.96 (P < 0	0.00001)		
e			
DASH score			
Agnoli and colleagues 2011 <sup>21</sup>	0.4%	0.75 [0.51, 1.10]	
Bertoia and colleagues 2014 <sup>72</sup>	0.3%	0.86 [0.54, 1.37]	
del Gobbo and colleagues 2015	1.5%	1.05 [0.88, 1.25]	
Djousse and colleagues 2014 <sup>40</sup>	0.9%	0.90 [0.70, 1.16]	
Fitzgerald and colleagues 2012	1.1%	0.87 [0.70, 1.08]	
Folsom and colleagues 2007 <sup>61</sup>	1.2%	0.93 [0.76, 1.14]	
Fung and colleagues 2008 <sup>62</sup>	3.0%	0.77 [0.70, 0.85]	-
George and colleagues 2014	1.8%	0.76 [0.65, 0.89]	
Harmon and colleagues 2015 M <sub>21</sub>	3.2%	0.83 [0.76, 0.91]	-
Harmon and colleagues 2015_W	3.0%	0.78 [0.71, 0.86]	-
Larsson and colleagues 2016 <sup>70</sup>	2.9%	0.86 [0.78, 0.95]	-
Lassale and colleagues 2016 <sup>34</sup>	3.0%	0.77 [0.70, 0.85]	-
Levitan and colleagues 2009 M <sup>63</sup>	1.4%	0.78 [0.65, 0.94]	
Levitan and colleagues 2009 W <sup>64</sup>	0.8%	0.63 [0.48, 0.83]	
Lin and colleagues 2013 <sup>66</sup>	0.3%	0.63 [0.41, 0.97]	
Mertens and colleagues 2017 <sup>57</sup>	1.2%	0.81 [0.66, 0.99]	
Park and colleagues 2016 <sup>9</sup>	0.4%	0.52 [0.35, 0.77]	
Reedy and colleagues 2014 M <sup>25</sup>	4.0%	0.86 [0.81, 0.91]	-
Reedy and colleagues 2014 W <sup>25</sup>	3.4%	0.78 [0.72, 0.84]	-
Yu and colleagues 2014 M <sup>59</sup>	1.2%	0.60 [0.49, 0.73]	
Yu and colleagues 2014 W <sup>59</sup>	1.6%	0.79 [0.67, 0.93]	
Subtotal (95% CI)	36.7%	0.80 [0.77, 0.84]	♦
Heterogeneity: $Tau^2 = 0.00$ : $Chi^2 = 39$	37, df = 20	(P = 0.006): I <sup>2</sup> = 49%	
Test for overall effect: $Z = 9.59$ (P < 0.	00001)		
Total (95% CI)	100.0%	0.78 [0.76, 0.80]	♦
Heterogeneity: Tau <sup>2</sup> = 0.00: Chi <sup>2</sup> = 97.	72, df = 50	(P < 0.0001): I <sup>2f</sup> = 49%	
Test for overall effect: $Z = 19.16$ (P < 0	0.00001)		0.5 0.7 1 1.5 2
Test for subgroup differences: Chi2 = 7	r = 0 $df = 0$	$(D = 0.02)$ $l^2 = 74.09/$	reduced risk increased risk

**Figure 3.** Forest plot showing pooled relative risks (RRs) with 95% CI for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for cardiovascular disease mortality or incidence. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup>*f*<sup>2</sup>=inconsistency.

		Risk Ratio	Risk Ratio
Study or Subgroup	Weight	IV, Random, 95% CI	IV, Random, 95% CI
HEI <sup>a</sup> 26			
Anic and colleagues 2016 <sup>20</sup>	2.1%	0.83 [0.77, 0.89]	-
Arem and colleagues 2013 <sup>22</sup>	1.4%	0.85 [0.74, 0.98]	
Chiwa and colleagues 2013 <sup>22</sup>	2.2%	0.92 [0.86, 0.98]	-
George and colleagues 2012	1.6%	0.90 [0.64, 0.96]	-
George and colleagues 2015 <sup>29</sup>	1.1%	1.11 [0.93, 1.32]	+
Harmon and colleagues 2015 M <sup>31<sup>b</sup></sup>	2.0%	0.76 [0.70, 0.83]	-
Harmon and colleagues 2015 W <sup>31<sup>c</sup></sup>	1.9%	0.89 [0.81, 0.98]	-
Kappeler and colleagues 20136	0.3%	0.75 [0.51, 1.10]	
Lassale and colleagues 2016 <sup>34</sup>	2.1%	0.87 [0.81, 0.93]	-
Li and colleagues 2013 <sup>14</sup>	0.5%	0.88 [0.65, 1.19]	
Li and colleagues 2013 <sup>14</sup>	0.5%	0.92 [0.67, 1.26]	
Li and colleagues 2013 <sup>14</sup>	0.6%	0.75 [0.57, 0.99]	
Li and colleagues 2013	0.2%	0.51 [0.31, 0.84]	
Li and colleagues 2014 M <sup>13</sup>	0.5%	0.72 [0.53, 0.98]	
Li and colleagues 2014 W <sup>13</sup>	0.4%	0.74 [0.61, 0.90]	
McCullough and colleagues 2000 M <sup>7</sup>	1.2%	1 12 [0 95 1 32]	<u>+</u>
McCullough and colleagues 2000 W <sup>8</sup>	1.9%	1.02 [0.93, 1.12]	+
Park and colleagues 2016 <sup>9</sup>	0.1%	0.53 [0.29, 0.97]	
Park and colleagues 2017 M <sup>35</sup>	1.3%	0.69 [0.59, 0.80]	
Park and colleagues 2017 W <sup>35</sup>	1.2%	0.82 [0.70, 0.96]	
Reedy and colleagues 2008 M <sup>15</sup>	1.3%	0.72 [0.62, 0.84]	
Reedy and colleagues 2008 W	0.8%	0.80 [0.64, 1.00]	
Reedy and colleagues 2014 M <sup>25</sup>	2.3%	0.76 [0.72, 0.80]	-
Reedy and colleagues 2014 W <sup>25</sup>	2.2%	0.82 [0.77, 0.87]	
Vargas and colleagues 2016 <sup>30</sup>	0.9%	0.73 [0.59, 0.90]	
Are and colleagues 2014 <sup>20</sup>	0.6%	0.85 [0.65, 1.11]	
Subtotal (95% CI)	35.7%	0.81 [0.69, 0.95]	•
Heterogeneity: $Tau^2 = 0.01$ · Chi <sup>2</sup> = 104	30. df = 3	8 (P < 0.00001) · 12 = 73%	•
Test for overall effect: $Z = 7.84$ (P < 0.0		o (i = 0.00001), i = 73%	
4	,		
AHEI			
Akbaraly and colleagues 201149	0.5%	0.80 [0.58, 1.10]	
Anic and colleagues 2016 <sup>26</sup>	2.1%	0.86 [0.80, 0.92]	-
Bosire and colleagues 2013 <sup>23</sup>	2.3%	0.93 [0.88, 0.98]	-
Chiuve and colleagues 2012	2.3%	0.94 [0.89, 0.99]	-
Djousse and colleagues 2014 <sup>40</sup>	0.8%	0.68 [0.54, 0.86]	
Dugue and colleagues 2016	0.4%	1.02 [0.73, 1.43]	
George and colleagues 2014 <sup>5</sup>	1.4%	0.93 [0.81, 1.07]	-
George and colleagues 2015 <sup>55</sup>	1.1%	0.98 [0.82, 1.17]	-
Harmon and colleagues 2015 M <sup>31</sup>	2.0%	0.87 [0.75, 0.90]	-
Harmon and colleagues 2015 W <sup>31</sup>	1.8%	0.85 [0.77, 0.94]	-
McCullough and colleagues 2002 M <sup>41</sup>	1.1%	1.03 [0.87, 1.22]	- <del>-</del> -
McCullough and colleagues 2002 W <sup>41</sup>	1.8%	0.97 [0.88, 1.07]	+
Mursu and colleagues 201352	1.7%	0.88 [0.79, 0.98]	-
Park and colleagues 2017 M <sup>35</sup>	1.4%	0.75 [0.65, 0.86]	-
Park and colleagues 2017 W <sup>35</sup>	1.4%	0.90 [0.78, 1.04]	
Reedy and colleagues 2008 M <sup>15</sup>	1.3%	0.71 [0.61, 0.83]	
Reedy and colleagues 2008 W <sup>15</sup>	0.8%	0.83 [0.66, 1.04]	
Reedy and colleagues 2014 M <sup>25</sup>	2.4%	0.82 [0.78, 0.86]	÷
Reedy and colleagues 2014 W <sup>25</sup>	2.3%	0.88 [0.83, 0.93]	-
Vargas and colleagues 2016	0.9%	0.86 [0.70, 1.06]	
Xie and colleagues 2014 M <sup>59</sup>	0.7%	1.03 [0.80, 1.33]	
Yu and colleagues 2014 W	1.2%	0.87 [0.74, 1.02]	-
Subtotal (95% CI)	35.0%	0.88 [0.85, 0.91]	•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 49.8	38, df = 23	(P = 0.0010); I <sup>2</sup> = 54%	
Test for overall effect: Z = 7.60 (P < 0.0	00001)		
DAOLL			
DASH score	-		
Anic and colleagues 2016 <sup>20</sup>	2.1%	0.84 [0.78, 0.90]	-
Lipousse and colleagues 2014	0.8%	0.93 [0.74, 1.17]	
George and colleagues 2014 h <sup>28</sup>	1.5%	0.80 [0.70, 0.91]	-
George and colleagues 2015 <sup>29</sup>	1 1%	1.00 [0.84 1 19]	+
Haridass 2015 <sup>55</sup>	1.7%	0.88 [0.79. 0.98]	
Harmon and colleagues 2015 M <sup>31</sup>	1.9%	0.78 [0.71. 0.86]	-
Harmon and colleagues 2015 W <sup>31</sup>	1.8%	0.86 [0.78, 0.95]	
Larsson and colleagues 2017 <sup>69</sup>	0.0%	0.36 [0.11, 1.18]	← → +
Larsson and colleagues 2017 <sup>69</sup>	0.3%	0.41 [0.26, 0.65]	
Larsson and colleagues 2017 <sup>69</sup>	0.2%	0.36 [0.20, 0.65]	
Lassale and colleagues 2016	2.1%	0.87 [0.81, 0.93]	
Miller and colleagues 2013 M <sup>-7</sup>	1.8%	0.75 [0.68, 0.83]	
Miller and colleagues 2013 W	1.4%	0.84 [0.73, 0.97]	
Park and colleagues 2017 M <sup>35</sup>	1.5%	0.00 [0.07, 1.27]	-
Park and colleagues 2017 W <sup>35</sup>	1.5%	0.86 [0.75 1 00]	
Reedy and colleagues 2014 M <sup>25</sup>	2.4%	0.80 [0.76. 0.84]	-
Reedy and colleagues 2014 W <sup>25</sup>	2.2%	0.82 [0.77, 0.87]	+
Vargas and colleagues 2016 <sup>36</sup>	0.8%	0.78 [0.62, 0.98]	
Yu and colleagues 2014 M <sup>59</sup>	1.2%	0.88 [0.75, 1.03]	
Yu and colleagues 2014 W <sup>59</sup>	1.4%	0.90 [0.78, 1.04]	1
Subtotal (95% CI)	29.3%	0.82 [0.80, 0.86]	•
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 40.2	28, df = 21	(P = 0.007); I <sup>2</sup> = 48%	
Test for overall effect: $Z = 10.23$ (P < 0	.00001)		
Total (95% CI)	100 0%	0.84 [0.82 0 87]	4
Heterogeneity: $Tau^2 = 0.01$ · $Chi^2 = 215$	02. df = 7	4 (P < 0.00001) I <sup>2</sup> = 66%	·····
Test for overall effect: $7 = 13.78 / P < 0$	.00001)	- (, - 0.00001), 1 - 00%	0.2 0.5 1 2 5
			reduced risk increased risk

**Figure 4.** Forest plot showing pooled relative risks (RRs) with 95% CI for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for cancer mortality or incidence. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup>l<sup>2</sup>=inconsistency.

		Risk Ratio	Risk Ratio
Study or Subgroup	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
HEI <sup>a</sup>			
Cespedes and colleagues 2016 <sup>27</sup>	6.4%	0.83 [0.78, 0.88]	-
Chiuve and colleagues 2012 <sup>11</sup>	6.0%	0.82 [0.76, 0.88]	-
Jacobs and colleagues 2015 M <sup>32</sup>	5.6%	0.93 [0.85, 1.02]	
Jacobs and colleagues 2015 W32	5.6%	0.92 [0.84, 1.01]	
Subtotal (95% Cl)	23.5%	0.87 [0.82, 0.93]	$\bullet$
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> =	7.78, df =	3 (P = 0.05); I <sup>2</sup> = 61%	
Test for overall effect: Z = 4.36 (P	< 0.0001)		
ALEI <sup>d</sup>			
Cospedes and colleagues 2016 <sup>27</sup>	6 3%	0 78 10 73 0 831	-
Chippedes and colleagues 2010	5.5%	0.67 [0.61, 0.74]	-
de Koning and colleagues 2012	1.2%	0.77 [0.67, 0.88]	
Europe and colloagues 2007 <sup>51</sup>	4.2 /0		_ <b>_</b>
Interact 201/ $^{40}$	4.1% 5.0%		_
lacobs and colleagues $2015 \text{ M}^{32}$	5.8%	0.88 [0.81, 0.96]	-
Jacobs and colleagues 2015 $W^{32}$	5.0%	0.88 [0.80, 0.97]	-
Otto and colleagues $2015^{47}$	2.6%	0.81 [0.65, 1.00]	
Oiao and colleagues $2013^{42}$	5.8%	0.76 [0.70, 0.83]	-
Tobias and colleagues 2012 <sup>44</sup>	1.3%	0.65 [0.46, 0.92]	
Subtotal (95% CI)	46.1%	0.80 [0.74, 0.86]	•
Heterogeneity: $Tau^2 = 0.01$ : Chi <sup>2</sup> =	37.45. df :	$= 9 (P < 0.0001); I^2 = 76\%$	
Test for overall effect: Z = 6.19 (P	< 0.00001)	)	
DASH score			
Cespedes and colleagues 2016 <sup>27</sup>	6.2%	0.74 [0.69, 0.79]	-
de Koning and colleagues 2011 <sup>12</sup>	4.1%	0.75 [0.65, 0.87]	
Interact 2014 <sup>40</sup>	4.6%	0.95 [0.84, 1.07]	
Jacobs and colleagues 2015 M <sup>32</sup>	5.9%	0.79 [0.73, 0.85]	
Jacobs and colleagues 2015 W <sup>32</sup>	5.4%	0.77 [0.70, 0.85]	-
Liese and colleagues 2009 <sup>65</sup>	0.6%	0.64 [0.37, 1.11]	
Otto and colleagues 2015 <sup>47</sup>	2.2%	1.02 [0.79, 1.30]	<del></del>
Tobias and colleagues 2012 <sup>44</sup>	1.4%	0.68 [0.49, 0.94]	
Subtotal (95% Cl)	30.4%	0.80 [0.74, 0.86]	•
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> =	18.05, df =	= 7 (P = 0.01); l² = 61%	
Test for overall effect: Z = 5.82 (P	< 0.00001)	)	
Total (95% CI)	100.0%	0.82 [0.78, 0.85] <sub>c</sub>	•
Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> =	75.69, df =	= 21 (P < 0.00001); l²¹= 72%	
Test for overall effect: Z = 9.17 (P	< 0.00001)	)	reduced risk increased risk
Test ferrer hansen differense est Ohi	2 - 1 00 -1		

Test for subgroup differences: Chi<sup>2</sup> = 4.09, df = 2 (P = 0.13), l<sup>2</sup> = 51.1% **Figure 5.** Forest plot showing pooled relative risks (RRs) with 95% Cl for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category for type 2 diabetes. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score. <sup>f</sup>/<sup>2</sup>=inconsistency.

	HEI	
	George and colleagues 2011 <sup>17</sup>	0.2%
	George and colleagues 2014 a	4.1%
	Jacobs and colleagues 2016 $M_{-c}^{33}$	11.0%
	Jacobs and colleagues 2016 W <sup>33</sup>	9.7%
	Pelser and colleagues 2014 <sup>18</sup>	11.2%
	Thomson and colleagues 2014 <sup>19</sup>	7.3%
	Subtotal (95% CI)	43.5%
	Heterogeneity: Tau <sup>2</sup> = 0.01; Chi <sup>2</sup> = 6	6.09, d
	Test for overall effect: Z = 2.34 (P =	0.02)
		0 70
	Fung and colleagues 2014	2.7%
	Izano and colleagues $2013$	6.5%
	Jacobs and colleagues 2016 M	12.1%
	Subtotal (95% CI)	8.8% 30.0%
	Heterogeneity: $Tau^2 = 0.01$ : $Chi^2 = 3$	375 d
	Test for overall effect: $Z = 0.62$ (P =	0.53)
	PAOL soon	
	DASH score	
	Fung and colleagues 2014	2.7%
	Izano and colleagues 2013	6.4%
	Jacobs and colleagues 2016 M	10.5%
	Subtotal (95% CI)	7.0% <b>26.5</b> %
	Heterogeneity: $Tau^2 = 0.00$ ; Chi <sup>2</sup> = $\frac{1}{2}$	1.30, d
	Test for overall effect: Z = 0.81 (P =	0.42)
	Total (95% CI)	100.0%
-	Heterogeneity: $Tau^2 = 0.00$ : Chi <sup>2</sup> =	12.86.
	Test for overall effect: $Z = 2.48$ (P =	0.01)
	······································	/

Study or Subgroup

а



**Risk Ratio** 

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Test for subgroup differences:  $Chi^2 = 1.36$ , df = 2 (P = 0.51),  $I^2 = 0\%$ 

Figure 8. Forest plot showing pooled relative risks (RRs) for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category with 95% CI for cancer mortality among cancer survivors. <sup>a</sup>HEI=Healthy Eating Index (includes the original version, HEI-2005, HEI-2010). <sup>b</sup>Men. <sup>c</sup>Women. <sup>d</sup>AHEI=Alternate Healthy Eating Index (includes the original version, and AHEI-2010). <sup>e</sup>DASH=Dietary Approaches to Stop Hypertension score.  $f_{l}^{2}$ =Inconsistency.

**Risk Ratio** 

0.2%

4.1%

9.7%

11.2%

7.3%

43.5%

2.7%

6.5%

12.1%

8.8%

30.0%

2.7%

6.4%

10.5%

7.0%

26.5%

100.0%

11.0%



**Figure 9.** Forest plot showing pooled relative risks (RRs) for the highest diet quality (HEI, AHEI, DASH) vs lowest diet quality category with 95% CI for different cancer types. <sup>a</sup>Men. <sup>b</sup>Women. <sup>c</sup>l<sup>2</sup>=inconsistency.



**Figure 10.** Funnel plot showing study precision against the relative risk with 95% CIs all-cause mortality. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 11.** Funnel plot showing study precision against the relative risk with 95% CIs for cardiovascular mortality or incidence. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 12.** Funnel plot showing study precision against the relative risk with 95% CIs for cancer mortality or incidence. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 13.** Funnel plot showing study precision against the relative risk with 95% Cls for type 2 diabetes. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 14.** Funnel plot showing study precision against the relative risk with 95% Cls for all-cause mortality among cancer survivors. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.



**Figure 15.** Funnel plot showing study precision against the relative risk with 95% Cls for cancer mortality among cancer survivors. <sup>a</sup>SE=standard error. <sup>b</sup>HEI=Healthy Eating Index. <sup>c</sup>AHEI=Alternate Health Eating Index. <sup>d</sup>DASH=Dietary Approaches to Stop Hypertension.

**Table 3.** US cohort studies: relative risk ratios (with 95% confidence intervals) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% CI	1 <sup>2</sup> , %
	0		0.70	0.76.0.00	50
All-cause mortality	9	All indexes combined	0.78	0.76-0.80	59
Cardiovascular disease mortality or incidence	17	All indexes combined	0.79	0.76-0.81	49
Cancer mortality or incidence	26	All indexes combined	0.84	0.82-0.86	67
Type 2 diabetes	9	All indexes combined	0.80	0.76-0.84	68
Neurodegenerative disease	4	All indexes combined	0.84	0.73-0.97	59
All-cause mortality among cancer survivors	7	All indexes combined	0.88	0.81-0.95	38
Cancer mortality among cancer survivors	7	All indexes combined	0.90	0.83-0.98	0

**Table 4.** Long-term follow up ( $\geq$ 8 years): Relative risk ratios (with 95% Cls) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% Cl	I <sup>2</sup> , %
All-cause mortality	12	All indexes combined	0.78	0.77-0.80	59
Cardiovascular disease mortality or incidence	25	All indexes combined	0.79	0.77-0.81	40
Cancer mortality or incidence	29	All indexes combined	0.85	0.83-0.87	67
Type 2 diabetes	7	All indexes combined	0.80	0.75-0.85	72
Neurodegenerative disease	4	All indexes combined	0.91	0.78-1.06	35
All-cause mortality among cancer survivors	4	All indexes combined	0.77	0.69-0.86	0
Cancer mortality among cancer survivors	4	All indexes combined	0.86	0.74-1.01	0

**Table 5.** High-quality studies ( $\geq$ 7 points Newcastle Ottawa scale): Relative risk ratios (with 95% Cls) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% Cl	<u>l</u> ², %
All-cause mortality	9	All indexes combined	0.79	0.77-0.80	47
Cardiovascular disease mortality or incidence	22	All indexes combined	0.78	0.76-0.80	49
Cancer mortality or incidence	28	All indexes combined	0.85	0.83-0.87	67
Type 2 diabetes	8	All indexes combined	0.82	0.79-0.86	75
Neurodegenerative disease	2	All indexes combined	0.90	0.76-1.05	50
All-cause mortality among cancer survivors	7	All indexes combined	0.88	0.81-0.95	38
Cancer mortality among cancer survivors	7	All indexes combined	0.90	0.83-0.98	0

**Table 6.** Women: relative risk ratios (with 95% CIs) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% Cl	l <sup>2</sup> , %
All-cause mortality	6	All indexes combined	0.78	0.77-0.79	2
Cardiovascular disease mortality or incidence	13	All indexes combined	0.77	0.75-0.79	0
Cancer mortality or incidence	14	All indexes combined	0.88	0.85-0.91	53
Type 2 diabetes	5	All indexes combined	0.80	0.76-0.84	63
Neurodegenerative disease	2	All indexes combined	0.94	0.84-1.05	1
All-cause mortality among cancer survivors	6	All indexes combined	0.82	0.75-0.89	1
Cancer mortality among cancer survivors	6	All indexes combined	0.83	0.74-0.93	0

**Table 7.** Men: Relative risk ratios (with 95% Cls) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% CI	l <sup>2</sup> , %
All-cause mortality	4	All indexes combined	0.77	0.74-0.79	80
Cardiovascular disease mortality or incidence	8	All indexes combined	0.76	0.72-0.80	73
Cancer mortality or incidence	10	All indexes combined	0.83	0.79-0.87	79
Type 2 diabetes	2	All indexes combined	0.83	0.77-0.90	68
Neurodegenerative disease	1	All indexes combined	1.83	0.65-5.15	NA <sup>a</sup>
All-cause mortality among cancer survivors	1	All indexes combined	1.01	0.91-1.13	2
Cancer mortality among cancer survivors	1	All indexes combined	0.99	0.85-1.14	0

<sup>a</sup>NA=not applicable.

**Table 8.** Fixed-effects meta-analysis: Relative risk ratios (with 95% CIs) of the association of diet quality as assessed by the Healthy Eating Index, Alternate Healthy Eating Index, or Dietary Approaches to Stop Hypertension score for all-cause mortality, cardiovascular mortality or incidence, cancer mortality or incidence, type 2 diabetes, neurodegenerative disease, and all-cause mortality and cancer mortality among cancer survivors

Outcome	No. of studies	Index	Risk ratio	95% Cl	l <sup>2</sup> , %
All-cause mortality	13	All indexes combined	0.78	0.77-0.79	59
Cardiovascular disease mortality or incidence	28	All indexes combined	0.78	0.77-0.80	49
Cancer mortality or incidence	31	All indexes combined	0.85	0.84-0.86	66
Type 2 diabetes	10	All indexes combined	0.81	0.80-0.83	72
Neurodegenerative disease	5	All indexes combined	0.85	0.78-0.92	51
All-cause mortality among cancer survivors	7	All indexes combined	0.89	0.84-0.95	38
Cancer mortality among cancer survivors	7	All indexes combined	0.90	0.83-0.98	0