Adherence to the Dutch dietary guidelines and 15-year incidence of heart failure in the EPIC-NL cohort

Marjolein C. Harbers[1], A. Marleen de Kroon[1], Jolanda M.A. Boer[2], Folkert W. Asselbergs[3,4,5], Johanna M. Geleijnse[6], W. M. Monique Verschuren[1,2], Yvonne T. van der Schouw[1], Ivonne Sluijs[1]

[1] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

[2] Centre for Nutrition, Prevention and Health Services, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands

[3] Department of Cardiology, Division Heart & Lungs, University Medical Center Utrecht, Utrecht University, Utrecht, the Netherlands

[4] Institute of Cardiovascular Science, Faculty of Population Health Sciences, University College London, London, United Kingdom

[5] Health Data Research UK and Institute of Health Informatics, University College London, London, United Kingdom

[6] Division of Human Nutrition and Health, Wageningen University, Wageningen, the Netherlands

Corresponding author:
Marjolein Harbers
E-mail: m.c.harbers@umcutrecht.nl

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Figure captions

Fig. 1 Flowchart of participant exclusions. [a] Implausible energy intake was defined as individuals within the lower and upper 0.5% ratio of energy intake over basal metabolic rate

ABSTRACT

Purpose: A healthy diet may contribute to the primary prevention of heart failure (HF), but evidence is still inconclusive. We aimed to study the association between adherence to the Dutch dietary guidelines and incidence of HF.

Methods: We studied 37,468 participants aged 20-70 years and free of HF at baseline from the EPIC-NL cohort. At baseline (1993-1997) data were collected on demographics, lifestyle and presence of chronic diseases. Dietary intake was assessed using a 178-item validated food frequency questionnaire. Dietary intake data were used to calculate scores on the Dutch Healthy Diet 2015 Index (DHD15-index) measuring adherence to the Dutch dietary guidelines. The DHD15-index is based on the average daily intake of 14 food groups resulting in a total score ranging between 0 and 140, with higher scores indicating better adherence. HF morbidity and mortality during follow-up were ascertained through linkage with national registries. Cox proportional hazards analysis was used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between DHD15 adherence and HF risk, adjusting for sociodemographic and lifestyle characteristics.

Results: The average score on the DHD15-index was 71 (SD=15). During a median follow-up of 15.2 years (IQR: 14.1 – 16.5), 674 HF events occurred. After adjustment for demographic and lifestyle characteristics, higher scores on the DHD15-index were associated with lower risk of HF (HR_{Q4vsQ1}: 0.73; 95% CI: 0.58 – 0.93; *P*-trend: 0.001).

Conclusion: In a large Dutch population of middle-aged adults, higher adherence to the Dutch dietary guidelines was associated with lower risk of HF.

Keywords: dietary patterns, heart failure, Dutch Healthy Diet 2015 index, Dutch dietary guidelines

INTRODUCTION

Heart failure (HF) is a chronic condition of the heart in which the heart is not sufficiently able to contract or relax, resulting in an inadequate supply of oxygen and nutrients to the rest of the body [1]. As a consequence, patients with HF experience symptoms such as shortness of breath and fatigue. HF is a growing public health concern worldwide, and typically presents at older age. Given the ageing population, the lifetime risk of HF is high, ranging between 20% and 45% [2]. Consequently, it is expected that the prevalence of HF will increase substantially in the future [3].

Coronary heart disease, hypertension, diabetes mellitus, obesity and smoking are responsible for 52% of incident cases of HF in the US [4]. Given the fact that an unhealthy diet is an important risk factor for coronary heart disease, hypertension, diabetes mellitus and obesity, it could be hypothesized that diet may be an important modifiable risk factor for the primary prevention of HF as well. Potential mechanisms by which healthy diets may be protective for HF development include decreased oxidative stress and inflammation, and increased antioxidant defence and nitric oxide bioavailability [5].

Previously, adherence to the DASH diet has been associated with 22-37% lower risk of HF [6,7] and improved left ventricular function [8], although another study remained inconclusive [9]. Similarly, high adherence to the Mediterranean diet has been associated with 21-31% lower risk of HF [10,11], although after adjustment for lifestyle characteristics this was not the case in a German cohort [12]. The heterogeneity in study findings may be due to differences in length of follow-up, ascertainment of HF, and age of study participants. As the evidence-base for the protective association of healthy dietary patterns with HF risk remains inconclusive, more prospective observational studies are warranted.

The Health Council of the Netherlands released an updated version of the Dutch dietary guidelines in 2015, in which they compiled all the evidence on nutrients, foods, and dietary patterns in relation to the ten most important chronic diseases and related risk factors – including cardiovascular disease and risk factors such as systolic blood pressure, LDL-cholesterol, and body weight. Therefore, higher adherence to the Dutch dietary guidelines potentially reduces the risk of HF. The DHD15-index was developed to measure adherence to the Dutch dietary guidelines [13]. Hence, the aim of the present study is to study the association between adherence to the DHD15-index and the incidence of HF in a Dutch population.

METHODS

Study population

EPIC-NL is the Dutch contribution to The European Prospective Investigation into Cancer and Nutrition- and consists of 40 011 participants from the MORGEN and PROSPECT cohorts [14]. For the MORGEN cohort (n=22,654), men and women from the general population aged 20 to 59 years were randomly sampled from three Dutch towns in the Netherlands (Amsterdam, Doetinchem, and Maastricht) between 1993 and 1997. For the Prospect cohort (n=17,357) women aged 49 to 70 years, participating in the breast cancer screening programme between 1993 and 1995, and living in Utrecht or its vicinity were recruited. Participants provided informed consent prior to study inclusion. Both studies complied with the Declaration of Helsinki and were approved by the medical ethics committee of the Netherlands Organization for Applied Scientific Research (TNO) (MORGEN), and the institutional review board of the University Medical Centre Utrecht (Prospect).

For the present study, participants were excluded who withheld permission for linkage with disease registries (n=1,756); had prevalent HF (n=22); did not participate in the food frequency questionnaire (n=179); had implausible energy intake (i.e., those in the lowest and highest 0.5% of the ratio of energy intake over basal metabolic rate; n=356); had missing data on the covariates in model 1 and model 2 (n=229); withdrew permission for use of the data for analyses (n=1). Consequently, the population for analysis comprised 37,468 participants (**Figure 1**).

Dietary intake assessment

Dietary intake was assessed using a self-administered validated food frequency questionnaire (FFQ) that included questions on the habitual frequency of consumption of 178 food items during the year preceding enrolment. Consumption frequency could be indicated in times per day, per week, per month or per year, or as never. Consumed amounts could be indicated using specified units (e.g. glass or slice). For selected foods, photographs with portion sizes assisted in portion size estimation [15]. Reproducibility and validity were previously assessed in 121 men and women [15,16]. The median validity of 16 food groups with 12 monthly 24-hour recalls as reference, was 0.61 for men and 0.53 for women. Correlation coefficients for specific food groups ranged from 0.21 for cooked vegetables to 0.78 for sugar and sweet products among men and from 0.31 for vegetables and 0.87 for alcoholic beverages among women. Average food intake (g/d) was calculated by multiplying the consumption frequency with the consumed amounts, and nutrient intakes were calculated using the Dutch food composition table of 1996 [17].

Calculation of Dutch Healthy Diet 2015-index score

Average food intake was used to construct scores on the DHD15-index [13]. The DHD15-Index represents adherence to the Dutch food-based dietary guidelines released by the Health Council of the Netherlands in 2015.

The DHD15-index has previously been validated by comparing mean scores as assessed by a food frequency questionnaire and two 24h recalls as a reference, which showed a correlation coefficient of 0.56 [13]. The calculation of the DHD15-Index in the EPIC-NL study population has been described previously [18]. In short, the index consists of 15 food groups which are assigned a proportional score between 0 and 10. In the present study, we included only fourteen components since no data was available on type of coffee (filtered vs. unfiltered) consumed. Consequently, scores on the DHD15-index could range between 0 (no adherence) to 140 (complete adherence) for each participant. The scoring system of the DHD15-Index is shown in **Online Resource Table 1**.

Ascertainment of heart failure

Hospitalisation for and death from HF were used to define HF incidence. Hospitalisation for HF was determined based on both primary and secondary hospital discharge diagnoses which were obtained from the Hospital Discharge Register (ICD9-code: 428). A primary hospital diagnosis was defined as the underlying disease for hospitalisation. A secondary hospital diagnosis was defined as a comorbidity of the primary hospital admission. The Hospital Discharge Register was linked to the EPIC-NL cohort on the basis of birth date, sex, postal code, and general practitioner by a validated probabilistic method [19]. Vitality information was obtained through the municipal registry and causes of death were obtained from the Cause of Death Register at Statistics Netherlands (ICD10-code: I50). Death from HF was based on both primary and secondary causes of death. A primary cause of death was defined as the underlying disease that led to death. A secondary cause of death was defined as either a complication of the primary cause, or another disease which might have contributed to the death. Follow-up was complete until December 31st 2010.

Assessment of covariates

A self-administered general questionnaire provided information on age, sex, educational level, smoking status, and physical activity. Educational level was categorized into low (lower vocational training or primary school), middle (secondary school and intermediate vocational training), or high (higher vocational training or university), and smoking status was categorized into current, former or never [14]. Physical activity was assessed using the validated EPIC questionnaire and categorised according to the Cambridge Physical Activity Index (CPAI) into active, moderately active, moderately inactive and inactive [20,21] . In the first year of the MORGEN study (1993, 14.2% of the study population), physical activity was not assessed with the EPIC questionnaire. The missing physical activity data were imputed using single imputation SPSS Missing Values Analysis procedure as described previously [22].

A physical examination at baseline provided information on blood pressure, weight, height, and waist and hip circumference. During this examination systolic and diastolic blood pressure measurements were performed twice in supine position, from which the mean was taken. For the MORGEN-EPIC these measurements were performed on the left arm using a random zero sphygmomanometer, and for the PROSPECT-EPIC on the right arm using a Boso Oscillomat (Bosch & Son, Jungingen, Germany). Participants were categorised as being hypertensive in case systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, when antihypertensive medications were used (self-reported) or if hypertension had been diagnosed by a physician. BMI was calculated as height divided by weight squared and waist-hip ratio was calculated as waist circumference divided by hip circumference.

Blood samples were drawn during the physical examination. Serum total cholesterol was measured using enzymatic methods and LDL- and HDL-cholesterol were measured using a homogeneous assay with enzymatic endpoint. The ratio between total/HDL cholesterol ratio was computed [14]. Presence of hyperlipidaemia was based on self reported diagnosis and / or use of medication.

Prevalent cases of type 2 diabetes were identified through linkage with the National medical registry (1990–1997) and by self-report using the general baseline questionnaire. Cases detected by either of these methods have been verified by consulting the general practitioners [14]. Only verified cases were used in the analyses.

Statistical analysis

Participant characteristics at baseline were shown by quartiles of DHD15-index scores. The characteristics were expressed as means with standard deviations for normally distributed variables, medians and interquartile range for skewed variables, or as counts and percentages for categorical variables.

Follow-up time was calculated from the date of enrolment into the study to the date of HF diagnosis, date of death or date of censoring. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between DHD15-index quartiles and incidence of HF, using the lowest quartile as reference. Additionally, a test for linear trend across DHD15-index quartiles was performed by assigning the median value for each quartile and modelling this variable as a continuous variable. The proportional hazard assumption was fulfilled according to inspection of log-log plots and by including time-dependent covariates in the Cox models ($p<0.05$).

The first model was adjusted for age and sex. The second model, which is considered to be the main model, was additionally adjusted for smoking status, physical activity, total energy intake, and educational level. Additionally, we conducted an explorative analysis where BMI, waist-hip ratio, diabetes mellitus type 2, systolic blood pressure, hyperlipidaemia, hypertension, and total/HDL cholesterol ratio were added to model 2, both simultaneously and individually. We did this in a separate model since these factors may be mediators in the association of DHD15-index and HF risk, rather than confounders. Only participants with complete information on these additional covariates were included in this explorative analysis (n=35,709), and a flowchart of participant exclusions is shown in **Online Resource Figure 1**. All analyses were stratified by cohort by including cohort in the strata statement in the Cox model, which allowed the hazard of HF to vary across cohorts.

Several sensitivity analyses were carried out. First, to minimise the possibility of reverse causation, the analyses were repeated after exclusion of the first two years of follow-up. Second, the analyses were repeated using the DHD15-index excluding the sodium component since the FFQ may not be a suitable method for estimating sodium intake [23]. Third, since participants with prevalent myocardial infarction (MI), type 2 diabetes, hypertension and stroke at baseline may receive lifestyle advice to change dietary behaviours, we conducted sensitivity analyses excluding these groups of participants. Fourth, given that MIs frequently precede HF, the analyses were repeated after exclusion of persons who developed MI during follow-up, to test whether this association is independent of MI.

Statistical analyses were performed using IBM SPSS Statistics 24 (IBM Analytics, United States of America, New York). A p-value below 0.05 was considered to be statistically significant.

RESULTS

The average score on the DHD15-index was 71 (SD=15), with a minimum score of 16 and a maximum score of 130. Participants with higher scores on the DHD15-index were more likely to be older, highly educated, and more physically active. Moreover, they were less likely to be male and to be a current smoker, and had lower BMI compared to participants with low scores on the DHD index (**Table 1**).

During a median follow up of 15.2 (IQR: 14.1; 16.5) years, 674 HF events occurred. Comparing extreme quartiles, the highest adherence to the DHD15-index was associated with a lower incidence of HF (HR: 0.73; 95% CI: 0.58 – 0.93; *P*-trend = 0.001) after adjustment for sociodemographic and lifestyle characteristics (**Table 2**).

The characteristics of the study population after exclusion of participants with missing data on BMI, waist-hip ratio, systolic blood pressure, hyperlipidaemia and total/HDL cholesterol ratio are shown in **Online Resource Table 2**. No substantial differences were observed between the characteristics of the main population and subpopulation after participant exclusions. The association between DHD15 adherence and HF incidence after adjustment for sociodemographic and lifestyle characteristics was similar in the subpopulation as compared to the main population (HR: 0.74; 95% CI: 0.57 – 0.95; *P*-trend: 0.003). When adjusting for potential intermediates simultaneously, the association between DHD15-index and incidence of HF attenuated to non-significant (HR: 0.93; 95% CI: 0.72 – 1.21; *P*-trend: 0.27). When these potential intermediates were added individually to the main model, adjustment for BMI led to the strongest attenuation (HR: 0.84; 95%CI: 0.65-1.08; *P*-trend: 0.06) (**Online Resource Table 3**).

Exclusion of cases in the first two years of follow-up or excluding the sodium component from the DHD15-index had no substantial impact on the results (**Online Resource Table 4**). Excluding participants with prevalent MI (n=504), type 2 diabetes (n=570) or stroke (n=443) at baseline also had little effect on the observed hazard-ratio’s. In comparison, exclusion of participants with hypertension (n=14,044) resulted in slight attenuation of the association. Exclusion of participants who experienced MI at follow-up (n=53) did not alter the results.

DISCUSSION

In the present study among Dutch middle-aged adults, we observed that high adherence to the DHD15-index was associated with 27% lower risk of HF. These findings suggest that adherence to the Dutch dietary guidelines may contribute to the prevention of HF.

Before we interpret our findings, some limitations of our study need to be addressed. The first limitation concerns the reliability of the calculated sodium intake in our study. Food frequency questionnaires are generally no suitable method for estimating sodium intake [23]. About 80% of sodium intake in the Netherlands comes from (processed) foods [24]. However, sodium content may differ among products brands, which is not captured by the FFQ since no questions are included on specific food brands consumed. Moreover, the amount of sodium added by consumers was not captured by the FFQ. This may have resulted in misclassification and bias of the HRs towards the null. Indeed, exclusion of sodium from the DHD15-index showed little change in the observed association, suggesting that sodium was captured inadequately. Additionally, the coffee component in the DHD15-index which represents the dietary recommendation to replace unfiltered coffee by filtered coffee, was not included in the calculation of DHD15-scores because no information was available on type of coffee consumed (filtered/unfiltered). Furthermore, dietary intake was self-reported using a validated FFQ. The validity of vegetable and fish consumption is of concern [15], and this may have contributed to diluted associations. More specifically, higher intakes of these food groups have been associated with lower risk of heart failure [25,26], which could imply that measurement error in these components may have attenuated the inverse risk observed in the present study. Consequently, the true risk associated with a DHD15 compliant dietary pattern may have been underestimated. Moreover, diet was assessed only once and may have changed during follow-up, resulting in non-differential misclassification that may have weakened the observed associations. Also, the number of HF events in our study population is likely an underestimation as HF may be unrecorded in patients who have other CVD [1]. Additionally, the validity of HF cases retrieved from the Hospital Discharge Registry may be of concern, as a previous study in the Netherlands showed low sensitivity (43%) but adequate positive predictive value (80%) when HF incidence from the Hospital Discharge Registry was compared with HF incidence obtained from a golden standard cardiovascular disease registry, potentially contributing to a further underestimation of HF cases in the present study [27]. Moreover, we only included cases of HF resulting from hospitalisation or death. Therefore, the generalizability of the present findings to less severe cases of HF treated in primary care is uncertain. Also, it is well-known that individuals participating in cohort studies are generally more health-conscious, and therefore may not fully reflect the general population. In addition, we did not have information on HF subtypes, such as based on preserved versus reversed ejection fraction. Therefore, it is not yet clear whether the association observed in the present study is different across subtypes of HF.

Strengths of our study include its prospective design, broad age range of the study population and extensive follow-up period. Moreover, we had detailed information on dietary intake. Finally, our associations were robust against exclusion of cases in the first two years of follow-up, minimizing the possibility that associations can be explained by reverse causation. Additionally, exclusion of patients participants with MI at baseline or follow-up, prevalent type 2 diabetes, or stroke at baseline showed similar findings. Exclusion of participants with prevalent hypertension attenuated the association, indicating that hypertension may be an intermediate in the diet-heart failure pathway.

Data on the association between adherence to a healthy dietary pattern – and to the DHD15-index in specific – with HF from large prospective observational studies are scarce. However, the association between the DHD-index reflecting the dietary guidelines of 2006 and incidence of CVD previously yielded a null association in the EPIC-NL cohort [28]. This may be due to the fact that HF was included in a composite end-point of incident CVD that may differ in disease pathology and effects of dietary modification from other CVD. Moreover, substantial differences exist between both indices in dietary components included, with the DHD15-having its primary focus on food groups whereas the DHD-index primarily includes individual nutrients and only a limited number of food groups (vegetables, fruit and fish) [13,29].

The inverse association observed in the present study is further substantiated by other prospective cohort studies investigating the association between healthy diet index scores, such as the DASH score and the Mediterranean diet score, and HF risk. First, adherence to the DASH diet was associated with 22 and 37% lower HF risk in two Swedish cohorts with evidence of a dose-response relationship, supporting our finding and suggesting that healthy eating patterns could protect against HF [6,7]. In contrast, a US cohort did not observe an association of the DASH score with HF risk [9]. Second, in the same two Swedish cohorts higher adherence to the modified Mediterranean diet score was also associated with 21 and 31% lower risk of HF [10,11]. In contrast to the present study, these inverse associations remained after inclusion of BMI, history of hypertension, hypercholesterolemia, and diabetes in the multivariable adjusted model. In an analysis in the EPIC-Potsdam study (Germany), high adherence to the traditional Mediterranean diet was associated with 41% lower risk of HF after adjustment for age, sex, and total energy intake [12]. Adjustment for lifestyle characteristics resulted in slight attenuation of the association. Furthermore, inclusion of BMI, waist circumference, diabetes, hypertension and hyperlipidaemia in this analysis resulted in further attenuation of the association to non-significance.

One of the potential explanations for these previous contrasting findings may be due to differences in HF ascertainment. The US cohort installed a centralized events committee which used all available outpatient and inpatient data to establish whether participants had a confirmed HF diagnosis by a treating physician, experienced HF symptoms and were on medical therapy. Similarly, in the EPIC-Potsdam study, HF was ascertained on the basis of self-reported diagnosis, death due to HF, hospital information system data, and validation of medication use typical for HF. Additionally, HF diagnosis was validated by the treating physician. In the Swedish cohort and in EPIC-NL however, only cases resulting from hospitalisation or death were included. Consequently, the Swedish cohorts and EPIC-NL may represent patients with more severe disease as compared to patients in the US and German cohorts. As heart failure is a heterogeneous syndrome with multiple subtypes, pathophysiology and the role of risk-factors – such as diet – may differ. For example, a study conducted by Ahmad et al. [30] showed that different HF phenotypes as established by cluster analysis, responded differently to therapeutic intervention and had distinct outcomes on selected end-points including all-cause hospitalisation and mortality. Therefore, it may be important to consider the subtypes of HF when studying the association between healthy dietary patterns and incident HF. Moreover, differences in background diet and the age of participants included may also explain these contrasting findings.

The effect size observed in the present study compares well to the inverse associations reported for other dietary scores, previously. However, some notable differences exist among the DHD15-index, the DASH score, and the Mediterranean diet score with regard to their composition and scoring. Compared to the DASH score and Mediterranean diet score, the DHD15-index is the most extensive diet score with more dietary components included. For example, the DASH score does not include fish or alcohol, which have been suggested as relevant food components for HF risk [31,32]. Similarly, the Mediterranean diet score does not include a tea of sugar-sweetened beverage component [33]. Additionally, the DHD15-index is based on absolute dietary cut-offs instead of scores being assigned relative to other participants in the study population, which may be more meaningful in terms of impact on disease risk. Finally, scoring of included components differs among the diet scores, with high intakes of dairy contributing in a detrimental direction for the Mediterranean diet score and in a beneficial direction for the DHD15-index and DASH score.

In conclusion, the present study showed that higher adherence to the Dutch Healthy Guidelines 2015 was associated with lower incidence of HF. Future research is warranted to study the association between healthy dietary patterns and HF risk in study populations including less severe cases of HF and different subtypes of HF.

Author contributions

IS, and MH developed the research plan; MdK and MH performed the statistical analysis; the first draft of the manuscript was written by MH and MdK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

The study complied with the Declaration of Helsinki and was approved by the medical ethics committee of the Netherlands Organization for Applied Scientific Research (TNO) (MORGEN), and the institutional review board of the University Medical Centre Utrecht (Prospect).

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Table 1. Baseline characteristics across quartiles of DHD15-index scores in the EPIC-NL cohort[a] (n=37,468)

	Quartiles of DHD15-index score			
	Q1 (16 – 61)	Q2 (61 – 71)	Q3 (71 – 81)	Q4 (81 – 130)
N (%)	9,367 (25.0)	9,367 (25.0)	9,367 (25.0)	9,367 (25.0)
Age, years	49 (36, 55)	52 (42, 57)	53 (45, 59)	53 (46, 59)
Cohort				
Morgen, n (%)	6,497 (69.4)	5,225 (55.8)	4,656 (49.7)	4,605 (49.2)
Prospect, n (%)	2,870 (30.6)	4,142 (44.2)	4,711 (50.3)	4,762 (50.8)
Sex				
Female, n (%)	6,070 (64.8)	6,973 (74.4)	7,476 (79.8)	7,457 (79.6)
Educational level				
Low, n (%)	6,179 (66.0)	5,866 (62.6)	5,498 (58.7)	4,218 (45.0)
Moderate, n (%)	2,143 (22.9)	2,004 (21.4)	1,918(20.5)	2,064 (22.0)
High, n (%)	1,045 (11.2)	1,497 (16.0)	1,951 (20.8)	3,085 (32.9)
Smoking status				
Never, n (%)	3,014 (32.2)	3,534 (37.7)	3,863 (41.2)	3,892 (41.6)
Former, n (%)	2,301 (24.6)	2,837 (30.3)	3,131 (33.4)	3,528 (37.7)
Current, n (%)	4,052 (43.3)	2,996 (32.0)	2,373 (25.3)	1,947 (20.8)
Physical activity				
Inactive, n (%)	956 (10.2)	715 (7.6)	618 (6.6)	523 (5.6)
Moderate Inactive, n (%)	2,346 (25.0)	2,405 (25.7)	2,408 (25.7)	2,165 (23.1)
Moderate active, n (%)	2,274 (24.3)	2,383 (25.4)	2,468 (26.3)	2,602 (27.8)
Active, n (%)	3,791 (40.5)	3,864 (41.3)	3,873 (41.3)	4,077 (43.5)
DHD15 food groups				
Vegetables, g/d	89 (65, 118)	98 (75, 128)	107 (82, 138)	124 (95, 161)
Fruit, g/d	115 (52, 185)	141 (96, 251)	190 (121, 274)	242 (147, 328)

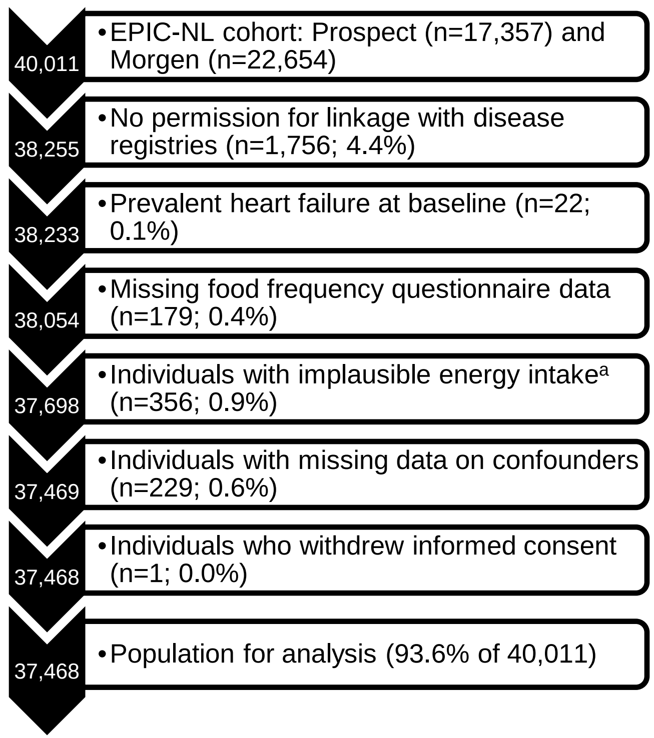
Whole grains, g/d	14 (2, 72)	47 (6, 106)	73 (19, 126)	99 (64, 135)
Legumes, g/d	4 (1, 10)	6 (2, 12)	7 (3, 14)	10 (5, 17)
Nuts, g/d	2 (0, 5)	3 (1, 7)	3 (1, 7)	6 (2, 14)
Dairy, g/d	330 (156, 644)	391 (224, 605)	405 (254, 586)	399 (277, 536)
Fish, g/d	4 (2, 11)	6 (2, 12)	7 (3, 14)	9 (4, 15)
Tea, ml/d	71 (3, 250)	179 (36, 375)	250 (125, 450)	375 (250, 450)
Soft fats and oils, g/d	10 (4, 20)	11 (5, 19)	11 (5, 18)	11 (6, 18)
Solid fats, g/d	12 (5, 23)	9 (4, 18)	7 (3, 15)	6 (2, 13)
Red Meat, g/d	83 (61, 102)	68 (42, 87)	54 (33, 78)	39 (21, 59)
Processed meat, g/d	37 (21, 60)	26 (14, 39)	18 (9, 31)	12 (4, 20)
Sugar-sweetened beverages, ml/d	155 (73, 267)	119 (48, 196)	99 (40, 161)	76 (28, 138)
Alcohol, g/d	5 (1, 21)	4 (1, 15)	4 (1, 14)	6 (1, 14)
Sodium, mg/d	2668 (2098, 3333)	2337 (1864, 2868)	2157 (1763, 2613)	2039 (1700, 2428)
BMI, kg/m^2	25.6 (23.2, 28.6)	25.4 (23.1, 28.1)	25.2 (23.1, 27.8)	24.5 (22.5, 26.9)
Hip-waist ratio	0.84 ± 0.09	0.83 ± 0.09	0.82 ± 0.09	0.81 ± 0.08
Type 2 diabetes, n (%)	167 (1.8)	162 (1.7)	145 (1.5)	96 (1.0)
Systolic blood pressure, mmHg	126 ± 19	127 ± 19	127 ± 19	126 ± 19
Diastolic blood pressure, mmHg	78 ± 11	78 ± 11	78 ± 11	77 ± 10
Hypertension, n (%)	3,476 (37.1)	3,631 (38.8)	3,631 (38.8)	3,306 (35.3)
Total/HDL cholesterol ratio	4.0 (3.2, 5.1)	3.9 (3.1, 4.9)	3.7 (3.0, 4.7)	3.6 (2.9, 4.5)
Hyperlipidaemia, n (%)	812 (8.7)	794 (8.5)	795 (8.5)	804 (8.6)

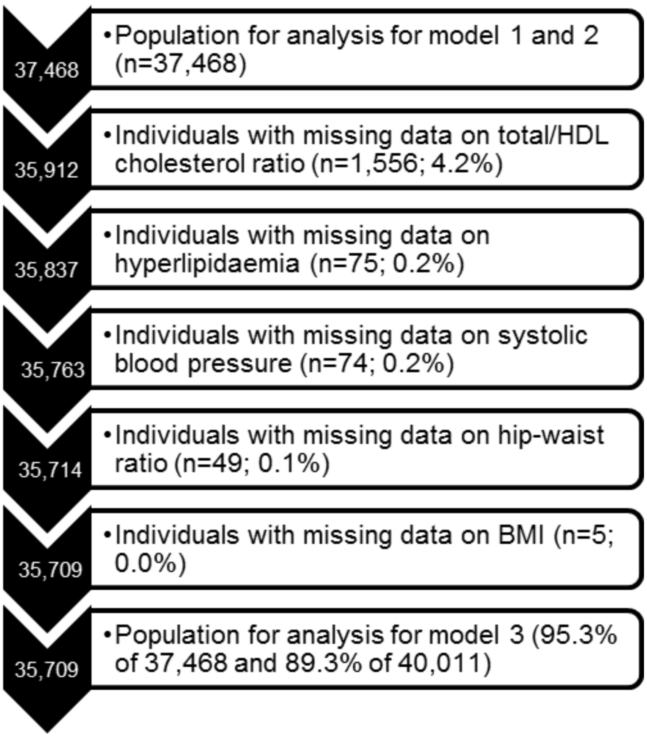
[a] Values are displayed as medians (P25, P75) or as means ± SD. Missing values, N (%): BMI 21 (0.1%), hip-waist ratio 68 (0.2%), systolic blood pressure 82 (0.2%), diastolic blood pressure 64 (0.2%), hyperlipidaemia 77 (0.2), cholesterol ratio 1,556 (4.2%).

Table 2. HRs (95% CI) for the association between quartiles of DHD15-index scores and incident HF (n = 37,468)

	Q1	Q2	Q3	Q4	P_{trend}
DHD15-index, range	16-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	148 / 9367	199 / 9367	172 / 9367	155 / 9367	
Person-years	139,516	138,494	139,020	138,893	
Univariable	1.00 (ref)	1.20 (0.97 – 1.49)	0.98 (0.79 – 1.23)	0.89 (0.71 – 1.11)	0.11
Model 1[a]	1.00 (ref)	1.04 (0.84 – 1.29)	0.79 (0.63 – 0.99)	0.66 (0.52 – 0.83)	<0.001
Model 2[b]	1.00 (ref)	1.09 (0.88 – 1.35)	0.85 (0.68 – 1.07)	0.73 (0.58 – 0.93)	0.001

[a] Model 1 was adjusted for age and sex; [b] Model 2 was additionally adjusted for educational level, energy intake, physical activity, and smoking status.


40,011
•EPIC-NL cohort: Prospect (n=17,357) and Morgen (n=22,654)
38,255
•No permission for linkage with disease registries (n=1,756; 4.4%)
38,233
•Prevalent heart failure at baseline (n=22; 0.1%)
38,054
•Missing food frequency questionnaire data (n=179; 0.4%)
37,698
•Individuals with implausible energy intake[a] (n=356; 0.9%)
37,469
•Individuals with missing data on confounders (n=229; 0.6%)
37,468
•Individuals who withdrew informed consent (n=1; 0.0%)
37,468
•Population for analysis (93.6% of 40,011)



Online Resource Fig. 1 Flowchart of additional participant exclusions for participants with missing data on potential intermediates

Online Resource Table 1. Components of the DHD15-index and corresponding dietary recommendations and their threshold (minimum score) and cut-off (maximum score) values.

DHD15-component	Dietary recommendation	Minimum score (0 points)	Maximum score (10 points)
1. Vegetables	Eat at least 200 g of vegetables daily	0 g/d	≥ 200 g/d
2. Fruit	Eat at least 200 g of fruit daily	0 g/d	≥ 200 g/d
3. Whole grain products[a]	a. Eat at least 90 g of wholegrain products daily	0 g/d	≥ 90 g/d
	b. Replace refined cereal products by whole-grain products	No consumption of whole grain products OR ratio whole grain to refined grain ≤ 0.7	No consumption of refined products OR ratio of whole grains to refined grains ≥ 11
4. Legumes	Eat legumes weekly.	0 g/d	≥10 g/d
5. Nuts	Eat at least 15 grams of unsalted nuts a day.	0 g/d	≥15 g/d
6. Dairy[b]	Eat a few portions of dairy produce daily, including milk or yoghurt.	0 g/d OR ≥750 g/d	300–450 g/d
7. Fish[c]	Eat one serving of fish weekly, preferably oily fish.	0 g/d	≥15 g/d
8. Tea	Drink three cups of black or green tea a day	0 g/d	≥450 g/d
9. Fats and oils	Replace butter, hard margarines, and cooking fats by soft margarines, liquid cooking fats, and vegetable oils	No consumption of soft margarines, liquid cooking fats and vegetable oils OR ratio of liquid cooking fats to solid cooking fats ≤ 0.6	No consumption of butter, hard margarines and cooking fats OR ratio of liquid cooking fats to solid cooking fats ≥ 13
10. Coffee[d]	Replace unfiltered coffee by filtered coffee.	Any consumption of unfiltered coffee	Consumption of only filtered coffee OR no coffee consumption
11. Red meat	Limit consumption of red meat.	≥ 100 g/d	≤45 g/d
12. Processed meat	Limit consumption of processed meat.	≥ 50 g/d	0 g/d
13. Sugar-sweetened beverages and fruit juices	Limit consumption of sweetened beverages and fruit juices.	≥ 250 g/d	0 g/d
14. Alcohol	If alcohol is consumed at all, intake should be limited to one Dutch unit (10 gram ethanol) daily	Women: ≥20 g ethanol/d Men: ≥30 g ethanol/d	Women: ≤10 g ethanol/d Men: ≤10 g ethanol/d
15. Sodium[e]	Limit consumption of table salt to 6 g daily	≥ 3.8 g sodium/d	≤ 1.9 g sodium/d

[a] This component comprises two sub-components of which each sub-component has a maximum score of 5 points; [b] Maximum of 40 g cheese can be included; [c] Maximum of 4 g lean fish can be included; [d] The coffee component was not included in the calculation of the DHD15-score as no data was available on type of coffee (filtered/unfiltered); [e] Sodium only originated from foods; intake from added salt was not captured by the FFQ.

Online Resource Table 2. Baseline characteristics across quartiles of DHD15-index scores after exclusion of participants with missing data on BMI, waist-hip ratio, systolic blood pressure, hyperlipidaemia, and total/HDL cholesterol ratio (n=35,709)[a]

	Quartiles of DHD15-index score			
	Q1 (16 – 61)	Q2 (61 – 71)	Q1 (71 – 81)	Q4 (81 – 130)
N (%)	8927 (25.0)	8927 (25.0)	8928 (25.0)	8927 (25.0)
Age in years	48 (36, 54)	51 (42, 57)	52 (44, 59)	53 (45, 59)
Cohort				
Morgen, n (%)	6385 (71.5)	5189 (58.1)	4628 (51.8)	4543 (50.9)
Prospect, n (%)	2542 (28.5)	3738 (41.9)	4300 (48.2)	4384 (49.1)
Sex				
Female, n (%)	5682 (63.6)	6553 (73.4)	7045 (78.9)	7037 (78.8)
Education				
Low, n (%)	5836 (65.4)	5526 (61.9)	5142 (57.6)	3978 (44.6)
Middle, n (%)	2079 (23.3)	1951 (21.9)	1880 (21.1)	1967 (22.0)
High, n (%)	1012 (11.3)	1450 (16.2)	1906 (21.3)	2982 (33.4)
Smoking status				
Never, n (%)	2871 (32.2)	3345 (37.5)	3668 (41.1)	3706 (41.5)
Former, n (%)	2170 (24.3)	2701 (30.3)	2972 (33.3)	3347 (37.5)
Current, n (%)	3886 (43.5)	2881 (32.3)	2288 (25.6)	1874 (21.0)
Physical activity				
Inactive, n (%)	890 (10.0)	660 (7.4)	573 (6.4)	488 (5.5)
Moderate Inactive, n (%)	2233 (25.0)	2278 (25.5)	2282 (25.6)	2061 (23.1)
Moderate active, n (%)	2179 (24.4)	2286 (25.6)	2369 (26.5)	2476 (27.7)
Active, n (%)	3625 (40.6)	3703 (41.5)	3704 (41.5)	3902 (43.7)
DHD15 food groups				

Vegetables, g/d	89 (65, 118)	98 (75, 128)	107 (82, 137)	124 (95, 161)
Fruit, g/d	113 (51, 182)	140 (95, 250)	190 (120, 273)	242 (145, 326)
Whole grains, g/d	14 (2, 72)	47 (6, 106)	73 (19, 127)	99 (64, 136)
Legumes, g/d	4 (1, 10)	6 (2, 12)	7 (3, 13)	10 (5, 17)
Nuts, g/d	2 (0, 5)	3 (1, 7)	3 (1, 7)	6 (2, 14)
Dairy, g/d	327 (156, 641)	390 (225, 606)	404 (253, 585)	399 (276, 536)
Fish, g/d	4 (2, 11)	6 (2, 12)	7 (3, 14)	9 (4, 15)
Tea, ml/d	71 (3, 250)	179 (36, 375)	250 (125, 450)	375 (250, 450)
Soft fats and oils, g/d	10 (4, 20)	11 (5, 19)	11 (5, 18)	11 (6, 18)
Solid fats, g/d	12 (5, 23)	9 (4, 18)	7 (3, 15)	6 (2, 13)
Red Meat, g/d	84 (61, 102)	69 (42, 87)	55 (33, 78)	39 (21, 60)
Processed meat, g/d	37 (22, 60)	26 (14, 40)	18 (9, 31)	12 (4, 20)
Sugar-sweetened beverages, ml/d	155 (73, 269)	120 (49, 198)	99 (40, 163)	76 (29, 138)
Alcohol, g/d	6 (1, 21)	5 (1, 16)	5 (1, 14)	6 (1, 14)
Sodium, mg/d	2687 (2113, 3345)	2349 (1885, 2884)	2165 (1768, 2626)	2045 (1707, 2437)
BMI[a], kg/m^2	25.6 (23.1, 28.5)	25.3 (23.1, 28.0)	25.1 (23.0, 27.7)	24.4 (22.5, 26.9)
Hip-waist ratio	0.84 ± 0.09	0.83 ± 0.09	0.82 ± 0.09	0.81 ± 0.08
Type 2 diabetes, n (%)	148 (1.7)	140 (1.6)	132 (1.5)	84 (0.9)
Systolic blood pressure, mmHg	125 ± 18	127 ± 19	127 ± 19	125 ± 19
Diastolic blood pressure, mmHg	78 ± 11	78 ± 11	78 ± 11	77 ± 10
Hypertension, n (%)	3244 (36.3)	3391 (38.0)	3385 (37.9)	3091 (34.6)
Total/HDL cholesterol ratio	4.0 (3.2, 5.0)	3.9 (3.1, 4.9)	3.7 (3.0, 4.7)	3.6 (2.9, 4.5)
Hyperlipidaemia, n (%)	767 (8.6)	745 (8.3)	744 (8.3)	763 (8.5)

[a] Values are displayed as medians (P25, P75) or as means ± SD.

Online Resource Table 3. HRs (95% CI) for the association between quartiles of DHD15-index scores and incident HF with both simultaneous and individual adjustment for potential intermediates in a subpopulation of EPIC-NL (n=35,709)[a]

	Q1	Q2	Q1	Q4	P_{trend}
DHD15-index, range	16 – 61	61 – 71	71 – 81	81 – 130	
Quartile median	53	66	76	88	
Cases / at risk (n)	130 / 8927	165 / 8927	135 / 8928	134 / 8927	
Person-years	133,338	132,419	132,843	132,578	
Model 2[b]	1.00 (ref)	1.05 (0.83 – 1.32)	0.78 (0.61 – 1.00)	0.74 (0.57 – 0.95)	0.003
Model 2[b] + all intermediates[c]	1.00 (ref)	1.16 (0.92 – 1.46)	0.89 (0.69 – 1.14)	0.93 (0.72 – 1.21)	0.27
Model 2[b] + BMI	1.00 (ref)	1.10 (0.88 – 1.40)	0.85 (0.66 – 1.09)	0.84 (0.65 – 1.08)	0.06
Model 2[b] + Waist-hip ratio	1.00 (ref)	1.07 (0.85 – 1.36)	0.82 (0.64 – 1.05)	0.79 (0.61 – 1.02)	0.02
Model 2[b] + Type 2 diabetes	1.00 (ref)	1.09 (0.86 – 1.37)	0.81 (0.63 – 1.04)	0.79 (0.61 – 1.03)	0.02
Model 2[b] + Systolic blood pressure	1.00 (ref)	1.08 (0.85 – 1.36)	0.81 (0.63 – 1.04)	0.79 (0.61 – 1.02)	0.02
Model 2[b] + Hyperlipidaemia	1.00 (ref)	1.05 (0.83 – 1.32)	0.78 (0.61 – 1.00)	0.73 (0.57 – 0.95)	0.003
Model 2[b] + Hypertension	1.00 (ref)	1.08 (0.85 – 1.36)	0.82 (0.64 – 1.05)	0.79 (0.61 – 1.03)	0.02
Model 2[b] + Total/HDL cholesterol ratio	1.00 (ref)	1.05 (0.83 – 1.32)	0.80 (0.62 – 1.02)	0.76 (0.59 – 0.99)	0.009

[a] Analyses were conducted after exclusion of participants with missing data on potential intermediates (Online Resource Figure 1); [b] Model 2 was adjusted for age, sex, educational level, energy intake, physical activity and smoking status ; [c] Additionally adjusted for all potential intermediates simultaneously, including BMI, hip-waist ratio, type 2 diabetes, systolic blood pressure, hypertension, hyperlipidaemia, total/HDL cholesterol ratio.

Online Resource Table 4. Sensitivity analyses excluding various subpopulations and using DHD15-index scores without the sodium component as end-point

	Q1	Q2	Q1	Q4	P_{trend}
First two years of follow-up excluded					
DHD15-index, range	16-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	143/9321	188/9293	160/9310	147/9307	
Person-years	139,457	138,410	138,956	138,820	
Univariable	1.00 (ref)	1.17 (0.94, 1.46)	0.94 (0.75, 1.18)	0.87 (0.69, 1.09)	0.07
Model 1[a]	1.00 (ref)	1.02 (0.82, 1.27)	0.76 (0.60, 0.95)	0.64 (0.51, 0.81)	<0.001
Model 2[b]	1.00 (ref)	1.07 (0.85, 1.33)	0.82 (0.65, 1.03)	0.72 (0.56, 0.92)	0.001
DHD15-index without sodium component					
DHD15-index, range	14-54	54-64	64-74	74-120	
Quartile median	47	59	68	80	
Cases / at risk (n)	172/9,367	178/9,367	175/9,367	149/9,367	
Person-years	139,252	138,815	138,915	138,940	
Univariable	1.00 (ref)	0.95 (0.77-1.17)	0.91 (0.73-1.12)	0.78 (0.63-0.97)	0.11
Model 1[a]	1.00 (ref)	0.85 (0.69-1.05)	0.75 (0.60-0.92)	0.60 (0.48-0.75)	<0.001
Model 2[b]	1.00 (ref)	0.92 (0.74-1.13)	0.84 (0.68-1.04)	0.71 (0.56-0.89)	0.001
Participants with prevalent MI at baseline excluded					
DHD15-index, range	16-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	130/9,231	184/9,233	160/9,228	145/9,257	
Person-years	137,775	136,737	137,095	137,382	
Univariable	1.00 (ref)	1.27 (1.01-1.59)	1.05 (0.83-1.32)	0.94 (0.74-1.20)	0.29
Model 1[a]	1.00 (ref)	1.10 (0.88-1.38)	0.84 (0.67-1.06)	0.70 (0.55-0.89)	<0.001
Model 2[b]	1.00 (ref)	1.14 (0.91-1.43)	0.90 (0.71-1.14)	0.77 (0.60-0.99)	0.007

Participants with prevalent type 2 diabetes at baseline excluded					
DHD15-index, range	16-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	125/9200	180/9205	159/9222	144/9271	
Person-years	137,320	136,348	136,980	137,592	
Univariable	1.00 (ref)	1.29 (1.02 – 1.62)	1.08 (0.85 – 1.37)	0.97 (0.76 – 1.23)	0.40
Model 1[a]	1.00 (ref)	1.11 (0.89 – 1.40)	0.87 (0.68 – 1.10)	0.72 (0.56 – 0.91)	0.001
Model 2[b]	1.00 (ref)	1.17 (0.93 – 1.47)	0.93 (0.73 – 1.19)	0.79 (0.62 – 1.02)	0.02
Participants with prevalent hypertension at baseline excluded					
DHD15-index, range	18-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	43/5891	58/5736	60/5736	58/6061	
Person-years	88,566	86,036	85,862	90,482	
Univariable	1.00 (ref)	1.20 (0.81 – 1.79)	1.18 (0.80 – 1.76)	1.08 (0.72 – 1.61)	0.82
Model 1[a]	1.00 (ref)	1.06 (0.71 – 1.58)	0.95 (0.64 – 1.41)	0.79 (0.53 – 1.19)	0.17
Model 2[b]	1.00 (ref)	1.09 (0.73 – 1.63)	1.01 (0.67 – 1.52)	0.87 (0.57 – 1.33)	0.41
Participants with prevalent stroke at baseline excluded					
DHD15-index, range	16-61	61-71	71-81	81-130	
Quartile median	53	66	76	88	
Cases / at risk (n)	141/9201	190/9219	160/9231	152/9246	
Person-years	137,126	136,361	137,142	137,193	
Univariable	1.00 (ref)	1.21 (0.97 – 1.50)	0.96 (0.76 – 1.21)	0.91 (0.72 – 1.15)	0.16
Model 1[a]	1.00 (ref)	1.05 (0.84 – 1.31)	0.77 (0.61 – 0.97)	0.67 (0.53 – 0.85)	<0.001
Model 2[b]	1.00 (ref)	1.10 (0.88 – 1.37)	0.82 (0.65 – 1.04)	0.75 (0.59 – 0.95)	0.002

Participants with MI during follow-up excluded					
DHD15-index, range	16 – 61	61 – 71	71 – 81	81 – 130	
Quartile median	53	66	76	88	
Cases / at risk (n)	139/9358	181/9349	158/9353	143/9355	
Person-years	139,409	138,273	138,873	138,752	
Univariable	1.00 (ref)	1.15 (0.92 – 1.44)	0.95 (0.75 – 1.19)	0.86 (0.68 – 1.09)	0.07
Model 1[a]	1.00 (ref)	1.00 (0.80 – 1.25)	0.76 (0.61 – 0.96)	0.64 (0.50 – 0.81)	<0.001
Model 2[b]	1.00 (ref)	1.05 (0.84 – 1.31)	0.82 (0.65 – 1.04)	0.71 (0.55 – 0.91)	0.001

[a] Model 1 was adjusted for age and sex; [b] Model 2 was additionally adjusted for educational level, energy intake, physical activity, and smoking status.