The Association between Life's Essential 8 and the Risk for Atrial Fibrillation in a Dutch Population

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ABSTRACT

BACKGROUND: This study examined the association between Life's Essential 8 (LE8) and the incidence of atrial fibrillation (AF).

METHODS: In total, 37,807 participants from the European Prospective Investigation Into Cancer and Nutrition-Netherlands (EPIC-NL) cohort were included (mean age 49.4 ± 11.9 years, 74.7% women). The components diet, physical activity, sleep health, nicotine exposure, body mass index, blood glucose, blood lipids, blood pressure were all given a score between 0 and 100 and an overall LE8 score was created. The overall LE8 score was averaged and categorized into low cardiovascular health (CVH, 0-49), moderate CVH (50-79), and high CVH (80-100). AF cases were obtained through linkage with registries.

RESULTS: During a median follow-up of 15.3 years (interquartile range: 14.1 – 26.5 years), 833 AF cases (2.3%) were identified. Compared to the high CVH score (19.5%), participants with a low CVH score (5%) had a 1.99 times higher hazard for incident AF (hazard ratio = 1.99, 95% confidence interval (CI) = 1.49 – 2.65) in a Cox proportional hazards model adjusted for age, sex, education level, heart failure, coronary heart disease, and alcohol consumption. Furthermore, an ideal component decrease was associated with a 1.11 times higher risk for incident AF (95% CI = 1.05 – 1.18).

CONCLUSIONS: The results show that a worse CVH, indicated by a lower LE8 score, is associated with an increased risk for incident AF.

KEY WORDS: Atrial fibrillation | Life's Essential 8 | Cardiovascular health

LAYMAN'S SUMMARY

Atrial fibrillation (AF) is a heart condition in which the heart rhythm is often too fast and irregular. People suffering from AF have a higher chance to die and to experience other cardiovascular diseases like a stroke. To prevent cardiovascular diseases, the American Heart Association developed a score called Life's Essential 8 (LE8). LE8 consists of eight risk factors for CVDs: diet, physical activity, sleep, smoking, body mass index, blood glucose values, blood cholesterol values, and blood pressure. Each component can be scored for an individual to create an overall LE8 score, with a higher score meaning a better cardiovascular health (CVH). The aim of this study was to find whether a higher LE8 score was associated with a lower occurrence of AF cases.

Data from 13,807 participants was used to study this association. Almost 75% of the participants were female and 2.3% of the participants developed AF during the study. For each participant a LE8 score was calculated and afterwards grouped into either low CVH, moderate CVH, or high CVH. After taking into account other risk factors like age, sex, education level, history of other cardiovascular diseases (heart failure and coronary heart disease), and alcohol consumption, participants with a low CVH had an almost 2-times higher risk of developing AF than participants with a high CVH score. This finding provides evidence that encouraging patients to improve their LE8 score might lead to prevention of the occurrence of AF.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice with a global estimated prevalence of 33.5 million patients.[1] Patients with AF have a 3-fold higher risk for all-cause mortality, a 2-fold higher risk for cardiovascular events, and have impaired quality of life compared to participants without AF.[2-4]

The concept of Life's Simple 7 (LS7) was developed by the American Heart Association (AHA) in 2010 with as an overarching goal to reduce the burden of cardiovascular diseases (CVD) through prevention.[5] LS7 consists of seven health and behavioral factors (diet, physical activity (PA), smoking, body mass index (BMI), blood pressure, blood glucose, and total cholesterol) and can be used as a scoring tool to generate a cardiovascular health (CVH) score. So far, several studies in Asia and the United States have investigated the relationship between LS7 and the incidence [5-8] and prevalence [9] of AF. All studies showed that a higher LS7 score was associated with a lower risk for AF.

In 2022, the AHA updated LS7 to the new score Life's Essential 8 (LE8). In LE8, scoring of the previous seven components was adjusted and a new component sleep health, measured by sleep duration, was added.[10] The relationship between sleep and AF has previously been studied in a biobank study in the United Kingdom.[11] In this study a "healthy" sleeping score, consisting of multiple factors including sleep duration, was associated with a reduced risk of AF.

The effect of LE8 on the incidence of AF has not been studied thus far, and especially in Europe information on the association between LS7 and AF is lacking. Hence, the purpose of this study was to examine the association between the AHA's LE8 and incident AF in a

general Dutch population using data from the EPIC-NL cohort (European Prospective Investigation Into Cancer and Nutrition-Netherlands).

METHODS

STUDY POPULATION

The EPIC-NL cohort consists of the MORGEN (Monitoring Project on Risk Factors for Chronic Diseases) and the Prospect cohorts. Both cohorts recruited participants between 1993 and 1997. The MORGEN cohort includes 10,260 men and 12,394 women from three Dutch towns (Amsterdam, Doetinchem, and Maastricht). The participants were between 20 and 59 at recruitment. The Prospect cohort consists of 17,357 women all residing in the city of Utrecht at time of recruitment and participating in the Dutch breast cancer screening program. All participants provided written informed consent. Further details about the design and rationale of the EPIC-NL cohort are provided elsewhere.[12]

Of the 40,010 participants in the EPIC-NL cohort, we excluded participants with prevalent AF (n = 40), people who did not give permission for linkage with registries (n = 1,721), people with implausible energy intake, indicated by a basal metabolic rate in the lower or upper 0.5% (n = 358), and people with missing information on the outcome (n = 84). After exclusions, 37,807 participants were included in the analysis. Patients were followed until the occurrence of AF, death, censoring, or until the end up the follow-up (January 1, 2011), whichever came first.

DATA COLLECTION

At study inclusion, all participants filled in a general questionnaire, a food frequency questionnaire (FFQ), had a physical examination, and non-fasting blood samples were drawn and stored in liquid nitrogen for later analyses. The general questionnaire contained questions about socio-demographic factors (age, sex, education level), lifestyle factors (alcohol consumption, smoking history, and PA, prevalent chronic diseases (self-reported diabetes, hypertension), time since last food consumption, and medication use. Information on PA was collected by asking participants how many hours in a typical week in the year prior to enrollment they spend participating in one of the following activities: walking, cycling, gardening, do-it-yourself activities at home, physical exercise, and housework.[13]

The self-administered FFQ included questions about the frequency of consumption of 79 main food categories in the year prior to enrollment. Overall, the average daily consumption of 178 foods can be estimated. The FFQ was validated before the start of the study.[14]

The physical examination included body weight, waist and hip circumference, and blood pressure measurement. Body weight was measured in light indoor clothing without shoes. BMI was calculated as weight divided by the square of height. Blood pressure was measured in duplicate and the average was used in the analysis.

Total cholesterol, high-density lipoprotein (HDL) cholesterol, and glucose were measured in the blood samples collected at baseline. In the MORGEN cohort, measurements were performed in the entire cohort. In the Prospect cohort, serum total cholesterol, citrate plasma cholesterol, or both were available in 90% of the participants. These measurements were standardized into one serum cholesterol value. Missing serum total cholesterol and HDL cholesterol were imputed using single imputation with non-Bayesian linear regression. Non-HDL cholesterol values were obtained by subtracting HDL cholesterol form total cholesterol.

Glucose measurements were available in the Prospect cohort in a subset of 10%. For participants with glucose measurements, it was determined whether the blood samples were obtained when the participant was fasting (last meal more than eight hours ago) or non-fasting (last meal less than eight hours ago). Hemoglobin A1c (HbA1c) was measured in a random sample of the baseline cohort (6.5%, 2604 participants).

Follow-up questionnaires three and four, sent to the participants in 2010/2011 and 2015/1016 respectively, contained questions about sleep health. Participants were asked how many hours they slept on average at night during the past four weeks. If participants responded to both follow-up questionnaires, the two values were averaged.

Extreme values of glucose (≥400 or ≤40 mg/dL), HbA1c (≥13.57%= or ≤3.29%), BMI (≥50 kg/m^2), and sleep duration (>12 hours) were removed and later on imputed using multiple imputation.

LE8 SCORE

The total LE8 score was based on the scores of the eight included components (diet, PA, nicotine exposure, sleep health, BMI, blood lipids, blood glucose, and blood pressure). Definitions used to score each component in this study and the distribution of the scores are shown in ***Supplemental Table 1***. The total LE8 score was created by summing the score for each component and dividing this score with eight. Subsequently, the score was categorized into low (0-49), moderate (50-79), and high (80-100) CVH. To create more stable groups, the LE8 score was also categorized into quartiles (quartile 1 ≤61.6; quartile 2 >61.6 – 69.9; quartile 3 >69.9 – 77.8; and quartile 4 >77.8).

The diet component of LE8 was scored according to the Dietary Approach to Stop Hypertension (DASH)-style diet as suggested by the AHA.[10] The DASH-style diet consists of

the following eight components: fruit, vegetables, nuts and legumes, whole grains, low-fat dairy, sodium, red and processed meat, and sweetened beverages.[10, 15] In EPIC-NL the participants are divided into sex-specific quantiles for each component.[16] Each component was scored between 1 and 5. For the components fruit, vegetables, nuts and legumes, whole grains, and low-fat dairy, the sex-specific quantile 1 was scored with 1 point (lowest intake) and sex-specific quantile 5 with 5 points (highest intake). For sodium, red and processed meat, and sweetened beverages this was reversed.

Leisure time PA was used to calculate the number of minutes participants exercised per week. Information on PA at work was only available as a categorical variable. Participants in the highest category of PA at work (heavy manual work) were automatically assigned to the highest group of the PA score, participants in the second-highest group (manual work) were assigned to the highest group of the PA if they also exercised more than one minute per week.

Different than proposed in the AHA guidelines, the nicotine exposure score used in this study does not contain exposure to nicotine delivery-systems as this data was not available for the participants.[10] Furthermore, according to the definitions proposed by the AHA, knowledge on the diabetes diagnosis together with fasting blood glucose or HbA1c values are needed to score blood glucose component.[10] Because our data showed some inconsistency when combining glucose or HbA1c values with a diabetes diagnosis, only information on diabetes diagnosis was used to assign participants to the highest or second-highest blood glucose score. Sleep health, BMI, blood lipids, and blood pressure were scored according to AHA guidelines.[10]

OUTCOME ASSESSMENT

The incidence of AF was defined by the hospitalization for and death from AF. Primary diagnosis of AF was provided by the National Medical Registry using the Dutch Hospital Discharge Diagnosis Database. This database was linked to the EPIC-NL cohort using information on the date of birth, sex, postal code, and general practitioner with a validated probabilistic method.[17] Vital status of the study participants was obtained via linkage with municipal registries. Primary and secondary causes of death were obtained through linkage with Statistics Netherlands. AF diagnosis was coded according to the International Classification of Diseases, Ninth Revision (ICD-9) code 427.3 and the International Classification of Diseases, Tenth Revision (ICD-10) code I48.

STATISTICAL ANALYSIS

Baseline characteristics were summarized for the overall cohort and stratified by the CVH score. Continuous variables were described using the mean and standard deviation or median and interquartile range. Categorical variables were described using percentages. To visualize the time until AF incidence, a Kaplan-Meier curve stratified by the three groups (low, moderate, and high CVH) was created. Missing data in the variables making up the LE8 components and confounders were imputed using the *mice* package in R statistical software. Data was imputed with ten iterations over ten imputations. Results of the ten separate analyses were pooled using Rubin's rules. The number and percentages of missing data are shown in ***Supplemental Table 2.***

A Cox proportional hazards model was used to calculate the hazard ratio (HR) and corresponding 95% confidence interval (CI) for the association between the grouped LE8 score, both by using low, moderate, and high CVH and by quartiles, and the incidence of AF. High

CVH and quartile 4 served as the reference group. Furthermore, a decrease in the number of ideal components was also studied in a Cox proportional hazards model. The number of ideal components was measured by the sum of the times a participant had an optimal score of 100 for a component. The contribution of each individual LE8 component was studied in a leave-one-out analysis. For every component a new LE8 score was created without that component and compared with the total LE8 score including that specific component. The proportional hazards assumption was checked by visual inspection of the Schoenfeld residuals. The models were adjusted for age, sex, education level, heart failure, coronary heart disease, and alcohol consumption. All analyses were stratified for the variable cohort to account for the two different cohorts participants originated from. In sensitivity analyses, the total LE8 score in all participants was compared with the LE8 score in participants with complete data on the sleep health component (n = 13,253), and in participants with complete data on the blood glucose component (n = 15,205). Furthermore, to account for the possibility of reverse causality, all AF events occurring in the first two years of follow up were excluded and this model was compared with the model containing all AF events. Statistical significance was defined as a p-value < 0.05. All statistical analyses were performed in R software version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

STUDY CHARACTERISTICS

In total, 37,807 participants were included in this study. During a median of 15.3 years (interquartile range: 14.1 – 26.5 years) of follow-up, 877 participants (2.3%) developed AF. Baseline characteristics for the entire cohort and stratified by CVH score are presented in ***Table***

1. The mean age of the entire cohort was 49.4 ± 11.9 years and the majority of the participants (74.7%) were female. Younger age, female sex and higher education level were some of the characteristics associated with a higher CVH score, as measured by a higher LE8 score.

Table 1. Baseline characteristics of the study population

	Total EPIC-NL cohort (N = 37807)	**High CVH (score ≥80) (N = 7372, 19.5%)**	**Moderate CVH (score 50-79) (N = 28543, 75.5%)**	**Low CVH (score <50) (N = 1892, 5.0%)**
Demographics				
Age (y)	49.4 ± 11.9	44.9 ± 12.9	50.2 ± 11.5	53.5 ± 8.1
% Females	74.7	78.8	74.3	65.6
% Higher education	20.2	35.6	17.0	8.2
Clinical measures				
SBP (mm Hg)	126.4 ± 19.0	115.4 ± 13.5	128.0 ± 18.6	144.2 ± 20.5
DBP (mm Hg)	77.9 ± 10.6	71.7 ± 8.2	78.8 ± 10.3	88.5 ± 11.1
Glucose (mg/dL)	90.0 [82.8 – 100.8]	86.4 [79.2 – 93.6]	91.8 [82.8 – 100.8]	102.6 [91.8 – 120.6]
Non-HDL (mg/dL)	158.0 ± 43.1	126.6 ± 32.0	163.3 ± 49.8	203.4 ± 40.4
BMI (kg/m^2)	25.2 [22.9 – 27.9]	23.1 [21.6 – 24.5]	25.6 [23.4 – 28.1]	30.6 [27.3 – 33.3]
Lifestyle factors				
DASH score	24.0 ± 4.8	26.8 ± 4.5	23.6 ± 4.7	20.2 ± 3.8
Average time sleeping/night (hr)	7.0 ± 1.2	7.3 ± 0.8	7.0 ± 1.2	6.5 ± 1.8
Current smokers	38.1	6.5	43.7	79.3
Never smokers	47.9	80.8	41.6	10.2
Leisure time physical activity (hr/day)	4.4 ± 2.2	4.4 ± 2.1	4.5 ± 2.2	4.3 ± 2.4
High (> 50 g/day) alcohol consumption	3.6	1.9	3.9	5.0
Comorbidities				
Hypertension	37.4	15.6	40.5	76.3
Diabetes	12.8	3.4	13.7	38.4
Coronary heart disease	1.8	0.7	1.9	4.7
Stroke	1.3	0.7	1.3	2.6
Heart failure	0.1	0.0	0.1	0.2

Values are presented as mean ± standard deviation, median [interquartile range] or as percentages. BMI = body mass index; DASH = dietary approaches to stop hypertension; DBP = diastolic blood pressure; EPIC-NL = European Prospective Investigation Into Cancer and Nutrition-Netherlands; HDL = high-density lipoprotein; SBP = systolic blood pressure.

The mean scores for each individual component stratified by the CVH score are shown in ***Figure 1***. In all eight components the mean score is lowest in the low CVH score and highest in the high CVH score. The differences between low, moderate, and high CVH are the smallest for the component PA with mean scores of 98.5, 99.8 and 99.9 respectively.

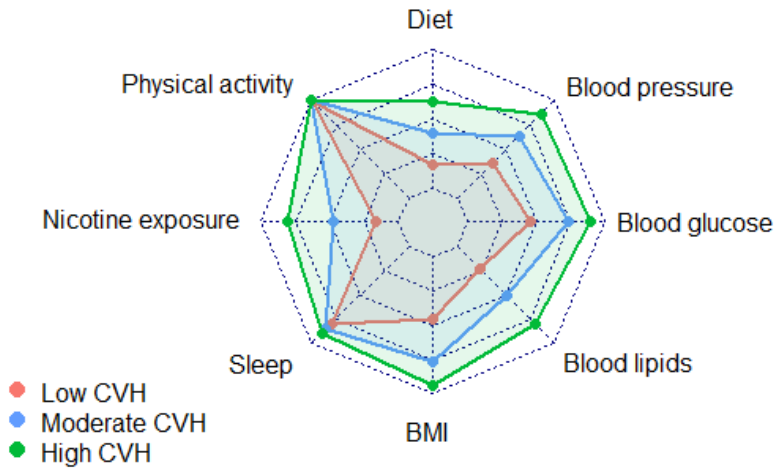

Figure 1. Radar plot of the individual mean LE8 score for each component in the Life's Essential 8 score. *The score for each component lies between 0 and 100, with 0 being closest to the center of the radar plot and 100 closest to the outside border of the radar plot.*

ASSOCIATION BETWEEN LE8 AND THE INCIDENCE OF AF

The Kaplan Meier-curve (***Figure 2***) shows that AF-free survival significantly differed between low, moderate and high CVH (logrank p-value <0.001). After adjusting for age, sex, education level, heart failure, coronary heart disease, and alcohol consumption, low CVH, as compared with high CVH, was associated with an increased risk for AF (HR = 1.99; 95% CI = 1.49 – 2.65; ***Table 2***). Moderate CVH compared to high CVH was associated with an increased risk for AF in the fully adjusted model although this effect was not significant (HR = 1.12; 95% CI = 0.91 – 1.38). In the crude model, moderate CVH compared to high CVH was significantly associated with an increased risk for AF (HR = 1.59; 95% CI = 1.29 – 1.95). Furthermore, an ideal component decrease was significantly associated with a higher AF risk (HR = 1.11; 95% CI = 1.05 – 1.18).

When using quartiles, only quartile 1 compared to quartile 4 is significantly associated with an increased risk for incident AF in the fully adjusted model (HR = 1.40; 95% CI = 1.14 – 1.72; ***Supplemental Table 3***). Quartile 2 compared to quartile 4 still showed a non-significant increased risk for incident AF (HR = 1.04; 95% CI = 0.84 – 1.29), but quartile 3 compared to quartile 4 was associated with a reduced risk for AF, even though still not significant (HR = 0.92; 95% CI = 1.73 – 1.15).

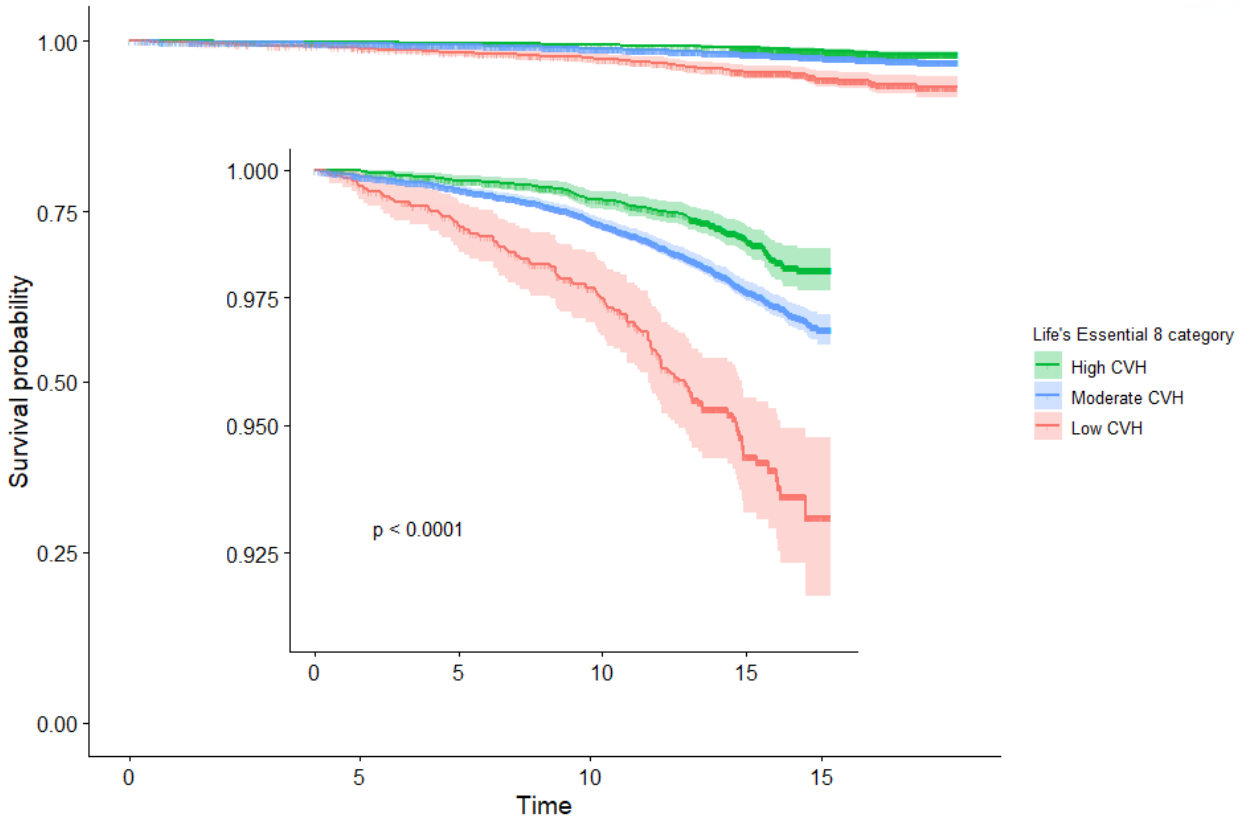

Figure 2. Kaplan-Meier curve of the AF-free survival across the three different CVH scores. *Insert depicts the zoomed in survival curve. Results of the logrank test (p<0.001) indicated significant differences between the three CVH scores. CVH = cardiovascular health.*

Table 2. Associations between Life's Essential 8 and incident atrial fibrillation

	Model 1	**Model 2**	**Model 3**
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Grouped LE8 score			
High (≥80)	Reference	Reference	Reference
Moderate (50-79)	1.59 (1.29 – 1.95)	1.19 (0.97 -1.47)	1.12 (0.91 – 1.38)
Low (<50)	3.80 (2.89 – 5.01)	2.45 (1.85 – 3.25)	1.99 (1.49 – 2.65)
Ideal component decrease	1.33 (1.25 – 1.40)	1.16 (1.10 – 1.23)	1.11 (1.05 – 1.18)

Model 1: crude model; model 2: adjusted for age, sex, and education level; model 3: additionally adjusted for heart failure, coronary heart disease, and alcohol consumption. CI = confidence interval; HR = hazard ratio; LE8 = Life's Essential 8.

LEAVE-ONE-OUT ANALYSIS

The impact of excluding a single component from the total LE8 score on the HRs and corresponding 95% CI is shown in ***Figure 3***. All models are adjusted for age, sex, education level, heart failure, coronary heart disease, and alcohol consumption. Excluding sleep health from the total LE8 score changes the direction of the association for moderate CVH compared to high CVH as it is associated with an reduced, although not significant, risk for incident AF (HR = 0.96; 95% CI = 0.78 – 1.19). Low CVH compared to high CVH is still associated with an increased risk for incident AF, although of a smaller magnitude (HR = 1.47; 95% CI = 1.14 – 1.90). Excluding one of the other seven components from the LE8 score only affects the magnitude and not the direction of the association. Excluding either the component BMI, PA, or blood pressure from the total LE8 score resulted in a lower HR for moderate CVH compared to high CVH (HR = 1.05; 95% CI = 0.84 – 1.30, HR = 1.07; 95% CI = 0.84 – 1.38, HR = 1.09; 95% CI = 0.91 – 1.33, respectively), and a lower HR for low CVH compared to high CVH (HR = 1.46; 95% CI = 1.09 – 1.95, HR = 1.60; 95% CI = 1.20 – 2.12, HR = 1.68; 95% CI = 1.26 – 2.25, respectively).

The HR of moderate compared to high CVH increases and becomes statistically significant when either the diet or nicotine exposure components is removed from the LE8 score (HR = 1.25; 95% CI = 1.04 – 1.51; and HR = 1.29; 95% CI = 1.05 – 1.57, respectively). Also, the HR of low compared to high CVH increases when excluding either diet or nicotine exposure (HR = 2.35; 95% CI =1.74 – 3.18, HR = 2.15; 95% CI = 1.59 – 2.90).

Excluding either blood glucose or blood lipids does not impact the moderate compared to high CVH but slightly lowers the HR for blood glucose (HR = 1.88; 95% CI = 1.41 – 2.49) and slightly increase the HR for blood lipids (HR = 2.17; 95% CI = 1.62 – 2.91) when comparing low CVH and high CVH.

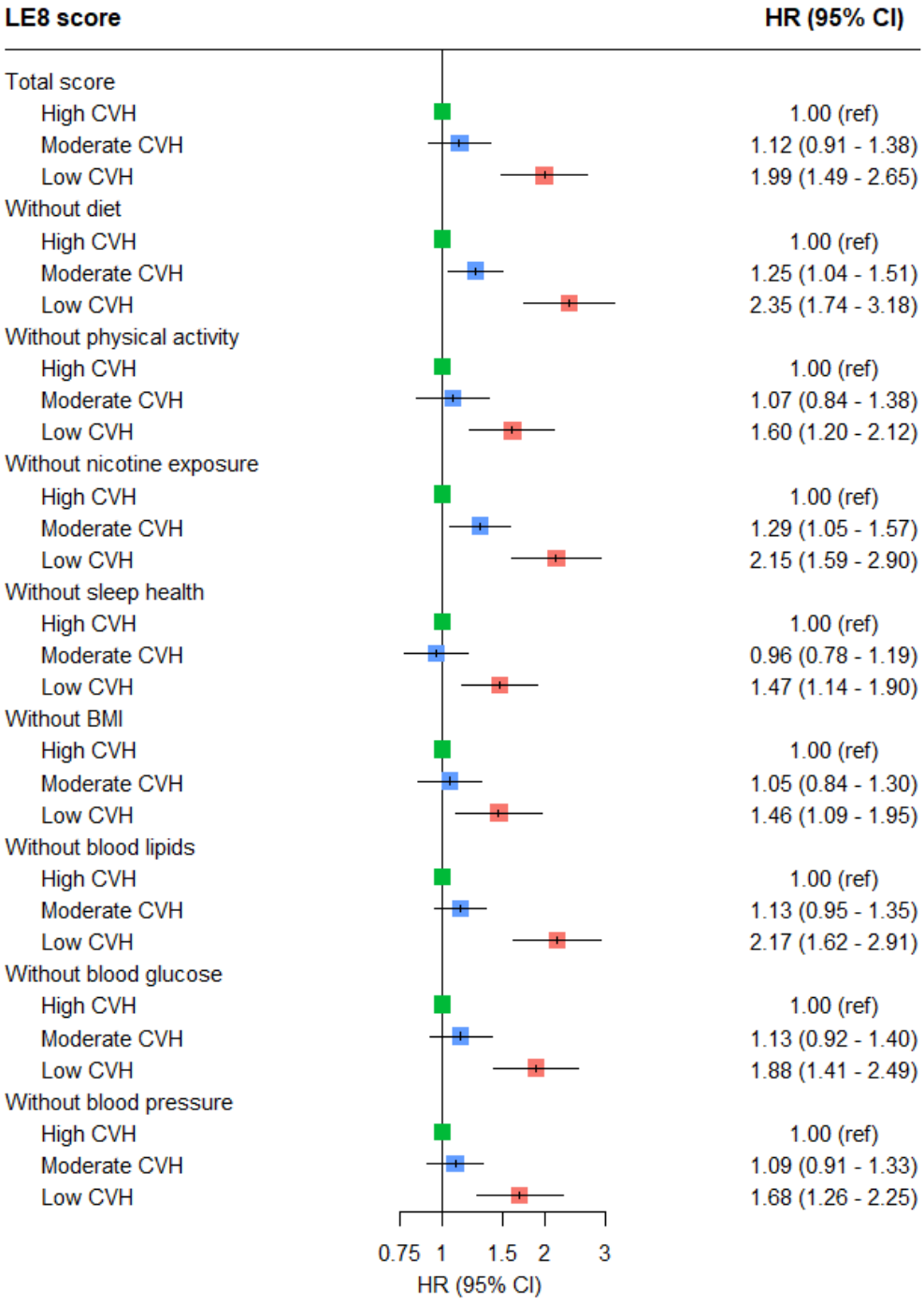

Figure 3. Leave-one-out analysis. *For every component, a new score is created without that component to visualize the impact of excluding that specific component. All models are adjusted for age, sex, education level, heart failure, coronary heart disease, and alcohol consumption. BMI = body mass index; CVH = cardiovascular health; CI = confidence interval. HR = hazard ratio; LE8 = Life's Essential 8.*

SENSITIVITY ANALYSIS

In a subset of participants with complete data for the component sleep health, the associations were less strong and were no longer statistically significant (***Supplemental Table 4***). The opposite effect was seen when only including participants with complete data on the blood glucose component, in this subset the associations were even stronger than in the entire cohort (***Supplemental Table 5***). Excluding AF events within the first two years of follow-up did not impact the results (***Supplemental Table 6***).

DISCUSSION

In this prospective Dutch cohort study, a low CVH score, indicated by a lower LE8 score, was associated with a 1.99 times higher risk for incident AF as compared to a high CVH score. An ideal component decrease was associated with a 1.11 times higher risk for incident AF. Only 19.5% of the participants in this cohort had a high CVH score, indicating that there is room for improvement in the overall health of the population possibly reducing the incidence of AF in the general population.

LE8 AND INCIDENT AF

So far no studies have been carried out that examine the association between LE8 and incident AF. The previous tool LS7 has been studied before in relation to incident AF, with similar findings as reported in the present study (***Table 3***).[5-9] This is the first study examining the role of ideal CVH in AF occurrence, either by using LS7 or LE8, in a European cohort. Past studies were conducted in Asia or the United States. All studies categorized the healthy lifestyle score into three groups, although there were differences in the exact definitions. Despite these different definitions, the highest group of the LS7 score was in all studies associated with a

significant reduction in the risk for incident AF or AF prevalence. Despite the changes in the scoring of individual components between LS7 and LE8 and the addition of the component sleep health, a higher CVH score was still associated with a lower incidence of AF. A moderate CVH score in this cohort did not significantly increase the risk for incident AF compared to a high CVH score. However, decreasing the number of ideal components was associated with a higher AF risk, indicating that small improvements in the CVH score could have beneficial effects in reducing the prevalence of AF.

Table 3. Comparison between the findings of the EPIC-NL study and previous studies on the association between ideal CVH and incident atrial fibrillation

	EPIC-NL	**REGARDS[5]**	**ARIC[6]**	**NHIS-Senior cohort[7]**	**MESA[8]**	**Jidong community[9]**
Country	Netherlands	United States	United States	Korea	United States	China
LS7 or LE8	LE8	LS7	LS7	LS7	LS7	LS7
Definitions of LS7/LE8 categories	Low CVH (<50), moderate CVH (50-79), and high CVH (≥80).	Low CVH (0-4), moderate CVH (5-9), and high CVH (10-14).	Low CVH (0-4), moderate CVH (5-9), and high CVH (10-14).	Low CVH (0-2 ideal metrics), moderate CVH (3-4 ideal metrics), and high CVH (5-6 ideal metrics); no diet information.	Low CVH (0-8), moderate CVH (9-10), and high CVH (11-14).	Low CVH (0-2 ideal metrics), moderate CVH (3-4 ideal metrics), and high CVH (5-7 ideal metrics).
Sample size	37,807	9,576	13,182	208,598	6,506	4,477
Adjusted for	Age, sex, education level, heart failure, coronary heart disease, and alcohol consumption. Stratified for the two different cohorts participants originated from.	Age, sex, race, education, income, geographic region, alcohol use, left ventricular hypertrophy, coronary heart disease, and stroke.	Age, sex, race, education, ARIC study site, alcohol consumption, and left ventricular hypertrophy.	Age, sex, medical history of hypertrophic cardiomyopathy, bleeding, hypothyroidism, thromboembolism, coagulation dysfunction, osteoporosis, chronic kidney disease, chronic obstructive pulmonary disease, and liver disease.	Age, sex, race/ethnicity, education, income, and health insurance.	Age, sex, alcohol consumption, previous heart failure, stroke, and myocardial infarction.
Outcome	Low CVH was associated with a 1.99 times higher risk for incident AF compared to high CVH.	High CVH score was associated with a 32% lower risk compared to the low CVH score.	High CVH score was associated with a 62% lower risk compared to the low CVH score.	High CVH score was associated with a 19% lower risk compared to the low CVH score.	High CVH score was associated with a 27% lower risk compared to the low CVH score.	High CVH score was associated with a 56% lower AF prevalence compared to the low CVH score.

Individual components	Protective effect of LE8 mostly driven through the components sleep health and BMI.	Ideal BMI and blood pressure reduced the risk for AF.	Ideal BMI, blood pressure, blood glucose, smoking, and physical activity reduced the risk for AF.	Ideal BMI, blood pressure, and physical activity reduced the risk for AF. Ideal cholesterol increased the risk for AF.	Ideal BMI, blood pressure, blood glucose, and smoking reduced the risk for AF.	Ideal physical activity was associated with lower AF prevalence.

ARIC = Atherosclerosis Risk in Communities; BMI = body mass index; CVH = cardiovascular health; EPIC-NL European Prospective Investigation Into Cancer and Nutrition-Netherlands; LE8 = Life's Essential 8; LS7 = Life's Simple 7; MESA = Multi-Ethnic Study of Atherosclerosis; NHIS-Senior = National Health Insurance Service-Senior; REGARDS = Reasons for Geographic and Racial Differences in Stroke.

INDIVIDUAL COMPONENTS OF LE8

Excluding either sleep health, BMI, PA, or blood pressure from the total LE8 score lowered the associated risks of incident AF when comparing low and moderate CVH with high CVH. This was most apparent for the components sleep health and BMI; the protective effect of LE8 subsequently seems mostly driven by the components sleep health and BMI. In the majority of studies examining the association between LS7 and AF, ideal levels of BMI and blood pressure were also significantly associated with a reduced risk for AF.[5-8] These findings are consistent with previous studies focusing on the association of those individual components with AF.[18-20] In this study, almost the entire cohort scored optimal for the component PA, therefore drawing conclusions should be considered with caution. In three of the studies examining the relationship between LS7 and AF, ideal levels of physical activity were associated with a lower AF risk.[7, 9, 21] However, two meta-analyses indicated a possible sex difference in the association between physical activity and AF with males performing intense physical activity having an increased risk for AF.[22, 23]

Excluding either diet or nicotine exposure from the total LE8 score resulted in an more extreme protective effect of LE8 on the incidence of AF. In the previous studies exploring the relationship between LS7 and AF, the component diet showed no significant association with incident AF, indicating that diet might have a smaller or negligible contribution to the AF risk

than the other components.[5, 6, 8, 9] In a meta-analysis, smoking was associated with an increased risk for AF and this increased risk was reduced both not completely reversed for current smokers.[24] However, only in the Atherosclerosis Risk in Communities (ARIC) and Multi-Ethnic Study of Atherosclerosis (MESA) studies, ideal levels of the component smoking significantly increased the risk for incident AF.[6, 8] Compared to LS7, the smoking component of LE8 also includes the exposure to secondhand smoke. The relation between exposure to secondhand smoke and AF has been studied a couple of times, all suggesting that exposure to secondhand smoke increases the risk for AF.[25-28] Why removing nicotine exposure from the total LE8 score in this study led to more extreme HRs is unclear.

Excluding blood glucose or blood lipids from total LE8 score did not impact the results in a large way. Diabetes and higher levels of blood glucose have been shown to increase the risk for AF in a meta-analysis among cohort studies.[29] Only in the ARIC and MESA study blood glucose was significantly associated with an increased AF risk.[6, 8] Excluding blood glucose from the score slightly lowered the HR of low CVH compared to high CVH. When only the participants with complete data on the blood glucose component were included in the analysis, as shown in the sensitivity analysis, the associations between LE8 and incident AF became even stronger. It could be possible that including only the subset of participants with complete data on the blood glucose component could lead to stronger reductions in the leave-on-out analysis excluding blood glucose. None of the studies showed an association between ideal levels of blood lipids and AF.[5-9] In the National Health Insurance Service-Senior cohort the opposite trend was seen; ideal levels of blood lipids were associated with an increased AF risk.[7]

IMPLICATIONS

In the last decades, the absolute number of deaths attributed to AF have risen and the percentage of hospitalizations due to AF have increased with 205.1% for women and with 161.7% for men in the Netherlands.[30] These numbers indicate the need for preventive measures. LE8 is a tool that is easy to interpret and can be easily applied by healthcare providers to encourage patients to make improvements in the shared risk factors for AF and other CVDs. Although this study shows that low CVH compared to high CVH is associated with an increased risk for AF, future research should focus on studying whether improvements in CVH do decrease the incidence of AF. Nonetheless, previous studies have shown that a lower CVH score, assessed by looking at the LS7 score, was associated with a higher AF burden later in life.[31]

STUDY STRENGTHS AND LIMITATIONS

Strengths of this study were the long follow-up time which allowed for AF cases to occur, a large sample size, and detailed data collection on both the LE8 components as possible other risk factors for AF.

This study also has some limitations. Firstly, AF cases not resulting in death were obtained using data from the Hospital Discharge Register (HDR). Only hospitalizations with AF as a primary diagnosis were detected and hospitalizations with AF as a secondary diagnosis or AF cases not detected in the hospital were therefore missed in this study. In a recent cohort study from the Netherlands, it was found that for 33.7% of the participants included in the study AF was diagnosed by a general practitioner.[32] The total number of AF cases could therefore be higher in this study, and some participants might be misclassified as non-cases. Furthermore, prevalent AF cases were also detected via linkage with the HDR and included only

hospitalizations with AF as primary diagnosis. Additionally, the HDR only goes back to one year prior to enrollment, prevalent AF cases who occurred more than one year prior to enrollment could therefore be missed. Only 40 prevalent AF cases (0.09%) were present in this cohort. This percentage is low compared to the expected prevalence in the Dutch population[33], so it could be that some of the incident AF cases were actually prevalent AF cases. Third, in this study we only looked at the association between the CVH score and incident AF by using baseline measurements. Therefore, we are unable to say whether changes in CVH score could reduce the risk for AF. Moreover, in some of the LE8 components there was a lot of missing data. Because sleep data was only available in later follow-up questionnaires, this might not reflect the sleep duration of the participants at baseline. Furthermore, a FFQ was used to assess the dietary intake needed to calculate the diet score. A FFQ is not the most ideal way to estimate dietary intake, especially for sodium. In the study used to validate the FFQ used in the EPIC-NL cohort it was also shown that the estimation of vegetable intake might be of concern when comparing the intake reported by participants in the FFQ to a 24-hour recall.[14] However, because the scores used in the DASH diet are based on the percentiles of intake of the food groups and not the actual intake, it might not be of a large concern in this study. At last, because of the observational nature of this cohort residual confounding cannot be ruled out.

CONCLUSION

In the general Dutch population, an unhealthy lifestyle, reflected by a lower LE8 score, was associated with an increased risk for incident AF. Prevention of AF could be accomplished by improvements in the components that make up the LE8 score; especially improvements in the components BMI and sleep health.

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