Title
Risk of Heart Failure: The Opportunity for Prevention with American Heart Association's Life's Simple 7

Brief title:
Life's Simple 7 and Heart Failure Risk

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Abstract:
Background: The American Heart Association recommends the concept of Life's Simple 7 (LS7); healthy behaviors that have shown to reduce cardiovascular disease.

Objectives: We examined whether combinations of specific LS7 components are associated with a reduced risk of heart failure (HF).

Methods: we included 37,803 participants from the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) cohort with a mean age of 49.4 (SD 11.9) years and 74.7% women. The LS7 score ranged from 0–14 and was calculated based on 0, 1, or 2 points for smoking, physical activity, body mass index (BMI), diet, blood pressure, total cholesterol, and blood glucose. 23.2% of participants had an overall ideal score (11-14 points), 35.3% an intermediate (9-10 point) and 41.5% an inadequate score (0-8 points).

Results: Over a median follow-up of 15.2 years [IQR 14.1;16.5] 690 participants (1.8%) developed HF. In Cox proportional hazard models, ideal and intermediate LS7 scores were associated with a reduced risk of HF compared to the inadequate category (hazard ratio (HR) 0.45, 95% confidence interval (95%CI) 0.34;0.60 and HR 0.53, 95%CI 0.44;0.64, respectively). Our analyses show that combinations with specific LS7 components, notably glucose, BMI, smoking or blood pressure, are associated with a lower incidence of HF.

Conclusions: A healthy lifestyle, as reflected in an ideal LS7 score, was associated with a 55% lower risk of HF compared to an inadequate LS7 score. Preventive strategies that target combinations of specific LS7 components could have a significant impact on decreasing incident HF in the population at large.

Condensed abstract:
The American Heart Association recommends the concept of Life's Simple 7 (LS7); healthy behaviors that have shown to reduce cardiovascular disease. We examined whether combinations of specific LS7 components are associated with a reduced risk of heart failure (HF) in a cohort of 37,803 participants from the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL). Our analyses suggest that combinations with specific LS7 components, notably glucose, BMI, smoking or blood pressure, are associated with decreased incidence of HF. Preventive strategies that target combinations of specific LS7 components could have a significant impact on decreasing HF in the population at large.

Keywords:
Life's Simple 7; Healthy lifestyle; Cardiovascular disease risk factors; Heart failure

Abbreviations list:
HF = heart failure, CVD = Cardiovascular disease, LS7 = Life's Simple 7, EPIC-NL = European Prospective Investigation into Cancer and Nutrition-Netherlands.

Introduction

Heart failure (HF) is one of the leading causes of morbidity and mortality and one of the main presentations of cardiovascular disease (CVD).(1) Similar to other types of CVD, the incidence of HF could be reduced by modifying lifestyle factors such as smoking, physical activity and diet. Previous research indeed suggests that adherence to a healthy lifestyle reduces the risk of HF.(2–5)

The American Heart Association recommends the concept of Life's Simple 7 (LS7); health behaviors that could reduce the burden of CVD.(6) LS7 consists of known CVD risk factors: smoking, physical activity, body mass index, diet, blood pressure, total cholesterol, and glucose. To date, several studies have established the relationship between LS7 and HF which showed that a reduced risk of HF was achieved with a more favorable LS7 score. (7–10) Thus, behavioral changes could improve cardiovascular health, but resources to achieve an "ideal" lifestyle are often lacking and it is known that it can be challenging to change one's lifestyle.(11) Therefore, questions as whether even modest improvements, such as reducing one or two specific LS7 components, could decrease the risk of HF are of interest. The European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) cohort has gathered data on individual components that could be responsible for reduced CVD risk.(12)

Hence, we sought to address the detailed relationship between health behaviors and the risk of HF. We studied American Heart Association LS7 and the risk of HF in a general Dutch population and aimed to provide insight in combinations of specific LS7 components that could reduce the risk of HF.

Methods

Study population

The EPIC-NL cohort consists of the MORGEN (Monitoring Project on Risk Factors for Chronic Diseases) and the Prospect cohorts. Details of the design and rationale of EPIC-NL have been described elsewhere.(12) Both cohorts were set up between 1993 and 1997. The MORGEN cohort included 10,260 men and 12,394 women aged 20–64 years and the Prospect cohort included 17,357 women aged 49–70 years. All participants gave written informed consent.

In total, we included n = 37,803 participants. Participants were ineligible if they had a HF diagnosis at baseline (n = 47). Participants were excluded if they did not give permission for linkage with disease or mortality registries (n = 1,630), had an implausible basal metabolic rate, defined as the top and bottom 0.5% of the ratio of reported energy intake over estimated energy requirement (n = 367) or had a missing outcome (n = 81). Participants were followed over time until HF diagnosis, censor date, death or end of follow-up (01-01-2011).

Baseline measurements

At cohort inclusion a general questionnaire and a food frequency questionnaire (FFQ) were filled out and a non-fasting blood sample was taken. The general questionnaire included demographic characteristics (sex, education), risk factors (smoking, physical activity, diet) and presence of chronic diseases (hypertension, hyperlipidemia, diabetes). Education level was categorized into high (higher vocational education and university) and other. Physical activity was assessed by combining activities of occupational and recreational nature during the past year in the Cambridge Physical Activity Index (CPAI).(13) During physical examination, height and weight were measured and Body Mass Index (BMI) was calculated as weight (kg)/height squared (m^2). At baseline, mean systolic (SBP) and diastolic blood pressure (DBP) were measured in 2 repeated measurements after at least 5 minutes of resting. Hypertension

and hyperlipidemia were either self-reported, based on measurements from physical examination or registered use of medication.(14)

The validated EPIC FFQ was used to assess food intake based on the usual consumption frequency of 79 main food categories during the year preceding enrolment.(15) Food groups incorporated in the LS7 diet component were fruit and vegetables (>400 grams/day), fish (>200 grams/week), whole grains (>50 grams/day), sodium (<1500 mg/day) and sugar sweetened beverages (<450 kcal/week).(6, 16) The diet score was adjusted for total energy intake (kcal/day) using the regression residual method.(17)

Biochemical measurements

Serum total cholesterol, high density lipoprotein (HDL) cholesterol and glucose were measured in samples collected at baseline. In the MORGEN cohort, the biochemical measurements were performed in all participants at baseline. In the Prospect cohort 90% of participants had either serum cholesterol, citrate plasma values of cholesterol or both measured in a later stage. These measurements were standardized into one serum cholesterol value. Single imputation with non-Bayesian linear regression was used to impute missing serum values for both total cholesterol and HDL cholesterol.

In the Prospect cohort, glucose was determined in a subpopulation of 1700 participants. For all participants with glucose measurements, we determined whether blood glucose was measured fasting (>=480 min since last meal or since last drink) or non-fasting (<480 min since last meal or since last drink). This was taken into account in calculating points for the glucose component in the LS7 score(**Online Table 1**). For those participants who did not have a glucose measurement at baseline we used information on self-reported diabetes, diabetes diagnosis abstracted from the Hospital Discharge Register or registered diabetes medication.

LS7 components

An overall healthy lifestyle score was calculated based on 7 known CVD risk factors (smoking, physical activity, body mass index, diet, blood pressure, total cholesterol, and blood glucose). All risk factors were scored as ideal: 2 points, intermediate: 1 point or inadequate: 0 points. **Online Table 1** shows the definitions of the LS7 components, the associated score and the distribution among the EPIC-NL participants. The healthy lifestyle score was summed and ranged from 0 to 14. The overall LS7 score was categorized approximating tertiles; a score from 0–8 = inadequate, 9–10 = intermediate, 11–14 = ideal.

Outcome measure

Hospitalization for and death from HF were used to define HF incidence. Primary and secondary hospital discharge diagnoses were obtained from the Hospital Discharge Register. The database was linked to the EPIC-NL cohort on the basis of birth date, sex, postal code, and general practitioner by a validated probabilistic method.(18) Information on vital status was obtained through the municipal registry and causes of death were obtained from the Cause of Death Register at Statistics Netherlands. Causes of death were coded according to ICD-9 codes until 1996, and after that, according to ICD-10 codes. (**Online Table 2**).

A primary diagnosis was defined as the underlying disease for hospitalization or the underlying cause of death. A secondary diagnosis was defined as a comorbidity of the primary hospital admission, a complication of the primary cause of death, or another disease which might have contributed to death.

Statistical analysis

All statistical analyses were performed in R software version 3.4.1. A Kaplan-Meier curve was created to visualize time to HF event, stratified by healthy lifestyle score. Missing data in the

baseline risk factors, except glucose, comorbidities and medication data, were imputed using multiple imputation from the *mice* algorithm in the statistical software package R. **Online Table 3** shows the percentage missing per baseline variable. Analyses were performed on 10 imputed datasets separately and results were pooled using Rubin's rules. Patient characteristics were summarized as mean (SD) or median [IQR] for continuous variables and percentages for categorical variables.

A Cox proportional hazard model was used to estimate the hazard ratios (HR) with 95% confidence interval (95% CI) for the association of the healthy lifestyle score with the outcome. The reference was the lowest category of the LS7 score (inadequate). We also estimated the HR and 95% CI for each individual component of the healthy lifestyle score in a multivariable Cox proportional hazard model. The proportional hazards assumption was verified by assessment of the Schoenfeld residuals. All analyses were adjusted for the potential confounders sex, age and educational level. Analyses for the separate LS7 components were additionally adjusted for the other components in the score. Due to the nature of the EPIC-NL cohort, the merging of two existing cohorts, we added cohort as a random effects variable in the model to adjust for cohort variability.

Finally, we separately compared clusters of one, two or three specific LS7 ideal components to a combined cluster of five, six and seven inadequate LS7 components in a Cox proportional hazard model to investigate whether combinations of specific LS7 components reduce the risk of HF. We selected clusters with a sample size of > 300 individuals for our analyses.

In sensitivity analyses we compared the healthy lifestyle score in a subset of participants in whom glucose had been measured at baseline (n = 20,694). Furthermore, we excluded sodium from the diet score in a sensitivity analysis, since no information was available on added salt via the FFQ which could have biased our LS7 diet component.

Results

Baseline characteristics

Baseline characteristics of the overall cohort as well as stratified by healthy lifestyle score are presented in **Table 1**. Overall, the population consisted of 74.7% females with a mean age of 49.4 years (11.9 SD). The individuals with an ideal healthy lifestyle score were generally younger, more often female and had higher education levels compared to individuals with an intermediate or inadequate score (all p-value <0.001).

Life's Simple 7 components and incidence of heart failure

Over a median follow-up of 15.2 years [IQR 14.1; 16.5] a total of 690 patients (1.8%) developed HF. A Kaplan-Meier curve for HF-free survival by healthy lifestyle score is shown in **Figure 1**. HF-free survival rate significantly differed between healthy lifestyle score groups (log rank, p-value < 0.001). The association between the healthy lifestyle score and incident HF is shown in **Table 2**. With inadequate healthy lifestyle score as a reference, we found a significantly decreased risk of HF incidence for individuals with an intermediate (HR 0.53, 95% CI 0.44; 0.64) and ideal healthy lifestyle score (HR 0.45, 95% CI 0.34; 0.60) after adjusting for age, sex and education level. Furthermore, we investigated the association of number of ideal LS7 components and incident HF (**Table 2**). Two or more ideal LS7 components showed a significant decreased risk of incident HF (HR 0.48, 95% CI 0.29; 0.80), with 0 ideal LS7 components as a reference and adjusted for age, sex and education level.

Individual components of LS7 and heart failure risk

The associations between individual components of the LS7 and incident HF are shown in **Figure 2**. Intermediate and ideal scores of glucose, smoking, BMI and blood pressure were all

significantly associated with a decreased HF incidence, compared to inadequate levels. Intermediate scores of diet and both intermediate and ideal scores of physical activity were associated with reduced incidence of HF, compared to inadequate scores in the model adjusted for age, sex and education level, but were not statistically significantly associated with incident HF in the fully adjusted model. No statistically significant association of cholesterol scores with incidence of HF was observed.

LS7 clusters and heart failure risk

Associations between clusters of LS7 ideal scores with incident HF are shown in **Figure 3**. The group with a score of five, six or seven inadequate LS7 components (N = 238) was used as reference. Individuals with two ideal components from the clusters of BMI – glucose, smoking – glucose and physical activity – smoking had a lower risk of HF incidence compared to the reference group. In individuals with three ideal components, the clusters with BMI – blood pressure – glucose, BMI – glucose – smoking, blood pressure – glucose – smoking and lastly glucose – physical activity – smoking showed a statistically significant lower incidence of HF. No statistical significant associations were observed between other clusters and incident HF.

Sensitivity analyses

Online Table 4 shows that associations of intermediate and ideal healthy lifestyle scores with incident HF were even stronger in the subset of patients with baseline glucose measurements available compared to the main analysis. In addition, removing salt from the LS7 diet component did not affect our results (**Online Table 5**).

Discussion

In this large cohort study with almost 20 years of follow-up we found that a healthy lifestyle score was associated with a reduced risk of HF. Individuals with intermediate and ideal healthy lifestyle scores had a 47% and 55% lower risk of incident HF compared to an inadequate healthy lifestyle score, respectively. In this cohort 41.5% individuals scored inadequately on the LS7 score, showing there is ample room for improvements in healthy lifestyle behavior that may reduce HF in the general population.

Life's Simple 7 and incident HF

Findings in this study are consistent with previous studies reporting on the association between LS7 and HF (**Table 3**).(7–10) All previous studies were conducted in cohorts from the United States (U.S.), and this study is the first examining LS7 in a European cohort. Nearly all studies categorized a healthy lifestyle in ideal, intermediate and inadequate, but definitions of these categories varied markedly. Even though different definitions were used, all studies found a reduced risk of incident heart failure in those with an ideal healthy lifestyle.(7–10) Of note, only 690 patients (1.8%) developed HF in our study. Compared to other cohorts, the incidence of HF is quite low. (7–10) This could be attributed to only having access to HF diagnoses in secondary care as outcome, while many HF patients are primarily known in primary care. Other reasons could be the relative young age of the participants (mean 49.4 years (11.9 SD) and almost 75% females in the study. It has been shown that the incidence of HF is considerably lower in females and younger individuals.(19) Still, we found strong associations between LS7 and incident HF. Associations could be even stronger in a balanced age and sex cohort.

Independent associations of Life's simple 7 components and incident HF

We extended the earlier findings with several new observations. Most studies did not investigate independent associations of individual components of LS7.(7, 9, 10) However, our

multivariable models showed that lower glucose levels, higher BMI , non-smoking and blood pressure <140/90 mmHg were all independently associated with a lower risk of incident HF. These associations are consistent with existing literature on these CVD risk factors.(19–23) Interestingly, our study also showed that not only an ideal healthy lifestyle was associated with a lower incidence of HF, also an intermediate healthy lifestyle yielded a considerable risk reduction of 47%. This shows that potentially modest improvements, i.e. from an inadequate healthy lifestyle to an intermediate healthy lifestyle would be beneficial in lowering HF incidence.

Our analyses showed that, after adjustments for age, sex and education level, physical activity (both ideal and intermediate) and an intermediate diet score were associated with reduced HF risk, which complements previous literature. Several studies reported that there is a dose-response relationship between physical activity and HF risk.(24–26) Conflicting results have been previously reported for the association between diet and HF.(2, 7, 27, 28) Despite the observed associations of physical activity and diet in our adjusted model, these components were not independently associated from the other LS7 components with a reduced risk of HF. Physical activity and diet are closely related to BMI, blood pressure and glucose and could influence these biological risk factors. Therefore, it could be hypothesized that the association of these factors with incident HF is mediated through the other LS7 components.(29–32) Lastly, it is known that total cholesterol is a strong predictor for coronary artery disease, which is one of the most common causes of HF.(33) Interestingly, previous studies observed no association between LS7 total cholesterol and HF, a finding that is confirmed in our study.(7, 8) A potential explanation could be that total cholesterol is only associated with HF with reduced ejection fraction. Further research is needed to confirm this hypothesis. Another explanation could be that cholesterol might not play a substantial role in HF. Results from the Controlled Rosuvastatin in Multinational Trial in Heart Failure (CORONA) study did not show

any beneficial effect of rosuvastatin in HF on the composite outcome of cardiovascular death, nonfatal myocardial infarction or stroke, while it did reduce LDL cholesterol.(34)

The current study is the first to examine the relationship between clusters of risk factors and incident HF. As it could be challenging to change one's lifestyle, we investigated whether specific combinations of LS7 components could reduce the risk of HF. Our analyses suggest that clusters with specific LS7 components, notably clusters including glucose, BMI, smoking or blood pressure, are associated with a lower incidence of HF. Therefore, it stands to reason that preventive strategies that target combinations of these specific LS7 components could have a large impact on decreasing incident HF in the general population. Yet, this should be further confirmed by intervention studies. Several clusters did not often occur in the population, which prevented us from studying all clusters of LS7 components thoroughly. We did observe a stepwise trend of the associations; clusters with two or three ideal LS7 components show a larger reduction in incident HF than one ideal component.

Strengths and limitations

Strengths of this study are the large sample size of the cohort, with rich data collection, including in depth information on risk factors. Another strength of this study was the long follow-up, which allowed for the assessment of incident HF. Our results are generalizable to other Western European populations; however, caution should be used comparing our results to U.S. populations due to more diversity in race distribution in U.S. cohorts. Several other limitations should be addressed. First, only baseline measurements of LS7 components were available, which might not reflect the risk factor status over time. In a subset of the EPIC-NL cohort repeated measurements were available and in an earlier study it was observed that in those who improve their baseline risk profile, compared to those with a stable profile over time, CVD incidence is up to two times lower.(35) Furthermore, the FFQ might not be an ideal

instrument to measure dietary intake, especially for sodium intake, which may have affected the association of diet with HF. Our sensitivity analysis showed, however, that excluding sodium from our diet score does not affect the results. Glucose measurements were available in the MORGEN cohort, while only in subset of participants of the PROSPECT cohort. Therefore, we used other information to determine glucose status, such as diabetes diagnosis and medication use. Patients with (yet) unrecognized diabetes from the PROSPECT cohort were not taken into account in these analyses, which is a limitation of our study. However, the results were robust in the sensitivity analysis. HF diagnoses were based on the Hospital Discharge Register and Cause of Death Register, however many HF patients are only known in primary care and not secondary care. Using these registries could have led to an underestimation of HF cases. Furthermore, we were unable to differentiate between HF phenotypes, since we had no access to detailed echocardiography estimates to assess systolic function. Lastly, due to the observational design of the study, residual confounding cannot be excluded.

Conclusions

A healthy lifestyle, as reflected in an ideal LS7 score, was associated with a 55% lower risk of HF. Given the robust associations between a healthy lifestyle and reduced incidence of HF, this study provides evidence that prevention of incident HF could be accomplished by implementing healthy lifestyle patterns. The American Heart Association LS7 could be seen as a way to improve cardiovascular health and to reduce morbidity and mortality from CVDs, and in particular HF.

Perspectives

Core Clinical Competencies

Resources to achieve an "ideal" lifestyle are often lacking and it is known that it can be challenging to change one's lifestyle. Our analyses suggest that clusters with specific LS7 components, notably clusters including glucose, BMI, smoking or blood pressure, are associated with a lower incidence of HF. Focusing on particular components of the American Heart Association LS7 could be seen as a way to improve cardiovascular health.

Translational Outlook implications

Preventive strategies that target combinations of specific LS7 components could have a large impact on decreasing incident HF in the general population. However, this should be further confirmed by intervention studies.

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Figure 1. Kaplan Meier for the probability of HF free survival

Caption Figure 1. Stratified by healthy lifestyle score: ideal (score 11–14), intermediate (score 9–10) and inadequate (score 0–8). Log-rank test for differences in event free survival based on healthy lifestyle score: p < 0.0001. Insert: zoomed in survival curves.

Central illustration:

Figure 2. Associations between individual components of the LS7 and incident HF

Caption Figure 2. Model 1 = adjusted for age, sex and education level, model 2 = adjusted for age, sex, education level and all LS7 components. N = 37,803, number of events = 690. Red boxes = Inadequate level of LS7 component, Blue boxes = intermediate level of LS7 component, Green boxes = Ideal level of LS7 component. BMI = Body Mass Index.

Figure 3. Associations between clusters of ideal LS7 components with incident HF

Legend Figure 3. Analyses are adjusted for age, sex and education level. Individuals with five, six and seven inadequate LS7 components were the reference group (N = 238). Hazard ratio (95% CI) = Hazard ratio (95% confidence interval). N = size of cluster, BMI = Body Mass Index, BP = Blood Pressure. Number of events displayed in **Online Table 6**.

Table 1. Baseline characteristics EPIC-NL cohort

	Overall EPIC-NL* cohort (n = 37,803)	LS7 score ideal (11 – 14) 23.2% (n = 8,770)	LS7 score intermediate (9 – 10) 35.3% (n = 13,345)	LS7 score inadequate (0 – 8) 41.5 % (n = 15,688)
Demographics				
Age (years)	49.4 (11.9)	43.8 (12.5)	48.9 (12.1)	52.6 (10.1)
Female sex (%)	74.7	77.2	76.2	71.9
High education (%)	20.2	30.7	21.2	13.5
Lifestyle factors (%)				
Smoking				
Current	30.3	6.1	25.9	49.0
Ex-smoker	31.5	39.5	32.6	23.1
Physical activity				
Active	41.6	64.9	45.1	25.5
Sedentary	7.6	0.9	3.5	14.8
Diet score				
0 – 1	29.1	12.7	25.2	41.7
2 – 3	68.4	82.5	72.3	57.1
4 – 5	2.5	4.8	2.5	1.1
Clinical measurements (mean (SD))				
Systolic blood pressure (mmHg)	126.4 (19)	114 (11.7)	123.8 (16.5)	135.4 (19.7)
Diastolic blood pressure (mmHg)	77.9 (10.6)	61.6 (7.9)	76.5 (9.5)	82.5 (10.7)
BMI (kg/m^2, median [IQR])	25.2 [4.9]	23.1 [2.9]	24.7 [4.2]	27.1 [5.1]
WHR	0.8 (0.1)	0.8 (0.1)	0.8 (0.1)	0.9 (0.1)
Total cholesterol (mg/dL)	214.6 (42.0)	185.3 (30.9)	207.7 (38.7)	233.3 (40.2)
HDL cholesterol (mg/dL)	56.6 (16.1)	59.4 (15.2)	57.9 (16.2)	53.3 (15.6)
Glucose (mg/dL, median [IQR])	90.1 [18.0]	84.7 [14.4]	88.3 [16.2]	95.5 [21.6]
Comorbidities (%)				
Hypertension	37.5	13.8	30.1	56.6
Diabetes mellitus	1.5	0.1	0.3	3.3
Myocardial infarction	1.3	0.6	1.1	1.9

* EPIC-NL = European Prospective Investigation into Cancer and Nutrition-Netherlands, BMI = Body Mass Index, WHR = Waist-Hip Ratio, HDL = High Density Lipoprotein, IQR = Inter Quartile Range.

Table 2. Associations between LS7 and incident HF

Associations of healthy lifestyle score with incident HF		
	Model 1	Model 2
	HR (95% CI)	HR (95% CI)
Inadequate (0 - 8)	1 (ref)	1 (ref)
Intermediate (9 - 10)	0.41 (0.34; 0.50)	0.53 (0.44; 0.64)
Ideal (11 - 14)	0.22 (0.17; 0.30)	0.45 (0.34; 0.60)
Associations of LS7 ideal components with incident HF		
	Model 1	Model 2
	HR (95% CI)	HR (95% CI)
0 ideal components	1 (ref)	1 (ref)
1 ideal components	1.03 (0.61; 1.72)	0.93 (0.56; 1.57)
2 ideal components	0.58 (0.35; 0.95)	0.48 (0.29; 0.80)
3 ideal components	0.40 (0.24; 0.66)	0.39 (0.23; 0.64)
4 ideal components	0.26 (0.16; 0.45)	0.35 (0.20; 0.59)
5 ideal components	0.11 (0.06; 0.22)	0.23 (0.12; 0.43)
6 - 7 ideal components	0.07 (0.02; 0.21)	0.20 (0.07; 0.59)

Model 1 = crude model, model 2 = adjusted for age, sex and education level. HR (95% CI) = Hazard ratio (95% Confidence interval). N = 37,803, number of events = 690.

Table 3. EPIC-NL main findings in context of previous studies

	Studies				
	EPIC-NL	**MESA study** (7)	**Jackson Heart Study** (8)	**Framingham Offspring Study** (9)	**ARIC study** (10)
Definition LS7 categories	Ideal (>= 11 points), intermediate (9 - 10 points), inadequate (<= 8 points)	Ideal (>= 11 points), intermediate (9 - 10 points), inadequate (<= 8 points)	Ideal >= 4 ideal components (>= 8 points), intermediate (5 - 7 points), inadequate = 0 - 2 ideal components (0 - 4 points)	Linear scale 0 - 14 points	Ideal (>= 10 points), intermediate (5 - 10 points), inadequate (<= 4 points)
Cohort size	37,803	6,506	4,195	3,201	13,462, for cardiac remodeling 6,538 participants

Adjustments	1) Adjusted for age, sex and education, 2) Adjusted for age, sex, education and all other LS7 components	Adjusted for age, sex, race/ethnicity, education, income and health insurance.	1) Adjusted for age and sex, 2) adjusted for age, sex and all other LS7 components	Adjusted for age and sex	Adjusted for inverse probability weights: 1) age, sex, race, and education at Visit 1, 2) age, sex, race, study center, education, prevalent HF and CAD, all other LS7 variables measured at Visit 1; systolic and diastolic blood pressure, heart rate, BMI, smoking and drinking status, diabetes, hypertension medication at Visit 4; and incident HF through 2011.
Outcome	Ideal score was associated with a 55% risk reduction compared to inadequate score. Strongest independent predictors for risk reduction in HF were glucose, smoking and BMI.	Ideal score was associated with 69% risk reduction compared to inadequate score.	Ideal score was associated with a 61% risk reduction compared to inadequate score. Achieving ideal blood pressure, BMI, glucose and smoking was associated with lower risk of adverse cardiac remodeling.	Each 1 point higher LS7 score was associated with a 23% risk reduction for incident HF, consistent across ejection fraction.	Ideal score associated with 14.4% lower lifetime risk of HF among middle-aged participants (45 - 64 years) compared to inadequate score.

Novelty	1) relationship between clusters of risk factors and incident HF: clusters including glucose, BMI, smoking or blood pressure are associated with a risk reduction of HF, 2) First time LS7 evaluated in a European cohort.	Across racial/ethnic groups a similar trend was observed for the association of LS7 and HF risk, Black participants had the highest incidence of HF and the poorest LS7 status followed by Hispanic, white and Chinese American participants.	Blood pressure, physical activity, smoking and glucose were independently associated with a risk reduction in HF. The combined population attributable risk for these components was 37.1%.	Higher LS7 scores were associated with a lower prevalence of adverse cardiac remodeling and echocardiographic measures including left ventricular wall thickness.	Ideal score associated with lower left ventricular hypertrophy and diastolic dysfunction.