

## Life's Essential 8 and the risk of cardiovascular disease death and all-cause mortality in Finnish men

# Nzechukwu M. Isiozor (1)<sup>1</sup>\*, Setor K. Kunutsor<sup>2</sup>, Ari Voutilainen<sup>3</sup>, and Jari A. Laukkanen<sup>1,3,4</sup>

<sup>1</sup>Institute of Clinical Medicine, University of Eastern Finland, Yliopistonranta 1, 70211 Kuopio, Finland; <sup>2</sup>Diabetes Research Centre, University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4WP, UK; <sup>3</sup>Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Yliopistonranta 1C, Canthia Building, FI-70211 Kuopio, Finland; and <sup>4</sup>Department of Internal Medicine, Central Finland Health Care District, Hoitajantie 3, 40620 Jyväskylä, Finland

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Aims	The aim of the study was to examine the association between Life's Essential 8 (LE8) and the risk of cardiovascular and all- cause mortality.
Methods and results	The LE8 was computed for 1662 men, aged 42–60 years, without pre-existing history of cardiovascular disease (CVD) at baseline in the Kuopio Ischaemic Heart Disease study. The LE8 factors include diet, physical activity, nicotine exposure, sleep, body mass index, blood pressure, blood glucose, and lipids. Each LE8 factor was scored between 0 and 100 points. The summation of all points generated the total LE8 score, which was categorized into quartiles $\leq$ -420, >420–485, >485–550, and >550. Multivariable Cox regression models were used to estimate hazard ratios and 95% confidence intervals of LE8 scores for the outcomes. During a median follow-up of 30 years, 402 and 987 men died from CVD and any cause, respectively. The total LE8 score among participants ranged from 185 to 750. The higher the LE8 scores, the lower the risk of dying from CVD and all-cause. Following adjustment for age, alcohol consumption, and socio-economic status, every 50-unit increase in LE8 score was associated with 17% and 14% lower risk of CVD and all-cause deaths, respectively. Men within LE8 top quartile had 60% lower risk of CVD mortality when compared with those within the bottom quartile.
Conclusion	Life's Essential 8 was strongly and inversely associated with the risk of CVD death and all-cause mortality among ageing men. Measures that promote optimal LE8 scores should be encouraged among the general population.
Lay Summary	<ul> <li>The association between the American Heart Association's Life's Essential 8 (LE8) and the risk of cardiovascular and all-cause mortality was examined using the Kuopio Ischaemic Heart Disease Risk Factor Study in Finland.</li> <li>The result supports continuous improvement in healthy behaviours and factors used in generating LE8 score, which may lower future risk of dying from heart disease.</li> <li>In this paper:</li> <li>Men who had total LE8 score more than 550 had lower risk of dying from heart disease or any cause of death compared with those with LE8 score ≤ 420.</li> <li>Increasing LE8 score by 50 can lower risk of dying from heart disease or any other cause.</li> </ul>
Keywords	Cardiovascular health metrics • Life Essential 8 • Cardiovascular disease • All-cause • Death • Cohort

\* Corresponding author. Tel: +358465670392, Email: nzechukwu.isiozor@uef.fi

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## Introduction

Cardiovascular disease (CVD) remains the leading cause of death worldwide, accounting for 32% of all global deaths and 22% of deaths among working age populations (15–64 years) in Finland.<sup>1,2</sup> Population-wide preventive approaches are important strategies for reducing the risk of CVD and its associated burdens. Thus, the recently updated metrics launched by the American Heart Association (AHA) for assessing cardiovascular health, termed Life's Essential 8 (LE8), could be beneficial for the prevention of CVD and overall improvement of cardiovascular health. The metrics is an upgraded modification and advancement to the earlier developed Life's Simple 7 (LS7).<sup>4</sup> The LE8 components include physical activity (PA), body mass index (BMI), and blood pressure (BP); and the updated factors are diet, nicotine exposure, blood lipids, and blood glucose, while the new factor is sleep. This latest addition highlights the importance of psychological components for better cardiovascular health. Sleep is an important factor affecting health. Although there is a research gap for substantial evidence to show how improving sleep duration or quality reduces CVD events, poor sleeping habits and sleep disorders such as insomnia and obstructive sleep appoea have been reported to impact negatively on cardiovascular health.<sup>5,6</sup> Some researchers, however, have demonstrated how minor changes in sleep can affect CVD-related risk factors, and sleep time can be altered.<sup>7</sup> This formed part of the basis for including sleep to the initial seven factors, in addition to the simplistic and improving reliable measurement tools.<sup>3</sup>

A major difference between LE8 from LS7 is the scoring system of the factors. Whereas each factor in the LS7 score system ranged from 0 to 2 (with an ideal factor assigned a maximum score of 2; intermediate factor = 1; and poor factor = 0), the new LE8 scoring system for each factor ranges from 0 to 100 points. The committee that developed the new scoring system considered the ease of programming the metric scores in software applications, online CVH assessment tools, and electronic health records.<sup>3</sup>

Earlier studies have shown how LS7 maintained at optimal levels can lower risk of cardiovascular events and mortality.<sup>8–13</sup> Over the years, LS7 has proved to be a useful tool for evaluating healthy lifestyle to improve cardiovascular health, also ascertained in meta-analyses reports.<sup>14,15</sup> However, to our knowledge, no study has evaluated the associations between the newly launched LE8 and adverse cardiovascular outcomes such as CVD death and all-cause mortality in European populations. Therefore, we sought to examine the prospective relationship between AHA's developed LE8 and the risk of CVD death and all-cause mortality using data from eastern Finland.

## Methods

#### Study population

Reporting of the study was conducted in accordance with Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines for reporting observational studies in epidemiology (STROBE checklist attached).

The population-based Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD) which comprised men aged 42–60 years, without pre-existing history of CVD at baseline, was used. The KIHD was initially designed to investigate various risk factors of atherosclerotic CVD and other chronic diseases among middle-aged and older men in Kuopio and its surrounding communities.<sup>9,16</sup> Men, aged 42–60 years, were randomly selected from the national population register at baseline (1984–89). Of the 3235 eligible men, 186 did not reply to invitation and 367 declined consents, leaving 2682 volunteer participants for the study. The present study is based on 1662 men with no history of CVD at baseline and non-missing data on relevant covariates (see Supplementary material online, *Figure S1*). The Research Ethics Committee of the University of Eastern Finland approved the KIHD research protocol (ref. number 143/97), and the study protocol

complied to the ethical guidelines of the Declaration of Helsinki. All participants gave informed consent.

#### Data collection

Each participant received a self-administered questionnaire before their visit to the study centre. Participants were invited to the study centre for interviews and clinical examination. A trained registered research nurse, with more than 6 years experience in epidemiological studies, performed the interviews. The participants also went through health examinations. Details of the assessment for BP, BMI, nutritional status, nicotine exposure, smoking status, alcohol intake, PA, prevalent medical conditions, and socioeconomic status (SES) have been previously described.<sup>9</sup> A 4-day food record diary was used to assess diet, and a 7-day PA diary was used to assess the conditioning PA (metabolic equivalents (METs)  $\geq$  3). A combination of self-reported answers to the following questions was used to assess nicotine exposure—'1) Have you ever smoked (yes or no), 2) Do you smoke currently (no, irregularly, or regularly), 3) When did you smoke last, and 4) How often do you have to be in a smoky room?'. Adulthood SES was assessed using self-reported questionnaires based on combined measures of income, occupational prestige, education, material standard of living, and housing conditions. Income was divided into quintiles over the past 12 months. The occupational status (occupational prestige) of participants based on self-reported primary lifetime occupation was classified into three groups as white collar (professional and managerial staff and low-paid clerical workers); blue collar (manual labourers in construction, mining, manufacturing, or forestry); and farmer, including those who spent most of their employed activities in the agricultural sector. Education was classified into four categories—less than an elementary education, completion of elementary education, completion of middle school or a part of middle school, and completion of high school or above. Standard of living was evaluated using a self-reported material possession index based on 12-item ownership (colour TV, video tape recorder, freezer, dish washer, car, motorcycle, telephone, summer cottage, house trailer, motor boat, sailing boat, and ski mobile). The combined SES scale ranged from 0 to 25, with higher values indicating lower SES.<sup>1</sup>

A self-reported answer to 'How many hours do you usually sleep a night?' was used to assess sleep health. The weight and height measured at baseline were used to calculate the BMI [weight in kilograms divided by height in meters squared (kg/m<sup>2</sup>)]. After a supine rest of 5 min, the BP was measured using a random-zero mercury sphygmomanometer (Hawskley, UK) between 8 a.m. and 10 a.m. with 5-min interval—three measurements in supine, two in sitting, and one in a standing position.<sup>18,19</sup> The average of six BP values was used for the systolic and diastolic BP.

Participants were to abstain from alcohol consumption for 3 days, smoking, and feeding for 12 h prior to blood specimen collection between 8 and 10 in the morning. After the subject had rested for 30 min in the supine position, blood sample was drawn from the antecubital vein with Terumo Venoject VT-100PZ vacuum (Terumo Corp., Tokyo, Japan), without the use of tourniquet. Blood glucose was measured by glucose dehydrogenase method (Merck, Darmstadt, Germany) after precipitation of proteins by trichloroacetic acid using a clinical chemistry analyser (Kone Specific, KONE Instruments Oy, Espoo, Finland), in addition to the following questionnaire items—'(a) do you have diet-controlled diabetes, (b) do you use oral diabetes medications, and (c) do you use insulin?".<sup>8,19,20</sup> Also, self-reported diabetes at baseline was considered. The cholesterol contents of serum lipoprotein fractions and triglycerides were measured enzymatically (CHOD-PAP, Boehringer, Mannheim, Germany). Using ultracentrifugation and precipitation, serum high-density lipoprotein cholesterol and its subfractions were separated from fresh serum samples.<sup>21</sup>

#### Life's Essential 8

The LE8 adopted for this study conformed with the recently updated AHA's cardiovascular health metrics, consisting of four health behaviours (diet, PA, nicotine exposure, and sleep health) and four health factors (BMI, blood lipids, blood glucose, and BP) (see Supplementary material online, *Table S1*).<sup>3</sup> The eight factors and how the points are allocated in this study are summarized in *Table 1*. The points for each factor at baseline ranged from 0 to 100. The highest and lowest points for each level of the factors are described below:

Table 1	Distribution of baseline Life's Essential 8 factors by cardiovascular disease death and all-cause death in KIHD
study	

Life's Essential 8			All participants N = 1662	Card disea N = 4	iovascular se death 02	All-ca mort N = 9	ause ality 87
Factors	Points	N	Mean point (SD)	n	P for trend	n	P for trend
Diet (MEPA)			29.38 (11.02)		0.632		0.538
0–3	0	40	( )	8		22	
4–7	25	1292		321		774	
8–11	50	329		73		191	
12–14	80	1		0		0	
15–16	100	_		_		_	
Physical activity (min/week)			56.83 (43.97)		0.86		0.614
0	0	548		136		337	
1–29	20	32		5		19	
30–59	40	107		22		57	
60–89	60	115		30		72	
90–119	80	108		28		59	
120–149	90	121		29		69	
≥150	100	631		152		374	
Nicotine exposure			54.49 (41.65)		0.177		<0.001
– Current smoker	0	560	( )	148		406	
- Former smoker and second-hand exposure (quit $<1$ year)	5	2		0		1	
- Former smoker (quit <1 year)	25	31		8		20	
- Former smoker and second-hand exposure (quit $1 - < 5$ years)	30	7		4		5	
- Former smoker (quit 1-<5 year)	50	47		7		20	
- Former smoker and second-hand exposure (quit $\geq$ 5 years)	55	28		4		10	
- Former smoker (quit $\geq$ 5years)	75	501		124		291	
- Never smoker, but second-hand exposure	80	25		5		11	
– Never smoker	100	461		102		223	
Sleep health (average hours/night)			91.21 (18.36)		0.499		0.053
<4	0			35		101	
4-<5	20			42		107	
5-<6 or ≥10	40	147		12		41	
6-<7	70	169		313		738	
9–<10	90	72					
7–<9	100	1274					
Body mass index (kg/m <sup>2</sup> )			73.78 (23.84)		0.004		0.009
≥40.0	0	5	( )	4		5	
35.0–39.9	15	40		12		27	
30.0–34.9	30	199		57		126	
25.0–29.9	70	858		213		526	
<25	100	560		116		303	
Blood lipids (mg/dL)			43.09 (28.90)		0.019		0.005
Non-HDL >220 mg/dL	0	228		64		144	
Non-HDL 190–219 mg/dL	20	318		91		208	
Non-HDL 160–189 mg/dL	40	501		118		300	
Non-HDL 130–159 mg/dL	60	407		94		231	
Non-HDL <130 mg/dL	100	208		35		104	
20 points subtracted for drug-treated levels	-			-			
Blood glucose			96.02 (14.53)		<0.001		<0.001
Insulin-treated diabetes	0	1		1		1	
Tablet-treated diabetes	20	16		9		16	

Continued

#### Table 1 Continued

Life's Essential 8			All participants N = 1662	Card disea N = 4	liovascular ase death 102	All-c mort N = 9	ause tality 987
Factors	Points	N	Mean point (SD)	n	P for trend	n	P for trend
Diet-treated diabetes	40	46		19		38	
No diabetes and FBG 100–125 mg/dL	60	62		19		40	
No diabetes and FBG <100 mg/dL	100	1537		354		892	
Blood pressure (SBP or DBP), mmHg			39.13 (29.71)		<0.001		<0.001
≥160 or ≥100	0	275		88		191	
140-159 or 90-99 treated	5	81		23		50	
140–159 or 90–99	25	457		137		287	
130-139 or 80-89 treated	30	39		15		26	
130–139 or 80–89	50	523		94		284	
120–129/<80 treated	55	4		2		3	
120–129/<80	75	102		19		54	
<120/<80 treated	80	4		0		2	
<120/<80	100	177		24		90	

DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL, high-density lipoprotein; MEPA, Mediterranean Eating Pattern for Americans; SBP, systolic blood pressure.

- (1) Diet: The Mediterranean Eating Pattern for Americans (MEPA) score was used. The lowest MEPA score range of 0–3 was assigned the least point of 0, while the highest MEPA score of 15–16 has highest point of 100.
- (2) Physical activity (PA): Moderate or vigorous PA of  $\geq$ 150 min/week = 100 points; no PA/week = 0 point.
- (3) Nicotine exposure (including cigarettes, inhaled nicotine delivery system, and second-hand exposure): Never smoked and no second-hand exposure = 100 points; current smokers = 0 point.
- (4) Sleep health (average sleep/night): 7-<9 h = 100 points; <4 h = 0 points.
- (5) Body mass index  $(kg/m^2)$ : <25 = 100 points;  $\geq 40.0 = 0$  point.
- (6) Blood lipids (non-high-density lipoprotein cholesterol, mg/dL): <130 = 100 points; ≥220 = 0 point. However, for drug-treated level, 20 points were subtracted.
- (7) Blood glucose (fasting, mg/dL or HbA1c, %): No history of diabetes and FBG <100 (or HbA1c < 5.7) = 100 points; diabetes with HbA1c  $\geq$  10 = 0 point.
- (8) Blood pressure (systolic/diastolic, mmHg): <120/<80 (optimal) = 100 points; systolic of ≥160 or diastolic of ≥100 = 0 point. If values are of treated level, 20 points were deducted.</p>

#### Ascertainment of follow-up events

All CVD and all-cause deaths from study enrolment to end of 2019 were ascertained by computer linkage to the national death registry using the Finnish personal identification code. There were no losses to follow-up. The CVD deaths were coded according to cause of death related to the ICD-9 (International Classification of Diseases, Ninth Revision, code numbers 390–459) or the ICD-10 (code numbers I00–I99). Censoring was carried out on the date from the baseline visit to CVD death, death, or the end of the observation period (31 December 2019).

#### Statistical analysis

Baseline characteristics of the participants were summarized using descriptive statistics. These were presented as mean  $\pm$  standard deviation or median (interquartile range) for continuous variables and as numbers (percentage) for categorical variables. The shape of the relationship between LE8 (as continuous variable) and the risk of outcomes was explored using restricted cubic splines with knots at the 5th, 35th, 65th, and 95th of LE8 distribution in a multivariable adjusted model. Multivariable Cox regression models were used to estimate the hazard ratios (HR) and 95%

confidence intervals (Cls) of CVD death and all-cause mortality for the baseline LE8 scores, after no major departure from the proportionality assumptions using Schoenfeld residuals was confirmed.<sup>22</sup>

For each LE8 factor, the worst category was assigned 0 point, whereas the best was assigned 100 points (*Table 1*). All the points from all factors were summed up to generate the total LE8 score. This score was categorized into quartiles—quartile 1 (Q1),  $\leq$ 420; quartile 2 (Q2), >420–485; quartile 3 (Q3), >485–550; quartile 4 (Q4), >550, with Q1 used as referent. Based on the two domains of CVH metrics, i.e. health behaviours and health factors, LE8 health behaviour and LE8 health factor scores were created. Subsidiary analysis was done to evaluate the effect the newly introduced factor, sleep, has on outcomes if only the initial LS7 factors were updated. Thus, an LE8 score excluding sleep health was generated.

Two adjusted models were used to estimate the HRs. The first model was adjusted for age, and the second model was adjusted for age, alcohol consumption, and SES. Sensitivity analysis was conducted with additional adjustments for family history of coronary heart disease, use of antihypertensive and cholesterol-lowering medications. Also, results were presented in age categories based on the median age of participants. We used receiver operating characteristic (ROC) to determine the best cut-off points of LE8 score, which could be used to predict the specified outcomes, with the predictive accuracy expressed as area under the curve (AUC). All statistical analyses were done using IBM SPSS Statistics 27 and R software (2022.07.0 + 548). A two-sided *P* value < 0.05 was considered statistically significant.

## Results

During a median follow-up of 30 years, 402 CVD and 987 all-cause deaths were recorded. The mean age of all participants was 52 years. On average, men who were older and had lower SES were more likely to die from CVD and any cause. The total LE8 score ranged from 185 to 750 with a mean score of 484 for all participants, 491 for men who did not die from CVD, and 508 for all survivors (*Table 2*). A restricted cubic spline showed that the risk of CVD death and all-cause mortality decreased continuously with increasing LE8 scores across the range of 0–800 (*Figure 1A* and *B*). *Table 1* shows the distribution of the LE8 components and points. For the diet factor, the mean point was 29.4 with more than 75% of the participants (129 men) scoring 25 points.

	All participants (N =	= 1662) No CVD death ( <i>n</i> =	1200) UVU death (n = 4				
Age (years)	$52.2 \pm 5.5$	51.5 ± 5.6	54.3 ± 4.4	<0.001 49.5 ± 5.6	54.0 <del>+</del> 4	4.5	<0.001
Socio-economic status	$11.6 \pm 5.1$	$11.3 \pm 5.1$	$12.6 \pm 4.9$	$< 0.001  10.2 \pm 4.8$	12.7 ± 5	5.0	<0.001
Alcohol/week (g)	33.4 (6.5–92.6)	34.6 (7.2–92.8)	30.7 (4.2–91.3)	0.575 29.8 (7.1–7	( <del>6</del> ) 36.5 (6.	6.4–109.9)	<0.001
Systolic blood pressure (n	134.0 ± 16.3 <b>mHg)</b> 134.0 ± 16.3	$132.4 \pm 15.9$	$138.8 \pm 16.7$	<0.001 130.6 ± 13	) 136.3±	± 17.4	<0.001
Smoker	516 (31.0)	373 (29.6)	143 (35.6)	0.024 133 (19.7)	383 (38	8.8)	<0.001
Body mass index (kg/m <sup>2</sup> )	$26.7 \pm 3.5$	$26.5 \pm 3.3$	$27.2 \pm 3.9$	$0.001  26.3 \pm 3.3$	26.7 ± 3	3.6	0.003
LE8 score	$483.9 \pm 91.8$	$490.6 \pm 91.1$	$463.2 \pm 90.8$	<0.001 508.0 ± 88	9 467.5±	± 90.1	<0.001
LE8 (in quartiles)				<0.001			<0.001
Q1, ≤420	423 (25.5)	289 (22.9)	134 (33.3)	112 (16.6)	311 (31	1.5)	
Q2, >420–485	436 (26.2)	324 (25.7)	112 (27.9)	160 (23.7)	276 (28	8.0)	
Q3, >485–550	397 (23.9)	307 (24.4)	90 (22.4)	183 (27.1)	214 (21	1.7)	
Q4, >550	406 (24.4)	340 (27.0)	66 (16.4)	220 (32.6)	186 (1	18.8)	



However, most men (1274) had healthy sleep, scoring 100 points with mean of 91.2 points among the participants—highest for the behavioural indicators. For the health factors, most men were in the category of no diabetes and fasting blood glucose <100 mg/dL, which also reflects the highest LE8 point achieved by the entire cohort. The distribution of baseline characteristics of participants by LE8 quartiles and age categories are shown in Supplementary material online, *Table S2*. Men at the bottom quartile and 54 years and above were of lower SES compared with those at the top quartile and younger.

The associations between LE8 and risk of CVD and all-cause deaths are displayed in *Table 3*. The higher the LE8 scores, the lower the risk of CVD death and all-cause death. Following adjustment for age, alcohol consumption, and SES, men in the top quartile (Q4) of LE8 had 60% and 48% lower risk of CVD and all-cause deaths when compared to those within the bottom quartile (Q1), respectively (*Figure 2*). Similarly, in the fully adjusted model, every 50-unit increase in total LE8 score was significantly associated with 17% lower risk of CVD death and 14% lower risk of all-cause death. Further evaluation on

	CVD death					All-cause d	eath			
	N/n	Model 1		Model 2		n/N	Model 1		Model 2	
		HR (95% CI)	P value	HR (95% CI)	P value		HR (95% CI)	P value	HR (95% CI)	P value
LE8 score (in e	quartiles)				-					
÷	134/423	-		-		311/423	1	Ι	~	I
7	112/436	0.644 (0.501–0.828)	0.001	0.667 (0.518–0.858)	0.002	276/436	0.696 (0.592–0.819)	<0.001	0.733 (0.622–0.863)	<0.001
e	90/397	0.513 (0.392–0.671)	<0.001	0.545 (0.416–0.714)	<0.001	214/397	0.539 (0.453–0.642)	<0.001	0.584 (0.490–0.697)	<0.001
4	66/406	0.354 (0.263–0.476)	<0.001	0.403 (0.298–0.545)	<0.001	186/406	0.441 (0.367–0.529)	<0.001	0.520 (0.431–0.626)	<0.001
Total LE8 sco	e (per 50-uni	t increase)								
	402/1662	0.805 (0.762–0.851)	<0.001	0.826 (0.780-0.874)	<0.001	987/1662	0.833 (0.804–0.862)	<0.001	0.861 (0.831–0.893)	<0.001
LS7 score <sup>a 8,9</sup>										
Inadequate	130/2607	-		~		676/1140	£-	Ι	-	I
Average	435/2607	0.57 (0.47–0.70)	<0.001	0.64 (0.52–0.78)	<0.001	585/1299	0.74 (0.66–0.83)	<0.001	0.79 (0.70–0.88)	<0.001
Optimal	44/2607	0.30 (0.21–0.42)	<0.001	0.35 (0.24–0.49)	<0.001	28/138	0.33 (0.23–0.49)	<0.001	0.35 (0.24–0.52)	<0.001
LE8 health be	haviour score	(per 50-unit increase)								
	402/1662	0.874 (0.814–0.939)	<0.001	0.908 (0.845–0.977)	0.010	987/1662	0.831 (0.795–0.870)	<0.001	0.867 (0.828–0.908)	<0.001
LE8 health fac	tor score (per	- 50-unit increase)								
	402/1662	0.709 (0.650–0.774)	<0.001	0.729 (0.668–797)	<0.001	987/1662	0.831 (0.787–0.878)	<0.001	0.863 (0.816–0.912)	<0.001
LE8 score with	iout sleep hea	ulth (per 50-unit increa	ise)							
	402/1662	0.798 (0.753–0.845)	<0.001	0.820 (0.773–0.870)	<0.001	987/1662	0.834 (0.804–0.864)	<0.001	0.864 (0.832–0.897)	<0.001
LE8 score quartiles: Model 1: adjusted fc Model 2: Model 1 pl CVU, cardiovascular <sup>a</sup> Published KIHD res	Quartile 1, ≤420; 1 rr age. us alcohol consum disease; HR, hazar ults on cardiovascu	Quartile 2, >420-485; Quartil. ption: socio-economic status. d ratio, LE8, Lifé's Essential 8; Jar health metrics based on ini	e 3, >485–550; ( LS7, Life's Simple itial seven factor	Quartile 4, >550. <sup>2</sup> 7; <i>n</i> /N, number of events/to <sup>1</sup> s (referenced in text, Isiozor ¢	tal. et al. <sup>8,</sup> ).					

 Table 3
 Association between LE8 and risk of CVD death and all-cause mortality



**Figure 2** Graphical representations for the associations between the American Heart Association's Life's Simple 7  $(LS7)^{8,9}$  and Life's Essential 8 (LE8) in quartiles (Q) and the risk of cardiovascular disease (CVD) death and all-cause mortality among the Kuopio Ischaemic Heart Disease Risk Factor Study participants.

the association between health behavioural and health factor scores of LE8 and risk of CVD death and all-cause death revealed statistical significance per 50-unit increase (Table 3). Analysis using the LE8 score without the newly AHA's introduced factor, sleep health, followed similar pattern such that without the sleep factor, each 50-unit rise in the LE8 score was significantly associated with lower risks of CVD death and all-cause death (HR, 95% CI: 0.82, 0.77-0.87 for CVD death and 0.86, 0.83–0.90 for all-cause death). Sensitivity analysis additionally including family history of coronary heart disease, use of cholesterol lowering drugs, and antihypertensive medications did not substantially alter the findings (see Supplementary material online, Table S3). Comparing the two age categories, men <54 years and  $\geq54$  years, following full adjustments, the HR for risk of CVD death decreased continuously across the LE8 quartiles; however, statistical significance was consistently observed among men  $\geq$  54 years. Similarly, there was statistically significant association between LE8 quartiles and risk of allcause death among men 54 years and above (see Supplementary material online, Table S3). Receiver operating characteristic analysis showed that a LE8 score threshold of 457.50 had 48.8% sensitivity and 64.8% specificity as a predictive marker for CVD mortality, with an AUC of 0.59. For all-cause mortality, the threshold was 482.5 with 56.1% sensitivity and 63.3% specificity and an AUC of 0.63.

#### Discussion

In this prospective study of middle-aged to ageing Finnish men, higher total LE8 score, a composite score and measure of AHA's recently updated CVH metrics, was associated with lower risk of CVD death and all-cause mortality. In general, survivors of both CVD and all-cause deaths had higher mean total LE8 scores than the deceased. Most of the participants who did not die from CVD were within the top quartile (Q4), whereas majority who died from CVD were within the least quartile (Q1). Similar patterns were also observed for all-cause mortality. Men in the top quartile had 60% and 48% lower risk of CVD death and all-cause mortality when compared to those within the lowest quartile, respectively. Compared to men within the lowest quartile (Q1), a graded increased protection from CVD death and all-cause mortality was observed from Q2, Q3, to Q4. More so, for each 50-unit increase in total LE8 score, there were associated 17% and 14% lower risk of CVD death and all-cause mortality, respectively. The lowest mean point achieved by participants was for the diet factor, whereas blood glucose factor had the highest mean point. The ROC analysis showed that the discriminative ability of LE8 score was limited.

This research is unique, being the first to report on the association of AHA's updated metrics and risk of CVD death in a general European population. Although the findings are consistent with earlier studies which evaluated the association between the older cardiovascular health metrics, LS7, and risk of CVD events and death,<sup>8,9</sup> it reveals and confirms the importance of optimal cardiovascular health to lower risk of CVD death and all-cause mortality. Our previous findings from the KIHD cohort using the AHA's initial seven factors (LS7) reported that men with optimal CVH had 75% lower risk of CVD death<sup>9</sup> and 65% lower risk of all-cause mortality.<sup>8</sup> This was similar with the reports from the Aerobics Center Longitudinal Study (ARIC) in the USA where there was significant association between optimal LS7 and lower risk of CVD death, but not with all-cause death.<sup>23</sup> Other regions of the world, outside of the USA, have evaluated the association between America's developed metrics and CVD death. For instance, in Europe, the Three-City Study in France reported significant relation between ideal CVH metrics using LS7 approach and risk of all-cause mortality,<sup>13</sup> which also falls in line with Dong and colleagues' study in China (Asia).<sup>12</sup> A meta-analysis on the LS7 and risk of CVD and all-cause mortality confirmed the inverse association between LS7 and risk of CVD death and all-cause mortality, thus reported that the highest LS7 score was associated with 75% lower risk of cardiovascular mortality and 45% lower risk of all-cause mortality.<sup>15</sup>

The proven benefits of optimal LS7 for better cardiovascular health are evident across diverse population groups. However, there is need for its refinement and calibration for inter- and intra-individual variances.<sup>24</sup> Based on this updated and modified metrics including more comprehensive data on lifestyle factors, LE8 was launched as an improved tool to assess cardiovascular health.<sup>3</sup> More so, the new scaling system can better address intra-individual changes and inter-individual differences. Notably, the updated factors in the current LE8 are diet, nicotine exposure, blood lipids, and blood glucose; and the new included factor is sleep health. Based on the diet score used in our current study, no participant had the highest point (i.e. MEPA score 15-16). In fact, there was only one participant who achieved a score of 12-14. With this finding, more public health efforts and programmes are needed to promote healthier diets. Focused programmes that can improve the least achieved factors would be crucial for cardiovascular benefits. For instance, in this population group, health measures and sensitizations towards healthier diets in the general population will be more beneficial than blood glucose awareness initiative, since our result shows that most men had the highest blood glucose points needed for better cardiovascular health. On how LE8 health behavioural scores relate to CVD and all-cause deaths, per 50-unit increase in the score was associated with 9% and 17% lower risk of CVD and all-cause deaths. For

example, using diet, this simply means that improving the diet score from '4–7' (25 points) to '12–14' (80 points) will significantly lower the risk of CVD death and all-cause death. Similarly, 50-unit rise in LE8 health factor score was associated with lower risk of CVD and all-cause death. In general, targeted programmes and health policies on LE8 factors with lower mean points are encouraged to improve the total LE8 scores at population level. When a high LE8 score is adopted and improved on by the populace, CVD mortality rates could be reduced.

Sleep, which is the newly added lifestyle factor, has been reported to be associated with cardiovascular events and all-cause mortality.<sup>25-28</sup> Meta-analysis evaluating this association reported a U-shaped relationship between sleep duration and risk of CVD and all-cause mortality, such that both short and long sleep duration increased the risk of CVD and all-cause mortality.<sup>26</sup> Recently, Jin<sup>28</sup> and colleagues confirmed this U-shaped association using the National Health and Nutrition Examination Survey (NHANES) and concluded that 7-h sleep was associated with the lowest mortality risk. But does sleep inclusion in LE8 make any difference from previous LS7 factors? Assuming only the definition and quantification of the original factors in the LS7 were updated, our subsidiary finding shows that per 50-unit rise in the LE8 score (without sleep) would be associated with 18% and 14% lower risk of CVD and all-cause death, respectively. However, more studies are needed to evaluate if sleep in the new cardiovascular health metrics makes a substantial difference to its protective effect.

In general, the updated CVH metrics can serve as personal guide for CVD prevention and overall health promotion strategies. Additionally, it can be useful to researchers, policymakers, and health systems in developing standardized tools to monitor and measure CVH at individual and population levels.

The strengths of this study include the novelty, being the first study to report the association between LE8 and risk of CVD death and all-cause mortality in the European population; the relatively large number of homogeneous participants with no CVD history at baseline; and the long followup period of the cohort which is adequate for the ascertainment of outcomes of interest. However, some limitations deserve mentioning. These are the inclusion of middle-aged to ageing Finnish men, which limits the generalizability of our results to women, other populations groups including younger and elderly populations, and ethnicities; misclassification bias given the use of self-administered questionnaires to obtain information on some of the components of the LE8; and the use of baseline CVH metrics due to the likelihood of changes in components of LE8 over the period of follow-up as a result of ageing, diseases, and lifestyle modification. We were unable to account for other cause-specific deaths as competing risk events due to the unavailability of data. The use of baseline assessments could underestimate the associations due to the potential for regression dilution bias. Therefore, it would be interesting to investigate further how the longitudinal evolution of the LE8 or interventions to improve total LE8 scores influences the rates of CVD death and all-cause mortality.

## Conclusions

Life's Essential 8 was strongly and inversely associated with the risk of CVD and all-cause mortality among ageing men, consistent with linear dose–response relationships. Increased sensitization for the overall improvement of the total LE8 score is needed, with targeted programmes towards the LE8 factors the population are deficient of higher points. Thus, measures that promote optimal LE8 scores should be encouraged among the general population.

## **Authors' contributions**

N.M.I., S.K.K., A.V., and J.A.L. contributed to the acquisition, analysis, and interpretation of the work. N.M.I. and A.V. contributed to the

conception and design. N.M.I. drafted the manuscript. All critically revised the manuscript and gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Ari Voutilainen (PhD), Jari A. Laukkanen (MD, PhD), Nzechukwu Michael Isiozor (MD, MHSc, PhD), and Setor K. Kunutsor (MD, PhD).

## Supplementary material

Supplementary material is available at European Journal of Preventive Cardiology.

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**Conflict of interest:** None declared.

## Data availability

The data underlying this article were provided by University of Eastern Finland, Institute of Public Health and Clinical Nutrition by permission. Data will be shared upon request to the corresponding author with permission of University of Eastern Finland.

#### References

- World Health Organization. Cardiovascular diseases (CVDs). https://www.who.int/ news-room/fact-sheets/detail/cardiovascular-diseases-(cvds) (Oct 29, 2022)
- Toppila I, Ukkola-Vuoti L, Perttilä J, Törnwall O, Sinisalo J, Hartikainen J, Lehto S. Cardiovascular event rate and death in high-risk secondary prevention patient cohort in Finland: a registry study. *Clin Cardiol* 2022;45:342–351.
- Lloyd-Jones DM, Allen NB, Anderson CAM, Black T, Brewer LC, Foraker RE, Grandner MA, Lavretsky H, Perak AM, Sharma G, Rosamond W; American Heart Association. Life's Essential 8: updating and enhancing the American Heart Association's Construct of Cardiovascular Health: a presidential advisory from the American Heart Association. *Circulation* 2022;**146**:e18-e43.
- 4. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, Arnett DK, Fonarow GC, Ho PM, Lauer MS, Masoudi FA, Robertson RM, Roger V, Schwamm LH, Sorlie P, Yancy CW, Rosamond WD. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. *Circulation* 2010;**121**:586–613.
- 5. Javaheri S, Redline S. Insomnia and risk of cardiovascular disease. Chest 2017;152: 435-444.
- Sánchez-de-la-Torre M, Campos-Rodriguez F, Barbé F. Obstructive sleep apnoea and cardiovascular disease. *Lancet Respir Med* 2013;1:61–72.
- Hale L, Troxel W, Buysse DJ. Sleep health: an opportunity for public health to address health equity. Annu Rev Public Health 2020;41:81–99.
- Isiozor NM, Kunutsor SK, Voutilainen A, Kurl S, Kauhanen J, Laukkanen JA. Association between ideal cardiovascular health and risk of sudden cardiac death and all-cause mortality among middle-aged men in Finland. *Eur J Prev Cardiol* 2020;28:294–300.
- Isiozor NM, Kunutsor SK, Voutilainen A, Kurl S, Kauhanen J, Laukkanen JA. American Heart Association's cardiovascular health metrics and risk of cardiovascular disease mortality among a middle-aged male Scandinavian population. *Ann Med* 2019;**51**:306– 313. doi:10.1080/07853890.2019.1639808
- Zhou L, Zhao L, Wu Y, Wu Y, Gao X, Li Y, Mai J, Nie Z, Ou Y, Guo M, Liu X. Ideal cardiovascular health metrics and its association with 20-year cardiovascular morbidity and mortality in a Chinese population. J Epidemiol Community Health 2018;**72**:752–758.
- Lachman S, Peters RJ, Lentjes MA, Mulligan AA, Luben RN, Wareham NJ, Khaw K, Boekholdt SM. Ideal cardiovascular health and risk of cardiovascular events in the EPIC-Norfolk prospective population study. *Eur J Prev Cardiol* 2016;23:986–994.
- Dong Y, Hao G, Wang Z, Wang X, Chen Z, Zhang L. Ideal cardiovascular health status and risk of cardiovascular disease or all-cause mortality in Chinese middle-aged population. *Angiology* 2019;**70**:523–529.

- Gaye B, Canonico M, Perier M, Samieri C, Berr C, Dartigues J, Tzourio C, Elbaz A, Empana J. Ideal cardiovascular health, mortality, and vascular events in elderly subjects: the three-city study. J Am Coll Cardiol 2017;69:3015–3026.
- Guo L, Zhang S. Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: a meta-analysis of prospective studies. *Clin Cardiol* 2017; 40:1339–1346.
- Fang N, Jiang M, Fan Y. Ideal cardiovascular health metrics and risk of cardiovascular disease or mortality: a meta-analysis. Int J Cardiol 2016;214:279–283.
- Salonen JT. Is there a continuing need for longitudinal epidemiologic research? The Kuopio Ischaemic Heart Disease Risk Factor Study. Ann Clin Res 1988;20:46–50.
- Jae SY, Kurl S, Bunsawat K, Franklin BA, Choo J, Kunutsor SK, Kauhanen J, Laukkanen JA. Impact of cardiorespiratory fitness on survival in men with low socioeconomic status. *Eur J Prev Cardiol* 2020;28:450–455.
- Isiozor NM, Kunutsor SK, Voutilainen A, Kauhanen J, Laukkanen JA. Life's Simple 7 and the risk of stroke in Finnish men: a prospective cohort study. *Prev Med* 2021;**153**: 106858. doi:10.1016/j.ypmed.2021.106858
- Voutilainen A, Brester C, Kolehmainen M, Tuomainen TP. Effects of data preprocessing on results of the epidemiological analysis of coronary heart disease and behaviourrelated risk factors. Ann Med 2021;53:890–899.
- Voutilainen A, Brester C, Kolehmainen M, Tuomainen T. Epidemiological analysis of coronary heart disease and its main risk factors: are their associations multiplicative, additive, or interactive? Ann Med 2022;54:1500–1510.

- Salonen JT, Salonen R, Seppänen K, Rauramaa R, Tuomilehto JHDL. HDL2, And HDL3 subfractions, and the risk of acute myocardial infarction. A prospective population study in eastern Finnish men. *Circulation* 1991;84:129–139.
- 22. Therneau TM, Grambsch PM. Modeling survival data: extending the cox model. New York: Springer-Verlag; 2000.
- Artero EG, España-Romero V, Lee D, Sui X, Church TS, Lavie CJ, Blair SN. Ideal cardiovascular health and mortality: Aerobics Center Longitudinal Study. *Mayo Clin Proc* 2012; 87:944–952.
- Ioachimescu OC. From seven sweethearts to life begins at eight thirty: a journey from Life's Simple 7 to Life's Essential 8 and beyond. J Am Heart Assoc 2022;11:e027658. doi: 10.1161/JAHA.122.027658
- 25. Nagai M, Hoshide S, Kario K. Sleep duration as a risk factor for cardiovascular disease a review of the recent literature. *Curr Cardiol Rev* 2010;**6**:54–61.
- 26. Yin J, Jin X, Shan Z, Li S, Huang H, Li P, Peng X, Peng Z, Yu K, Bao W, Yang W, Chen X, Liu L. Relationship of sleep duration with all-cause mortality and cardiovascular events: a systematic review and dose-response meta-analysis of prospective cohort studies. J Am Heart Assoc 2017;6:e005947.
- Kripke DF, Simons RN, Garfinkel L, Hammond EC. Short and long sleep and sleeping pills. Is increased mortality associated? Arch Gen Psychiatry 1979;36:103–116.
- Jin Q, Yang N, Dai J, Zhao Y, Zhang X, Yin J, Yan Y. Association of sleep duration with all-cause and cardiovascular mortality: a prospective cohort study. *Front Public Health* 2022;**10**:880276.