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FULL RESEARCH PAPER
Cardiovascular disease

Ideal cardiovascular health and cardiovascular-related events: a systematic review and meta-analysis

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Aims The aim of this study was to systematically review and quantitatively summarize the evidence on the association between Life Simple's 7 (LS7) and multiple cardiovascular diseases (CVDs) and cardiometabolic diseases (CMDs).

Methods and results EMBASE and PubMed were searched from January 2010 to March 2022 for observational studies that investigated the association between ideal cardiovascular health (CVH) with CVD or CMD outcomes in an adult population. Two reviewers independently selected studies according to the eligibility criteria, extracted data, and evaluated risk of bias. Data were analysed with a random-effects meta-analysis. This meta-analysis included 59 studies (1 881 382 participants). Participants with ideal CVH had a considerably lower risk of a variety of CVDs and CMDs as compared with those with poor CVH, varying from 40% lower risk for atrial fibrillation (AF) {hazard ratio [HR] = 0.60 [95% confidence interval (CI) 0.44–0.83]} to 82% lower risk for myocardial infarction [HR = 0.18 (95% CI 0.12–0.28)]. Intermediate CVH was associated with 27–57% lower risk in CVDs and CMDs compared with poor CVH, with the highest hazard for AF [HR = 0.73 (95% CI 0.59–0.91)] and the lowest hazard for peripheral arterial disease [HR = 0.43 (95% CI 0.30–0.60)].

Conclusion Ideal and moderate CVH were associated with a lower incidence of CVDs and CMDs than poor CVH. Life Simple's 7 holds significant potential for promoting overall CVH and thereby contributing to the prevention of CVDs.

Lay summary Healthy lifestyle is very important to prevent cardiovascular diseases (CVDs) and cardiometabolic diseases (CMDs), such as diabetes and kidney diseases. Therefore, in 2010, the American Heart Association introduced Life's Simple 7 (LS7), a scoring system using seven lifestyle factors to measure cardiovascular health in populations, and these factors are diet, physical activity, smoking, blood pressure, blood lipids, blood sugar, and weight. In this review, we investigated the relationship between LS7 score and CVDs or CMDs.

Key findings
- Higher Life's Simple 7 (LS7) score, meaning a healthier lifestyle score, was related to lower risks of cardiovascular diseases (CVDs).
- Promoting healthy lifestyle (higher LS7 score) could possibly lead to prevention of CVDs.

Keywords Life's Simple 7 • Cardiovascular health • Cardiovascular diseases • Cardiometabolic diseases • Preventive medicine • American Heart Association

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Introduction

Cardiovascular diseases (CVDs) and cardiometabolic diseases (CMDs) are significant health problems worldwide and reported by the World Health Organization to be the leading cause of death and disability.[1] Therefore, in 2010, the American Heart Association (AHA) emphasized that promoting ideal cardiovascular health (CVH) in the population can be accomplished through increased emphasis on prevention, promoting healthy behaviours, and prioritizing control of risk factors.[2] Ideal CVH was defined as achieving optimal CVH for seven cardiovascular (CV) risk factors: four modifiable health behaviours (no tobacco use, healthy weight, healthy diet, and moderate physical activity) and three health factors (normal blood pressure, blood glucose, and cholesterol levels). These seven metrics, also known as Life Simple's 7 (LS7), categorize individuals into three levels: ideal, intermediate, and poor CVH.[2]

To date, many observational studies reported an inverse relationship between LS7 scores and incidence of CVDs and CMDs, indicating a lower risk for these outcomes with higher CVH.[3,4] Systematic reviews in 2018 and 2023 suggested an inverse association between higher adherence to ideal CVH and CVD incidence, such as coronary heart disease (CHD), myocardial infarction (MI), stroke, and CV mortality.[4,5] This review aims to extend the previous evidence by including outcomes that were not included in previous reviews, such as atrial fibrillation (AF), type 2 diabetes (T2D), chronic kidney disease (CKD), heart failure (HF), peripheral arterial disease (PAD), stroke, and venous thromboembolism (VTE). We hypothesize that an inverse association also holds for these outcomes. Furthermore, we investigate the association between number of ideal metrics and incidence of CVDs and CMDs.

Thus, the aim of this study was to investigate the associations between meeting intermediate or ideal CVH, compared with poor CVH, and mortality or incidence of multiple CVDs and CMDs by conducting a systematic review and meta-analysis.

Methods

A priori registration

Our systematic review was registered in PROSPERO in May 2022 (CRD42022335273). This systematic review is reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[6]

Search methods for identification of studies

In March 2022, a systematic literature search was performed in PubMed and Embase to identify observational studies that investigated the association between ideal CVH and CVD and CMD outcomes. We limited our search to studies from 2010 to 2022, as the LS7 metrics were defined by the AHA in 2010 and did not place any language restrictions. Full electronic search strategies are shown in Supplementary material online, *Table S1*.

Selection processes

Studies were included in the systematic review based on the following inclusion criteria: (i) observational studies—cohort, cross-sectional, and case-control studies—assessing the association between AHA's ideal CVH and CV and cardiometabolic (CM) events, (ii) adult population (>18 years old), and (iii) reporting data on hazard ratios (HRs), odds ratios (ORs), or risk ratios (RRs) with confidence intervals (CIs) for the outcome of interest. Outcomes of interest included incidence and mortality due to CVD, including AF, CHD, HF, MI, PAD, stroke, and VTE, and CMD (T2D and CKD).

We did not restrict our selection to the general population but also included studies which were conducted in secondary prevention populations (populations with participants already diagnosed with one of our outcomes of interest) and in risk factor populations, e.g. hypertension, smokers, and hypercholesterolaemia. Furthermore, the studies using adaptations of LS7, for example, not comprising all metrics, were included to examine the relationship between LS7 and one of our outcomes.

Every article was assessed independently by two authors (randomly distributed between S.F., F.t.H., K.W., M.S., Q.S., Z.W.) for eligibility. First, the title and abstract were screened for eligibility. If deemed appropriate for inclusion, the full text of the article was screened. Any conflicts were discussed and solved amongst the two screeners or during a group discussion with all screeners and, when appropriate, by an adjudicator (A.U., R.W.M.V.). Reasons for exclusion were recorded for the articles screened during full-text review. The study selection process is illustrated in a PRISMA flowchart (*Figure 1*).[6]

Data extraction

A data collection form was developed in Excel that contained the following variables: author, year of publication, study design, study location, study population, follow-up time, sample size, baseline characteristics of participants (*N*, mean/median age, age range, sex), exposure (description of LS7 groups and the description of each LS7 metric, LS7 score range, number of participants in each LS7 group), outcome (description of outcome, number of events, risk estimate, and CIs), which confounders the authors adjusted for, percentage of missing data, and whether subgroup analysis was performed. The data from all articles were extracted by two authors; one author first entered the data into the data collection form created in Excel, and the second author verified its accuracy. Conflicts were solved by discussion and, when appropriate, by an adjudicator.

Risk of bias assessment

To assess the risk of bias for each study, two reviewers graded the studies independently using the Newcastle-Ottawa Scale (NOS) for both cohort and cross-sectional studies.[7] Disagreements were resolved by third-party decision or through consensus discussion. The number of stars in the three domains (selection, comparability, and outcome) is summed to get a NOS score. Based on the Agency for Health Research and Quality (AHRQ) standards, the reviewers judged the quality of the study, which was either good, fair, or poor. Studies were assigned a poor quality when there were $\leq$1 stars in the selection or outcome domain or 0 stars in the comparability domain; a fair quality when they received 2 stars in the selection domain, $\leq$2 stars in the comparability domain, and $\leq$3 stars in the outcome domain; and a good quality when studies had $\geq$3 stars in selection domain, $\geq$1 stars in the comparability domain, and $\geq$2 stars in the outcome domain. The detailed scales can be found in Supplementary material online, *Tables S2 and S3*.

Definition of ideal, intermediate, and poor cardiovascular health

To assess the association between AHA's definition of ideal CVH and our outcomes of interest, studies that calculated ideal CVH scores using LS7 were included. Methodological heterogeneity with respect to LS7 was identified across studies. Studies differed in the number of metrics [body mass index (BMI), diet, smoking, physical activity, blood pressure, blood glucose, and blood lipids] they included and also in the way they investigated CVH. Studies could have investigated CVH in a categorized manner (e.g. ideal, intermediate, and poor CVH), in a continuous manner (point or ideal metric increase), or by looking at the number of metrics having an ideal level. In the present review, we followed the definitions used by the authors of the included papers for both describing the results and the meta-analysis. Studies were handled as follows: (i) studies grouping 0–2, 3–4, and 5–7 ideal metrics or grouping a LS7 score of 0–4, 5–9, and 10–14 were included into this review as poor, intermediate, and ideal respectively, (ii) when articles grouped 6–7 ideal metrics together and compared this to 0–2 or 0–1 ideal metrics, we used the risk estimate of 6–7 ideal metrics as ideal and did not include an intermediate risk estimate, and (iii) if both are not reported, RRs were calculated using information from the article by combining 0–2, 3–4, and 5–7 ideal metrics to indicate poor, intermediate, and ideal CVH, respectively. Supplementary material online, *Table S4* shows how each of the included studies categorized CVH and how we included the studies in our meta-analysis.

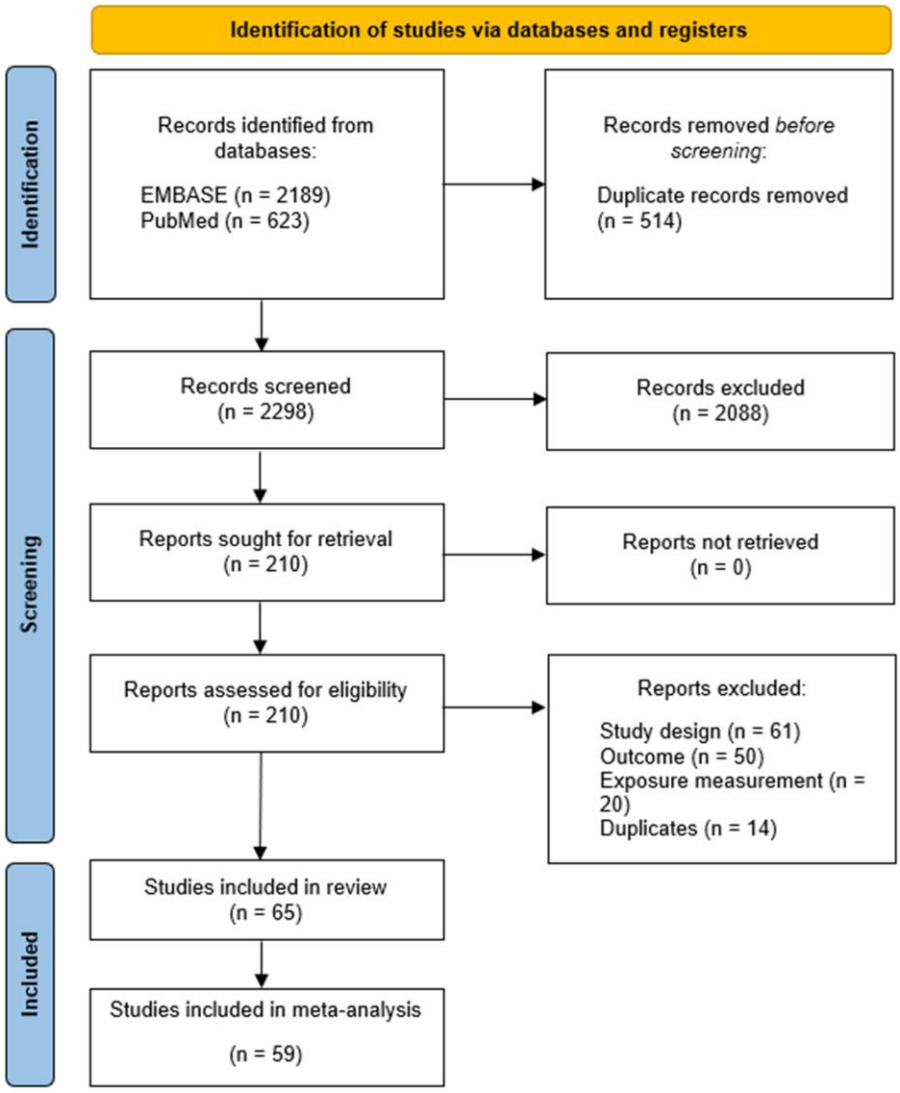

Figure 1 Flowchart of the identification of included studies in this review.

Statistical analysis

We pooled risk estimates of ideal vs. poor and intermediate vs. poor CVH for the different outcomes using random-effects models. Furthermore, risk estimates for one point increases in CVH or ideal metric increases in CVH were also pooled using random-effects models. We chose the random-effects model to meta-analyse our results because we expected the studies to differ in participant, exposure, and outcome-characteristics. The generic inverse variance approach has been used in the random-effects models to calculate pooled relative effects (DerSimonian–Laird). The between-study variance τ^2 and CI were estimated using restricted maximum likelihood estimator and Q-profile method, respectively.[8] For the sensitivity analysis, the leave-one-out method was used. Furthermore, we assessed the effect of combining HRs/ORs/RRs by doing the analysis separately for each effect estimate.[9] If there were more than 10 studies in one disease outcome, we drew a funnel plot and tested the asymmetry by using the 'Begg' method to check for publication bias.[10] We used the *meta* package in R statistical software (version 4.1.0) for the meta-analysis.

When possible, subgroup analyses were conducted for mean age (<55, 55–75, and >75 years old), proportion of women (<35%, between 35% and 65%, and >65%), geographical area (USA, Asia, Europe, and Australia), and follow-up time (<5, 5–15, >15 years). For all analyses except the subgroup analyses, a *P*-value smaller than 0.05 was considered statistically significant; for the subgroup analyses, the *P*-value threshold was 0.10.[11]

Results

Literature search

The electronic literature search retrieved 2812 articles. After title and abstract screening, 210 full-text articles were assessed for eligibility. During full-text screening, 145 articles were excluded. Reasons for exclusion based on the full-text screening were (i) study design (i.e. conference abstracts, reviews; 61 articles), (ii) outcome (i.e. outcomes not CVD or CMD; 50 articles), and (iii) exposure measurement (i.e. changes in CVH; 20 articles). In the end, 65 articles[12–76] met the inclusion criteria and were included in the review (*Figure 1*). Of these 65 articles, 6 were only described narratively due to a lack of (statistical) information on outcomes to calculate a pooled effect,[19,20,51,55,64,73] and 59 were in included the meta-analysis across the outcomes.

Table 1 Characteristics of the included studies

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Aboagye-Mensah *et al.* 2020[12]	USA	729	48.0*	0	AAMWW Study	Cross-sectional	Type 2 diabetes	Age and insurance status	General population	5
Ahmad *et al.* 2019[13]	USA	6766	59.1*	53.9	NHANES III Study	14**	Composite of CVD mortality	Age, sex, race, annual income levels, alcohol use, CRP, prior congestive heart failure, and stroke	General population	7
Ahmed *et al.* 2020[14]	UK	7274	50.0*	0	British Regional Heart Study	19.8**	Stroke	Age, social class, and alcohol intake	General population	7
Artero *et al.* 2012[15]	USA	11 993	46.0*	24.3	ACLS Study	11.6*	Composite of CVD mortality	Age, sex, examination year, alcohol intake, and parental history of CVD	General population	8
Bundy *et al.* 2020[16]	USA	30 447	55.0*	60.6		16.2*	Composite of CVD events	Stratified for age, sex, and race	General population	7
Cao *et al.* 2021[17]	UK	354 976	56.2*	54.7	UK Biobank	11**	Stroke	Age (timescale), sex, ethnicity, education attainment, employment status, Townsend deprivation index, consumption of alcohol intake, CRP, and family history of stroke	General population	9
Climie *et al.* 2019[18]	UK	6234	49.8*	30.3	Whitehall II Study	24.8**	Type 2 diabetes	Age (timescale), sex, ethnicity, education, occupation, marital status, alcohol, fasting glycaemia, and family history of diabetes at baseline	General population	7
Crisan *et al.* 2019[19]	USA	1513			NHANES III Study	14.2*	Composite of CVD events	Age, sex, and race/ethnicity	Risk factor population (COPD)	7
Díez-Espino *et al.* 2020[20]	Spain	7447	67.0*		PREDIMED	4.8**	Composite of CVD events	Age, sex, centre, and intervention group	Risk factor population (HTN, hypercholesterolaemia, overweight, smoking, and a family history of premature CVD)	7
Dong *et al.* 2012[21]	USA	2981	69.0*	63.7	NOMAS Study	11**	Composite of CVD events, CVD mortality, stroke, and MI	Age, sex, and race/ethnicity	General population	8

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Effoe *et al.* 2017[22]	USA	2668	54.7*	65.4	Jackson Heart Study	7.6**	Type 2 diabetes	Age, sex, education, and income, hs-CRP, and HOMA-IR	General population	8
Folsom *et al.* 2011[23]	USA	12 744	54*	56.1	ARIC Study	18.7**	Composite of CVD events	Age, sex, and race	General population	8
Folsom *et al.* 2015[24]	USA	13 462	54.1*	54.6	ARIC Study	22.5**	Heart failure	Age, sex, race, prevalent CHD, and competing risk of death	General population	8
Foraker *et al.* 2016[25]	USA	4140	54.5**	64.8	Jackson Heart Study	9	Stroke	No confounders	General population	6
Foraker *et al.* 2016[26]	USA	115 306		100	WHI Study	12.9**	Composite of CVD events	Age, enrolment observational study/clinical trial, race/ethnicity, marital status, and family history of CVD or cancer	General population	6
Fretts *et al.* 2014[27]	USA	1639	38*	63	SHF Study	5*	Type 2 diabetes	Age, sex, site, education, and family history of diabetes	General population	7
Gao *et al.* 2020[28]	China	45 657	49.2*	57.5		9.7*	Composite of CVD mortality	Age, sex, educational level, alcohol intake, health insurance, and urbanization	General population	8
Garg *et al.* 2018[29]	USA	13 182	54.0*	56	ARIC Study	25.1**	Atrial fibrillation	Age, sex, education, ARIC study site, alcohol consumption, and left ventricular hypertrophy	General population	8
Garg *et al.* 2018[30]	USA	9576	63*	57	REGARDS Study	9.4**	Atrial fibrillation	Age, gender, race, income, education, geographic region, left ventricular hypertrophy, alcohol use, CHD, and stroke	General population	7
Garg *et al.* 2018[31]	USA	12 865	54*	55	ARIC Study	24.4**	Peripheral arterial disease	Age, sex, race, education ARIC study site, alcohol consumption, aspirin use, and left ventricular hypertrophy	General population	8
Gaye *et al.* 2017[32]	France	7371	73.8*	63.3	Three-City Study	8.6**	Stroke and CHD	Age, education, sex, race, income, alcohol use, eGFR, urine ACR, and hs-CRP	General population	8
González *et al.* 2016[33]	USA	15 825		52.2	HSHS/SOL Study	Cross-sectional	Stroke and CHD	Age, sex, household income, health insurance, language, Hispanic/Latino heritage, marital status, and nativity/US residency	General population	5

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Greenlee *et al.* 2017[34]	USA	3491	72.0*	61.4	CHS Study	15**	Composite of CVD events and composite of CVD mortality	Age, self-rated health, race/ethnicity, income, education, sex, marital status, non-steroidal anti-inflammatory drug use, and limitations in instrumental activities of daily living	General population	8
Guo *et al.* 2016[35]	China	11 417	53.0*	53.8		Cross-sectional	Stroke	Age, marital status, education, family income, and drinking status	General population	8
Han *et al.* 2016[36]	China	91 443	51.5*	20.6	Kailuan Study		CKD	Age, sex, education level, income level, alcohol consumption, CRP blood concentration, and eGFR	General population	6
Isiozor *et al.* 2019[37]	Finland	2607	53.1*	0	KIHD Study	25.8**	Composite of CVD mortality	Age, alcohol consumption, socioeconomic status, HDL cholesterol, use of cholesterol-lowering medications, use of antihypertensive, history of CHD, and history of type II DM	General population	8
Isiozor *et al.* 2019[38]	Finland	2584	53.1*	0	KIHD Study	25.2**	MI	Age, alcohol consumption, socioeconomic status, history of CHD, and history of type 2 DM	General population	8
Isiozor *et al.* 2021[39]	Finland	2520	53.0*	0	KIHD Study	26.0**	Stroke	Age, alcohol consumption, socioeconomic status, use of antihypertensive and cholesterol-lowering medications, and history of type 2 diabetes	General population	8
Isiozor *et al.* 2021[40]	Finland	2577	53.1*	0	KIHD Study	25.8**	MI mortality	Age, alcohol consumption, socioeconomic status, history of CHD, and history of type 2 diabetes	General population	6
Joseph *et al.* 2016[41]	USA	5348	61.9*	53.5	MESA Study	11.1**	Type 2 diabetes	Age, education, sex, study site, race/ethnicity, occupational status, alcohol use, and eGFR	General population	9

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Joseph *et al.* 2019[42]	USA	7758	63*	56.5	REGARDS Study	9.5**	Type 2 diabetes	Age, education, sex, race, income, alcohol use, eGFR, urine ACR, and hs-CRP	General population	8
Kim *et al.* 2013[43]	South Korea	12 538	47.5*	0			Composite of CVD mortality	Age, educational attainment, alcohol consumption, and family history of CVD	General population	6
Kim *et al.* 2021[44]	South Korea	197 241	70*	68.4	Korea National Health Insurance Service-Senior cohort database	7.2**	MI mortality	Age, sex, economic status, CHD, HTN, DM, anaemia, and COPD	General population	8
Kulshreshtha *et al.* 2013[45]	USA	22 914	65.0*	58	REGARDS Study	4.9***	Stroke	Age, race, sex, income, alcohol use, education, and geographic region	General population	8
Lachman *et al.* 2016[46]	Europe	10 043	57.0*	55.9	EPIC-Norfolk Study	10*	Composite of CVD events, stroke, and CHD	Age and sex	General population	8
Lee *et al.* 2021[47]	South Korea	208 598	70**	56.4	Korea NHIS Study	7.2**	Atrial fibrillation	Age, sex, economic status, medical histories of hypertrophic cardiomyopathy, bleeding, hypothyroidism, hyperthyroidism, thromboembolism, coagulation, dysfunction, osteoporosis, CKD, COPD, and liver disease	General population	7
Liu *et al.* 2014[48]	China	95 429	51.5*	20.3	Kailuan Study	4.0**	Composite of CVD mortality	Age, sex, average income, education level, alcohol use, and history of MI, stroke, and cancer	General population	7
Miao *et al.* 2015[49]	China	91 598	51.6*	20.5	Kailuan Study	6.8*	Composite of CVD events, stroke, and MI	Age, gender, alcohol consumption, income, education, history of CVD, heart rate, uric acid, and high-sensitivity CRP	General population	8
Mok *et al.* 2018[50]	USA	13 079	54.5*	56	ARIC Study	24.2**	MI	Age at baseline, sex, and race	General population[a]	8
Muntner *et al.* 2013[51]	USA	3093	72.2*	54.9	REGARDS Study	4**	CKD	Age, sex, race, geographic region of residence, education, and history of stroke and CHD	Secondary prevention population (CKD)	7

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Nayor *et al.* 2015[52]	USA	3201	59*	53.2	Framingham Offspring Study	12.3*	Heart failure	Age, sex, LVM, interim MI, log(BNP), and UACR	General population	8
Ogunmoroti *et al.* 2017[53]	USA	6506	62*	53	MESA Study	12.2**	Heart failure	Age, sex, race/ethnicity, education, income, and health insurance	General population	9
Ogunmoroti *et al.* 2018[54]	USA	6506	62.0*	53	MESA Study	11.2**	Atrial fibrillation	Age, sex, race/ethnicity, education, income, and health insurance	General population	9
Olson *et al.* 2015[55]	USA	16 491	65.0*	55	REGARDS Study	4.7**	Venous thromboembolism	Age, sex, income, education, race, region, and race–region interaction	General population	7
Ommerborn *et al.* 2016[56]	USA	4702		65.9	Jackson Heart Study	8.3**	Composite of CVD events	Age, sex, income, and education	General population	8
Pase *et al.* 2016[57]	USA	2631	62*	55	Framingham Offspring Study	10***	Stroke	Sex and age	General population	9
Peng *et al.* 2017[58]	Australia	7002		50.7	2011–2012 Australian Health Survey	Cross-sectional	Composite of CVD events	Age, sex, educational attainment, income, and residence region	General population	9
Peng *et al.* 2017[59]	Australia	7002		55.6	2011–2012 Australian Health Survey	Cross-sectional	CHD	Age, sex, education attainment, income, and residence region	General population	9
Perak *et al.* 2020[60]	USA	4836	24.9*	54.8	CARDIA Study	31.9	Composite of CVD events, heart failure, stroke, MI, and composite of CVD mortality	Sex, age, race, and total education	General population	9
Polonsky *et al.* 2017[61]	USA	5961	62.8*	53.3	MESA Study	10.3*	Composite of CVD events, and CHD	Age, sex, race/ethnicity, and education	General population	8
Rebholz *et al.* 2016[62]	USA	14 832	54.0*	55	ARIC Study	22.0**	CKD	Age, sex, race, and baseline eGFR	General population	9
Spahillari *et al.* 2017[63]	USA	4195	54.4*	65	Jackson Heart Study	9.9**	Heart failure	Age, sex, incident MI, and fatal CHD	General population	8
Su *et al.* 2022[64]	Europe and South America	5483	66**	42	DIET-HD Study	3.8**	CVD mortality	Age, sex, secondary education, serum albumin, serum haemoglobin, serum calcium, serum phosphorus, history of CVD, HTN, diabetes, pulmonary disease, statins, dialysis vintage, vascular access type, Kt/V, energy intake, and body mass index	Secondary prevention population (CKD)	7

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Tsai *et al.* 2021[65]	China	6048	43**	50.2	TwSHHH Study	14.3**	Composite of CVD events	Sex, age, education, average month income, marital status, parental history of CVD, menopause status, oestrogen exposure, baseline HTN, baseline DM, history of hyperlipidaemia, SBP, DBP, triglyceride, non-HDL, fasting glucose, and HbA1c	General population	8
Uijl *et al.* 2019[66]	Netherlands	37 803	49.4*	74.7	EPIC-NL	15.2**	Heart failure	Age, sex, and educational level	General population	9
Unkart *et al.* 2019[67]	USA	5529	61.3*	53	MESA Study	9.2**	Peripheral arterial disease	Age, sex, and race/ethnicity	General population	9
Wang *et al.* 2019[68]	China	111 765	56.4*	66.1	China Cardiometabolic Disease and Cancer Cohort Study	3.8*	Composite of CVD events	Age, sex, education attainment, family history of diabetes, family history of CVD, and diabetes duration	General population[b]	8
Wang *et al.* 2020[69]	China	3916	53.7*	38.3	APAC Study	2	Peripheral arterial disease	Sex, age, education, average income op the family members, and family history of stroke	General population	8
Xanthakis *et al.* 2014[70]	USA	1826	58.3*	58.7	Framingham Offspring Study	16***	Composite of CVD events	Age, sex, PAI-1, GDF-15, BNP, and subclinical disease	General population	8
Yang *et al.* 2012[71]	USA	13 312	45.0*	51.8	NHANES III Study	14.5**	Composite of CVD mortality and CHD mortality	Age, sex, race/ethnicity, educational attainment, alcohol intake, family history of CVD, smoking status, physical activity, body mass index, health diet score, total cholesterol level, blood pressure, and glycated haemoglobin level	General population	7
Yang *et al.* 2017[72]	China	4477	53.0*	50.5		Cross-sectional	Atrial fibrillation	Age, sex, drinking, previous heart failure, stroke, and MI	General population	7

Continued

Table 1 *Continued*

Reference, year	Country	Sample size	Age (y)	Women (%)	Study name	Follow-up (y)	Outcome	Adjusted for	Study population	NOS score
Ying *et al.* 2020[73]	China	4662	41.3*	50.1		5.7*	Stroke	Age, sex, education, alcohol consumption, DM, depression, family history of stroke, years of HTN, antihypertensive medication, low-density lipoprotein, SBP, DBP, uric acid, triglyceride, total homocysteine, and creatinine	Risk factor population (HTN)	8
Zhang *et al.* 2013[74]	China	91 698	51.5*	21	Kailuan Study	4	Stroke	Age, sex, hospital, education, and income	General population	7
Zhou *et al.* 2018[75]	China	938	45.8*	50.4	PRC-USA Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology	20.3**	Composite of CVD events, stroke, CHD, and composite of CVD mortality	Age, sex, urban or rural, north or south, types of work, education, and drinking status at baseline	General population	8
Zhu *et al.* 2021[76]	China	**95 167**	51.5	79.8	Kailuan Study	10.3**	Heart failure	Age, sex, history of MI, history of atrial fibrillation, monthly income, alcohol consumption, educational level, and antihypertensive, hypoglycaemic, and lipid-lowering drug use	General population	8

Italic studies were not included in the meta-analysis.
ACR, albumin-to-creatinine ratio; BNP, B-type natriuretic peptide; CHD, coronary heart disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVD, cardiovascular disease; DM, diabetes mellitus; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GDF-15, growth differentiation factor-15; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; HTN, hypertension; LVM, left ventricular mass; MI, myocardial infarction; PAI-1, plasminogen activator inhibitor-1; SBP, systolic blood pressure; UACR, urine albumin-to-creatinine ratio; NOS, Newcastle-Ottowa Scale.
[a]This article also investigates the association between CVH and heart failure, stroke, MI, and CVD mortality in MI patients. That sample had a smaller sample size, higher mean age, lower percentage of women, and a shorter follow-up period.
[b]This article investigates the association between CVH and composite of CVD events in patients with normal glucose regulation, prediabetes, and diabetes. In the analysis, we combined all three to resemble the general population.
*, mean; **, median; ***, maximum.

Study characteristics

Table 1 summarizes the characteristics of the studies included. Sample sizes ranged from 729[12] to 354 976 participants.[17] In total, the studies in this review included 1 936 562 participants, of which 1 881 382 participants were included in the meta-analysis. The mean/median age varied between 24.9 and 73.8 years old. The average proportion of women in all studies combined was 47%. Most studies ($n = 35$) were performed in the USA.[12,13,15,16,19,21–27,29–31,33,34,41,42,45,50–57,60–63,67,70,71] Thirteen studies were conducted in China, four in Finland, three in the UK and South Korea, two in Australia, and one in Spain, France, and the Netherlands. One study was conducted in multiple countries in Europe and one in multiple countries in Europa and South America. Six studies were cross-sectional studies,[12,33,35,58,59,72] and the remainder were cohort studies. All but one[26] of the included studies adjusted for multiple a set of confounders. All—except the study previously mentioned—adjusted for age, and the majority of the studies, including both men and women, furthermore adjusted for sex. The study by Guo *et al.*[35] did not adjust for sex but did include both men and women. The majority of the included studies ($n = 60$) was conducted in the general population. Three of the included studies were done in a risk factor population (chronic obstructive pulmonary disease,[19] multiple risk factors,[20] and hypertensive individuals[73]) and two in a secondary prevention population (both in individuals with CKD[51,64]). The studies included in our review cover a broad range of outcomes which were diagnosed differently across studies. Supplementary material online, *Table S5* shows how events were diagnosed across the included studies.

Exposure measurements

Most of the studies ($n = 56$) included all seven metrics in their analysis. Six studies[14,18,22,44,47,73] included only six, two studies[12,28] included only five, and one study[64] included only four metrics in their analysis. Diet was not included as a component in five studies.[12,14,28,44,47] Also, glucose was missing in five studies; four of these studies[12,18,22,42] had T2D as an outcome and therefore did not include glucose as a component. The other study[64] investigated the relationship between LS7 and CVD mortality in patients with CKD. Next to missing the component glucose, this study also did not have information on the metrics BMI and cholesterol. Blood pressure was missing in the study by Ying *et al.*,[73] which included hypertensive patients, and physical activity was missing in the study by Gao *et al.*.[28] Smoking was included as a component in all the studies.

The number of food groups incorporated into the diet component differed amongst studies. Six studies only incorporated salt intake as a food group in their diet score.[35,36,48,49,74,76] Although sleep is not part of LS7, two studies did incorporate sleep in their physical activity score.[52,74]

Across 64 articles, the average proportion of participants with an ideal, intermediate, and poor CVH was 18.8%, 52.1%, and 29.1%, respectively. Only the study by Nayor *et al.*[52] was not included in this calculation because they did not share how many participants had ideal, intermediate, or poor CVH. After pooling the studies, ideal levels of the individual metrics of LS7 were achieved in 10% for diet, 28.2% for blood pressure, 36.4% for BMI, 42.3% for physical activity, 44% for cholesterol, 63.6% for smoking, and 68.3% for glucose.

Risk of bias assessment

For all 59 cohort studies, the total NOS score ranged from 6 to 9 with an average score of 7.7 (see Supplementary material online, *Table S2*), 51 studies (86.4%) had a good quality, and 8 studies (13.6%) had a poor quality and were therefore assessed to have high risk of bias. The reason for downgrading was the outcome domain for the majority of the studies (seven out of the eight studies).[27,30,36,48,51,55,74] All seven articles did not provide any information on the participants lost to follow-up. Besides this, in six of the seven articles, the follow-up period was considered inadequate because it was shorter than the predefined period of 5 years, and in one article, the outcome assessment was done using self-reported data.[30] One of the cohort studies was downgraded due to the comparability domain, because it did not adjust for any confounders.[25]

For all six cross-sectional studies, the total NOS score ranged from 5 to 9 with an average score of 7.2 (see Supplementary material online, *Table S3*). Three studies (50%) had a good quality according to the AHRQ standard, one study (16.7%) was assessed as having fair quality, and two studies (33.3%) were judged to be of poor quality. Downgrading of the studies by Aboagye-Mensah *et al.*[12] and González *et al.*,[33] who were judged to have poor quality, was due to the selection and outcome domain, given that the sample size was not justified due to a lack of power calculation, and no description of the non-respondents was provided. Furthermore, the outcome assessment was not described or done using a non-standard method. The article by Yang *et al.*[72] was judged to have fair quality due to downgrading of the selection domain; sample size was not justified, and there was an unsatisfactory recruitment rate for the non-respondents.

Association between ideal cardiovascular health metrics and cardiovascular and cardiometabolic events

There was an inverse-graded relationship between the degree of CVH and the incidence or mortality of CVDs and CMDs (*Figures 2* and *3*). Participants with ideal or intermediate CVH profiles, compared with poor CVH, had a lower risk of developing AF [ideal HR = 0.60 (95% CI 0.44–0.83), $I^2 = 93\%$; intermediate HR = 0.73 (95% CI 0.59–0.91), $I^2 = 90\%$]. The pooled HR for CKD was the second highest [ideal HR = 0.42 (95% CI 0.36–0.48), $I^2 = 0\%$], followed by the HR for stroke [ideal HR = 0.37 (95% CI 0.30–0.45), $I^2 = 69\%$; intermediate HR = 0.65 (95% CI 0.61–0.70), $I^2 = 30\%$]. Moreover, the pooled results are approximately equal for CVD mortality [ideal HR = 0.35 (95% CI 0.25–0.48), $I^2 = 72\%$; intermediate HR = 0.51 (95% CI 0.48–0.54), $I^2 = 0\%$] and HF [ideal HR = 0.33 (95% CI 0.25–0.45), $I^2 = 93\%$; intermediate HR = 0.56 (95% CI 0.49–0.63), $I^2 = 79\%$]. In addition, for MI [ideal HR = 0.18 (95% CI 0.12–0.28), $I^2 = 64\%$; intermediate HR = 0.45 (95% CI 0.34–0.61), $I^2 = 50\%$] and PAD [ideal HR = 0.20 (95% CI 0.08–0.54), $I^2 = 84\%$; intermediate HR = 0.43 (95% CI 0.30–0.60), $I^2 = 70\%$], we observed the strongest associations, stronger than for T2D [ideal HR = 0.27 (95% CI 0.17–0.43), $I^2 = 82\%$; intermediate HR = 0.61 (95% CI 0.51–0.74), $I^2 = 77\%$], CHD [ideal HR = 0.28 (95% CI 0.18–0.43), $I^2 = 29\%$; intermediate HR = 0.58 (95% CI 0.51–0.66), $I^2 = 0\%$], and composite of CVD events [ideal HR = 0.26 (95% CI 0.20–0.34), $I^2 = 92\%$; intermediate HR = 0.57 (95% CI 0.50–0.64), $I^2 = 92\%$].

An ideal metric increase in CVH score was associated with a lower risk for AF [HR = 0.89 (95% CI 0.82–0.96), $I^2 = 94\%$], the composite of CVD events [HR = 0.80 (95% CI 0.76–0.84), $I^2 = 29\%$], and T2D [HR = 0.75 (95% CI 0.67–0.84), $I^2 = 74\%$; *Figure 4*].

Similar to an ideal metric increase in CVH score, a one point increase in CVH score was associated with an 8% lower risk of AF [HR = 0.92 (95% CI 0.88–0.97), $I^2 = 95\%$; *Figure 5*]. The pooled HR of stroke [HR = 0.85 (95% CI 0.82–0.88), $I^2 = 90\%$] and the composite of CVD [HR = 0.82 (95% CI 0.72–0.93), $I^2 = 92\%$] were approximately equal. Stronger observations were seen for PAD [HR = 0.79 (95% CI 0.71–0.87), $I^2 = 85\%$], HF [HR = 0.78 (95% CI 0.67–0.89), $I^2 = 65\%$], and MI [HR = 0.75 (95% CI 0.66–0.86), $I^2 = 87\%$].

For the outcome VTE, only one article was found during the literature search.[55] Both high and intermediate CVH showed a significantly lower risk for incident VTE when compared with low CVH [ideal

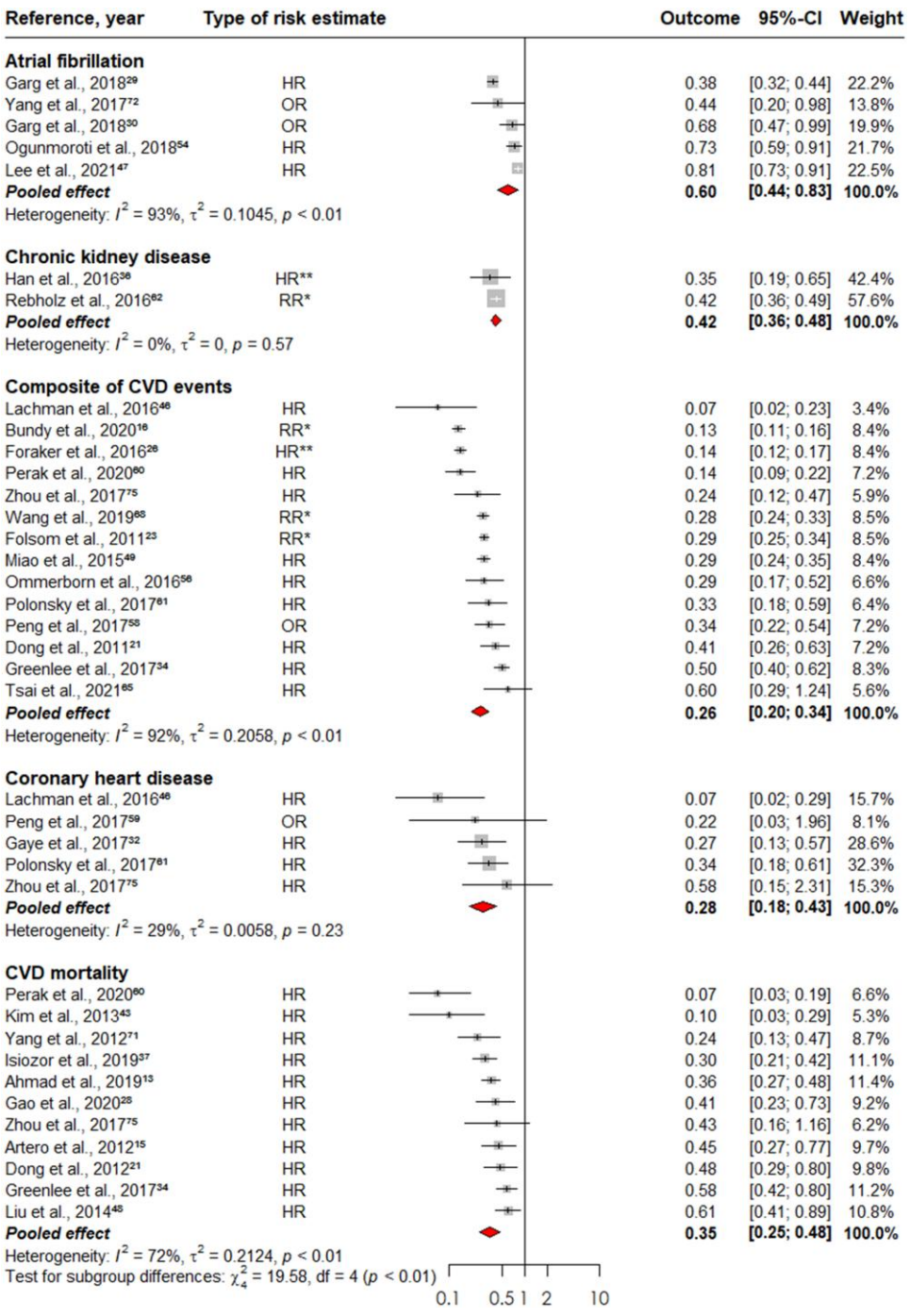

Figure 2 Hazard ratio [95% confidence intervals (CIs)] for cardiovascular and cardiometabolic events for ideal vs. poor cardiovascular health (CVH) profile. Weights are from random-effects analysis. Poor CVH is used as the reference category. CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MI, myocardial infarction; OR, odds ratio; RR, risk ratio. *RR is calculated using data from article; therefore unadjusted. **HR is the inverse of the HR reported in the article.

HR = 0.56 (95% CI 0.38–0.82); intermediate HR = 0.62 (95% CI 0.43–0.89)].

In patients with COPD[19] and patients with multiple risk factors like hypertension, smoking, and overweight,[20] the association between LS7 and the composite of CVD events was similar as for the general population [5–7 ideal metrics compared with 0–1 ideal metrics HR = 0.53 (95% CI 0.21–1.36) and HR = 0.34 (95% CI 0.21–0.53), respectively]. In patients with hypertension, 5–6 ideal metrics compared with 0 ideal metrics was associated with a 0.28 times lower hazard (95% CI 0.12–0.63) for incident stroke.[73] Patients with CKD showed a reduced risk for CVD mortality when having a high CVH compared with a low CVH [HR = 0.65 (95% CI 0.49–0.85)].[64] The hazard for progression

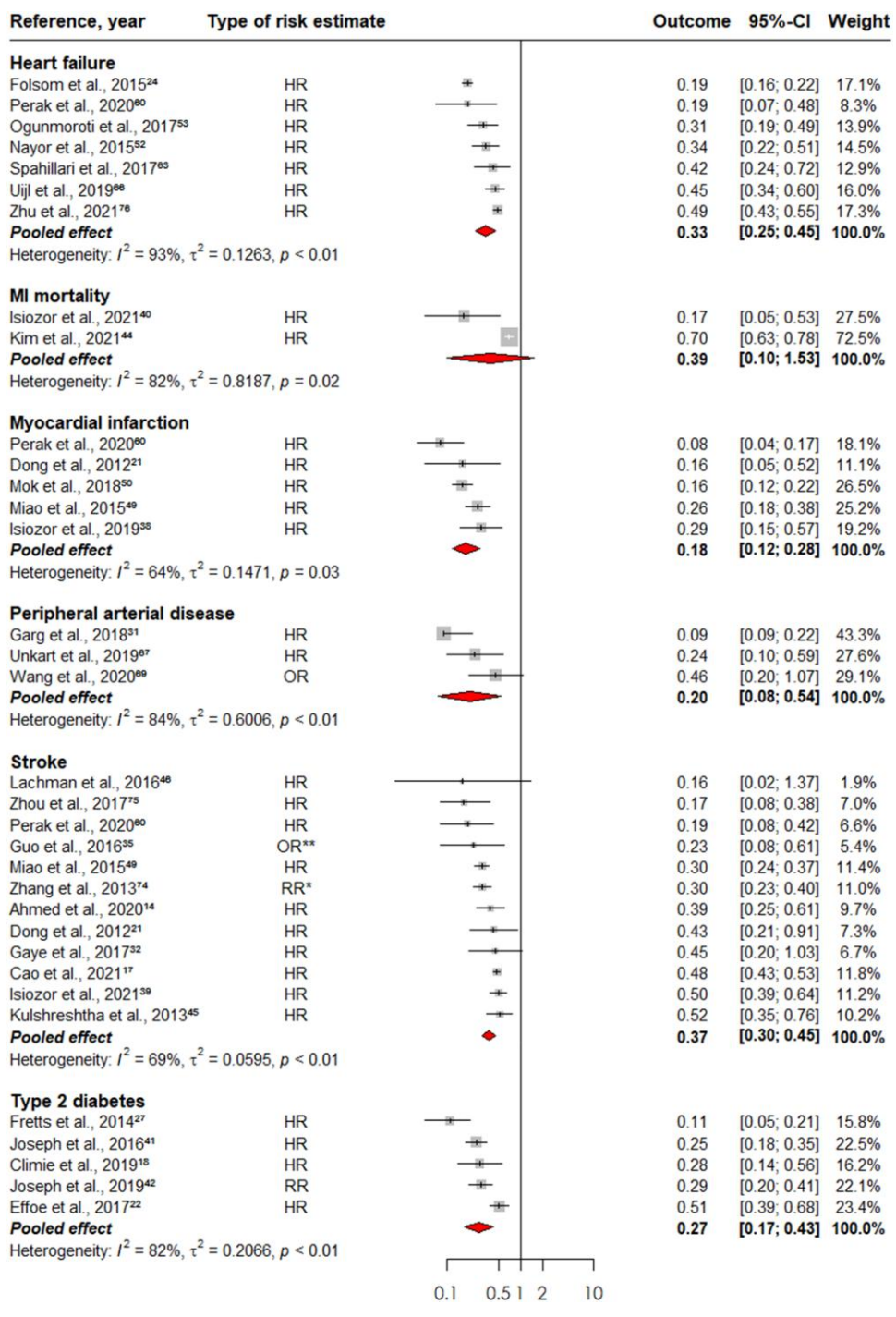

Figure 2 Continued

to end-stage renal disease in CKD patients was 0.52 (95% CI 0.27–0.98) for 4 compared with 0–1 ideal metrics.[51] No events occurred in the highest group of ideal metrics (5–7).

Subgroup analysis

All significant subgroup analyses are shown in Supplementary material online, *Figures S1–S4*. Younger participants (<55 years) had a lower risk for incident CVDs and CMDs compared with older participants for the outcomes AF, composite of CVD events, CVD mortality, HF, MI, MI mortality, PAD, stroke, and T2D. There is a statistically significant quantitative subgroup effect for region for stroke comparing ideal ($P < 0.01$) and intermediate ($P < 0.01$) CVH with poor CVH. Heterogeneity was decreased (ideal: studies in USA $I^2 = 57\%$, studies in Europe $I^2 = 0\%$, and studies in Asia $I^2 = 0\%$; intermediate: studies in USA $I^2 = 27\%$, studies in Europe $I^2 = 22\%$, and studies in Asia $I^2 = 0\%$). In Asian studies, ideal and intermediate CVH compared with poor CVH showed the greatest risk reduction for incident stroke [ideal HR = 0.29 (95% CI

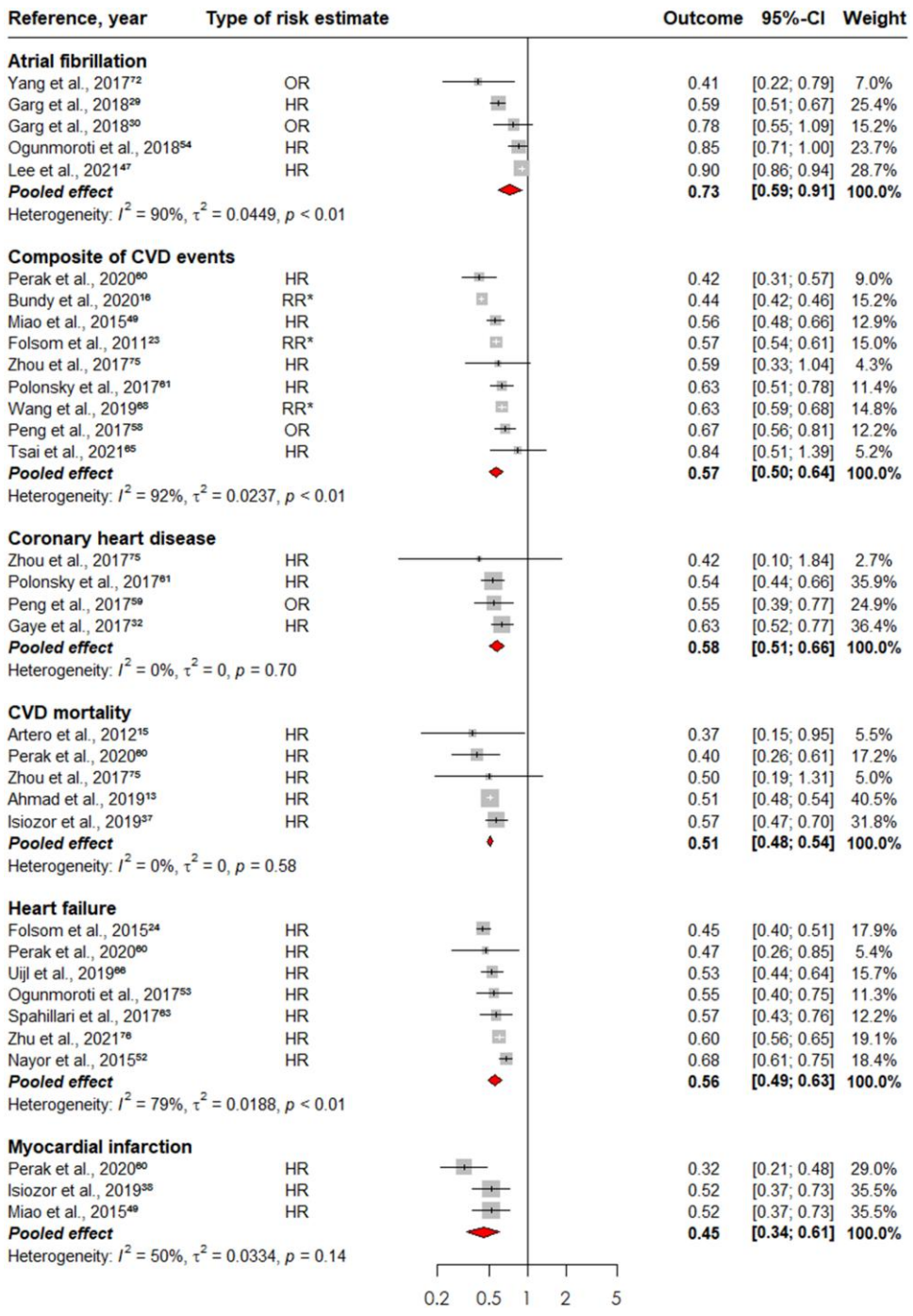

Figure 3 Hazard ratio [95% confidence intervals (CIs)] for cardiovascular and cardiometabolic events for intermediate vs. poor cardiovascular health (CVH) profile. Weights are from random-effects analysis. Poor CVH is used as the reference category. CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; MI, myocardial infarction; OR, odds ratio; RR, risk ratio. *RR is calculated using data from article; therefore unadjusted. **OR is the inverse of the OR reported in the article.

0.25–0.34); intermediate HR = 0.61 (95% CI 0.55–0.66)]. For the outcome composite of CVD events, there was a significant subgroup effect of geographical region for ideal compared with poor CVH only (P = 0.10). However, the HRs among the different regions were similar, and heterogeneity only decreased among Asian studies (I^2 = 31%).

Sensitivity analyses

Only combining studies that report the same effect estimate (HR/OR/RR) did not alter our results (see Supplementary material online, *Figures S5–S8*). Furthermore, no apparent changes in the pooled HR were observed when individual studies were left out in the leave-one-out

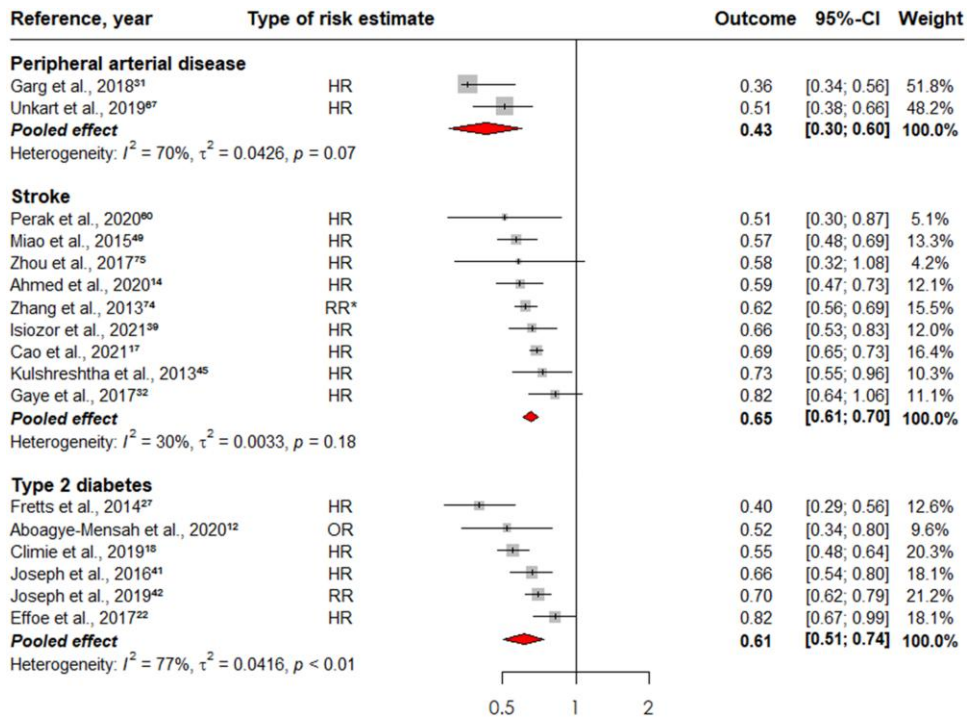

Figure 3 Continued

analysis, indicating that none of the included studies had a large influential effect on the pooled effect estimate (see Supplementary material online, *Figures S9–S12*). The Begg tests for the association between ideal (compared with poor) CVH and composite of CVD events, CVD mortality, and stroke were all non-significant ($P = 0.55$, $P = 0.07$, and $P = 0.49$), but the funnel plots showed some asymmetry (see Supplementary material online, *Figure 13*), indicating a possibility of publication bias.

Discussion

The findings of this review and meta-analysis, including 1 881 382 participants, suggest that LS7 has a graded relationship with CVD and CMD risk. Participants with ideal CVH have a considerably lower risk of a variety of CV and CM events as compared with those with poor CVH, varying from 40% lower risk for AF to 82% lower risk for MI. Having an intermediate CVH profile led to 27–57% lower risk of CVDs and CMDs compared with a poor CVH profile, with the lowest risk reduction for AF and the highest risk reduction for PAD. Furthermore, the one point and one ideal metric increase also led to 11–25% and 8–25% lower risk of incident CV and CM events, respectively. Although results could not be pooled, similar trends were seen among risk factor and secondary prevention populations.

Expanding and confirming results of existing studies

This systematic review expands the current evidence towards the importance of promoting ideal CVH to prevent CVDs and CMDs. To our knowledge, this is the most comprehensive meta-analysis with the largest sample size, including various CVDs and CMDs, with a rigorous systematic review methodology.

In the previous systematic review and the meta-analysis published in 2018, Ramírez-Vélez *et al.*[4] found that achieving a greater number of ideal or intermediate CVH metrics was associated with a 31–77% lower incidence of different CVDs (stroke, MI, incident HF, VTE, CHD, and a composite variable of CVD events) in 210 443 participants. In the present study, these positive findings have been confirmed and expanded by including more studies and additional outcomes to provide an overview of the available evidence regarding the association between ideal CVD and CVDs and CMDs. This review, including 59 studies and combined 1 881 382 participants, expanded the CVD and CMD outcomes to include AF, T2D, CVD mortality, CKD, and PAD and described the association between these and ideal CVH. Furthermore, we also grouped studies reporting an ideal metric or point increase in CVH score to identify the dose-dependent association shown in many previous studies and found a graded association between the ideal metric increase and point increase in CVH score and lower incidence of CVDs and CMDs.

In another systematic review, published in 2023, Radovanovic *et al.*[5] included 22 studies and found that higher adherence to ideal CVH was associated with a 62–82% lower incidence of different CVDs (composite CVD, CHD, MI, and stroke). Both systematic reviews highlighted that promoting intermediate CVH as a short-term goal may be beneficial in the primary prevention of CVD. Ramírez-Vélez *et al.*[4] reported that achieving intermediate CVH was associated with a 55%, 46%, 42%, 51%, 31%, and 44% lower incidence of composite CVD, MI, stroke, HF, VTE, and CHD, respectively. Likewise, Radovanovic *et al.*[5] reported that achieving intermediate CVH was associated with a 39%, 37%, 30%, and 49% lower incidence of composite CVD, MI, stroke, and CHD, respectively. In our study, we similarly found that achieving intermediate CVH was associated with a 43%, 55%, 35%, 44%, and 42% lower incidence of composite CVD, MI, stroke, HF, and CHD, respectively. In addition, we also showed that the one point increase in LS7 score also led to 18%, 25%, 15%, and 22% lower risk of

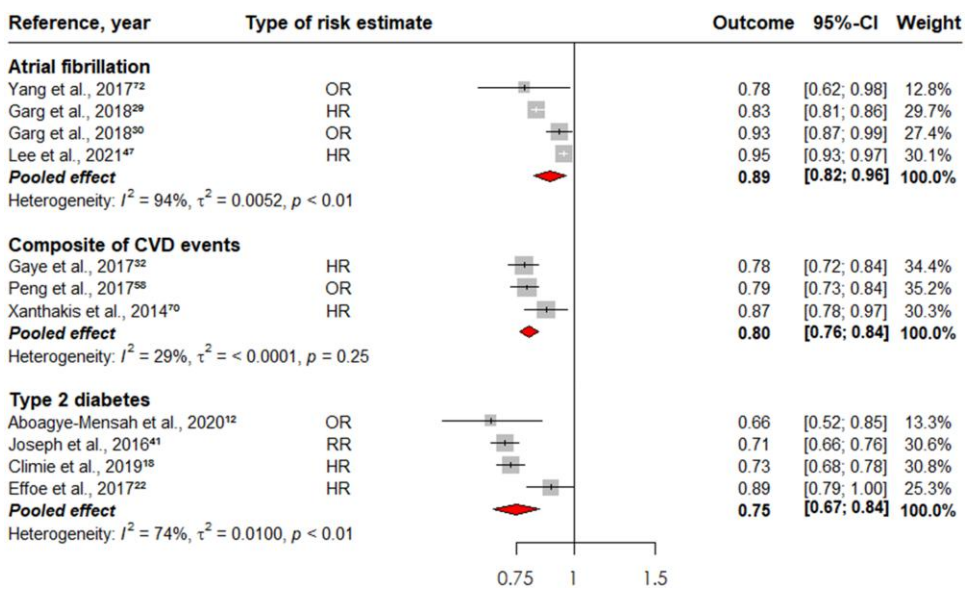

Figure 4 Hazard ratio [95% confidence intervals (CIs)] for cardiovascular and cardiometabolic events per ideal metric increase in cardiovascular health (CVH) score. Weights are from random-effects analysis. CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; OR, odds ratio.

incident composite CVD, MI, stroke, and HF events, respectively. Moreover, an ideal metric increase also led to 20% lower risk of incident composite CVD events. This inverse association between a one point or one ideal metric increase and CVD incidence for various outcomes supports the hypothesis that even minor adjustments to the ideal CVH can enhance the primary prevention of CVDs.

In contrast to previous reviews, we did not pool the effect estimates for different CVD and CMD outcomes, as the high heterogeneity between different outcomes could hamper drawing conclusions.[77] We conducted subgroup analyses to explore sources of heterogeneity, although not all heterogeneity could be explained by our subgroups. There may be several reasons for this. Almost all included studies adjusted for age and sex, and many of these studies adjusted for additional potential confounders such as education, socioeconomic status, and alcohol consumption. Nevertheless, the possibility of some unmeasured or residual confounding cannot be ruled out.[9] To preserve the causal design of the study, we included the result of the final model adjusted for all available confounders, as, a consequence, it was not possible to run subgroup analyses for all available confounders. Furthermore, the different definitions of LS7 used across the included studies and differences in the way outcomes were diagnosed could also be sources of heterogeneity. To decrease the source of heterogeneity, individual patient data meta-analysis can be performed in the future to further elaborate on the influence of patient characteristics on the CVD and CMD outcomes.

Implication of cardiovascular health status

Our systematic review and meta-analysis included studies from various diverse populations and showed that the concept of ideal, intermediate, and poor CVH assessed by the combination of health behaviours (diet quality, physical activity, weight, and current smoking) and health factors (total cholesterol, blood pressure, and fasting plasma glucose) is a powerful and feasible way to identify individuals at various low, intermediate, and high risk of a broad variety of CV conditions. Since we have shown that LS7 relates to a variety of CV outcomes, this suggests that assessment of CVH may help to achieve the AHA's new mission and 2030 Impact Goal on healthy life expectancy regardless of race and ethnicity, economic status, or other demographic or geographic characteristics.[78]

Beyond Life's Simple 7: Life's Essential 8

During the conduct of this systematic review, a publication of the AHA became available introducing Life's Essential 8 (LE8) as an updated LS7 version, which modified the quantifications of the measurements in each original LS7 metric and added sleep as the eighth component to the final score.[79] The variability in the measurement of the dietary component across the studies included in our systematic review supports that the LS7 dietary component is difficult to apply in research settings and that the new dietary assessment in LE8 scoring may be more appropriate, as it allows for the population-level assessment using the Dietary Approaches to Stop Hypertension (DASH) diet score.[79] The use of quantiles can make it possible to assess the overall diet score, even if some measurements are incomplete or measured differently than the original definition. Moreover, many of the studies in our systematic review used different definitions to calculate ideal CVH, such as ideal point increase and ideal metric increase; therefore ,it is conceivable that the novel quantitative assessment of LE8 scoring can be more universally applied and will be more useful for comparing studies.

To date, six articles reported the relationship between LE8 and the incidence or mortality of CV-related events.[80–84] These results demonstrated a significantly inverse relationship between LE8 scores and incidence or mortality of CV and CM events. In the future, it would be of interest to conduct a meta-analysis of the association between LE8 and CVDs and CMDs to deepen our understanding on how the updated LE8 concept could improve CVD and CMD prevention.

Strengths and limitations

Our systematic review has important strengths. First, we implemented a comprehensive search in the two largest search engines for nine different outcomes to enlighten the relationship between LS7 and many different CVDs and CMDs. We also included studies in the risk and secondary prevention populations.

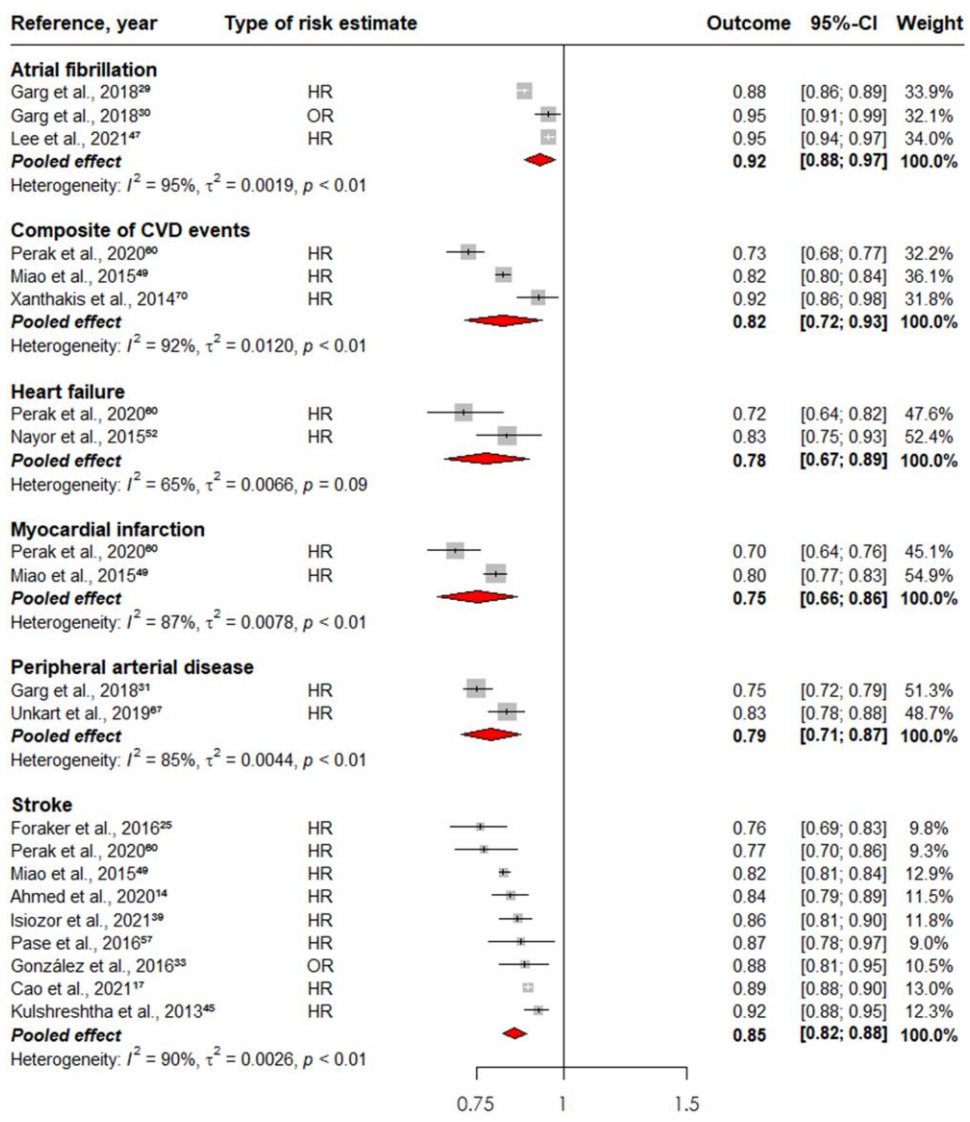

Figure 5 Hazard ratio [95% confidence intervals (CIs)] for cardiovascular and cardiometabolic events per point increase in cardiovascular health (CVH) score. Weights are from random-effects analysis. CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; OR, odds ratio.

Nonetheless, the results presented in this review must be interpreted with caution, and a number of limitations should be borne in mind. Although all of the following limitations may affect the results of this review, they are not strictly methodological limitations, but limitations on the comparability of the papers we have included. First, there were not enough studies in the risk and secondary prevention group to conduct meta-analyses. However, the dose-dependent relationship between ideal CVH and reduced number of events was observed in all studies.[19,20,50,51,64,73] Second, not all studies used the same definition or measurement of the LS7 metrics. Nevertheless, the majority of the studies used a similar approach (i.e. based on the number of ideal CVH metrics, participants were categorized into three groups: poor CVH group (participants with 0–2 ideal CVH metrics, used as the reference group), intermediate CVH group (participants with 3 and 4 ideal CVH metrics), and ideal CVH group (participants with 5–7 ideal CVH metrics). Third, although most of the studies reported HRs as effect estimates, some studies reported different effect estimates such as ORs and RRs.[12,16,23,29,33,35,41,42,58,62,68,69,72,74] Therefore, we pooled different effect measures such as HRs, RRs, and ORs together and used a random-effects model assuming underlying variation of true effect between studies.[85] Besides that, due to the very low number of cross-sectional studies, we analysed them together with cohort studies. Fourth, many of the included studies had different diagnostic criteria and different outcome definitions or diagnostic pathways for these outcomes. This may have contributed to the high rates of heterogeneity in the meta-analyses; however, the effect estimates of most studies show similar results (i.e. higher CV risk for lower CVH). Fifth, for many outcomes, the studies were not evenly distributed between the subgroups and there were less than ten studies; therefore, our subgroup effects may be biased.[11,86] For example, there were not enough studies to draw robust conclusions across geographical regions. However, we did find that the association between ideal and intermediate CVH and risk of stroke was stronger in studies from Asia.

Conclusions

This review shows compelling evidence of the association between LS7 across the spectrum of CVDs and CMDs. Individuals with ideal CVH had a substantial reduction in the risk of CVDs and CMDs, ranging from a 40% lower risk for AF to 82% lower risk for MI. Some of the outcomes had high levels of heterogeneity; this could be due to differences in how the concept LS7 was scored or how the outcome was diagnosed. Nonetheless, these findings underscore the potential of LS7 as a tool to enhance overall CVH and the prevention of CVDs and CMDs.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology*.

Author contribution

S.F., F.t.H., K.W., M.S., Q.S., and Z.W. drafted the work and undertaken the statistical analyses. F.t.H., M.S., and Q.S. were involved in writing the manuscript. M.L.B., Y.T.V.d.S., A.U., and R.W.M.V. were involved in the revision of the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Conflict of interest: none declared.

Data availability

All data are extracted from published original articles and in some cases through correspondence with the authors. Our data set is available upon request.

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