Preventive Medicine Reports 46 (2024) 102853

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: www.elsevier.com/locate/pmedr

# Improving life's essential 8 mitigates myocardial infarction risk attributed to abnormal birth weight in later life

Da Luo [a,b,c], Xiaoying Wang [d], Si Li [e], Yunlong Guan [e], Changwu Xu [a,b,c], Bofang Zhang [a,b,c], Shuo Yang [a,b,c], Xingjie Hao [e,*], Jing Chen [a,b,c,*]

[a] Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China
[b] Cardiovascular Research Institute of Wuhan University, Wuhan, China
[c] Hubei Key Laboratory of Cardiology, Wuhan, China
[d] Department of Cardiology, The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China
[e] Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

ARTICLE INFO

*Keywords:*
Life's essential 8
Myocardial infarction
Birth weight
Additive interaction
Cardiovascular health

ABSTRACT

*Background:* To prospectively assess the individual and joint effects of birth weight and the life's essential 8 (LE8)-defined cardiovascular health (CVH) on myocardial infarction (MI) risk in later life.
*Methods:* In 144,803 baseline MI-free participants who were recruited in the UK Biobank cohort between 2006 and 2010, Cox proportional hazard models were used to estimate the associations of birth weight, LE8 score, and their interactions with incident MI. LE8 was defined on the basis of diet, physical activity, nicotine exposure, sleep health, body mass index, blood pressure, blood glucose, and blood lipids.
*Results:* Low birth weight was associated with higher risk of MI [hazard ratio (HR) 1.17, 95% confidence interval 1.02–1.35, $P = 0.025$], while no significant correlation between high birth weight and MI was observed after adjustment. Low CVH was associated with higher MI risk [HR 6.43 (3.71–11.15), $P < 0.001$). Participants with low birth weight and low CVH (vs. participants with normal birth weight and high CVH) had HR of 5.97 (2.94–12.14) for MI incidence. The relative excess risk due to interaction of low birth weight and low CVH on MI was −4.11 (−8.12, −0.11), indicating a negative interaction on an additive scale. A consistent decreasing trend of MI risk along with increased LE8 score was observed across all three birth weight groups.
*Conclusion:* Low birth weight was associated with increased MI risk, emphasizing the importance of the prenatal factor in risk prediction and prevention of MI. Improving LE8 can mitigate MI risk attributed to low birth weight.

## 1. Introduction

In the past three decades, there has been remarkable progress in improving clinical outcomes for acute myocardial infarction (MI) due to prompt myocardial reperfusion and the advancement of post-MI heart failure therapies (Collet et al., 2021; Heidenreich et al., 2022; Lawton et al., 2022). However, the estimated overall MI prevalence is 3.2% in Americans ≥20 years of age in 2020 (Tsao et al., 2023). Similarly, in 57 European Society of Cardiology member countries, the median age-standardised incidence estimate of ischaemic heart disease was 293.3 per 100,000 people in 2019 (Byrne et al., 2023). China has also experienced an increasing trend in MI-related mortality from 2002 to 2018, reaching 78.5 per 100,000 people in 2018 (Writing Committee Of The Report On Cardiovascular Health And Diseases In China, 2022). These alarming statistics highlight the ongoing challenges in MI prevention and treatment.

Low birth weight, a surrogate indicator of poor fetal growth and development, was first identified by Dr. David Barker as an early life

*Abbreviations:* AF, attributable fraction; AHA, American Heart Association; AP, attributable proportion due to interaction; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; CVH, cardiovascular health; HR, hazard ratio; LE8, life's essential 8; MI, myocardial infarction; RCS, restricted cubic spline; RERI, relative excess risk due to interaction; S, synergy index.

* Corresponding authors at: Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, 13 Hangkong Road, 430030, Wuhan, Hubei, China (X. Hao). Department of Cardiology, Renmin Hospital of Wuhan University, 238 Jiefang Road, Wuchang, Wuhan 430060, Hubei, China (J. Chen).
*E-mail addresses:* xingjie@hust.edu.cn (X. Hao), chenjing1982@whu.edu.cn (J. Chen).

https://doi.org/10.1016/j.pmedr.2024.102853
Received 29 January 2024; Received in revised form 3 August 2024; Accepted 5 August 2024
Available online 10 August 2024

exposure associated with adult ischaemic heart disease (Barker et al., 1989). The Barker hypothesis proposed that fetal environment and intrauterine growth retardation permanently programme the body's metabolism, leading to long-lasting alterations in cardiovascular structure and function, and thus predispose individuals to future adult disease (Barker et al., 1989; Barker, 1995). It shifts the primary prevention of adult disease to early life. Several studies have confirmed association between low birth weight and risk of cardiovascular disease (CVD) and diabetes (Mr et al., 2018; Raisi-Estabragh et al., 2023; Tian et al., 2019). However, limited studies have specifically analysed the association between birth weight and subsequent MI incidence in an exposure–response manner.

Lifestyle factors in later life have been well-established as determinants of cardiovascular health (CVH) (Biddinger et al., 2022; Dempsey et al., 2022; Larsson et al., 2020; Srour et al., 2019). In 2022, the American Heart Association (AHA) released an enhanced approach to define and quantify CVH: Life's Essential 8 (LE8) (Lloyd-Jones et al., 2022a). Although several previous studies have explored the association between LE8 and the morbidity and mortality of CVD, it remains unclear whether the later life risk of MI attributed to birth weight could be modified by adherence to high CVH in adulthood (Isiozor et al., 2023; Sun et al., 2023; Zhang et al., 2023).

To bridge the above gaps in knowledge, this study aims to elucidate the association of birth weight and LE8 with the risk of MI later in life. We also investigated the interactions and joint effects of birth weight and CVH defined by LE8 on the incidence of MI.

## 2. Methods

### 2.1. Study population

The UK Biobank is a large prospective cohort study involving over 500,000 participants aged 40–69 years recruited between 2006 and 2010 across the United Kingdom, with details previously described (Sudlow et al., 2015). This work was covered by the ethical approval for UK Biobank studies from the UK National Health Service National Research Ethics Service (Ref 11/NW/0382). We excluded the participants with an MI history at baseline and those with missing or invalid records on birth weight and eight metrics of CVH in the current study, leaving a total of 144,803 participants for further analyses (Fig. 1). The data regarding this project were from Application No. 88159 of the UK Biobank resource.

### 2.2. Assessment of birth weight and life's essential 8

The birth weight information was self-reported by participants and recorded either in kilograms (kg) or in ounces and pounds, and subsequently converted to kg for consistency. Birth weight was then categorized into a three-level variable according to prior literature: low birth weight, <2.5 kg; normal birth weight, 2.5–4.0 kg; high birth weight, >4.0 kg (Blencowe et al., 2019). The LE8 score consists of eight component metrics: diet, physical activity, nicotine exposure, sleep health, body mass index (BMI), blood pressure, blood glucose, and blood lipids. The total LE8 score (0 to 100 points) is calculated by summing the scores of each metric and dividing by eight, according to the AHA algorithm (Lloyd-Jones et al., 2022a). In this study, LE8 score of 80 to 100 is considered high CVH, 50 to 79 is moderate CVH, and 0 to 49 is low CVH. The healthy diet was evaluated based on the Dietary Approaches to Stop Hypertension (Supplemental Table 1). Physical activity is quantified by calculating the minutes per week spent on moderate and vigorous activity. Smoking status is categorized as never, former, or current smoker at the time of in-person baseline interview at the UK Biobank Assessment Centre. Sleep duration is self-reported in hours. BMI was calculated by dividing the weight by squared height in meters (kg/$m^2$). Blood lipids level was calculated as total cholesterol minus high-density lipoprotein cholesterol. Blood glucose is measured using

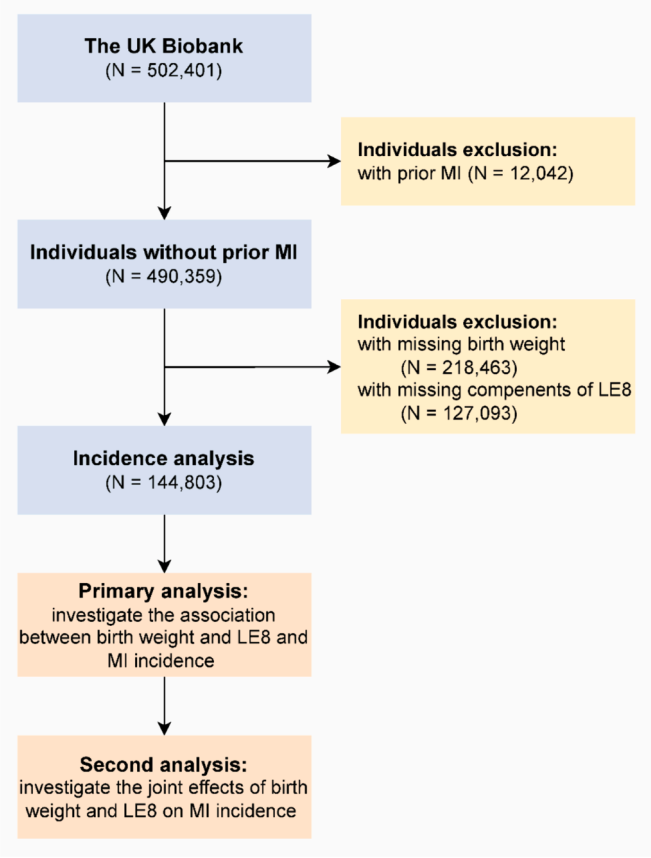


**Fig. 1.** The flowchart of screening eligible adults in the United Kingdom, 2006–2017. LE8, life's essential 8; MI, myocardial infarction.

Haemoglobin A1c (HbA1c) and considering the history of diabetes. Systolic and diastolic blood pressure are assessed by averaging two consecutive measurements. Additional detailed information on definitions and scoring for the LE8 metrics are displayed in Supplemental Table 2.

### 2.3. Ascertainment of myocardial infarction

The primary outcome of this study was incident MI. The date of MI was determined as the date of the first reported occurrence of MI. As aforementioned, recurrent cases of MI were not considered for further analyses. The study included outcomes that occurred from baseline up until the latest available censor date, which extended to May 31, 2017.

### 2.4. Assessment of covariates

To identify potential confounders, directed acyclic graph (Supplemental Fig. 1) was plotted to clarify the relationships between confounding factors, exposure, and outcomes based on the prior literature (Li et al., 2023, 2015; Raisi-Estabragh et al., 2023; Zhang et al., 2023). The covariates included sociodemographic characteristics and health-related factors: age at recruitment, sex, race, Townsend deprivation index, education level, drinking status, nicotine exposure, physical activity, diet, aspirin use, family history of heart disease and diabetes and hypertension.

### 2.5. Statistical analysis

Categorical variables were reported as frequencies (percentages) and continuous variables were presented as mean ± SD. For missing data, we applied a missing indicator category for categorical variables and

imputed the median value for continuous variables. Person-time in years was calculated from the baseline to the date of first diagnosis of MI, death, end of the follow-up, or the latest available censor dates, whichever came first.

Cox proportional hazard models were used to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the association between birth weight, LE8 score and risk of MI. The assumption of proportionality was tested using the scaled Schoenfeld residuals, and we did not find any violation of the assumption. The cumulative risks of MI incidence for birth weight and LE8 score were calculated and the Kaplan-Meier curves were plotted after adjusting for covariates using inverse probability of treatment weighting. In addition, to investigate the exposure–response relationships of birth weight, LE8 scores, and the risk of MI, restricted cubic spline (RCS) with 4 knots in the fully adjusted Cox models was used.

To evaluate the joint effects of birth weight and LE8 score on MI incidence, we divided the participants into nine groups according to the categorized birth weight and LE8 score. The relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP), and the synergy index (S) were used to assess the addictive interaction between birth weight and LE8 score (Li and Chambless, 2007).

Stratification analyses were performed to evaluate potential effect modification and find special populations. We also conducted several sensitivity analyses to test the robustness of our findings by (1) excluding participants who experienced MI events within the first two years of follow-up, (2) excluding participants with incomplete variables. Statistical significance was defined as a two-tailed *P* value of <0.05. All statistical analyses were performed using R software (Version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria).

## 3. Results

### 3.1. Baseline characteristics of study population

The mean age of 144,803 participants was 54.7 ± 8.1 years, 58.7% were female and 86.6% identified as Caucasian (Table 1). The mean birth weight was 3.3 ± 0.7 kg and the mean score of LE8 was 61.7 ± 10.7. A total of 5201 (3.6%) were of high CVH, 119,623 (82.6%) were of moderate CVH, and 19,979 (13.8%) were of low CVH. Over a median follow-up period of 8.3 years, equivalent to 1,180,150 person-years of observation, 2,092 incident MI cases were documented. Participants who experienced incident MI were more likely to be older, male, with abnormal birth weight and lower CVH, and exhibited higher Townsend deprivation index and lower education level.

### 3.2. Association between birth weight and incident MI

Higher birth weight was associated with a reduction in MI risk (both $P < 0.001$, Table 2, Model 2 and 3). The RCS revealed a linear exposure–response relationship between birth weight and the MI risk (*P* for

**Table 1**
Baseline characteristics of the non-myocardial infarction and incident myocardial infarction participants in the United Kingdom, 2006–2017.

| Characteristics | Levels | Total (N=144803) | No Incident MI (N=142711) | Incident MI (N=2092) | *P* value* |
|---|---|---|---|---|---|
| Age, n (%) | <60 yrs. | 95,557 (66) | 94,643 (66.3) | 914 (43.7) | <0.001 |
| | ≥60 yrs. | 49,246 (34) | 48,068 (33.7) | 1178 (56.3) | |
| Sex, n (%) | Female | 85,056 (58.7) | 84,391 (59.1) | 665 (31.8) | <0.001 |
| | Male | 59,747 (41.3) | 58,320 (40.9) | 1427 (68.2) | |
| Race, n (%) | Caucasian | 125,385 (86.6) | 123,553 (86.6) | 1832 (87.6) | 0.195 |
| | Others | 19,418 (13.4) | 19,158 (13.4) | 260 (12.4) | |
| Townsend deprivation index, n (%) | Low | 48,249 (33.3) | 47,639 (33.4) | 610 (29.2) | <0.001 |
| | Medium | 48,282 (33.3) | 47,591 (33.3) | 691 (33) | |
| | High | 48,272 (33.3) | 47,481 (33.3) | 791 (37.8) | |
| Education level, n (%) | Higher degree | 59,942 (41.4) | 59,284 (41.5) | 658 (31.5) | <0.001 |
| | Ang school degree | 59,877 (41.4) | 59,120 (41.4) | 757 (36.2) | |
| | Vocational qualifications | 8491 (5.9) | 8281 (5.8) | 210 (10) | |
| | Unknown | 16,493 (11.4) | 16,026 (11.2) | 467 (22.3) | |
| Drinking status, n (%) | Never | 5036 (3.5) | 4939 (3.5) | 97 (4.6) | <0.001 |
| | Current | 135,311 (93.4) | 133,423 (93.5) | 1888 (90.2) | |
| | Previous | 4394 (3) | 4287 (3) | 107 (5.1) | |
| | Unknown | 62 (0) | 62 (0) | 0 (0) | |
| Family history of heart disease, n (%) | No | 80,738 (55.8) | 79,809 (55.9) | 929 (44.4) | <0.001 |
| | Yes | 64,065 (44.2) | 62,902 (44.1) | 1163 (55.6) | |
| Family history of diabetes, n (%) | No | 112,235 (77.5) | 110,660 (77.5) | 1575 (75.3) | 0.015 |
| | Yes | 32,568 (22.5) | 32,051 (22.5) | 517 (24.7) | |
| Family history of hypertension, n (%) | No | 67,158 (46.4) | 66,111 (46.3) | 1047 (50) | <0.001 |
| | Yes | 77,645 (53.6) | 76,600 (53.7) | 1045 (50) | |
| Aspirin use, n (%) | No | 129,670 (89.5) | 128,085 (89.8) | 1585 (75.8) | <0.001 |
| | Yes | 15,133 (10.5) | 14,626 (10.2) | 507 (24.2) | |
| Birth weight, n (%) | Normal birth weight | 111,387 (76.9) | 109,856 (77) | 1531 (73.2) | <0.001 |
| | High birth weight | 19,277 (13.3) | 18,948 (13.3) | 329 (15.7) | |
| | Low birth weight | 14,139 (9.8) | 13,907 (9.7) | 232 (11.1) | |
| CVH, n (%) | High | 5201 (3.6) | 5188 (3.6) | 13 (0.6) | <0.001 |
| | Moderate | 119,623 (82.6) | 118,150 (82.8) | 1473 (70.4) | |
| | Low | 19,979 (13.8) | 19,373 (13.6) | 606 (29) | |
| Total LE8 score, mean ± SD | | 61.7 ± 10.7 | 61.8 ± 10.7 | 55.5 ± 11.0 | <0.001 |
| LE8 metrics, mean ± SD | Diet | 35.5 ± 15.7 | 35.5 ± 15.6 | 37.0 ± 17.0 | <0.001 |
| | Physical activity | 76.2 ± 36.5 | 76.3 ± 36.4 | 71.2 ± 39.7 | <0.001 |
| | Nicotine exposure | 80.3 ± 31.8 | 80.4 ± 31.6 | 68.0 ± 38.0 | <0.001 |
| | Sleep duration | 90.0 ± 17.9 | 90.0 ± 17.9 | 86.5 ± 21.2 | <0.001 |
| | BMI | 70.2 ± 28.5 | 70.3 ± 28.4 | 60.8 ± 29.5 | <0.001 |
| | Blood lipids | 48.0 ± 29.2 | 48.1 ± 29.2 | 40.4 ± 28.8 | <0.001 |
| | Blood glucose | 40.2 ± 5.5 | 40.2 ± 5.5 | 40.0 ± 8.5 | 0.123 |
| | Blood pressure | 53.1 ± 27.2 | 53.2 ± 27.1 | 40.5 ± 24.1 | <0.001 |

BMI, body mass index; CVH, cardiovascular health; LE8, life's essential 8; MI, myocardial infarction; SD, standard deviation.
* For continuous variables, *P* values were derived from t-tests, while for categorical variables, *P* values were derived from chi-square tests.

**Table 2**
Associations of birth weight and cardiovascular health with risk of incident myocardial infarction among adults in the United Kingdom, 2006–2017.

| Levels | Cases/N (%) | Person-year | Incidence Density (‰) | Model 1 HR (95% CI) | Model 2 HR (95% CI) | Model 3 HR (95% CI) |
|---|---|---|---|---|---|---|
| Birth weight | | | | | | |
| Continuous | 2092/144,803 (1.44) | 1,180,150 | 1.77 | 1.00 (0.94, 1.07) | **0.89 (0.83, 0.94)** | **0.90 (0.84, 0.95)** |
| Normal birth weight | 1531/111,387 (1.37) | 908,146 | 1.69 | 1.00 (Ref.) | 1.00 (Ref.) | 1.00 (Ref.) |
| High birth weight | 329/19,277 (1.71) | 156,776 | 2.10 | **1.25 (1.11, 1.40)** | 1.00 (0.89, 1.13) | 0.95 (0.85, 1.08) |
| Low birth weight | 232/14,139 (1.64) | 115,228 | 2.01 | **1.19 (1.04, 1.37)** | **1.27 (1.10, 1.46)** | **1.17 (1.02, 1.35)** |
| CVH | | | | | | |
| Continuous | 2092/144,803 (1.44) | 1,180,150 | 1.77 | **0.95 (0.95, 0.96)** | **0.95 (0.95, 0.96)** | **0.96 (0.95, 0.96)** |
| High CVH | 13/5201 (0.25) | 42,834 | 0.30 | 1.00 (Ref.) | 1.00 (Ref.) | 1.00 (Ref.) |
| Moderate CVH | 1473/119,623 (1.23) | 975,955 | 1.51 | **4.99 (2.89, 8.61)** | **3.27 (1.90, 5.66)** | **2.96 (1.72, 5.12)** |
| Low CVH | 606/19,979 (3.03) | 161,361 | 3.76 | **12.42 (7.17, 21.52)** | **7.86 (4.54, 13.63)** | **6.43 (3.71, 11.15)** |

Model 1 was not adjusted for any covariable. Model 2 was adjusted for age and sex. Model 3 for birth weight was further adjusted for race, nicotine exposure, drinking status, physical activity, diet, Townsend deprivation index, education level, aspirin use, family history of heart disease, family history of diabetes, and family history of hypertension. Model 3 for CVH was further adjusted for race, Townsend deprivation index, education level, drinking status, aspirin use, family history of heart disease, family history of diabetes, and family history of hypertension, based on Model 2. The boldface value indicates significant differences ($P < 0.05$). CI, confidence interval; CVH, cardiovascular health; HR, hazard ratio; LE8, life's essential 8.

overall association < 0.001, and *P* for non-linear association = 0.116, as illustrated in Fig. 2A). A significant inverse association was found below an optimal threshold of 3.3 kg of birth weight. In addition, the cumulative MI risk was higher in the participants with low birth weight than in those with either normal or high birth weight (log-rank $P < 0.001$, Fig. 3A). Compared with normal birth weight, low birth weight was associated with a higher MI risk (adjusted HR 1.17, 95% CI 1.02–1.35, $P = 0.025$, Table 2, Model 3). However, there was no significant association observed between high birth weight and incident MI after adjustment (adjusted HR 0.95, 95% CI 0.85–1.08, $P = 0.444$, Table 2).

### 3.3. Association between LE8 and incident MI

A higher LE8 score was associated with a reduction in MI risk, in both the unadjusted and fully adjusted models (all $P < 0.001$, Table 2). The RCS showed a monotonically inverse linear exposure–response relationship between birth weight and the MI risk (*P* for overall association < 0.001, and *P* for non-linear association = 0.408, as illustrated in Fig. 2B). A significant increase in the hazard of incident MI was observed along with LE8 score below an optimal threshold of 62 points. The cumulative MI risk was highest in the participants with low LE8 score (Fig. 3B). The adjusted HRs of incident MI for moderate and low CVH in comparison with high CVH were 2.96 (1.72–5.12), and 6.43 (3.71–11.15), respectively (Table 2, Model 3).

### 3.4. Joint analysis of birth weight and LE8 score with incident MI

A consistent decreasing trend of MI risk associated with increased LE8 score was observed across all categories of birth weight (Supplemental Fig. 2). Additionally, a joint effect of birth weight and LE8 score on the risk of incident MI was presented in Fig. 4. Low CVH defined by low LE8 score can significantly aggravate the MI risk in different birth weight groups, especially in normal birth weight group (HR 7.71, 95% CI 3.98–14.93), when compared to high CVH. Furthermore, interactions between birth weight and CVH on MI incidence were further investigated, and negative additive interactions (antagonistic effect) were found (Supplemental Table 3).

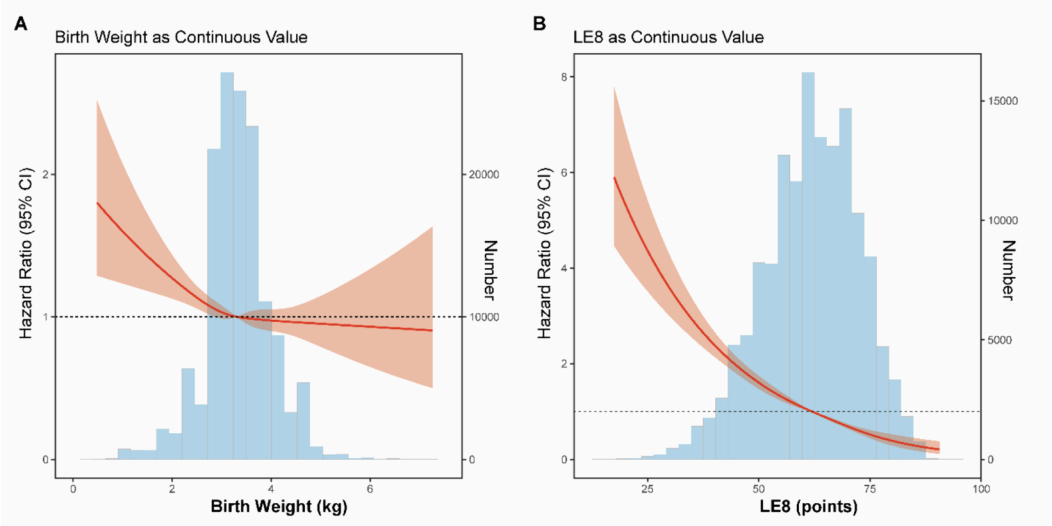


**Fig. 2.** Exposure-response relationships of birth weight (A) and life's essential 8 score (B) with the risk of incident myocardial infarction among adults in the United Kingdom, 2006–2017. Associations between birth weight (A), and LE8 (B) with incident MI were evaluated by restricted cubic splines after adjustment for the covariables. (A) HRs were adjusted for age, sex, race, diet, physical activity, nicotine exposure, drinking status, Townsend deprivation index, education levels, aspirin use, family history of heart disease, family history of diabetes, and family history of hypertension; (B) HRs were adjusted for age, sex, race, Townsend deprivation index, education levels, drinking status, aspirin use, family history of heart disease, family history of diabetes, and family history of hypertension. CI, confidence interval; HR, hazard ratio; LE8, life's essential 8; MI, myocardial infarction.

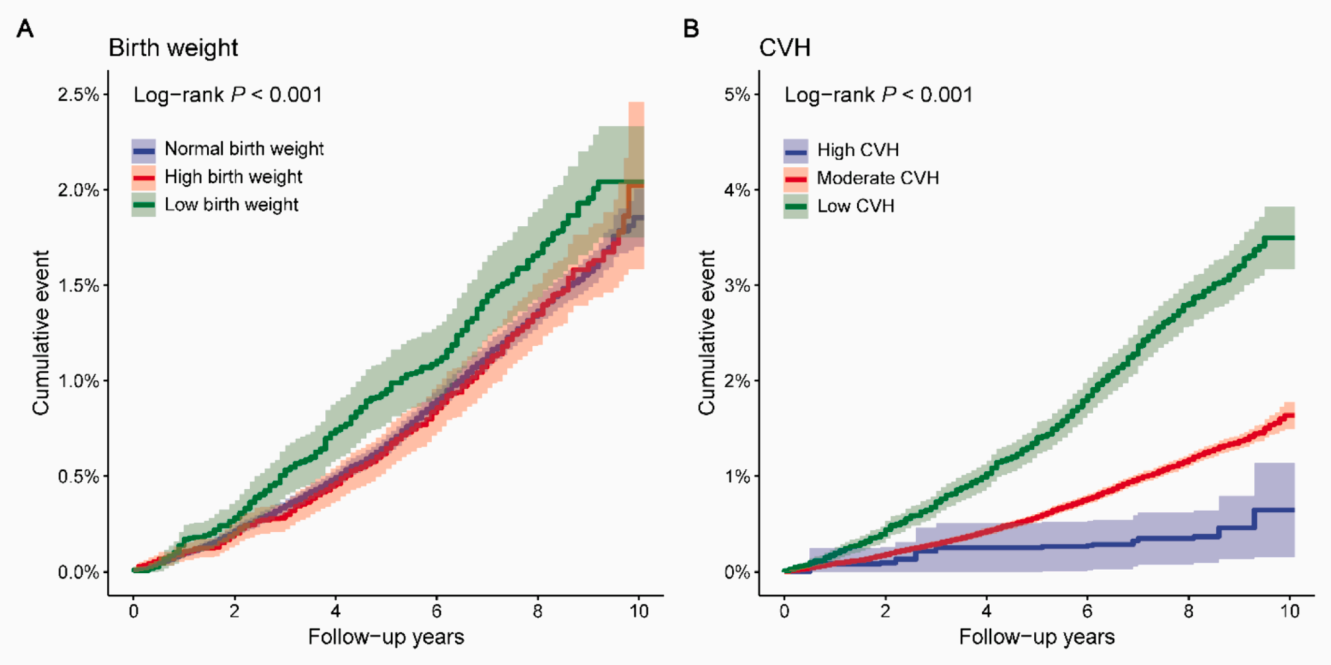


**Fig. 3.** Kaplan-Meier curves of incident myocardial infarction stratified by birth weight and cardiovascular health among adults in the United Kingdom, 2006–2017. Cumulative incidence of MI based on different birth weight (A) and CVH levels (B), is presented respectively. HRs were adjusted for age and sex using inverse probability of treatment weighting. CI, confidence interval; CVH, cardiovascular health; HR, hazard ratio; MI, myocardial infarction.

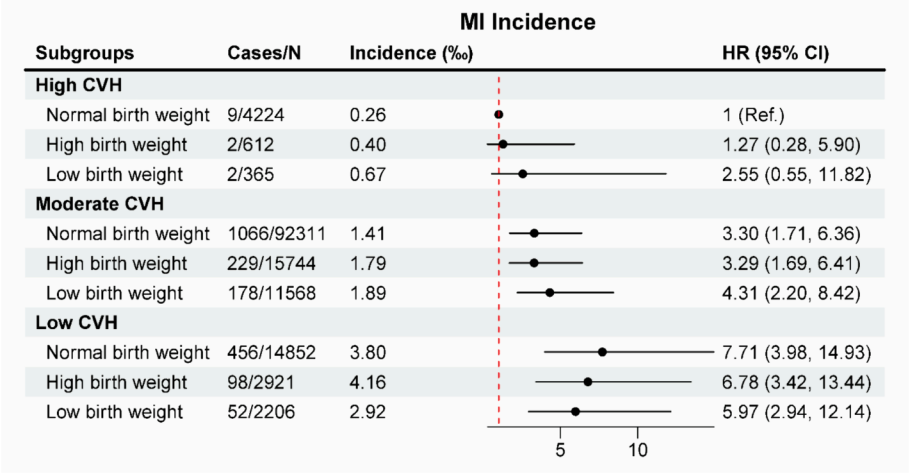


**Fig. 4.** Joint effects of birth weight and cardiovascular health on the risk of incident myocardial infarction among adults in the United Kingdom, 2006–2017. The model was adjusted for age, sex, race, Townsend deprivation index, education level, drinking status, aspirin use, family history of heart disease, family history of diabetes, and family history of hypertension. CI, confidence interval; CVH, cardiovascular health; HR, hazard ratio; MI, myocardial infarction.

### *3.5. Stratification and sensitivity analyses*

The effects of LE8 on incident MI were further evaluated using stratification analyses (Supplemental Table 4). Significant differences were observed based on age and family history of heart disease in the association between LE8 and the MI risk (both $P$ for interaction $< 0.05$). Our findings regarding the associations between LE8 score and MI risk remained consistent even after excluding participants who experienced incident MI within two years from baseline (Supplemental Table 5) or those with imputed covariables (Supplemental Table 6).

## 4. Discussion

In this prospective cohort study, we explored the association between birth weight, LE8 score, and their potential interactions and joint effects on the risk of MI in adulthood. Our findings indicated that low birth weight was related to a higher risk of later life MI. Moderate to high CVH can significantly reduce the risk of incident MI across three birth weight groups, especially in normal birth weight group. Furthermore, significant negative additive interactions (antagonistic effect) were observed between low birth weight and low CVH on the incidence of MI. These findings emphasize the importance of protection of fetal growth to reduce the risk of MI in later life, and improving LE8 during adulthood could be an effective preventive measure.

Early life exposures may exert a varying degree of influence on cardio-metabolic syndrome at different stages of the life cycle. Accumulating evidence has demonstrated that individuals with low birth weight are at a higher risk of developing CVD in adulthood (Huang et al.,

2022; Mr et al., 2018; Raisi-Estabragh et al., 2023). The fetal origins hypothesis and its subsequent concept "developmental origins of health and disease (DOHaD)" propose that intrauterine undernutrition might have profound and lasting impacts on susceptibility to nutrition-related cardio-metabolic diseases (Barker, 1995; Hoffman et al., 2021). It can be attributed to underlying mechanisms involving physiological responses, adapted metabolism, and altered body composition as a result of growth retardation (Hoffman et al., 2021; Visentin et al., 2014). Moreover, subsequent rapid postnatal catch-up growth may ameliorate the severity of metabolic deficits (Singhal and Lucas, 2004). Several studies have reported both low and high birth weight were significantly associated with a higher BMI as well as obesity in adulthood (Eriksson et al., 2001; Newby et al., 2005). It is well-established that obesity is closely intertwined with the development of comorbid conditions related to cardio-metabolic diseases (Juonala et al., 2011; Kahn et al., 2006).

On the other hand, existing evidence has also reported that high birth weight was associated with a greater risk of CVD (Mohseni et al., 2020; Osler et al., 2009). Maternal gestational diabetes and obesity have been identified as factors leading to high birth weight, which in turn is linked to an elevated risk of developing diabetes in later life (Fall and Kumaran, 2019). However, it is worth noting that some studies did not observe a significant association between high birth weight and CVD risk (Huang et al., 2022; Raisi-Estabragh et al., 2023). Furthermore, a comprehensive meta-analysis has revealed J-shaped associations of birth weight with CVD, and the lowest risks for CVD was observed at 4.0–4.5 kg, indicating high birth weight may serve as a protective factor against future CVD (Mr et al., 2018). Given the intricate relationship between birth weight and other etiologic factors in determining MI over extended periods, it is necessary to conduct further studies regarding the interplay of genetic and environmental factors.

These observations underscore the significance of early-life interventions aimed at fostering healthier developmental trajectories to attenuate the MI risk in later life. Therefore, early nutritional interventions, particularly regarding protein-energy and micronutrients during pregnancy, are crucial for under-nourished populations (Fall and Kumaran, 2019). However, interventions initiated after the first trimester may not be early enough, as it results in the oversight of key events such as fetal organogenesis during the early pregnancy period. Thus, there remains a question of whether any modifications can be made to mitigate the adverse effects of low birth weight on their long-term CVH for individuals who have missed the optimal window for intervention or are born with low birth weight.

Substantial studies have revealed the association between healthy lifestyles and favourable cardiovascular outcomes (Cho et al., 2023; Isiozor et al., 2023; Zhang et al., 2023, 2021). Our study also demonstrated a significant inverse relationship between LE8 score and MI risk, and individuals with low CVH have a higher MI risk in later life, which were in accordance with previous research (Arnett et al., 2019; Lv et al., 2017). A higher LE8 score is often indicative of a more favourable social and economic environment, better access to healthcare, and a greater tendency to engage in healthier lifestyle behaviours, all of which contribute to a reduced risk of MI. In addition, the potential mechanisms underlying the cardiovascular protective effects of LE8 encompass various pathways involving inflammation, endothelial function, haemostatic factors, and so forth (Lloyd-Jones et al., 2022a).

Several studies have explored the potential associations between birth weight and the single component of LE8 (Li et al., 2015; Qiao et al., 2017; Shi et al., 2022). However, there is currently a lack of relevant research investigating the interaction between birth weight and integrated LE8 on the subsequent risk of CVD or MI. In this study, we found that a low LE8 score can aggravate the association between birth weight and adult MI risk. Specifically, LE8 score may have a stronger influence on cardiovascular health outcomes in individuals born with normal birth weight. In contrast, for individuals with abnormal birth weight, the impact of low LE8 score on MI risk was not as pronounced compared to those with normal birth weight. It could be attributed to the negative additive interactions between abnormal birth weight and LE8 score. Another notable finding is that LE8 score demonstrates potential as a practical and effective strategy for preventing MI, especially among specific populations. The stratification analysis revealed that the cardiovascular protective effect of LE8 was more prominent in individuals under the age of 60, and those without family history of heart disease. These results corroborate the findings of a great deal of the previous work (Lloyd-Jones et al., 2022b; Ramírez-Vélez et al., 2018; Wells et al., 2022).

Generally, we found a significant interaction between birth weight and LE8 score regarding the risk of later MI in adulthood. Our finding suggests that abnormal birth weight-related MI risk varies according to LE8 score, highlighting opportunities where improving LE8 may attenuate the developmental programming effects. Furthermore, we observed that the protective effect of an ideal CVH profile, as indicated by high LE8 score, was more pronounced in individuals with normal birth weight compared to those with abnormal birth weight. These results emphasize the importance of both normal birth weight and improving LE8 in reducing the risk of MI and promoting the integration of preventive strategies from early life to adulthood.

Several study limitations deserve mention. Firstly, our study relied on self-reported information regarding birth weight, diet, sleep duration, and physical activity, which may be subject to recall bias and misclassification of CVH. Secondly, LE8 score were calculated at one time point, and the continuous trajectory of eight metrics over time was not well tracked. Thus, potential lifestyle changes may occur during the follow-up period. Thirdly, our findings are derived from a specific population in the United Kingdom, primarily consisting of individuals of white British descent. As a result, caution should be advised when attempting to generalize these findings to other racial or ethnic groups with distinct sociodemographic characteristics.

In conclusion, low birth weight was associated with increased MI risk in later life, emphasizing the importance of the prenatal factor in risk prediction and prevention of MI. While timely interventions during pregnancy are ideal, individuals born with low birth weight can still take measures to mitigate the adverse effects by improving LE8.

## CRediT authorship contribution statement

**Da Luo:** Writing – original draft, Methodology, Funding acquisition, Conceptualization. **Xiaoying Wang:** Writing – original draft, Visualization, Validation. **Si Li:** Methodology, Formal analysis, Data curation. **Yunlong Guan:** Methodology, Formal analysis, Data curation. **Changwu Xu:** Methodology, Formal analysis, Data curation. **Bofang Zhang:** Visualization, Validation. **Shuo Yang:** Visualization, Validation. **Xingjie Hao:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization. **Jing Chen:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

The authors do not have permission to share data.

## Acknowledgments

None.

*Funding*

Chinese Society of Cardiology's Foundation (grant number:

CSCF2021A02), National Natural Science Foundation of China (grant number: 82003561), and the Science Foundation of Health Commission of Hubei Province, China (grant number: WJ2021M145).

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2024.102853.

## References


Arnett, D.K., Khera, A., Blumenthal, R.S., 2019. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: Part 1. Lifestyle and behavioral factors. JAMA Cardiol. 4, 1043–1044. https://doi.org/10.1001/jamacardio.2019.2604.

Barker, D.J., 1995. Fetal origins of coronary heart disease. BMJ 311, 171–174. https://doi.org/10.1136/bmj.311.6998.171.

Barker, D.J., Winter, P.D., Osmond, C., Margetts, B., Simmonds, S.J., 1989. Weight in infancy and death from ischaemic heart disease. Lancet Lond. Engl. 2, 577–580. https://doi.org/10.1016/s0140-6736(89)90710-1.

Biddinger, K.J., Emdin, C.A., Haas, M.E., Wang, M., Hindy, G., Ellinor, P.T., Kathiresan, S., Khera, A.V., Aragam, K.G., 2022. Association of habitual alcohol intake with risk of cardiovascular disease. JAMA Netw. Open 5, e223849. https://doi.org/10.1001/jamanetworkopen.2022.3849.

Blencowe, H., Krasevec, J., de Onis, M., Black, R.E., An, X., Stevens, G.A., Borghi, E., Hayashi, C., Estevez, D., Cegolon, L., Shiekh, S., Ponce Hardy, V., Lawn, J.E., Cousens, S., 2019. National, regional, and worldwide estimates of low birthweight in 2015, with trends from 2000: a systematic analysis. Lancet Glob. Health 7, e849–e860. https://doi.org/10.1016/S2214-109X(18)30565-5.

Byrne, R.A., Rossello, X., Coughlan, J.J., Barbato, E., Berry, C., Chieffo, A., Claeys, M.J., Dan, G.-A., Dweck, M.R., Galbraith, M., Gilard, M., Hinterbuchner, L., Jankowska, E. A., Jüni, P., Kimura, T., Kunadian, V., Leosdottir, M., Lorusso, R., Pedretti, R.F.E., Rigopoulos, A.G., Rubini Gimenez, M., Thiele, H., Vranckx, P., Wassmann, S., Wenger, N.K., Ibanez, B., ESC Scientific Document Group, 2023. 2023 ESC Guidelines for the management of acute coronary syndromes. Eur. Heart J. ehad191. https://doi.org/10.1093/eurheartj/ehad191.

Cho, S.M.J., Koyama, S., Honigberg, M.C., Surakka, I., Haidermota, S., Ganesh, S., Patel, A.P., Bhattacharya, R., Lee, H., Kim, H.C., Natarajan, P., 2023. Genetic, sociodemographic, lifestyle, and clinical risk factors of recurrent coronary artery disease events: a population-based cohort study. Eur. Heart J., ehad380 https://doi.org/10.1093/eurheartj/ehad380.

Collet, J.-P., Thiele, H., Barbato, E., Barthélémy, O., Bauersachs, J., Bhatt, D.L., Dendale, P., Dorobantu, M., Edvardsen, T., Folliguet, T., Gale, C.P., Gilard, M., Jobs, A., Jüni, P., Lambrinou, E., Lewis, B.S., Mehilli, J., Meliga, E., Merkely, B., Mueller, C., Roffi, M., Rutten, F.H., Sibbing, D., Siontis, G.C.M., ESC Scientific Document Group, 2021. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur. Heart J. 42, 1289–1367. https://doi.org/10.1093/eurheartj/ehaa575.

Dempsey, P.C., Rowlands, A.V., Strain, T., Zaccardi, F., Dawkins, N., Razieh, C., Davies, M.J., Khunti, K.K., Edwardson, C.L., Wijndaele, K., Brage, S., Yates, T., 2022. Physical activity volume, intensity, and incident cardiovascular disease. Eur. Heart J. 43, 4789–4800. https://doi.org/10.1093/eurheartj/ehac613.

Eriksson, J., Forsén, T., Tuomilehto, J., Osmond, C., Barker, D., 2001. Size at birth, childhood growth and obesity in adult life. Int. J. Obes. Relat. Metab. Disord. J. Int. Assoc. Study Obes. 25, 735–740. https://doi.org/10.1038/sj.ijo.0801602.

Fall, C.H.D., Kumaran, K., 2019. Metabolic programming in early life in humans. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 374, 20180123 https://doi.org/10.1098/rstb.2018.0123.

Heidenreich, P.A., Bozkurt, B., Aguilar, D., Allen, L.A., Byun, J.J., Colvin, M.M., Deswal, A., Drazner, M.H., Dunlay, S.M., Evers, L.R., Fang, J.C., Fedson, S.E., Fonarow, G.C., Hayek, S.S., Hernandez, A.F., Khazanie, P., Kittleson, M.M., Lee, C.S., Link, M.S., Milano, C.A., Nnacheta, L.C., Sandhu, A.T., Stevenson, L.W., Vardeny, O., Vest, A.R., Yancy, C.W., 2022. 2022 AHA/ACC/HFSA guideline for the management of heart failure. J. Am. Coll. Cardiol. 79, e263–e421. https://doi.org/10.1016/j.jacc.2021.12.012.

Hoffman, D.J., Powell, T.L., Barrett, E.S., Hardy, D.B., 2021. Developmental origins of metabolic diseases. Physiol. Rev. 101, 739–795. https://doi.org/10.1152/physrev.00002.2020.

Huang, X., Liu, J., Qi, L., Adachi, J.D., Wu, J., Li, Z., Meng, Q., Li, G., Lip, G.Y.H., 2022. Birth weight and the risk of cardiovascular outcomes: a report from the large population-based UK biobank cohort study. Front. Cardiovasc. Med. 9, 827491 https://doi.org/10.3389/fcvm.2022.827491.

Isiozor, N.M., Kunutsor, S.K., Voutilainen, A., Laukkanen, J.A., 2023. Life's Essential 8 and the risk of cardiovascular disease death and all-cause mortality in Finnish men. Eur. J. Prev. Cardiol. 30, 658–667. https://doi.org/10.1093/eurjpc/zwad040.

Juonala, M., Magnussen, C.G., Berenson, G.S., Venn, A., Burns, T.L., Sabin, M.A., Srinivasan, S.R., Daniels, S.R., Davis, P.H., Chen, W., Sun, C., Cheung, M., Viikari, J. S.A., Dwyer, T., Raitakari, O.T., 2011. Childhood adiposity, adult adiposity, and cardiovascular risk factors. N. Engl. J. Med. 365, 1876–1885. https://doi.org/10.1056/NEJMoa1010112.

Kahn, S.E., Zinman, B., Haffner, S.M., O'Neill, M.C., Kravitz, B.G., Yu, D., Freed, M.I., Herman, W.H., Holman, R.R., Jones, N.P., Lachin, J.M., Viberti, G.C., ADOPT Study Group, 2006. Obesity is a major determinant of the association of C-reactive protein levels and the metabolic syndrome in type 2 diabetes. Diabetes 55, 2357–2364. https://doi.org/10.2337/db06-0116.

Larsson, S.C., Mason, A.M., Bäck, M., Klarin, D., Damrauer, S.M., Program, M.V., Michaëlsson, K., Burgess, S., 2020. Genetic predisposition to smoking in relation to 14 cardiovascular diseases. Eur. Heart J. 41, 3304–3310. https://doi.org/10.1093/eurheartj/ehaa193.

Lawton, J.S., Tamis-Holland, J.E., Bangalore, S., Bates, E.R., Beckie, T.M., Bischoff, J.M., Bittl, J.A., Cohen, M.G., DiMaio, J.M., Don, C.W., Fremes, S.E., Gaudino, M.F., Goldberger, Z.D., Grant, M.C., Jaswal, J.B., Kurlansky, P.A., Mehran, R., Metkus, T. S., Nnacheta, L.C., Rao, S.V., Sellke, F.W., Sharma, G., Yong, C.M., Zwischenberger, B.A., 2022. 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation 145, e18–e114. https://doi.org/10.1161/CIR.0000000000001038.

Li, R., Chambless, L., 2007. Test for additive interaction in proportional hazards models. Ann. Epidemiol. 17, 227–236. https://doi.org/10.1016/j.annepidem.2006.10.009.

Li, Y., Ley, S.H., Tobias, D.K., Chiuve, S.E., VanderWeele, T.J., Rich-Edwards, J.W., Curhan, G.C., Willett, W.C., Manson, J.E., Hu, F.B., Qi, L., 2015. Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. The BMJ 351, h3672. https://doi.org/10.1136/bmj.h3672.

Li, X., Ma, H., Wang, X., Feng, H., Qi, L., 2023. Life's essential 8, genetic susceptibility, and incident cardiovascular disease: A prospective study. Arterioscler. Thromb. Vasc. Biol. https://doi.org/10.1161/ATVBAHA.123.319290.

Lloyd-Jones, D.M., Allen, N.B., Anderson, C.A.M., Black, T., Brewer, L.C., Foraker, R.E., Grandner, M.A., Lavretsky, H., Perak, A.M., Sharma, G., Rosamond, W., Association, A.H., 2022a. 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 146, e18–e43. https://doi.org/10.1161/CIR.0000000000001078.

Lloyd-Jones, D.M., Ning, H., Labarthe, D., Brewer, L., Sharma, G., Rosamond, W., Foraker, R.E., Black, T., Grandner, M.A., Allen, N.B., Anderson, C., Lavretsky, H., Perak, A.M., 2022b. Status of Cardiovascular Health in US Adults and Children Using the American Heart Association's New "Life's Essential 8" Metrics: Prevalence Estimates From the National Health and Nutrition Examination Survey (NHANES), 2013 Through 2018. Circulation 146, 822–835. https://doi.org/10.1161/CIRCULATIONAHA.122.060911.

Lv, J., Yu, C., Guo, Y., Bian, Z., Yang, L., Chen, Y., Tang, X., Zhang, W., Qian, Y., Huang, Y., Wang, X., Chen, J., Chen, Z., Qi, L., Li, L., China Kadoorie Biobank Collaborative Group, 2017. Adherence to healthy lifestyle and cardiovascular diseases in the chinese population. J. Am. Coll. Cardiol. 69, 1116–1125. https://doi.org/10.1016/j.jacc.2016.11.076.

Mohseni, R., Mohammed, S.H., Safabakhsh, M., Mohseni, F., Monfared, Z.S., Seyyedi, J., Mejareh, Z.N., Alizadeh, S., 2020. Birth weight and risk of cardiovascular disease incidence in adulthood: a dose-response meta-analysis. Curr. Atheroscler. Rep. 22, 12. https://doi.org/10.1007/s11883-020-0829-z.

Mr, K., Tt, G., Aw, G., R, D., C, L., Sh, L., T, H., 2018. Birth weight and risk of type 2 diabetes mellitus, cardiovascular disease, and hypertension in adults: A meta-analysis of 7 646 267 participants from 135 studies. J. Am. Heart Assoc. 7. https://doi.org/10.1161/JAHA.118.008870.

Newby, P.K., Dickman, P.W., Adami, H.-O., Wolk, A., 2005. Early anthropometric measures and reproductive factors as predictors of body mass index and obesity among older women. Int. J. Obes. 2005 (29), 1084–1092. https://doi.org/10.1038/sj.ijo.0802996.

Osler, M., Lund, R., Kriegbaum, M., Andersen, A.-M.-N., 2009. The influence of birth weight and body mass in early adulthood on early coronary heart disease risk among Danish men born in 1953. Eur. J. Epidemiol. 24, 57–61. https://doi.org/10.1007/s10654-008-9301-z.

Qiao, Y., Zhang, T., Liu, H., Katzmarzyk, P.T., Chaput, J.-P., Fogelholm, M., Johnson, W. D., Kuriyan, R., Kurpad, A., Lambert, E.V., Maher, C., Maia, J.A.R., Matsudo, V., Olds, T., Onywera, V., Sarmiento, O.L., Standage, M., Tremblay, M.S., Tudor-Locke, C., Zhao, P., Hu, G., ISCOLE Research Group, 2017. Joint association of birth weight and physical activity/sedentary behavior with obesity in children ages 9–11 years from 12 countries. Obes. Silver Spring Md 25, 1091–1097. https://doi.org/10.1002/oby.21792.

Raisi-Estabragh, Z., Cooper, J., Bethell, M.S., McCracken, C., Lewandowski, A.J., Leeson, P., Neubauer, S., Harvey, N.C., Petersen, S.E., 2023. Lower birth weight is linked to poorer cardiovascular health in middle-aged population-based adults. Heart 109, 535–541. https://doi.org/10.1136/heartjnl-2022-321733.

Ramírez-Vélez, R., Saavedra, J.M., Lobelo, F., Celis-Morales, C.A., Pozo-Cruz, B.D., García-Hermoso, A., 2018. Ideal cardiovascular health and incident cardiovascular disease among adults: A systematic review and meta-analysis. Mayo Clin. Proc. 93, 1589–1599. https://doi.org/10.1016/j.mayocp.2018.05.035.

Shi, D., Dang, J., Ma, N., Liu, Y., Zhong, P., Cai, S., Ma, Y., Zou, Z., Dong, Y., Song, Y., Ma, J., 2022. The combined effect of birth weight and lifestyle on clustered cardio-metabolic risk factors in children and adolescents: a national school-based cross-sectional survey. Nutrients 14, 3131. https://doi.org/10.3390/nu14153131.

Singhal, A., Lucas, A., 2004. Early origins of cardiovascular disease: is there a unifying hypothesis? Lancet Lond. Engl. 363, 1642–1645. https://doi.org/10.1016/S0140-6736(04)16210-7.

Srour, B., Fezeu, L.K., Kesse-Guyot, E., Allès, B., Méjean, C., Andrianasolo, R.M., Chazelas, E., Deschasaux, M., Hercberg, S., Galan, P., Monteiro, C.A., Julia, C., Touvier, M., 2019. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Santé). BMJ 365, l1451. https://doi.org/10.1136/bmj.l1451.

Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., Downey, P., Elliott, P., Green, J., Landray, M., Liu, B., Matthews, P., Ong, G., Pell, J., Silman, A.,

Young, A., Sprosen, T., Peakman, T., Collins, R., 2015. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 12, e1001779 https://doi.org/10.1371/journal.pmed.1001779.

Sun, Y., Yu, Y., Zhang, K., Yu, B., Yu, Y., Wang, Y., Wang, B., Tan, X., Wang, Yu., Lu, Y., Wang, N., 2023. Association between Life's Essential 8 score and risk of premature mortality in people with and without type 2 diabetes: A prospective cohort study. Diabetes Metab. Res. Rev., e3636 https://doi.org/10.1002/dmrr.3636.

Tian, G., Guo, C., Li, Q., Liu, Y., Sun, X., Yin, Z., Li, H., Chen, X., Liu, X., Zhang, D., Cheng, C., Liu, L., Liu, F., Zhou, Q., Wang, C., Li, L., Wang, B., Zhao, Y., Liu, D., Zhang, M., Hu, D., 2019. Birth weight and risk of type 2 diabetes: A dose-response meta-analysis of cohort studies. Diabetes Metab. Res. Rev. 35, e3144.

Tsao, C.W., Aday, A.W., Almarzooq, Z.I., Anderson, C.A.M., Arora, P., Avery, C.L., Baker-Smith, C.M., Beaton, A.Z., Boehme, A.K., Buxton, A.E., Commodore-Mensah, Y., Elkind, M.S.V., Evenson, K.R., Eze-Nliam, C., Fugar, S., Generoso, G., Heard, D.G., Hiremath, S., Ho, J.E., Kalani, R., Kazi, D.S., Ko, D., Levine, D.A., Liu, J., Ma, J., Magnani, J.W., Michos, E.D., Mussolino, M.E., Navaneethan, S.D., Parikh, N.I., Poudel, R., Rezk-Hanna, M., Roth, G.A., Shah, N.S., St-Onge, M.-P., Thacker, E.L., Virani, S.S., Voeks, J.H., Wang, N.-Y., Wong, N.D., Wong, S.S., Yaffe, K., Martin, S.S., American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee, 2023. Heart Disease and Stroke Statistics-2023 update: A report from the American Heart Association. Circulation 147, e93–e621. https://doi.org/10.1161/CIR.0000000000001123.

Visentin, S., Grumolato, F., Nardelli, G.B., Di Camillo, B., Grisan, E., Cosmi, E., 2014. Early origins of adult disease: low birth weight and vascular remodeling. Atherosclerosis 237, 391–399. https://doi.org/10.1016/j.atherosclerosis.2014.09.027.

Wells, I., Simons, G., Davenport, C., Mallen, C.D., Raza, K., Falahee, M., 2022. Acceptability of predictive testing for ischemic heart disease in those with a family history and the impact of results on behavioural intention and behaviour change: a systematic review. BMC Public Health 22, 1751. https://doi.org/10.1186/s12889-022-14116-6.

Writing committee of the report on cardiovascular health and diseases in china, 2022. Report on cardiovascular health and diseases in China 2021: an updated summary. Biomed. Environ. Sci. BES 35, 573–603. https://doi.org/10.3967/bes2022.079.

Zhang, Y.-B., Chen, C., Pan, X.-F., Guo, J., Li, Y., Franco, O.H., Liu, G., Pan, A., 2021. Associations of healthy lifestyle and socioeconomic status with mortality and incident cardiovascular disease: two prospective cohort studies. The BMJ 373, n604. https://doi.org/10.1136/bmj.n604.

Zhang, J., Chen, G., Habudele, Z., Wang, X., Cai, M., Li, H., Gao, Y., Lip, G.Y.H., Lin, H., 2023. Relation of life's essential 8 to the genetic predisposition for cardiovascular outcomes and all-cause mortality: results from a national prospective cohort. Eur. J. Prev. Cardiol., zwad179 https://doi.org/10.1093/eurjpc/zwad179.