Nutrition 62 (2019) 186–193

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Applied nutritional investigation

# Fetal and childhood malnutrition during the Korean War and metabolic syndrome in adulthood

Changwoo Han M.D. [a], Yun-Chul Hong M.D., Ph.D. [a,b,c,*]

[a] Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea
[b] Institute of Environmental Medicine, Seoul National University Medical Research Center, Seoul, Korea
[c] Environmental Health Center, Seoul National University College of Medicine, Seoul, Korea

ARTICLE INFO

*Article History:*
Received 15 November 2018
Received in revised form 4 January 2019
Accepted 9 January 2019

*Keywords:*
Malnutrition
Metabolic syndrome
Developmental programming
Korean War

ABSTRACT

*Objectives:* Koreans experienced unexpected shortages of food and refugee life during the Korean War (1950–1953). In the present study, we used the Korean War as a natural experiment for early life malnutrition with the aim of evaluating the risk for metabolic syndrome in adulthood according to participant exposure status during the Korean War.

*Methods:* We used data from 25 708 participants from the fourth through seventh Korean National Health and Nutrition Examination Survey, a nationally representative database of Korea. By years of birth, we divided the study participants into non-exposed (1959–1963 and 1954–1958), fetal-exposed (1951–1953), early childhood–exposed (1946–1950), late-childhood-exposed (1941–1945), and adolescent-exposed (1936–1940) groups according to participants' ages during the Korean War. We calculated the risk for metabolic syndrome in adult life using logistic regression analysis.

*Results:* Compared with the non-exposed group, women exposed to the Korean War while in utero and during early childhood were associated with increased risk for abdominal obesity and elevated triacylglycerol levels, whereas men showed low high-density lipoprotein cholesterol levels. Fetal and early childhood exposure increased the risk for metabolic syndrome in adults compared with the non-exposed group (fetal-exposed men: odds ratio [OR], 1.28; 95% confidence interval [CI], 0.93–1.76; fetal-exposed women: OR, 1.35; 95% CI, 1.01–1.80; early-childhood–exposed men OR, 1.25; 95% CI, 0.82–1.90; and early-childhood–exposed women OR, 1.41; 95% CI, 0.97–2.06).

*Conclusions:* Fetal and early childhood experiences during the Korean War were associated with increased risk for some components of metabolic syndrome. The present study suggested that early life malnutrition due to the Korean War may be associated with metabolic syndrome in later life.



## Introduction

Metabolic syndrome is a cluster of metabolic risk factors that includes abdominal obesity, hypertension, glucose intolerance, and dyslipidemia [1]. It is associated with increased risk for type 2 diabetes and cardiovascular disease morbidity and mortality [2,3]. The prevalence of metabolic syndrome is increasing worldwide and about 30% to 35% of Korean and U.S. adults have metabolic syndrome [2,3]. The causes of metabolic syndrome are believed to be overweight, physical inactivity, and genetic factors; however, the exact mechanisms and linkages between each risk factor of the syndrome are not fully understood [1].

One explanation for the pathogenesis of metabolic disease is developmental origins of chronic disease hypothesis [4,5]. According to findings from the Helsinki Birth Cohort, low birthweight is associated with increased risk for coronary heart disease, stroke, hypertension, and type 2 diabetes in later life [6]. In addition, the risks increased in children who had low birthweight and in those who experienced rapid increase of body mass index (BMI) in their childhood. These findings suggest that the nutritional environment during pregnancy may be associated with lifelong risk for metabolic disease and a mismatch between the early (poor) and later life (improved) nutritional status may exacerbate the risk [6,7].

The linkages between early life exposure to malnutrition and adverse health outcomes in adults have been proposed by the

CH designed the study; had full access to all data; analyzed the data, contributed to the discussion, data interpretation, and writing of the manuscript writing; and takes responsibility for the integrity of data and the accuracy of data analysis. YCH contributed to the discussion, interpretation of data, writing of the manuscript, and supervised the study. The authors have no conflicts of interest to declare.

* Corresponding author: Tel: +82 2 740-8394; Fax: +82 2 747 4830.
*E-mail address:* ychong1@snu.ac.kr (Y.-C. Hong).

https://doi.org/10.1016/j.nut.2019.01.003
0899-9007/

Dutch and the Chinese famine studies. By analyzing newborn infants born during the Dutch famine period, it was shown that early life exposure to famine is associated with type 2 diabetes, coronary heart disease, atherogenic lipid profile, increased BMI, and abdominal obesity [8–13]. However, exposure to the Dutch famine was not significantly associated with metabolic syndrome, although it showed positive association [14].

According to the Chinese famine studies, fetal and early childhood exposure to famine was associated with increased risk for metabolic syndrome [15–18]. In addition, early exposure to the Chinese famine was associated with type 2 diabetes, non-alcoholic fatty liver disease, hypertension, and increased BMI [19–23]. However, because famine studies are based on rare historical events, there are limited number of studies that replicated the Dutch and the Chinese famine study findings.

In June 1950, sudden invasion from North Korea initiated the Korean War, and South Korea lost 90% of its territory in the first 2 mo of the war. After the United Nation's support, South Korea rehabilitated its territory and headed toward the North (November 1950), but the joining of the Chinese communist force with North Korea led to a battle that lasted until the armistice in July 1953. The occupation of Seoul (the South Korean capital city) changed four times during the war, and many civilians had to endure 3 y of war and life as a refugee. About 70% of textile and chemical industries and 40% of agricultural and machinery industries were destroyed during the first 4 mo of the war, and >40% of factories and production facilities were damaged by the middle of 1951 [24]. About 800 000 to 999 000 South Korean civilians were sacrificed, injured, or abducted; and total war damage was estimated at USD $6.9 billion (which was 86% of the gross national product of South Korea at the end of the war) [24]. Among 50 wars in recent history worldwide, the Korean War ranks third in scale, intensity, and scope, behind World Wars I and II [25].

According to a recent survey, >50% of adult Koreans responded “yes” to having heard about their family members' refugee experiences during the Korean War [26]. Despite emergency aids and ration distributions, refugees experienced chronic shortages of food and water during the war [27]. Destruction of agricultural facilities, impoverished soil, and decreased manpower during the war resulted in >33% reduction in agricultural productivity in 1952 compared with the years between 1945 and 1950 [24].

Therefore, it is plausible to assume that young Koreans experienced unexpected shortages of food and refugee life during the Korean War. On the basis of the developmental origins of chronic disease hypothesis and based on previous findings from Dutch and Chinese famine studies, we hypothesized that early life exposure to malnutrition during the Korean War is associated with metabolic syndrome in adults. To prove this hypothesis, we analyzed data from the Korean National Health and Nutrition Examination Survey (KNHANES), a nationally representative database of Korea, using the Korean War as a natural experiment for early life malnutrition.

## Materials and methods

### *Study participants*

We used the yearly survey data from the fourth (2007–2009), fifth (2010–2012), sixth (2013–2015), and seventh (2016) cycles of KNHANES. Detailed study design and survey contents were published previously [28]. In summary, KNHANES is an ongoing national surveillance system that assesses the health and nutritional status of Koreans. Since the fourth survey cycle, KNHANES adopted a stratified, multistage, probability sampling design to generate nationally representative values. We used health interview and physical examination data, which included anthropometric measurements, biochemical blood tests, and participants' characteristic information.

Among the 81 503 participants from the fourth to seventh KNHANES cycles, we identified 29 300 who were born between 1936 and 1963. After excluding 3592 participants with missing questionnaire answers, anthropometric measurements, and biochemical blood tests, we included data from 25 708 participants (men: 11 180; women: 14 528; Supplementary Fig. 1).

### *Korean War exposure classification*

We divided the study participants into non-exposed (born between 1959 and 1963; born between 1954 and 1958), fetal-exposed (born between 1951 and 1953), early childhood–exposed (born between 1946 and 1950), late-childhood-exposed (born between 1941 and 1945), and adolescent-exposed (born between 1936 and 1940) groups according to the participants' age at the beginning of the Korean War (June 1950; Supplementary Fig. 2). We referred to the seven stages of the human life cycle suggested by Bogin, which was adopted in previous famine studies [8,15]. Number of study participants per group and their weighted percentage and sex ratio (men to women) are summarized in Supplementary Table 1. The sex ratio (men to women) per each exposure group varied from 0.72 to 1.01, similar to the sex ratio of 2010 and 2015 population census data.

### *Definition of the metabolic syndrome*

We used the National Cholesterol Education Program—Third Adult Treatment Panel criteria to define metabolic syndrome and its risk components [29]. Participants with three or more findings on the following risk variables were regarded as having MetS:

- waist circumference ≥90 cm in men or ≥80 cm in women;
- fasting plasma glucose ≥100 mg/dL or undergoing treatment;
- low high-density lipoprotein cholesterol <40 mg/dL in men or <50 mg/dL in women or undergoing treatment;
- high serum triacylglycerols ≥150 mg/dL or undergoing treatment; and
- increased blood pressure ≥130/85 mm Hg or undergoing treatment

The modified waist circumference criteria for Asian-Pacific population was applied to the present study.

For a sensitivity analysis, we used the International Diabetes Federation (IDF) criteria to define metabolic syndrome [30]. Anyone with abdominal obesity (waist circumference ≥90 cm in men or ≥80 cm in women) and two or more of the following four risk parameters was classified as having a metabolic syndrome:

- fasting plasma glucose ≥100 mg/dL or previously diagnosed type 2 diabetes;
- low HDL cholesterol <40 mg/dL in men or <50 mg/dL in women or undergoing treatment;
- high serum triacylglycerols ≥150 mg/dL or undergoing treatment; and
- increased blood pressure ≥130/85 mm Hg or undergoing treatment.

### *Study variables*

The health interview, physical examination, and biochemical blood tests were performed by trained staff and interviewers at the KNHANES mobile examination centers. The following variables from the health interview were selected as potential confounders based on a previous literature review: age; household income (high; middle high; middle low; low); smoking status (yes, those who smoked more than five packs of cigarettes; no, person who never smoked or smoked less than five packs of cigarettes; don't know); drinking status (yes, current drinker or past drinker; no, never drinker; don't know); exercise status (number of days with muscle exercise per week, ≥3 d or more; 1–2 d; never; don't know); and current treatment (yes; no; don't know) of hypertension, diabetes (type 1 and type 2), or hyperlipidemia.

All participants were instructed to fast for >12 h before the blood test. Venous blood samples were collected at the mobile center and sent to a certified laboratory for an analysis. Fasting plasma glucose and cholesterol levels were analyzed enzymatically using Advia 1650 (Siemens, New York, NY, USA) and Hitachi Automatic Analyzer 7600 (Hitachi, Japan).

Trained examiners measured participants' height, weight, waist circumference, and blood pressure, following KNHANES standard physical examination protocols. Height and weight were measured using portable stadiometer (Seriter, Bismarck, ND,USA) and calibrated balance beam scale (Giant-150 N; Hana, Seoul, Korea), respectively. BMI was calculated as weight in kilograms divided by height in meter square ($kg/m^2$). Waist circumference was measured at the end of the normal expiration by measuring the lower borders of the rib cage and the iliac crest. Systolic and diastolic blood pressures were measured twice using a mercury sphygmomanometer (Baumanometer; Baum, Hopague, NY, USA) in a sitting position after 10 min of rest. Average values of systolic and diastolic blood pressure were used in the present analysis. Total daily energy intake level and percentage

of energy from carbohydrates, protein, and fat were calculated based on 24-h recall nutritional survey results. The percentage of energy from carbohydrates, protein, and fat were calculated as the ratio of energy from each nutrient to total daily energy intake.

*Statistical analysis*

All statistical analyses were performed by reflecting the sampling design and sample population weights of KNHANES. Because four cycles of KNHANES survey were used, we recalculated new sample weights for each participant according to the KNHANES analysis guidelines. All analyses were conducted with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and a conventional two-tailed $\alpha$ level of 0.05 was applied to the analysis.

First, we used the SURVEYFREQ procedure to compare categorical baseline characteristics of the study participants according to exposure status of the Korean War. Second, we compared the least square geometric means (LSGMs) of continuous variables related to metabolic syndrome (height, weight, BMI, waist circumference, blood pressure, fasting blood glucose, triacylglycerols, and HDL cholesterol) by exposure status of the Korean War. We used the SURVEYREG procedure to construct multivariable regression models adjusting for age, household income, smoking, drinking, exercise status, and KNHANES survey cycle to calculate LSGMs.

Last, the risk of metabolic syndrome and its individual features (abdominal obesity, hypertension, glucose intolerance, and dyslipidemia) were estimated by exposure status of the Korean War using logistic regression model with SURVEYLOGISTIC procedure. The logistic regression model was adjusted for age, household income, smoking, drinking, exercise status, and KNHANES survey cycle. According to previous famine studies with sex-specific results, we conducted sex-stratified analysis.

Several sensitivity analyses were conducted to confirm the robustness of the study findings. First, we used a different metabolic syndrome definition, the IDF criteria, and conducted the same analysis. Second, because the small number of participants with "don't know" answers may lead to potential bias, we excluded participants who responded with "don't know" in the sensitivity analysis. Third, because menstrual status may affect middle-age and elderly women's health, we further adjusted for menstrual status (having a period; pregnant; in menopause; others; don't know) in our sensitivity analysis. Fourth, because early life exposure to malnutrition may lead to preference of high-fat diet in adulthood [10], we compared the total daily energy intake levels and percentage of energy from carbohydrates, protein, and fat by the exposure status of the Korean War. We conducted sensitivity analysis by additionally adjusting for nutritional status in our main analysis model.

## Results

Table 1 shows the weighted characteristics of study participants by their exposure status to the Korean War. Owing to the cross-sectional survey design of KNHANES, adolescent- and childhood-exposed groups were generally older than non-exposed groups. In men, non-exposed groups tended to report that their household income was high and were more likely to be drinkers than other groups. Early childhood–exposed groups were more likely to be smokers, exercise frequently, and currently be taking hyperlipidemia medication. The late childhood-exposed group took hypertension and diabetes mellitus medications more frequently than the other groups. In women, the non-exposed group tended to report that their household income was high and were more likely to be smokers and drinkers, but also exercise frequently. Those in the early childhood–exposed group tended to take hyperlipidemia medication, whereas those in the adolescent-exposed group were more likely to be smokers and were taking hypertension and diabetes medications.

The LSGMs of the risk factors of metabolic syndrome are summarized in Table 2. In men, LSGMs of height, weight, BMI, waist circumference, and blood pressure were highest in the non-exposed group. However, fasting plasma glucose and triacylglycerol levels were highest in the fetal-exposed group; whereas the late-childhood–exposed group showed the lowest HDL-cholesterol levels. In women, height and fasting plasma glucose levels were highest in the non-exposed group; whereas the HDL-cholesterol levels were lowest in the adolescent-exposed group. However, weight, waist circumference, and systolic blood pressure were highest in the early-childhood–exposed group. BMI was highest in the fetal-exposed group, and triacylglycerol was highest in the late-childhood–exposed group. Figure 1 shows the patterns of LSGMs of BMI and waist circumference by participants' exposure status of the Korean War. Although men showed monotonic increasing pattern with the highest estimates in the Korean War non-exposed group, the point estimates of BMI and waist circumference were highest in the fetal-exposed group of women.

Table 3 shows the weighted association between metabolic syndrome and participants' exposure status to the Korean War. Compared with the Korean War non-exposed group born between 1959 and 1963, the fetal-exposed and early-childhood–exposed groups showed increased risk for metabolic syndrome in women (odds ratio [OR], 1.35; 95% confidence interval [CI], 1.01–1.80; OR, 1.41; 95% CI, 0.97–2.06, for fetal-exposed and early-childhood–exposed groups, respectively). Although not statistically significant, fetal-exposed and early-childhood–exposed men also showed increased risk for metabolic syndrome (fetal-exposed OR, 1.28; 95% CI, 0.93–1.76; early-childhood–exposed OR, 1.25; 95% CI, 0.82–1.90).

With the additional analysis of each risk component of metabolic syndrome, fetal-exposed and early-childhood–exposed women showed increased risk for abdominal obesity (fetal-exposed: OR, 1.66; 95% CI, 1.25–2.20); early-childhood–exposed: OR, 1.59; 95% CI, 1.10–2.29) and high fasting triacylglycerol levels or hyperlipidemia treatment (fetal-exposed: OR, 1.56; 95% CI, 1.18–2.07; early-childhood–exposed: OR, 1.55; 95% CI, 1.08–2.22) compared with the non-exposed group. In men, fetal-exposed and early-childhood–exposed groups showed increased risk for reduced HDL-cholesterol levels or hyperlipidemia treatment (fetal-exposed: OR, 1.55; 95% CI, 1.13–2.12; early-childhood–exposed: OR, 1.67; 95% CI, 1.10–2.52).

By using a different metabolic syndrome definition with central obesity as an obligatory component, we found similar results in women but attenuated risk estimate in men (Supplementary Table 2). The analysis without participants who answered "don't know" in the questionnaire survey showed similar results to the main findings (Supplementary Tables 3). Further adjustment for menstrual cycles in women did not change the present study results (Supplementary Table 4). Preference for fatty foods was not observed in the fetal-exposed or early-childhood–exposed groups (Supplementary Table 5). Further adjustment for nutritional status (total daily energy intake or percentage of energy from carbohydrates, protein, and fat) did not change the study results (Supplementary Tables 6, 7).

## Discussion

In the present study, we used the Korean War as a natural experiment for early life exposure to malnutrition and evaluated the risk for metabolic syndrome according to the participants' exposure status during the Korean War (non-exposed, fetal-exposed, early- and late-childhood–exposed, and adolescent-exposed). Fetal and early-childhood exposure to the Korean War was associated with increased risk for metabolic syndrome in women. Although it was not statistically significant, fetal and early-childhood exposure to the Korean War in men also was associated with increased risk for metabolic syndrome.

Series of meta-analyses suggested that low birthweight, a surrogate marker for fetal malnutrition, is associated with type 2 diabetes and hypertension in adult life [31,32]. The Dutch famine and the Chinese famine studies replicated the results by using historical famine events as a natural experiment for malnutrition during early life. By analyzing data from the European Prospective

**Table 1**
Weighted characteristics* of the study population by the Korean War exposure status (N = 25,708)

| Characteristics | Adolescent-exposed (born between 1936-1940) | Late childhood-exposed (born between 1941-1945) | Early childhood-exposed (born between 1946-1950) | Fetal-exposed (born between 1951-1953) | Non-exposed (born between 1954-1958) | Non-exposed (born between 1959-1963) |
|---|---|---|---|---|---|---|
| Age at the beginning of the Korean War (years) | 10-14 | 5-9 | 0-4 | fetal period-3 | | |
| **Men** | n = 1,667 | n = 1,777 | n = 2,106 | n = 1,208 | n = 2,189 | n = 2,233 |
| Mean age (years) | 73.66 (0.09) | 68.66 (0.08) | 63.55 (0.07) | 59.62 (0.08) | 55.55 (0.06) | 50.72 (0.07) |
| Household income | | | | | | |
| High | 150 (9.3) | 223 (13.4) | 440 (20.8) | 383 (30.9) | 848 (37.7) | 886 (38.7) |
| Middle high | 226 (13.2) | 301 (17.7) | 541 (25.6) | 351 (30.6) | 599 (27.2) | 672 (30.6) |
| Middle low | 426 (24.4) | 598 (32.7) | 688 (32.8) | 299 (24.9) | 517 (23.7) | 474 (21.7) |
| Low | 865 (53.1) | 655 (36.2) | 437 (20.8) | 175 (13.7) | 225 (11.3) | 201 (9.1) |
| Smoking | | | | | | |
| Yes | 1320 (79.4) | 1399 (78.4) | 1716 (81.2) | 954 (79.5) | 1780 (81.1) | 1811 (81) |
| No | 321 (18.6) | 357 (20.1) | 370 (17.5) | 239 (18.9) | 382 (17.4) | 404 (18) |
| Don't know | 26 (2.1) | 21 (1.5) | 20 (1.3) | 15 (1.5) | 27 (1.5) | 18 (1) |
| Drinking | | | | | | |
| Yes | 1456 (87) | 1615 (91.2) | 1951 (92) | 1123 (92.6) | 2070 (94.4) | 2126 (94.6) |
| No | 187 (11) | 146 (7.6) | 137 (6.8) | 70 (5.8) | 95 (4.1) | 89 (4.4) |
| Don't know | 24 (1.9) | 16 (1.2) | 18 (1.1) | 15 (1.5) | 24 (1.4) | 18 (1) |
| Exercise (/week) | | | | | | |
| 3 or more times | 328 (19.7) | 415 (23.7) | 585 (27.2) | 303 (25.3) | 468 (21.4) | 462 (20.7) |
| 1-2 times | 104 (5.8) | 164 (9.2) | 223 (10.4) | 163 (14.6) | 318 (14.6) | 346 (15.5) |
| Never | 1198 (71.6) | 1165 (64.7) | 1266 (60.3) | 711 (57.2) | 1347 (61.3) | 1365 (60.8) |
| Don't know | 37 (2.9) | 33 (2.4) | 32 (2.1) | 31 (3) | 56 (2.7) | 60 (2.9) |
| HTN medication | | | | | | |
| Yes | 746 (46.1) | 837 (47.9) | 872 (40.8) | 416 (33.4) | 589 (27.1) | 428 (19.3) |
| No | 898 (52) | 926 (51.2) | 1208 (57.5) | 771 (64.5) | 1559 (71) | 1766 (78.7) |
| Don't know | 23 (1.9) | 14 (0.9) | 26 (1.7) | 21 (2.1) | 41 (1.9) | 39 (2) |
| HLD medication | | | | | | |
| Yes | 187 (11.4) | 262 (15.2) | 411 (19.1) | 218 (17.6) | 325 (14.2) | 283 (12) |
| No | 1459 (86.9) | 1501 (84) | 1669 (79.2) | 970 (80.4) | 1819 (83.5) | 1911 (86) |
| Don't know | 21 (1.8) | 14 (0.9) | 26 (1.8) | 20 (2) | 45 (2.2) | 39 (2) |
| DM medication | | | | | | |
| Yes | 271 (15.5) | 337 (19.1) | 363 (17.6) | 197 (16.4) | 233 (11) | 162 (6.8) |
| No | 1376 (82.8) | 1426 (80) | 1717 (80.7) | 992 (81.7) | 1915 (87) | 2033 (91.2) |
| Don't know | 20 (1.7) | 14 (0.9) | 26 (1.8) | 19 (1.9) | 41 (2) | 38 (1.9) |
| **Women** | n = 2,113 | n = 2,273 | n = 2,505 | n = 1,511 | n = 2,934 | n = 3,192 |
| Mean age (years) | 74.09 (0.08) | 68.82 (0.07) | 63.56 (0.07) | 59.79 (0.07) | 55.57 (0.07) | 50.83 (0.06) |
| Household income | | | | | | |
| High | 166 (8) | 215 (9.1) | 367 (14.3) | 338 (22.1) | 904 (30) | 1212 (37.1) |
| Middle high | 222 (10.6) | 310 (13.4) | 491 (19.7) | 375 (26.4) | 798 (27.9) | 933 (29) |
| Middle low | 438 (20) | 602 (26.6) | 806 (32.2) | 494 (31.4) | 805 (28) | 740 (24) |
| Low | 1287 (61.4) | 1146 (50.9) | 841 (33.8) | 304 (20.1) | 427 (14.2) | 307 (9.9) |
| Smoking | | | | | | |
| Yes | 159 (8.5) | 112 (4.7) | 125 (4.9) | 74 (5.6) | 169 (6.5) | 232 (8.1) |
| No | 1904 (88.5) | 2128 (93.6) | 2354 (93.7) | 1422 (93) | 2743 (92.6) | 2921 (90.4) |
| Don't know | 50 (3) | 33 (1.7) | 26 (1.4) | 15 (1.4) | 22 (0.9) | 39 (1.5) |
| Drinking | | | | | | |
| Yes | 1152 (54.1) | 1372 (60.6) | 1689 (67.2) | 1111 (73.9) | 2285 (79) | 2630 (82.6) |
| No | 915 (43.1) | 872 (37.9) | 797 (31.8) | 385 (24.8) | 627 (20.1) | 526 (16) |
| Don't know | 46 (2.8) | 29 (1.5) | 19 (1) | 15 (1.4) | 22 (0.9) | 36 (1.4) |
| Exercise (/week) | | | | | | |
| 3 or more times | 91 (4.7) | 163 (6.9) | 252 (10.2) | 150 (9.3) | 322 (10.3) | 363 (12) |
| 1-2 times | 53 (2.5) | 104 (4.6) | 133 (5.1) | 102 (6.8) | 247 (8.8) | 317 (9.8) |
| Never | 1907 (89.3) | 1960 (85.5) | 2079 (82.6) | 1230 (81.8) | 2316 (78.9) | 2435 (75.4) |
| Don't know | 62 (3.4) | 46 (3) | 41 (2.1) | 29 (2.1) | 49 (2) | 77 (2.8) |
| HTN medication | | | | | | |
| Yes | 1201 (58.5) | 1172 (52.4) | 1044 (42) | 486 (34.2) | 722 (24.3) | 473 (14.6) |
| No | 885 (39.8) | 1063 (45.3) | 1432 (56.6) | 997 (63.9) | 2176 (74.3) | 2656 (83) |
| Don't know | 27 (1.6) | 38 (2.3) | 29 (1.4) | 28 (1.9) | 36 (1.4) | 63 (2.4) |
| HLD medication | | | | | | |
| Yes | 436 (22.1) | 642 (29.3) | 746 (29.8) | 410 (27) | 627 (21.1) | 379 (11.6) |
| No | 1651 (76.3) | 1591 (68.2) | 1729 (68.6) | 1074 (71.2) | 2276 (77.7) | 2748 (85.9) |
| Don't know | 26 (1.6) | 40 (2.6) | 30 (1.5) | 27 (1.8) | 31 (1.2) | 65 (2.5) |
| DM medication | | | | | | |
| Yes | 395 (20.7) | 399 (17.6) | 331 (13) | 159 (10.9) | 170 (6.1) | 128 (4.2) |
| No | 1689 (77.5) | 1838 (80.2) | 2149 (85.8) | 1328 (87.4) | 2734 (92.7) | 3006 (93.6) |
| Don't know | 29 (1.8) | 36 (2.2) | 25 (1.2) | 24 (1.7) | 30 (1.1) | 58 (2.3) |

HTN, hypertension; HLD, hyperlipidemia; DM, diabetes mellitus.
*Results are shown as N (weighted percent) for categorical variables and mean (standard error) for continuous variables.

**Table 2**
Weighted blood and body measurements* of the study population by the Korean War exposure status (N = 25,708)

| | Adolescent-exposed (born between 1936-1940) | Late childhood-exposed (born between 1941-1945) | Early childhood-exposed (born between 1946-1950) | Fetal-exposed (born between 1951-1953) | Non-exposed (born between 1954-1958) | Non-exposed (born between 1959-1963) |
|---|---|---|---|---|---|---|
| Men | | | | | | |
| Height (cm) | 166.72 (0.62) | 167.14 (0.43) | 167.00 (0.28) | 166.75 (0.28)† | 167.14 (0.32) | 167.65 (0.47) |
| Weight (kg) | 65.01 (1.02)† | 66.27 (0.71) | 67.26 (0.48) | 67.34 (0.48) | 67.82 (0.53) | 68.58 (0.78) |
| Body Mass Index (kg/m$^2$) | 23.36 (0.32) | 23.70 (0.23) | 24.09 (0.16) | 24.19 (0.16) | 24.24 (0.17) | 24.35 (0.25) |
| Waist circumference (cm) | 83.11 (0.92)† | 84.26 (0.64) | 85.46 (0.43) | 85.87 (0.42) | 85.86 (0.47) | 86.33 (0.70) |
| Systolic blood pressure (mmHg) | 121.72 (1.83) | 123.36 (1.27) | 124.09 (0.83) | 124.41 (0.82) | 124.73 (0.94) | 124.87 (1.45) |
| Diastolic blood pressure (mmHg) | 75.37 (1.13) | 76.56 (0.78) | 77.80 (0.49) | 78.41 (0.49) | 78.87 (0.57) | 78.89 (0.89) |
| Fasting blood glucose (mg/dL) | 102.75 (3.17) | 106.85 (2.39) | 109.32 (1.50) | 111.11 (1.47) | 109.31 (1.64) | 107.70 (2.35) |
| Triglycerides (mg/dL) | 132.35 (13.49) | 137.39 (9.23) | 143.43 (5.68) | 154.41 (6.33) | 152.73 (6.42) | 149.49 (10.38) |
| HDL (mg/dL) | 44.92 (1.20) | 44.84 (0.86) | 45.25 (0.58) | 45.43 (0.56) | 45.72 (0.61) | 46.69 (0.91) |
| Women | | | | | | |
| Height (cm) | 153.02 (0.52)† | 154.33 (0.37) | 154.86 (0.27) | 154.59 (0.25)† | 154.77 (0.27)† | 155.32 (0.38) |
| Weight (kg) | 56.10 (0.78) | 57.42 (0.56) | 58.24 (0.39) | 58.06 (0.38) | 57.36 (0.41) | 57.21 (0.59) |
| Body Mass Index (kg/m$^2$) | 23.96 (0.31) | 24.11 (0.22) | 24.28 (0.15)† | 24.29 (0.15)† | 23.92 (0.17) | 23.69 (0.24) |
| Waist circumference (cm) | 81.49 (0.92) | 81.94 (0.64) | 82.60 (0.44)† | 82.58 (0.43)† | 81.26 (0.47) | 80.61 (0.69) |
| Systolic blood pressure (mmHg) | 120.41 (1.65) | 122.17 (1.17) | 123.07 (0.85) | 122.18 (0.87) | 122.04 (0.88) | 120.90 (1.27) |
| Diastolic blood pressure (mmHg) | 72.72 (0.98) | 74.33 (0.68) | 75.61 (0.47) | 75.77 (0.48) | 75.99 (0.51)† | 74.99 (0.74) |
| Fasting blood glucose (mg/dL) | 97.10 (2.21)† | 99.09 (1.69) | 102.17 (1.24) | 103.83 (1.36) | 103.27 (1.21) | 104.24 (1.72) |
| Triglycerides (mg/dL) | 145.69 (9.08) | 148.75 (6.88) | 143.08 (5.19) | 141.66 (4.56) | 137.49 (4.92)† | 130.51 (6.4) |
| HDL (mg/dL) | 49.36 (1.13) | 50.13 (0.82) | 50.28 (0.62) | 50.19 (0.65) | 51.37 (0.72) | 51.42 (0.97) |

HDL, high-density lipoprotein.
*Estimates are least square geometric means and SE calculated from multivariable regression models. Model adjusted for age, household income, smoking, drinking, exercise status, and KNHANES survey cycle.
†$P < 0.05$ compared to Non-exposed group (1959-1963).

Investigation into Cancer and Nutrition study, self-reported degree of the Dutch famine exposure during childhood (ages 0–9 y) and adolescence (ages 10–17 y) were associated with increased type 2 diabetes in elderly women [8]. In addition, self-reported degree of famine exposure during adolescence was positively associated with coronary heart disease [9].

By analyzing the Dutch Famine Birth Cohort and other related retrospective cohort data, researchers found that exposure to famine during the early gestational period was associated with increased atherogenic lipid profile and increased risk for taking lipid-lowering medication in later life [10,33]. In addition, prenatal exposure to famine was associated with increased blood pressure, impaired glucose tolerance, increased risk of coronary artery disease, and obesity [11,12,34–36]. However, by analyzing 783 members of the Dutch Famine Birth Cohort, exposure to famine in utero was not significantly associated with metabolic syndrome, although it showed positive association (OR, 1.2; 95% CI, 0.9–1.7) [14]. In addition, analysis with the risk factors of metabolic syndrome in the study showed that fetal exposure to famine was associated with

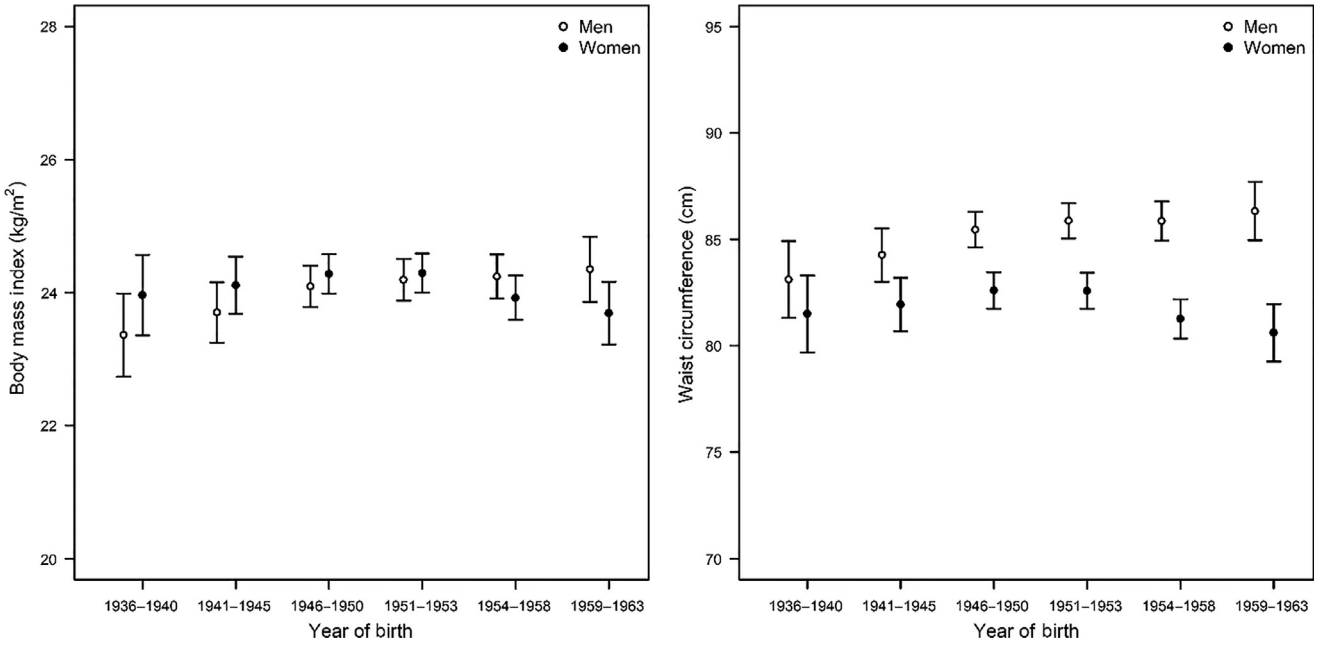


**Fig. 1.** Body mass index and waist circumference by exposure status to the Korean War. Estimates were calculated from multivariable regression models. The data point represents least square geometric means; error bars represent 95% confidence intervals. Models adjusted for age, household income, smoking, drinking, exercise status, and Korean National Health and Nutrition Examination Survey cycle.

**Table 3**
Weighted association [Odds ratio (95%CI)]* between the Korean War exposure status and metabolic health outcomes in elderly individuals

| | Adolescent-exposed (born between 1936-1940) | Late childhood-exposed (born between 1941-1945) | Early childhood-exposed (born between 1946-1950) | Fetal-exposed (born between 1951-1953) | Non-exposed (born between 1954-1958) | Non-exposed (born between 1959-1963) |
|---|---|---|---|---|---|---|
| Men | | | | | | |
| Increased BMI (≥ 23 kg/m$^2$) | 0.62 (0.30-1.28) | 0.78 (0.43-1.38) | 0.95 (0.61-1.46) | 0.97 (0.7-1.33) | 0.90 (0.73-1.11) | 1.00 (ref) |
| Increased WC (≥ 90 cm) | 0.58 (0.27-1.24) | 0.70 (0.38-1.26) | 0.89 (0.57-1.38) | 0.82 (0.59-1.16) | 0.85 (0.68-1.06) | 1.00 (ref) |
| Raised BP† or having HTN tx | 0.62 (0.31-1.27) | 0.83 (0.47-1.45) | 0.93 (0.61-1.41) | 0.96 (0.70-1.32) | 0.93 (0.76-1.14) | 1.00 (ref) |
| Raised glucose‡ or having DM tx | 0.49 (0.24-0.99) | 0.79 (0.45-1.37) | 0.93 (0.61-1.40) | 1.15 (0.84-1.56) | 1.11 (0.91-1.36) | 1.00 (ref) |
| Raised TG§ or having HLD tx | 0.60 (0.30-1.21) | 0.77 (0.44-1.33) | 0.92 (0.62-1.38) | 1.07 (0.78-1.46) | 0.99 (0.82-1.20) | 1.00 (ref) |
| Reduced HDL¶ or having HLD tx | 1.38 (0.68-2.77) | 1.55 (0.89-2.68) | 1.67 (1.10-2.52) | 1.55 (1.13-2.12) | 1.25 (1.03-1.53) | 1.00 (ref) |
| Metabolic Syndrome | 0.69 (0.34-1.41) | 0.95 (0.54-1.68) | 1.25 (0.82-1.90) | 1.28 (0.93-1.76) | 1.14 (0.93-1.39) | 1.00 (ref) |
| Women | | | | | | |
| Increased BMI (≥ 23 kg/m$^2$) | 1.16 (0.62-2.15) | 1.34 (0.81-2.21) | 1.45 (1.00-2.1) | 1.46 (1.10-1.94) | 1.15 (0.96-1.37) | 1.00 (ref) |
| Increased WC (≥ 80 cm) | 1.18 (0.63-2.20) | 1.32 (0.80-2.17) | 1.59 (1.10-2.29) | 1.66 (1.25-2.20) | 1.19 (1.01-1.42) | 1.00 (ref) |
| Raised BP† or having HTN tx | 0.85 (0.45-1.60) | 0.96 (0.58-1.60) | 1.14 (0.79-1.64) | 1.00 (0.76-1.33) | 1.04 (0.86-1.25) | 1.00 (ref) |
| Raised glucose‡ or having DM tx | 0.84 (0.45-1.56) | 1.03 (0.62-1.71) | 1.09 (0.75-1.56) | 1.23 (0.92-1.64) | 1.10 (0.92-1.32) | 1.00 (ref) |
| Raised TG§ or having HLD tx | 1.01 (0.55-1.87) | 1.34 (0.83-2.19) | 1.55 (1.08-2.22) | 1.56 (1.18-2.07) | 1.32 (1.10-1.57) | 1.00 (ref) |
| Reduced HDL¶ or having HLD tx | 1.00 (0.53-1.90) | 1.24 (0.75-2.04) | 1.27 (0.88-1.83) | 1.27 (0.95-1.70) | 1.10 (0.92-1.31) | 1.00 (ref) |
| Metabolic Syndrome | 0.90 (0.47-1.70) | 1.17 (0.70-1.96) | 1.41 (0.97-2.06) | 1.35 (1.01-1.80) | 1.15 (0.96-1.37) | 1.00 (ref) |

BMI, body mass index; WC, waist circumference; BP, blood pressure; HTN, hypertension; DM, diabetes mellitus; TG, triglycerides; HLD, hyperlipidemia; HDL, high-density lipoprotein.
*Model adjusted for age, household income, smoking, drinking, exercise status, and Korean National Health and Nutritional Examination Survey cycle.
†Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg.
‡Raised fasting plasma glucose (≥ 110 mg/dL).
§Raised fasting triglyceride (≥ 150 mg/dL).
¶40 mg/dL > (men) and 50 mg/dL > (women).

increased blood triacylglycerol levels in both men and women and lower HDL-cholesterol levels in men [14].

According to the Chinese famine study, early life exposure to famine was associated with metabolic syndrome. By analyzing 7874 adults from the 2002 China National Nutritional and Health Survey, exposure to famine during fetal life and early childhood was associated with three times higher risk of metabolic syndrome in adulthood compared with the non-famine exposed group (OR, 3.13; 95% CI, 1.24–7.89) [16]. By analyzing the annual physical examination data of 5040 participants from the public health center in Chongqing, China, fetal and early childhood (0–2 y) exposure to famine was associated with an increased risk for metabolic syndrome in women (fetal-exposed: OR, 1.87; 95% CI, 1.15–3.04; early-childhood–exposed: OR, 1.50; 95% CI, 1.20_1.87) [17]. From a population-based cross-sectional survey of East China with 6445 participants, fetal and childhood exposure (0–10 y) to the Chinese famine was associated with higher prevalence of metabolic syndrome in women (fetal-exposed: OR, 1.47; 95% CI, 1.05_2.07; childhood-exposed: OR, 1.80; 95% CI, 1.22–2.67) [15]. By analyzing 7915 participants from Dongfeng-Tonji cohort, early-, mid-, and late- childhood exposure to the Chinese famine was associated with increased risk for metabolic syndrome, particularly in women (early childhood–exposed women: OR, 1.26; 95% CI, 1.02–1.56; mid-childhood–exposed women: OR, 1.43; 95% CI, 1.14–1.78; late-childhood–exposed women: OR, 1.47; 95% CI, 1.18–1.84) [18]. In addition, prenatal exposure to Chinese famine was associated with type 2 diabetes, non-alcoholic fatty liver disease, hypertension, and increased BMI in adult life [19–23,37,38].

In the present study, we demonstrated that fetal and early-childhood exposures to famine were significantly associated with increased BMI, waist circumference, triacylglycerol levels, and metabolic syndrome in women. Previous famine studies also showed sex-specific results suggesting that early life exposure to malnutrition shows more profound effects on women. Exposure to the Dutch famine during early gestational stages was associated with increased BMI and waist circumference in women by age 50 y, but not in men [12]. In the Chinese famine study, effects of early life famine exposure on metabolic syndrome, non-alcoholic fatty liver disease, and increased BMI were significant in women, but not in men [15,17–19,37,38].

These sex-specific results of famine studies can be explained by the mortality selection of fetuses and the cultural background of East-Asian countries [15,39]. Boys are considered to be more susceptible to malnutrition during the fetal period. Boys tend to grow faster during the fetal period and become longer than girls in relation to their placenta size, which suggests lower nutritional reservoir capacity and greater risk for undernourishment during the gestational stage [40]. In the Dutch famine birth cohort, the percentage of male births was lower in the famine-exposed group [12]. Similarly, the effects of malnutrition during the Korean War might have increased fetal male mortality, resulting in the selection of healthier males. In addition, Korea has a lifelong history of a son-preference culture [41]. Therefore, male children may have been relatively better fed and better treated during the war than female children, which might have resulted in significant adverse health effects of malnutrition in women. However, although the results were not statistically significant, fetal and early-childhood exposure to the Korean War was positively associated with metabolic syndrome in men in the present study.

The key assumption of the developmental origin of disease hypothesis is that fetuses and infants program their bodies against unfavorable external environments to increase short-term survival [5]. However, changes in the external environment results in mismatches between personal adaptation and the environment, which might increase the risk for long-term disease development [7]. Paradoxically, adaptation to ensure increased survival might cause diseases in later life.

In the case of famine exposure, fetuses and young children program their neuroendocrine, pancreatic, skeletal muscle, and adipose tissues to prepare for an undernourishing external environment [5]. However, this adaptation leads to increased adiposity, insulin resistance, and impaired insulin secretion in later life, and these adverse health outcomes are more apparent when

individuals face improved nutritional environment later in life. For example, in the Dutch famine study, early exposure to famine during the gestational period was associated with impaired glucose tolerance, and it is believed to be mediated by defective β-cell function of the pancreas in a famine-exposed group compared with the non-famine–exposed group [35,42].

Fetal-exposed and early-childhood–exposed groups in the present study might have experienced severe malnutrition during their early life because of the Korean War. However, after the war, their nutritional status was much improved compared with their early life. Therefore, the mismatch between nutritional status during early and later life might have increased the risk for metabolic syndrome in the birth cohorts born during or just before the Korean War.

The non-exposed group born between 1954 and 1958 showed elevated risks for increased waist circumference and triacylglycerol levels in women and decreased HDL-cholesterol levels in men. However, the effect sizes were smaller compared with the fetal-exposed and early-childhood–exposed groups. Similar findings were observed in the Chinese famine studies, and these results can be partially explained by the desperate situation in the country after the Korean War or the Chinese famine. Although nutritional status was improved compared with the war period, destruction of facilities and desolate rural areas required additional time for the country to recover. Therefore, a child born after the war also could be affected by malnutrition during their early life, although the degree of malnutrition would not have been as profound as the malnutrition experienced by the birth cohorts who were born during or just before the Korean War.

Although we explained that the present study results showed effects on early life malnutrition, there could be other external stressors during the war period that also might have affected one's health in later life. Factors such as early parental loss or separation during the traumatic event may affect one's mental and physical health after the war [43,44]. Therefore, we may not conclude that increased risks for metabolic syndrome in fetal-exposed and young-childhood–exposed groups are solely from the early life experiences of malnutrition. However, it is impossible to disentangle the effects of malnutrition and other external stressors. In addition, marked decreases in agricultural productivity and an unexpected refugee life experience combined with chronic shortage of food and water during the Korean War support the hypothesis of using the Korean War as natural experiment of early life malnutrition [24,26,27].

To our knowledge, this was the first study to evaluate specific long-term health effects of childhood malnutrition, using the Korean War as a natural experiment. However, several limitations should be addressed. First, our findings are conditional to survivors enrolled in KNHANES (2007–2016). Previous studies showed increased risk for coronary heart disease or other chronic disease among famine-exposed groups. Similarly, malnutrition from the Korean War might have led to increased mortality, and survivors might be constituted by people with better health and social resources. However, such mortality selection should shift our results toward the null.

Second, owing to the cross-sectional survey design of KNHANES, ages of the study participants for each Korean War exposure groups were uneven. However, because most Koreans were exposed to the war, we were unable to find age-matched comparable control groups who were not exposed. Similar problems arose in previous Chinese famine studies, and we adjusted the age effect by including age at KNHANES enrollment in our statistical model, similar to previous Chinese famine studies [15]. In addition, if participants' age was the major determinant of metabolic syndrome, we might have observed monotonically increasing or decreasing patterns of the size of the effect estimates. However, effect estimates for the risk for metabolic syndrome were highest in the fetal-exposed or early-childhood–exposed groups in both men and women.

Third, we were unable to estimate the individual-level severity of the early life malnutrition during the Korean War period. In the Dutch famine studies, researchers directly assessed the degree of the famine using the self-administered questionnaires (by asking place of residence, experience of hunger, and degree of weight loss during the Dutch famine period) [8]. However, owing to the limited information in KNHANES data, we were unable to estimate the degree of malnutrition on an individual level. Therefore, by referring to the previous Chinese famine studies [15], we assessed the severity of malnutrition using the information of the birth year. In addition, several famine studies suggested that the health effects of fetal malnutrition may be dependent on the period of gestation (early, mid, and late gestation) [13]. Owing to the limited birth information of KNHANES, we were unable to confirm this association.

## Conclusions

The present study used the Korean War as a natural experiment for early life malnutrition experience and evaluated the risk for metabolic syndrome in adulthood according to participants' age at the beginning of the Korean War. Fetal and early childhood exposure to the Korean War was associated with increased risk for metabolic syndrome in women. Although it was not statistically significant, fetal and early-childhood exposure to the Korean War in men was also associated with increased risk for metabolic syndrome. Therefore, early experience of malnutrition during the Korean War may be associated with metabolic syndrome in adult life. Our results serve as additional evidence for the developmental origins of chronic disease hypothesis.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2019.01.003.

## References

[1] Alberti K, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–5.
[2] Lim S, Shin H, Song JH, Kwak SH, Kang SM, Yoon JW, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998–2007. Diabetes Care 2011;34:1323–8.
[3] Mozumdar A, Liguori G. Persistent increase of prevalence of metabolic syndrome among US adults: NHANES III to NHANES 1999–2006. Diabetes Care 2011;34:216–9.
[4] Barker DJP. Mothers, babies and health in later life. 2nd Edition, Churchill Livingstone, Edinburgh: Elsevier Health Sciences; 1998.
[5] Calkins K, Devaskar SU. Fetal origins of adult disease. Curr Probl Pediatr Adolesc Health Care 2011;41:158–76.
[6] Barker DJ, Osmond C, Kajantie E, Eriksson JG. Growth and chronic disease: findings in the Helsinki Birth Cohort. Ann Human Biol 2009;36:445–58.
[7] Bateson P, Barker D, Clutton-Brock T, Deb D, D'udine B, Foley RA, et al. Developmental plasticity and human health. Nature 2004;430:419.
[8] van Abeelen AF, Elias SG, Bossuyt PM, Grobbee DE, van der Schouw YT, Roseboom TJ, et al. Famine exposure in the young and the risk of type 2 diabetes in adulthood. Diabetes 2012;61:2255–60.
[9] van Abeelen AF, Elias SG, Bossuyt PM, Grobbee DE, van der Schouw YT, Roseboom TJ, et al. Cardiovascular consequences of famine in the young. Eur Heart J 2011;33:538–45.
[10] Lussana F, Painter RC, Ocke MC, Buller HR, Bossuyt PM, Roseboom TJ. Prenatal exposure to the Dutch famine is associated with a preference for fatty foods and a more atherogenic lipid profile. Am Clin Nutr 2008;88:1648–52.
[11] Painter RC, de Rooij SR, Bossuyt PM, Simmers TA, Osmond C, Barker DJ, et al. Early onset of coronary artery disease after prenatal exposure to the Dutch famine. Am J Clin Nutr 2006;84:322–7.

[12] Ravelli AC, van der Meulen JH, Osmond C, Barker DJ, Bleker OP. Obesity at the age of 50 y in men and women exposed to famine prenatally. Am J Clin Nutr 1999;70:811–6.
[13] Roseboom T, de Rooij S, Painter R. The Dutch famine and its long-term consequences for adult health. Early Hum Dev 2006;82:485–91.
[14] de Rooij SR, Painter RC, Holleman F, Bossuyt PM, Roseboom TJ. The metabolic syndrome in adults prenatally exposed to the Dutch famine. Am J Clin Nutr 2007;86:1219–24.
[15] Wang N, Wang X, Li Q, Han B, Chen Y, Zhu C, et al. The famine exposure in early life and metabolic syndrome in adulthood. Clin Nutr 2017;36:253–9.
[16] Li Y, Jaddoe VW, Qi L, He Y, Wang D, Lai J, et al. Exposure to the Chinese famine in early life and the risk of metabolic syndrome in adulthood. Diabetes Care 2011;34:1014–8.
[17] Zheng X, Wang Y, Ren W, Luo R, Zhang S, Zhang J, et al. Risk of metabolic syndrome in adults exposed to the great Chinese famine during the fetal life and early childhood. Eur J Clin Nutr 2012;66:231.
[18] Yu C, Wang J, Wang F, Han X, Hu H, Yuan J, et al. Victims of Chinese famine in early life have increased risk of metabolic syndrome in adulthood. Nutrition 2018;53:20–5.
[19] Wang N, Chen Y, Ning Z, Li Q, Han B, Zhu C, et al. Exposure to famine in early life and nonalcoholic fatty liver disease in adulthood. J Clin Endocrinol Metab 2016;101:2218–25.
[20] Wang N, Wang X, Han B, Li Q, Chen Y, Zhu C, et al. Is exposure to famine in childhood and economic development in adulthood associated with diabetes? J Clin Endocrinol Metab 2015;100:4514–23.
[21] Wang PX, Wang J-J, Lei Y-X, Xiao L, Luo Z-C. Impact of fetal and infant exposure to the Chinese Great Famine on the risk of hypertension in adulthood. PLoS One 2012;7:e49720.
[22] Li Y, He Y, Qi L, Jaddoe VW, Feskens EJ, Yang X, et al. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. Diabetes 2010;59:2400–6.
[23] Huang C, Li Z, Wang M, Martorell R. Early life exposure to the 1959–1961 Chinese famine has long-term health consequences. J Nutr 2010;140:1874–8.
[24] Lee JW. The impact of the Korean War on the Korean economy. International J Korean Stud 2001;5.
[25] David SJ, Melvin S. The wages of war, 1816–1965: a statistical handbook. New York: John Wiley and Sons; 1972.
[26] Gallop Korea. Awareness on Korean War. Seoul, South Korea: The Gallup Korea Daily Opinion; 2015.
[27] Lee C. In utero exposure to the Korean War and its long-term effects on socioeconomic and health outcomes. J Health Econ 2014;33:76–93.
[28] Kweon S, Kim Y, M-j Jang, Kim Y, Kim K, Choi S, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014;43:69–77.
[29] Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112:2735–52.
[30] Alberti KGM, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet 2005;366:1059–62.
[31] Whincup PH, Kaye SJ, Owen CG, Huxley R, Cook DG, Anazawa S, et al. Birth weight and risk of type 2 diabetes: a systematic review. JAMA 2008;300:2886–97.
[32] Mu M, Wang S-F, Sheng J, Zhao Y, Li H-Z, Hu C-L, et al. Birth weight and subsequent blood pressure: a meta-analysis. Arch Cardiovasc Dis 2012;105:99–113.
[33] Roseboom TJ, van der Meulen JH, Osmond C, Barker DJ, Ravelli AC, Bleker OP. Plasma lipid profiles in adults after prenatal exposure to the Dutch famine. Am J clin Nutr 2000;72:1101–6.
[34] Stein AD, Zybert PA, Van der Pal-de Bruin K, Lumey L. Exposure to famine during gestation, size at birth, and blood pressure at age 59 y: evidence from the Dutch Famine. Eur J Epidemiol 2006;21:759–65.
[35] Ravelli AC, van der Meulen JH, Michels R, Osmond C, Barker DJ, Hales C, et al. Glucose tolerance in adults after prenatal exposure to famine. Lancet 1998;351:173–7.
[36] Roseboom TJ, van der Meulen JH, Osmond C, Barker DJ, Ravelli AC, Schroeder-Tanka JM, et al. Coronary heart disease after prenatal exposure to the Dutch famine, 1944–45. Heart 2000;84:595–8.
[37] Wang Y, Wang X, Kong Y, Zhang JH, Zeng Q. The Great Chinese Famine leads to shorter and overweight females in Chongqing Chinese population after 50 y. Obesity 2010;18:588–92.
[38] Yang Z, Zhao W, Zhang X, Mu R, Zhai Y, Kong L, et al. Impact of famine during pregnancy and infancy on health in adulthood. Obesity Rev 2008;9:95–9.
[39] Mu R, Zhang X. Why does the Great Chinese Famine affect the male and female survivors differently? Mortality selection versus son preference. Econ Hum Biol 2011;9:92–105.
[40] Eriksson JG, Kajantie E, Osmond C, Thornburg K, Barker DJ. Boys live dangerously in the womb. Am J Hum Biol 2010;22:330–5.
[41] Das Gupta M, Zhenghua J, Bohua L, Zhenming X, Chung W, Hwa-Ok B. Why is son preference so persistent in East and South Asia? A cross-country study of China, India and the Republic of Korea. J Int Dev 2003;40:153–87.
[42] De Rooij SR, Painter RC, Phillips DI, Osmond C, Michels RP, Godsland IF, et al. Impaired insulin secretion after prenatal exposure to the Dutch famine. Diabetes Care 2006;29:1897–901.
[43] Catani C, Jacob N, Schauer E, Kohila M, Neuner F. Family violence, war, and natural disasters: a study of the effect of extreme stress on children's mental health in Sri Lanka. BMC Psychiatry 2008;8:33.
[44] Alastalo H, Räikkönen K, Pesonen A-K, Osmond C, Barker DJ, Kajantie E, et al. Cardiovascular health of Finnish war evacuees 60 years later. Ann Med 2009;41:66–72.