

# **Supplemental Material**

**Table S1. Odds ratio (95% confidence interval) for Cardiovascular Diseases risks according to famine exposure.**

<b>All participants (N=234219)</b>	<b>Non-exposed (1963-1974) N=54525</b>	<b>Fetal-exposed (1959-1962) N=29387</b>	<b>Childhood-exposed (1949-1958) N=102370</b>	<b>Adolescent-exposed (1941-1948) N=47937</b>
<b>Total CVD [Case (%)]</b>	593(1.09)	750(2.55)	5836(5.70)	5382(11.23)
Model 1 *	1.00 (ref.)	<b>1.34 (1.19-1.50)</b>	<b>1.57 (1.38-1.78)</b>	<b>1.49 (1.25-1.78)</b>
Model 2 †	1.00 (ref.)	<b>1.35 (1.20-1.52)</b>	<b>1.60 (1.41-1.82)</b>	<b>1.55 (1.30-1.86)</b>
Model 3 #	1.00 (ref.)	<b>1.16 (1.02-1.30)</b>	<b>1.23 (1.07-1.41)</b>	1.15 (0.96-1.39)
<b>MI [Case (%)]</b>	55(0.10)	62(0.21)	442(0.43)	325(0.68)
Model 1 *	1.00 (ref.)	<b>1.57 (1.06-2.32)</b>	<b>2.14 (1.47-3.12)</b>	<b>1.97 (1.20-3.23)</b>
Model 2 †	1.00 (ref.)	<b>1.51 (1.01-2.24)</b>	<b>2.00 (1.36-2.93)</b>	<b>1.85 (1.12-3.07)</b>
Model 3 #	1.00 (ref.)	1.36 (0.91-2.05)	<b>1.65 (1.05-2.59)</b>	1.42 (0.78-2.61)
<b>Stroke [Case (%)]</b>	145(0.27)	170(0.58)	1335(1.30)	1263(2.63)
Model 1 *	1.00 (ref.)	<b>1.34 (1.06-1.70)</b>	<b>1.66 (1.33-2.08)</b>	<b>1.68 (1.25-2.25)</b>
Model 2 †	1.00 (ref.)	<b>1.37 (1.08-1.73)</b>	<b>1.72 (1.37-2.17)</b>	<b>1.80 (1.34-2.43)</b>
Model 3 #	1.00 (ref.)	1.11 (0.87-1.41)	1.17 (0.91-1.50)	1.07 (0.77-1.49)
<b>CHD [Case (%)]</b>	422(0.77)	561(1.91)	4452(4.35)	4171(8.70)
Model 1 *	1.00 (ref.)	<b>1.42 (1.24-1.63)</b>	<b>1.77 (1.53-2.05)</b>	<b>1.79 (1.47-2.19)</b>
Model 2 †	1.00 (ref.)	<b>1.45 (1.27-1.67)</b>	<b>1.84 (1.59-2.14)</b>	<b>1.91 (1.56-2.34)</b>
Model 3 #	1.00 (ref.)	<b>1.22 (1.06-1.41)</b>	<b>1.36 (1.17-1.59)</b>	<b>1.34 (1.09-1.65)</b>

\* Model 1 adjusted for age, sex, BMI, education status, smoking and drinking status, physical activity, famine severity, healthy diet (yes/no), components of metabolic syndrome (hypertension/central obesity/elevated TG/decreased HDL-c/hyperglycemia);

† Model 2 adjusted for age, sex, BMI, education status, smoking and drinking status, physical activity, famine severity, healthy diet (yes/no), metabolic syndrome (yes/no), area (rural/urban), economic status (high/low), marriage status (married/unmarried/cohabitation/divorced/separated/widowed/other), occupation (worker/farmer/soldier/cadre/medical/self-employed/businessman/government officials/housewife/retired/other);

# Model 3 adjusted for natural logarithm-transformed age, sex, BMI, education status, smoking and drinking status, physical activity, famine severity, healthy diet (yes/no), and metabolic syndrome.

CVD: cardiovascular disease; MI: myocardial infarction; CHD: coronary heart disease.

Significant results in bold.

**Table S2. Odds ratio (95% confidence interval) for Cardiovascular Diseases risks according to famine severity.**

<b>All participants (N=234219)</b>	<b>Fetal-exposed (1959-1962) N=29387</b>	<b>Childhood-exposed (1949-1958) N=102370</b>	<b>Adolescent-exposed (1941-1948) N=47937</b>
<b>Total CVD</b>			
Less severely affected famine area	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Severely affected famine area	<b>1.84 (1.52-2.22)</b>	<b>1.87 (1.75-2.00)</b>	<b>1.69 (1.57-1.82)</b>
<b>MI</b>			
Less severely affected famine area	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Severely affected famine area	1.28 (0.63-2.58)	<b>1.68 (1.32-2.14)</b>	<b>1.53 (1.16-2.01)</b>
<b>Stroke</b>			
Less severely affected famine area	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Severely affected famine area	<b>1.48 (1.01-2.17)</b>	<b>1.64 (1.43-1.88)</b>	<b>1.34 (1.16-1.56)</b>
<b>CHD</b>			
Less severely affected famine area	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
Severely affected famine area	<b>2.06 (1.65-2.56)</b>	<b>2.00 (1.85-2.15)</b>	<b>1.75 (1.61-1.90)</b>

Adjusted for age, sex, BMI, education status, smoking and drinking status, physical activity, famine severity, healthy diet (yes/no), metabolic syndrome, area (rural/urban), economic status (high/low), marriage status (married/unmarried/cohabitation/divorced/separated/widowed/other), occupation (worker/farmer/soldier/cadre/medical/self-employed/businessman/government officials/housewife/retired/ other);

CVD: cardiovascular disease; MI: myocardial infarction; CHD: coronary heart disease. Significant results in bold.

**Table S3. Odds ratio (95% confidence interval) for Cardiovascular Diseases risks using the younger and older exposure groups as reference.**

	<b>Non-exposed (1963-1966) + Adolescent-exposed (1945-1948)</b>	<b>Fetal-exposed (1959-1962)</b>	<b>Childhood-exposed (1955-1958)</b>
<b>Total CVD</b>			
Model 1	1.00 (ref)	<b>1.17 (1.07-1.28)</b>	<b>1.23 (1.18-1.28)</b>
Model 2	1.00 (ref)	<b>1.14 (1.04-1.25)</b>	<b>1.20 (1.15-1.26)</b>
<b>MI</b>			
Model 1	1.00 (ref)	1.08 (0.81-1.44)	<b>1.29 (1.12-1.49)</b>
Model 2	1.00 (ref)	1.10 (0.81-1.48)	<b>1.32 (1.14-1.53)</b>
<b>Stroke</b>			
Model 1	1.00 (ref)	1.05 (0.87-1.25)	<b>1.17 (1.07-1.27)</b>
Model 2	1.00 (ref)	1.05 (0.87-1.27)	<b>1.16 (1.07-1.27)</b>
<b>CHD</b>			
Model 1	1.00 (ref)	<b>1.15 (1.04-1.28)</b>	<b>1.23 (1.17-1.29)</b>
Model 2	1.00 (ref)	<b>1.13 (1.01-1.25)</b>	<b>1.20 (1.14-1.26)</b>

Model 1 adjusted for age and sex; Model 2 was further adjusted for BMI, education status, smoking and drinking status, physical activity, famine severity, healthy diet (yes/no), metabolic syndrome (yes/no).

Significant results in bold.

**Figure S1. Study population selection and classification.**

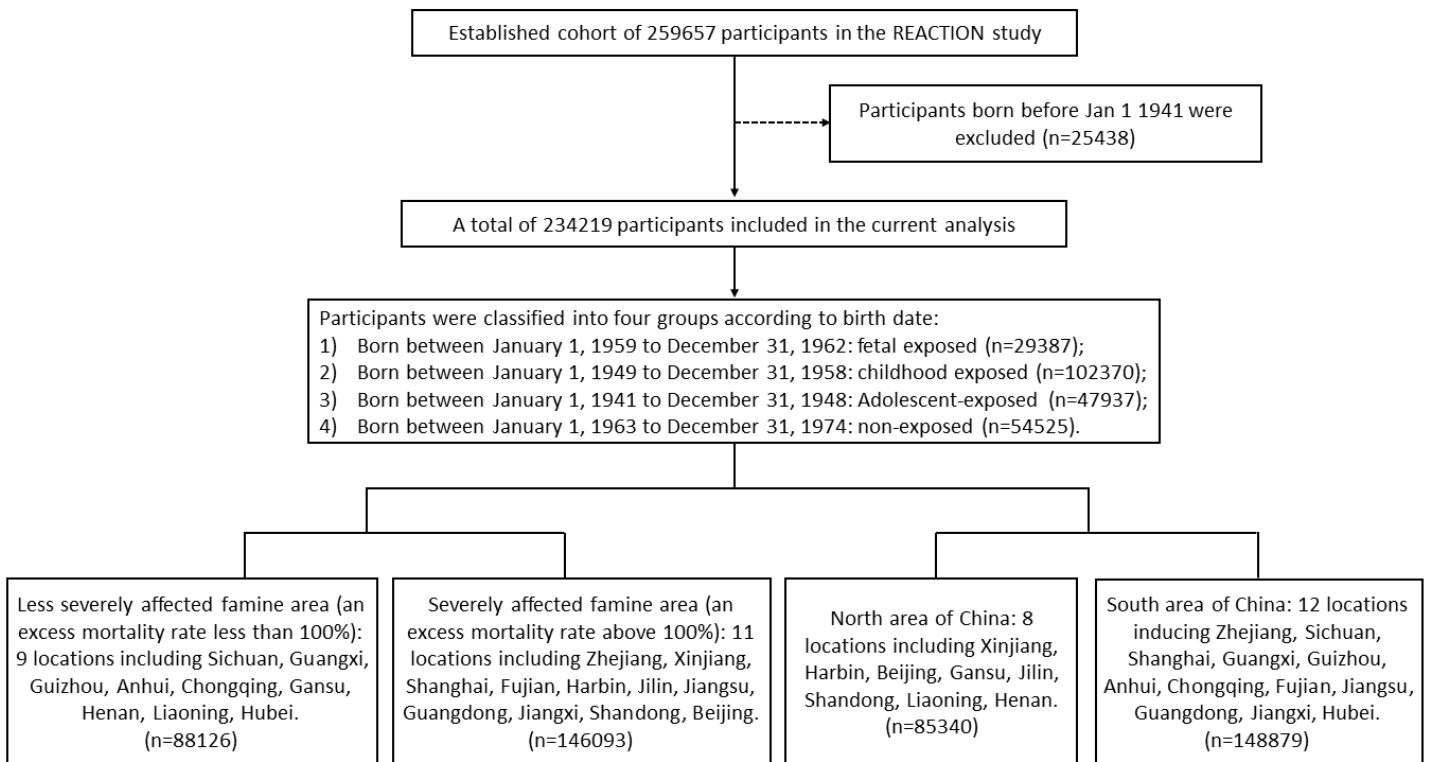


Figure S2. Famine severity and risk of CVD among men (a, b, c) and women (d, e, f).

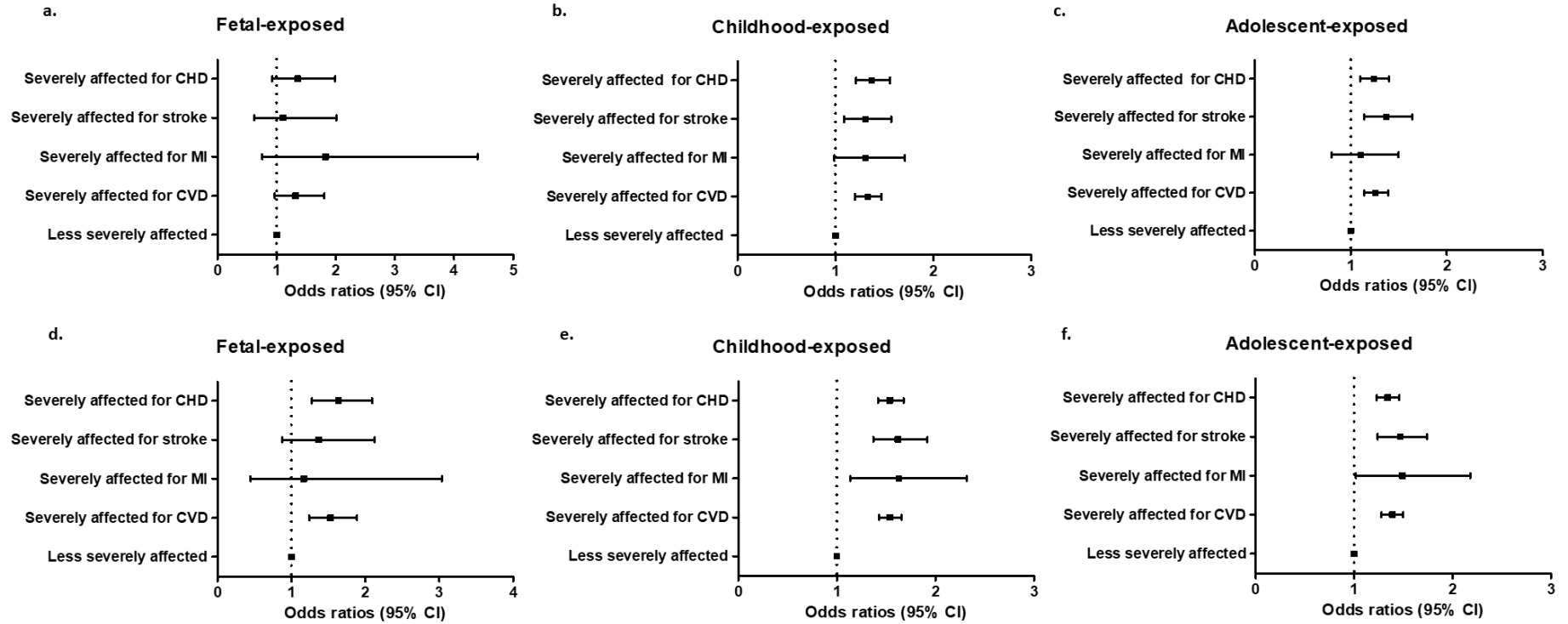
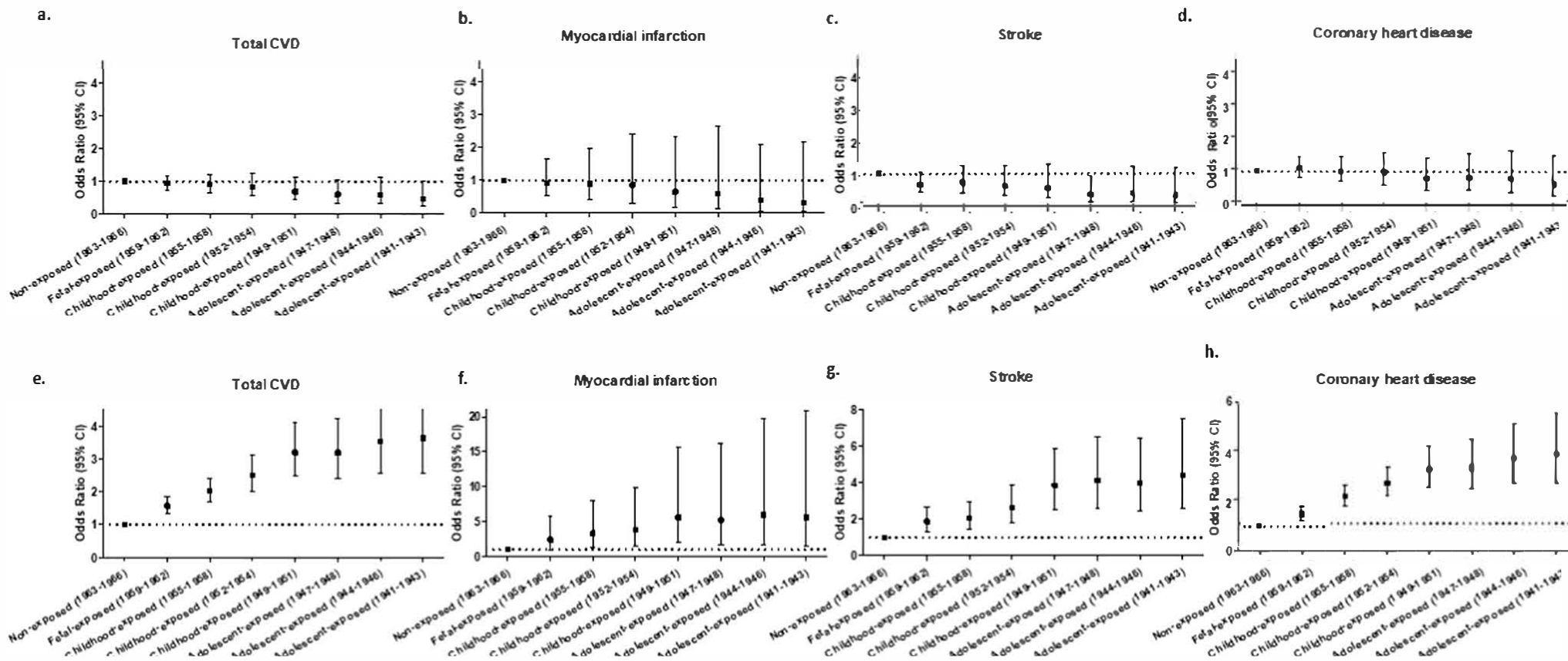
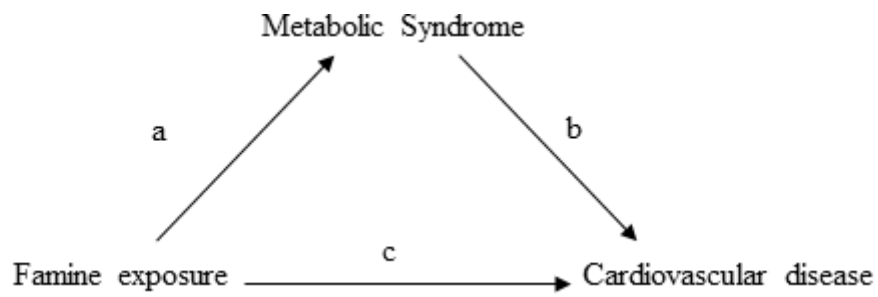


Figure S3. Finer classification according to famine exposure duration in the estimation of risk for CVD in men (a, b, c, d) and women (e, f, g, h).





<u>Path</u>	<u>Effect</u>	<u>95%CI</u>	<u>P value</u>
a	0.0098	0.0049~ 0.0147	<0.0001
b	0.0213	0.0191~ 0.0235	<0.0001
c	-0.0070	-0.0095~ -0.0045	<0.0001
c'	-0.0072	-0.0097~ -0.0047	<0.0001

**Supplementary Figure 4.** Mediation analysis of MetS with famine exposure for CVD risk.