

Sex-specific effects of fetal exposure to the 1959-61 Chinese Famine on risk of adult hypertension

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Background

- Adverse exposure/ undernutrition in fetal growth → adult chronic disease
 - Adult body size
 - Diabetes
 - Cardiovascular disease (CVD)
 - BP/hypertension??
- Most studies performed in European cohorts, short duration (i.e. Dutch Hunger Winter famine [5 mo.], Siege of Leningrad [28 mo.])

Chinese Famine

- “Three years of natural disasters”, “Three years of difficult period” ... “Three bitter years”
- Great Leap Forward: Mao Zedong
- 1959-1961
- Rural farms → communes
 - Prohibited private farm ownership
 - Fewer farmers
- Drought, floods, policy changes → nationwide famine

Chinese Famine (2)

- Crop production: ↓ from 200 million tons (1958) to 143.5 million tons (1960)
- Population: ↓ by ~13.5 million
- Birth rate: ↓ 2.9% (1958) to 2.1% (1960)
- Death rate: ↑ from 1.2% (1958) to 2.5% (1960)
 - “15 million excess deaths”

Chinese Famine (3)

- US Collaborative Project for NTD Prevention: increased hypertension in those from rural areas with postnatal exposure to famine
- 2002 China National Nutrition and Health Survey (CNNHS): higher BP, hypertension risk in those who lived in severely affected areas

Purpose

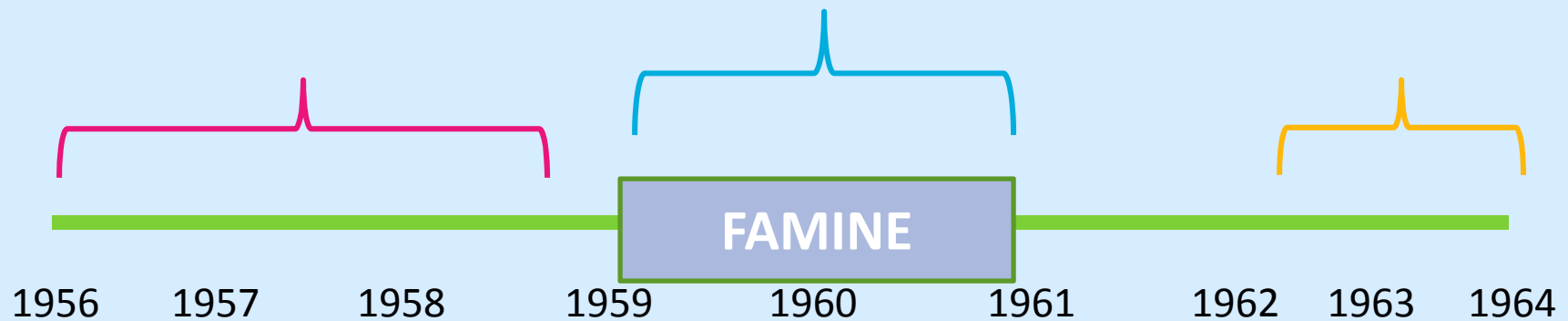
- Using 2009 follow-up data on famine cohort from China Health and Nutrition Survey, explore whether persons prenatally exposed to famine have increased risk of hypertension in adulthood (middle-age)

Methods

- Retrospective cohort study
 - Longitudinal data from CHNS
- Subjects: Participants in 2009 CHNS
 - 9 provinces in China
 - Born between Sept 1, 1956–Dec 31, 1964
 - n= 1415 (734 ♀, 681 ♂)
- Counties stratified on income, weighted sampling → random selection of 4 counties

Variables

- Exposure
 - Fetal-infant: born 10/1/1959–9/30/1961
 - Early childhood: born 10/1/1956–9/30/1958
 - Post-famine: born 10/1/1962–9/30/1964



Variables (2)

- Outcome
 - Hypertension (BP measurement, self-report, medication)
- Covariates
 - Marital status, BMI, waist circumference, tobacco or alcohol use

Analysis

- Descriptive statistics
- Chi-square/ ANOVA
- Multivariable linear regression
- Multivariable logistic regression
- Stratified analysis: men and women separately

Table 1 Demographic and health characteristics of men and women born in China 1959–1961 by exposure cohort, China Health and Nutrition Survey, 2009

	Timing of exposure to famine			<i>P</i> value
	Unexposed (n = 623)	Fetal exposed (n = 321)	Early child exposed (n = 471)	
Birth date	10/1/1962–9/30/1964	10/1/1959–9/30/1961	10/1/1956–9/30/1958	
	n (%)	n (%)	n (%)	
Sex, female	313 (50.2)	169 (52.6)	252 (53.5)	0.54
Smoking, yes (%)				
Men	210 (67.7)	107 (70.4)	145 (66.2)	0.70
Women	10 (3.2)	3 (1.8)	11 (4.4)	0.34
All subjects	220 (35.3)	110 (34.3)	156 (33.1)	0.75
Alcohol use, yes (%)				
Men	222 (71.6)	99 (65.1)	149 (68.0)	0.34
Women	38 (12.1)	18 (10.7)	18 (7.1)	0.14
All subjects	260 (41.7)	117 (36.4)	167 (35.5)	0.08
Marital status, yes (%)				
Men	289 (93.2)	144 (94.7)	205 (93.6)	0.82
Women	298 (95.2)	157 (92.9)	240 (95.2)	0.50
All subjects	587 (94.2)	301 (93.8)	445 (94.5)	0.92

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	Timing of exposure to famine			<i>P</i> value
	Unexposed (n = 623)	Fetal exposed (n = 321)	Early child exposed (n = 471)	
Birth date	10/1/1962–9/30/1964 Mean (SD)	10/1/1959–9/30/1961 Mean (SD)	10/1/1956–9/30/1958 Mean (SD)	<i>P</i> value
Age				
Men	46.06 (0.63)	49.22 (0.57)	51.96 (0.63)	<0.01
Women	46.07 (0.57)	49.10 (0.60)	52.09 (0.60)	<0.01
All subjects	46.07 (0.60)	49.16 (0.59)	52.03 (0.62)	<0.01
Weight (kg)				
Men	68.75 (11.00)	68.61 (10.60)	65.93 (10.41)	0.01
Women	60.30 (9.52)	59.16 (9.81)	59.39 (9.87)	0.39
All subjects	64.46 (11.10)	63.64 (11.22)	62.36 (10.62)	0.01
Height (cm)				
Men	168.40 (6.40)	167.31 (5.93)	166.78 (6.08)	0.01
Women	158.22 (5.32)	156.36 (6.01)	156.46 (5.75)	<0.01
All subjects	163.24 (7.77)	161.55 (8.10)	161.17 (7.83)	<0.01
BMI (kg/m ²)				
Men	24.17 (3.23)	24.41 (3.26)	23.64 (3.12)	0.07
Women	24.07 (3.47)	24.15 (3.34)	24.23 (3.57)	0.86
All subjects	24.12 (3.35)	24.27 (3.30)	23.96 (3.38)	0.45
Waist circumference (cm)				
Men	86.36 (10.06)	85.83 (10.35)	85.65 (9.67)	0.71
Women	81.30 (8.96)	82.19 (9.75)	83.21 (10.63)	0.08
All subjects	83.80 (9.84)	83.90 (10.18)	84.32 (10.27)	0.71

Table 2 Mean blood pressure (Mean \pm SD) and prevalence (%) of hypertension among the unexposed (C1), fetal-infant exposed (C2) and early child exposed (C3) cohorts from the China Health and Nutrition Survey, 2009

	Unexposed (C1)	Fetal exposed (C2)	Early child exposed (C3)	C2 versus C1 D (95 % CI)	C3 versus C1 D (95 % CI)	C3 versus C2 D (95 % CI)
Systolic blood pressure (SBP)^a						
Men	124.13 (13.94)	125.32 (15.27)	126.00 (14.16)	1.19 (-1.51-3.89)	2.55 (0.23-4.88)*	-1.68 (-4.64-1.27)
Women	119.74 (14.52)	124.18 (16.96)	123.93 (16.21)	4.24 (1.50-6.98)**	3.86 (1.48-6.25)**	0.48 (-2.55-3.50)
All subjects)	121.93 (14.39)	124.72 (16.17)	124.89 (15.31)	2.75 (0.83-4.66)**	3.21 (1.54-4.88)**	-0.46 (-2.56-1.64)
Diastolic blood pressure (DBP)^a						
Men	83.44 (10.09)	82.52 (10.97)	83.75 (10.09)	-1.00 (-2.91-0.92)	0.74 (-0.95-2.43)	-1.84 (-3.96-0.28)
Women	79.03 (9.99)	81.04 (11.56)	81.33 (8.96)	1.80 (-0.05-3.64)	1.88 (0.41-3.36)*	0.01 (-1.87-1.89)
All subjects	81.22 (10.27)	81.74 (11.29)	82.46 (9.57)	0.48 (-0.85-1.80)	1.35 (0.23-2.47)*	-0.76 (-2.16-0.64)

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	Unexposed (C1)	Fetal exposed (C2)	Early child exposed (C3)	C2 versus C1	C3 versus C1	C3 versus C2
	N (%)	N (%)	N (%)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
Diagnosis of hypertension						
Men	32 (10.3)	18 (11.8)	22 (10.0)	1.09 (0.58–2.06)	1.07 (0.60–1.94)	1.02 (0.52–2.04)
Women	22 (7.0)	24 (14.2)	32 (12.7)	2.16 (1.16–4.02)*	1.87 (1.03–3.39)*	1.33 (0.73–2.45)
All subjects	54 (8.7)	42 (15.1)	54 (11.5)	1.57 (1.02–2.44)*	1.41 (0.93–2.12)	1.16 (0.74–1.82)
Currently taking anti-hypertension drugs						
Men	24 (7.7)	14 (9.2)	14 (6.4)	1.13 (0.55–2.32)	0.91 (0.45–1.85)	1.19 (0.53–2.66)
Women	13 (4.2)	19 (11.2)	25 (9.9)	2.81 (1.32–5.97)**	2.45 (1.19–5.05)*	1.33 (0.69–2.59)
All subjects	37 (5.9)	33 (10.3)	39 (8.3)	1.82 (1.10–3.01)*	1.50 (0.93–2.44)	1.26 (0.76–2.09)
Systolic hypertension (SBP \geq 140)						
Men	37 (11.9)	23 (15.1)	37 (16.9)	1.32 (0.74–2.36)	1.65 (0.99–2.74)	0.74 (0.41–1.34)
Women	26 (8.3)	25 (14.8)	36 (14.3)	2.01 (1.09–3.70)*	1.83 (1.04–3.22)*	1.12 (0.63–1.99)
All subjects	63 (10.1)	48 (15.0)	73 (15.5)	1.58 (1.05–2.40)*	1.71 (1.18–2.48)*	0.93 (0.62–1.40)
Diastolic hypertension (DBP \geq 90)						
Men	70 (22.6)	31 (20.4)	46 (21.0)	0.86 (0.52–1.42)	0.98 (0.64–1.51)	0.81 (0.47–1.39)
Women	43 (13.7)	34 (20.1)	42 (16.7)	1.60 (0.95–2.70)	1.12 (0.68–1.85)	1.41 (0.83–2.42)
All subjects	113 (18.1)	65 (20.2)	88 (18.7)	1.15 (0.80–1.64)	1.04 (0.76–1.44)	1.10 (0.76–1.60)
Adult hypertension^b						
Men	86 (27.7)	42 (27.6)	67 (30.6)	0.97 (0.61–1.54)	1.26 (0.85–1.86)	0.74 (0.46–1.21)
Women	55 (17.6)	43 (25.4)	71 (28.2)	1.62 (1.01–2.61)*	1.78 (1.15–2.74)**	0.94 (0.59–1.52)
All subjects	141 (22.6)	85 (26.5)	138 (29.5)	1.24 (0.90–1.73)	1.48 (1.11–1.98)**	0.85 (0.61–1.19)

Discussion

- Strengths of study
 - Large time period
 - Sex-specific effects
 - Unique population
- Weaknesses
 - Relatively small sample size
 - Measure of “exposure”
 - No one truly “unexposed”

More for discussion

- Fit Bradford-Hill Criteria?
- Other covariates to consider?
- Meaningful results?