Does childhood meat eating contribute to sex differences in risk factors for ischaemic heart disease in a developing population?

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ABSTRACT

Background A male epidemic of ischaemic heart disease (IHD) emerges with economic development. It has previously been hypothesised that this epidemic is due to nutritionally driven levels of pubertal sex steroids, which lead to a more atherogenic body shape and lipid profile in boys but not girls, without any sex-specific effects on glucose metabolism. This study tests this hypothesis by examining the association of childhood meat eating with IHD risk in a developing Chinese population.

Methods Multivariable linear and censored regression was used in a cross-sectional study of 19 418 Chinese older (≥50 years) men and women from the Guangzhou Biobank Cohort Study (phases 2 and 3) to assess the adjusted associations of childhood meat eating with waist to hip ratio (WHR), high-density lipoprotein cholesterol and fasting plasma glucose.

Results Adjusted for age, childhood hunger, life-course socioeconomic position and current lifestyle childhood almost daily meat eating compared with less than weekly meat eating was associated with higher WHR (0.007, 95% CI 0.0003 to 0.01) in men but not women. No association with fasting glucose was observed.

Conclusions Given the potential limitations of this study, especially the crude nature of the exposure and modest findings, the results should be considered as preliminary. However, they do lend support to the hypothesis that the male epidemic of premature IHD and sexual divergence in IHD rates that occur with economic development may be nutritionally driven in childhood. In elucidating the developmental origins of non-communicable chronic diseases, more attention should be focused on the sociohistorical context and the role of puberty.

An epidemic of premature ischaemic heart disease (IHD) occurred in the 20th century in men in most industrialised countries, with sex differences in IHD mortality becoming more evident in the later half of the 20th century.[1 2] It is not yet clear why IHD mortality rose so rapidly in men compared with women. We have previously suggested, based on physiological evidence elsewhere[3–6] and our results in China,[7–12] that with economic development nutritionally driven differences in sex steroids and pubertal development have sex-specific effects on lipids and fat patterning, but not diabetes, which are detrimental in men and protective in women.[7–9 11] Consistent with this postulate, some aspects of IHD risk, such as high-density lipoprotein (HDL) cholesterol are known to be context specific, suggesting environmental factors may play a role.[13] Moreover, with economic development in the west, there has been some increase in the rate of diabetes in men compared with women but not to the same extent as IHD.[14]

We have previously shown in recently developed or developing populations that generally less limited childhood environments are associated with a higher risk of IHD mortality or a more atherogenic lipid profile and body shape in men but not women, perhaps mediated by nutrition.[7–9] Pubertal diet affects sex steroids and pubertal development in humans[15–17] and animals, in whom underfeeding reduces testosterone[18 19] and oestrogen levels.[20] Testosterone is associated with lower HDL-cholesterol and oestrogen with higher HDL-cholesterol in pubertal boys and girls, respectively.[4] Diet has sex-specific effects on HDL-cholesterol in adolescents,[21 22] in whom, for example, greater energy and lower carbohydrate and fat intake have been associated with higher HDL-cholesterol in girls only.[21] During puberty, and not before, and driven largely by sex steroids, marked sexual dimorphism in body shape and composition emerges.[23] Girls develop a more gynecoid body shape (increased fat around the hips) and boys a more android body shape (increased abdominal fat).[23]

We took advantage of a sample of older people from southern China to test two related hypotheses concerning the developmental origins of IHD. Does childhood meat eating have sex-specific associations with body shape (measured by the waist to hip ratio; WHR) and lipid profile (measured by HDL-cholesterol)? Conversely, are the same exposures associated with fasting glucose for either or both sexes? For completeness we examined the relation of childhood meat eating with systolic blood pressure (SBP) and diastolic blood pressure (DBP) and fasting low-density lipoprotein (LDL) cholesterol.

MATERIALS AND METHODS

Participants

The Guangzhou Biobank Cohort Study is an ongoing collaboration among the Guangzhou People's Number 12 Hospital, the Universities of Hong Kong and Birmingham, which has been described in detail elsewhere.[24] Recruitment of participants draws from 'The Guangzhou Health and Happiness Association for the Respectable Elders' (GHHARE), a community social and welfare association unofficially aligned with the municipal government in which membership is open to older persons for a monthly fee of 4 Yuan (50 US cents). Approximately 7% of permanent Guangzhou residents aged 50 years and over are members of GHHARE, of whom 11% (approximately 10 000 participants) enrolled each time for phases one, two and three and were included if they were capable of consenting, were ambulatory and were not receiving treatment modalities that if omitted may result in immediate life-threatening risk, such as chemotherapy or radiotherapy for cancer, or dialysis for renal failure. Those with less immediate risk, such as a history of vascular disease or associated risk factors, including diabetes and hypertension, were not excluded from the study. Of those eligible, 90% of the men and 99% of the women participated. We added questions about the participant's family background in phase 2, recruited from April 2005 to May 2006, which were also included in phase 3 (September 2006 to January 2008). These questions included recollection of childhood environment and experiences. The Guangzhou Medical Ethics Committee of the Chinese Medical Association approved the study and all participants gave written, informed consent before participation.

Participants underwent a detailed medical interview and a physical examination. In brief, seated blood pressure was taken as the average of the last two of three measurements, using the Omron 705CP sphygmomanometer (Omron Corporation, Kyoto, Japan). Fasting total serum cholesterol, HDL-cholesterol, LDL-cholesterol and fasting plasma glucose levels were determined by Shimadzu CL-8000 Automatic Chemical Analyzer (Shimadzu Corporation, Kyoto, Japan) in the hospital laboratory. Waist circumference was measured as the smallest horizontal circumference between the ribs and iliac crest, or, for obese participants, the circumference at the level of the navel. Hip circumference was measured at the greatest circumference around the buttocks below the iliac crest. WHR was calculated as the ratio of waist circumference to hip circumference.

Historical nutritional setting

Undernutrition was common in China until recently, because essentially pre-industrial conditions prevailed until the mid 20th century.[25] Diet was limited to cereals (mainly rice in southern China), vegetables, few animal foods and negligible dairy products.[26] Living standards improved following the establishment of the People's Republic of China in 1949. Between 1952 and 1973 the intake of animal protein increased from 11 kg to 13 kg per capita per year,[26 27] although was much lower than current intakes in urban China (65.3 kg) or the USA (112 kg).[26 27]

Outcomes

In total, six outcome measures of IHD risk were considered: WHR, HDL-cholesterol, SBP and DBP and LDL-cholesterol. The main outcomes were WHR and HDL-cholesterol, risk factors for IHD in which sexual dimorphism becomes more pronounced at puberty due to the action of sex steroids. With pubertal development, WHR increases in males and decreases in females,[28] while HDL-cholesterol falls in males and remains constant in females.[3 6 29] Compared with other measures of adiposity, WHR is one of the best predictors of IHD.[30] A secondary outcome was a risk factor for IHD whose precursors also change at puberty but more likely as a function of growth hormone rather than sex steroids, that is, fasting plasma glucose.[31] For completeness, we also considered the other biological risk factors in the Framingham equation, that is SBP and DBP and fasting LDL-cholesterol as outcomes. SBP increases during puberty but to a greater extent in boys.[32] LDL-cholesterol does not show sex-specific changes during puberty.[6]

Childhood socioeconomic position

Contemporaneous information on the participant's childhood conditions is not available in this or similar settings. Instead, we specifically selected a set of broad markers of family living conditions, similar to proxies such as car ownership in the west, using possession of simple, notable items appropriate to China in the mid-20th century.[33 34] We asked about parental possession of three items during the participants' childhood: a watch, a sewing machine and a bicycle. Childhood socioeconomic position (SEP) was categorised as low (no such parental possessions), medium (one or two) and high (all three) as previously.[7]

Exposure

Childhood meat eating was assessed by asking participants how frequently they ate meat in childhood as 'never', 'yearly', 'monthly', 'about once a week' or 'almost daily'. Fewer than 1% reported 'never' eating meat in childhood; 'monthly' and 'yearly' meat eating represented similar, minimal meat intake, therefore these three categories were combined into one group giving a three-point scale: 'less than weekly', 'about 1 day per week' and 'almost daily'.

Statistical analysis

Multivariable censored regression[35] was used to assess the association of childhood meat eating with HDL-cholesterol, fasting blood glucose, LDL-cholesterol, and SBP and DBP because some people were taking medication for hypertension (n=4093), lipids (n=1177) or diabetes (n=1316). Multivariable linear regression was used to assess the association of childhood meat eating with WHR. From these models we reported adjusted mean differences (β) with 95% CI. Potential confounders considered, categorised as per table 1, were age, educational level, childhood SEP, recall of childhood hunger, current annual personal income, job type, smoking status, alcohol use, physical activity. We present two models: model 1 adjusted for age; model 2 additionally adjusted for all other potential confounders listed above.

We examined whether the effects of meat eating were consistent by sex from the heterogeneity of effect across strata and statistical significance of the interaction term between sex and meat eating. In addition, as some outcomes have different associations with age by sex, and meat eating is correlated with age, we also included an interaction term between sex and age when assessing whether the association of meat eating with any of the outcomes varied by sex. We similarly examined whether the effects of meat eating were consistent by age, using age as a continuous variable. Finally, we also examined for the statistical significance of a combined interaction term for age, sex and meat eating.

Linear regression was used to assess the association of childhood meat eating with validation outcomes of height in men and women, age of menarche in women and age of pubertal landmarks in men, adjusted for sex (if appropriate).

Data analysis was performed using STATA version 8.2.

RESULTS

Of the 20 077 participants there were 5375 men and 14 702 women. Of these, 5172 men (96%) and 14 243 women (97%) had complete data for all variables. Men were aged from 50 to 96 years, with a mean of 63.1 years (SD 7.0). Women were aged from 50 to 95 years, mean of 59.5 years (SD 7.1). Childhood meat eating was similar in men and women, with 52.6% of men

Table 1 Participant characteristics by sex and childhood meat eating (figures given as % unless indicated otherwise)

	Men					Women				
	Almost daily meat eating (n=542)	Meat eating about 1 day/week (n=1912)	Less than weekly meat eating (n=2718)	Overall (n=5172)	p Value†	Almost daily meat eating (n=1710)	Meat eating about 1 day/week (n=5311)	Less than weekly meat eating (n=7225)	Overall (n=14246)	p Value†
Age group (years)										
≥70	19.0	14.7	22.3	19.2	<0.001	9.4	7.6	13.9	11	<0.001
65-69	20.7	19.4	23.1	21.5		11.6	11.0	15.3	13.3	
60-64	24.7	26.7	23.1	24.6		15.3	14.4	17.4	16	
55-59	20.7	23.2	20.9	21.7		23.9	28.3	26.6	26.9	
50-54	14.9	16.1	10.5	13.0		39.8	38.7	26.8	32.8	
Childhood hunger										
Never	79.3	64.7	49.3	58.1	<0.001	85.8	73.0	53.7	64.8	<0.001
Less than weekly	15.7	23.0	20.6	21.0		11.0	18.8	20.5	18.7	
At least weekly	5.0	12.3	30.1	20.9		3.2	8.2	25.7	16.5	
Highest educational attainment‡										
Less than primary	1.1	1.0	4.0	2.6	<0.001	3.6	5.7	16.2	10.8	<0.001
Primary	19.2	21.1	31.0	26.1		22.6	26.4	39.0	32.3	
Junior middle	25.8	32.5	29.1	30.0		29.2	30.2	24.3	27.1	
Senior middle or higher	53.9	45.4	36.0	41.3		44.6	37.8	20.6	29.9	
Childhood SEP§										
Low	33.3	55.7	80.8	66.5	<0.001	24.5	45.3	74.6	57.6	<0.001
Medium	20.5	22.6	11.6	16.6		23.2	25.4	15.5	20.1	
High	46.1	21.7	7.6	16.9		52.3	29.3	10.0	22.3	
Occupational type										
Manual¶	51.2	52.5	55.9	54.2	0.100	54.9	61.7	71.4	65.8	<0.001
Non-manual	33.3	31.8	29.9	30.9		23.2	18.4	11.5	15.5	
Other	15.5	15.7	14.2	14.9		21.9	19.9	17.1	18.7	
Current annual personal income (8 Yuan=US$1)										
≤10 000 Yuan	21.4	21.1	25.4	23.4	0.001	22.3	27.0	40.5	33.3	<0.001
10–15 000 Yuan	36.4	37.0	37.7	37.3		54.7	53.9	44.1	49	
>15 000 Yuan	38.2	36.1	32.4	34.4		21.1	16.7	10.9	14.3	
Don't know	4.1	5.8	4.6	5.0		1.9	2.4	4.5	3.4	
Physical activity (IPAQ)										
Inactive	12.9	12.5	12.2	12.4	0.030	11.1	12.3	11.3	11.6	0.080
Minimally active	42.8	49.5	46.1	47.0		40.1	42.1	42.4	42	
HEPA active††	44.3	38.0	41.7	40.6		48.8	45.6	46.3	46.3	
Smoking status										
Never	34.7	41.1	37.1	38.3	0.006	96.8	97.4	96.7	97	<0.001
Ex-smoker	28.4	25.7	29.5	28.0		1.1	0.7	1.6	1.2	
Current	36.4	33.0	32.9	33.3		1.4	1.5	1.5	1.5	
Alcohol use										
Never	42.9	47.4	48.2	47.3	0.010	68.7	71.7	74.9	73.0	<0.001
<1/week	31.8	29.7	27.9	29.0		25.2	22.7	18.9	21.1	
1–4/week	5.9	7.9	6.2	6.8		1.7	1.6	1.8	1.7	
≥5/week	14.0	9.8	11.8	11.3		1.4	1.2	1.4	1.3	
Ex-drinker	5.5	5.3	5.9	5.6		3.0	2.9	2.9	2.9	

*p<0.05; **p<0.01; ***p<0.001.
†For unadjusted comparisons using χ^2 analyses.
‡These correspond approximately to the following number of years of schooling, less than primary: no formal education, primary school: 0–6 years, junior middle: 7–9 years, and senior middle or higher: ≥10 years.
§These correspond to parental possession of none (low), 1–2 (medium) and 3 (high) of: sewing machine, watch and bicycle.
¶Worker, farmer or seller.
††Health-enhancing physical activity (HEPA), that is, vigorous activity at least 3 days a week achieving at least 1500 MET min per week or activity on 7 days of the week achieving at least 3000 MET min per week.
IPAQ, International Physical Activity Questionnaire; SEP, socioeconomic position.

and 50.7% of women reporting less than weekly meat eating. The men had more education, with 71.3% of men and 57.1% of women having attended junior middle school or above. The mean age of menarche was 15.0 years (SD 2.4).

Table 1 shows that less frequent childhood meat eating was associated with older age. Meat eating was associated with higher educational attainment, higher childhood SEP, recall of never experiencing childhood hunger and greater current personal income; it was also associated with current smoking and greater alcohol use and with non-manual occupation in women. Table 2 shows that daily meat eating was associated with lower HDL-cholesterol in men. Less frequent childhood meat eating was associated with higher SBP in men and with lower HDL-cholesterol, higher fasting blood glucose, lower LDL-cholesterol, and higher SBP and DBP in women.

There was evidence that the association of meat eating with WHR, HDL-cholesterol and DBP varied with sex, but that the association of meat eating with fasting plasma glucose, LDL-

Table 2 Cardiovascular risk by sex and childhood meat eating (figures given as mean and SD unless indicated otherwise)

	Men				
	Almost daily meat eating (n=542)	Meat eating about 1 day/week (n=1912)	Less than weekly meat eating (n=2178)	Overall (n=5172)	p-Value*
WHR	0.91 (0.06)	0.90 (0.06)	0.90 (0.06)	0.90 (0.06)	0.003
HDL-cholesterol (mmol/l)	1.46 (0.37)	1.48 (0.38)	1.50 (0.40)	1.49 (0.39)	0.034
Fasting plasma glucose (mmol/l)	5.64 (1.66)	5.61 (1.69)	5.59 (1.42)	5.60 (1.55)	0.740
LDL-cholesterol (mmol/l)	3.24 (0.63)	3.21 (0.65)	3.18 (0.65)	3.20 (0.65)	0.120
SBP (mm Hg)	131.55 (20.94)	130.29 (20.40)	133.14 (2178)	131.92 (21.23)	<0.001
DBP (mm Hg)	76.38 (11.19)	74.97 (11.01)	75.94 (11.28)	75.63 (11.19)	0.004
	Women				
	Almost daily meat eating (n=1710)	Meat eating about 1 day/week (n=5311)	Less than weekly meat eating (n=7225)	Overall (n=14246)	p-Value*
WHR	0.85 (0.07)	0.84 (0.06)	0.86 (0.07)	0.85 (0.07)	<0.001
HDL-cholesterol (mmol/l)	1.71 (0.44)	1.72 (0.42)	1.69 (0.42)	1.70 (0.42)	0.002
Fasting plasma glucose (mmol/l)	5.61 (1.61)	5.53 (1.58)	5.65 (1.66)	5.60 (1.63)	<0.001
LDL-cholesterol (mmol/l)	3.53 (0.73)	3.47 (0.70)	3.46 (0.71)	3.47 (0.71)	<0.001
SBP (mm Hg)	125.18 (21.25)	124.9 (21.18)	128.63 (22.06)	126.83 (21.71)	<0.001
DBP (mm Hg)	71.68 (10.90)	71.40 (10.89)	72.01 (10.80)	71.74 (10.85)	0.008

*For unadjusted comparisons using analysis of variance.
DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; WHR, waist to hip ratio.

cholesterol and SBP did not, from the heterogeneity of effect across strata and statistical significance of interaction terms (tables 3 and 4). However, the interaction term between meat eating and sex with HDL-cholesterol as the outcome was no longer significant when interaction terms between sex and two other factors, education and childhood SEP, were also included in the model (p=0.36). Results for all outcomes are presented combined (table 3) and for men and women separately (table 4).

Table 4 shows that daily childhood meat eating was associated with greater WHR in men and smaller WHR in women after adjustment for age (model 1); further adjustment for education, childhood hunger, childhood and adulthood SEP and lifestyle factors (model 2) did not affect the results in men, but attenuated those in women. Effect sizes, however, were small corresponding to approximately one tenth of a SD. Similarly, adjusted for age only more frequent childhood meat eating was associated with lower HDL-cholesterol in men, but the association was attenuated by further adjustment (model 2). In women, weekly meat eating was associated with higher HDL-cholesterol. Again, effect sizes were small. In men and women childhood meat eating had little association with fasting glucose. Adjusted for age, childhood meat eating was associated with higher LDL-cholesterol in both men and women; these findings were attenuated by further adjustment (model 2). There was no clear pattern of association between childhood meat eating and blood pressure in men.

There was some evidence that the association of childhood meat eating with WHR varied by age group by significance of interaction term (table 3) but not by stratification by age group (see supplementary table 1, available online only). Weekly and

Table 3 Adjusted associations of childhood meat eating with WHR, HDL-cholesterol, fasting plasma glucose, LDL-cholesterol and SBP and DBP for men and women together

	Model	Less than weekly meat eating †	Meat eating about 1 Day/week β	95% CI	Almost daily meat eating β	95% CI	p Value for interaction term between sex and meat eating‡	p Value for interaction term between age and meat eating‡ Men	Women	All	p Value for interaction term between sex, age meat eating
WHR	1	-	−0.007***	−0.009 to −0.005	−0.004*	−0.007 to −0.0005	<0.001	0.14	0.08	0.03	0.63
	2	-	−0.004***	−0.006 to −0.002	0.002	−0.001 to 0.005	<0.001	0.08	0.21	0.04	0.22
HDL-cholesterol (mmol/l)	1	-	0.006	−0.008 to 0.02	−0.00002	−0.02 to 0.02	0.02	0.42	0.48	0.30	0.61
	2	-	0.012	−0.002 to 0.03	0.0008	−0.02 to 0.02	0.0006	0.87	0.52	0.41	0.86
Fasting plasma glucose (mmol/l)	1	-	−0.04	−0.09 to 0.009	0.02	−0.06 to 0.10	0.19	0.99	0.43	0.34	0.76
	2	-	−0.01	−0.07 to 0.04	0.06	−0.02 to 0.15	0.31	0.99	0.52	0.36	0.89
LDL-cholesterol (mmol/l)	1	-	0.02	−0.003 to 0.04	0.09***	0.06 to 0.12	0.83	0.44	0.69	0.46	0.84
	2	-	0.006	−0.02 to 0.03	0.06**	0.02 to 0.09	0.95	0.41	0.89	0.62	0.87
SBP (mm Hg)	1	-	−1.46***	−2.22 to −0.70	−1.28*	−2.43 to −0.14	0.58	0.52	0.84	0.64	0.72
	2	-	−0.90*	−1.72 to −0.09	−0.37	−1.62 to 0.88	0.54	0.44	0.65	0.42	0.92
DBP (mm Hg)	1	-	−0.54	−0.94 to −0.14	−0.02	−0.62 to 0.58	0.05	0.68	0.57	0.73	0.47
	2	-	−0.46*	−0.88 to −0.03	0.10	−0.55 to 0.75	0.03	0.54	0.81	0.52	0.57

Model 1: adjusted for age.
Model 2: additionally adjusted for education, childhood hunger, life-course socioeconomic position and lifestyle factors.
*p<0.05;**p<0.01;***p<0.001.
†Reference category.
‡Model also includes interaction between age and sex.
DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; WHR, waist to hip ratio.

Table 4 Adjusted associations of childhood meat eating with WHR, HDL-cholesterol, fasting plasma glucose, LDL-cholesterol and SBP and DBP for men and women separately

	Men						Women				
	Model	Less than weekly meat eating†	Meat eating about 1 Day/week		Almost daily meat eating		Less than weekly meat eating†	Meat eating about 1 Day/week		Almost daily meat eating	
			β	95% CI	β	95% CI		β	95% CI	β	95% CI
WHR	1	.	−0.0009	−0.005 to 0.003	0.009**	0.003 to 0.01	.	−0.01***	−0.01 to −0.008	−0.007***	−0.01 to −0.004
	2	.	−0.002	−0.006 to 0.002	0.007*	0.0003 to 0.01	.	−0.005***	−0.007 to −0.003	0.0006	−0.003 to 0.004
HDL-cholesterol (mmol/l)	1	.	−0.02	−0.04 to 0.007	−0.04*	−0.08 to −0.004	.	0.02*	0.002 to 0.03	0.01	−0.01 to 0.03
	2	.	−0.002	−0.03 to 0.02	−0.03	−0.07 to 0.02	.	0.02	−0.001 to 0.03	0.008	−0.02 to 0.03
Fasting plasma glucose (mmol/l)	1	.	0.05	−0.06 to 0.13	0.08	−0.10 to 0.20	.	−0.07*	−0.13 to −0.008	0.01	−0.08 to 0.10
	2	.	0.03	−0.08 to 0.13	0.05	−0.12 to 0.21	.	−0.02	−0.09 to 0.04	0.07	−0.03 to 0.17
LDL-cholesterol (mmol/l)	1	.	0.02	−0.02 to 0.06	0.07*	0.006 to 0.13	.	0.03*	0.001 to 0.06	0.10***	0.06 to 0.14
	2	.	0.01	−0.03 to 0.05	0.05	−0.02 to 0.12	.	0.002	−0.03 to 0.03	0.06**	0.02 to 0.10
SBP (mm Hg)	1	.	−1.68*	−3.12 to 0.23	−0.36	−2.63 to 1.92	.	−1.39**	−2.28 to −0.50	−1.53*	−2.85 to −0.21
	2	.	−1.74*	−3.27 to −0.21	−0.34	−2.81 to 2.12	.	−0.59	−1.54 to 0.37	−0.36	−1.81 to 1.08
DBP (mm Hg)	1	.	−1.11**	−1.88 to −0.34	0.74	−0.48 to 1.96	.	−0.42	−0.89 to 0.04	−0.21	−0.89 to 0.48
	2	.	−1.26**	−2.08 to −0.45	0.42	−0.90 to 1.74	.	−0.15	−0.66 to 0.34	0.02	−0.74 to 0.77

Model 1: adjusted for age.
Model 2: additionally adjusted for education, childhood hunger, life-course socioeconomic position and lifestyle factors.
*$p<0.05$; **$p<0.01$; ***$p<0.01$.
†Reference category.
DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; WHR, waist to hip ratio.

daily meat eating were associated with greater height in men and women, earlier age of menarche in women and earlier age of voice breaking, pubarche and first nocturnal emission in men (see supplementary table 2, available online only).

DISCUSSION

Consistent with our hypothesis, in an older population from a developing country, there were sex-specific associations of childhood meat eating with measures of body shape (WHR) and HDL-cholesterol, but not with fasting glucose. However, effect sizes were small and the clinical significance of such findings was unclear. Men, but not women, with more frequent childhood meat eating had a less favourable body shape, and perhaps lower HDL-cholesterol. Childhood meat eating was also associated with higher LDL-cholesterol in both sexes, and had no clear association with SBP or DBP.

We were unable to identify previous papers in the literature that had examined the effects of meat eating in childhood on individual biological IHD risk factors in adulthood. Only one study, a case–control study of Hong Kong Chinese people, has examined the effects of childhood meat eating on adulthood IHD. Crude, subgroup analyses showed more frequent childhood meat eating was associated with a reduced risk of acute myocardial infarction in younger men only; however, this association was not robust to adjustment and meat eating was only available for 40% of cases.[36] Two cohort studies in developed countries have examined the relation between childhood diet (at 4 and 8 years of age) and adulthood cardiovascular disease (morbidity and mortality).[37 38] However, neither examined childhood meat eating, differences by sex or individual IHD risk factors; moreover the populations were comparatively well fed, with very different levels of nutrition from mid-20th century China. In developing countries, supplementation studies usually focus on infants or young children and provide a wide range of nutrients,[39 40] which may have quite different effects from specific nutrients in older children or adolescents.

There are several limitations in the present study. First, the infrastructure to facilitate fully representative studies in most developing countries, such as China, is not readily available. However, waiting until all the appropriate infrastructure is in place before embarking on studies from the developing world would preclude the study of a large proportion of the global population during a period of immense transition. Although our sample could not be totally representative, this would invalidate our results only if we have systematically missed people with a specific relation between childhood meat eating and IHD risk—for example, if we are missing men with raised HDL-cholesterol and women with low HDL-cholesterol who ate meat daily in childhood. Second, we relied on recalled experience of childhood meat eating. Random misclassification would make the findings conservative. There is no reason to suspect differential recall bias as the participants were unaware of the hypothesis at the time of data collection. Alternatively, reported childhood meat eating may be a reflection of an atherogenic current diet in men, but not women. We did not adjust for potential confounding by diet, because of the difficulty of obtaining reliable and accurate dietary data in large-scale studies of free-living participants,[41] particularly among the Chinese who share several dishes during a meal and individual intake is doubly difficult to gauge. However, daily meat eating was associated with better childhood socioeconomic conditions (table 1), greater height in men and women, earlier age of menarche in women and earlier age of puberty in men (see supplementary table 2, available online only). Third, our measure of childhood nutrition, meat eating, is relatively crude, without timing, type, quantity or associated dietary patterns. The earliest childhood memories related to self occur after 3 or 4 years of age, later in Chinese populations.[42 43] Childhood meat eating, as recorded here, probably reflects the memory of consumption after the age of 5 years, most likely of pork or chicken,[44] in limited amount.[26 27] As such, our findings are perhaps more generalisable to developing countries with similar low levels of meat consumption. Neither can we comment regarding other aspects of diet that may have been associated with childhood meat eating. It could be that childhood meat eating is a proxy for a generally more nutritious diet. However, adjustment for childhood hunger (a proxy for overall intake) made no difference to our findings. Finally, the differences we observed are modest, certainly from a clinical perspective. However, given the crude nature of our exposure it is likely our findings are underestimated and even a marginal magnitude of effect could translate into a large health impact at the population level.

Our findings could reflect childhood meat eating as a proxy for other aspects of pre-adult living conditions, including maternal conditions and thus birth weight or childhood environment. However, we adjusted for childhood SEP, which may in fact also reflect childhood meat eating, and thus make our findings conservative. Moreover, we do not know if it is specifically meat eating or more generally a better diet, or specific constituents of the diet associated with meat, such as fat, which underlie our observations.

Alternatively, our findings could reflect a changing psychosocial context, which influenced the sexes differently. For example, smoking prevalence in China is much higher in men than women (50.2% compared with 2.8%, respectively).[45] However, adjustment for smoking had little effect on our results. Furthermore, population studies worldwide (including China) have shown that although smoking rates predict secular changes in lung cancer, they do not predict changes in sex differences for coronary heart disease.[1 46]

Despite these potential limitations, our findings lend some support to our biologically based hypothesis that nutritionally driven increases in sex steroid levels at puberty generate a lifelong less favourable HDL-cholesterol profile and body shape in boys while having the opposite effect in girls, without causing sex differences in precursors of diabetes.[11 47]

Our hypothesis does not of course negate other risk factors for IHD; it merely adds a sociohistorical dimension. Nevertheless, it implies that the IHD epidemic that emerged in men with economic development could have arisen as a result of corresponding population-wide improvements in nutrition during childhood and adolescence. More importantly, it implies that in the developing world improved nutrition could already be generating a subsequent epidemic of IHD in men, although there may be other benefits, such as better cognition.[48] Conversely, in women the cardioprotective effects of childhood and adolescent nutrition may be counterbalanced by an increased risk of hormonally modulated cancers (such as breast cancer),[49 50] similarly driven by sex steroids as previously suggested.[9]

CONCLUSION

Given the potential limitations of this study, especially the crude nature of our exposure and small effect sizes, our results should be considered as preliminary. However, they lend some support to the hypothesis that sexual divergence in IHD may be nutritionally driven in childhood. In addition, this study highlights the value of evidence from developing countries interpreted within its socioeconomic and historical context.

What this paper adds

- Men developed much higher rates of IHD than women in most developed countries in the early 20th century. The reasons for this male epidemic of IHD remain unclear.
- This study tests the hypothesis that childhood meat eating is associated with more atherogenic body shape (high WHR) and lipid profile (low HDL-cholesterol) in later adulthood in men but not women without sex-specific effects on diabetes risk (fasting plasma glucose).
- Childhood meat eating had sex-specific associations with WHR and possibly HDL-cholesterol. More frequent childhood meat eating was associated with higher WHR and lower HDL-cholesterol in men but the reverse among women. However, these findings were attenuated by further adjustment for life-course SEP, childhood hunger and lifestyle. Furthermore, effect sizes were small and as such findings should be considered as preliminary.

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