British Journal of Nutrition (2017), **117**, 572–581
doi:10.1017/S000711451700040X

Hb level, iron intake and mortality in Chinese adults: a 10-year follow-up study

Zumin Shi[1,2]*†, Shiqi Zhen[1]†, Yonglin Zhou[1] and Anne W. Taylor[2]

[1]*Department of Nutrition and Foodborne Disease Prevention, Jiangsu Provincial Centre for Disease Control and Prevention, Nanjing 210009, People's Republic of China*
[2]*Discipline of Medicine, The University of Adelaide, L7, SAHMRI, North Terrace, Adelaide 5000, Australia*

(Submitted 1 June 2016 – Final revision received 31 January 2017 – Accepted 1 February 2017)

Abstract

Anaemia is prevalent in developing countries and is commonly Fe deficiency related. We aimed to assess the association between Fe status, Fe intake and mortality among Chinese adults. We prospectively studied 8291 adults aged 20–98 years with a mean follow-up of 9·9 years. All participants were measured for Hb at baseline in 2002. Food intake, measured by 3-d weighed food record (*n* 2832), and fasting serum ferritin were measured. We documented 491 deaths (including 192 CVD and 165 cancer deaths) during 81 527 person-years of follow-up. There was a U-shaped association between Hb levels and all-cause mortality. Compared with the second quartile of Hb (121 g/l), the first (105) and fourth quartile (144) had hazard ratios (HR) of 2·29 (95 % CI 1·51, 3·48) and 2·31 (95 % CI 1·46, 3·64) for all-cause mortality in women. In men, compared with third quartile of Hb (143 g/l), first (122) and fourth quartiles (154) had 61 and 65 % increased risk of all-cause mortality. Anaemia was associated with an increased risk of all-cause and CVD mortality in men but not in women after adjusting for potential confounders. Low and high Fe intake as percentage of Chinese recommended nutrient intake (RNI) were positively associated with all-cause mortality in women but not in men. In women, across quartiles of relative Fe intake, HR for all-cause mortality were 2·55 (95 % CI 0·99, 6·57), 1·00, 3·12 (95 % CI 1·35, 7·18) and 2·78 (95 % CI 1·02, 7·58). Both low and high Hb levels are related to increased risk of all-cause mortality. Both low and high intake of Fe as percentage of RNI was positively associated with mortality in women.

Key words: Hb: Iron: Mortality: Chinese adults: Cohort studies

Anaemia is a major health problem especially in developing countries. It affected 32·9 % of the world population in 2010[1] and is often Fe deficiency related. Despite the rapid economic development and substantial drop in the prevalence of anaemia, it still affected 15 % of Chinese adults in 2002[2]. Fe deficiency is one of the most common causes of anaemia[3]. Other nutritional factors, for example vitamins (vitamin A, vitamin C and vitamin B_2) and minerals (Mg), are also associated with anaemia but have attracted less attention[4,5]. Fe supplementation is widely used to prevent anaemia especially in developing countries including China. However, in recent years, high levels of serum ferritin and Fe intake, especially haem Fe, were found to be associated with an increased risk of diabetes[6–9]. The hypothesised mechanisms include oxidative stress and insulin resistance caused by Fe. An increasing number of studies have reported a positive association between Fe intake (especially haem Fe) and mortality[10–12]. This association seems to support the 'Fe hypothesis' proposed by Sullivan[13] (i.e. a high Fe level in the body increases the risk of CVD). However, there are controversial and mixed results on the relationship between Fe intake and mortality[14]. For example, a U-shape association between non-haem Fe intake and mortality has also been reported[11]. Furthermore, supplemental Fe was not associated with the increased risk of CVD mortality in the Iowa Women's Health study[11]. In a Japanese study, total Fe intake was positively associated with mortality in men but not in women[10].

The adverse health effects of anaemia are well known. However in UK, a U-shaped association between Hb levels and mortality has been found in the general population[15] and for postmenopausal women in the USA[16]. The relationship between Fe status, Fe intake and mortality among adults has not been thoroughly studied in developing countries. No large cohort study has assessed the association between Hb and mortality among adults in developing countries.

We aimed to assess the association between Hb levels, serum ferritin, Fe intake and mortality in Chinese adults.

Method

Study population

The Jiangsu Nutrition Study is an ongoing cohort study investigating the association of nutrition and other factors with the risk

Abbreviations: CDC, Centre for Disease Control and Prevention; CKD, chronic kidney disease; HR, hazard ratio; RNI, recommended nutrient intake.

* **Corresponding author:** Associate Professor Z. Shi, fax +61 8 8313 1228, email Zumin.shi@adelaide.edu.au

† Both authors contributed equally to this work.

of non-communicable chronic disease[8,17]. The sample was based on a subsample of the Chinese national nutrition and health survey representing the Jiangsu province and the year 2002 was used as a baseline. The rural sample was selected from six counties (Jiangyin, Taichang, Shuining, Jurong, Sihong and Haimen). From each of the six counties, three smaller towns were randomly selected. The urban sample was selected from the capital cities of the two prefectures, Nanjing and Xuzhou; and from each capital city three streets were randomly selected. The six counties and the two prefectures represented a geographically and economically diverse population. In each town/street, two villages/neighbourhoods were randomly selected, and ninety households were further selected randomly from each village/neighbourhood. All the members in the households were invited to take part in the study. In total, 9326 adults aged 20 years and above participated in the baseline survey. Of the participants, 1035 (609 men and 426 women) participated in the questionnaire survey but did not have their Hb measured. Those who did not have their Hb measured were younger as compared with those with measured Hb (mean age 43·3 (SD 16·5) *v.* 46·6 (SD 14·7) years), however the BMI was similar (mean 23·8 (SD 2·98) *v.* 23·4 (SD 3·4) kg/m^2). Thus the final analytical sample in the study was 8291.

In addition, one-third of the households were interviewed about their dietary intake and had their fasting blood samples measured for glucose and serum ferritin at baseline. In total, 2832 adults aged 20 years and above participated in this part of the survey.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects/patients were approved by Jiangsu Provincial Centre for Disease Control and Prevention (CDC). Written informed consent was obtained from all the participants.

Data collection and measurements

Participants were interviewed at their homes by health workers using a standard questionnaire to collect information on health status, demographics and lifestyle factors[2].

Exposure variables – baseline Hb, ferritin, iron intake

Hb and serum ferritin. An overnight fasting blood sample was collected at baseline in 2002. The blood samples were analysed for Hb by the cyanmethemoglobin method in the local CDC according to a standard protocol[18]. Anaemia was defined as a Hb level below 130 g/l for men and 120 g/l for women[19]. Serum ferritin was analysed in a laboratory in the National Centre for Disease Control and Prevention in Beijing using commercially available RIA kits (RIA kit for serum ferritin; Beijing North Institute of Biological Technology). Serum ferritin was recoded into four categories: <50, 50–99, 100–199 and ≥200 μg/l. The quality control of all the laboratory measures were managed by the Chinese CDC in Beijing. For onsite measure of Hb, results of the blind samples (for quality control purpose) were reported to the Chinese CDC by telephone daily. Oral confirmation by telephone from the Chinese CDC was needed before the Hb testing was conducted.

Dietary intake. Nutrients intake (e.g. Fe intake) was assessed using a 3-d weighed food diary which recorded all foods consumed by each individual, on 3 consecutive days at baseline[20]. Food consumption data were analysed using the Chinese Food Composition Table[21].

Outcome variable-death ascertainment. The underlying cause of mortality was defined according to the WHO International Classification of Disease, 10th revision (ICD-10). Information regarding deaths in the household was collected in 2012 by household visit, as well as by linking with the death registry database in the local CDC in 2012. Thus the identification of participant deaths were virtually complete. CVD mortality included ICD-10 codes I00–99. Cancers mortality was defined as ICD-10 C00–97.

Baseline covariates

Cigarette smoking was assessed by asking frequency of daily cigarette smoking. Alcohol consumption was assessed by asking the frequency and amount of alcohol/wine intake. Daily leisure time physical activity was classified into three categories: 0, 1–29 and ≥30 min. Education was recoded into three categories based on six categories of education levels in the questionnaire: 'Low': illiteracy, primary school; 'Medium': junior middle school; 'High': high middle school or higher. Occupation was recoded into manual or non-manual based on a question with twelve occupational categories. We defined diabetes as fasting plasma glucose > 7·0 mmol/l or having known diabetes (self-reported doctor diagnosed). Blood pressure was measured twice by mercury sphygmomanometer on the right upper arm of the participant, who was seated for 5 min before the measurement. The mean of these two measurements was used in the analyses. Hypertension was defined as systolic blood pressure above 140 mmHg and/or diastolic blood pressure above 90 mmHg, or using antihypertensive drugs. Height was measured without shoes and weight was measured with light clothing. Obesity was defined as BMI ≥28 kg/m^2 as recommended for Chinese adults[22].

Statistical analysis

χ^2 Tests were used to compare differences in categorical and ANOVA in continuous variables. The cohort was divided into sex-specific quartiles on the basis of Hb level as well as Fe intake. For each participant, person-years of follow-up were calculated from the date of baseline survey to the date of death or the date of last follow-up (1 December 2012), whichever came first. The association between Hb and Fe status and the risk of CVD and cancer mortality was analysed using competing risks regression[23] and the association between Hb, Fe intake and ferritin and all-cause mortality was analysed using Cox proportional hazard models, adjusting for multiple covariates. Using the first quartile of Hb as a reference, we found the lowest risk of mortality were those in the second quartile of Hb in women and third quartile in men. In order to use the lowest risk group as a reference, we choose the second quartile of Hb as the reference in women and the third quartile of Hb as the reference in men. Three models

assessed the association between Hb and mortality. The first model controlled for age (continuous); the second model further adjusted for socio-demographic (education, occupation, urban/rural, south/north) and lifestyle factors (smoking, alcohol consumption and leisure time physical activity), BMI (linear and square terms) and hypertension. In the third model, we excluded those who died within 2 years of follow-up (*n* 66) as they may have suffered from serious health problems which may have led to a change in dietary intake and other lifestyle factors at baseline. Excluding participants who died during the first several years of follow-up is a common practice in nutritional epidemiological studies. It is often used as a sensitivity analysis. We used model 2 as the final model and model 3 as a sensitivity analysis. As the sample sizes were above 97 % of the whole sample in the full model, we did not impute the missing data. The proportional hazards assumption in the Cox model was assessed with graphical methods and with models including time-by-covariate interactions. In general, all proportionality assumptions were appropriate. Similar model building approaches were used for the association between Fe intake and mortality with additional adjustment of intake of energy in all models and diabetes, active commuting, sedentary activity, intake of fat and fibre in model 2 and 3. We tested for linear trends across categories of dietary Fe exposure by assigning each participant the median value for the category and modelling this value as a continuous variable. As the recommended Fe intake for women differs by age, we also used Fe intake as percentage of 2013 Chinese recommended nutrient intake (RNI) for Fe (20 and 12 mg/d for those aged 18–49 years and 50 years and above, respectively) as an exposure variable in women in the multivariable analyses[24].

We next investigated the dose–response relation between Hb level and mortality. We flexibly modelled Hb as quantitative predictor of mortality using restricted cubic splines with three knots at fixed percentiles (10th, 50th and 90th) of its distribution. An overall *P* value for the association was then obtained by testing the regression coefficient of the two splines simultaneously equal to 0. As the simpler linear response model is a special case of the spline model, a *P* value for non-linearity was obtained by testing the regression coefficient of the second spline equal to zero[25]. The results were graphically presented with the distribution of Hb (Fig. 1).

Because there was a significant sex difference between Hb level and mortality, sex-specific analyses were performed. We also assessed the interaction between serum ferritin and anaemia in relation to all-cause mortality in both sexes by adding a multiplicative term in a parsimonious model adjusting for age, income, physical activity, smoking and BMI (linear and square terms). All the regression analyses were adjusted for household cluster. Statistical significance was considered when $P < 0{\cdot}05$ (two-sided). All analyses were performed using Stata 14 (StataCorp).

Results

At baseline, compared with participants in the second/third quartile of Hb (selected as reference quartiles due to the lowest risk of mortality in women/men, respectively, see description of statistical analyses), those in the lowest quartiles of Hb were older, less likely to be obese and to live in the urban area, whereas those in the highest quartiles of Hb were more likely to be younger, obese and to live in the urban area (Table 1). The prevalence of anaemia was 30·2 (24·2 in men and 35·1 % in women), whereas 19·7 % of women had Hb between 110 and 120 g/l and 13·2 % of men had Hb between 120 and 130 g/l. Fe intake as percentage of RNI was positively associated with serum ferritin in women but not in men (online Supplementary Fig. S1).

Of the 8291 participants with Hb measurements, we documented 491 deaths (including 192 CVD deaths and 165 cancer deaths) during 81 527 person-years of follow-up. There was a U-shape association between Hb levels and all-cause mortality in both men and women, with the mortality risk lowest of Hb at 125 g/l in women and 140 g/l in men (Fig. 1). In men, the first quartile (hazard ratio (HR) 1·61 95 % CI 1·13, 2·29) and fourth quartile (HR 1·65 95 % CI 1·11, 2·47) of Hb had increased risks of all-cause mortality as compared with the third quartile (mean 143 g/l, which is above the WHO cut-off (130 g/l) for

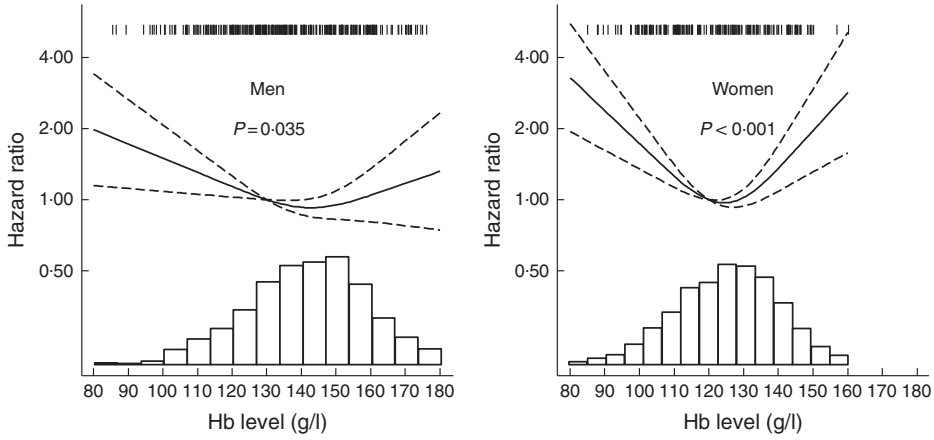

Fig. 1. Hazard ratios for all-cause mortality according to Hb levels among Chinese adults. Data were fitted by using Cox proportional hazard regression. Estimates were adjusted for age, sex, smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), BMI (continuous and square of BMI), and hypertension. ——, Estimates using restrict cubic splines ($P_{\text{for non-linearity}} = 0{\cdot}035$ in men and <0·001 in women). - - - - -, 95 % CI for the non-linear response model. The reference value is Hb of 130 g/l in men and 120 g/l in women, and the histogram shows the distribution of Hb levels in the cohort. Tick marks at the top of the figure represent the position of the cases of death.

Table 1. Sample characteristics according to quartiles (Q) of Hb among Chinese adults (Mean values and standard deviations; percentages)

	Quartiles of Hb								
	Q1		Q2		Q3		Q4		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*
n	2109		2041		2071		2070		
Hb (g/l)	112	12	128	9	139	9	153	12	<0·001
Age (years)	49·4	15·4	46·9	14·6	45·7	14·3	44·5	14·0	<0·001
BMI (kg/m^2)	23·0	3·2	23·2	3·3	23·5	3·5	24·0	3·5	<0·001
Obesity (%) (BMI ≥ 28 kg/m^2)	6·9		8·2		10·5		13·0		<0·001
Men (%)	45·8		44·0		44·8		44·9		0·740
Income (%)									<0·001
Low	23·2		26·9		37·2		47·4		
Medium	41·9		40·1		32·5		24·8		
High	34·9		33·0		30·3		27·8		
Low education (%)	52·6		47·9		48·4		46·1		<0·001
Region (%)									<0·001
South	59·6		54·8		49·7		44·2		
North	40·4		45·2		50·3		55·8		
Manual job (%)	55·1		55·2		56·5		54·3		0·570
Urban (%)	21·2		24·0		24·2		28·6		<0·001
Hypertension (%)	24·0		27·1		28·1		30·1		<0·001
Diabetes (%)	2·6		2·2		3·3		5·9		<0·001
Anaemia (%)	96·9		22·6		0·0		0·0		<0·001
Smoker (%)	27·5		27·8		25·8		27·6		0·440
Alcohol drinker (%)	22·3		24·1		24·4		26·0		0·047
No leisure time physical activity (%)	93·6		92·5		91·9		89·6		<0·001

Table 2(a). Mortality from all-cause, CVD and cancer according to Hb levels or anaemia status in men (*n* 3720)* (Hazard ratios (HR) and 95 % confidence intervals)

	Quartiles of Hb								Anaemia status			
	Q1 (122 g/l)†		Q2 (137 g/l)		Q3 (143 g/l)	Q4 (154 g/l)		$P_{\text{for trend}}$	No	Yes		
	HR	95 % CI	HR	95 % CI	HR	HR	95 % CI	(quadratic)	HR	HR	95 % CI	*P*
Participants at risk (*n*)	965		899		927	929			2821	899		
Person-years	9150		8804		9175	9091			27 739	8483		
All-cause mortality												
Cases	120		66		49	60			177	118		
Model 1‡	1·59	1·15, 2·20	1·18	0·82, 1·69	1	1·45	1·00, 2·10	0·008	1	1·39	1·10, 1·77	0·006
Model 2§	1·61	1·13, 2·29	1·24	0·84, 1·82	1	1·65	1·11, 2·47	0·004	1	1·34	1·03, 1·74	0·027
Model 3‖	1·45	1·00, 2·11	1·12	0·75, 1·67	1	1·65	1·10, 2·48	0·005	1	1·26	0·96, 1·67	0·095
CVD mortality												
Cases	46		20		19	17			57	45		
Model 1	1·24	0·72, 2·11	0·82	0·44, 1·54	1	1·02	0·53, 1·96	0·262	1	1·35	0·91, 2·01	0·136
Model 2	1·65	0·93, 2·92	0·84	0·44, 1·59	1	0·94	0·47, 1·91	0·116	1	1·90	1·20, 3·01	0·007
Model 3	1·46	0·80, 2·69	0·75	0·38, 1·49	1	0·93	0·44, 1·95	0·165	1	1·74	1·05, 2·88	0·030
Cancer mortality												
Cases	46		28		17	27			73	45		
Model 1	1·78	1·02, 3·11	1·46	0·80, 2·66	1	1·80	0·98, 3·30	0·067	1	1·32	0·90, 1·93	0·156
Model 2	1·42	0·79, 2·53	1·29	0·71, 2·35	1	1·89	1·01, 3·54	0·092	1	1·08	0·72, 1·64	0·703
Model 3	1·46	0·80, 2·66	1·19	0·63, 2·22	1	1·95	1·02, 3·72	0·043	1	1·15	0·75, 1·76	0·520

Q, quartiles.
* Anaemia was defined as Hb < 130 g/l in men.
† Mean Hb of the quartile.
‡ Model 1 adjusted for age.
§ Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region (south/north), BMI (linear and square terms) and hypertension.
‖ Model 3, further excluded those died within 2 years.

anaemia in men) (Table 2(a)). In women, the HR was almost identical for low and high Hb levels (Table 2(b)). Compared with the second quartile of Hb (mean 121 g/l, which is approximately the cut-off for anaemia in women based on WHO definition), the HR for all-cause mortality was 2·29 (95 % CI 1·51, 3·48) and 2·31 (95 % CI 1·46, 3·64) in the first and fourth quartile of Hb, respectively. High Hb level was associated with cancer mortality in men but not in women.

Anaemia was associated with an increased risk of all-cause and CVD mortality in men (Table 2(a)) but not in women (Table 2(b)).

Table 2(b). Mortality from all-cause, CVD and cancer according to Hb levels or anaemia status in women (*n* 4571)* (Hazard ratios (HR) and 95 % confidence intervals)

	Quartiles of Hb								Anaemia status			
	Q1 (105 g/l)†		Q2 (121 g/l)	Q3 (131 g/l)		Q4 (144 g/l)		$P_{for\ trend}$ (quadratic)	No	Yes		
	HR	95 % CI	HR	HR	95 % CI	HR	95 % CI		HR	HR	95 % CI	*P*
Participants at risk (*n*)	1112		1124	1159		1203			2965	1606		
Person-years	11 147		11 411	11 432		11 317			29 520	15 786		
All-cause mortality												
Cases	83		34	30		49			102	94		
Model 1‡	2·19	1·46, 3·28	1	0·94	0·57, 1·54	1·91	1·23, 2·96	<0·001	1	1·29	0·97, 1·72	0·076
Model 2§	2·29	1·51, 3·48	1	1·12	0·68, 1·84	2·31	1·46, 3·64	<0·001	1	1·17	0·87, 1·57	0·303
Model 3‖	2·08	1·34, 3·24	1	1·00	0·59, 1·70	2·00	1·24, 3·24	<0·001	1	1·19	0·86, 1·64	0·301
CVD mortality												
Cases	33		16	15		26			54	36		
Model 1	1·53	0·83, 2·80	1	1·00	0·49, 2·02	2·22	1·20, 4·13	0·007	1	0·79	0·52, 1·22	0·289
Model 2	1·54	0·82, 2·91	1	1·13	0·56, 2·29	2·38	1·27, 4·44	0·010	1	0·75	0·47, 1·19	0·224
Model 3	1·64	0·83, 3·23	1	1·10	0·51, 2·34	2·38	1·21, 4·68	0·010	1	0·79	0·48, 1·31	0·361
Cancer mortality												
Cases	21		7	8		11			24	23		
Model 1	2·61	1·09, 6·23	1	1·17	0·43, 3·22	1·77	0·68, 4·55	0·028	1	1·46	0·80, 2·66	0·220
Model 2	2·78	1·12, 6·89	1	1·48	0·50, 4·33	2·28	0·80, 6·51	0·024	1	1·18	0·64, 2·16	0·600
Model 3	2·27	0·81, 6·35	1	1·65	0·50, 5·44	2·24	0·67, 7·47	0·123	1	0·97	0·49, 1·90	0·928

Q, quartiles.
* Anaemia was defined as Hb <120 g/l in women.
† Mean Hb of the quartile.
‡ Model 1 adjusted for age.
§ Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region(south/north), BMI (linear and square terms), and hypertension.
‖ Model 3, further excluded those died within 2 years.

Among the 2832 adults aged 20 years and above with information on Fe intake at baseline, there were 184 deaths (including 70 CVD deaths, 63 cancer deaths) during on average 9·8 year follow-up (in total 27 742 person-years).

Absolute Fe intake was positively associated with all-cause mortality in women but not in men (Tables 3(a) and (b)). Compared with the first quartile of Fe intake, other levels of Fe intake were associated with an HR of 2·24 (95 % CI 1·18, 4·27) for all-cause mortality in women and 0·89 (95 % CI 0·53, 1·51) in men. A positive association between Fe intake and CVD and cancer mortality was observed in women (Table 3(b)). However, the above associations changed if we used Fe intake as a percentage of RNI in women. Compared with the second quartile of Fe intake (%RNI) (median: 127·8; range: 98·7–130·5), both low (first quartile) and high (third and fourth quartile) Fe intake had an increased risk of all-cause mortality (Table 3(c)). In women, across the quartiles of relative Fe intake, HR for all-cause mortality were 2·55 (95 % CI 0·99, 6·57), 1·00, 3·12 (95 % CI 1·35, 7·18) and 2·78 (95 % CI 1·02, 7·58), respectively. In sensitivity analysis, after excluding those died within 2 years, low relative Fe intake was associated with a significant increased risk of all-cause mortality with HR of 4·10 (95 % CI 1·24, 13·52). Further adjusting for red meat consumption did not change the above association (data not shown). Excluding those age below 40 years, the above association did not change (data not shown).

Serum ferritin levels were not associated with mortality in both men and women (Tables 4(a) and (b)). However, in a parsimonious model adjusting for age, smoking, leisure time physical activity, income and BMI, significant interaction between quartiles of serum ferritin and anaemia (Hb <130 g/l in men, Hb <120 g/l in women) in relation to all-cause mortality was found in women but not in men (online Supplementary Table S1).

Discussion

In this prospective study, we found there was an U-shaped association between Hb levels and mortality. Both low Fe intake and high Fe intake as percentage of RNI were associated with an increased risk of mortality in women but not in men.

A U-shape association between Hb and mortality is consistent with findings from developed countries[15]. There was a sex difference with the associations. In women, the mortality risk increased at the level of Hb 130 g/l. However, in China, anaemia is diagnosed when Hb is below 110 g/l for women and 120 g/l for men[26]. Based on the distribution of Hb in the sample, among the anaemic participants, about 55 % had Hb levels between 120 and 130 g/l in men and 110 and 120 g/l in women, which would be diagnosed as normal based on the Chinese criteria. This would mean that half of anaemic patients would be missed for proper treatment under the Chinese anaemia diagnostic criteria. Meanwhile, when Hb level is above 150 g/l, the mortality risk also increased. The safe window for Hb seems relatively narrow especially in women. This may be related to menopause in women and Fe induced oxidative stress. Although Hb is an indicator of Fe status, it may also be affected by other factors. For example, contracted plasma volume caused by hypertension may lead to an increase of Hb. In our sample, a positive association between hypertension and high Hb was observed. The association

Table 3(a). Mortality from all-cause, CVD and cancer according to quartiles (Q) of iron intake in men (Hazard ratios (HR) and 95 % confidence intervals)

	Quartiles of Fe intake								Q2–Q4 *v.* Q1			
	Q1 17·7 mg/d (median)	Q2 (23·0)		Q3 (28·6)		Q4 (40·1)			Q1	Q2–Q4		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$	HR	HR	95 % CI	*P*
Participants at risk (*n*)	325	325		325		325			325	975		
Person-years	3075	3163		3201		3173			3075	9537		
All-cause mortality												
Cases	40	28		17		25			40	70		
Model 1*	1	1·12	0·69, 1·82	0·72	0·38, 1·38	1·33	0·67, 2·64	0·409	1	1·02	0·64, 1·63	0·923
Model 2†	1	1·04	0·61, 1·77	0·63	0·31, 1·29	1·11	0·48, 2·53	0·943	1	0·89	0·53, 1·51	0·674
Model 3‡	1	1·06	0·60, 1·88	0·53	0·25, 1·15	1·08	0·43, 2·70	0·972	1	0·86	0·49, 1·51	0·604
CVD mortality												
Cases	17	6		8		7						
Model 1	1	0·67	0·25, 1·79	1·30	0·45, 3·71	1·54	0·48, 4·89	0·399	1	0·96	0·43, 2·15	0·925
Model 2	1	0·62	0·21, 1·84	1·69	0·53, 5·35	1·09	0·32, 3·72	0·686	1	0·92	0·39, 2·18	0·854
Model 3	1	0·85	0·29, 2·49	1·45	0·41, 5·16	1·04	0·33, 3·27	0·821	1	1·02	0·41, 2·52	0·969
Cancer mortality												
Cases	16	9		8		11						
Model 1	1	0·73	0·31, 1·68	0·68	0·27, 1·73	0·97	0·33, 2·80	0·935	1	0·75	0·36, 1·56	0·443
Model 2	1	0·68	0·28, 1·62	0·57	0·21, 1·56	0·85	0·24, 3·02	0·863	1	0·65	0·29, 1·43	0·279
Model 3	1	0·68	0·27, 1·72	0·55	0·19, 1·58	0·88	0·22, 3·50	0·919	1	0·64	0·28, 1·48	0·295

* Model 1 adjusted for age and energy intake.
† Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region (south/north), BMI (linear and square terms), diabetes, hypertension, intake of energy, fat and fibre.
‡ Model 3, further excluded those died within 2 years.

Table 3(b). Mortality from all-cause, CVD and cancer according to quartiles (Q) of iron intake in women (Hazard ratios (HR) and 95 % confidence intervals)

	Quartiles of Fe intake								Fe intake			
	Q1 14·8 mg/d (median)	Q2 (19·2)		Q3 (23·4)		Q4 (33·8)			Q1	Q2–Q4		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$	HR	HR	95 % CI	*P*
Participants at risk (*n*)	383	383		383		383			383	1149		
Person-years	3753	3766		3793		3817			3753	11 377		
All-cause mortality												
Cases	24	23		14		13			24	50		
Model 1*	1	2·19	1·17, 4·09	2·09	0·91, 4·79	2·09	0·85, 5·11	0·166	1	2·15	1·17, 3·95	0·013
Model 2†	1	2·36	1·22, 4·56	2·05	0·89, 4·72	1·83	0·65, 5·12	0·367	1	2·24	1·18, 4·27	0·013
Model 3‡	1	3·72	1·74, 7·93	2·49	0·89, 6·98	2·73	0·92, 8·09	0·183	1	3·37	1·60, 7·09	0·001
CVD mortality												
Cases	10	12		4		6						
Model 1	1	3·79	1·47, 9·77	2·32	0·60, 8·90	4·05	1·08, 15·13	0·073	1	3·50	1·37, 8·95	0·009
Model 2	1	5·08	1·71, 15·12	2·60	0·60, 11·28	2·88	0·74, 11·24	0·173	1	4·22	1·42, 12·56	0·010
Model 3	1	8·98	2·69, 30·02	4·40	0·84, 23·07	5·83	1·25, 27·29	0·046	1	7·90	2·36, 26·49	0·001
Cancer mortality												
Cases	2	6		9		2						
Model 1	1	5·31	1·02, 27·59	11·89	1·85, 76·51	2·96	0·34, 26·06	0·517	1	6·83	1·36, 34·41	0·020
Model 2	1	4·81	0·83, 27·80	10·21	1·39, 75·12	3·17	0·25, 39·91	0·587	1	6·73	1·25, 36·08	0·026
Model 3	1	13·45	1·38, 131·21	20·10	1·38, 292·12	12·54	0·89, 177·75	0·371	1	14·85	1·47, 150·39	0·022

* Model 1 adjusted for age and energy intake.
† Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region (south/north), BMI (linear and square terms), diabetes, hypertension, intake of energy, fat and fibre.
‡ Model 3, further excluded those died within 2 years.

between Hb and mortality could be confounded by hypertension. Although hypertension was adjusted in the analyses, residual confounding is possible.

The positive association between high Fe intake and mortality is in line with findings from other studies in Japan[10] and the USA[12]. In contrast to the Japanese study[10], we only found a positive association between Fe intake and mortality among women. The association was independent of red meat consumption. Consistent with a positive association between low Hb and mortality in women, low intake of Fe as percentage of RNI was also positively associated with all-cause mortality. In women, the lowest risk of mortality was those in the quartile with Fe intake between 99 and 131 % of RNI. The sex difference on the association between Fe intake and mortality may be due to the fact that women have a different risk of having anaemia before and after menopause. Our findings have public health significance.

British Journal of Nutrition

Table 3(c). Mortality from all-cause, CVD and cancer according to quartiles (Q) of iron intake as a percentage of recommended nutrient intake (RNI) in women
(Hazard ratios (HR) and 95 % confidence intervals)

	Quartiles of Fe intake as percentage of RNI						
	Q1 96·0 (median)		Q2 (127·8)	Q3 (170·5)		Q4 (286·1)	
	HR	95 % CI	HR	HR	95 % CI	HR	95 % CI
Participants at risk (*n*)	383		383	383		383	
Person-years	3829		3810	3751		3737	
All-cause mortality							
Cases	11		10	27		26	
Model 1*	2·11	0·82, 5·43	1·00	2·44	1·13, 5·29	2·67	1·08, 6·59
Model 2†	2·55	0·99, 6·57	1·00	3·12	1·35, 7·18	2·78	1·02, 7·58
Model 3‡	4·10	1·24, 13·52	1·00	5·93	1·96, 17·96	4·77	1·30, 17·55
CVD mortality							
Cases	5		3	14		10	
Model 1	2·41	0·46, 12·64	1·00	5·00	1·37, 18·28	4·89	1·22, 19·58
Model 2	7·48	0·72, 78·12	1·00	14·84	1·92, 114·88	8·87	1·01, 77·76
Model 3	10·15	0·40, 257·68	1·00	38·45	1·65, 895·75	25·85	1·01, 663·22
Cancer mortality							
Cases	1		2	5		11	
Model 1	0·55	0·05, 6·02	1·00	2·30	0·43, 12·26	6·57	1·12, 38·69
Model 2	0·51	0·05, 5·75	1·00	1·75	0·32, 9·62	6·78	1·04, 44·12
Model 3§	1·00			8·33	0·88, 79·24	27·72	2·83, 271·21

* Model 1 adjusted for age and energy intake.
† Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region (south/north), BMI (linear and square terms), diabetes, hypertension, intake of energy, fat and fibre.
‡ Model 3, further excluded those died within 2 years.
§ As the number of cancer death was 1, 0, 5, 8 across quartiles of Fe intake after excluding those died within 2 years, we combined Q1 and Q2 as reference group.

Table 4(a). Mortality by serum ferritin level in men
(Hazard ratios (HR) and 95 % confidence intervals)

	Serum ferritin level (μg/l)							
	<50		50–99	100–199		≥200		
	HR	95 % CI	HR	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$*
Participants at risk (*n*)	206		368	481		241		
Person-years	1970		3529	4729		2344		
All-cause mortality								
Cases	21		41	30		18		
Model 1†	0·75	0·45, 1·27	1	0·63	0·40, 0·99	0·56	0·31, 1·02	0·120
Model 2‡	0·67	0·38, 1·20	1	0·68	0·41, 1·11	0·68	0·35, 1·33	0·614
Model 3§	0·66	0·36, 1·23	1	0·65	0·38, 1·12	0·55	0·26, 1·16	0·343
CVD mortality								
Cases	6		11	16		5		
Model 1	0·78	0·30, 2·07	1	1·41	0·65, 3·07	0·62	0·20, 1·89	0·966
Model 2	0·78	0·27, 2·21	1	1·37	0·57, 3·28	0·88	0·23, 3·34	0·575
Model 3	1·10	0·37, 3·29	1	1·83	0·65, 5·18	0·69	0·14, 3·35	0·974
Cancer mortality								
Cases	9		18	10		7		
Model 1	0·73	0·32, 1·69	1	0·47	0·22, 1·01	0·54	0·22, 1·32	0·190
Model 2	0·68	0·28, 1·65	1	0·51	0·23, 1·14	0·74	0·29, 1·89	0·639
Model 3	0·80	0·32, 1·99	1	0·47	0·20, 1·11	0·72	0·25, 2·02	0·436

* Ordinal number (1, 2, 3, 4) representing four levels of serum ferritin was used to test $P_{for\ trend}$.
† Model 1 adjusted for age.
‡ Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), residence (urban/rural), region (south/north), BMI (linear and square terms), diabetes, hypertension, intake of energy, fat and fibre.
§ Model 3, further excluded those died within 2 years.

The Fe intake in the Chinese population is over 23 mg/d[27], which is above the 2013 Chinese RNI (12 mg/d for men aged 18–80 years, 20 mg/d for women aged 18–49 years)[24]. The Fe intake level in our sample is similar to the mean intake in China, but much higher than western countries. The main source of Fe in the study sample was from plant-based food (non-haem Fe)[7].

Table 4(b). Mortality by serum ferritin level in women (Hazard ratios (HR) and 95 % confidence intervals)

	Serum ferritin level (μg/l)							
	<50		50–99	100–199		≥200		
	HR	95 % CI	HR	HR	95 % CI	HR	95 % CI	$P_{for\ trend}$*
Participants at risk (*n*)	792		373	272		89		
Person-years	7923		3665	2627		855		
All-cause mortality								
Cases	15		24	27		8		
Model 1†	0·99	0·48, 2·03	1	1·18	0·67, 2·10	0·98	0·42, 2·27	0·743
Model 2‡	0·87	0·42, 1·79	1	1·22	0·66, 2·26	0·93	0·36, 2·38	0·586
Model 3§	0·71	0·28, 1·83	1	1·29	0·66, 2·54	0·82	0·29, 2·32	0·491
CVD mortality								
Cases	7		7	16		2		
Model 1	1·75	0·53, 5·70	1	2·50	1·00, 6·26	0·83	0·16, 4·25	0·863
Model 2	1·54	0·51, 4·66	1	2·39	0·80, 7·13	0·63	0·08, 4·90	0·981
Model 3	1·95	0·49, 7·77	1	2·11	0·65, 6·82	0·27	0·02, 3·05	0·366
Cancer mortality								
Cases	3		7	6		3		
Model 1	0·37	0·09, 1·59	1	0·93	0·30, 2·88	1·34	0·34, 5·27	0·180
Model 2	0·36	0·09, 1·45	1	1·15	0·38, 3·50	1·34	0·36, 4·90	0·100
Model 3		–	1	0·68	0·20, 2·29	1·27	0·28, 5·85	0·054

* Ordinal number (1, 2, 3, 4) representing four levels of serum ferritin was used to test $P_{for\ trend}$.
† Model 1 adjusted for age.
‡ Model 2 further adjusted for smoking (0, 1–19, ≥20 cigarettes/d), alcohol drinking (no, 1–2 times/week, 3–4 times/week, daily), leisure time physical activity (no, 1–29 min/d, >30 min/d), education (low, medium, high), occupation (manual/non-manual), BMI (linear and square terms), diabetes, hypertension, intake of energy, fat and fibre.
§ Model 3, further excluded those died within 2 years.

Use of Fe supplement was found to be rare at the baseline survey. Because of the high prevalence of anaemia in China, Fe-fortified soy sauce was used to prevent anaemia at the population level[28]. However, anaemia in our study area is multifactorial and associated with overall dietary patterns, individual foods, micronutrients and early life famine exposure[29]. Fe supplement may benefit women with Fe intake below the Chinese RNI in terms of mortality, which is about one in every four participants. Among women with Fe intake that meets the RNI, adding extra Fe may increase the risk of mortality. However, we are not able to assess the effect of Fe supplement in relation to mortality in this study. Further research is needed.

We have previously reported that anaemia coexisted with metabolic syndrome and its components[30]. In addition, it is common that people with chronic kidney disease (CKD) have an increased risk of anaemia. In China the prevalence of CKD is about 10 %[31]. Thus anaemia should not be treated in isolation without considering its causes. Among people with CKD, complete correction of anaemia using erythropoiesis-stimulating agents is associated with adverse outcomes[32]. We have previously reported that a low intake of riboflavin is associated with an increased risk of anaemia in the population. When riboflavin intake is adequate, there is no association between Fe intake and anaemia in the Chinese population[5]. Given the link between Fe and diabetes as well as the increasing high burden of diabetes in China, our results do not support the use of Fe supplements as a population prevention strategy for anaemia. Studies have shown that fetal exposure to the Chinese famine (1959–1961) increased the risk of anaemia[33], hypertension[34] and diabetes[35]. Those born during the Chinese famine have now reached 50 years old. Special attention should be paid to this group. In fact, only 0·2 % men and 6·6 % women above 50 years of age had Fe intake below the RNI (data not shown). Providing extra Fe to this specific group may cause harm, however, further research is needed.

The overall null association between ferritin and mortality is in line with findings from National Health and Nutrition Examination Survey[36]. A high level of ferritin has been shown to be associated with diabetes and the metabolic syndrome in the Chinese population. Interestingly we found a significant interaction between serum ferritin and anaemia in relation to all-cause mortality in women. This is consistent with a positive association between a high Hb/high Fe intake (%RNI) and mortality in women in our sample. It is also in line with a positive association between Fe intake (%RNI) and serum ferritin in women. Furthermore, high serum ferritin may provide a good reservoir of Fe among those with anaemia. However, a null association between Fe intake, serum ferritin and mortality in our study in men remains a puzzle. Several possibilities could be hypothesised. First, because of the low intake of riboflavin in the Chinese population, the ability to mobilise Fe from ferritin is limited[37,38]. Second, other factors (inflammation and infection) may also affect ferritin levels[3]. However, in the current study we are not able to adjust for these factors (e.g. C-reactive protein was not measured).

Our study has several limitations. First, we do not have information on CKD. Some studies found an interaction between anaemia and CKD in relation to mortality. Second, only a third of the sample had dietary information. We have limited sample power to undertake further subgroup analyses for the association between Fe intake and mortality. Third, although a 5-year follow-up was conducted, the follow-up rate was low (approximately 50 %) due to migration and city construction[39]. Thus these follow-up data were not used in the current analyses. Our findings may be biased by the incident chronic conditions (obesity, diabetes and hypertension) as well as the change of dietary habits during the 10-year follow-up. Covariates were

British Journal of Nutrition

only measured at baseline on average 5·3 years before death. The strength of the study is the relatively large sample size of participants with Hb measurements, as well as the detailed information on socio-demographic and lifestyle factors.

In conclusion, both low and high Hb levels are related to an increased risk of all-cause mortality in the study population. Both low and high intake of Fe as percentage of RNI are associated with increased risk of mortality in women. Both Fe intake and ferritin levels are not associated with mortality in men. Further research is needed in other regions of China.

Acknowledgements

The authors thank the participating regional Centres for Disease Control and Prevention in Jiangsu province, including the Nanjing, Xuzhou, Jiangyin, Taicang, Suining, Jurong, Sihong, and Haimen Centres for their support for data collection. The research was supported by The University of Adelaide and Jiangsu Provincial Centre for Disease Control and Prevention.

Z. S. contributed to the statistical analysis and manuscript writing. Z. S., S. Z. and Y. Z. contributed to the design, conduct and data collection. Z. S., S. Z., Y. Z. and A. W. T. contributed to manuscript revision. A. W. T. contributed to data analysis. All authors read and approved the final manuscript.

The authors declare that there are no conflicts of interest.

Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S000711451700040X

References

1. Kassebaum NJ, Jasrasaria R, Naghavi M, *et al.* (2014) A systematic analysis of global anemia burden from 1990 to 2010. *Blood* **123**, 615–624.
2. Li L, Rao K, Kong L, *et al.* (2005) A description on the Chinese national nutrition and health survey in 2002. *Zhonghua Liu Xing Bing Xue Za Zhi* **26**, 474–484.
3. Zimmermann MB & Hurrell RF (2007) Nutritional iron deficiency. *Lancet* **370**, 511–520.
4. Fishman SM, Christian P & West KP (2000) The role of vitamins in the prevention and control of anaemia. *Public Health Nutr* **3**, 125–150.
5. Shi Z, Zhen S, Wittert GA, *et al.* (2014) Inadequate riboflavin intake and anemia risk in a Chinese population: five-year follow up of the Jiangsu Nutrition Study. *PLOS ONE* **9**, e88862.
6. Bao W, Rong Y, Rong S, *et al.* (2012) Dietary iron intake, body iron stores, and the risk of type 2 diabetes: a systematic review and meta-analysis. *BMC Med* **10**, 119.
7. Shi Z, Zhou M, Yuan B, *et al.* (2010) Iron intake and body iron stores, anaemia and risk of hyperglycaemia among Chinese adults: the prospective Jiangsu Nutrition Study (JIN). *Public Health Nutr* **13**, 1319–1327.
8. Shi Z, Hu X, Yuan B, *et al.* (2006) Association between serum ferritin, hemoglobin, iron intake, and diabetes in adults in Jiangsu, China. *Diabetes Care* **29**, 1878–1883.
9. Basuli D, Stevens RG, Torti FM, *et al.* (2014) Epidemiological associations between iron and cardiovascular disease and diabetes. *Front Pharmacol* **5**, 117.
10. Zhang W, Iso H, Ohira T, *et al.* (2012) Associations of dietary iron intake with mortality from cardiovascular disease: the JACC study. *J Epidemiol* **22**, 484–493.
11. Lee DH, Folsom AR & Jacobs DR Jr (2005) Iron, zinc, and alcohol consumption and mortality from cardiovascular diseases: the Iowa Women's Health Study. *Am J Clin Nutr* **81**, 787–791.
12. Hunnicutt J, He K & Xun P (2014) Dietary iron intake and body iron stores are associated with risk of coronary heart disease in a meta-analysis of prospective cohort studies. *J Nutr* **144**, 359–366.
13. Sullivan JL (1981) Iron and the sex difference in heart disease risk. *Lancet* **i**, 1293–1294.
14. Sempos CT & Looker AC (2001) Iron status and the risk of coronary heart disease: an example of the use of nutritional epidemiology in chronic disease research. *J Nutr Biochem* **12**, 170–182.
15. Kengne AP, Czernichow S, Hamer M, *et al.* (2012) Anaemia, haemoglobin level and cause-specific mortality in people with and without diabetes. *PLOS ONE* **7**, e41875.
16. Kabat GC, Kim MY, Verma AK, *et al.* (2016) Association of hemoglobin concentration with total and cause-specific mortality in a cohort of postmenopausal women. *Am J Epidemiol* **183**, 911–919.
17. Ruel G, Shi Z, Zhen S, *et al.* (2014) Association between nutrition and the evolution of multimorbidity: the importance of fruits and vegetables and whole grain products. *Clin Nutr* **33**, 513–520.
18. Dallman PR (1984) Diagnosis of anemia and iron deficiency: analytic and biological variations of laboratory tests. *Am J Clin Nutr* **39**, 937–941.
19. World Health Organization (1968) Nutritional anaemias. Report of a WHO scientific group. *World Health Organ Tech Rep Ser* **405**, 5–37.
20. Shi Z, Hu X, He K, *et al.* (2008) Joint association of magnesium and iron intake with anemia among Chinese adults. *Nutrition* **24**, 977–984.
21. Yang Y (2005) *Chinese Food Composition Table 2004*. Beijing: Peking University Medical Press.
22. Zhou BF, Cooperative Meta-Analysis Group of the Working Group on Obesity in C (2002) Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults – study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed Environ Sci* **15**, 83–96.
23. StataCorp (2015) *Stata 14 Base Reference Manual*. College State, TX: Stata Press.
24. Chinese Nutrition Society (2013) *Chinese DRIs Handbook*. Beijing: Standards Press of China.
25. Orsini N & Greenland S (2011) A procedure to tabulate and plot results after flexible modeling of a quantitative covariate. *Stata J* **11**, 1–29.
26. Wang X, Wu Z, Chen Y, *et al.* (2015) Increased prevalence and incidence of anemia among adults in transforming rural China: two cross-sectional surveys. *BMC Public Health* **15**, 1–6.
27. Zhai F, Wang H, Du S, *et al.* (2007) Lifespan nutrition and changing socio-economic conditions in China. *Asia Pac J Clin Nutr* **16**, Suppl. 1, 374–382.
28. Huo JS, Yin JY, Sun J, *et al.* (2015) Effect of NaFeEDTA-fortified soy sauce on anemia prevalence in China: a systematic review and meta-analysis of randomized controlled trials. *Biomed Environ Sci* **28**, 788–798.
29. Shi Z & Taylor A (2015) Nutritional determinants of anemia among adults in Eastern China. *World J Transl Med* **4**, 55–59.
30. Shi Z, Hu X, Yuan B, *et al.* (2008) Coexistence of anaemia and the metabolic syndrome in adults in Jiangsu, China. *Asia Pac J Clin Nutr* **17**, 505–513.

31. Zhang L, Wang F, Wang L, *et al.* (2012) Prevalence of chronic kidney disease in China: a cross-sectional survey. *Lancet* **379**, 815–822.
32. Provatopoulou ST & Ziroyiannis PN (2011) Clinical use of erythropoietin in chronic kidney disease: outcomes and future prospects. *Hippokratia* **15**, 109–115.
33. Shi Z, Zhang C, Zhou M, *et al.* (2013) Exposure to the Chinese famine in early life and the risk of anaemia in adulthood. *BMC Public Health* **13**, 904.
34. Huang C, Li Z, Wang M, *et al.* (2010) Early life exposure to the 1959–1961 Chinese famine has long-term health consequences. *J Nutr* **140**, 1874–1878.
35. Li Y, He Y, Qi L, *et al.* (2010) Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. *Diabetes* **59**, 2400–2406.
36. Sempos CT, Looker AC, Gillum RE, *et al.* (2000) Serum ferritin and death from all causes and cardiovascular disease: the NHANES II Mortality Study. National Health and Nutrition Examination Study. *Ann Epidemiol* **10**, 441–448.
37. Powers HJ, Wright AJ & Fairweather-Tait SJ (1988) The effect of riboflavin deficiency in rats on the absorption and distribution of iron. *Br J Nutr* **59**, 381–387.
38. Sirivech S, Frieden E & Osaki S (1974) The release of iron from horse spleen ferritin by reduced flavins. *Biochem J* **143**, 311–315.
39. Shi Z, Yuan B, Hu G, *et al.* (2011) Dietary pattern and weight change in a 5-year follow-up among Chinese adults: results from the Jiangsu Nutrition Study. *Br J Nutr* **105**, 1047–1054.

British Journal of Nutrition