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#### Anemia and associated factors among the elderly in an urban district in China: a large-scale cross-sectional study

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1	Anemia and associated factors among the elderly in an urban
2	district in China: a large-scale cross-sectional study
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3	1	Abstract
4 5	2	<b>Objective</b> : Anemia leads to poor health outcomes in the elderly however most
5	- 3	current research in China has focused on younger adults. The present study aimed to
7	1	investigate the prevalence of anemia and its associated risk factors in elderly
8	4	individuals in an urban district in China
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10	6	Design: A cross-sectional study.
12	7	Setting: A urbanization region Shenzhen of China
13	,	Setting. A urbanization region, Shenzhen of China.
14	8	<b>Participants</b> : A total of 121,981 participants aged $\geq$ 65 years were recruited at local
15	9	community health service centers in Shenzhen from January to December 2018.
10 17	10	Primary outcomes: Their hemoglobin (Hb) levels and the prevalence of anemia were
18	11	analyzed and potential associated factors were evaluated.
19	12	<b>Results</b> : The mean Hb level was $13.64 \pm 1.67$ g/dL and the prevalence of anemia was
20	13	15.43%. Anemia was positively associated with older age, being underweight (odds
21	14	ratio $(OR)$ : 2.06, 95% confidence interval $(CI)$ : 1.93–2.20) diabetes $(OR)$ : 1.23, 95%
22	15	CI: 1.19-1.28) and chronic kidney disease (OR: 1.41, 95% CI: 1.36-1.46) and
23 24	10	inversely with higher education level current smoker ( $OP: 0.84, 0.5\%, CI: 0.78, 0.80$ )
25	10	inversely with higher ( $OB$ : 0.86, 0.50/ $CL$ : 0.81, 0.02), habitual drinker ( $OB$ : 0.81, 0.50/
26	17	non-nabitual drinker ( $OR$ : 0.86, 95% $CI$ : 0.81–0.92), nabitual drinker ( $OR$ : 0.81, 95% $CI$ : 0.87, 0.67)
27	18	CI: 0.75-0.87, overweight ( $OR: 0.67, 95%$ $CI: 0.64-0.70$ ), obesity ( $OR: 0.57, 95%$
28 20	19	CI: $0.53-0.61$ ), central obesity (OR: $0.86$ , $95\%$ CI: $0.82-0.89$ ), hypertension (OR:
30	20	0.86, 95% <i>CI</i> : 0.83–0.89), and dyslipidemia ( <i>OR</i> : 0.81, 95% <i>CI</i> : 0.78–0.84).
31	21	Conclusion: Anemia is prevalent among people aged 65 years and older in China.
32	22	Prevention, screening of key populations, and treatment of senile anemia should be a
33	23	top priority in Shenzhen, and should be listed as important public health intervention
34 35	24	measures for implementation.
36	25	<b>Keywords</b> : elderly, anemia, epidemiologic study, risk factor
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#### Strengths and limitations of this study

This is the first large-scale cross-sectional study to assess the prevalence of anemia and its factors in an urban district in China. 

■ This study had a sufficient sample size to detect statistical significance in the prevalence of anemia among elderly.

Convenience sampling was used to enroll the population sample. 

The data set used in this study did not provide information on dietary behaviour of to been teriewoony the participants. 

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#### 1. Introduction

Anemia, characterized by decreased hemoglobin (Hb) levels, occurs when low numbers of red blood cells reduce the ability of the blood to carry oxygen to meet the body's physiological needs. Although anemia may occur at any stage of life, older people are particularly vulnerable,<sup>1, 2</sup> and anemia in the elderly is a risk factor for a variety of adverse health outcomes, such as hospitalization, disability, and death.<sup>1</sup>, <sup>3-5</sup>Anemia is also an independent risk factor for declining physical performance, and has a negative impact on quality of life, physical function, and muscle strength in older people.<sup>6-8</sup> 

Globally, 11.0% of men and 10.2% of women aged > 65 years are anemic<sup>9</sup>. Ruan et al. revealed that the prevalence of anemia among middle-aged and elderly residents in China was 31.0%<sup>10</sup>, while Qin et al. reported a prevalence of 12.86% among similar populations from 2011 to 2012.<sup>11</sup> Although China has seen a significant reduction in anemia among middle-aged and elderly residents in the past decade, its occurrence among the elderly cannot be neglected. 

A total of 150 million Chinese were aged 65 years or above in 2016, accounting for 10.8% of the population.<sup>12</sup> Improving anemia in the elderly thus has important public health implications. Previous studies have investigated the prevalence of anemia in middle-aged and elderly people, but there is a lack of large-scale studies on anemia in the urban elderly population.<sup>10, 11, 13</sup> The current study therefore aimed to assess the prevalence of anemia and associated factors among elderly people in an 4.6 urban district in China. 

#### 2. Materials and methods

#### a) Study population

We used convenience sampling to select our population sample by recruiting people aged 65 years and older from the lists of all residents registered at local community health centers in Shenzhen, China, from January 2018 through December 2018. Recruitment activities include pasting posters or placing foldings in local community health centers and other public places. Electronic posters also be distributed via all the open WeChat groups of local community health centers' staff, to make the survey available to the close contacts easily. Moreover, the staff of the local community health centers recruited the elderly adults in their service community to participate in the survey by telephone. The eligibility criteria were as follows: (1) having lived in Shenzhen for more than 6 months; and (2) able to participate in the study and give informed consent. A total of 141,684 individuals were recruited in this study, accounting for 36.9% (141,684/383,700) of the resident elderly population in Shenzhen according to the 2015 population census. Data were collected at examination centers in local community health centers in the participants' residential areas. Participants were asked to complete a questionnaire, provide a fasting blood sample, and undergo physical examinations. A total of 19,703 respondents were excluded because of failure to fulfil one or all of these requirements. Finally, 121,981 participants (86.09%) were included in the final data analysis. 

#### 1 2.2 Questionnaire survey

Prior to the study, all investigators completed a training course to understand the
methodology and process of the study. Working manuals containing questionnaire
techniques, blood pressure measurement, anthropometric measurements, biological
sample collection, and processing information were distributed to all the investigators.

Data were recorded by face-to-face interview 1 hour after blood collection. All participants completed a standardized questionnaire including questions on sociodemographic status (e.g., date of birth, sex, education level, marital status), past medical history (e.g., history of previous disease, operation history, history of trauma), family health history (e.g., hypertension, diabetes, coronary heart disease, malignant tumor, stroke), lifestyle (e.g., smoking, physical activity, alcohol consumption), and medication use, under the supervision of trained general practitioners and nurses. Educational level was categorized into three groups according to the number of years of education: illiterate, no education; primary education, 1–6 years of education; and junior high school education and above, seven or more years of education. Regarding drinking habits, participants were classified as habitual drinkers (drink at least once a day), non-habitual drinkers (six times a week to once a month), or non-drinker (almost never).<sup>14</sup> Based on a previous study, we divided participants into current smokers, ex-smokers, and never-smokers.<sup>15</sup> 

#### 20 2.3 Physical examination

Anthropometric examinations were carried out in the morning after overnight fasting, and body measurements were taken by trained examiners based on a standardized protocol. The physical examination methods were described as previous study.<sup>12</sup> Height and weight were measured with the participants wearing light clothing without shoes, using analogue scales. Waist circumference (WC) was measured at the end of normal expiration at the midpoint level of the mid-axillary line between the 12th rib head and the superior anterior iliac spine. Body mass index (BMI) was calculated by dividing body weight (in kilograms) by height squared (in meters). Blood pressure were measured in both arms and recorded the higher one. Calibrated electronic sphygmomanometers were used to measure blood pressure on the arm supported at heart level with sitting position, carried out twice. The average of the two measurements was used for the statistical analysis. To obtain accurate readings, the participants were asked to rest for at least 5 min before the measurement, or, if having engaged in excessive exercise prior to the visit, for at least 30 min before the measurement.

#### **2.4 Blood sample collection and biochemical analyses**

Venous blood samples were taken after overnight fasting for at least 8 hours. All blood samples were analyzed in clinical laboratories at the grade 2 hospitals to which the community health centers were directly affiliated. All the laboratories had successfully completed a standardization and competency program. Fasting venous blood was used to measure levels of Hb, plasma glucose, creatinine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) using an automatic biochemistry analyzer. Biochemical analysis of fresh blood samples was completed within 4 hours. 

1 Serum creatinine was used to calculate the estimated glomerular filtration rate (eGFR)

2 using the full age spectrum equation.<sup>16</sup>

#### **2.5 Definitions**

Anemia was defined as a Hb concentration < 13 g/dL in men and < 12 g/dL in women, according to World Health Organization standards.<sup>17</sup> Chronic kidney disease (CKD) was defined as eGFR  $< 60 \text{ mL/min}/1.73 \text{ m}^{2.18}$  A diagnosis of hypertension was considered when three consecutive high readings ( $\geq 140$  systolic and/or  $\geq 90$ mm Hg diastolic) with 2-week intervals were registered or treatment with antihypertensive medication within the previous 2 weeks was self-reported.<sup>19, 20</sup> Participants who met one of the following three criteria were diagnosed with diabetes: (1) previously diagnosed by professional doctors, (2) fasting plasma glucose (FBG)  $\geq$ 7.0 mmol/L, and (3) 2-hour plasma glucose level  $\geq$  11.1 mmol/L.<sup>21</sup> High TC, high TG, high LDL-C, and low HDL-C were diagnosed according to the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults.<sup>22</sup> In this study, we defined dyslipidemia as an abnormal concentration of one or more lipid components or the use of anti-dyslipidemia medications in the past 2 weeks. 

17Participants were divided into four groups based on the adult weight criteria18published by the Ministry of Health of China (WS/T 428-2013): BMI < 18.5 kg/m²</td>19(low weight), BMI  $\ge 18.5$  kg/m² and <24.0 kg/m² (normal weight), BMI  $\ge 24.0$  kg/m²20and < 28.0 kg/m² (overweight), and BMI  $\ge 28.0$  kg/m² (obesity). A WC  $\ge 90$  cm for21men and  $\ge 85$  cm for women was defined as central obesity.

#### **2.6 Statistical analyses**

Descriptive statistics, including means and standard deviations, were used to compute continuous variables. Numerical data were expressed as percentages and compared by  $\chi^2$  tests. Multivariate logistic regression analysis was performed to explore the association between prevalence of amemia and associated risk factors. In the multivariate logistic regression model, the prevalence of anemia was defined as the dependent variable, and gender, education level, age group, smoking status, drinking habit, BMI, central obesity, diabetes, hypertension, dyslipidemia and CKD were defined as the independent variables. Data analysis was carried out using SAS 9.4 (Institute, Cary, NC, USA). A two-sided value of P < 0.05 was considered to be statistically significant. 

33 2.7 Participants and public involvement

Neither the study participants nor the public were involved in the design, recruitment or conduct of the study. All the participants had the option of receiving a health check and biochemical results when they visited the local community health centers.

#### **2.8 Ethical Approval Statement**

The study received ethnicity approval from the Center for Chronic Disease Control in Shenzhen(Grant No: SZCCC-201802, SZCCC-2020-018-01-PJ). The study complies with the guidelines of the Declaration of Helsinki. Written informed consent was received by all participants before the collection of data and conducting of the research. Where participants were illiterate, we obtained written informed consent from their proxies.

## 1 3. Results

### 3.1 Characteristics of participants

The characteristics of the study participants are shown in Table 1. The mean age was  $71.28 \pm 5.58$  years (range 65–103 years). There were 54,649 men and 69,358 women, and > 50% of participants had a minimum of a junior school education. Among the study population, 8.22% were current smokers and 6.35% were habitual drinkers. The mean Hb, BMI, SBP, DBP, WC, FBG, TC, TG, LDL-C, HDL-C, and eGFR values among all 121,981 participants were  $13.64 \pm 1.67$  g/dL,  $23.83 \pm 3.17$ kg/m<sup>2</sup>, 134.71  $\pm$  17.69 mmHg, 77.23  $\pm$  10.31 mmHg, 85.10  $\pm$  8.82 cm, 5.96  $\pm$  1.90 mmol/L,  $5.21 \pm 2.00 mmol/L$ ,  $1.57 \pm 1.14 mmol/L$ ,  $3.09 \pm 1.05 mmol/L$ ,  $1.39 \pm 1.05$ mmol/L, and  $68.74 \pm 16.70$  mL/min/1.73m<sup>2</sup>, respectively. A total of 100,762 participants (82.60%) had at least one chronic disease, with hypertension (55.61%), dyslipidemia (44.73%), CKD (31.09%), and diabetes (22.31%) being the most prevalent (data not shown). 

## **3.2 Prevalence of anemia in different subgroups**

The overall prevalence anemia was 15.43%. The prevalence of anemia among subpopulations is shown in Table 2. Anemia was significantly more prevalent in women than in men and generally increased with age. The prevalence was lower among individuals with at least primary-level education, and lower in current smokers and habitual drinkers compared with their counterparts. The prevalence of anemia was higher in participants with low weight and lower in those with overweight, obesity, central obesity, hypertension, or dyslipidemia. Individuals with diabetes or CKD had a higher prevalence of anemia than those without these conditions. 

## **3.3** Association between anemia and related variables

Binary logistic regression analysis was carried out with presence or absence of anemia as the dependent variable, and factors in univariate analysis as independent variables to determine the factors influencing anemia. Higher education level, current-smoker, drinker, overweight, obesity, central obesity, hypertension, and dyslipidemia were independently associated with lower odds for the presence of anemia (Fig. 1), while older age, underweight, diabetes, and CKD were independently associated with greater odds (Fig. 1). However, there was no significant difference in the risk of anemia in relation to sex. 

## **4. Discussion**

In this study, the prevalence of anemia among elderly individuals in an urban district in China was 15.43%. This was higher than the 12.86% reported in previous national studies in China,<sup>11</sup> but lower than the 18.90% prevalence reported in the 2009 national survey in China.<sup>23</sup> The difference in prevalence rates among these studies may have been caused by differences in study design, sample size, and/or the age of the study participants.

41 The current study found a significant negative correlation between anemia42 prevalence and educational level. This was consistent with studies conducted in Nepal

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and Pakistan, which confirmed that a low educational level was a risk factor for anemia.<sup>24</sup> This relationship probably occurs because higher levels of education enable people to earn more and thus escape from the poverty trap. Multivariate analysis also identified older age as an independent risk factor for anemia, consistent with the findings of other related studies.<sup>9, 25</sup> The prevalence of anemia increased with age, with a two-to-three-fold increase (26.89% vs. 12.72%) in people aged > 80 years, suggesting the need for routine screening for anemia in this high-risk subgroup.

8 Current smokers had a lower risk of anemia than never smokers, and habitual 9 drinking was also associated with a decreased risk of anemia (odds ratio: 0.81). 10 However, these findings were not consistent with an Indian study.<sup>26</sup> Considering the 11 potential risks to human health from alcohol or tobacco use, we do not recommend 12 that alcohol or tobacco should be used as protective factors against anemia.

We also found a negative association between increased BMI and anemia prevalence, in accord with other studies conducted in China, the United States, Nepal, and Pakistan.<sup>24, 27</sup> The reasons for being underweight may include poor distribution of inadequate food within the family, food insecurity, poverty, and micronutrient deficiencies, which tend to coexist with other macronutrient deficiencies. The underlying mechanism accounting for the significant negative association between overweight or obesity and anemia risk is unclear; however there are several possible explanations. First, obese participants are less likely to be malnourished, because excess calorie intake leads to obesity,<sup>28</sup> and overnutrition in obese participants may thus be associated with a significant reduction in anemia risk. Second, obese participants may have a variety of other diseases that could increase Hb levels, such as obstructive sleep apnea and other obesity-related breathing disorders, which lead to chronic tissue hypoxia and increased red blood cells.<sup>29</sup> 

We found that older people with diabetes had higher rates of anemia than non-diabetics, consistent with previous studies.<sup>30</sup> Evidence indicates that the incidence and prevalence of anemia in diabetic patients is often associated with erythropoietin deficiency caused by diabetic kidney damage.<sup>31</sup> Other researchers have also shown a link between anemia and hypertension, as shown in our current study.<sup>18</sup>

This study showed that the prevalence of anemia was low among individuals with dyslipidemia. A study by Zaribaf et al. found a significant positive correlation between Hb levels and dyslipidemia.<sup>32</sup> However, this study differed from our study in that it assessed the relationship between anemia and lipids in premenopausal women, whereas our study focused on older adults (aged 65–113 years).<sup>32</sup> In contrast, a study conducted by other researchers in women of childbearing age found no significant association between serum LDL and anemia.<sup>32</sup> The reasons for the different results in terms of the relationship between dyslipidemia and anemia deserve further investigation. Patients with CKD have defects in renal endocrine function, resulting in decreased erythropoietin secretion by the kidney, leading to nephrogenic anemia.<sup>33</sup> Nearly half of all patients with CKD have anemia.<sup>33</sup> The current study found the similar results.

This study had some limitations. First, it was a cross-sectional study and could only
infer correlation, not causation. Second, we adopted a convenient sampling method to

recruit elderly participants. This is a major factor preventing true extrapolation of the results to the general population. Finally, renal disease was assessed based on a one-time GFR measurement, possibly leading to overestimation of the actual prevalence of CKD. However, these limitations do not affect the significance of the results, which provide the first evidence of the prevalence and risk factors of anemia among elderly individuals in urban China.

#### 5. Conclusion

In conclusion, anemia is prevalent among the elderly population in China, with older age, underweight, diabetes, CKD, and anemia being positively associated with anemia, and higher education level, current-smoker, drinker, overweight, obesity, central obesity, hypertension, and dyslipidemia being negatively associated. The prevention, screening of key populations, and treatment of senile anemia should be a top priority in Shenzhen, and should be listed as important public health intervention measures for implementation.

#### 18 Acknowledgments

We are grateful to all the volunteers for participating in the present study, and to all the investigators for their support and hard work during this survey.

#### Author Contributions

WN, XY, and JX: study conception and design. WN, XY, JZ, PL, HZ, YZ, and JX: performance of research. XY and JZ: data analysis and interpretation. WN and XY: writing the original draft. WN and JX: Writing the review and editing. All authors have read and agreed to the published version of the manuscript.

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#### **Conflicts of Interest**

The authors declare no conflict of interest.

#### Patient consent for publication

Not required.

#### 40 Ethics approval

This study was approved by the ethical review committee of the Center for Chronic Disease Control of Shenzhen.

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3	1	Data s	sharing statement
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## 1 Tables

Table 1 Sociodemographic and other characteristics of older adults living in
 Shenzhen community (N=121981)

Characteristics	General
Age (years)	$71.28 \pm 5.58$
Hb(g/dL)	$13.64 \pm 1.67$
BMI (Kg/m2)	$23.83 \pm 3.17$
SBP (mm Hg)	$134.71 \pm 17.69$
DBP (mm Hg)	$77.23 \pm 10.31$
WC (cm)	$85.1 \pm 8.82$
FBG (mmol/L)	$5.96 \pm 1.9$
TC(mmol/L)	$5.21 \pm 2$
TG(mmol/L)	$1.57 \pm 1.14$
LDL-C(mmol/L)	$3.09 \pm 1.05$
HDL-C(mmol/L)	$1.39 \pm 0.51$
eGFR	$68.74 \pm 16.7$
Gender, n(%)	
Male	54649 (44.07%)
Female	69358 (55.93%)
Education level, n(%)	
Illiterate	9888 (8.11%)
Primary education	43441 (35.61%)
Junior school education and above	68652 (56.28%)
Smoking status, n (%)	
Current smoker	10023 (8.22%)
Ex-smoker	7546 (6.19%)
Never-smoker	104412 (85.6%)
Drinking habit, n (%)	
Non-drinker	101661 (83.34%)
Non-habitual drinker	12571 (10.31%)
Habitual drinker	7749 (6.35%)

<sup>5</sup> 2 according to sociodemograph	ic and other char	acteristics				
6 Characteristics	Total	Ν	%	$\chi^2$ Value	Р	Value
Total	121981	18820	15.43			
Gender				22.36		< 0.001
<sup>10</sup> Male	53743	7946	14.79			
Female	68238	10874	15.94			
<sup>2</sup> Education level				263.21		< 0.001
4 Illiterate	9888	2027	20.50			
<sup>5</sup> Primary education	43441	7240	16.67			
Junior school education and above	68652	9553	13.92			
8 Age group				1201.99		< 0.001
9 65~	60043	7635	12.72			
$^{20}_{11}$ 70~	32750	4730	14.44			
$22 75 \sim$	16599	3070	18.50			
$^{23}$ 80 $\sim$	12589	3385	26.89			
$\frac{24}{5}$ Smoking status				68.89		< 0.001
6 Current smoker	10023	1253	12.50			
27 Ex-smoker	7546	1047	13.87			
<sup>28</sup> Never-smoker	104412	16520	15.82			
Drinking habit				130.24		< 0.001
Non-drinker	101661	16302	16.04			
<sup>32</sup> Non-habitual drinker	12571	1589	12.64			
Habitual drinker	7749	929	11.99			
B5 BMI				1522.11		< 0.001
<sup>36</sup> Low weight	4496	1504	33.45			
<sup>37</sup> Normal weight	61532	11041	17.94			
<sup>38</sup> Overweight	44644	5175	11.59			
0 Obesity	11309	1100	9 73			
<sup>41</sup> Central obesity	11507	1100	5.15	540 10		< 0.001
2 Yes	49051	5897	12.02	010110		\$0.001
A No	72930	12923	17.72			
5 Diabetes	12950	12725	17.72	27.05		< 0.001
Ves	27220	4520	16.61	27.05		<0.001
No	94761	14300	15.09			
9 Hypertension	74/01	14500	15.07	63 27		< 0.001
0 Vec	67835	0883	14 57	05.27		< 0.001
1 No	5/1/6	2005 8037	16.51			
2 IV 3 Dyslinidemia	54140	0751	10.31	211 72		< 0 001
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	0/41/	11400	17.01	671 21		~0.001
/ UND 18 Vas	27027	7571	10.07	024.34		~0.001
<sup>1</sup> 1 es 59 NL	5/92/	/3/4	19.9/			
50 <u>INO</u>	84054	11246	13.38			

#### 1 Figure legends

Fig 1 Risk factors analyses on the prevalence of anemia in older adults living inShenzhen community

tor occreation with

1	Characteristics	OR(95%CI)
3	Gender	
4	Female	1
5	Mala	
6 7		1.00 (0.97–1.04)
8	Education level	
9	Illiterate	1
10	Primary education	0.89 (0.84–0.94)
12	Junior school education and above	0.72 (0.68–0.76)
13	Age group	, , , , , , , , , , , , , , , , , , ,
15	65~	1
16	70	1 10 (1 06_1 15)
17		1.10 (1.00–1.13)
18	75~	1.37 (1.31–1.44)
20	80~	1.96 (1.86–2.06)
21	Smoking status	
22	Never-smoker	1
23 24		0 84 (0 78–0 89)
25		
26	Ex-smoker	1.00 (0.93–1.08)
27	Drinking habit	
28 29	Non-drinker	1
30	Non-habitual drinker	0.86 (0.81–0.92)
31	Habitual drinker	0.81 (0.75–0.87)
32	RMI	, , , , , , , , , , , , , , , , , , ,
34		
35		1
36	Underweight	2.06 (1.93–2.20)
38	Overweight	0.67 (0.64–0.70)
39	Obesity	0.57 (0.53–0.61)
40	Central obesity	
42	No	1
43		
44		0.86 (0.82-0.89)
45 46	Diabetes	
47	No	1
48	Yes	1.23 (1.19–1.28)
49 50	Hypertension	
51	No	1
52	Yes	0.86 (0.83–0.89)
54	Dyslinidemia	
55	No	4
56	INU	1
57 58	Yes	0.81 (0.78–0.84)
59	СКД	
60	No	1
	Yes	1.41 (1.36–1.46)

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Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5-6
Bias	9	Describe any efforts to address potential sources of bias	Page 6
Study size	10	Explain how the study size was arrived at	Page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Not applicable
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
Results			

#### STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	Page 4
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Page7
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	Page 7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Page 7
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	Page 7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	Page 8-9
		magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	Page 7-9
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	Page 9
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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#### Anemia and associated factors among older adults in an urban district in China: a large-scale cross-sectional study

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Keywords:	Anaemia < HAEMATOLOGY, EPIDEMIOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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5 4 5	1	Anemia and associated factors among older adults in an urban
6 7	2	district in China: a large-scale cross-sectional study
8 9 10	3	
11 12 13	4	Wenqing Ni <sup>1#</sup> , Xueli Yuan <sup>1#</sup> , Yuanying Sun <sup>1</sup> , Hongmin Zhang <sup>1</sup> ,
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#### 1 Abstract

Objective: Anemia leads to poor health outcomes in older adults; however, most
current research in China has focused on younger adults. The present study aimed to
investigate the prevalence of anemia and its associated factors in older adults in an
urban district in China.

- **Design**: A cross-sectional study.
- 7 Setting: A urbanized region, Shenzhen, China.

**Participants**: A total of 121,981 participants aged  $\geq$  65 years were recruited at local 9 community health service centers in Shenzhen from January to December 2018.

Primary outcomes: The prevalence of anemia was analyzed and potential associated
 factors were evaluated.

**Results**: The mean Hemoglobin level was $13.64 \pm 1.67$ g/dL and the prevalence of anemia was 15.43%. Prevalence of mild, moderate and severe anemia were 12.24%, 2.94% and 0.25% respectively. Anemia was positively associated with older age, being underweight (adjusted odds ratio (AOR): 2.06, 95% confidence interval (CI): 1.93-2.20), diabetes (AOR: 1.23, 95% CI: 1.19-1.28), and chronic kidney disease (AOR: 1.41, 95% CI: 1.36–1.46), and inversely with higher education level, current-smoker (AOR: 0.84, 95% CI: 0.78–0.89), non-habitual drinker (AOR: 0.86, 95% CI: 0.81-0.92), habitual drinker (AOR: 0.81, 95% CI: 0.75-0.87), overweight (AOR: 0.67, 95% CI: 0.64-0.70), obesity (AOR: 0.57, 95% CI: 0.53-0.61), central obesity (AOR: 0.86, 95% CI: 0.82–0.89), hypertension (AOR: 0.86, 95% CI: 0.83– 0.89), and dyslipidemia (AOR: 0.81, 95% CI: 0.78–0.84). 

Conclusion: Anemia is prevalent among people aged 65 years and older in China.
 Screening of high-risk populations, and treatment of senile anemia should be a top
 priority in Shenzhen, and should be listed as important public health intervention
 measures for implementation.

27 Keywords: older adults, anemia, epidemiologic study, risk factor

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#### Strengths and limitations of this study

■ This was the first large-scale cross-sectional study to assess the prevalence of anemia and its factors in an urban district in China. 

This study had a sufficiently large sample size to detect significant differences in the prevalence of anemia among older adults.

Convenience sampling was used to enroll the population sample. 

The dataset used in this study did not provide information on the dietary behavior T To been teriew only of the participants. 

#### 1 1. Introduction

Anemia results from an inadequate number of erythrocytes which leads to a decreased ability to carry oxygen to meet the body's physiological demands. It is characterized by reduced levels of hemoglobin (Hb) in the blood in affected individuals. Anemia may occur at all stages of life, however, older people are among the most vulnerable.<sup>1,2</sup> Globally, 11.0% of men and 10.2% of women aged 65 years and older are anemic.<sup>3</sup> Anemia is a risk factor for a variety of adverse outcomes in the older population, including hospitalization, disability and mortality.<sup>1</sup> Previous studies found higher mortality rates in people aged 65 years and older hospitalized for myocardial infarction, patients with systolic and diastolic chronic heart failure (CHF), and in older CHF patients with anemia.<sup>4-6</sup> Anemia is also an independent risk factor for decline in physical performance and has a negative impact on quality of life, physical functioning, and muscle strength in older individuals.<sup>7-9</sup> Early identification and treatment of anemia is therefore an important strategy to improve the quality of life of older adults with anemia. 

In China, 13.5% of the total population (approximately 190.64 million people) were aged 65 years or older in 2020,<sup>10</sup> and increasing life expectancy and declining fertility rates mean that China is experiencing an ongoing aging process. In line with the aging of the population, anemia has become an important public health problem in China. The China Health and Retirement Longitudinal Study showed a prevalence of anemia in middle-aged and older Chinese residents of 12.86% from 2011 to 2012,<sup>11</sup> and the 2010–2012 China National Nutrition and Health Survey found a prevalence of anemia in older Chinese people of 12.6%.<sup>12</sup> Preventing anemia and improving the health of older adults in China are thus urgent issues. However, the only previous trial for preventing anemia examined the use of iron-fortified soy sauce in some cities in China, which aimed to reduce the prevalence of iron-deficiency anemia among women of reproductive age.<sup>13</sup> The prevention of anemia in older adults thus still presents a challenge, and limited measures have been taken to address this public health problem.

Identifying the factors affecting the occurrence of anemia would help to determine effective interventional targets. Economic development and living standards are important factors affecting anemia.<sup>14</sup> Most previous studies focused on the prevalence of anemia among middle-aged and older adults in urban and rural districts of China, but there is a lack of large-sample studies of anemia among older adults in urban districts.<sup>11,12,15,16</sup> This study therefore aimed to examine the prevalence of anemia and its related factors among people aged 65 or older in an urban district of China, to help develop strategies for future interventions and the prevention of anemia in older adults living in urban districts in China. 

39 2. Materials and methods

#### **2.1Study population**

We used convenience sampling to select our study population by recruiting people
aged 65 years and older from the lists of all residents registered at local community

health centers in Shenzhen, China, from January 2018 to December 2018. Recruitment activities include pasting posters or placing leaflets in local community health centers and other public places. Electronic posters were also distributed via all the open WeChat groups of local community health center staff, to make the survey easily available to close contacts . The staff of the local community health centers also recruitedolder adults adults in their community to participate in the survey by telephone. The eligibility criteria were as follows: (1) lived in Shenzhen for more than 6 months; (2) able to participate in the study and give informed consent; and (3) conscious and able to cooperate to complete the face-to-face interview, medical examinations and biomedical tests. We excluded residents living in prisons. A total of 141,684 individuals were recruited in this study, accounting for 36.9% (141,684/383,700) of the resident older adult population in Shenzhen according to the 2015 population census. Data were collected at examination centers in local community health centers in the participants' residential areas. Participants were asked to complete a questionnaire, provide a fasting blood sample, and undergo physical examinations. A total of 19,703 respondents were excluded because of failure to fulfil one or all of these requirements. Finally, 121,981 participants (86.09%) were included in the final data analysis. 

#### **2.2 Questionnaire survey**

Prior to the study, all investigators completed a training course to understand the
methodology and process of the study. Working manuals containing questionnaire
techniques, blood pressure measurement, anthropometric measurements, biological
sample collection, and processing information were distributed to all the investigators.

Data were recorded by face-to-face interview 1 hour after blood collection. All participants completed a standardized questionnaire including questions on sociodemographic status (e.g., date of birth, sex, education level, marital status), past medical history (e.g., history of previous disease, operation history, history of trauma), family health history (e.g., hypertension, diabetes, coronary heart disease, malignant tumor, stroke), lifestyle (e.g., smoking, physical activity, alcohol consumption), and medication use, under the supervision of trained general practitioners and nurses. Educational level was categorized into three groups according to the number of years of education: not educated; primary education(1-6 years of education); and junior high school education and above ( $\geq 7$  years of educatio). Regarding drinking habits, participants were classified as habitual drinkers (drink at least once a day), non-habitual drinkers (six times a week to once a month), or non-drinker (almost never).<sup>17</sup> Based on a previous study, we divided participants into current smokers, ex-smokers, and never-smokers.<sup>18</sup> 

38 2.3 Physical examination

Anthropometric examinations were carried out in the morning after overnight fasting, and body measurements were taken by trained examiners based on a standardized protocol. Height and weight were measured with the participants wearing light clothing without shoes, using analogue scales. Waist circumference (WC) was measured at the end of normal expiration at the midpoint level of the mid-axillary line between the 12th rib head and the superior anterior iliac spine. Body

#### **BMJ** Open

mass index (BMI) was calculated by dividing body weight (in kilograms) by height squared (in meters). Blood pressure was measured twice in both arms supported at heart level with the participants in a sitting position, using a calibrated electronic sphygmomanometer and the higher level was recorded and used for statistical analysis. To obtain accurate readings, the participants were asked to rest for at least 5 min before the measurement, or if they had engaged in excessive exercise prior to the visit, to rest for at least 30 min before the measurement.

## 8 2.4 Blood sample collection and biochemical analyses

Venous blood samples were taken after overnight fasting for at least 8 hours. All blood samples were analyzed in clinical laboratories at the grade 2 hospitals to which the community health centers were directly affiliated. All the laboratories had successfully completed a standardization and competency program. Fasting venous blood was used to measure levels of Hb, plasma glucose, creatinine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) using an automatic biochemistry analyzer. Biochemical analysis of fresh blood samples was completed within 4 hours. Serum creatinine was used to calculate the estimated glomerular filtration rate (eGFR) using the full age spectrum equation.<sup>19</sup> 

### 19 2.5 Operational definitions/measurements

Anemia was defined as a Hb concentration < 13 g/dL in men and < 12 g/dL in women, according to World Health Organization standards.<sup>20</sup> The severity of anemia was classified as mild (11-11.9 g/dL (women), 11-12.9 g/dL (men)), moderate (8-10.9 g/dL), and severe (<8 g/dL).<sup>20</sup> Chronic kidney disease (CKD) was defined as  $eGFR < 60 mL/min/1.73 m^{2.21}$  A diagnosis of hypertension was considered in participants with three consecutive high readings ( $\geq 140$  systolic and/or  $\geq 90$  mm Hg diastolic) with 2-week intervals or treatment with antihypertensive medication within the previous 2 weeks was self-reported.<sup>22, 23</sup> Participants who met one of the following three criteria were diagnosed with diabetes: (1) previously diagnosed by professional doctors, (2) fasting plasma glucose (FBG)  $\geq$  7.0 mmol/L, and (3) 2-hour plasma glucose level  $\geq$  11.1 mmol/L.<sup>24</sup> High TC, high TG, high LDL-C, and low HDL-C were diagnosed according to the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults.<sup>25</sup> In this study, we defined dyslipidemia as an abnormal concentration of one or more lipid components or the use of anti-dyslipidemia medications in the past 2 weeks. 

Participants were divided into four groups based on the adult weight criteria published by the Ministry of Health of China (WS/T 428-2013): BMI < 18.5 kg/m<sup>2</sup> (low weight), BMI  $\ge$  18.5 kg/m<sup>2</sup> and <24.0 kg/m<sup>2</sup> (normal weight), BMI  $\ge$  24.0 kg/m<sup>2</sup> and < 28.0 kg/m<sup>2</sup> (overweight), and BMI  $\ge$  28.0 kg/m<sup>2</sup> (obesity). A WC  $\ge$  90 cm for men and  $\ge$ 85 cm for women was defined as central obesity.<sup>26</sup>

**2.6 Statistical analyses** 

41 Descriptive statistics, including means and standard deviations, were used to 42 compute continuous variables. Numerical data were expressed as percentages and 43 compared by  $\chi^2$  tests. Multivariate logistic regression analysis was performed to 44 explore the associations between the prevalence of anemia and associated risk factors. **BMJ** Open

In the multivariate logistic regression model, the prevalence of anemia was defined as the dependent variable, and sex, education level, age group, smoking status, drinking habit, BMI, central obesity, diabetes, hypertension, dyslipidemia and CKD were defined as the independent variables. Data analysis was carried out using SAS 9.4 (Institute, Cary, NC, USA). A two-sided value of P < 0.05 was considered to be statistically significant.

#### 7 2.7 Participants and public involvement

8 Neither the study participants nor the public were involved in the design, 9 recruitment or conduct of the study. All the participants had the option of receiving a 10 health check and biochemical results when they visited the local community health 11 centers.

#### 12 2.8 Ethical Approval Statement

The study received ethical approval from the Center for Chronic Disease Control in Shenzhen(Grant No: SZCCC-201802, SZCCC-2020-018-01-PJ). The study complied with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all participants before the collection of data and conducting of the research. If the participants were not educated, we obtained written informed consent from their proxies (son, daughter, daughter-in-law, son-in-law, etc).

#### 19 3. Results

#### **3.1 Characteristics of participants**

The characteristics of the study participants are shown in Table 1. The mean age was  $71.28 \pm 5.58$  years (range 65–103 years). There were 54,649 men and 69,358 women, and > 50% of participants had a minimum of a junior school education. Among the study population, 8.22% were current smokers and 6.35% were habitual drinkers. The mean Hb, BMI, SBP, DBP, WC, FBG, TC, TG, LDL-C, HDL-C, and eGFR values among all 121,981 participants were  $13.64 \pm 1.67$  g/dL,  $23.83 \pm 3.17$  $kg/m^2$ , 134.71 ± 17.69 mmHg, 77.23 ± 10.31 mmHg, 85.10 ± 8.82 cm, 5.96 ± 1.90 mmol/L,  $5.21 \pm 2.00 mmol/L$ ,  $1.57 \pm 1.14 mmol/L$ ,  $3.09 \pm 1.05 mmol/L$ ,  $1.39 \pm 1.05$ mmol/L, and  $68.74 \pm 16.70$  mL/min/1.73m<sup>2</sup>, respectively. A total of 100,762 participants (82.60%) had at least one chronic disease, with hypertension (55.61%), dyslipidemia (44.73%), CKD (31.09%), and diabetes (22.31%) being the most prevalent (data not shown). 

#### 46 33

The overall prevalence anemia was 15.43% and the prevalence (95% confidence intervals(CI)) of mild, moderate and severe anemia were 12.24% (12.05-12.42), 2.94% (2.84-3.03) and 0.25% (0.23-0.28) respectively. The prevalence of anemia among subpopulations is shown in Table 2. Anemia was significantly more prevalent in women than in men and generally increased with age. The prevalence was lower among individuals with at least primary-level education, and lower in current smokers and habitual drinkers compared with their counterparts. The prevalence of anemia was higher in participants with low weight and lower in those with overweight, obesity, central obesity, hypertension, or dyslipidemia. Individuals with diabetes or CKD had a higher prevalence of anemia than those without these conditions. 

3.2 Prevalence of anemia in different subgroups

**3.3** Association between anemia and related variables

Binary logistic regression analysis was carried out with presence or absence of anemia as the dependent variable, and factors in univariate analysis as independent variables to determine the factors influencing anemia. Primary education(adjusted odds ratio (AOR)=0.89, 95%CI:0.84-0.94), junior school education and above (AOR=0.72, 95%CI:0.68-0.76) current-smoker (AOR=0.84, 95%CI:0.78-0.89), non-habitual drinker (AOR=0.86, 95%CI:0.81-0.92), habitual drinker (AOR=0.81, 95%CI:0.75-0.87), overweight (AOR=0.67, 95%CI:0.64-0.70), obesity(AOR=0.57, 95%CI:0.53-0.61), central obesity (AOR=0.86, 95%CI:0.82-0.89), hypertension (AOR=0.86, 95%CI:0.83-0.89), and dyslipidemia (AOR=0.81, 95%CI:0.78-0.84) were independently associated with lower odds for the presence of anemia (Fig. 1), while age 70-74 years (AOR=1.10, 95%CI:1.06-1.15), age 75-79 years (AOR=1.37, 95%CI:1.31-1.44), age  $\geq$  80 years (AOR=1.96, 95%CI:1.86-2.06), underweight (AOR=2.06, 95%CI:1.93-2.20), diabetes (AOR=1.23, 95%CI:1.19-1.28), and CKD (AOR=1.41, 95%CI:1.36-1.46) were independently associated with greater odds (Fig. 1). However, there was no significant difference in the risk of anemia in relation to sex. 

#### 18 4. Discussion

This was the first large-scale cross-sectional survey to report the prevalence of anemia in older adults (aged 65 years or older) living in an urban district of China. This study demonstrated that the prevalence of anemia was relatively high, representing a public health problem in Shenzhen. After controlling for the confounding factors we found that the prevalence of anemia varied with education level, age group, smoking status, drinking habit, BMI, central obesity, and some non-communicable diseases.

The prevalence of anemia among older adults in an urban district in China in current study was 15.43%, which was higher than the 12.86% reported in previous national studies in China,<sup>11</sup> but lower than the 18.90% reported in the 2009 national survey in China.<sup>13</sup> The difference in prevalence rates among these studies may have been caused by differences in study design, sample size, and/or the age of the study participants.

The current study found a significant negative correlation between anemia prevalence and educational level. This was consistent with studies conducted in Nepal and Pakistan, which confirmed that a low educational level was a risk factor for anemia.<sup>27</sup> This relationship probably occurs because higher levels of education enable people to earn more and thus escape from the poverty trap. Multivariate analysis also identified older age as an independent risk factor for anemia, consistent with the findings of other related studies.<sup>3, 28</sup> The prevalence of anemia increased with age, with a two-to-three-fold increase (26.89% vs. 12.72%) in people aged > 80 years, suggesting the need for routine screening for anemia in this high-risk subgroup. 

41 Current smokers had a lower risk of anemia than never smokers. Similarly,
 42 previous studies showed that smoking was negatively correlated with the risk of
 43 anemia.<sup>29,30</sup> A multiple logistic regression analysis of the health check-up database of

St. Luke's International Hospital in Tokyo between April 2016 and March 2017 revealed that Japanese women (35-49 years) who were current smokers had a 25% lower risk of anemia compared with non-smokers, after adjusting for the covariates.<sup>30</sup> Increased Hb levels in smokers were associated with elevated carboxyhemoglobin (HbCO), a stable complex of Hb and carbon monoxide (CO), because of the exposure to excess CO caused by smoking.<sup>31</sup> The form of HbCO decreases oxygen delivery, and smokers had compensatory elevated Hb to increase erythropoiesis and maintain oxygen transportation.<sup>32</sup> This might explain why adaptation to excess CO during smoking was reflected by increases in Hb and RBC mass.<sup>33</sup> Habitual drinking was also associated with a decreased risk of anemia, with a corresponding OR of 0.81, consistent with a Korean study.<sup>29</sup> However, the direct causality of this negative correlation between alcohol drinking and anemia is still unclear.<sup>29</sup> Given the potential risks of alcohol and tobacco consumption to human health, we do not recommend increasing alcohol consumption or smoking to protect against anemia. 

We also found a negative association between increased BMI and anemia prevalence, in accord with other studies conducted in China, the United States, Nepal, and Pakistan.<sup>27, 34</sup> The reasons for being underweight may include poor distribution of inadequate food within the family, food insecurity, poverty, and micronutrient deficiencies, which tend to coexist with other macronutrient deficiencies. The underlying mechanism accounting for the significant negative association between overweight or obesity and anemia risk is unclear; however there are several possible explanations. First, obese participants are less likely to be malnourished, because excess calorie intake leads to obesity,<sup>35</sup> and overnutrition in obese participants may thus be associated with a significant reduction in anemia risk. Second, obese participants may have a variety of other diseases that could increase Hb levels, such as obstructive sleep apnea and other obesity-related breathing disorders, which lead to chronic tissue hypoxia and increased red blood cells.<sup>36</sup> 

We found that older people with diabetes had higher rates of anemia than non-diabetics, consistent with previous studies.<sup>37</sup> Evidence indicates that the incidence and prevalence of anemia in diabetic patients is often associated with erythropoietin deficiency caused by diabetic kidney damage.<sup>38</sup> Other researchers have also shown a link between anemia and hypertension, as shown in our current study.<sup>21</sup>

This study showed that the prevalence of anemia was low among individuals with dyslipidemia. A study by Zaribaf et al. found a significant positive correlation between Hb levels and dyslipidemia.<sup>39</sup> However, this study differed from our study in that it assessed the relationship between anemia and lipids in premenopausal women, whereas our study focused on older adults (aged 65–113 years).<sup>39</sup> In contrast, a study conducted by other researchers in women of childbearing age found no significant association between serum LDL and anemia.<sup>39</sup> The reasons for the different results in terms of the relationship between dyslipidemia and anemia deserve further investigation. Patients with CKD have defects in renal endocrine function, resulting in decreased erythropoietin secretion by the kidney, leading to nephrogenic anemia.<sup>40</sup> Nearly half of all patients with CKD have anemia.<sup>40</sup> The current study found the similar results. 

This study had some limitations. First, it was a cross-sectional study and could only infer correlation, not causation. Second, randomized sampling would represent the best design for testing the prevalence of anemia and its associated factors among older adults; however, large random sampling was not practically feasible and we therefore adopted a convenient sampling method to recruit older adult participants. This was a major factor preventing the extrapolation of the results to the general population. Finally, renal disease was assessed based on a one-time GFR measurement, possibly leading to overestimation of the actual prevalence of CKD. However, these limitations do not affect the significance of the results, which provide the first evidence of the prevalence and risk factors of anemia among older adults in urban China. 

#### 12 5. Conclusion

In conclusion, anemia is prevalent among the older adult population in China, with older age, underweight, diabetes, CKD, and anemia being positively associated with anemia, and higher education level, current-smoker, drinker, overweight, obesity, central obesity, hypertension, and dyslipidemia being negatively associated. Screening of high risk populations, and treatment of senile anemia should be top priorities in Shenzhen, and should be listed as important public health intervention measures for implementation.

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#### 27 Author Contributions

WN, XY, and JX: study conception and design. WN, XY, YS, HZ, YZ, and JX: performance of research. XY and YS: data analysis and interpretation. WN and XY: writing the original draft. WN and JX: Writing the review and editing. All authors have read and agreed to the published version of the manuscript.

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#### **Conflicts of Interest**

The authors declare no conflict of interest.

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9	5	This study was approved by	the ethical review committee of the Center for
10	6	Chronic Disease Control of Shenzhe	en.
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12	8	Data sharing statement	
14	9	All data generated or analyze	d during this study are included in this published
15	10	rticle. No additional data are availa	ble.
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6 7	3	Tables		
8 9	4	Table 1 Sociodemographic and other c	characteristics of older a	dults living in
10	5	Shenzhen community $(N=121, 981)$		
11		Characteristics	Total	95%CI
12		Age (years)	$71.28 \pm 5.58$	71.25-71.31
14		Hb(g/dL)	$13.64 \pm 1.67$	13 63-13 65
15		$BMI(Kg/m^2)$	23 83 + 3 17	23 81-23 85
16		SDD (mm Hg)	$25.05 \pm 5.17$ 124 71 ± 17 60	124 61 124 91
17		SDF (IIIII FIG)	$134.71 \pm 17.09$	134.01-134.01
18		DBP (mm Hg)	$77.23 \pm 10.31$	//.18-//.29
19 20		WC (cm)	$85.1 \pm 8.82$	85.05-85.15
20		FBG (mmol/L)	$5.96 \pm 1.9$	5.95-5.97
22		TC(mmol/L)	$5.21 \pm 2$	5.20-5.23
23		TG(mmol/L)	$1.57 \pm 1.14$	1.57-1.58
24		LDL-C(mmol/L)	$3.09 \pm 1.05$	3.08-3.09
25		HDL-C(mmol/L)	$1.39 \pm 0.51$	1 39-1 39
20 27		eGER	6874 + 167	68 65-68 83
28		$rac{1}{2}$	$00.74 \pm 10.7$	00.05-00.05
29		Sex, II(76)	54(40 (44 070/)	12 70 11 21
30		Male	54649 (44.07%)	43./8-44.34
31		Female	69358 (55.93%)	55.66-56.22
32 22		Education level, n(%)		
34		Not educated	9888 (8.11%)	7.95-8.26
35		Primary education	43441 (35.61%)	35.34-35.88
36		Junior school education and above	68652 (56.28%)	56.00-56.56
37		Smoking status, n (%)		
38		Current smoker	10023 (8 22%)	8 06-8 37
39 40		Ex-smoker	7546 (6 19%)	6 05-6 32
41		Navar smokar	104412 (85 50%)	0.05 0.52 85 40 85 70
42		$\mathbf{D}_{\mathbf{v}} = \mathbf{D}_{\mathbf{v}} = \mathbf{D}_{\mathbf{v}} + \mathbf{D}_{\mathbf{v}} = \mathbf{D}_{\mathbf{v}} = \mathbf{D}_{\mathbf{v}} + \mathbf{D}_{\mathbf{v}} = $	104412 (83.3978)	03.40-03.79
43		Drinking nabit, n (%)		00.10.00.55
44		Non-drinker	101661 (83.34%)	83.13-83.55
45 46		Non-habitual drinker	12571 (10.31%)	10.14-10.48
40		Habitual drinker	7749 (6.35%)	6.22-6.49
48	6			
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3 Table 2 Prevalence of and	emia in old	er adults liv	ving in Sł	enzhen comm	nunity,	
4 according to sociodemograph	nic and other	characteristic	cs			
Characteristics	Total	Ν	%	95%CI	$\chi^2$ Value	P
Total	121981	18820	15.43	15.23-15.63		
Sex					22.36	<
Male	53743	7946	14.79	14.49-15.09		
Female	68238	10874	15.94	15.66-16.21		
Education level					263.21	<
Not educated	9888	2027	20.50	19.70-21.30		
Primary education	43441	7240	16.67	16.32-17.02		
Junior school education and above	68652	9553	13.92	13.66-14.17		
Age group					1201.99	<
65~69	60043	7635	12.72	12.45-12.98		
70~74	32750	4730	14.44	14.06-14.82		
75~79	16599	3070	18.50	17.90-19.09		
80~	12589	3385	26.89	26.11-27.66		
Smoking status					68.89	<
Current smoker	10023	1253	12.50	11.85-13.15		
Ex-smoker	7546	1047	13 87	13 09-14 65		
Never-smoker	104412	16520	15.82	15 60-16 04		
Drinking habit	101112	10020	10.02	10.00 10.01	130.24	<
Non-drinker	101661	16302	16 04	15 81-16 26	150.21	
Non-habitual drinker	12571	1589	12.64	12.06-13.22		
Habitual drinker	7749	929	11 99	11 27-12 71		
BMI	7777	)_)	11.77	11.27 12.71	1522 11	<
Low weight	1196	1504	33.45	32 07-34 83	1322.11	
Normal weight	61532	11041	17.04	17 64 18 25		
Overweight	01552 44644	5175	11.54	11 20 11 80		
Obosity	11200	1100	0.72	0.18.10.27		
Central obesity	11309	1100	9.13	9.10-10.27	540.10	/
Vas	40051	5007	12.02	11 72 12 21	340.10	
No	+2021 72020	12027	12.02	11./3-12.31		
Dishatas	12930	12923	1/./2	17.44-18.00	77 05	/
Vas	27220	1500	1661	16 16 17 05	27.05	<
	27220	4520	10.01	10.10-1/.00		
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rypertension X <sub></sub>	(7025	0002	1457	14 20 14 02	03.27	<
r es	0/855	9883	14.5/	14.30-14.83		
	54146	8937	16.51	16.19-16.82	011 70	
Dyslipidemia			10.40	10 10 10 54	211.72	<
Yes	54564	7354	13.48	13.19-13.76		
No	6/41/	11466	17.01	16./2-1/.29		
CKD					624.34	<

Yes	37927	7574	19.97	19.57-20.37
No	84054	11246	13.38	13.15-13.61
1	A two-sided value of $P < 0.05$ was cons	sidered to be sta	tistically s	ignificant.
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6 7	2	Figure legends
8 9	3	Fig 1 Risk factor analyses of the prevalence of anemia in older adults living in
10	4	Shenzhen community
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Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe	Page 5-6
Bias	9	Describe any efforts to address potential sources of bias	Page 6
Study size	10	Explain how the study size was arrived at	Page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Not applicable
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	Page 4
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Page7
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	Page 7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Page 7
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	Page 7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	Page 8-9
		magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	Page 7-9
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	Page 9
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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### Anemia and associated factors among older adults in an urban district in China: a large-scale cross-sectional study

Journal:	BMJ Open
Manuscript ID	bmjopen-2021-056100.R2
Article Type:	Original research
Date Submitted by the Author:	30-Nov-2021
Complete List of Authors:	Ni, Wenqing; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Yuan, Xueli; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Sun, Yuanying; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Hong; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Yan; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Yan; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Xu, Jian; Shenzhen Nanshan Center for Chronic Disease Control, Department of Elderly Health Management
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	Anaemia < HAEMATOLOGY, EPIDEMIOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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5 4 5	1	Anemia and associated factors among older adults in an urban
6 7	2	district in China: a large-scale cross-sectional study
o 9 10	3	
11 12 13	4	Wenqing Ni <sup>1#</sup> , Xueli Yuan <sup>1#</sup> , Yuanying Sun <sup>1</sup> , Hongmin Zhang <sup>1</sup> ,
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# 1 Abstract

Objective: Anemia leads to poor health outcomes in older adults; however, most
current research in China has focused on younger adults. The present study aimed to
investigate the prevalence of anemia and its associated factors in older adults in an
urban district in China.

- **Design**: A cross-sectional study.
- **Setting**: An urbanized region, Shenzhen, China.
  - **Participants**: A total of 121,981 participants aged  $\geq$  65 years were recruited at local 9 community health service centers in Shenzhen from January to December 2018.
  - Primary outcomes: The prevalence of anemia was analyzed and potential associated
     factors were evaluated.

**Results**: The mean hemoglobin level was $13.64 \pm 1.67$ g/dL and the prevalence of anemia was 15.43%. The prevalences of mild, moderate, and severe anemia were 12.24%, 2.94%, and 0.25% respectively. Anemia was positively associated with older age, being underweight (adjusted odds ratio (AOR): 2.06, 95% confidence interval (CI): 1.93–2.20), diabetes (AOR: 1.23, 95% CI: 1.19–1.28), and chronic kidney disease (AOR: 1.41, 95% CI: 1.36–1.46), and inversely with higher education level, current-smoker (AOR: 0.84, 95% CI: 0.78–0.89), non-habitual drinker (AOR: 0.86, 95% CI: 0.81-0.92), habitual drinker (AOR: 0.81, 95% CI: 0.75-0.87), overweight (AOR: 0.67, 95% CI: 0.64-0.70), obesity (AOR: 0.57, 95% CI: 0.53-0.61), central obesity (AOR: 0.86, 95% CI: 0.82–0.89), hypertension (AOR: 0.86, 95% CI: 0.83– 0.89), and dyslipidemia (AOR: 0.81, 95% CI: 0.78–0.84). 

Conclusion: Anemia is prevalent among people aged 65 years and older in China.
 Screening of high-risk populations and treatment of senile anemia should be a top
 priority in Shenzhen, and should be listed as important public health intervention
 measures for implementation.

27 Keywords: older adults, anemia, epidemiologic study, risk factor

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#### Strengths and limitations of this study

■ This was the first large-scale cross-sectional study to assess the prevalence of anemia and its factors in an urban district in China. 

This study had a sufficiently large sample size to detect significant differences in the prevalence of anemia among older adults.

Convenience sampling was used to enroll the population sample. 

The dataset used in this study did not provide information on the dietary behavior T To been teriew only of the participants. 

## 1 1. Introduction

Anemia results from an inadequate number of erythrocytes which leads to a decreased ability to carry oxygen to meet the body's physiological demands. It is characterized by reduced levels of hemoglobin (Hb) in the blood in affected individuals. Anemia may occur at all stages of life, however, older people are among the most vulnerable.<sup>1,2</sup> Globally, 11.0% of men and 10.2% of women aged 65 years and older are anemic.<sup>3</sup> Anemia is a risk factor for a variety of adverse outcomes in the older population, including hospitalization, disability and mortality.<sup>1</sup> Previous studies found higher mortality rates in people aged 65 years and older hospitalized for myocardial infarction, patients with systolic and diastolic chronic heart failure (CHF), and in older CHF patients with anemia.<sup>4-6</sup> Anemia is also an independent risk factor for decline in physical performance and has a negative impact on quality of life, physical functioning, and muscle strength in older individuals.<sup>7-9</sup> Early identification and treatment of anemia is therefore an important strategy to improve the quality of life of older adults with anemia. 

In China, 13.5% of the total population (approximately 190.64 million people) were aged 65 years or older in 2020,<sup>10</sup> and increasing life expectancy and declining fertility rates mean that China is experiencing an ongoing aging process. In line with the aging of the population, anemia has become an important public health problem in China. The China Health and Retirement Longitudinal Study showed a prevalence of anemia in middle-aged and older Chinese residents of 12.86% from 2011 to 2012,<sup>11</sup> and the 2010–2012 China National Nutrition and Health Survey found a prevalence of anemia in older Chinese people of 12.6%.<sup>12</sup> Preventing anemia and improving the health of older adults in China are thus urgent issues. However, the only previous trial for preventing anemia examined the use of iron-fortified soy sauce in some cities in China, which aimed to reduce the prevalence of iron-deficiency anemia among women of reproductive age.<sup>13</sup> The prevention of anemia in older adults thus still presents a challenge, and limited measures have been taken to address this public health problem.

Clarifying the risk factors of anemia in the older adults will help to identify the population at risk of anemia, and promote the development of targeted screening and intervention measures. Economic development and living standards are important factors affecting anemia.<sup>14</sup> Most previous studies focused on the prevalence of anemia among middle-aged and older adults in urban and rural districts of China, but there is a lack of large-sample studies of anemia among older adults in urban districts.<sup>11,12,15,16</sup> This study therefore aimed to examine the prevalence of anemia and its related factors among people aged 65 or older in an urban district of China, to help develop strategies for future interventions and the prevention of anemia in older adults living in urban districts in China. 

- 40 2. Materials and methods
- **2.1 Study population**
- 42 We used convenience sampling to select our study population by recruiting people

aged 65 years and older from the lists of all residents registered at local community health centers in Shenzhen, China, from January 2018 to December 2018. Recruitment activities include pasting posters or placing leaflets in local community health centers and other public places. Electronic posters were also distributed via all the open WeChat groups of local community health center staff, to make the survey easily available to close contacts. The staff of the local community health centers also recruited older adults in their community to participate in the survey by telephone. The eligibility criteria were as follows: (1) lived in Shenzhen for more than 6 months; (2) able to participate in the study and give informed consent; and (3) conscious and able to cooperate to complete the face-to-face interview, medical examinations and biomedical tests. Prisoners are not free to visit community health centres, and we excluded residents living in prisons. A total of 141,684 individuals were recruited in this study, accounting for 36.9% (141,684/383,700) of the resident older adult population in Shenzhen according to the 2015 population census. Data were collected at examination centers in local community health centers in the participants' residential areas. Participants were asked to complete a questionnaire, provide a fasting blood sample, and undergo physical examinations. A total of 19,703 respondents were excluded because of failure to fulfil one or all of these requirements. Finally, 121,981 participants (86.09%) were included in the final data analysis. 

#### **2.2 Questionnaire survey**

Prior to the study, all investigators completed a training course to understand the methodology and process of the study. Working manuals containing questionnaire techniques, blood pressure measurement, anthropometric measurements, biological sample collection, and processing information were distributed to all the investigators.

Data were recorded by face-to-face interview 1 hour after blood collection. All participants completed a standardized questionnaire including questions on sociodemographic status (e.g., date of birth, sex, education level, marital status), past medical history (e.g., history of previous disease, operation history, history of trauma), family health history (e.g., hypertension, diabetes, coronary heart disease, malignant tumor, stroke), lifestyle (e.g., smoking, physical activity, alcohol consumption), and medication use, under the supervision of trained general practitioners and nurses. Educational level was categorized into three groups according to the number of years of education: not educated; primary education(1-6 years of education); and junior high school education and above ( $\geq 7$  years of education). Regarding drinking habits, participants were classified as habitual drinkers (drink at least once a day), non-habitual drinkers (six times a week to once a month), or non-drinker (almost never).<sup>17</sup> Based on a previous study, we divided participants into current smokers, ex-smokers, and never-smokers.<sup>18</sup> 

## **2.3 Physical examination**

40 Anthropometric examinations were carried out in the morning after overnight 41 fasting, and body measurements were taken by trained examiners based on a 42 standardized protocol. Height and weight were measured with the participants 43 wearing light clothing without shoes, using analogue scales. Waist circumference 44 (WC) was measured at the end of normal expiration at the midpoint level of the

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mid-axillary line between the 12th rib head and the superior anterior iliac spine. Body mass index (BMI) was calculated by dividing body weight (in kilograms) by height squared (in meters). Blood pressure was measured twice in both arms supported at heart level with the participants in a sitting position, using a calibrated electronic sphygmomanometer and the higher level was recorded and used for statistical analysis. To obtain accurate readings, the participants were asked to rest for at least 5 min before the measurement, or if they had engaged in excessive exercise prior to the visit, to rest for at least 30 min before the measurement. 

## 9 2.4 Blood sample collection and biochemical analyses

Venous blood samples were taken after overnight fasting for at least 8 hours. All blood samples were analyzed in clinical laboratories at the grade 2 hospitals to which the community health centers were directly affiliated. All the laboratories had successfully completed a standardization and competency program. Fasting venous blood was used to measure levels of Hb, plasma glucose, creatinine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) using an automatic biochemistry analyzer. Biochemical analysis of fresh blood samples was completed within 4 hours. Serum creatinine was used to calculate the estimated glomerular filtration rate (eGFR) using the full age spectrum equation.<sup>19</sup> 

#### **2.5** C

### 0 2.5 Operational definitions/measurements

Anemia was defined as a Hb concentration < 13 g/dL in men and < 12 g/dL in women, according to World Health Organization standards.<sup>20</sup> The severity of anemia was classified as mild (11–11.9 g/dL (women), 11–12.9 g/dL (men)), moderate (8– 10.9 g/dL), and severe (<8 g/dL).<sup>20</sup> Chronic kidney disease (CKD) was defined as  $eGFR < 60 mL/min/1.73 m^{2.21}$  A diagnosis of hypertension was considered in participants with three consecutive high readings ( $\geq 140$  systolic and/or  $\geq 90$  mm Hg diastolic) with 2-week intervals or self-reported treatment with antihypertensive medication within the previous 2 weeks.<sup>22, 23</sup> Participants who met one of the following three criteria were diagnosed with diabetes: (1) previously diagnosed by professional doctors, (2) fasting plasma glucose (FBG)  $\geq$  7.0 mmol/L, and (3) 2-hour plasma glucose level  $\geq$  11.1 mmol/L.<sup>24</sup> High TC, high TG, high LDL-C, and low HDL-C were diagnosed according to the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults.<sup>25</sup> In this study, we defined dyslipidemia as an abnormal concentration of one or more lipid components or the use of anti-dyslipidemia medications in the past 2 weeks. 

Participants were divided into four groups based on the adult weight criteria published by the Ministry of Health of China (WS/T 428-2013): BMI < 18.5 kg/m<sup>2</sup> (low weight), BMI  $\ge$  18.5 kg/m<sup>2</sup> and <24.0 kg/m<sup>2</sup> (normal weight), BMI  $\ge$  24.0 kg/m<sup>2</sup> and < 28.0 kg/m<sup>2</sup> (overweight), and BMI  $\ge$  28.0 kg/m<sup>2</sup> (obesity). A WC  $\ge$  90 cm for men and  $\ge$ 85 cm for women was defined as central obesity.<sup>26</sup>

#### **2.6 Statistical analyses**

42 Descriptive statistics, including means and standard deviations, were used to 43 compute continuous variables. Numerical data were expressed as percentages and 44 compared by  $\chi^2$  tests. Multivariate logistic regression analysis was performed to 1 explore the associations between the prevalence of anemia and associated risk factors.

In the multivariate logistic regression model, the prevalence of anemia was defined as
the dependent variable, and sex, education level, age group, smoking status, drinking
habit, BMI, central obesity, diabetes, hypertension, dyslipidemia and CKD were
defined as the independent variables. Data analysis was carried out using SAS 9.4

6 (Institute, Cary, NC, USA). A two-sided value of P < 0.05 was considered to be 7 statistically significant.

## 8 2.7 Participants and public involvement

9 Neither the study participants nor the public were involved in the design, 10 recruitment or conduct of the study. All the participants had the option of receiving a 11 health check and biochemical results when they visited the local community health 12 centers.

#### 13 2.8 Ethical Approval Statement

The study received ethical approval from the Center for Chronic Disease Control in Shenzhen(Grant No: SZCCC-201802, SZCCC-2020-018-01-PJ). The study complied with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from uneducated participants before the collection of data and conducting of the study. For participants who were not educated, the participants and a proxy (family member) who accompanied the participant in the survey were informed orally (participant) and in writing (proxy) about the purpose, process, methods, benefits, and health risks of the study. During the informed consent process, uneducated older adults and their proxies were able to consult the investigators with questions at any time. After explaining the concept of informed consent, uneducated older adults provided verbal agreement, and written informed consent to participate in the study was provided by their proxy. The consent processes were approved by the committee of the Center for Chronic Disease Control of Shenzhen. 

## **3. Results**

## **3.1 Characteristics of participants**

The characteristics of the study participants are shown in Table 1. The mean age was  $71.28 \pm 5.58$  years (range 65–103 years). There were 54,649 men and 69,358 women, and > 50% of participants had a minimum of a junior school education. Among the study population, 8.22% were current smokers and 6.35% were habitual drinkers. The mean Hb, BMI, SBP, DBP, WC, FBG, TC, TG, LDL-C, HDL-C, and eGFR values among all 121,981 participants were  $13.64 \pm 1.67$  g/dL,  $23.83 \pm 3.17$  $kg/m^2$ , 134.71 ± 17.69 mmHg, 77.23 ± 10.31 mmHg, 85.10 ± 8.82 cm, 5.96 ± 1.90 mmol/L,  $5.21 \pm 2.00 mmol/L$ ,  $1.57 \pm 1.14 mmol/L$ ,  $3.09 \pm 1.05 mmol/L$ ,  $1.39 \pm 1.05$ mmol/L, and  $68.74 \pm 16.70$  mL/min/1.73m<sup>2</sup>, respectively. A total of 100,762 participants (82.60%) had at least one chronic disease, with hypertension (55.61%), dyslipidemia (44.73%), CKD (31.09%), and diabetes (22.31%) being the most prevalent (data not shown).

## **3.2** Prevalence of anemia in different subgroups

The overall prevalence anemia was 15.43% and the prevalences (95% confidence intervals(*CI*)) of mild, moderate and severe anemia were 12.24% (12.05-12.42),

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2.94% (2.84-3.03) and 0.25% (0.23-0.28) respectively. The prevalence of anemia among subpopulations is shown in Table 2. Anemia was significantly more prevalent in women than in men and generally increased with age. The prevalence was lower among individuals with at least primary-level education, and lower in current smokers and habitual drinkers compared with their counterparts. The prevalence of anemia was higher in participants with low weight and lower in those with overweight, obesity, central obesity, hypertension, or dyslipidemia. Individuals with diabetes or CKD had a higher prevalence of anemia than those without these conditions. 

### **3.3** Association between anemia and related variables

Binary logistic regression analysis was carried out with presence or absence of anemia as the dependent variable, and factors in univariate analysis as independent variables to determine the factors influencing anemia. Primary education(adjusted odds ratio (AOR)=0.89, 95%CI:0.84-0.94), junior school education and above 95%CI:0.68-0.76) current-smoker (AOR=0.84, 95%CI:0.78-0.89), (AOR=0.72, non-habitual drinker (AOR=0.86, 95%CI:0.81-0.92), habitual drinker (AOR=0.81, 95%CI:0.75-0.87), overweight (AOR=0.67, 95%CI:0.64-0.70), obesity(AOR=0.57, 95%CI:0.53-0.61), central obesity (AOR=0.86, 95%CI:0.82-0.89), hypertension (AOR=0.86, 95%CI:0.83-0.89), and dyslipidemia (AOR=0.81, 95%CI:0.78-0.84) were independently associated with lower odds for the presence of anemia (Fig. 1), while age 70-74 years (AOR=1.10, 95%CI:1.06-1.15), age 75-79 years (AOR=1.37, 95%CI:1.31-1.44), age  $\geq 80$  years (AOR=1.96, 95%CI:1.86-2.06), underweight (AOR=2.06, 95%CI:1.93-2.20), diabetes (AOR=1.23, 95%CI:1.19-1.28), and CKD (AOR=1.41, 95%CI:1.36-1.46) were independently associated with greater odds (Fig. 1). However, there was no significant difference in the risk of anemia in relation to sex. 

# **4. Discussion**

This was the first large-scale cross-sectional survey to report the prevalence of anemia in older adults (aged 65 years or older) living in an urban district of China. This study demonstrated that the prevalence of anemia was relatively high, representing a public health problem in Shenzhen. After controlling for the confounding factors we found that the prevalence of anemia varied with education level, age group, smoking status, drinking habit, BMI, central obesity, and some non-communicable diseases.

The prevalence of anemia among older adults in an urban district in China in the current study was 15.43%, which was higher than the 12.86% reported in previous national studies in China,<sup>11</sup> but lower than the 18.90% reported in the 2009 national survey in China.<sup>13</sup> The difference in prevalence rates among these studies may have been caused by differences in study design, sample size, and/or the age of the study participants.

The current study found a significant negative correlation between anemia
prevalence and educational level. This was consistent with studies conducted in Nepal
and Pakistan, which confirmed that a low educational level was a risk factor for
anemia.<sup>27</sup> This relationship probably occurs because higher levels of education enable

people to earn more and thus escape from the poverty trap. Multivariate analysis also identified older age as an independent risk factor for anemia, consistent with the findings of other related studies.<sup>3, 28</sup> The prevalence of anemia increased with age, with a two-to-three-fold increase (26.89% vs. 12.72%) in people aged > 80 years, suggesting the need for routine screening for anemia in this high-risk subgroup.

Current smokers had a lower risk of anemia than never smokers. Similarly, previous studies showed that smoking was negatively correlated with the risk of anemia.<sup>29,30</sup> A multiple logistic regression analysis of the health check-up database of St. Luke's International Hospital in Tokyo between April 2016 and March 2017 revealed that Japanese women (35-49 years) who were current smokers had a 25% lower risk of anemia compared with non-smokers, after adjusting for the covariates.<sup>30</sup> Increased Hb levels in smokers were associated with elevated carboxyhemoglobin (HbCO), a stable complex of Hb and carbon monoxide (CO), because of the exposure to excess CO caused by smoking.<sup>31</sup> The form of HbCO decreases oxygen delivery, and smokers had compensatory elevated Hb to increase erythropoiesis and maintain oxygen transportation.<sup>32</sup> This might explain why adaptation to excess CO during smoking was reflected by increases in Hb and RBC mass.33 Habitual drinking was also associated with a decreased risk of anemia, with a corresponding OR of 0.81, consistent with a Korean study.<sup>29</sup> However, the direct causality of this negative correlation between alcohol drinking and anemia is still unclear.<sup>29</sup> Given the potential risks of alcohol and tobacco consumption to human health, we do not recommend increasing alcohol consumption or smoking to protect against anemia. 

We also found a negative association between increased BMI and anemia prevalence, in accord with other studies conducted in China, the United States, Nepal, and Pakistan.<sup>27, 34</sup> The reasons for being underweight may include poor distribution of inadequate food within the family, food insecurity, poverty, and micronutrient deficiencies, which tend to coexist with other macronutrient deficiencies. The underlying mechanism accounting for the significant negative association between overweight or obesity and anemia risk is unclear; however there are several possible explanations. First, obese participants are less likely to be malnourished, because excess calorie intake leads to obesity,<sup>35</sup> and overnutrition in obese participants may thus be associated with a significant reduction in anemia risk. Second, obese participants may have a variety of other diseases that could increase Hb levels, such as obstructive sleep apnea and other obesity-related breathing disorders, which lead to chronic tissue hypoxia and increased red blood cells.<sup>36</sup> 

We found that older people with diabetes had higher rates of anemia than non-diabetics, consistent with previous studies.<sup>37</sup> Evidence indicates that the incidence and prevalence of anemia in diabetic patients is often associated with erythropoietin deficiency caused by diabetic kidney damage.<sup>38</sup> Other researchers have also shown a link between anemia and hypertension, as shown in our current study.<sup>21</sup>

This study showed that the prevalence of anemia was low among individuals with
dyslipidemia. A study by Zaribaf et al. found a significant positive correlation
between Hb levels and dyslipidemia.<sup>39</sup> However, this study differed from our study in
that it assessed the relationship between anemia and lipids in premenopausal women,

whereas our study focused on older adults (aged 65–113 years).<sup>39</sup> In contrast, a study conducted by other researchers in women of childbearing age found no significant association between serum LDL and anemia.<sup>39</sup> The reasons for the different results in terms of the relationship between dyslipidemia and anemia deserve further investigation. Patients with CKD have defects in renal endocrine function, resulting in decreased erythropoietin secretion by the kidney, leading to nephrogenic anemia.<sup>40</sup> Nearly half of all patients with CKD have anemia.<sup>40</sup> The current study found the similar results. 

This study had some limitations. First, it was a cross-sectional study and could only infer correlation, not causation. Second, randomized sampling would represent the best design for testing the prevalence of anemia and its associated factors among older adults; however, large random sampling was not practically feasible and we therefore adopted a convenient sampling method to recruit older adult participants. This was a major factor preventing the extrapolation of the results to the general population. Finally, renal disease was assessed based on a one-time GFR measurement, possibly leading to overestimation of the actual prevalence of CKD. However, these limitations do not affect the significance of the results, which provide the first evidence of the prevalence and risk factors of anemia among older adults in urban China. 

#### 5. Conclusion

In conclusion, anemia is prevalent among the older adult population in China, with older age, underweight, diabetes, CKD, and anemia being positively associated with anemia, and higher education level, current-smoker, drinker, overweight, obesity, central obesity, hypertension, and dyslipidemia being negatively associated. Screening of high-risk populations, and treatment of senile anemia should be top priorities in Shenzhen, and should be listed as important public health intervention measures for implementation. 

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#### **Author Contributions**

WN, XY, and JX: study conception and design. WN, XY, YS, HZ, YZ, and JX: performance of research. XY and YS: data analysis and interpretation. WN and XY: writing the original draft. WN and JX: Writing the review and editing. All authors have read and agreed to the published version of the manuscript. 

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21	15	
22	16	Data sharing statement
25 74	10	All data generated or analyzed during this study are included in this published
25	17	All data generated of analyzed during this study are included in this published
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6 7	3	Tables		
8 9	4	Table 1 Sociodemographic and other c	characteristics of older a	dults living in
10	5	Shenzhen community $(N=121, 981)$		
11		Characteristics	Total	95%CI
12		Age (years)	$71.28 \pm 5.58$	71.25-71.31
14		Hb(g/dL)	$13.64 \pm 1.67$	13 63-13 65
15		$BMI(Kg/m^2)$	23 83 + 3 17	23 81-23 85
16		SDD (mm Hg)	$25.05 \pm 5.17$ 124 71 ± 17 60	124 61 124 91
17		SDF (IIIII FIG)	$134.71 \pm 17.09$	134.01-134.01
18		DBP (mm Hg)	$77.23 \pm 10.31$	//.18-//.29
19 20		WC (cm)	$85.1 \pm 8.82$	85.05-85.15
20		FBG (mmol/L)	$5.96 \pm 1.9$	5.95-5.97
22		TC(mmol/L)	$5.21 \pm 2$	5.20-5.23
23		TG(mmol/L)	$1.57 \pm 1.14$	1.57-1.58
24		LDL-C(mmol/L)	$3.09 \pm 1.05$	3.08-3.09
25		HDL-C(mmol/L)	$1.39 \pm 0.51$	1 39-1 39
20 27		eGER	6874 + 167	68 65-68 83
28		$rac{1}{2}$	$00.74 \pm 10.7$	00.05-00.05
29		Sex, II(76)	54(40 (44 070/)	12 70 11 21
30		Male	54649 (44.07%)	43./8-44.34
31		Female	69358 (55.93%)	55.66-56.22
32 22		Education level, n(%)		
34		Not educated	9888 (8.11%)	7.95-8.26
35		Primary education	43441 (35.61%)	35.34-35.88
36		Junior school education and above	68652 (56.28%)	56.00-56.56
37		Smoking status, n (%)		
38		Current smoker	10023 (8 22%)	8 06-8 37
39 40		Ex-smoker	7546 (6 19%)	6 05-6 32
41		Navar smokar	104412 (85 50%)	0.05 0.52 85 40 85 70
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43		Drinking nabit, n (%)		00.10.00.55
44		Non-drinker	101661 (83.34%)	83.13-83.55
45 46		Non-habitual drinker	12571 (10.31%)	10.14-10.48
40		Habitual drinker	7749 (6.35%)	6.22-6.49
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5 2 6 3 T	able ? Prevalence	of anemi	a in older a	dulte living ir	Shenzhen c	ommunity	
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8 4 4	ceording to socioden	lographic	and other char	Provolonco	05% CI		
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10 Chara 11	ciensiics	Total	anemia	01		χ <sup>-</sup> value	
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<sup>13</sup> Total		121981	18820	15.43	15.23-15.63		
14 15 <sub>0</sub>						22.36	< 0.001
16 Male		537/3	7946	14 79	14 49-15 09	22.30	< 0.001
17 <sup>Ivraic</sup>		68738	10874	14.79	14.49-13.09		
19 ducation level		08238	100/4	15.74	15.00-10.21	263 21	< 0.001
<sup>20</sup> Not educated		9888	2027	20.50	19 70-21 30	205.21	<0.001
21 Primary educati	on	43441	7240	16.67	16 32-17 02		
23 $1$ $1$ $1$	1 (* 11	(0(5)	0552	12.02	12.66.14.17		
24 Junior school ec	lucation and above	68652	9553	13.92	13.66-14.17		
<sup>25</sup> Age group						1201.99	< 0.001
$\frac{20}{27}65 \sim 69$		60043	7635	12.72	12.45-12.98		
<sub>28</sub> 70~74		32750	4730	14.44	14.06-14.82		
$2975 \sim 79$		16599	3070	18.50	17.90-19.09		
$^{30}_{31}80\sim$		12589	3385	26.89	26.11-27.66		
3 moking status						68.89	< 0.001
33 Current smoker		10023	1253	12.50	11.85-13.15		
<sup>34</sup> <sub>35</sub> Ex-smoker		7546	1047 <	13.87	13.09-14.65		
<sup>36</sup> Never-smoker		104412	16520	15.82	15.60-16.04		
<sup>3</sup> Drinking habit						130.24	< 0.001
<sup>39</sup> <sup>40</sup> Non-drinker		101661	16302	16.04	15.81-16.26		
41 42 Non-habitual dr	inker	12571	1589	12 64	12 06-13 22		
43 Habitual drinker	r	7749	929	11 99	11 27-12 71		
<sup>4</sup> BMI	L	1119	/ _ /	11.77	11.27 12.71	1522 11	< 0.001
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47 Normal weight		61532	11041	17.94	17.64-18.25		
<sup>48</sup> Overweight		44644	5175	11.59	11 29-11 89		
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50 central obesity		11009	1100	5.70	, <u>,</u> ,	540.10	< 0 001
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<sup>53</sup> No		72930	12923	17.72	17.44-18.00		
54 5Diabetes						27.05	< 0.001
56 Yes		27220	4520	16.61	16.16-17.05		
<sup>57</sup> No		94761	14300	15.09	14.86-15.32		
58 Hypertension						63.27	< 0.001
60 Yes		67835	9883	14.57	14.30-14.83		
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8 9	3	Fig 1 Risk factor analyses of the prevalence of anemia in older adults living in
10	4	Shenzhen community
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Section/Topic	ltem #	Recommendation	Reported on page #	
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1	
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4	
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4	
Methods				
Study design	4	Present key elements of study design early in the paper	Page 4	
Setting	5 Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection			
Participants 6 (a) Give the eligibility criteria, and the sources and methods of selection of participants		Page 4		
'ariables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable		Page 5-6		
Data sources/	ata sources/ 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe		Page 5-6	
Bias	9	Describe any efforts to address potential sources of bias	Page 6	
Study size	10	Explain how the study size was arrived at	Page 4	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6	
		(b) Describe any methods used to examine subgroups and interactions	Not applicable	
		(c) Explain how missing data were addressed	Not applicable	
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable	
		(e) Describe any sensitivity analyses	Not applicable	
Results				

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	Page 4
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Page7
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	Page 7
Aain results       16       (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence)		Page 7	
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	Page 7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	Page 8-9
		magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	Page 7-9
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	Page 9
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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### Anemia and associated factors among older adults in an urban district in China: a large-scale cross-sectional study

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Manuscript ID	bmjopen-2021-056100.R3
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Date Submitted by the Author:	30-Jan-2022
Complete List of Authors:	Ni, Wenqing; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Yuan, Xueli; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Sun, Yuanying; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Hong; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Yan; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Zhang, Yan; Shenzhen Center for Chronic Disease Control, Department of Elderly Health Management Xu, Jian; Shenzhen Nanshan Center for Chronic Disease Control, Department of Elderly Health Management
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	Anaemia < HAEMATOLOGY, EPIDEMIOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

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5 4 5	1	Anemia and associated factors among older adults in an urban
6 7	2	district in China: a large-scale cross-sectional study
8 9 10	3	
11 12 13	4	Wenqing Ni <sup>1#</sup> , Xueli Yuan <sup>1#</sup> , Yuanying Sun <sup>1</sup> , Hongmin Zhang <sup>1</sup> ,
14 15 16	5	Yan Zhang <sup>1</sup> , Jian Xu <sup>1</sup>
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19	7	Control, Shenzhen, Guangdong, 518020, China
20 21 22	8	# These authors contributed equally to this work.
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# 1 Abstract

Objective: Anemia leads to poor health outcomes in older adults; however, most
current research in China has focused on younger adults. The present study aimed to
investigate the prevalence of anemia and its associated factors in older adults in an
urban district in China.

- **Design**: A cross-sectional study.
- **Setting**: An urbanized region, Shenzhen, China.
  - **Participants**: A total of 121,981 participants aged  $\geq$  65 years were recruited at local 9 community health service centers in Shenzhen from January to December 2018.

**Primary outcomes**: The prevalence of anemia was analyzed and potential associated 11 factors were evaluated.

**Results**: The mean hemoglobin level was $13.64 \pm 1.67$ g/dL and the prevalence of anemia was 15.43%. The prevalences of mild, moderate, and severe anemia were 12.24%, 2.94%, and 0.25%, respectively. Anemia was positively associated with older age, being underweight (adjusted odds ratio (AOR): 2.06, 95% confidence interval (CI): 1.93-2.20), diabetes (AOR: 1.23, 95% CI: 1.19-1.28), and chronic kidney disease (AOR: 1.41, 95% CI: 1.36–1.46), and inversely with higher education level, current-smoker (AOR: 0.84, 95% CI: 0.78–0.89), non-habitual drinker (AOR: 0.86, 95% CI: 0.81-0.92), habitual drinker (AOR: 0.81, 95% CI: 0.75-0.87), overweight (AOR: 0.67, 95% CI: 0.64-0.70), obesity (AOR: 0.57, 95% CI: 0.53-0.61), central obesity (AOR: 0.86, 95% CI: 0.82–0.89), hypertension (AOR: 0.86, 95% CI: 0.83–0.89), and dyslipidemia (AOR: 0.81, 95% CI: 0.78–0.84). 

Conclusion: Anemia is prevalent among people aged 65 years and older in China.
Screening of high-risk populations and treatment of senile anemia should be a top
priority in Shenzhen, and should be listed as important public health intervention
measures for implementation.

27 Keywords: older adults, anemia, epidemiologic study, risk factor

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#### Strengths and limitations of this study

■ This was the first large-scale cross-sectional study to assess the prevalence of anemia and its factors in an urban district in China. 

This study had a sufficiently large sample size to detect significant differences in the prevalence of anemia among older adults.

Convenience sampling was used to enroll the population sample. 

The dataset used in this study did not provide information on the dietary behavior T To been teriew only of the participants.
### 1 1. Introduction

Anemia results from an inadequate number of erythrocytes which leads to a decreased ability to carry oxygen to meet the body's physiological demands. It is characterized by reduced levels of hemoglobin (Hb) in the blood in affected individuals. Anemia may occur at all stages of life, however, older people are among the most vulnerable.<sup>1,2</sup> Globally, 11.0% of men and 10.2% of women aged 65 years and older are anemic.<sup>3</sup> Anemia is a risk factor for a variety of adverse outcomes in the older population, including hospitalization, disability and mortality.<sup>1</sup> Previous studies found higher mortality rates in people aged 65 years and older hospitalized for myocardial infarction, patients with systolic and diastolic chronic heart failure (CHF), and in older CHF patients with anemia.<sup>4-6</sup> Anemia is also an independent risk factor for decline in physical performance and has a negative impact on quality of life, physical functioning, and muscle strength in older individuals.<sup>7-9</sup> Early identification and treatment of anemia is therefore an important strategy to improve the quality of life of older adults with anemia. 

In China, 13.5% of the total population (approximately 190.64 million people) were aged 65 years or older in 2020,<sup>10</sup> and increasing life expectancy and declining fertility rates mean that China is experiencing an ongoing aging process. In line with the aging of the population, anemia has become an important public health problem in China. The China Health and Retirement Longitudinal Study showed a prevalence of anemia in middle-aged and older Chinese residents of 12.86% from 2011 to 2012,<sup>11</sup> and the 2010–2012 China National Nutrition and Health Survey found a prevalence of anemia in older Chinese people of 12.6%.<sup>12</sup> Preventing anemia and improving the health of older adults in China are thus urgent issues. However, the only previous trial for preventing anemia examined the use of iron-fortified soy sauce in some cities in China, which aimed to reduce the prevalence of iron-deficiency anemia among women of reproductive age.<sup>13</sup> The prevention of anemia in older adults thus still presents a challenge, and limited measures have been taken to address this public health problem.

Clarifying the risk factors of anemia in the older adults will help to identify the population at risk of anemia, and promote the development of targeted screening and intervention measures. Economic development, living standards, body mass index (BMI), chronic disease and specific risk factors, chronic kidney disease (CKD), older age are important factors affecting anemia.<sup>1,3,14,15</sup> Most previous studies focused on the prevalence of anemia among middle-aged and older adults in urban and rural districts of China, but there is a lack of large-sample studies of anemia among older adults in urban districts.<sup>11,12,16,17</sup> This study therefore aimed to examine the prevalence of anemia and its related factors among people aged 65 or older in an urban district of China, to help develop strategies for future interventions and the prevention of anemia in older adults living in urban districts in China. 

- **2. Materials and methods**
- **2.1 Study population**

We recruited participants aged 65 years and older from the lists of all residents registered at local community health centers in Shenzhen by convenient sampling method, from January 2018 to December 2018. The staff of the local community health centers recruited older adults in their community to participate in the survey by pasting posters, placing leaflets, telephone, distributed electronic posters via Wechat. The eligibility criteria were as follows: (1) lived in Shenzhen for more than 6 months; (2) able to participate in the study and give informed consent; and (3) conscious and able to cooperate to complete the face-to-face interview, medical examinations and biomedical tests. Prisoners are not free to visit community health centres, and we excluded residents living in prisons. A total of 141,684 individuals were recruited in this study, accounting for 36.9% (141,684/383,700) of the resident older adult population in Shenzhen according to the 2015 population census. Data were collected at examination centers in local community health centers in the participants' residential areas. Participants were asked to complete a questionnaire, provide a fasting blood sample, and undergo physical examinations. A total of 19,703 respondents were excluded because of failure to fulfil one or all of these requirements. Finally, 121,981 participants (86.09%) were included in the final data analysis. 

### **2.2 Questionnaire survey**

Prior to the study, all investigators completed a training course to understand the methodology and process of the study. Working manuals containing questionnaire techniques, blood pressure measurement, anthropometric measurements, biological sample collection, and processing information were distributed to all the investigators.

Data were recorded by face-to-face interview 1 hour after blood collection. Detailed sociodemographic characteristics and health parameters were collected by a standardized questionnaire including age, sex, education level, marital status, past medical history, family health history, lifestyle behaviors, and medication use. Participants were categorized according to the level of education into three categories: not educated; primary education; and junior high school education and above. Regarding drinking habits, participants were classified as habitual drinkers (drink at least once a day), non-habitual drinkers (six times a week to once a month), or non-drinker (almost never).<sup>18</sup> Based on a previous study, we divided participants into current smokers, ex-smokers, and never-smokers.<sup>19</sup> 

#### **2.3 Physical examination**

Anthropometric examinations were carried out in the morning after overnight fasting by standard methods. Body height, weight and waist circumference (WC) of the participants were measured, and BMI was calculated. Blood pressure was measured twice in both arms supported at heart level with the participants in a sitting position, using a calibrated electronic sphygmomanometer and the higher level was recorded and used for statistical analysis. To obtain accurate readings, the participants were asked to rest for at least 5 min before the measurement, or if they had engaged in excessive exercise prior to the visit, to rest for at least 30 min before the measurement. 

#### **2.4 Blood sample collection and biochemical analyses**

44 Venous blood samples were taken after overnight fasting for at least 8 hours. All

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blood samples were analyzed in clinical laboratories at the grade 2 hospitals to which the community health centers were directly affiliated. All the laboratories had successfully completed a standardization and competency program. Fasting venous blood was used to measure levels of Hb, plasma glucose, creatinine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) using an automatic biochemistry analyzer. Biochemical analysis of fresh blood samples was completed within 4 hours. Serum creatinine was used to calculate the estimated glomerular filtration rate (eGFR) using the full age spectrum equation.<sup>20</sup> 

#### 2.5 Operational definitions/measurements

Anemia was defined as a Hb concentration < 13 g/dL in men and < 12 g/dL in women, according to World Health Organization standards.<sup>21</sup> The severity of anemia was classified as mild (11-11.9 g/dL (women), 11-12.9 g/dL (men)), moderate (8-10.9 g/dL), and severe (<8 g/dL).<sup>21</sup> CKD was defined as eGFR < 60 mL/min/1.73 m<sup>2,22</sup> A diagnosis of hypertension was considered in participants with three consecutive high readings ( $\geq$  140 mm Hg systolic blood pressure and/or  $\geq$  90 mm Hg diastolic blood pressure) with 2-week intervals or self-reported treatment with antihypertensive medication within the previous 2 weeks.<sup>23, 24</sup> Participants who met one of the following three criteria were diagnosed with diabetes: (1) previously diagnosed by professional doctors, (2) fasting plasma glucose (FBG)  $\geq$  7.0 mmol/L, and (3) 2-hour plasma glucose level  $\geq$  11.1 mmol/L.<sup>25</sup> High TC, high TG, high LDL-C, and low HDL-C were diagnosed according to the 2016 Chinese Guidelines for the Management of Dyslipidemia in Adults.<sup>26</sup> In this study, we defined dyslipidemia as an abnormal concentration of one or more lipid components or the use of anti-dyslipidemia medications in the past 2 weeks. 

Participants were divided into four groups based on the adult weight criteria published by the Ministry of Health of China (WS/T 428-2013): BMI < 18.5 kg/m<sup>2</sup> (low weight), BMI  $\geq$  18.5 kg/m<sup>2</sup> and <24.0 kg/m<sup>2</sup> (normal weight), BMI  $\geq$  24.0 kg/m<sup>2</sup> and  $< 28.0 \text{ kg/m}^2$  (overweight), and BMI  $\ge 28.0 \text{ kg/m}^2$  (obesity). A WC  $\ge 90 \text{ cm}$  for men and  $\geq 85$  cm for women was defined as central obesity.<sup>27</sup> 

#### 2.6 Statistical analyses

Descriptive statistics, including means and standard deviations, were used to compute continuous variables. Numerical data were expressed as percentages and compared by  $\chi^2$  tests. Multivariate logistic regression analysis was performed to explore the associations between the prevalence of anemia and associated risk factors. In the multivariate logistic regression model, the prevalence of anemia was defined as the dependent variable, and sex, education level, age group, smoking status, drinking habit, BMI, central obesity, diabetes, hypertension, dyslipidemia and CKD were defined as the independent variables. Data analysis was carried out using SAS 9.4 (Institute, Cary, NC, USA). A two-sided value of P < 0.05 was considered to be statistically significant. 

2.7 Participants and public involvement

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Neither the study participants nor the public were involved in the design, recruitment or conduct of the study. All the participants had the option of receiving a 

health check and biochemical results when they visited the local community health
 centers.

### **2.8 Ethical Approval Statement**

The study received ethical approval from the Center for Chronic Disease Control in Shenzhen(Grant No: SZCCC-201802, SZCCC-2020-018-01-PJ). The study complied with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all participants before the collection of data and conducting the study. For participants who were not educated, the participants and a proxy (family member) who accompanied the participant in the survey were informed orally (participant) and in writing (proxy) about the purpose, process, methods, benefits, and health risks of the study. During the informed consent process, uneducated older adults and their proxies were able to consult the investigators with questions at any time. After explaining the concept of informed consent, uneducated older adults provided verbal agreement, and written informed consent to participate in the study was provided by their proxy. The consent processes were approved by the committee of the Center for Chronic Disease Control of Shenzhen. 

# **3. Results**

# **3.1 Characteristics of participants**

The characteristics of the study participants are shown in Table 1. The mean age was  $71.28 \pm 5.58$  years (range 65–103 years). There were 54,649 men and 69,358 women, and > 50% of participants had a minimum of a junior school education. Among the study population, 8.22% were current smokers and 6.35% were habitual drinkers. The mean Hb, BMI, SBP, DBP, WC, FBG, TC, TG, LDL-C, HDL-C, and eGFR values among all 121,981 participants were  $13.64 \pm 1.67$  g/dL,  $23.83 \pm 3.17$ kg/m<sup>2</sup>, 134.71  $\pm$  17.69 mmHg, 77.23  $\pm$  10.31 mmHg, 85.10  $\pm$  8.82 cm, 5.96  $\pm$  1.90 mmol/L,  $5.21 \pm 2.00 mmol/L$ ,  $1.57 \pm 1.14 mmol/L$ ,  $3.09 \pm 1.05 mmol/L$ ,  $1.39 \pm 1.05$ mmol/L, and 68.74 ± 16.70 mL/min/1.73m<sup>2</sup>, respectively. A total of 100,762 participants (82.60%) had at least one chronic disease, with hypertension (55.61%), dyslipidemia (44.73%), CKD (31.09%), and diabetes (22.31%) being the most prevalent (data not shown). 

# **3.2** Prevalence of anemia in different subgroups

The overall prevalence anemia was 15.43% and the prevalences (95% confidence intervals(CI)) of mild, moderate and severe anemia were 12.24% (12.05-12.42), 2.94% (2.84-3.03) and 0.25% (0.23-0.28), respectively. The prevalence of anemia among subpopulations is shown in Table 2. Anemia was significantly more prevalent in women than in men and generally increased with age. The prevalence was lower among individuals with at least primary-level education, and lower in current smokers and habitual drinkers compared with their counterparts. The prevalence of anemia was higher in participants with low weight and lower in those with overweight, obesity, central obesity, hypertension, or dyslipidemia. Individuals with diabetes or CKD had a higher prevalence of anemia than those without these conditions. 

- **3.3** Association between anemia and related variables
- 43 Binary logistic regression analysis was carried out with presence or absence of

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anemia as the dependent variable, and factors in univariate analysis as independent 1 variables to determine the factors influencing anemia. Primary education(adjusted 2 odds ratio (AOR)=0.89, 95%CI:0.84-0.94), junior school education and above 3 (AOR=0.72, 95%CI:0.68-0.76) current-smoker (AOR=0.84, 95%CI:0.78-0.89), 4 non-habitual drinker (AOR=0.86, 95%CI:0.81-0.92), habitual drinker (AOR=0.81, 5 6 95%CI:0.75-0.87), overweight (AOR=0.67, 95%CI:0.64-0.70), obesity(AOR=0.57, 95%CI:0.53-0.61), central obesity (AOR=0.86, 95%CI:0.82-0.89), hypertension 7 (AOR=0.86, 95%CI:0.83-0.89), and dyslipidemia (AOR=0.81, 95%CI:0.78-0.84) were 8 independently associated with lower odds for the presence of anemia (Fig. 1), while 9 age 70-74 years (AOR=1.10, 95%CI:1.06-1.15), age 75-79 years (AOR=1.37, 10 95%CI:1.31-1.44), age  $\geq 80$  years (AOR=1.96, 95%CI:1.86-2.06), underweight 11 (AOR=2.06, 95%CI:1.93-2.20), diabetes (AOR=1.23, 95%CI:1.19-1.28), and CKD 12 (AOR=1.41, 95%CI:1.36-1.46) were independently associated with greater odds (Fig. 13 1). However, there was no significant difference in the risk of anemia in relation to 14 sex. 15

### 16 **4. Discussion**

This was the first large-scale cross-sectional survey to report the prevalence of anemia in older adults (aged 65 years or older) living in an urban district of China. This study demonstrated that the prevalence of anemia was relatively high, representing a public health problem in Shenzhen. After controlling for the confounding factors we found that the prevalence of anemia varied with education level, age group, smoking status, drinking habit, BMI, central obesity, and some non-communicable diseases.

The prevalence of anemia among older adults in an urban district in China in the current study was 15.43%, which was higher than the 12.86% reported in previous national studies in China,<sup>11</sup> but lower than the 18.90% reported in the 2009 national survey in China.<sup>13</sup> The difference in prevalence rates among these studies may have been caused by differences in study design, sample size, and/or the age of the study participants.

The current study found a significant negative correlation between anemia 30 prevalence and educational level. This was consistent with studies conducted in Nepal 31 and Pakistan, which confirmed that a low educational level was a risk factor for 32 anemia.<sup>28</sup> This relationship probably occurs because higher levels of education enable 33 people to earn more and thus escape from the poverty trap. Multivariate analysis also 34 identified older age as an independent risk factor for anemia, consistent with the 35 findings of other related studies.<sup>3, 29</sup> The prevalence of anemia increased with age, 36 with a two-to-three-fold increase (26.89% vs. 12.72%) in people aged > 80 years, 37 suggesting the need for routine screening for anemia in this high-risk subgroup. 38

Current smokers had a lower risk of anemia than never smokers. Similarly,
previous researches revealed that smoking was decrease the risk of anemia.<sup>15,30</sup>
Sharma and co-researchers found that women aged 35-49 years who were current
smokers had a 25% lower risk of anemia compared with non-smokers, after adjusting
for the covariates.<sup>30</sup> Elevated Hb levels in smokers were associated with elevated

carboxyhemoglobin (HbCO), a stable compound of Hb and carbon monoxide (CO), due to exposure to excess CO as a result of smoking.<sup>31</sup> The form of HbCO reduces oxygen delivery, and smokers had compensatory elevated Hb to increase erythropoiesis and maintain oxygen transportation.<sup>32</sup> This might explain why adaptation to excess CO during smoking was shown by increase in Hb and red blood cell mass.<sup>33</sup> Habitual drinking was also associated with a decreased risk of anemia, with a corresponding OR of 0.81, consistent with a Korean study.<sup>15</sup> However, the direct causality of this negative correlation between alcohol drinking and anemia is still unclear.<sup>15</sup> Given the potential risks of alcohol and tobacco consumption to human health, we do not recommend increasing alcohol consumption or smoking to protect against anemia. 

We also found a negative association between increased BMI and anemia prevalence, in accord with other studies conducted in China, the United States, Nepal, and Pakistan.<sup>28, 34</sup> The reasons for being underweight may include poor distribution of inadequate food within the family, food insecurity, poverty, and micronutrient deficiencies, which tend to coexist with other macronutrient deficiencies. The underlying mechanism accounting for the significant negative association between overweight or obesity and anemia risk is unclear; however there are several possible explanations. First, obese participants are less likely to be malnourished, because excess calorie intake leads to obesity,<sup>35</sup> and overnutrition in obese participants may thus be associated with a significant reduction in anemia risk. Second, obese participants may have a variety of other diseases that could increase Hb levels, such as obstructive sleep apnea and other obesity-related breathing disorders, which lead to chronic tissue hypoxia and increased red blood cells.<sup>36</sup> 

We found that older people with diabetes had higher rates of anemia than non-diabetics, consistent with previous studies.<sup>37</sup> Evidence indicates that the incidence and prevalence of anemia in diabetic patients is often associated with erythropoietin deficiency caused by diabetic kidney damage.<sup>38</sup> Other researchers have also shown a link between anemia and hypertension, as shown in our current study.<sup>22</sup>

This study showed that the prevalence of anemia was low among individuals with dyslipidemia. A study by Zaribaf et al. found a significant positive correlation between Hb levels and dyslipidemia.<sup>39</sup> However, this study differed from our study in that it assessed the relationship between anemia and lipids in premenopausal women, whereas our study focused on older adults (aged 65–113 years).<sup>39</sup> In contrast, a study conducted by other researchers in women of childbearing age found no significant association between serum LDL and anemia.<sup>39</sup> The reasons for the different results in terms of the relationship between dyslipidemia and anemia deserve further investigation. Patients with CKD have defects in renal endocrine function, resulting in decreased erythropoietin secretion by the kidney, leading to nephrogenic anemia.<sup>40</sup> Nearly half of all patients with CKD have anemia.<sup>40</sup> The current study found the similar results. 

This study had some limitations. First, it was a cross-sectional study and could only
infer correlation, not causation. Second, randomized sampling would represent the
best design for testing the prevalence of anemia and its associated factors among older

adults; however, large random sampling was not practically feasible and we therefore adopted a convenient sampling method to recruit older adult participants. This was a major factor preventing the extrapolation of the results to the general population. Finally, renal disease was assessed based on a one-time GFR measurement, possibly leading to overestimation of the actual prevalence of CKD. However, these limitations do not affect the significance of the results, which provide the first evidence of the prevalence and risk factors of anemia among older adults in urban China. 

#### 5. Conclusion

In conclusion, anemia is prevalent among the older adult population in China, with older age, underweight, diabetes, and CKD being positively associated with anemia, and higher education level, current-smoker, drinker, overweight, obesity, central obesity, hypertension, and dyslipidemia being negatively associated. Screening of high-risk populations, and treatment of senile anemia should be top priorities in Shenzhen, and should be listed as important public health intervention measures for implementation. 

#### Acknowledgments

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### **Author Contributions**

WN, XY, and JX: study conception and design. WN, XY, YS, HZ, YZ, and JX: performance of research. XY and YS: data analysis and interpretation. WN and XY: writing the original draft. WN and JX: Writing the review and editing. All authors have read and agreed to the published version of the manuscript. 

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#### **Conflicts of Interest**

The authors declare no conflict of interest.

- Patient consent for publication
- Not required.

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9	5	Data sharing statement
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11	7	article. No additional data are available.
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6 7	3	Tables		
8 9	4	Table 1         Sociodemographic and other	characteristics of older a	dults living in
10	5	Shenzhen community $(N=121, 981)$		
11		Characteristics	Total	95%CI
12		Age (years)	$71.28 \pm 5.58$	71.25-71.31
13		Hb(g/dL)	$13.64 \pm 1.67$	13 63-13 65
15		$BML(K \alpha/m^2)$	$23.83 \pm 3.17$	23 81-23 85
16		SDD (mm Hg)	$25.05 \pm 5.17$ 124 71 ± 17 60	124 61 124 91
17		SDF (IIIII FIG)	$134.71 \pm 17.09$	134.01-134.01
18		DBP (mm Hg)	$77.23 \pm 10.31$	//.18-//.29
19		WC (cm)	$85.1 \pm 8.82$	85.05-85.15
20		FBG (mmol/L)	$5.96 \pm 1.9$	5.95-5.97
22		TC(mmol/L)	$5.21 \pm 2$	5.20-5.23
23		TG(mmol/L)	$1.57 \pm 1.14$	1.57-1.58
24		LDL-C(mmol/L)	$3.09 \pm 1.05$	3.08-3.09
25		HDL-C(mmol/L)	$1 39 \pm 0 51$	1 39-1 39
20 27		eGER	6874 + 167	68 65-68 83
28		$\operatorname{Corr}_{n(0/)}$	$00.74 \pm 10.7$	00.05-00.05
29		Sex, n(%)		42 70 44 24
30		Male	54649 (44.07%)	43./8-44.34
31		Female	69358 (55.93%)	55.66-56.22
32		Education level, n(%)		
33 34		Not educated	9888 (8.11%)	7.95-8.26
35		Primary education	43441 (35.61%)	35.34-35.88
36		Junior school education and above	68652 (56.28%)	56.00-56.56
37		Smoking status n (%)		
38		Current smoker	10023 (8 22%)	8 06-8 37
39		Ex smoker	7546 (6 10%)	6 05 6 32
40 41		Ex-shlokel	104412 (85 500/)	0.03-0.32
42		Never-smoker	104412 (85.59%)	85.40-85.79
43		Drinking habit, n (%)		
44		Non-drinker	101661 (83.34%)	83.13-83.55
45		Non-habitual drinker	12571 (10.31%)	10.14-10.48
46 47		Habitual drinker	7749 (6.35%)	6.22-6.49
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5 2 6 3 T	able ? Prevalence	of anemi	a in older a	dulte living ir	Shenzhen c	ommunity	
7 1 a	cording to socioder	or anomic	and other char	acteristics		ommunity,	
8 4 4	ceording to socioden	lographic	and other char	Provolonco	05% CI		
9 10 Chara	atoristics	Total	Number of	of	9370CI	w <sup>2</sup> Walua	D Value
10 Chara 11	ciensiics	Total	anemia	01		χ <sup>-</sup> value	
12				allellina (70)			
<sup>13</sup> Total		121981	18820	15.43	15.23-15.63		
14 15 <sub>0</sub>						22.36	< 0.001
16 Male		537/3	7946	14 79	14 49-15 09	22.30	< 0.001
17 <sup>Ivraic</sup>		68738	10874	14.79	14.49-13.09		
19 ducation level		08238	100/4	15.74	15.00-10.21	263 21	< 0.001
<sup>20</sup> Not educated		9888	2027	20.50	19 70-21 30	205.21	<0.001
21 Primary educati	on	43441	7240	16.67	16 32-17 02		
23 $1$ $1$ $1$	1 4 1 1	(0(5)	0552	12.02	12.66.14.17		
24 Junior school ec	lucation and above	68652	9553	13.92	13.66-14.17		
<sup>25</sup> Age group						1201.99	< 0.001
$\frac{20}{27}65 \sim 69$		60043	7635	12.72	12.45-12.98		
<sub>28</sub> 70~74		32750	4730	14.44	14.06-14.82		
$2975 \sim 79$		16599	3070	18.50	17.90-19.09		
$^{30}_{31}80\sim$		12589	3385	26.89	26.11-27.66		
3 moking status						68.89	< 0.001
33 Current smoker		10023	1253	12.50	11.85-13.15		
<sup>34</sup> <sub>35</sub> Ex-smoker		7546	1047 <	13.87	13.09-14.65		
<sup>36</sup> Never-smoker		104412	16520	15.82	15.60-16.04		
<sup>3</sup> Drinking habit						130.24	< 0.001
<sup>39</sup> <sup>40</sup> Non-drinker		101661	16302	16.04	15.81-16.26		
41 42 Non-habitual dr	inker	12571	1589	12 64	12 06-13 22		
43 Habitual drinker	r	7749	929	11 99	11 27-12 71		
<sup>4</sup> BMI	L	1119	/ _ /	11.77	11.27 12.71	1522 11	< 0.001
45 Low weight		4496	1504	33 45	32 07-34 83		
47 Normal weight		61532	11041	17.94	17.64-18.25		
<sup>48</sup> Overweight		44644	5175	11.59	11 29-11 89		
<sup>49</sup> Obesity		11309	1100	9 73	9 18-10 27		
50 central obesity		11009	1100	5.70	, <u>,</u> ,	540.10	< 0 001
52 Yes		49051	5897	12.02	11.73-12.31		
<sup>53</sup> No		72930	12923	17.72	17.44-18.00		
54 5Diabetes						27.05	< 0.001
56 Yes		27220	4520	16.61	16.16-17.05		
<sup>57</sup> No		94761	14300	15.09	14.86-15.32		
58 Hypertension						63.27	< 0.001
60 Yes		67835	9883	14.57	14.30-14.83		
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3 No			54146	8937	16 51	16 19-16 82		
4 Dyslinider	nia		01110	0,01	10.01	10.17 10.02	211 72	< 0.001
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10 Y es			37927	/5/4	19.97	19.57-20.37		
12 <sup>No</sup>			84054	11246	13.38	13.15-13.61		
13	1	A two-sided value of <i>P</i>	< 0.05 was	considered to	be statistical	lly significant.		
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6 7	2	Figure legends
8 9	3	Fig 1 Risk factor analyses of the prevalence of anemia in older adults living in
10	4	Shenzhen community
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Section/Topic	ltem #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Page 1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4
Methods			
Study design	4	Present key elements of study design early in the paper	Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 4
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Page 4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 5-6
Data sources/	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 5-6
Bias	9	Describe any efforts to address potential sources of bias	Page 6
Study size	10	Explain how the study size was arrived at	Page 4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Not applicable
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Page 6
		(b) Describe any methods used to examine subgroups and interactions	Not applicable
		(c) Explain how missing data were addressed	Not applicable
		(d) If applicable, describe analytical methods taking account of sampling strategy	Not applicable
		(e) Describe any sensitivity analyses	Not applicable
Results			

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Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	Page 4
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential	Page7
		confounders	
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures	Page 7
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence	Page 7
		interval). Make clear which confounders were adjusted for and why they were included	
		(b) Report category boundaries when continuous variables were categorized	Page 7
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 7-8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and	Page 8-9
		magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from	Page 7-9
		similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on	Page 9
		which the present article is based	

\*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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