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## Sex differences and risk factors of Metabolic syndrome in adults aged more than 40 in Northeast China: Results from the National Stroke Screening Survey

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## Original Article

### Title Page

# Sex differences and risk factors of Metabolic syndrome in adults aged more than 40 in Northeast China: Results from the National Stroke Screening Survey

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23 factor.  
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## ABSTRACT

**Objectives** To determine the gender differences and risk factors of Metabolic syndrome (MS) among the populations in northeast China.

**Study design** This study analyzed a part of the cross-sectional survey data of the National Stroke Screening and Prevention Program of China from 2016. The MS is defined as the presence of any three of the five risk factors: abnormal waist circumference, triglyceride, high-density lipoprotein cholesterol, blood pressure, fasting plasma glucose. Multiple regression analysis was used to investigate the sex-specific prevalence and risk factors of MS.

**Setting** The study was conducted in the Dehui city, Jilin province, China.

**Participants** A total of 4052 participants with complete questionnaire information and laboratory examinations were included in this analysis.

**Results** The prevalence of MS in northeast China ( $\geq 40$  years old) was 50.1%. In the male group, increase in age ( $\geq 65$  years old, OR=1.460, 95%CI: 1.065-2.002), high Body Mass Index (BMI) (overweight: OR=3.324, 95%CI: 2.403-4.598), abnormal neck circumference (OR=2.078, 95%CI: 1.569-2.751), and physical inactivity (OR=1.437, 95%CI: 1.064-1.941) significantly increased the risk of MS. In the female group, increase in age (OR=1.938, 95%CI: 1.466-2.561), high BMI (overweight: OR=3.273, 95%CI: 2.602-4.116), and abnormal neck circumference (OR=1.853, 95%CI: 1.521-2.258) were the underlying cause of MS. People with a junior middle school diploma (OR=0.633, 95%CI: 0.495-0.809) and being underweight (less BMI) (OR=0.238, 95%CI: 0.107-0.529) were less likely to develop MS.

**Conclusions** The prevalence of MS in women is significantly higher than that in men in northeast China. While increase in age, abnormal neck circumference and BMI

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3 significantly increase the risk of MS in women and men, physical inactivity increases  
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5 the risk of MS only in men. Additionally, higher education reduces the risk of MS in  
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7 women. Active lifestyle, preventive interventions and improvement in the level of  
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9 education could reduce the prevalence of MS.  
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12 **Key words:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
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### Strengths and limitations of this study

1. This cross-sectional study involves a large representative sample of Chinese people.
2. We used a uniform pre-coded questionnaire designed by the Stroke Screening and Prevention Program of the National Health and Family Planning Commission of China (CNSSS).
3. Partial results are based on self-reported data from the investigators, which inevitably has the drawback of recall bias.
4. Our survey excluded people who were sick or too weak to complete the interview.



## INTRODUCTION

Metabolic syndrome (MS) is a metabolic disorder, mainly related to insulin resistance and abdominal obesity.<sup>1</sup> It is a non-communicable disease. In developed countries, the prevalence of MS is higher and shows a trend of increase in every year,<sup>2</sup> which is inseparable from people's daily living habits.<sup>2</sup> MS is not an independent disease, but it is a risk factor for multiple cardiovascular diseases.<sup>3 4</sup> Moreover, there is a significant difference in the prevalence of MS between men and women. And the risk factors that affect MS vary by gender.<sup>5</sup> This paper aims to analyze the differences in the prevalence of MS between men and women in the population in northeast China.

## POTULATION and METHODS

### Data source and study participants

This population-based cross-sectional study was a part of the Stroke Screening and Prevention Program of the National Health and Family Planning Commission of China (CNSSS), among the resident population aged 40 years or above from January 2016 to March 2016. CNSSS is a national epidemiological survey of cerebrovascular diseases to obtain timely and reliable information on the morbidity, prevalence, and mortality of stroke in Chinese people over the age of 40.<sup>6</sup> The sampling method in this experiment has been described in detail in other articles.<sup>7</sup> The sample size (N) for this survey was acquired by calculation on a 2.37% stroke prevalence (p) among adults aged above 40 years in China,<sup>7</sup> using the formula  $N=(Z_{\alpha}^2pq)/d^2$  (where  $Z_{\alpha}=1.96$ ,  $\alpha=0.05$ ,  $q=1-p$ , and  $d=0.2p$ ).

A multistage stage stratified random cluster sampling method was applied to obtain the sample population. In the first stage, 30 villages and 10 towns were randomly selected from 308 villages (rural) and 14 towns (urban) in the Dehui City using the probability proportional to size (PPS) sampling method. In the second stage, 5

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3 villagers' groups or communities were randomly sampled from both rural and urban  
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5 strata using PPS. In the third stage, 1 participant aged  $\geq 40$  years was randomly  
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7 selected from each household of the selected villagers' groups or communities.  
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9 Respondents who were unwilling to participate in the survey or judged to be very frail  
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11 were excluded. We had selected permanent residents aged  $\geq 40$  years to attend the  
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13 study (a calculated total of 4445 participants with added 10% loss rate), and then,  
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15 4100 participants of them completed the face-to-face survey, with a good response  
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17 rate of 92.2%. In this sub-study of the CNSSS, we used data from participants who  
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19 finally completed the study. After excluding 48 participants with incomplete  
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21 questionnaire information or laboratory examinations, a total of 4052 participants  
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23 were included in this analysis. The sample selection framework is presented in Figure  
24  
25 1. The study protocol was approved by the Human Ethics and Research Ethics  
26  
27 committees of the First Hospital of Jilin University. Written informed consent was  
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29 obtained from all study participants before recruitment and data collection.  
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### 36 **Patient and public involvement**

37  
38 Patients and the public were not involved in the development of the research  
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40 questionnaire or outcome measures, study design, or recruitment to and conduct of  
41  
42 this study. There is no plan to disseminate the research findings to the participants.  
43  
44

### 45 **Data collection and measurement**

46  
47 All patients completed a questionnaire that included general information  
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49 (sociodemographic and health-related information). Physical examination included  
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51 height, weight, neck circumference, waist circumference, hip circumference, and  
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53 blood pressure. Height and weight were measured according to the standard. Subjects  
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55 removed their shoes and hats and wore light clothes. The measurement accuracy was  
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57 0.1cm and 0.1kg. Blood pressure was measured by doctors using the OMRON  
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3 automatic sphygmomanometer (OMRON HEM-7200, KYOTO, Japan). Blood  
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5 pressure was measured on the right arm, parallel to the heart. The subjects rested for  
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7 20 minutes, and then blood pressure was measured twice, and the mean value was  
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9 taken. Blood samples were measured overnight (at least 8 hours) on an empty  
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11 stomach for fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC),  
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13 low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol  
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15 (HDL-C). The samples were sent to the clinical laboratory of Changchun Kingmed  
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17 center for testing.  
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### 21 **Screening protocol and assessment criteria**

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23 The definition of MS we adopted in this study was published by International  
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25 Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung,  
26  
27 and Blood Institute (AHA/NHLBI).<sup>8</sup> The presence of any 3 of the 5 risk factors  
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29 constitutes a diagnosis of MS: 1. Waist circumference:  $\geq 90$ cm for men,  $\geq 80$ cm for  
30  
31 women; 2. TG:  $\geq 1.70$ mmol/L ( drug treatment for elevated TG is an alternate  
32  
33 indicator ) ; 3. HDL-C:  $< 1.0$ mmol/L for men,  $< 1.3$ mmol/ L for women, (drug  
34  
35 treatment for reduced HDL-C is an alternate indicator); 4. Blood pressure: systolic  
36  
37 blood pressure (SBP)  $\geq 130$  and/or diastolic blood pressure (DBP)  $\geq 85$ mmHg  
38  
39 (antihypertensive drug treatment in a patient with a history of hypertension is an  
40  
41 alternate indicator); and 5. FPG:  $\geq 5.6$ mmol/l (drug treatment of elevated glucose is an  
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43 alternate indicator).  
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49 In addition to gender grouping, the participants were divided into the middle-aged  
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51 group (40-64 years old) and the elderly group ( $\geq 65$  years old). Evaluation criteria for  
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53 other factors are shown in supplementary table S1. Those factors include overweight,  
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55 physical inactivity, smoking, abnormal neck circumference, and alcohol consumption.  
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### 59 **Statistical analysis**

Continuous variables were presented as median (IQR). Categorical data were presented as number and proportions. Sex differences were compared using Mann-Whitney U test and  $\chi^2$ -test. Multivariable binary logistic regressions were used to explore independent prevalence factors of MS among adults, and the OR and 95% confidence intervals (CIs) were calculated. All statistical analyses were performed using IBM SPSS 23.0 (SPSS, Inc., New York, NY, USA).  $P < 0.05$  was considered statistically significant.

## RESULTS

### 1. General data

There were 4052 participants in the survey. Among them, there were 1619 males and 2433 females with a median age of 53 (47, 62) years. Compared with the females, age, BMI, waist circumference, hip circumference, neck circumference and blood pressure were higher in males, whereas HDL-C and TC were lower ( $P < 0.001$ ). In addition, the proportion of smoking, exercising, living in the rural areas, and drinking alcohol were higher in men, whereas education level (Junior middle school and above) was higher in men, and the difference was statistically significant (except education level and living region  $P < 0.05$ , else  $P < 0.001$ ), as shown in Table 1.

Table 1 General characteristics of participants

	Men (N=1619)	Women (N=2433)	Total (N=4052)	$z/\chi^2$	<i>P</i> value
Age(years)	55(48,63)	53(47,61)	53(47,62)	-4.796	<0.001
BMI(kg/m <sup>2</sup> )	24.69(22.48,27.06)	23.97(21.94,26.32)	24.23(22.19,26.64)	-5.883	<0.001
WC(cm)	89(82,94)	84(77,90)	85(80,92)	14.949	<0.001
HC(cm)	100(94,104)	95(90,100)	96(90,102)	16.774	<0.001

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4	<b>NC(cm)</b>	36(35,38)	32(31,34)	34(32,36)	39.004	<0.001
5						
6	<b>Blood pressure</b>					
7						
8						
9	<b>SBP (mmHg)</b>	139.5(128.5,155)	136(124,153.5)	137.5(125.5,154.4)	-4.935	<0.001
10						
11	<b>DBP (mmHg)</b>	91.5(83.5,100)	85.5(79.5,94)	87.5(81,96.5)	-13.862	<0.001
12						
13						
14	<b>Lipid (mmol/l)</b>					
15						
16						
17	<b>HDL-C</b>	1.24(1.11,1.35)	1.25(1.13,1.39)	1.25(1.12,1.36)	-5.549	<0.001
18						
19	<b>TC</b>	5.26(4.59,5.96)	5.37(4.7,6.12)	5.34(4.66,6.05)	-3.582	<0.001
20						
21						
22	<b>LDL-C</b>	1.89(1.5,2.65)	1.9(1.54,2.63)	1.89(1.52,2.65)	-0.833	0.405
23						
24	<b>TG</b>	1.57(1.1,2.37)	1.62(1.17,2.38)	1.6(1.14,2.38)	-1.520	0.129
25						
26						
27	<b>FBG</b>	4.9(4.44,5.6)	5(4.5,5.6)	4.9(4.5,5.6)	-1.583	0.114
28						
29						
30	<b>Physical inactivity</b>				15.099	<0.001
31	<b>n (%)</b>					
32						
33	<b>No</b>	1309(80.9)	1841(75.7)	3150(77.7)		
34						
35	<b>Yes</b>	310(19.1)	592(24.3)	902(22.3)		
36						
37	<b>Alcohol consumption</b>				1340.38	<0.001
38	<b>n (%)</b>					
39						
40	<b>Never</b>	693(42.8)	2285(93.9)	2978(73.5)		
41						
42	<b>Heavy</b>	421(26)	12(0.5)	433(10.7)		
43						
44	<b>Light/moderate</b>	505(31.2)	136(5.6)	641(15.8)		
45						
46						
47	<b>Region, n (%)</b>				5.907	0.016
48						
49	<b>Urban</b>	788(48.7)	1279(52.6)	2067(51)		
50						
51	<b>Rural</b>	831(51.3)	1154(47.4)	1985(49)		
52						
53						
54	<b>Education, n(%)</b>				12.123	0.006
55						
56	<b>≤Primary school</b>	526(32.5)	920(37.8)	1446(35.7)		
57						
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<b>Junior middle school</b>	715(44.2)	981(40.3)	1696(41.9)		
<b>Senior middle school</b>	222(13.7)	315(12.9)	537(13.3)		
<b>College and above</b>	156(9.6)	217(8.9)	373(9.2)		
<b>Fruit consumption n(%)</b>				0.728	0.696
<b>≥ 5days/week</b>	1423(87.9)	2157(88.7)	3580(88.4)		
<b>3-4 days/week</b>	151(9.3)	208(8.5)	359(8.9)		
<b>≤ 2 days/week</b>	45(2.8)	68(2.8)	113(2.8)		
<b>Smoke, n(%)</b>				249.210	<0.001
<b>No</b>	563(34.8)	1462(60.1)	2025(50.0)		
<b>Yes</b>	1056(65.2)	971(39.9)	2027(50.0)		

Abbreviations: BMI, body mass index; WC, Waist circumference; HC, Hip circumference; NC, Neck circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; FBG, fasting blood glucose.

Values are expressed as median (IQR) or n (percentage).

## 2. MS prevalence

Among the 4052 subjects, 2030 met MS diagnosis, with a prevalence of 50.1% (38.4% in males and 57.9% in females). The gender difference was statistically significant ( $P < 0.001$ ). Among female population, the prevalence of MS in different age groups was 55.3% and 71.7%, respectively. There were statistical differences between the groups ( $P < 0.001$ ), as shown in Table 2a.

Table 2a Prevalence of Metabolic Syndrome

Characteristics	40-64 (N=3370)	65- (N=682)	Total (N=4052)	$\chi^2$	P value
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<b>Men (N=1619)</b>	501(38.00)	121(40.20)	622(38.40)	0.495	0.481
<b>Women (N=2433)</b>	1135(55.30)	273(71.70)	1408(57.90)	35.197	<0.001
<b>Total</b>	1636(48.50)	394(57.80)	2030(50.10)	19.309	<0.001
<b><math>\chi^2</math></b>	96.155	68.194	147.135		
<b>P</b>	<0.001	<0.001	<0.001		

Values are expressed as n (percentage).

### 3. Distribution of MS in different genders and different populations

Among middle-aged people (age 40-64), the proportions of waist circumference abnormality in males and females were 84.6% and 91.1%, respectively. The proportions of HDL-C abnormality in males and females were 28.7% and 77.2%, respectively, and the proportions of TG abnormality in males and females were 81.8% and 59.6%, respectively. The proportions of FBG abnormality in males and females were 45.7% and 40.30%, respectively. The proportion of blood pressure abnormality in males and females were 96.6% and 87.2%, respectively. The intergroup statistics were statistically significant (except FBG  $P < 0.05$ , residual  $P < 0.001$ ). In the elderly group, the proportions of HDL-C abnormality were 26.4% and 74.4%, respectively, and inter-group statistics of which were statistically significant ( $P < 0.001$ ), as shown in Table 2b.

Table 2b The distribution of Metabolic Syndrome in different genders in the populations of age 40-64 and age  $\geq 65$

Characteristics (Abnormality)	Age 40-64				Age $\geq 65$			
	Men (N=501)	Women (N=1135)	$\chi^2$	P value	Men (N=121)	Women (N=273)	$\chi^2$	P value
<b>WC, n(%)</b>	424(84.60)	1034(91.10)	15.008	<0.001	107(88.40)	256(93.80)	3.302	0.069

<b>HDL, n(%)</b>	144(28.70)	876(77.20)	347.384	<0.001	32(26.40)	203(74.40)	79.961	<0.001
<b>TG, n(%)</b>	410(81.80)	676(59.60)	77.292	<0.001	79(65.30)	190(69.60)	0.718	0.397
<b>FBG, n(%)</b>	229(45.70)	457(40.30)	4.231	0.04	59(48.80)	127(46.50)	0.169	0.681
<b>BP, n(%)</b>	484(96.60)	990(87.20)	34.293	<0.001	117(96.70)	262(96.00)	0.12	0.729

*Abbreviations: WC, Waist circumference; HDL, high-density lipoprotein; TC, total cholesterol; FBG, fasting blood glucose.*

*Values are expressed as n (percentage).*

#### 4. Univariate analysis of MS in different genders

In the male group, compared with the non-MS group, BMI, hip circumference and neck circumference of the population with MS were significantly higher. The population with MS was mostly distributed in urban regions, with a higher proportion of abnormal neck circumference, heavier alcohol consumption, less physical exercise, and lower education level. The difference between groups was statistically significant (except in alcohol consumption and education level  $P < 0.05$ , residual  $P < 0.001$ ). In the female group, compared with the non-MS group, the age, BMI, hip circumference, and neck circumference were significantly higher ( $P < 0.001$ ). The population with MS were mostly distributed in the rural region and had a higher proportion of abnormal neck circumference, lower education level, and no alcohol consumption (except alcohol consumption  $P < 0.05$ , residual  $P < 0.001$ ), as shown in Table 3.

Table 3 Univariate analysis of Metabolic Syndrome in different genders

Characteristics	Male			Female		
	MS (N=622)	Non-MS (N=997)	P value	MS (N=1408)	Non-MS (N=1025)	P value
Age (year)	55(48,63)	55(48,62)	0.828	56(49,63)	50(45,57)	<0.001



<b>BMI (Kg/m<sup>2</sup>)</b>	26.85 (25.15,28.51)	23.51 (21.47,25.26)	<0.001	25.15 (23.34,27.29)	22.41 (20.70,24.16)	<0.001
<b>HC (cm)</b>	103(100,107)	96(91,100)	<0.001	97(93,102)	90(84,95)	<0.001
<b>NC (cm)</b>	38(36,40)	35(34,37)	<0.001	33(32,35)	32(30,33)	<0.001
<b>Smoke, n(%)</b>			0.472			<0.001
No	223(35.9)	340(34.1)		798(56.7)	664(64.8)	
Yes	399(64.1)	657(65.9)		610(43.3)	361(35.4)	
<b>Physical inactivity n(%)</b>			<0.001			0.235
No	153(24.6)	157(15.7)		355(25.2)	237(23.0)	
Yes	469(75.4)	840(84.3)		1053(74.8)	788(77.0)	
<b>Alcohol consumption, n(%)</b>			0.006			0.010
Never	251(40.4)	442(44.3)		1340(95.2)	945(92.2)	
Light/moderate	182(29.3)	323(32.4)		63(4.5)	73(7.1)	
Heavier	189(30.4)	232(23.3)		5(0.4)	7(0.7)	
<b>Region, n(%)</b>			<0.001			<0.001
Urban	357(57.4)	431(43.2)		666(47.3)	613(59.8)	
Rural	265(42.6)	566(56.8)		742(52.7)	412(40.2)	
<b>Fruit consumption, n(%)</b>			0.690			0.254
≥5days per week	546(87.8)	877(88.0)		1236(87.8)	921(89.9)	
3-4 days per week	61(9.8)	90(9.0)		128(9.1)	80(7.8)	
≤2 days per week	15(2.4)	30(3.0)		44(3.1)	24(2.3)	
<b>BMI, n(%)</b>				<0.001		<0.001
Normal	88(14.1)	568(57.0)		465(33.0)	707(69.0)	

Underweight	3(0.5)	13(1.3)	8(0.6)	40(3.9)
Overweight	144(23.2)	238(23.9)	377(26.8)	162(15.8)
Apparently overweight	183(29.4)	106(10.6)	281(20.0)	81(7.9)
Obesity	204(32.8)	72(7.2)	277(19.7)	35(3.4)
<b>NC, n(%)</b>			<0.001	<0.001
Normal	160(25.7)	662(66.4)	550(39.1)	694(67.7)
Abnormal	462(74.3)	335(33.6)	858(60.9)	331(32.3)
<b>Age,n(%)</b>			0.481	<0.001
40-64 years	501(80.5)	817(81.9)	1135(80.6)	917(89.5)
≥65 years	121(19.5)	180(18.1)	273(19.4)	108(10.5)
<b>Education, n(%)</b>			0.006	<0.001
≤Primary school	176(28.3)	350(35.1)	630(44.7)	290(28.3)
Junior middle school	280(45.0)	435(43.6)	549(39.0)	432(42.1)
Senior middle school	104(16.7)	118(11.8)	149(10.6)	166(16.2)
College and above	62(10.0)	94(9.4)	80(5.7)	137(13.4)

*Abbreviations: MS, Metabolic syndrome; BMI, body mass index; HC, Hip circumference; NC, Neck circumference.*

*Values are expressed as median (IQR) or n (percentage).*

## 5. Multifactor logistics analysis results

Non-exercising males were more likely to develop MS than those with regular exercise (OR=1.437, 95%CI: 1.064-1.941). Elderly men were more likely to develop MS than middle-aged men (OR=1.460, 95%CI: 1.065-2.002). The risk of developing MS in the male group with neck circumference enlargement was higher than the one with normal neck circumference (OR=2.078, 95%CI: 1.569-2.751). People with

higher BMI (overweight) were more likely to develop MS than those with normal BMI (OR=3.324, 95%CI: 2.403-4.598) and the risk of MS was higher for people with higher BMI.

In the female group, elderly women were more likely to develop MS than middle-aged women (OR=1.938, 95%CI: 1.466-2.561). People with higher BMI (overweight) were more likely to develop MS than those with normal BMI (OR=3.273, 95%CI: 2.602-4.116) and the risk of MS was higher for people with higher BMI. People with a lower BMI (underweight) were less likely to develop MS than those with normal BMI (OR=0.238, 95%CI: 0.107-0.529). People with abnormal neck circumference were more likely to develop MS than those with normal neck circumference (OR=1.853, 95%CI: 1.521-2.258). People with a higher education level (at least a junior middle school diploma) were less likely to develop MS than those with a lower education level (primary school diploma and below) (OR=0.633, 95% CI: 0.495-0.809). The risk of MS decreased with higher education level, as shown in Table 4.

Table 4 Multivariate Logistic Regression Analyses on Risk Factors for the Prevalence of Metabolic Syndrome in male and female group

		Men		Women	
Category	Subcategory	OR (95%CI)	P value	OR (95%CI)	P value
Age	40-64	1(reference)		1(reference)	
	≥65	1.460(1.065-2.002)	0.019	1.938(1.466-2.561)	<0.001
Education	≤Primary school	1(reference)		1(reference)	
	Junior middle school	0.903(0.654-1.247)	0.536	0.633(0.495-0.809)	<0.001

	<b>Senior middle school</b>	1.062(0.673-1.675)	0.796	0.524(0.368-0.745)	<0.001
	<b>College and above</b>	0.672(0.401-1.125)	0.130	0.371(0.247-0.557)	<0.001
<b>Region</b>	<b>Urban</b>	1(reference)		1(reference)	
	<b>Rural</b>	0.878(0.636-1.213)	0.430	1.020(0.787-1.321)	0.883
<b>BMI</b>	<b>Normal</b>	1(reference)		1(reference)	
	<b>Underweight</b>	1.539(0.419-5.653)	0.516	0.238(0.107-0.529)	<0.001
	<b>Overweight</b>	3.324(2.403-4.598)	<0.001	3.273(2.602-4.116)	<0.001
	<b>Apparently overweight</b>	8.470(5.872-12.22)	<0.001	4.291(3.21-5.737)	<0.001
	<b>Obesity</b>	11.872(7.929-17.776)	<0.001	8.025(5.416-11.89)	<0.001
<b>NC</b>	<b>Normal</b>	1(reference)		1(reference)	
	<b>Abnormal</b>	2.078(1.569-2.751)	<0.001	1.853(1.521-2.258)	<0.001
<b>Smoke</b>	<b>No</b>	1(reference)		1(reference)	
	<b>Yes</b>	1.248(0.952-1.636)	0.109	1.227(0.982-1.533)	0.071
<b>Sport frequently</b>	<b>Yes</b>	1(reference)		1(reference)	
	<b>No</b>	1.437(1.064-1.941)	0.018	1.203(0.964-1.502)	0.103
<b>Alcohol consumption</b>	<b>Never</b>	1(reference)		1(reference)	
	<b>Higher drinking</b>	1.300(0.957-1.765)	0.093	0.418(0.115-1.518)	0.185
	<b>Light/moderate</b>	0.869(0.651-1.159)	0.338	0.698(0.471-1.034)	0.073

Abbreviations: BMI, body mass index; NC, Neck circumference; OR, odds ratio.

## DISCUSSION

MS has become one of the major public health threat in China. In the current study, the prevalence of MS in northeast China is significantly higher than that in entire

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2  
3 China (33.9%).<sup>9</sup> However in our study, the prevalence of MS was 50.1%. It is higher  
4 than previous study. In our study, it is also found that the prevalence of MS in women  
5 (57.9%) was higher than that in men (38.4%). In terms of age groups, the prevalence  
6 of MS in women was higher than that in men, no matter in the middle-aged group or  
7 the elderly group. In addition to gender differences, the prevalence of MS among  
8 female groups showed a trend of increase with the increase in age. The prevalence of  
9 MS in the elderly group (57.8%) was significantly higher than that in the middle-aged  
10 group (48.5%). In most studies, the prevalence of MS in females was higher than that  
11 in males,<sup>9,10</sup> but Firmann M's study found that the prevalence of MS in Caucasian  
12 males is higher than that in females,<sup>11</sup> which may be related to the difference in the  
13 selected race, the investigated population, and the selection criteria. The prevalence of  
14 MS is significantly different between regions and races. The gender difference in MS  
15 prevalence is mainly related to the increase in insulin resistance and the abnormal  
16 lipid metabolism resulting from the decrease in estrogen level after menopause  
17 following the increase in age. This change is related to hormone level, but not with  
18 aging.<sup>12</sup> In addition, relevant studies have shown that the prevalence of MS in women  
19 is significantly higher than that in men, and such a gender-related correlation was  
20 strengthened with the increase in age, which is consistent with our findings.

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45 In this study, we also found that the proportion of abnormal waist circumference  
46 and HDL in women was significantly higher than that in men, which was the main  
47 reason for the higher prevalence of MS in women than in men. This difference was  
48 significant in middle-aged group. This is consistent with the study of Dallongeville, a  
49 J.<sup>13</sup> The increase in waist circumference is significantly correlated with the occurrence  
50 of cardiovascular diseases.<sup>14</sup> In our study, the prevalence of abnormal TG in  
51 middle-aged men was significantly higher than that in middle-aged women, but there  
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3 was no such difference in the elderly population. This is same as reported in the  
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5 previous studies.<sup>15,16</sup> Therefore, we should mainly observe the occurrence of  
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7 abdominal obesity in middle-aged and elderly women.  
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10 Multivariate regression analysis showed that the prevalence of MS in men was  
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12 mainly influenced by BMI, and the risk of MS increases with the increase in BMI.  
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14 The abnormality of neck circumference, increase in age, and physical inactivity are  
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16 also the main factors influencing the prevalence risk of MS, which was the same as  
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18 reported in the research results of Zhou JY.<sup>17</sup> Infrequent physical activity increases  
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20 the risk of MS in men, but not in women. This finding is similar to that of  
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22 Díaz-Martínez X.<sup>18</sup> In the female group, both the growth in age and the abnormality  
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24 of neck circumference increase the risk of MS. There is a significant relationship  
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26 between MS prevalence in females and age, BMI, and neck circumference. Higher  
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28 education level of females can reduce the prevalence of MS; however, this correlation  
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30 is not found in the male population. The prevalence of MS in females shows a  
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32 correlation with education, whereas a negative correlation trend is observed in males,  
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34 which is similar to the results of Kim OY.<sup>19</sup>  
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41 Education level is the most important measure of the social economic status of  
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43 people, which is not only closely related to the prevalence of cerebrovascular  
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45 disease,<sup>20</sup> but also affects the prevalence of MS. The specific mechanism by which  
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47 education affects the prevalence of MS is not clear. It has been considered that  
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49 education affects people's health mainly by influencing lifestyle, positive attitudes  
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51 toward health, and accessing the chance of preventive health services.<sup>21</sup> In addition,  
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53 according to Kim OY's research, the prevalence of MS in South Korea is negatively  
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55 correlated with education level, which is largely related to the food consumption  
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57 pattern of Korean people (especially women).<sup>19</sup>  
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### **Strengths and limitations**

There are several limitations in the study. First, some parts of the results are based on the investigators' self-reported data, with the drawback of inevitable recall bias. Second, people who were sick or too weak to complete the interview were excluded in our survey. Despite these limitations, the main advantage of this study is the use of a large population cohort. After rigorous training prior to the survey, we used a uniform pre-coded questionnaire designed by CNSSS. A reliable method was applied to the study.

### **CONCLUSION**

In our study, the prevalence of MS in women is significantly higher than that in men in northeast China. Higher age, larger neck circumference, and higher BMI significantly increase the risk of MS in women and men, whereas physical inactivity increases the risk of MS only in men, higher education level reduces the prevalence of MS in women. It is important to control abnormal BMI and neck circumference in both men and women, particularly, in women with a low level of education and men with physical inactivity. Such a control can be achieved by influencing lifestyle, positive attitudes toward health, and accessing preventive interventions. Collectively, these efforts will help in lowering the prevalence of MS.

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### **CONTRIBUTORS**

Conception and design: Y Y, and Z-N G. Acquisition of the data: F-L Z and H-Y L.

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4 Data analysis: F-E L, D L, F-L Z. Drafting and revising the manuscript: F-E L.  
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7 Critical revision: Z-N G, and Y Y. All of the authors approved the final version for  
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9 publication.

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## 26 27 **CONFLICTS OF INTEREST**

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30 None declared.

## 31 32 **ETHICS APPROVAL**

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35 This subject was approved by the human ethics and research ethics committee of the  
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37 First Hospital of Jilin University (approval No: 2015-R-250), and written informed  
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39 consent was obtained from all of the participants.  
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## 42 43 **PROVENANCE AND PEER REVIEW**

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## 47 48 **DATA SHARING STATEMENT**

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51 The dataset supporting the conclusions of this article can be made available upon  
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53 request.  
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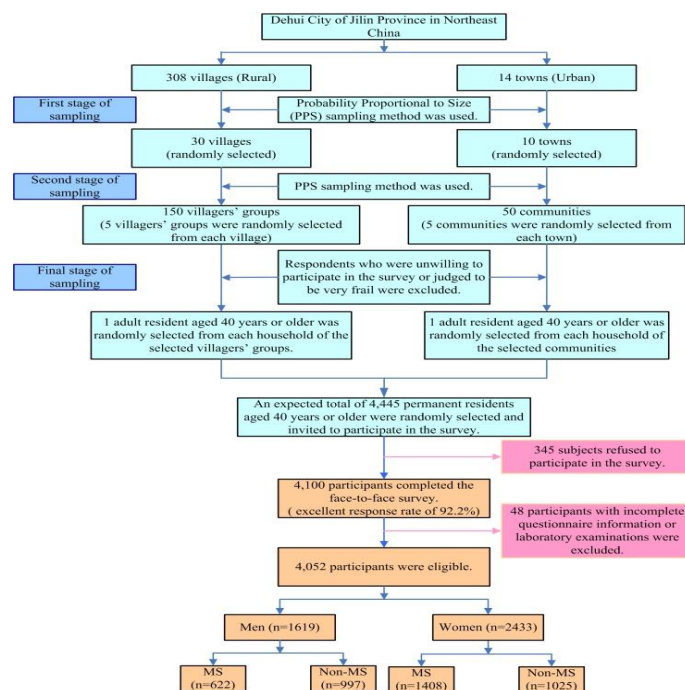
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9 Fig. 1 Sampling process in the study  
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For peer review only



Sex differences and risk factors of Metabolic syndrome in adults aged more than 40 in Northeast China: Results from the National Stroke Screening Survey  
Feng-e Li *et al*

**Supplementary Table S1** Definitions of metabolic syndrome-related risk factors in the survey.

Variables	Criteria	References
BMI	BMI was grouped into five categories for our study: underweight (BMI < 18.5 kg/m <sup>2</sup> ), normal (18.5 ≤ BMI < 24 kg/m <sup>2</sup> ), overweight (24 ≤ BMI < 26 kg/m <sup>2</sup> ), apparently overweight (26 ≤ BMI < 28 kg/m <sup>2</sup> ), obesity (BMI ≥ 28 kg/m <sup>2</sup> ).	Guidelines for diabetes prevention and treatment in China <sup>1</sup>
Abnormal neck circumference	≥37cm for male and ≥33cm for female	Neck circumference as an independent predictive contributor of cardio-metabolic syndrome <sup>2</sup>
Physical inactivity	Physical inactivity is defined as insufficient physical activity; Physical activity is defined as the performance of heavy physical labor or regular physical exercise for more than one year, more than 3 times per week, and for at least 30 minutes per session.	CHNS guidelines <sup>3</sup>
Smoking	A smoker was defined as one who reported smoking one or more cigarettes or was passively exposed to tobacco smoke every day in general for more than 6 consecutive months. A non-smoker was defined as the one who had never smoked, nor passively exposed to tobacco smoke; or, had history of smoking but quit smoking for at least 6 consecutive months previous to the study.	Technical specification of stroke screening and prevention in China <sup>4</sup>
Drinking	The NIAAA sets the standard drink size at about 14g of absolute ethanol, advising limits of no more than three drinks per day or seven drinks per week for men and women. Drinking status was divided into three categories according to the participants' self-report in the previous 6 months: non-drinkers: had never drunk alcoholic beverage; light/moderate drinkers: less than or upto NIAAA limits; heavier drinkers: in excess of NIAAA limits.	NIAAA guidelines <sup>5</sup>
Fruit consumption	Fruit consumption was grouped into three categories for our study: less than or equal to two days per week (≤ 2 d/w), three to four days per week (3–4 d/w), and greater than or equal to five days per week (≥ 5 d/w). And the weight of consumed fruits should reach or exceed two servings per day, and the definition of a serving of a fruit was calculated as 80g.	Fruit and vegetable consumption and stroke: meta-analysis of cohort studies <sup>6</sup>

**Abbreviation:** BMI, body mass index; CHNS, China Health and Nutrition Survey; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	6, 7
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			



Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	(7)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11,12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-17
		(b) Report category boundaries when continuous variables were categorized	12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18,19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
<b>Other information</b>			
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 which the present article is based	21

\*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](http://www.strobe-statement.org).

# BMJ Open

## Sex differences and risk factors for Metabolic syndrome in adults aged more than 40 years in Northeast China: Results from the National Stroke Screening Survey

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4 1 Original Article  
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7 2 **Title Page**  
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9 3 **Sex differences and risk factors for metabolic syndrome in adults**  
10 4 **aged more than 40 years in Northeast China: Results from the**  
11 5 **National Stroke Screening Survey**  
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51 20  
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55 21 **Authors contributions:** Conception and design: Y Y, and Z-N G. Acquisition of the  
56 22 data: F-L Z and H-Y L. Statistical methods and data analysis: F-e L, P Z, D L, F-L Z.  
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1 Drafting and revising the manuscript: F-e L. Critical revision: Z-N G, and Y Y. All of  
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8 Health and Family Planning Commission in China (GN-2016R0010).

9 **Search terms:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
10 factor.

11 **Word count: abstract 300 words; text 3429 words; 48 references; 5 tables and**  
12 **figures.**

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## 1 ABSTRACT

2 **Objectives** Low levels of income and education are also risk factors for metabolic  
3 syndrome (MS) in the population Northeast China, which has a high incidence of MS  
4 and cardiovascular diseases. This study aimed to determine sex-specific differences  
5 associated with the prevalence of and risk factors for MS among people older than 40  
6 years in Northeast China, which has not been previously investigated.

7 **Study design** This study analyzed a portion of the large sample data of the national  
8 cross-sectional screening of China from 2016. MS was defined as the presence of any  
9 three of the following five risk factors: abnormal waist circumference, high  
10 concentrations of triglycerides, high-density lipoprotein cholesterol, or fasting plasma  
11 glucose, and elevated blood pressure. Multiple regression analysis was used to  
12 investigate sex-specific differences in the prevalence of and risk factors for MS.

13 **Setting** The study was conducted in Dehui City, Jilin Province, China.

14 **Participants** A total of 4052 participants with complete questionnaire information and  
15 laboratory examinations were included.

16 **Results** The prevalence of MS was 50.1% overall (38.4% in males and 57.9% in  
17 females;  $p < 0.001$ ). High body mass index (BMI) and neck circumference significantly  
18 increased the risk of MS for both sexes. In addition, physical inactivity and alcohol  
19 consumption in males (odds ratios [ORs] 95% CIs: 1.506[1.117-2.031];  $p = 0.007$  and  
20 1.341[1.001-1.796];  $p = 0.049$ ) and advanced age in females (ORs 95% CIs:  
21 1.999[1.516-2.634];  $p < 0.001$ ) were factors associated with MS. Women who had a  
22 level of education above junior middle school and those who were underweight (BMI  
23  $< 18.5 \text{ kg/m}^2$ ) were less likely to develop MS, whereas for men, college education was  
24 a protective factor against MS.

25 **Conclusions** It is necessary to understand sex-specific differences and accurately

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1 identify high-risk groups, which could help formulate better public health policies and  
2 educational initiatives to fundamentally reduce the incidence of MS and cardiovascular  
3 diseases.

5 **Key words:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
6 factor.

For peer review only

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3 **1 Strengths and limitations of this study**  
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5 2 1. This cross-sectional study included a large, representative sample of Chinese  
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8 3 population.

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10 4 2. We used a uniform, pre-coded questionnaire designed by the Stroke Screening and  
11  
12 5 Prevention Program of the National Health and Family Planning Commission of China  
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14 6 (CNSSS).

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17 7 3. Some results were partially based on self-reported data collected by investigators,  
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19 8 which inevitably increased the risk of recall bias.

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21 9 4. Our survey excluded participants who were sick or too weak to complete the  
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23 10 interview.

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26 11 5. As a major limitation of all epidemiological investigations, conclusions based on  
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28 12 cross-sectional studies cannot be used for causal inferences.  
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## 2 INTRODUCTION

3  
4 Metabolic syndrome (MS) is associated with a cluster of cardiometabolic risk factors  
5 and has become one of the major public health threats in China. The higher prevalence  
6 of MS greatly increases the burden of morbidity and mortality of cardiovascular  
7 diseases worldwide.<sup>1-3</sup> This burden has increased every year, although it is difficult to  
8 differentiate it from unhealthy habits of daily living.<sup>4</sup> There is a significant difference  
9 in the prevalence of and risk factors for MS between men and women.<sup>5</sup> To control and  
10 reduce the risk of MS and cardiovascular diseases more effectively, it is necessary to  
11 identify high-risk populations and understand the sex-specific, modifiable lifestyle  
12 determinants of MS. Northeast China, with its low income level, has a high incidence  
13 of MS and cardiovascular diseases, especially the highest incidence and mortality of  
14 stroke (365 and 159/100 000 person-years) in China.<sup>6</sup> Thus, this study aimed to analyze  
15 the sex-specific differences in the prevalence of MS and its related risk factors in a  
16 population from northeast China.

## 18 POPULATION and METHODS

### 20 Data source and study participants

21  
22 This population-based cross-sectional study was a part of the Stroke Screening and  
23 Prevention Program of the National Health and Family Planning Commission of China

1 (CNSSS), which assessed a population of residents aged 40 years or older, from January  
2 to March 2016. The CNSSS is a national epidemiological survey of cerebrovascular  
3 diseases conducted to obtain timely and reliable information on the morbidity,  
4 prevalence, and mortality of stroke in Chinese people over the age of 40.<sup>7</sup> The sampling  
5 method employed in this study has been described in detail in other articles.<sup>8</sup> The  
6 sample size (N) required for this survey was calculated on a 2.37% stroke prevalence  
7 (p) among adults 40 years and older in China,<sup>8</sup> using the formula:  
8 
$$N = (Z_{\alpha}^2 pq) / d^2$$
 (where  $Z_{\alpha} = 1.96$ ,  $\alpha = 0.05$ ,  $q = 1-p$ , and  $d = 0.2p$ )

9 A multistage stratified, random cluster sampling method was applied to obtain the  
10 sample population. In the first stage, 30 villages and 10 towns were randomly selected  
11 from a total of 308 villages (rural) and 14 towns (urban) in Dehui City using the  
12 probability proportional to size (PPS) sampling method. In the second stage, five groups  
13 of villages or communities were randomly sampled from both the rural and urban strata  
14 using the PPS sampling. In the third stage, one participant aged  $\geq 40$  years was  
15 randomly selected from each household of the selected groups of villages or  
16 communities. Respondents who were unwilling to participate in the survey or who were  
17 judged to be very frail were excluded. We selected permanent residents aged  $\geq 40$  years  
18 for inclusion in the study (a calculated total of 4445 participants with an additional 10%  
19 loss rate); ultimately, 4100 participants completed the face-to-face survey, with a good  
20 response rate of 92.2%. In this sub-study of the CNSSS, we used data from participants  
21 who completed the study. After excluding 48 participants with incomplete  
22 questionnaire information or laboratory examinations, a total of 4052 participants were  
23 included in this analysis. The flowchart of the study selection process is shown in Figure  
24 1. The study protocol was approved by the Human Ethics and Research Ethics  
25 Committee of the First Hospital of Jilin University, Chang Chun, Jilin, China. Written

1 informed consent was obtained from all study participants before recruitment and data  
2 collection.

3

#### 4 **Patient and public involvement**

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6 Patients and the public were not involved in the development of the research  
7 questionnaire, its outcome measures, study design, recruitment methods or the conduct  
8 of this study. There is no plan to disseminate the research findings to the participants.

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#### 10 **Data collection and measurement**

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12 All participants completed a questionnaire that included an assessment of general  
13 sociodemographic and health-related information. Physical examinations included  
14 assessments of height, weight, neck circumference, waist circumference, hip  
15 circumference, and blood pressure. Height and weight were measured according to the  
16 standard methods; the subjects removed their shoes and hats and wore light clothes.  
17 The measurement accuracy was within 0.1 cm and 0.1 kg for the height and weight,  
18 respectively. Blood pressure was measured by physicians using an OMRON automatic  
19 sphygmomanometer (OMRON HEM-7200, KYOTO, Japan), on the right arm, after  
20 placing it parallel to the heart. The subjects were made to rest for 20 minutes before the  
21 blood pressure was measured twice, and mean value was recorded. Blood samples were  
22 collected following overnight fasting (at least eight hours) on an empty stomach to  
23 assess fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC), low-  
24 density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol  
25 (HDL-C) concentrations. The samples were sent to the clinical laboratory of

1 Changchun Kingmed Center (Chang Chun, Jilin, China) for testing.

### 3 **Screening protocol and assessment criteria**

5 The definition of MS used in this study was published by the International Diabetes  
6 Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood  
7 Institute (AHA/NHLBI).<sup>9</sup> The presence of any three of the following five risk factors  
8 constituted a diagnosis of MS: 1) Waist circumference:  $\geq 90$  cm for men, and  $\geq 80$  cm  
9 for women; 2) TG concentration:  $\geq 1.70$  mmol/L (drug treatment for elevated TG levels  
10 is an alternative indicator); 3) HDL-C concentration:  $< 1.0$  mmol/L for men, and  $< 1.3$   
11 mmol/L for women (drug treatment for reduced HDL-C levels is an alternative  
12 indicator); 4) blood pressure: systolic blood pressure (SBP)  $\geq 130$  mmHg and/or  
13 diastolic blood pressure (DBP)  $\geq 85$  mmHg (antihypertensive drug treatment in a  
14 patient with a history of hypertension is an alternative indicator); and 5) FPG  
15 concentration:  $\geq 5.6$  mmol/L (drug treatment for elevated glucose levels is an  
16 alternative indicator).

17 In addition to stratifying by sex, participants were stratified by age into a middle-  
18 aged group (40–64 years old) and an elderly group ( $\geq 65$  years old). The evaluation  
19 criteria for the other factors, including BMI, level of physical inactivity, smoking status,  
20 and alcohol consumption are shown in Supplementary Table S1.

### 22 **Statistical analysis**

24 The normalities of the data distributions were tested using the Kolmogorov-Smirnov  
25 test. Non-normally distributed continuous variables are presented as medians (IQRs).

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4 1 The Mann-Whitney U test was used to assess differences between two groups of data  
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6 2 with non-normal distributions. Categorical data are presented as numbers and  
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9 3 proportions. The differences between groups were assessed using the  $\chi^2$ -test.  
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11 4 Significant variables (those with  $P < 0.05$ ) identified in the univariate analysis were  
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14 5 selected for the multivariate analyses. Multiple logistic regression analysis was used to  
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17 6 explore the independent risk factors of MS in the two sexes, and the odds ratios (ORs)  
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20 7 and 95% confidence intervals (CIs) were calculated. All statistical analyses were  
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23 8 performed using IBM Statistical Package for the Social Sciences (SPSS) version 23.0  
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25 9 (SPSS, Inc., New York, NY, USA).  $P < 0.05$  was considered statistically significant.  
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## 11 **RESULTS**

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13 13 Among the 4,100 participants who completed the face-to-face survey, 4,052 were  
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15 14 included in the analysis. A total of 2,030 individuals met the criteria for MS, and the  
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17 15 prevalence was 50.1% overall (38.4% in males and 57.9% in females;  $p < 0.001$ ). Of  
18  
19 16 all the 4,052 participants, 1,619 were men (40.0%) and 2,433 were women (60.0%),  
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21 17 with a median age of 53 (IQR: 47- 62) years. The population were likely to have a lower  
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23 18 educational level. In total, 76.7% of the participants had a level of education not higher  
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25 19 than that of junior middle school.  
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### 21 **1. Demographic characteristics of all participants with MS**

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23 23 Table 1 shows that compared to males, the female participants with MS had the  
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1 following associated risk factors: a primary school and lower level of educational  
 2 attainment (44.7% vs. 28.3%;  $p < 0.001$ ), living in a rural area, a normal or underweight  
 3 BMI, an abnormal HDL-C concentration, and a higher concentration of total cholesterol  
 4 and LDL-C. Women were also less likely to have an abnormal neck or hip  
 5 circumference, hypertension, abnormal levels of triglycerides and fasting blood glucose,  
 6 live in urban areas, and smoke and drink alcohol.

7  
 8 Table 1. Sex differences in demographic characteristics and risk factors among  
 9 participants with metabolic syndrome (MS).

	Total	Male	Female	P value
<b>Participants, n (%)</b>	4052(100)	1619 (40.0)	2433 (60.0)	
<b>Cases, n (%)</b>	2030 (50.1)	622 (38.4)	1408 (57.9)	
<b>Age, years, median (IQR)</b>	56(49,63)	55.72(48,63)	56.19(49,63)	0.216
<b>Age group, n (%)</b>				0.973
40-64 years	1636(80.6)	501(80.5)	1135(80.6)	
≥65 years	394(19.4)	121(19.5)	273(19.4)	
<b>Waist circumference, n (%)</b>	1821(89.7)	531(85.4)	1290(91.6)	<0.001
<b>Neck circumference, median (IQR)</b>	34(32,37)	38.23(36,40)	33.27(32,35)	<0.001
<b>Hip circumference, n (%)</b>	100(95,104)	103.63(100,107)	97.76(93,102)	<0.001
<b>TCHO, mmol/L, median (IQR)</b>	5.52(4.83,6.25)	5.50(4.73,6.12)	5.63(4.87,6.29)	0.004
<b>LDLC, mmol/L, median (IQR)</b>	1.93(1.56,2.64)	2.08(1.5,2.57)	2.19(1.57,2.65)	0.001
<b>HDLC, n (%)</b>	1255(61.8)	176(28.3)	1079(76.6)	<0.001
<b>TG, n (%)</b>	1503(74.0)	508(81.7)	995(70.7)	<0.001
<b>FBG, n (%)</b>	881(43.4)	291(46.8)	590(41.9)	<0.001
<b>Hypertension, n (%)</b>	1853(91.3)	601(96.6)	1252(88.9)	<0.001
<b>Education, n (%)</b>				<0.001
≤Primary school	806(39.7)	176(28.3)	630(44.7)	
Junior middle school	829(40.8)	280(45)	549(39)	
Senior middle school	253(12.5)	104(16.7)	149(10.6)	
College and above	142(7.0)	62(10.0)	80(5.7)	
<b>Region, n (%)</b>				<0.001
Urban	1023(50.4)	357(57.4)	666(47.3)	
Rural	1007(49.6)	265(42.6)	742(52.7)	
<b>Smoke, n (%)</b>				<0.001
No	1021(50.3)	223(35.9)	798(56.7)	
Yes	1009(49.7)	399(64.1)	610(43.3)	
<b>Physical inactivity, n (%)</b>				0.768

No	1522(75.0)	469(75.4)	1053(74.8)
Yes	508(25.0)	153(24.6)	355(25.2)
<b>Alcohol consumption, n (%)</b>			<0.001
Never	1591(78.4)	251(40.4)	1340(95.2)
Light/moderate	245(12.1)	182(29.3)	63(4.5)
Heavier	194(9.6)	189(30.4)	5(0.4)
<b>Fruit consumption, n (%)</b>			0.609
≥5days per week	1782(87.8)	546(87.8)	1236(87.8)
3-4 days per week	189(9.3)	61(9.8)	128(9.1)
≤2 days per week	59(2.9)	15(2.4)	44(3.1)
<b>BMI, n (%)</b>			<0.001
Normal	553(27.2)	88(14.1)	465(33.0)
Underweight	11(0.5)	3(0.5)	8(0.6)
Overweight	521(25.7)	144(23.2)	377(26.8)
Apparently overweight	464(22.9)	183(29.4)	281(20.0)
Obesity	481(23.7)	204(32.8)	277(19.7)

Abbreviations: TCHO, total serum cholesterol; LDLC, Low Density Lipoprotein Cholesterol; HDLC, high-density lipoprotein; TG, triglyceride; FBG, fasting blood glucose; BMI, body mass index.

Values are expressed as n (percentage).

## 2. Univariate analysis of factors associated with MS by sex

Table 2 shows the prevalence of MS according to different demographic characteristics and risk factors in men and women. The prevalence of MS in woman was significantly higher than that in men ( $P < 0.001$ ). The prevalence of MS was higher in the elderly (men: 40.2%; women: 71.7%), especially in older women (Figure 2). In the female group, age, BMI, hip and neck circumference, smoking, alcohol drinking, geographical region, and level of educational attainment were associated with MS, whereas physical inactivity and fruit consumption were not. In men, the risk factors associated with MS were similar, except for age and smoking. Unlike in women, physical inactivity was also a risk factor in men.

Table 2 Distribution of metabolic syndrome (MS) in men and women according to different demographic characteristics

Characteristics	Male			Female		
	Total	case, (n%)	P value	Total	case, (n%)	P value
<b>Cases, n (%)</b>	1619	622(38.4)	-	2433	1408(57.9)	-
<b>Age, year, median (IQR)</b>	55(48,63)	55(48,63)	0.828	53(47,61)	56(49,63)	<0.001
<b>Age group, n (%)</b>			0.481			<0.001
40-64 years	1318	501(38.0)		2052	1135(55.3)	
≥65 years	301	121(40.2)		381	273(71.7)	
<b>BMI, Kg/m<sup>2</sup>, median (IQR)</b>	24.69 (22.48,27.06)	26.85 (25.15,28.51)	<0.001	23.97 (21.94,26.32)	25.15 (23.34,27.29)	<0.001
<b>BMI, n (%)</b>			<0.001			<0.001
Normal	656	88(13.4)		1172	465(39.7)	
Underweight	16	3(18.8)		48	8(16.7)	
Overweight	382	144(37.7)		539	377(69.9)	
Apparently overweight	289	183(63.3)		362	281(77.6)	
Obesity	276	204(73.9)		312	277(88.8)	
<b>HC, cm, median (IQR)</b>	100(94,104)	103(100,107)	<0.001	95(90,100)	97(93,102)	<0.001
<b>NC, cm, median (IQR)</b>	36(35,38)	38(36,40)	<0.001	32(31,34)	33(32,35)	<0.001
<b>Smoke, n (%)</b>			0.472			<0.001
No	563	223(39.6)		1462	798(54.6)	
Yes	1056	399(37.8)		971	610(62.8)	
<b>Physical inactivity n (%)</b>			<0.001			0.235
Yes	1309	153(49.4)		1841	355(60.0)	
No	310	469(35.8)		592	1053(57.2)	
<b>Alcohol consumption n (%)</b>			0.006			0.010
Never	693	251(36.2)		2285	1340(58.6)	
Light/moderate	505	182(36.0)		136	63(46.3)	
Heavier	421	189(44.9)		12	5(41.7)	
<b>Region, n (%)</b>			<0.001			<0.001
Urban	788	357(45.3)		1279	666(53.1)	
Rural	831	265(31.9)		1154	742(64.3)	
<b>Fruit consumption n (%)</b>			0.690			0.254
≥5days per week	1423	546(38.4)		2157	1236(57.3)	
3-4 days per week	151	61(40.4)		208	128(61.5)	
≤2 days per week	45	15(33.3)		68	44(64.7)	
<b>Education, n (%)</b>			0.006			<0.001
≤Primary school	526	176(33.5)		920	630(68.5)	
Junior middle school	715	280(39.2)		981	549(56.0)	
Senior middle school	222	104(46.8)		315	149(47.3)	
College and above	156	62(39.7)		217	80(36.9)	

1 Abbreviations: BMI, body mass index; HC, Hip circumference; NC, Neck  
2 circumference.

3 Values are expressed as median (IQR) or n (percentage).

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### 1 3. Relationship between risk factors and MS in the multivariate logistic regression 2 analysis

3  
4 The multivariate analysis in Table 3 shows that BMI and neck circumference were  
5 significantly associated with MS in both men and women. Higher educational  
6 attainment and an underweight BMI were not associated with MS in either sex.

7 In the male group, the ORs (95% CIs) were 3.202 (2.321–4.419;  $p < 0.001$ ) for the  
8 overweight BMI, 7.932 (5.530–11.376;  $p < 0.001$ ) for the apparently overweight BMI,  
9 and 11.059 (7.431–16.459;  $p < 0.001$ ) for the obese BMI groups compared to the  
10 reference value for a normal BMI; for neck circumference, it was 2.095 (1.584–2.772;  
11  $p < 0.001$ ). Physical inactivity and higher alcohol consumption were associated with  
12 MS in men (OR 1.506, 95% CI [1.117–2.031],  $p = 0.007$ ; and OR 1.341, 95% CI [1.001–  
13 1.796],  $p = 0.049$ , respectively). An OR of 0.584 (0.353–0.968;  $p = 0.037$ ) was observed  
14 for a college level of education and higher compared to the reference value for primary  
15 school education.

16 In the female group, the ORs (95% CIs) were 3.262 (2.594–4.101;  $p < 0.001$ ) for the  
17 overweight BMI, 4.251 (3.181–5.680;  $p < 0.001$ ) for the apparently overweight BMI,  
18 and 8.023 (5.415–11.885;  $p < 0.001$ ) for the obese BMI groups compared to the  
19 reference value for a normal BMI. For neck circumference, the OR was 1.865 (1.531–  
20 2.272;  $p < 0.001$ ). Advanced age ( $\geq 65$  years) was associated with MS in women (OR  
21 1.999, 95% CI [1.516–2.634];  $p < 0.001$ ). For the underweight BMI, the OR (95% CI)  
22 was 0.238 ([0.107–0.529];  $p < 0.001$ ). In women, for a level of educational attainment  
23 of junior middle school, the OR was 0.630 ([0.492–0.805];  $p < 0.001$ ); for senior middle  
24 school, it was 0.526 ([0.370–0.748];  $p < 0.001$ ), and for college and above, it was 0.376  
25 ([0.251–0.564];  $p < 0.001$ ).

1

2 Table 3 Multivariate logistic regression analyses on risk factors for the prevalence of  
3 metabolic syndrome (MS) in males and females.

Category	Reference	Male		Female	
		OR (95% CI)	P	OR (95% CI)	P
<b>Age group</b>	<b>40-64 years</b>				
≥65years		-	-	1.999(1.516-2.634)	< 0.001
<b>Education</b>	<b>≤Primary school</b>				
Junior middle school		0.859(0.624-1.183)	0.351	0.630(0.492-0.805)	< 0.001
Senior middle school		0.986(0.629-1.548)	0.952	0.526(0.370-0.748)	< 0.001
College and above		0.584(0.353-0.968)	0.037	0.376(0.251-0.564)	< 0.001
<b>Region</b>	<b>urban</b>				
Rural		0.889(0.647-1.221)	0.466	0.994(0.769-1.285)	0.963
<b>BMI</b>	<b>Normal</b>				
Overweight		3.202(2.321-4.419)	< 0.001	3.262(2.594-4.101)	< 0.001
Apparently overweight		7.932(5.530-11.376)	< 0.001	4.251(3.181-5.680)	< 0.001
Obesity		11.059(7.431-16.459)	< 0.001	8.023(5.415-11.885)	< 0.001
<b>Neck circumference</b>	-	2.095(1.584-2.772)	< 0.001	1.865(1.531-2.272)	< 0.001
<b>Smoke</b>	<b>No</b>				
Yes		-	-	1.217(0.975-1.519)	0.083
<b>Physical inactivity</b>	<b>Physical activity</b>				
Yes		1.506(1.117-2.031)	0.007	-	-
<b>Alcohol consumption</b>	<b>Never</b>				
Light/moderate drinking		0.883(0.667-1.170)	0.386	0.701(0.473-1.040)	0.077
Higher drinking		1.341(1.001-1.796)	0.049	0.435(0.120-1.575)	0.205

4 Abbreviations: BMI, body mass index; OR, odds ratio.

## 7 DISCUSSION

8  
9 In this study, we evaluated sex differences in the prevalence of MS and its relative  
10 determinants in a low-income population from Northeast China. We found that a high  
11 BMI and large neck circumference were risk factors for MS, and a higher BMI was  
12 associated with a higher prevalence of MS in both sexes. In addition, higher educational  
13 attainment was a protective factor against MS in both sexes, although the effect was  
14 greater in women. An underweight BMI was also a protective factor in women.  
15 Advanced age ( $\geq 65$  years) was a risk factor only for women, whereas physical

1 inactivity and excessive alcohol consumption were risk factors only in men.

2       The prevalence of MS has been steadily increasing due to unhealthy lifestyles in low-  
3 and high-income regions,<sup>10 11</sup> and there are known sex differences. The prevalence of  
4 MS in those living in the Chinese mainland for both the low–middle- and high-income  
5 populations was shown to be 33.9% in 2010;<sup>1</sup> however, in our study, it was 50.1%. This  
6 may be due to the fact that most of the participants in our study population had a lower  
7 educational level and income, which may have had an additive effect on the main,  
8 increasing trend. In most studies, the prevalence of MS in females was higher than that  
9 in males;<sup>1 12</sup> for example, in Mexico, the prevalence in females was 55.6%, whereas in  
10 males, it was 38.2%.<sup>13</sup> Similar sex disparities have been found in Middle Eastern  
11 countries, although few sex differences have been reported in populations from the  
12 European Union that have a lower MS prevalence.<sup>14</sup> Contrarily, there are also studies,  
13 which have reported that the prevalence of MS in males is higher than that in females  
14 in Caucasian,<sup>15</sup> in American adolescents,<sup>16</sup> and in Far East Asian and Japanese  
15 population, and the rate was twice as high as that in women from Macau.<sup>17</sup> These  
16 differences may be related to race, the period in which the studies were conducted, the  
17 geographic region, and the selection criteria used.<sup>18 19 20</sup> Our results were consistent  
18 with those reported in most countries that women had a higher prevalence of MS than  
19 men,<sup>21 22 23 24</sup> (57.9% in females and 38.4% in males;  $p < 0.001$ ). In addition, these sex-  
20 related differences were shown to be greater in women of advanced age, but remained  
21 relatively stable with respect to age in men in East China,<sup>25</sup> consistent with our own  
22 findings. Females  $\geq 65$  years old had a 1.999- fold risk of MS and 95%CI(1.516-2.634)  
23 compared to younger ones (40-65 years old). The sex differences may be mainly related  
24 to the increase in insulin resistance and abnormal lipid metabolism resulting from the  
25 decrease in estrogen levels after menopause as women age. Thus, this change may be

1 related to changes in hormone levels, rather than aging itself.<sup>26</sup>

2 It is well known that MS prevalence increases as BMI increases,<sup>27</sup> and a previous  
3 study found a BMI over 30.0 kg/m<sup>2</sup> was a risk factor;<sup>28</sup> our study also found that  
4 higher BMI, the higher the risk of MS. Compared to a normal BMI, the risk was 3.262-,  
5 4.251-, and 8.023-fold higher in overweight, significantly overweight, and obese  
6 women, respectively; in men, the risk increased 3.202-, 7.932-, and 11.059-fold,  
7 respectively. These findings suggest that weight gain in men (BMI  $\geq$  24) increases the  
8 risk of MS more significantly than it does in women; this has been reported in both  
9 sexes in a study of Turkish adults.<sup>29</sup> An Israeli cohort study claimed that a normal BMI  
10 had a high negative predictive value in both men (98%) and women (96%) with respect  
11 to MS.<sup>30</sup> As reported in a 2018 meta-analysis, neck circumference was not associated  
12 with MS;<sup>31</sup> however, a 2018 Chinese community-based study of those over 50 years old  
13 showed that neck circumference was associated with MS, although the two studies used  
14 different definitions.<sup>32</sup> In our study, the risk of MS increased by 1.865-fold in women  
15 and 2.095-fold in men for every 1 cm increase in neck circumference. Neck  
16 circumference combined with BMI are effective indicators of being overweight or  
17 obese, and such individuals are more prone to developing MS.

18 Educational level is the most important measure of socioeconomic status, which has  
19 been shown to not only affect the prevalence of MS, but is also closely related to the  
20 prevalence of cerebrovascular disease.<sup>33</sup> The specific mechanism by which education  
21 affects the prevalence of MS is unclear, although it has been considered that education

1 affects people's health mainly by influencing their lifestyles and positive attitudes  
2 toward health, and by increasing their access to preventive health services.<sup>34</sup> In addition,  
3 MS prevalence has been negatively correlated with educational level in South Korea,  
4 which is largely related to the dietary patterns of Koreans (especially in women).<sup>35</sup> In  
5 the female group in our study, compared to a level of education of primary school or  
6 less, the ORs indicated a 0.630-fold, 0.526-fold, and 0.376-fold risk of developing MS  
7 in those who had completed junior middle-school, senior middle-school, and college  
8 and above, respectively. This suggested that a higher educational level can reduce the  
9 risk of MS; however, in the male population, this advantage was found only in those  
10 who had a college education, with an OR of 0.584 (95% CI: 0.353–0.968). The negative  
11 association between MS prevalence and educational level was significant in females,  
12 which is similar to the results of a previous study.<sup>35</sup> A study of the third National Health  
13 and Nutrition Examination Survey found that low income and educational levels were  
14 associated with a higher prevalence of MS in females than in males.<sup>36</sup> Our study  
15 population is characterized by having both a low income and a low level of education,  
16 both of which contribute to a higher MS prevalence. The high percentage of females  
17 and males with a primary school education or below was 37.8% and 32.5%,  
18 respectively, which may partially explain the high prevalence of MS in women.<sup>24</sup>

19 Alcohol consumption and physical inactivity were the main risk factors in the male  
20 group, consistent with the findings of a previous study.<sup>37</sup> Infrequent physical activity  
21 results in a 1.506-fold increased risk of MS in men, but not in women, in agreement  
22 with previous findings;<sup>38</sup> however, physical activity has been suggested to be a low risk

1 factor for MS, as has beer consumption.<sup>39</sup> Conversely, it has also been shown that heavy  
2 alcohol consumption with binge drinking increased the risk of MS in Korean men,  
3 regardless of their BMI.<sup>40</sup> Similarly, our study also showed that the population with  
4 higher consumption of alcohol had a 1.341- fold increased risk of MS incidence and  
5 95%CI(1.001-1.796), compared to the population that never consumed alcohol.  
6 Additionally, the population with physical inactivity had a 1.506- fold increased risk of  
7 MS and 95%CI(1.117-2.031), compared to the population with physical activity.  
8 Chinese studies have found that smoking was associated with increased MS prevalence,  
9 regardless of sex or BMI classification.<sup>41</sup> In addition, smoking was independently  
10 associated with MS<sup>42</sup> in a dose-dependent manner,<sup>43</sup> and increased cigarette  
11 consumption of more than 20 pack-years is associated with a 1.81-fold increased MS  
12 prevalence compared to that in non-smokers in women.<sup>39</sup> The association between fruit  
13 consumption, geographical region, hip circumference, and MS risk remains unclear; in  
14 our study, there was no significant differences in MS risk related to these factors  
15 between men and women.

16 Lifestyle interventions resulted in a 2.61-fold reduced risk of MS compared with the  
17 control group in a previous study,<sup>44</sup> and an investigation of dietary patterns showed that  
18 the Chinese pattern (high in grains, vegetables, fruit, salted fish and eggs, soyabean,  
19 and etc.) was associated with a lower risk of MS than the animal food pattern (high in  
20 meats, fish and shrimp, eggs, seafood, alcoholic beverages, etc.).<sup>45</sup> Sex differences  
21 in the ways dietary patterns were associated with increased MS prevalence have been  
22 reported; for example, an increased prevalence was observed in men consuming an

1 "animal and fried food" diet, and women consuming a "high-salt and energy" diet.<sup>19</sup>  
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1 "animal and fried food" diet, and women consuming a "high-salt and energy" diet.<sup>19</sup>  
2 Muscle strength and cardiorespiratory fitness may independently and jointly reduce the  
3 incidence of MS,<sup>46</sup> as increased physical activity decreased the risk by 19–24%,<sup>47</sup> in  
4 men, every hour of exercise may decrease MS risk by 2%.<sup>48</sup> Weekly exercise while  
5 consuming > 2,000 kcal per day may strongly protect middle-aged men not only from  
6 obesity, but also from MS. To prevent the onset of MS, a better understanding of  
7 modifiable lifestyle factors is needed in high-risk populations; for example, in men who  
8 are physically inactive and regularly consume alcohol, further effort should be made to  
9 control body weight, especially by focusing on reducing high BMI and neck  
10 circumference. For women, especially the elderly, efforts should be made to control  
11 their weight more actively to maintain their BMI and neck circumference at a normal  
12 level or below to reduce the risk of MS, and a focus should be directed at changes in  
13 hormone levels. In the long run, a higher level of educational attainment can reduce the  
14 risk of MS. Understanding these factors and the sex differences between them, as well  
15 as accurately identify high-risk groups could help to develop better public health  
16 policies and educational initiatives and reduce the incidence of MS and vascular  
17 diseases.

18

## 19 **CONCLUSION**

20 In our study, the prevalence of MS in women was significantly higher than that in men  
21 in Northeast China. It is necessary to accurately identify groups at high risk of MS  
22 based on sex-specific factors. We observed that those at the highest risk were elderly

1 women with a low level of education and men with physical inactivity, excessive  
2 alcohol consumption, and a lower than college level of education. Abnormal BMI and  
3 large neck circumference were risk factors in both sexes. Health management and  
4 disease prevention organizations need to actively publicize such information to increase  
5 public attention and encourage those at risk to actively change their lifestyle and reduce  
6 the impact of preventable risk factors. These changes could fundamentally reduce the  
7 growing incidence of MS and the cardiovascular disease burden. These changes could  
8 fundamentally reduce the growing incidence of MS and the cardiovascular disease  
9 burden. There were also several limitations to this study, such as some self-reported  
10 data collected, blood samples measured only once, a lack of consideration of certain  
11 lifestyle factors or residual confounders, people sick or too weak excluded. Besides, the  
12 conclusion from cross-sectional studies cannot be used for causal inferences, and  
13 prospective and randomized studies are needed.

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#### 4 **CONFLICTS OF INTEREST**

5 None declared.

#### 6 **ETHICS APPROVAL**

7 This subject was approved by the human ethics and research ethics committee of the  
8 First Hospital of Jilin University (approval No: 2015-R-250), and written informed  
9 consent was obtained from all of the participants.

#### 10 **PROVENANCE AND PEER REVIEW**

11 Not commissioned; externally peer reviewed.

#### 12 **DATA SHARING STATEMENT**

13 The dataset supporting the conclusions of this article can be made available upon  
14 request.

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27 10 Fig. 1 Sampling process in the study

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29 11 Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study

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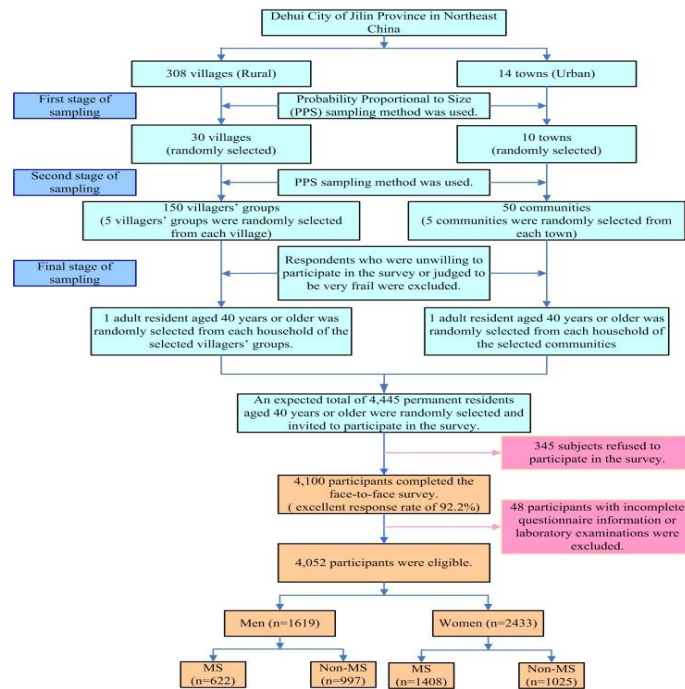
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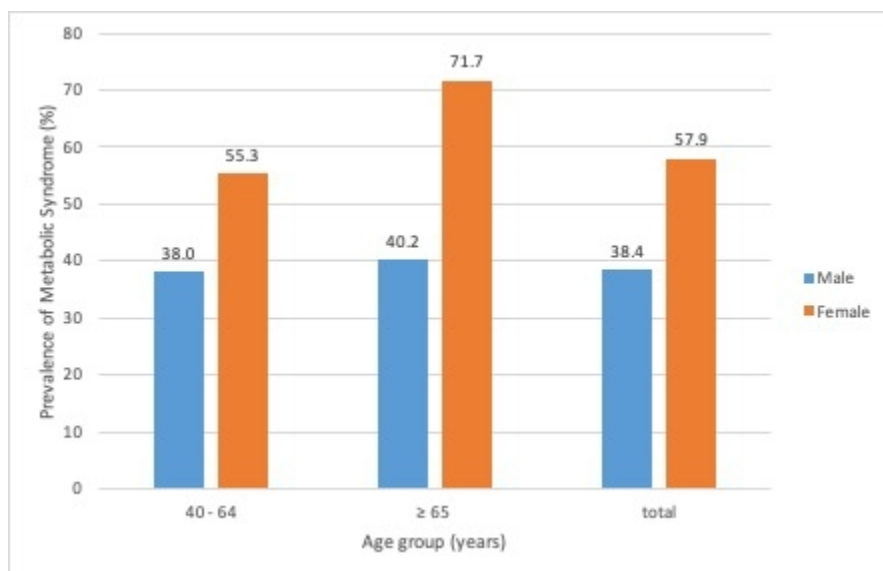


Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study

156x99mm (72 x 72 DPI)

**Supplementary Table S1** Definitions of metabolic syndrome-related risk factors in the survey.

Variables	Criteria	References
BMI	BMI was grouped into five categories for our study: underweight (BMI < 18.5 kg/m <sup>2</sup> ), normal (18.5 ≤ BMI < 24 kg/m <sup>2</sup> ), overweight (24 ≤ BMI < 26 kg/m <sup>2</sup> ), apparently overweight (26 ≤ BMI < 28 kg/m <sup>2</sup> ), obesity (BMI ≥ 28 kg/m <sup>2</sup> ).	Guidelines for diabetes prevention and treatment in China <sup>1</sup>
Abnormal neck circumference	≥37cm for male and ≥33cm for female	Neck circumference as an independent predictive contributor of cardio-metabolic syndrome <sup>2</sup>
Physical inactivity	Physical inactivity is defined as insufficient physical activity; Physical activity is defined as the performance of heavy physical labor or regular physical exercise for more than one year, more than 3 times per week, and for at least 30 minutes per session.	CHNS guidelines <sup>3</sup>
Smoking	A smoker was defined as one who reported smoking one or more cigarettes or was passively exposed to tobacco smoke every day in general for more than 6 consecutive months. A non-smoker was defined as the one who had never smoked, nor passively exposed to tobacco smoke; or, had history of smoking but quit smoking for at least 6 consecutive months previous to the study.	Technical specification of stroke screening and prevention in China <sup>4</sup>
Drinking	The NIAAA sets the standard drink size at about 14g of absolute ethanol, advising limits of no more than three drinks per day or seven drinks per week for men and women. Drinking status was divided into three categories according to the participants' self-report in the previous 6 months: non-drinkers: had never drunk alcoholic beverage; light/moderate drinkers: less than or upto NIAAA limits; heavier drinkers: in excess of NIAAA limits.	NIAAA guidelines <sup>5</sup>
Fruit consumption	Fruit consumption was grouped into three categories for our study: less than or equal to two days per week (≤ 2 d/w), three to four days per week (3–4 d/w), and greater than or equal to five days per week (≥ 5 d/w). And the weight of consumed fruits should reach or exceed two servings per day, and the definition of a serving of a fruit was calculated as 80g.	Fruit and vegetable consumption and stroke: meta-analysis of cohort studies <sup>6</sup>

**Abbreviation:** BMI, body mass index; CHNS, China Health and Nutrition Survey; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	6, 7
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	(7)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11,12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-17
		(b) Report category boundaries when continuous variables were categorized	12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18,19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
<b>Other information</b>			
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 which the present article is based	21

\*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](http://www.strobe-statement.org).



# BMJ Open

## Sex-based differences in and risk factors for metabolic syndrome in adults aged 40 years and above in Northeast China: Results from the National Stroke Screening Survey

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-038671.R2
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Complete List of Authors:	Li, Feng-e ; Jilin University First Hospital, Stroke Center, Department of Neurology; The Affiliated Hospital of Beihua University, Stroke Center, Department of Neurology Zhang, Fu-Liang; The First Hospital of Jilin University, Stroke Center, Department of Neurology Zhang, Peng; The First Hospital of Jilin University, Liu, Dong; The Affiliated Hospital of Beihua University, Stroke Center, Department of Neurology Liu, Hao-Yuan; Jilin University First Hospital, Stroke Center, Department of Neurology Guo, Zhen-Ni ; Jilin University First Hospital, Clinical Trail and Research Center for Stroke, Department of Neurology Yang, Yi; Jilin University First Hospital, Stroke Center, Department of Neurology; Jilin University First Hospital, Clinical Trail and Research Center for Stroke, Department of Neurology
<b>Primary Subject Heading</b>:	Nutrition and metabolism
Secondary Subject Heading:	Nutrition and metabolism, Epidemiology, Sports and exercise medicine, Public health, Health informatics
Keywords:	Other metabolic, e.g. iron, porphyria < DIABETES & ENDOCRINOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PREVENTIVE MEDICINE, Sex steroids & HRT < DIABETES & ENDOCRINOLOGY, Lipid disorders < DIABETES & ENDOCRINOLOGY, Hypertension < CARDIOLOGY

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11 4 **adults aged 40 years and above in Northeast China: Results from the**  
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13 5 **National Stroke Screening Survey**  
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16 6 Feng-e Li<sup>1,2</sup>, MD; Fu-Liang Zhang<sup>1</sup>, MD, PhD; Peng Zhang<sup>3</sup>, MD; Dong Liu<sup>2</sup>, MD;  
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18 7 Hao-Yuan Liu<sup>1</sup>; MD; Zhen-Ni Guo<sup>3</sup>, MD, PhD<sup>#</sup>; Yi Yang<sup>1,3</sup>, MD, PhD<sup>#</sup>.  
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51 20  
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55 21 **Authors contributions:** Conception and design: Y Y, and Z-N G. Acquisition of the  
56  
57 22 data: F-L Z and H-Y L. Statistical methods and data analysis: F-e L, P Z, D L, F-L Z.  
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9 **Search terms:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
10 factor.

11 **Word count: abstract 282 words; text 3359 words;** 52 references; 3 tables and 2  
12 figures.

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# 1 ABSTRACT

## 2 Objectives

3 Low levels of income and education are risk factors for metabolic syndrome (MS) in  
4 the population of Northeast China, which has a high incidence of MS and  
5 cardiovascular diseases. This study aimed to determine sex-based differences  
6 associated with the prevalence of and risk factors for MS among people older than 40  
7 years in Northeast China; this has not been previously investigated.

## 9 Study design

10 This study analyzed a portion of the large sample data of the national cross-sectional  
11 screening of China from 2016. MS was defined as the presence of any three of the  
12 following five risk factors: abnormal waist circumference; high levels of triglycerides,  
13 high-density lipoprotein cholesterol, or fasting plasma glucose; and elevated blood  
14 pressure. Multiple regression analysis was used to investigate sex-based differences in  
15 the prevalence of and risk factors for MS.

16 **Setting** The study was conducted in Dehui City, Jilin Province, China.

17 **Participants** A total of 4052 participants with complete questionnaire information and  
18 laboratory examination results were included.

19 **Results** The prevalence of MS was 50.1% overall (38.4% in males and 57.9% in  
20 females;  $p < 0.001$ ). High body mass index (BMI) and hip circumference were  
21 associated with MS in both sexes. In addition, physical inactivity (odds ratio [OR] and  
22 95% confidence interval [CI]: 1.441 [1.055, 1.969];  $p = 0.022$ ) in males and advanced  
23 age (OR and 95% CI: 1.536 [1.154, 2.043];  $p = 0.003$ ) in females were factors  
24 associated with MS. Women with junior high school education or above and living in

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4 1 rural areas were less likely to have MS, unlike men.  
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6 2 **Conclusions** The risk factors for MS have both similarities and differences in different  
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9 3 sexes; thus, the prevention and treatment of MS should be based on these sex  
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12 4 differences.  
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16 6 **Key words:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
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3 **1 Strengths and limitations of this study**  
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5 2 1. This cross-sectional study included a large, representative sample of Chinese  
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8 3 population.

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10 4 2. We used a uniform, pre-coded questionnaire designed by the Stroke Screening and  
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12 5 Prevention Program of the National Health and Family Planning Commission of China  
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14 6 (CNSSS).

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17 7 3. Some results were partially based on self-reported data collected by investigators,  
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19 8 which inevitably increased the risk of recall bias.

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21 9 4. Our survey excluded participants who were sick or too weak to complete the  
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23 10 interview.

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26 11 5. As a major limitation of all epidemiological investigations, conclusions based on  
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28 12 cross-sectional studies cannot be used for causal inferences.  
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## 1 INTRODUCTION

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3 Metabolic syndrome (MS) is associated with a cluster of cardiometabolic risk factors  
4 and has become one of the major public health threats in China. The higher prevalence  
5 of MS greatly increases the burden of morbidity and mortality of cardiovascular  
6 diseases worldwide.<sup>1-3</sup> This burden has increased every year, although it is difficult to  
7 differentiate it from unhealthy habits of daily living.<sup>4</sup> There is a significant difference  
8 in the prevalence of and risk factors for MS between men and women.<sup>5</sup> To control and  
9 reduce the risk of MS and cardiovascular diseases more effectively, it is necessary to  
10 identify high-risk populations and understand the sex-specific, modifiable lifestyle  
11 determinants of MS. Northeast China, with its low income level, has a high incidence  
12 of MS and cardiovascular diseases, especially the highest incidence and mortality of  
13 stroke (365 and 159/100 000 person-years) in China.<sup>6</sup> Thus, this study aimed to analyze  
14 the sex-specific differences in the prevalence of MS and its related risk factors in a  
15 population from Northeast China.

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## 17 POPULATION and METHODS

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### 19 Data source and study participants

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21 This population-based cross-sectional study was a part of the Stroke Screening and  
22 Prevention Program of the National Health and Family Planning Commission of China  
23 (CNSSS), which assessed a population of residents aged 40 years or older, from January



1 to March 2016. The CNSSS is a national epidemiological survey of cerebrovascular  
2 diseases conducted to obtain timely and reliable information on the morbidity,  
3 prevalence, and mortality of stroke in Chinese people over the age of 40.<sup>7</sup> The sampling  
4 method employed in this study has been described in detail in other articles.<sup>8</sup> The  
5 sample size (N) required for this survey was calculated on a 2.37% stroke prevalence  
6 (p) among adults 40 years and older in China,<sup>8</sup> using the formula:

$$7 \quad N = (Z_{\alpha}^2 pq) / d^2 \text{ (where } Z_{\alpha} = 1.96, \alpha = 0.05, q = 1-p, \text{ and } d = 0.2p)$$

8     A multistage stratified, random cluster sampling method was applied to obtain the  
9 sample population. In the first stage, 30 villages and 10 towns were randomly selected  
10 from a total of 308 villages (rural) and 14 towns (urban) in Dehui City using the  
11 probability proportional to size (PPS) sampling method. In the second stage, five groups  
12 of villages or communities were randomly sampled from both the rural and urban strata  
13 using the PPS sampling. In the third stage, one participant aged  $\geq 40$  years was  
14 randomly selected from each household of the selected groups of villages or  
15 communities. Respondents who were unwilling to participate in the survey or who were  
16 judged to be very frail were excluded. We selected permanent residents aged  $\geq 40$  years  
17 for inclusion in the study (a calculated total of 4445 participants with an additional 10%  
18 loss rate); ultimately, 4100 participants completed the face-to-face survey, with a good  
19 response rate of 92.2%. In this sub-study of the CNSSS, we used data from participants  
20 who completed the study. After excluding 48 participants with incomplete  
21 questionnaire information or laboratory examinations, a total of 4052 participants were  
22 included in this analysis. The flowchart of the study selection process is shown in Figure  
23 1. The study protocol was approved by the Human Ethics and Research Ethics  
24 Committee of the First Hospital of Jilin University, Chang Chun, Jilin, China. Written  
25 informed consent was obtained from all study participants before recruitment and data

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9 **3 Patient and public involvement**  
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13 5 Patients and the public were not involved in the development of the research  
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16 6 questionnaire, its outcome measures, study design, recruitment methods or the conduct  
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19 7 of this study. There is no plan to disseminate the research findings to the participants.  
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23 **9 Data collection and measurement**  
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28 11 All participants completed a questionnaire that included an assessment of general  
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30 12 sociodemographic and health-related information. Physical examinations included  
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32 13 assessments of height, weight, neck circumference, waist circumference, hip  
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34 14 circumference, and blood pressure. Height and weight were measured according to the  
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36 15 standard methods; the subjects removed their shoes and hats and wore light clothes.  
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38 16 The measurement accuracy was within 0.1 cm and 0.1 kg for the height and weight,  
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40 17 respectively. Blood pressure was measured by physicians using an OMRON automatic  
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42 18 sphygmomanometer (OMRON HEM-7200, KYOTO, Japan), on the right arm, after  
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44 19 placing it parallel to the heart. The subjects were made to rest for 20 minutes before the  
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46 20 blood pressure was measured twice, and mean value was recorded. Blood samples were  
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48 21 collected on an empty stomach following overnight fasting (at least 8 hours) to assess  
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50 22 fasting plasma glucose (FPG), triglyceride (TG), total cholesterol (TC), low-density  
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52 23 lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)  
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54 24 concentrations. The samples were sent to the clinical laboratory of Changchun  
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56 25 Kingmed Center (Chang Chun, Jilin, China) for testing.  
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## 2 **Screening protocol and assessment criteria**

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4 The definition of MS used in this study was published by the International Diabetes  
5 Federation and the American Heart Association/National Heart, Lung, and Blood  
6 Institute (AHA/NHLBI).<sup>9</sup> The presence of any three of the following five risk factors  
7 constituted a diagnosis of MS: 1) Waist circumference:  $\geq 90$  cm for men, and  $\geq 80$  cm  
8 for women; 2) TG concentration:  $\geq 1.70$  mmol/L (drug treatment for elevated TG levels  
9 is an alternative indicator); 3) HDL-C concentration:  $< 1.0$  mmol/L for men, and  $< 1.3$   
10 mmol/L for women (drug treatment for reduced HDL-C levels is an alternative  
11 indicator); 4) blood pressure: systolic blood pressure (SBP)  $\geq 130$  mmHg and/or  
12 diastolic blood pressure (DBP)  $\geq 85$  mmHg (antihypertensive drug treatment in a  
13 patient with a history of hypertension is an alternative indicator); and 5) FPG  
14 concentration:  $\geq 5.6$  mmol/L (drug treatment for elevated glucose levels is an  
15 alternative indicator).

16 In addition to stratifying by sex, participants were stratified by age into a middle-  
17 aged group (40–64 years old) and an elderly group ( $\geq 65$  years old). The evaluation  
18 criteria for the other factors, including BMI, level of physical inactivity, smoking status,  
19 and alcohol consumption are shown in Supplementary Table S1.

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## 21 **Statistical analysis**

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23 The normality of the data was tested using the Kolmogorov–Smirnov test. Non-  
24 normally distributed continuous variables are presented as medians (IQRs). The Mann-  
25 Whitney U test was used to assess differences between two groups of data with non-

1 normal distributions. Categorical data are presented as numbers and proportions. The  
2 differences between groups were assessed using the  $\chi^2$ -test. Significant variables (those  
3 with  $P < 0.05$ ) identified in the univariate analysis were selected for the multivariate  
4 analyses. Multiple logistic regression analysis was used to explore the independent risk  
5 factors of MS in the two sexes, and the odds ratios (ORs) and 95% confidence intervals  
6 (CIs) were calculated. All statistical analyses were performed using IBM Statistical  
7 Package for the Social Sciences (SPSS) version 23.0 (SPSS, Inc., New York, NY, USA).  
8  $P < 0.05$  was considered statistically significant.

## 10 RESULTS

12 Among the 4,100 participants who completed the face-to-face survey, 4,052 were  
13 included in the analysis. A total of 2,030 individuals met the criteria for MS, and the  
14 prevalence was 50.1% overall (38.4% in males and 57.9% in females;  $p < 0.001$ ). Of  
15 all the 4,052 participants, 1,619 were men (40.0%) and 2,433 were women (60.0%),  
16 with a median age of 53 years (IQR: 47–62). Overall, 76.7% of the participants had a  
17 level of education not higher than that of junior middle school.

### 19 1. Demographic characteristics of all participants with MS

21 Table 1 shows that compared with that in males (38.4%), the prevalence of MS in  
22 females (57.9%) was significantly higher. Among the 2,030 individuals with MS, the  
23 median age was 56 years (IQR: 49–63) and more than 80% of participants with MS,

1 both males and females, were in the group of 40–64 years. The rate of abnormal waist  
 2 circumference in females (91.6%) was higher than that in males (85.4%). The median  
 3 neck circumference and hip circumference in males were higher than those in females.  
 4 Compared with males, females were more likely to have the following associated risk  
 5 factors: a lower level of educational attainment, living in a rural area, a normal BMI,  
 6 an abnormal HDL-C concentration, and higher concentrations of TC and LDL-C. Men  
 7 were also more likely to have hypertension, abnormal levels of triglycerides and  
 8 fasting blood glucose, live in urban areas, and smoke and drink alcohol.

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 10 Table 1. Sex differences in demographic characteristics and risk factors among  
 11 participants with metabolic syndrome (MS).

	Total	Male	Female
<b>Participants, n (%)</b>	4052(100)	1619 (40.0)	2433 (60.0)
<b>Cases, n (%)</b>	2030 (50.1)	622 (38.4)	1408 (57.9)
<b>Age, years, median (IQR)</b>	56.00(49, 63)	55.72(48, 63)	56.19(49, 63)
<b>Age group, n (%)</b>			
40-64 years	1636(80.6)	501(80.5)	1135(80.6)
≥65 years	394(19.4)	121(19.5)	273(19.4)
<b>Waist circumference, n (%)</b>	1821(89.7)	531(85.4)	1290(91.6)
<b>Neck circumference, median (IQR)</b>	34.00(32, 37)	38.23(36, 40)	33.27(32, 35)
<b>Hip circumference, n (%)</b>	100.00(95, 104)	103.63(100, 107)	97.76(93, 102)
<b>TCHO, mmol/L, median (IQR)</b>	5.52(4.83, 6.25)	5.50(4.73, 6.12)	5.63(4.87, 6.29)
<b>LDLC, mmol/L, median (IQR)</b>	1.93(1.56, 2.64)	2.08(1.5, 2.57)	2.19(1.57, 2.65)
<b>HDLC, n (%)</b>	1255(61.8)	176(28.3)	1079(76.6)
<b>TG, n (%)</b>	1503(74.0)	508(81.7)	995(70.7)
<b>FBG, n (%)</b>	881(43.4)	291(46.8)	590(41.9)
<b>Hypertension, n (%)</b>	1853(91.3)	601(96.6)	1252(88.9)
<b>Education, n (%)</b>			
≤Primary school	806(39.7)	176(28.3)	630(44.7)
Junior middle school	829(40.8)	280(45)	549(39)
Senior middle school	253(12.5)	104(16.7)	149(10.6)
College and above	142(7.0)	62(10.0)	80(5.7)
<b>Region, n (%)</b>			
Urban	1023(50.4)	357(57.4)	666(47.3)
Rural	1007(49.6)	265(42.6)	742(52.7)
<b>Smoke, n (%)</b>			

No	1021(50.3)	223(35.9)	798(56.7)
Yes	1009(49.7)	399(64.1)	610(43.3)
<b>Physical inactivity, n (%)</b>			
No	1522(75.0)	469(75.4)	1053(74.8)
Yes	508(25.0)	153(24.6)	355(25.2)
<b>Alcohol consumption, n (%)</b>			
Never	1591(78.4)	251(40.4)	1340(95.2)
Light/moderate	245(12.1)	182(29.3)	63(4.5)
Heavier	194(9.6)	189(30.4)	5(0.4)
<b>Fruit consumption, n (%)</b>			
≥5days per week	1782(87.8)	546(87.8)	1236(87.8)
3-4 days per week	189(9.3)	61(9.8)	128(9.1)
≤2 days per week	59(2.9)	15(2.4)	44(3.1)
<b>BMI, n (%)</b>			
Normal	553(27.2)	88(14.1)	465(33.0)
Underweight	11(0.5)	3(0.5)	8(0.6)
Overweight	521(25.7)	144(23.2)	377(26.8)
Apparently overweight	464(22.9)	183(29.4)	281(20.0)
Obesity	481(23.7)	204(32.8)	277(19.7)

1 *Abbreviations: TCHO, total serum cholesterol; LDLC, Low Density Lipoprotein*  
 2 *Cholesterol; HDLC, high-density lipoprotein; TG, triglyceride; FBG, fasting blood*  
 3 *glucose; BMI, body mass index.*

4 *Values are expressed as n (percentage).*

## 6 2. Univariate analysis of factors associated with MS by sex

8 Table 2 shows the results of univariable logistic regression for factors associated with  
 9 MS in men and women. The prevalence of MS was higher in the elderly (men: 40.2%;  
 10 women: 71.7%), especially in older women (Figure 2; OR [95% CI] = 2.042 [1.608,  
 11 2.594];  $P < 0.001$ ). For females, age, BMI, hip and neck circumference, smoking,  
 12 higher alcohol consumption, geographical region, and level of educational attainment  
 13 were associated with MS, whereas physical inactivity and fruit consumption were not.  
 14 For males, the risk factors associated with MS were similar, except for age, smoking,  
 15 and higher alcohol consumption. Unlike in women, physical inactivity and  
 16 light/moderate alcohol consumption were also risk factors in men.

1 Table 2 Univariate logistic regression analyses on risk factors for the prevalence of  
2 metabolic syndrome (MS) in males and females

Category	Reference	Male		Female	
		OR (95% CI)	P	OR (95% CI)	P
<b>Age group</b>	<b>40-64 years</b>				
≥65years		1.096(0.849, 1.416)	0.482	2.042(1.608, 2.594)	<0.001
<b>HP</b>	-	1.199(1.175, 1.224)	<0.001	1.157(1.141, 1.173)	<0.001
<b>NC</b>	-	1.442(1.378, 1.509)	<0.001	1.365(1.31, 1.422)	<0.001
<b>Region</b>	<b>Urban</b>				
Rural		0.565(0.462, 0.692)	<0.001	1.658(1.408, 1.951)	<0.001
<b>Smoke</b>	<b>No</b>				
Yes		0.926(0.751, 1.142)	0.472	1.406(1.191, 1.660)	<0.001
<b>Physical inactivity</b>	<b>Physical activity</b>				
Yes		1.745(1.360, 2.240)	<0.001	1.121(0.928, 1.354)	0.235
<b>Alcohol consumption</b>	<b>Never</b>				
Light/moderate drinking		1.435(1.121, 1.836)	0.004	0.504(0.159, 1.592)	0.243
Higher drinking		0.992(0.782, 1.260)	0.949	0.609(0.430, 0.861)	0.005
<b>Fruit consumption</b>	<b>≥5days/week</b>				
3-4 days per week		1.089(0.773, 1.533)	0.627	1.192(0.890, 1.597)	0.238
≤2 days per week		0.803(0.428, 1.506)	0.494	1.366(0.825, 2.263)	0.226
<b>Education</b>	<b>≤Primary school</b>				
Junior middle school		1.280(1.012, 1.620)	0.040	0.585(0.485, 0.706)	<0.001
Senior middle school		1.753(1.273, 2.413)	0.001	0.413(0.318, 0.537)	<0.001
College and above		1.312(0.908, 1.896)	0.149	0.269(0.197, 0.366)	<0.001
<b>BMI</b>	<b>Normal</b>				
Underweight		1.490(0.416, 5.332)	0.540	0.304(0.141, 0.655)	0.002
Overweight		3.905(2.878, 5.300)	<0.001	3.538(2.845, 4.401)	<0.001
Apparently overweight		11.143(8.026, 15.470)	<0.001	5.275(4.013, 6.934)	<0.001
Obesity		18.288(12.885, 25.955)	<0.001	12.033(8.307, 17.431)	<0.001

3 Abbreviations: BMI, body mass index; HC, Hip circumference; NC, Neck  
4 circumference.

5 Values are expressed as median (IQR) or n (percentage).

### 6 7 8 **3. Relationship between risk factors and MS in the multivariate logistic regression** 9 **analysis**

10 Multivariate analysis reveals that BMI and hip circumference were significantly  
11 associated with MS in both men and women (Table 3). Age, region, and educational  
12 attainment were associated with MS in females, while physical inactivity was

1 associated with MS in males. Neck circumference, an underweight BMI, smoking, and  
2 alcohol consumption were not associated with MS in either sex.

3 For males, BMI, hip circumference, and physical inactivity were associated with MS.  
4 The ORs (95% CIs) were 2.067 (1.475, 2.896;  $p < 0.001$ ) for overweight BMI, 3.771  
5 (2.539, 6.601;  $p < 0.001$ ) for apparently overweight BMI, and 3.253 (2.019, 5.241;  $p <$   
6  $0.001$ ) for obese BMI. For hip circumference, the OR (95% CI) was 1.115 (1.086, 1.146;  
7  $p < 0.001$ ). Physical inactivity was associated with MS in males (OR 1.441, 95% CI  
8 [1.055, 1.969],  $p = 0.022$ ).

9 For females, BMI, hip circumference, and advanced age were associated with MS.  
10 Rural residence and junior middle school education or above were negatively associated  
11 with MS. The higher the education attainment, the lower the risk of MS. The ORs (95%  
12 CIs) were 2.091 (1.633, 2.677;  $p < 0.001$ ) for overweight BMI, 2.014 (1.455, 2.786;  $p$   
13  $< 0.001$ ) for apparently overweight BMI, and 2.546 (1.623, 3.995;  $p < 0.001$ ) for obese  
14 BMI groups. For hip circumference, the OR (95% CI) was 1.098 (1.077, 1.119;  $p <$   
15  $0.001$ ). The OR (95% CI) for advanced age ( $\geq 65$  years) was 1.536 (1.154, 2.043);  $p =$   
16  $0.003$ ). The OR (95% CI) for living in a rural region was 0.737 (0.561, 0.967;  $p = 0.028$ ).  
17 For an educational level of junior middle school, the OR (95% CI) was 0.616 (0.479,  
18 0.791;  $p < 0.001$ ); for senior middle school, it was 0.580 (0.404, 0.833;  $p = 0.003$ ), and  
19 for college and above, it was 0.434 (0.286, 0.660;  $p < 0.001$ ).

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21 Table 3 Multivariate logistic regression analyses on risk factors for the prevalence of  
22 metabolic syndrome (MS) in males and females.

Category	Reference	Male		Female	
		OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
<b>Age group</b>	<b>40-64 years</b>				
≥65years		-	-	1.536(1.154,2.043)	0.003
<b>Education</b>	<b>≤Primary school</b>				
Junior middle school		0.918(0.662, 1.272)	0.606	0.616(0.479, 0.791)	<0.001



Senior middle school		1.014(0.639, 1.609)	0.953	0.580(0.404, 0.833)	0.003
College and above		0.727(0.431, 1.225)	0.231	0.434(0.286, 0.660)	<0.001
<b>Region</b>	<b>Urban</b>				
Rural		0.815(0.586, 1.133)	0.223	0.737(0.561, 0.967)	0.028
<b>BMI</b>	<b>Normal</b>				
Underweight		2.464(0.578, 10.502)	0.223	0.569(0.248, 1.304)	0.183
Overweight		2.067(1.475, 2.896)	<0.001	2.091(1.633, 2.677)	<0.001
Apparently overweight		3.771(2.539, 5.601)	<0.001	2.014(1.455, 2.786)	<0.001
Obesity		3.253(2.019, 5.241)	<0.001	2.546(1.623, 3.995)	<0.001
<b>Neck circumference</b>	<b>-</b>	1.193(0.951, 1.498)	0.128	1.193(0.951, 1.498)	0.128
<b>Smoke</b>	<b>No</b>				
Yes		-	-	1.193(0.951, 1.498)	0.128
<b>Physical inactivity</b>	<b>Physical activity</b>				
Yes		1.441(1.055, 1.969)	0.022	-	-
<b>Alcohol consumption</b>	<b>Never</b>				
Light/moderate drinking		0.883(0.662, 1.179)	0.4	0.720(0.479, 1.080)	0.112
Higher drinking		1.320(0.978, 1.783)	0.07	0.431(0.114, 1.628)	0.215
<b>Hip circumference</b>		1.115(1.086, 1.146)	<0.001	1.098(1.077, 1.119)	<0.001

Abbreviations: BMI, body mass index; OR, odds ratio.

## DISCUSSION

In this study, we evaluated sex-based differences in the prevalence of MS and its relative determinants in a low income population from Northeast China. We found that in addition to being significantly more prevalent in females than in males, a high BMI and large hip circumference were risk factors for MS in both sexes. In addition, advanced age ( $\geq 65$  years) was a risk factor only for females, whereas physical inactivity was a risk factor only for males. Furthermore, educational attainment and living in a rural region were negatively associated with MS in women, but not in men.

The prevalence of MS has been steadily increasing due to unhealthy lifestyles in low- and high-income regions,<sup>10 11</sup> and there are known sex differences. The prevalence of MS in those living in the Chinese mainland for both the low–middle- and high-income populations was shown to be 33.9% in 2010;<sup>1</sup> however, in our study, it was 50.1%. This may be due to the fact that most of the participants in our study population had a lower educational level and income, which may have had an additive effect on the primary,

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3 1 increasing trend. In most studies, the prevalence of MS in females was higher than that  
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5 2 in males;<sup>1 12</sup> for example, in Mexico, the prevalence in females was 55.6%, whereas in  
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7 3 males, it was 38.2%.<sup>13</sup> Similar sex disparities were observed in Middle Eastern  
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9 4 countries, but few sex differences have been reported in the European Union which has  
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11 5 a lower MS prevalence overall.<sup>14</sup> Contrarily, the prevalence of MS in males is higher  
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13 6 than that in females in Caucasians,<sup>15</sup> American adolescents,<sup>16</sup> and Far East Asian and  
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15 7 Japanese populations, and twice that in women from Macau.<sup>17</sup> These differences may  
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17 8 be related to race, the period in which the studies were conducted, the geographic region,  
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19 9 and the selected criteria used.<sup>18 19 20</sup> Our results were consistent with those reported in  
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21 10 most countries that women had a higher prevalence of MS than men<sup>21 22 23 24</sup>. In addition,  
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23 11 these sex-related differences were shown to be greater in women of advanced age, but  
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25 12 remained relatively stable with respect to age in men in East China.<sup>25</sup> This was  
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27 13 consistent with our own findings that females aged  $\geq 65$  years had a 1.536-fold higher  
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29 14 risk of MS than those aged 40–65 years. As estrogen levels decrease in women after  
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31 15 menopause, an increase in insulin resistance and abnormal lipid metabolism result.  
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33 16 Thus, the sex differences observed may be related to changes in hormone levels, rather  
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35 17 than aging itself.<sup>26</sup>

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44 18 It is well known that MS prevalence increases when BMI ( $\geq 24$  kg/m<sup>2</sup>) is higher than  
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46 19 normal. Compared with that with a normal BMI, the risk of metabolic syndrome with  
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48 20 an overweight and obese BMI was 3.11- and 17.18-fold in Korean females and 4.30-  
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50 21 and 10.91-fold in Korean males without diabetes mellitus, respectively.<sup>27</sup> Our study  
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52 22 also found that compared with a normal BMI, a higher BMI was associated with higher  
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54 23 odds of MS. The risk was 2.091-, 2.014-, and 2.546-fold higher in overweight,  
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56 24 significantly overweight, and obese females, respectively; in males, the risk increased

1 2.067-, 3.771-, and 3.253-fold, respectively. These findings also suggest that weight  
2 gain in males ( $\text{BMI} \geq 26 \text{ kg/m}^2$ ) increases the risk of MS more substantially than it does  
3 in females; this positive association has also been reported in a study of Turkish  
4 adults.<sup>28</sup> An Israeli cohort study claimed that a normal BMI had a high negative  
5 predictive value in both men (98%) and women (96%) with respect to MS.<sup>29</sup> The  
6 inverse association was found between hip circumference and metabolic risk factors in  
7 Tehranian women.<sup>30</sup> Further, weak predictive ability was found for hip circumference.  
8 In our study, the risk of MS increased 1.098-fold in women and 1.115-fold in men for  
9 every 1 cm increase in hip circumference but not in neck circumference. Thus, BMI  
10 combined with hip circumference is an effective indicator of being overweight or obese,  
11 and such individuals are more prone to developing MS. Whether obesity or insulin  
12 resistance is a cause or consequence of MS is still under debate.<sup>31</sup> Adipokines produced  
13 by abnormal adipocytes cause insulin resistance, and visceral obesity may be a causal  
14 factor of metabolic disease.<sup>32</sup>

15 Physical inactivity was a main risk factor for males in our study, consistent with the  
16 findings of a previous study.<sup>33</sup> Infrequent physical activity results in a 1.441-fold  
17 increased risk of MS in men, but not in women, in agreement with previous findings,<sup>34</sup>  
18 and physical activity has been suggested to be associated with a low risk for MS.<sup>35</sup>  
19 Studies have also found that binge drinking and smoking were associated with  
20 increased MS prevalence, regardless of sex or BMI.<sup>36, 37</sup> The association between fruit  
21 consumption, neck circumference, and MS risk remains unclear; in our study, no  
22 significant associations were observed among alcohol consumption, smoking, fruit

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4 1 consumption, or neck circumference.  
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6 2 Educational level is the most important measure of socioeconomic status, which has  
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9 3 been shown to not only affect the prevalence of MS, but is also closely related to the  
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11 4 prevalence of cerebrovascular disease.<sup>38</sup> The specific mechanism by which education  
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14 5 affects the prevalence of MS is unclear, although it has been considered that education  
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17 6 influences people's lifestyles and positive attitudes toward health, and increases their  
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20 7 access to preventive health services.<sup>39</sup> In addition, it is reported in South Korea that  
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22 8 negative correlation between educational level and MS prevalence is largely related to  
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25 9 the dietary patterns of Koreans (especially in women).<sup>40</sup> For females in our study, the  
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28 10 ORs indicated a 0.616-fold, 0.580-fold, and 0.434-fold risk of developing MS in those  
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31 11 who had completed junior middle-school, senior middle-school, and college and above,  
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34 12 respectively. This suggests that a higher educational level can reduce the risk of MS;  
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37 13 however, this relationship was not found in males. The negative association between  
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40 14 MS prevalence and educational level was significant in females, which is similar to the  
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43 15 results of a previous study.<sup>40</sup> A National Survey found that low income and educational  
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46 16 levels were associated with a higher prevalence of MS in females than in males.<sup>41</sup> Our  
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49 17 study population is characterized by having both a low income and a low level of  
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52 18 education, both of which contribute to a higher MS prevalence. The high percentage of  
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55 19 included females with a primary school education or below was 37.8%, which may  
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58 20 partially explain the high prevalence of MS in women.<sup>24</sup> Urban adults ( $\geq 18$  years old)  
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60 21 in China were more likely to have MS than those in rural areas in 2009,<sup>42</sup> but the  
22 22 opposite was true among urban adults in Jiangxi province, China in 2015, and rural

1 females were more likely to have MS than urban ones, unlike males.<sup>43</sup> In our study, MS  
2 was negatively associated with living in rural regions (OR: 0.737 [0.561, 0.967],  $p =$   
3 0.028) but not with living in urban regions. The differences may be caused by the degree  
4 of economic development, life habits, and dietary patterns; for example, rural women  
5 have lower fat intake and more activity than urban women.<sup>44</sup>

6 Lifestyle interventions resulted in a 2.61-fold reduced risk of MS compared with the  
7 control group in a previous study,<sup>45</sup> and an investigation of dietary patterns showed that  
8 the Chinese pattern (high in grains, vegetables, fruit, salted fish and eggs, soyabean,  
9 and etc.) was associated with a lower risk of MS than the animal food pattern (high in  
10 meats, fish and shrimp, eggs, seafood, alcoholic beverages, etc.).<sup>46</sup> Sex differences  
11 in the ways dietary patterns were associated with increased MS prevalence have been  
12 reported; for example, an increased prevalence was observed in men consuming an  
13 "animal and fried food" diet, and women consuming a "high-salt and energy" diet.<sup>19</sup>  
14 Muscle strength and cardiorespiratory fitness may independently and jointly reduce the  
15 incidence of MS,<sup>47</sup> as increased physical activity decreased the risk by 19–24%,<sup>48</sup> in  
16 men, every hour of exercise may decrease MS risk by 2%.<sup>49</sup> Whereas the daily  
17 sedentary behavior linearly increases the risk of metabolic syndrome by 1.09 times per  
18 hour.<sup>50</sup> To prevent the onset of MS, a better understanding of modifiable lifestyle  
19 factors is needed in high-risk populations; for example, in men who are physically  
20 inactive, further effort should be made to control body weight, especially by focusing  
21 on reducing high BMI and hip circumference. Moreover, exercise can result in high  
22 brain insulin sensitivity, which can help to lose more body weight and body fat with a

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4 1 lower regain.<sup>51</sup> For women, especially the elderly outside rural regions, efforts should  
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6 2 be made to control weight to maintain BMI and hip circumference at normal levels to  
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9 3 reduce the risk of MS, and a focus should be directed at changes in hormone levels,  
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11 4 especially low concentrations of sex hormone-binding globulin and testosterone,  
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14 5 which increase the odds of MS.<sup>52</sup> In the long run, a higher level of educational  
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17 6 attainment can reduce the risk of MS. Understanding these factors and the sex  
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20 7 differences between them, as well as accurately identifying high-risk groups, could help  
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22 8 to develop better public health policies and educational initiatives and reduce the  
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25 9 incidence of MS and vascular diseases.  
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### 31 **Strengths and limitations**

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33 12 There were also several limitations to this study. Some data was self-reported, each  
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35 13 parameter in blood was only sampled and measured once, and some lifestyle factors  
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38 14 and potential residual confounders were not assessed. Furthermore, people who were  
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41 15 sick or too weak to participate were excluded, which may impact the generalizability  
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44 16 of the results. Moreover, cross-sectional studies cannot be used to make causal  
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47 17 inferences, and subsequent prospective and randomized studies are needed.  
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### 50 **CONCLUSION**

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53 20 In our study, we found that risk factors for MS have both sex-based similarities and  
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56 21 differences; thus, the prevention and treatment of MS should consider patients' sex.  
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## 14 **CONFLICTS OF INTEREST**

15 None declared.

## 17 **ETHICS APPROVAL**

18 This subject was approved by the human ethics and research ethics committee of the  
19 First Hospital of Jilin University (approval No: 2015-R-250), and written informed  
20 consent was obtained from all of the participants.

## 21 **PROVENANCE AND PEER REVIEW**

22 Not commissioned; externally peer reviewed.

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**DATA SHARING STATEMENT**

The dataset supporting the conclusions of this article can be made available upon request.

For peer review only



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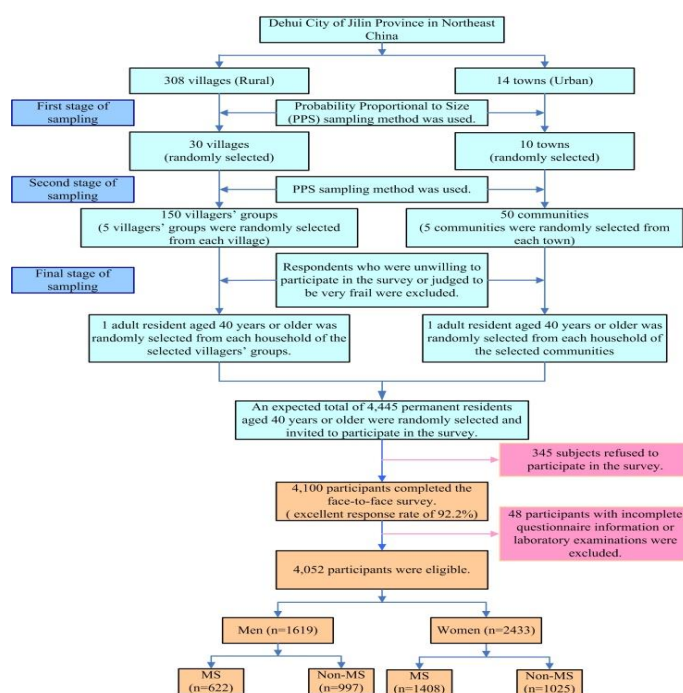
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Fig. 1 Sampling process in the study

Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study



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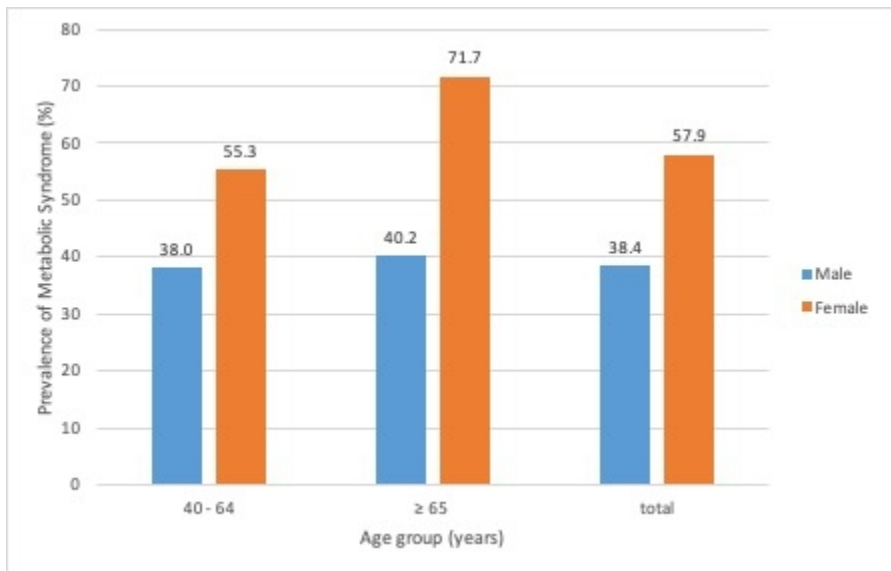


Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study  
156x99mm (72 x 72 DPI)



Sex differences and risk factors of Metabolic syndrome in adults aged more than 40 in Northeast China: Results from the National Stroke Screening Survey  
Feng-e Li *et al*

**Supplementary Table S1** Definitions of metabolic syndrome-related risk factors in the survey.

Variables	Criteria	References
BMI	BMI was grouped into five categories for our study: underweight (BMI < 18.5 kg/m <sup>2</sup> ), normal (18.5 ≤ BMI < 24 kg/m <sup>2</sup> ), overweight (24 ≤ BMI < 26 kg/m <sup>2</sup> ), apparently overweight (26 ≤ BMI < 28 kg/m <sup>2</sup> ), obesity (BMI ≥ 28 kg/m <sup>2</sup> ).	Guidelines for diabetes prevention and treatment in China <sup>1</sup>
Abnormal neck circumference	≥37cm for male and ≥33cm for female	Neck circumference as an independent predictive contributor of cardio-metabolic syndrome <sup>2</sup>
Physical inactivity	Physical inactivity is defined as insufficient physical activity; Physical activity is defined as the performance of heavy physical labor or regular physical exercise for more than one year, more than 3 times per week, and for at least 30 minutes per session.	CHNS guidelines <sup>3</sup>
Smoking	A smoker was defined as one who reported smoking one or more cigarettes or was passively exposed to tobacco smoke every day in general for more than 6 consecutive months. A non-smoker was defined as the one who had never smoked, nor passively exposed to tobacco smoke; or, had history of smoking but quit smoking for at least 6 consecutive months previous to the study.	Technical specification of stroke screening and prevention in China <sup>4</sup>
Drinking	The NIAAA sets the standard drink size at about 14g of absolute ethanol, advising limits of no more than three drinks per day or seven drinks per week for men and women. Drinking status was divided into three categories according to the participants' self-report in the previous 6 months: non-drinkers: had never drunk alcoholic beverage; light/moderate drinkers: less than or upto NIAAA limits; heavier drinkers: in excess of NIAAA limits.	NIAAA guidelines <sup>5</sup>
Fruit consumption	Fruit consumption was grouped into three categories for our study: less than or equal to two days per week (≤ 2 d/w), three to four days per week (3–4 d/w), and greater than or equal to five days per week (≥ 5 d/w). And the weight of consumed fruits should reach or exceed two servings per day, and the definition of a serving of a fruit was calculated as 80g.	Fruit and vegetable consumption and stroke: meta-analysis of cohort studies <sup>6</sup>

**Abbreviation:** BMI, body mass index; CHNS, China Health and Nutrition Survey; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	6, 7
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	(7)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11,12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-17
		(b) Report category boundaries when continuous variables were categorized	12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18,19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
<b>Other information</b>			
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 which the present article is based	21

\*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](http://www.strobe-statement.org).

# BMJ Open

## Sex-based differences in and risk factors for metabolic syndrome in adults aged 40 years and above in Northeast China: Results from the cross-sectional China national stroke screening survey

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Keywords:	Other metabolic, e.g. iron, porphyria < DIABETES & ENDOCRINOLOGY, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PREVENTIVE MEDICINE, Sex steroids & HRT < DIABETES & ENDOCRINOLOGY, Lipid disorders < DIABETES & ENDOCRINOLOGY, Hypertension < CARDIOLOGY

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4 1 Original Article  
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6 2 **TITLE PAGE**  
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9 3 **Sex-based differences in and risk factors for metabolic syndrome in**  
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11 4 **adults aged 40 years and above in Northeast China: Results from the**  
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13 5 **cross-sectional China national stroke screening survey**  
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17 6 Feng-e Li<sup>1,2</sup>, MD; Fu-Liang Zhang<sup>1</sup>, MD, PhD; Peng Zhang<sup>3</sup>, MD; Dong Liu<sup>2</sup>, MD;  
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56 21 **Authors contributions:** Conception and design: Y Y, and Z-N G. Acquisition of the  
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58 22 data: F-L Z and H-Y L. Statistical methods and data analysis: F-e L, P Z, D L, F-L Z.  
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25 9 **Search terms:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
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29 11 **Word count: abstract 300 words; text 3339 words;** 52 references; 3 tables and 2  
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## 1 ABSTRACT

2 **Objectives** Low levels of income and education are risk factors for metabolic syndrome  
3 in the population of Northeast China, which has a high incidence of metabolic  
4 syndrome and cardiovascular diseases. This study aimed to determine sex-based  
5 differences associated with the prevalence of and risk factors for metabolic syndrome  
6 among people older than 40 years in Northeast China; this has not been previously  
7 investigated.

8 **Design** This study analyzed a portion of the large sample data of the national cross-  
9 sectional screening of China from 2016. Metabolic syndrome was defined as the  
10 presence of any three of the following five risk factors: abnormal waist circumference;  
11 high levels of triglycerides, high-density lipoprotein cholesterol, or fasting plasma  
12 glucose; and elevated blood pressure. Multiple regression analysis was used to  
13 investigate sex-based differences in the prevalence of, and risk factors for metabolic  
14 syndrome.

15 **Setting** The study was conducted in Dehui City, Jilin Province, China.

16 **Participants** A total of 4052 participants with complete questionnaire information and  
17 laboratory examination results were included.

18 **Results** The prevalence of metabolic syndrome was 50.1% overall (38.4% in males and  
19 57.9% in females;  $p < 0.001$ ). High body mass index and hip circumference were  
20 associated with metabolic syndrome in both sexes. In addition, physical inactivity (odds  
21 ratio [OR] and 95% confidence interval [CI]: 1.441 [1.055, 1.969];  $p = 0.022$ ) in males  
22 and advanced age (OR and 95% CI: 1.536 [1.154, 2.043];  $p = 0.003$ ) in females were  
23 factors associated with metabolic syndrome. Women with junior high school education  
24 or above and living in rural areas were less likely to have metabolic syndrome. For men,  
25 education and rural or urban living had no association with metabolic syndrome.

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1 **Conclusions** The risk factors for metabolic syndrome have similarities and differences  
2 in different sexes; thus, the prevention and treatment of metabolic syndrome should be  
3 based on these sex differences.

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5 **Key words:** metabolic syndrome, prevalence, sex difference, cross-sectional, risk  
6 factor.

For peer review only



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- 3 1. This cross-sectional study included a large, representative sample of the Chinese
- 4 population.
- 5 2. We used a uniform, pre-coded questionnaire designed by the national stroke
- 6 screening survey of China.
- 7 3. Some results were partially based on self-reported data collected by investigators,
- 8 which inevitably increased the risk of recall bias.
- 9 4. Our survey excluded participants who were sick or too weak to complete the
- 10 interview.
- 11 5. As a major limitation of all epidemiological investigations, conclusions based on
- 12 cross-sectional studies cannot be used for causal inferences.

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## 2 INTRODUCTION

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4 Metabolic syndrome (MS) is associated with a cluster of cardiometabolic risk factors  
5 and has become one of the major public health threats in China. Higher prevalence of  
6 MS greatly increases the burden of morbidity and mortality due to cardiovascular  
7 diseases worldwide.<sup>1-3</sup> This burden has increased every year, although it is difficult to  
8 differentiate it from unhealthy habits of daily living.<sup>4</sup> There is a significant difference  
9 in the prevalence of, and risk factors for MS between men and women.<sup>5</sup> To control and  
10 reduce the risk of MS and cardiovascular diseases more effectively, it is necessary to  
11 identify high-risk populations and understand the sex-specific, modifiable lifestyle  
12 determinants of MS. Northeast China, with its low-income level, has a high incidence  
13 of MS and cardiovascular diseases, Specifically, it has the highest incidence and  
14 mortality rate of stroke (365 and 159/100 000 person-years) in China.<sup>6</sup> Thus, this study  
15 aimed to analyze the sex-specific differences in the prevalence of MS and its related  
16 risk factors in a population from Northeast China.

## 18 POPULATION and METHODS

### 20 Data source and study participants

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22 This population-based cross-sectional study was a part of the Stroke Screening and  
23 Prevention Program of the National Health and Family Planning Commission of China

1 (CNSSS). It assessed a population of residents aged 40 years or older, from January to  
2 March 2016. The CNSSS is a national epidemiological survey of cerebrovascular  
3 diseases conducted to obtain timely and reliable information on the morbidity,  
4 prevalence, and mortality of stroke in Chinese people over the age of 40.<sup>7</sup> The sampling  
5 method employed in this study has been described in detail in other articles.<sup>8</sup> The  
6 sample size (N) required for this survey was calculated on a 2.37% stroke prevalence  
7 (p) among adults 40 years and older in China,<sup>8</sup> using the formula:  
8 
$$N = (Z_{\alpha}^2 pq) / d^2$$
 (where  $Z_{\alpha} = 1.96$ ,  $\alpha = 0.05$ ,  $q = 1-p$ , and  $d = 0.2p$ )

9 A multistage stratified, random cluster sampling method was applied to obtain the  
10 sample population. In the first stage, 30 villages and 10 towns were randomly selected  
11 from a total of 308 villages (rural) and 14 towns (urban) in Dehui City, using the  
12 probability proportional to size (PPS) sampling method. In the second stage, five groups  
13 of villages or communities were randomly sampled from both the rural and urban strata  
14 using PPS sampling. In the third stage, one participant aged  $\geq 40$  years was randomly  
15 selected from each household of the selected groups of villages or communities.  
16 Respondents who were unwilling to participate in the survey or who were judged to be  
17 very frail were excluded. We selected permanent residents aged  $\geq 40$  years for inclusion  
18 in the study (a calculated total of 4445 participants with an additional 10% loss rate);  
19 ultimately, 4100 participants completed the face-to-face survey, with a good response  
20 rate of 92.2%. In this sub-study of the CNSSS, we used data from participants who  
21 completed the study. After excluding 48 participants with incomplete questionnaire  
22 information or laboratory examinations, a total of 4052 participants were included in  
23 this analysis. The flowchart of the study selection process is shown in Figure 1. The  
24 study protocol was approved by the Human Ethics and Research Ethics Committee of  
25 the First Hospital of Jilin University, Chang Chun, Jilin, China (2015-R-250). Written

1 informed consent was obtained from all study participants before recruitment and data  
2 collection.  
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#### 10 **Patient and public involvement**

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16 Patients and the public were not involved in the development of the research  
17 questionnaire, its outcome measures, study design, recruitment methods, or the conduct  
18 of this study. There is no plan to disseminate the research findings to the participants.  
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#### 26 **Data collection and measurement**

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30 All participants completed a questionnaire that included an assessment of general  
31 sociodemographic and health-related information. Physical examinations included  
32 assessments of height, weight, neck, waist, and hip circumferences, and blood pressure.  
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34 Height and weight were measured according to the standard methods; the subjects  
35 removed their shoes and hats and wore light clothes. The measurement accuracy was  
36 within 0.1 cm and 0.1 kg for the height and weight, respectively. Blood pressure was  
37 measured by physicians using an OMRON automatic sphygmomanometer (OMRON  
38 HEM-7200, KYOTO, Japan), on the right arm, after placing it parallel to the heart. The  
39 subjects were made to rest for 20 minutes before the blood pressure was measured twice,  
40 and mean value was recorded. Blood samples were collected on an empty stomach  
41 following overnight fasting (at least 8 hours) to assess fasting plasma glucose (FPG),  
42 triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C),  
43 and high-density lipoprotein cholesterol (HDL-C) concentrations. The samples were  
44 sent to the clinical laboratory of Changchun Kingmed Center (Chang Chun, Jilin, China)  
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### 3 **Screening protocol and assessment criteria**

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5 The definition of MS used in this study was published by the International Diabetes  
6 Federation and the American Heart Association/National Heart, Lung, and Blood  
7 Institute (AHA/NHLBI).<sup>9</sup> The presence of any three of the following five risk factors  
8 constituted a diagnosis of MS: 1) Waist circumference:  $\geq 90$  cm for men, and  $\geq 80$  cm  
9 for women; 2) TG concentration:  $\geq 1.70$  mmol/L (drug treatment for elevated TG levels  
10 was an alternative indicator); 3) HDL-C concentration:  $< 1.0$  mmol/L for men, and  $< 1.3$   
11 mmol/L for women (drug treatment for reduced HDL-C levels was an alternative  
12 indicator); 4) blood pressure: systolic blood pressure (SBP)  $\geq 130$  mmHg and/or  
13 diastolic blood pressure (DBP)  $\geq 85$  mmHg (antihypertensive drug treatment in a  
14 patient with a history of hypertension was an alternative indicator); and 5) FPG  
15 concentration:  $\geq 5.6$  mmol/L (drug treatment for elevated glucose levels was an  
16 alternative indicator).

17 In addition to stratification by sex, participants were also stratified by age into a  
18 middle-aged group (40–64 years old) and an elderly group ( $\geq 65$  years old). The  
19 evaluation criteria for other factors, including BMI, level of physical inactivity,  
20 smoking status, and alcohol consumption are shown in Supplementary Table S1.

21

### 22 **Statistical analysis**

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24 The normality of the data was tested using the Kolmogorov–Smirnov test. Non-  
25 normally distributed continuous variables are presented as medians (IQRs). Categorical

1 data are presented as numbers and proportions. Significant variables (those with  $P <$   
2 0.05) identified in the single variable analysis were selected for the multivariable  
3 analyses. Multiple logistic regression analysis was used to explore the independent risk  
4 factors of MS in the two sexes, and the odds ratios (ORs) and 95% confidence intervals  
5 (CIs) were calculated. All statistical analyses were performed using IBM Statistical  
6 Package for the Social Sciences (SPSS) version 23.0 (SPSS, Inc., New York, NY, USA).  
7  $P < 0.05$  was considered statistically significant.

## 9 RESULTS

11 Among the 4,100 participants who completed the face-to-face survey, 4,052 were  
12 included in the analysis. A total of 2,030 individuals met the criteria for MS, and the  
13 prevalence was 50.1% overall (38.4% in males and 57.9% in females;  $p < 0.001$ ). Of  
14 all the 4,052 participants, 1,619 were men (40.0%) and 2,433 were women (60.0%),  
15 with a median age of 53 years (IQR: 47–62). Overall, 76.7% of the participants were  
16 educated up to either primary and below or junior middle-school level.

### 18 1. Demographic characteristics of all participants with MS

20 Table 1 shows that compared with that in males (38.4%), the prevalence of MS in  
21 females (57.9%) was significantly higher. Among the 2,030 individuals with MS, the  
22 median age was 56 years (IQR: 49–63), and for both males and females, more than 80%  
23 of the participants with MS were in the group of 40–64 years. The rate of abnormal  
24 waist circumference in females (91.6%) was higher than that in males (85.4%). The

1 median neck and hip circumferences in males were higher than those in females were.  
 2 Compared with males, females had a higher proportion of the following associated risk  
 3 factors: a lower level of educational attainment, living in a rural area, an abnormal  
 4 HDL-C concentration, and higher concentrations of TC and LDL-C. However, a higher  
 5 proportion of men than women had hypertension, abnormal levels of triglycerides and  
 6 fasting blood glucose, abnormal BMI, resided in urban areas, had a smoke habit, and  
 7 consumed alcohol.

8  
 9 Table 1. Sex differences in demographic characteristics and risk factors among  
 10 participants with metabolic syndrome (MS).

	Total	Male	Female
<b>Participants, n (%)</b>	4052(100)	1619 (40.0)	2433 (60.0)
<b>Cases, n (%)</b>	2030 (50.1)	622 (38.4)	1408 (57.9)
<b>Age, years, median (IQR)</b>	56.00(49, 63)	55.72(48, 63)	56.19(49, 63)
<b>Age group, n (%)</b>			
40-64 years	1636(80.6)	501(80.5)	1135(80.6)
≥65 years	394(19.4)	121(19.5)	273(19.4)
<b>Waist circumference, n (%)</b>	1821(89.7)	531(85.4)	1290(91.6)
<b>Neck circumference, median (IQR)</b>	34.00(32, 37)	38.23(36, 40)	33.27(32, 35)
<b>Hip circumference, n (%)</b>	100.00(95, 104)	103.63(100, 107)	97.76(93, 102)
<b>TCHO, mmol/L, median (IQR)</b>	5.52(4.83, 6.25)	5.50(4.73, 6.12)	5.63(4.87, 6.29)
<b>LDL-C, mmol/L, median (IQR)</b>	1.93(1.56, 2.64)	2.08(1.5, 2.57)	2.19(1.57, 2.65)
<b>HDL-C, n (%)</b>	1255(61.8)	176(28.3)	1079(76.6)
<b>TG, n (%)</b>	1503(74.0)	508(81.7)	995(70.7)
<b>FBG, n (%)</b>	881(43.4)	291(46.8)	590(41.9)
<b>Hypertension, n (%)</b>	1853(91.3)	601(96.6)	1252(88.9)
<b>Education, n (%)</b>			
≤Primary school	806(39.7)	176(28.3)	630(44.7)
Junior middle-school	829(40.8)	280(45)	549(39)
Senior middle-school	253(12.5)	104(16.7)	149(10.6)
College and above	142(7.0)	62(10.0)	80(5.7)
<b>Region, n (%)</b>			
Urban	1023(50.4)	357(57.4)	666(47.3)
Rural	1007(49.6)	265(42.6)	742(52.7)
<b>Smoke, n (%)</b>			
No	1021(50.3)	223(35.9)	798(56.7)
Yes	1009(49.7)	399(64.1)	610(43.3)
<b>Physical inactivity, n (%)</b>			
No	1522(75.0)	469(75.4)	1053(74.8)

Yes	508(25.0)	153(24.6)	355(25.2)
<b>Alcohol consumption, n (%)</b>			
Never	1591(78.4)	251(40.4)	1340(95.2)
Light/moderate	245(12.1)	182(29.3)	63(4.5)
Heavier	194(9.6)	189(30.4)	5(0.4)
<b>Fruit consumption, n (%)</b>			
≥5days per week	1782(87.8)	546(87.8)	1236(87.8)
3-4 days per week	189(9.3)	61(9.8)	128(9.1)
≤2 days per week	59(2.9)	15(2.4)	44(3.1)
<b>BMI, n (%)</b>			
Normal	553(27.2)	88(14.1)	465(33.0)
Underweight	11(0.5)	3(0.5)	8(0.6)
Overweight	521(25.7)	144(23.2)	377(26.8)
Apparently overweight	464(22.9)	183(29.4)	281(20.0)
Obesity	481(23.7)	204(32.8)	277(19.7)

Abbreviations: TCHO, total serum cholesterol; LDL-C, low-Density Lipoprotein Cholesterol; HDL-C, high-density lipoprotein; TG, triglyceride; FBG, fasting blood glucose; BMI, body mass index.

Values are expressed as n (percentage).

## 2. Univariable analysis of factors associated with MS stratified by sex

Table 2 shows the results of univariable logistic regression for factors associated with MS in men and women. The prevalence of MS was higher in the elderly (men: 40.2%; women: 71.7%), especially in older women (Figure 2; OR [95% CI] = 2.042 [1.608, 2.594];  $P < 0.001$ ). For females, age, BMI, hip and neck circumference, smoking, higher alcohol consumption, geographical region, and level of educational attainment were associated with MS, whereas physical inactivity and fruit consumption were not. For males, the risk factors associated with MS were similar, except for age, smoking, and higher alcohol consumption. Unlike in women, physical inactivity and light/moderate alcohol consumption were also risk factors in men.

Table 2 Univariable logistic regression analyses on risk factors for the prevalence of metabolic syndrome (MS) in males and females



Category	Reference	Male		Female	
		OR (95% CI)	P	OR (95% CI)	P
<b>Age group</b>	<b>40-64 years</b>				
≥65years		1.10(0.85, 1.42)	0.482	2.04(1.61, 2.59)	<0.001
<b>HP</b>	-	1.20(1.18, 1.22)	<0.001	1.16(1.14, 1.17)	<0.001
<b>NC</b>	-	1.44(1.38, 1.51)	<0.001	1.37(1.31, 1.42)	<0.001
<b>Region</b>	<b>Urban</b>				
Rural		0.57(0.46, 0.69)	<0.001	1.66(1.41, 1.95)	<0.001
<b>Smoke</b>	<b>No</b>				
Yes		0.93(0.75, 1.14)	0.472	1.41(1.19, 1.66)	<0.001
<b>Physical inactivity</b>	<b>Physical activity</b>				
Yes		1.75(1.36, 2.24)	<0.001	1.12(0.93, 1.35)	0.235
<b>Alcohol consumption</b>	<b>Never</b>				
Light/moderate drinking		1.44(1.12, 1.84)	0.004	0.50(0.16, 1.59)	0.243
Higher drinking		0.99(0.78, 1.26)	0.949	0.61(0.43, 0.86)	0.005
<b>Fruit consumption</b>	<b>≥5days/week</b>				
3-4 days per week		1.09(0.77, 1.53)	0.627	1.19(0.89, 1.60)	0.238
≤2 days per week		0.80(0.43, 1.51)	0.494	1.37(0.83, 2.26)	0.226
<b>Education</b>	<b>≤Primary school</b>				
Junior middle-school		1.28(1.01, 1.62)	0.040	0.59(0.49, 0.71)	<0.001
Senior middle-school		1.75(1.27, 2.41)	0.001	0.41(0.32, 0.54)	<0.001
College and above		1.31(0.91, 1.90)	0.149	0.27(0.20, 0.37)	<0.001
<b>BMI</b>	<b>Normal</b>				
Underweight		1.49(0.42, 5.33)	0.540	0.30(0.14, 0.66)	0.002
Overweight		3.91(2.88, 5.30)	<0.001	3.54(2.85, 4.40)	<0.001
Apparently overweight		11.143(8.03, 15.47)	<0.001	5.28(4.01, 6.93)	<0.001
Obesity		18.29(12.89, 25.96)	<0.001	12.03(8.31, 17.43)	<0.001

1 Abbreviations: BMI, body mass index; HC, Hip circumference; NC, Neck  
2 circumference.

3 Values are expressed as median (IQR) or n (percentage).

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### 3. Relationship between risk factors and MS in the multivariable logistic regression analysis

Multivariable analysis revealed that BMI and hip circumference were significantly associated with MS in both men and women (Table 3). Age, region, and educational attainment were associated with MS in females, while physical inactivity was associated with MS in males. Neck circumference, an underweight BMI, smoking, and alcohol consumption were not associated with MS in either sex.

1 For males, BMI, hip circumference, and physical inactivity were associated with MS.  
 2 The ORs (95% CIs) were 2.067 (1.475, 2.896;  $p < 0.001$ ) for overweight BMI, 3.771  
 3 (2.539, 6.601;  $p < 0.001$ ) for apparently overweight BMI, and 3.253 (2.019, 5.241;  $p <$   
 4 0.001) for obese BMI. For hip circumference, the OR (95% CI) was 1.115 (1.086, 1.146;  
 5  $p < 0.001$ ). Physical inactivity was associated with MS in males (OR 1.441, 95% CI  
 6 [1.055, 1.969],  $p = 0.022$ ).

7 For females, BMI, hip circumference, and advanced age were associated with MS.  
 8 Rural residence and junior middle-school education or above were negatively  
 9 associated with MS. The higher the education attainment, the lower the risk of MS. The  
 10 ORs (95% CIs) were 2.091 (1.633, 2.677;  $p < 0.001$ ) for overweight BMI, 2.014 (1.455,  
 11 2.786;  $p < 0.001$ ) for apparently overweight BMI, and 2.546 (1.623, 3.995;  $p < 0.001$ )  
 12 for obese BMI groups. For hip circumference, the OR (95% CI) was 1.098 (1.077, 1.119;  
 13  $p < 0.001$ ). The OR (95% CI) for advanced age ( $\geq 65$  years) was 1.536 (1.154, 2.043);  
 14  $p = 0.003$ ). The OR (95% CI) for living in a rural region was 0.737 (0.561, 0.967;  $p =$   
 15 0.028). For an educational level of junior middle-school, the OR (95% CI) was 0.616  
 16 (0.479, 0.791;  $p < 0.001$ ); for senior middle-school, it was 0.580 (0.404, 0.833;  $p =$   
 17 0.003), and for college and above, it was 0.434 (0.286, 0.660;  $p < 0.001$ ).

18  
 19 Table 3 Multivariable logistic regression analyses on risk factors for the prevalence of  
 20 metabolic syndrome (MS) in males and females.

Category	Reference	Male		Female	
		OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
<b>Age group</b>	<b>40-64 years</b>				
	$\geq 65$ years	-	-	1.54(1.15,2.04)	0.003
<b>Education</b>	<b><math>\leq</math>Primary school</b>				
	Junior middle-school	0.92(0.66, 1.27)	0.606	0.616(0.48, 0.79)	<0.001
	Senior middle-school	1.01(0.64, 1.61)	0.953	0.58(0.40, 0.83)	0.003
	College and above	0.73(0.43, 1.23)	0.231	0.43(0.29, 0.66)	<0.001
<b>Region</b>	<b>Urban</b>				
	Rural	0.82(0.59, 1.13)	0.223	0.74(0.56, 0.97)	0.028

<b>BMI</b>	<b>Normal</b>				
Underweight		2.46(0.58, 10.50)	0.223	0.57(0.25, 1.30)	0.183
Overweight		2.07(1.48, 2.90)	<0.001	2.09(1.63, 2.68)	<0.001
Apparently overweight		3.77(2.54, 5.60)	<0.001	2.01(1.46, 2.79)	<0.001
Obesity		3.25(2.02, 5.24)	<0.001	2.55(1.62, 4.00)	<0.001
<b>Neck circumference</b>	<b>-</b>	1.19(0.95, 1.50)	0.128	1.19(0.95, 1.50)	0.128
<b>Smoke</b>	<b>No</b>				
Yes		-	-	1.19(0.95, 1.50)	0.128
<b>Physical inactivity</b>	<b>Physical activity</b>				
Yes		1.44(1.06, 1.97)	0.022	-	-
<b>Alcohol consumption</b>	<b>Never</b>				
Light/moderate drinking		0.88(0.66, 1.18)	0.400	0.72(0.48, 1.08)	0.112
Higher drinking		1.32(0.98, 1.78)	0.07	0.431(0.11, 1.63)	0.215
<b>Hip circumference</b>		1.12(1.09, 1.15)	<0.001	1.10(1.08, 1.12)	<0.001

Abbreviations: BMI, body mass index; OR, odds ratio.

## DISCUSSION

In this study, we evaluated sex-based differences in the prevalence of MS and its relative determinants in a low-income population from Northeast China. We found that in addition to being significantly more prevalent in females than in males, a high BMI, and large hip circumference were risk factors for MS in both sexes. In addition, advanced age ( $\geq 65$  years) was a risk factor only for females, whereas physical inactivity was a risk factor only for males. Furthermore, educational attainment and living in a rural region were negatively associated with MS in women, but not in men. The prevalence of MS has been steadily increasing due to unhealthy lifestyles in low- and high-income regions,<sup>10 11</sup> and there are known sex differences.

The prevalence of MS in those living in the Chinese mainland for both the low-, middle-, and high-income populations was shown to be 33.9% in 2010;<sup>1</sup> however, in our study, it was 50.1%. This may be because most of the participants in our study population had a lower educational level and income, which may have had an additive effect on the primary, increasing trend. In most studies, the prevalence of MS in females was higher than that in males;<sup>1 12</sup> for example, in Mexico, the prevalence in females

1 was 55.6%, whereas in males, it was 38.2%.<sup>13</sup> Similar sex disparities were observed in  
2 Middle Eastern countries, but few sex differences have been reported in the European  
3 Union, which has a lower MS prevalence overall.<sup>14</sup> In Contrast , the prevalence of MS  
4 in males is higher than that in females in Caucasians,<sup>15</sup> American adolescents,<sup>16</sup> Far  
5 East Asian and Japanese populations, and in Macau, it is twice that in women from.<sup>17</sup>  
6 These differences may be related to race, the period in which the studies were conducted,  
7 the geographic region, and the selection criteria used.<sup>18 19 20</sup> Our results were consistent  
8 with those reported in most countries that women had a higher prevalence of MS than  
9 men<sup>21 22 23 24</sup>. In addition, these sex-related differences were shown to be greater in  
10 women of advanced age, but remained relatively stable with respect to age in men in  
11 East China.<sup>25</sup> This was consistent with our own findings that females aged  $\geq 65$  years  
12 had a 1.536-fold higher risk of MS than those aged 40–65 years. A decrease in estrogen  
13 levels in women after menopause, results in an increase in insulin resistance and  
14 abnormal lipid metabolism result. Thus, the sex differences observed may be related to  
15 changes in hormone levels, rather than aging itself.<sup>26</sup>

16 It is well known that MS prevalence increases when BMI ( $\geq 24$  kg/m<sup>2</sup>) is higher than  
17 normal. Compared with individuals with a normal BMI, the risk of metabolic syndrome  
18 with an overweight and obese BMI was 3.11- and 17.18-fold in Korean females, and  
19 4.30- and 10.91-fold in Korean males without diabetes mellitus, respectively.<sup>27</sup> Our  
20 study also found that compared with a normal BMI, a higher BMI was associated with  
21 higher odds of MS. The risk was 2.091-, 2.014-, and 2.546-fold higher in overweight,  
22 significantly overweight, and obese females, respectively. In males, the risk increased  
23 2.067-, 3.771-, and 3.253-fold, respectively. These findings also suggest that weight  
24 gain in males (BMI  $\geq 26$  kg/m<sup>2</sup>) increases the risk of MS more substantially than it does  
25 in females; this positive association has also been reported in a study of Turkish

1 adults.<sup>28</sup> An Israeli cohort study claimed that a normal BMI had a high negative  
2 predictive value in both men (98%) and women (96%) with respect to MS.<sup>29</sup> The  
3 inverse association was found between hip circumference and metabolic risk factors in  
4 Tehranian women.<sup>30</sup> Further, weak predictive ability was found for hip circumference.  
5 In our study, the risk of MS increased 1.098-fold in women and 1.115-fold in men for  
6 every 1 cm increase in hip circumference but not in neck circumference. Thus, BMI  
7 combined with hip circumference is an effective indicator of being overweight or obese,  
8 and such individuals are more prone to developing MS. Whether obesity or insulin  
9 resistance is a cause or consequence of MS is still under debate.<sup>31</sup> Adipokines produced  
10 by abnormal adipocytes cause insulin resistance, and visceral obesity may be a causal  
11 factor of metabolic disease.<sup>32</sup>

12 Physical inactivity was a main risk factor for males in our study, consistent with the  
13 findings of a previous study.<sup>33</sup> Infrequent physical activity results in a 1.441-fold  
14 increased risk of MS in men, but not in women, this is consistent with previous  
15 findings.<sup>34</sup> Moreover, physical activity has been suggested to be associated with a low  
16 risk for MS.<sup>35</sup> Studies have also found that binge drinking and smoking were associated  
17 with increased MS prevalence, regardless of sex or BMI.<sup>36, 37</sup> The association between  
18 fruit consumption, neck circumference, and MS risk remains unclear; in our study, no  
19 significant associations were observed among alcohol consumption, smoking, fruit  
20 consumption, or neck circumference.

21 Educational level is the most important measure of socioeconomic status, which has  
22 been shown to not only affect the prevalence of MS, but is also closely related to the  
23 prevalence of cerebrovascular disease.<sup>38</sup> The specific mechanism by which education  
24 affects the prevalence of MS is unclear. It has, however, been considered that education  
25 influences people's lifestyles and positive attitudes toward health, and increases their

1 access to preventive health services.<sup>39</sup> In addition, it is reported in South Korea, that the  
2 negative correlation between educational level and MS prevalence is largely related to  
3 the dietary patterns of Koreans (especially in women).<sup>40</sup> For females in our study, the  
4 ORs indicated a 0.616-fold, 0.580-fold, and 0.434-fold risk of developing MS in those  
5 who had completed junior middle-school, senior middle-school, as well as college and  
6 above, respectively. This suggests that a higher educational level can reduce the risk of  
7 MS; however, this relationship was not found in males. The negative association  
8 between MS prevalence and educational level was significant in females, which is  
9 similar to the results of a previous study.<sup>40</sup> A National Survey found that low income  
10 and educational levels were associated with a higher prevalence of MS in females than  
11 in males.<sup>41</sup> Our study population was characterized by having both a low income and a  
12 low level of education, both of which contributed to a higher MS prevalence. The  
13 percentage of included females with a primary school education or below was 37.8%,  
14 which may partially explain the high prevalence of MS in women.<sup>24</sup> Urban adults ( $\geq 18$   
15 years old) in China were more likely than rural adults to have MS in 2009,<sup>42</sup> The  
16 opposite was true among urban adults in Jiangxi province, China in 2015, as females  
17 living in rural areas were more likely than urban females to have MS. These findings  
18 were not observed among males.<sup>43</sup> In our study, MS was negatively associated with  
19 living in rural regions (OR: 0.737 [0.561, 0.967],  $p = 0.028$ ) but not with living in urban  
20 regions. The differences may be caused by the degree of economic development,  
21 lifestyle habits, and dietary patterns; for example, rural women have lower fat intake  
22 and more activity than urban women.<sup>44</sup>

23 Lifestyle interventions resulted in a 2.61-fold reduced risk of MS compared with the  
24 control group in a previous study.<sup>45</sup> An investigation of dietary patterns showed that the  
25 Chinese pattern (high in grains, vegetables, fruit, salted fish and eggs, soyabean, and

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3 1 etc.) was associated with a lower risk of MS than the animal food pattern (high in meats,  
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5 2 fish and shrimp, eggs, seafood, alcoholic beverages, etc.).<sup>46</sup> Sex differences in the  
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7 3 dietary patterns were associated with increased MS prevalence; for example, an  
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9 4 increased prevalence was observed in men consuming an "animal and fried food" diet,  
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11 5 and women consuming a "high-salt and energy" diet.<sup>19</sup> Muscle strength and  
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13 6 cardiorespiratory fitness may independently and jointly reduce the incidence of MS,<sup>47</sup>  
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15 7 as increased physical activity decreased the risk by 19–24%.<sup>48</sup> In men, every hour of  
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17 8 exercise may decrease MS risk by 2%.<sup>49</sup> In contrast, daily sedentary behavior linearly  
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19 9 increases the risk of metabolic syndrome by 1.09 times per hour.<sup>50</sup> To prevent the onset  
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21 10 of MS, a better understanding of modifiable lifestyle factors is needed in high-risk  
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23 11 populations; for example, in men who are physically inactive, further effort should be  
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25 12 made to control body weight, especially by focusing on reducing high BMI and hip  
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27 13 circumference. Moreover, exercise can result in high brain insulin sensitivity, which  
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29 14 can help to lose more body weight and body fat with a lower regain.<sup>51</sup> For women,  
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31 15 especially the elderly outside rural regions, efforts should be made to control weight to  
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33 16 maintain BMI and hip circumference at normal levels to reduce the risk of MS. Focus  
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35 17 should also be directed at changes in hormone levels, especially the low concentrations  
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37 18 of sex hormone-binding globulin and testosterone, which increase the odds of MS.<sup>52</sup>  
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39 19 In the long run, a higher level of educational attainment can reduce the risk of MS.  
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41 20 Understanding these factors and the sex differences between them, as well as accurately  
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43 21 identifying high-risk groups, could help to develop better public health policies,  
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45 22 educational initiatives and reduce the incidence of MS and vascular diseases. There  
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47 23 were also several limitations to this study. Some data was self-reported, each parameter  
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49 24 in blood was only sampled and measured once, and some lifestyle factors and potential  
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51 25 residual confounders were not assessed. Furthermore, people who were sick or too  
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1 weak to participate were excluded, which may impact the generalizability of the results.  
2 Moreover, cross-sectional studies cannot be used to make causal inferences, and  
3 subsequent prospective and randomized studies are needed.

4

## 5 **CONCLUSION**

6 In our study, we found that risk factors for MS have both sex-based similarities and  
7 differences; thus, the prevention and treatment of MS should consider patients' sex.

8

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14

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## 22 **CONFLICTS OF INTEREST**

23 None declared.



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6 2 **ETHICS APPROVAL**7  
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9 3 This subject was approved by the human ethics and research ethics committee of the  
10 4 First Hospital of Jilin University (approval No: 2015-R-250), and written informed  
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14 5 consent was obtained from all of the participants.  
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19 7 **PROVENANCE AND PEER REVIEW**20  
21  
22 8 Not commissioned; externally peer reviewed.  
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27 10 **DATA SHARING STATEMENT**28  
29 11 The dataset supporting the conclusions of this article can be made available upon  
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31 12 request.  
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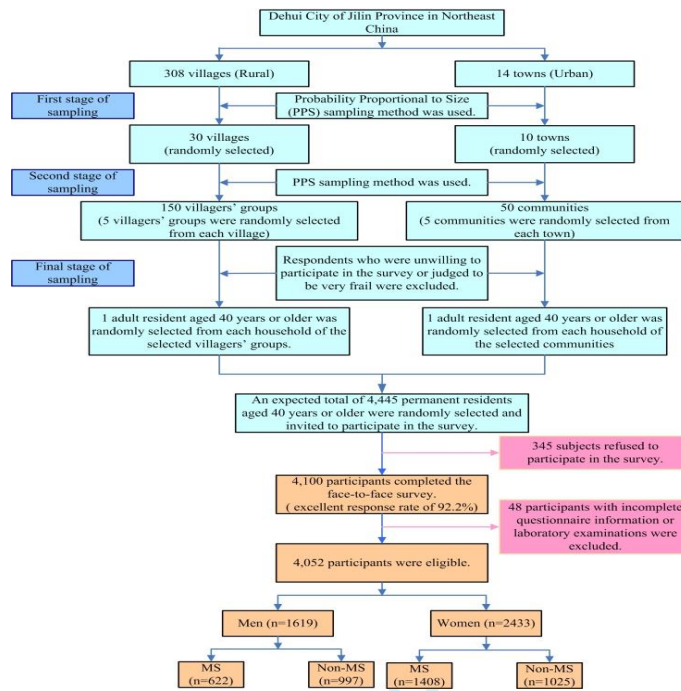
18 Fig. 1 Sampling process in the study

19 Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study

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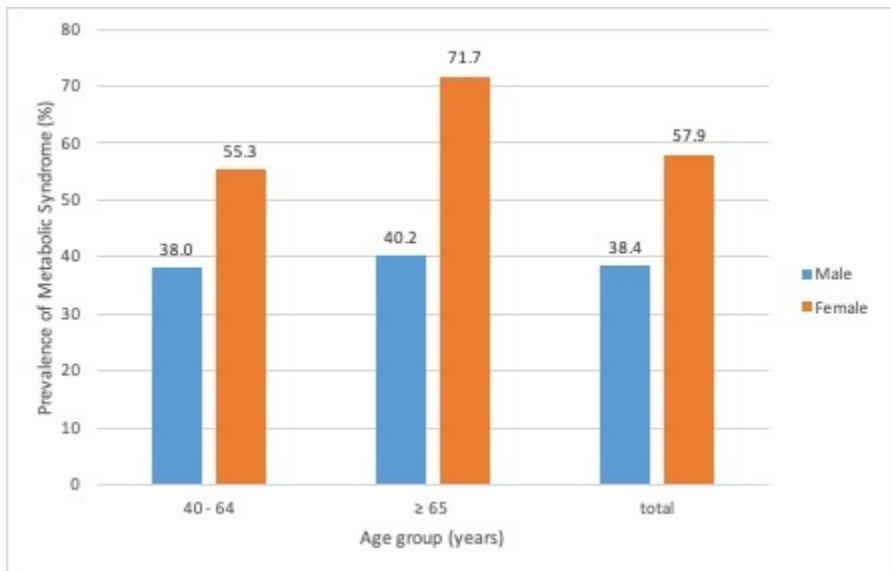


Fig. 2 Prevalence of metabolic syndrome in different sexes and ages in the study  
156x99mm (72 x 72 DPI)

Sex differences and risk factors of Metabolic syndrome in adults aged more than 40 in Northeast China: Results from the National Stroke Screening Survey  
Feng-e Li *et al*

**Supplementary Table S1** Definitions of metabolic syndrome-related risk factors in the survey.

Variables	Criteria	References
BMI	BMI was grouped into five categories for our study: underweight (BMI < 18.5 kg/m <sup>2</sup> ), normal (18.5 ≤ BMI < 24 kg/m <sup>2</sup> ), overweight (24 ≤ BMI < 26 kg/m <sup>2</sup> ), apparently overweight (26 ≤ BMI < 28 kg/m <sup>2</sup> ), obesity (BMI ≥ 28 kg/m <sup>2</sup> ).	Guidelines for diabetes prevention and treatment in China <sup>1</sup>
Abnormal neck circumference	≥37cm for male and ≥33cm for female	Neck circumference as an independent predictive contributor of cardio-metabolic syndrome <sup>2</sup>
Physical inactivity	Physical inactivity is defined as insufficient physical activity; Physical activity is defined as the performance of heavy physical labor or regular physical exercise for more than one year, more than 3 times per week, and for at least 30 minutes per session.	CHNS guidelines <sup>3</sup>
Smoking	A smoker was defined as one who reported smoking one or more cigarettes or was passively exposed to tobacco smoke every day in general for more than 6 consecutive months. A non-smoker was defined as the one who had never smoked, nor passively exposed to tobacco smoke; or, had history of smoking but quit smoking for at least 6 consecutive months previous to the study.	Technical specification of stroke screening and prevention in China <sup>4</sup>
Drinking	The NIAAA sets the standard drink size at about 14g of absolute ethanol, advising limits of no more than three drinks per day or seven drinks per week for men and women. Drinking status was divided into three categories according to the participants' self-report in the previous 6 months: non-drinkers: had never drunk alcoholic beverage; light/moderate drinkers: less than or upto NIAAA limits; heavier drinkers: in excess of NIAAA limits.	NIAAA guidelines <sup>5</sup>
Fruit consumption	Fruit consumption was grouped into three categories for our study: less than or equal to two days per week (≤ 2 d/w), three to four days per week (3–4 d/w), and greater than or equal to five days per week (≥ 5 d/w). And the weight of consumed fruits should reach or exceed two servings per day, and the definition of a serving of a fruit was calculated as 80g.	Fruit and vegetable consumption and stroke: meta-analysis of cohort studies <sup>6</sup>

**Abbreviation:** BMI, body mass index; CHNS, China Health and Nutrition Survey; NIAAA, National Institute on Alcohol Abuse and Alcoholism.

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

Section/Topic	Item #	Recommendation	Reported on page #
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	3,4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	6-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
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	7-8
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	NA
		(c) Explain how missing data were addressed	NA
		(d) If applicable, describe analytical methods taking account of sampling strategy	6, 7
		(e) Describe any sensitivity analyses	NA
<b>Results</b>			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9-11
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	(7)
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-11
		(b) Indicate number of participants with missing data for each variable of interest	NA
Outcome data	15*	Report numbers of outcome events or summary measures	11,12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	13-17
		(b) Report category boundaries when continuous variables were categorized	12
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	20
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18,19
Generalisability	21	Discuss the generalisability (external validity) of the study results	20
<b>Other information</b>			
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 which the present article is based	21

\*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](http://www.strobe-statement.org).