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Sex differences in non-communicable disease prevalence in China: a cross-sectional analysis of the China Health and Retirement Longitudinal Study in 2011

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ABSTRACT

Objectives To describe the sex differences in the prevalence of non-communicable diseases (NCDs) in adults aged 45 years or older in China.

Design Cross-sectional study.

Setting Nationally representative sample of the Chinese population 2011.

Participants 8401 men and 8928 women over 45 years of age who participated in the first wave of the China Health and Retirement Longitudinal Study (CHARLS).

Outcome measures Self-reported data on overall health and diagnosis of hypertension, dyslipidaemia, diabetes, heart disease, stroke, chronic lung disease, cancer or arthritis. Sex differences in NCDs were described using logistic regression to generate odds ratios (OR) with adjustment for sociodemographic factors and health-related behaviours. All analyses were stratified by age group for 45–64-year-old and ≥65-year-old participants.

Results In both age groups, men reported better overall health than women. The crude prevalence of heart disease, cancer and arthritis was higher while that of stroke and chronic lung disease was lower in women than in men. After adjustment, ORs (95% CI) for the 45–64 and ≥65 year age groups were 0.70 (0.58 to 0.84) and 0.66 (0.54 to 0.80), respectively, for arthritis for men compared with women. In contrast, ORs were 1.66 (1.09 to 2.52) and 2.12 (1.36 to 3.30) for stroke and 1.51 (1.21 to 1.89) and 1.43 (1.09 to 1.88) for chronic lung disease for men compared with women. ORs for heart disease (0.65 (0.52 to 0.80)) were lower in men than in women only in the 45–64 year age group.

Conclusions Odds of arthritis were lower while those of stroke and chronic lung disease were higher in men than in women in both age groups. However, odds of heart disease were lower in men than in women, but only in the group of individuals aged 45–64 years.

Strengths and limitations of this study

- The strength of the study lies in the use of a nationally representative sample of adults aged 45 years or older in China.
- The study is limited by its cross-sectional design, and recall bias may have arisen because the health outcomes and health-related behaviours were self-reported.
- The study is also limited by the differential opportunity to be diagnosed based on socioeconomic status and cultural norms around healthcare seeking.
- There is potential for residual confounding.

BACKGROUND

Non-communicable diseases (NCDs) are one of the major health challenges worldwide.[1] It has been estimated that 34.5 million deaths globally were due to NCDs in 2010, which reflected a significant increase from 1990.[2] Furthermore, previous research across the world has revealed significant differences in health status and NCD prevalence between men and women.[3–5] Women are more likely than men to report worse overall health and to have disabling non-lethal conditions including functioning problems globally.[6 7]

The rising burden of NCDs is particularly marked in low- and middle-income countries.[1] One such country is China where the morbidity and mortality related to NCDs has increased markedly during the past two decades. In 2014, the age-standardised death rate for NCDs reached 636 per 100 000 people, accounting for 87% of all-cause mortality.[8] A greater increase in self-reported chronic disease prevalence in China was observed among women than men between 2003 and 2008.[9] In 2012, the average life expectancy was 72 years in Chinese men and 77 years in Chinese women.[10] In nationally representative studies of adults the prevalence of diabetes in 2007–8 and hypertension in 2010 was significantly higher among men than among women in China.[11–13] Chronic

obstructive pulmonary disease (COPD) was also more prevalent among men than among women aged 40 years and older in China.[14] Furthermore, lung cancer has been identified as the most common cancer among Chinese men while breast cancer was the most common cancer among Chinese women.[15]

While there have been many studies examining sex differences in the prevalence of NCDs in China, more recent studies of nationally representative populations are scarce. Therefore, the aim of this study is to describe the sex differences in NCD prevalence in adults aged 45 years or older in China using data collected in 2011 in the first wave of the nationally representative China Health and Retirement Longitudinal Study (CHARLS).

METHODS

Data

For this cross-sectional study we analysed baseline data of the China Health and Retirement Longitudinal Study (CHARLS), which is a nationally representative longitudinal survey of the mainland Chinese population aged 45 years or older. The baseline survey was conducted in 2011 with subsequent follow-up surveys planned every 2 years. In 2011, after excluding empty or non-resident dwellings, individuals from 12 740 households were assigned as potential study participants. Final interviews were conducted in 17 708 respondents from 10 257 households in urban and rural areas in 150 of the 1442 counties and in 28 of the 34 provincial level administrative divisions in China.

The core CHARLS questionnaires included sections requesting information on: demographic factors, family structure and changes, health status and functioning, healthcare and insurance, work, retirement and pension, income and consumption, and assets (individual and household). Information was collected by interview by trained staff. The CHARLS team created separate weights for households and individuals corrected for non-response and sampling frame errors in each step of the CHARLS. Individuals recruited in 2011 were eligible for this analysis if they were aged 45 or older and had complete data on sex, health outcomes and individual weights. Details of the sampling methodology and the core CHARLS questionnaire have been described previously.[16]

Variables

For this study the following data were used: sociodemographic factors including age (middle-aged (45–64 years) and elderly (≥65 years)), sex, formal level of education (no formal education, elementary school, middle school, high school/vocational school, associate degree or over), marital status (never married, married, separated/divorced, widowed) and regional location (eastern, central and western China). Health status included self-reported data on overall health (excellent, very good, good, fair, poor or very poor) and on whether the respondent had been diagnosed by a doctor with hypertension, dyslipidaemia (elevation of LDL-C, triglycerides, total cholesterol or low HDL-C), diabetes, heart disease (defined as heart attack, coronary heart disease, angina, congestive heart failure or other heart problems), stroke, chronic lung diseases (such as chronic bronchitis or emphysema but excluding cancer), cancer or arthritis. The study participants also reported whether they received treatment for any of the conditions diagnosed by their doctor, health-related behaviours including three independent categories of physical activity (PA) (doing vigorous PA or not, doing moderate PA or not, walking or not), smoking status (current smoker, former smoker, non-smoker), alcohol consumption (more than once a month, less than once a month, never) and the number of meals eaten per day. All study participants signed informed consent to participate and the study was approved by Peking University Biomedical Ethics Committee (IRB00001052-14013-exemption).

Statistical analysis

Due to low frequencies in some of the cells, we merged some of the categories in variables representing smoking, alcohol consumption, meals per day and self-reported health. The new variable for meals, smoking and drinking were binary variables (two meals or less per day vs three meals or more per day; smoking (current smoker) vs not smoking (former smoker, non-smoker); drinking alcohol (drink alcohol more than once a month) vs not drinking alcohol (drink alcohol but less than once a month, none of these)). We also created a new self-reported health variable consisting of four categories: excellent/very good, good, fair and poor/very poor health.

All analyses were stratified by age group for 45–64 and ≥65-year-old participants. All variables were categorical and are presented as counts and percentages, respectively. Sex differences in participants' characteristics were explored using χ^2 tests. The association between sex and health outcomes was explored using logistic regression with three models. In Model 1, a crude model, we explored how health outcomes differ by sex while ignoring potential confounders. In Model 2 we included potential confounders including education level, marital status, region in China and urban status. Health-related behaviours have been identified as risk factors contributing to chronic NCDs,[17] therefore Model 3 includes additional adjustment for physical activity (doing any PA (vigorous and/or moderate and/or walking) vs not doing any PA), smoking status, alcohol consumption and diet.

Individual weights in the CHARLS data were applied in all descriptions and analyses to take into account selection probability, non-response patterns and post-stratification factors. Taylor linearised variance estimation was used to take into account potential clustering as a result of the sampling strategy. All analyses were performed using STATA/SE Version 12.0 software. Tests were considered statistically significant if $P<0.05$.

Table 1 Sociodemographic characteristics of men and women in the CHARLS 2011

	Men	Women	
	n=8401	n=8928	P value
Age (years)			
45–64	5747 (68.1)	6302 (69.4)	0.0925
≥65	2654 (31.9)	2626 (30.6)	
Rural	5098 (50.9)	5239 (49.3)	0.0037
Education			
No formal education	1083 (11.7)	3648 (38.8)	<0.001
Elementary school	3696 (42.2)	3084 (33.7)	
Middle school	2216 (26.4)	1372 (16.4)	
High school/ vocational school	1107 (15.3)	676 (8.8)	
Associate degree or over	288 (4.4)	132 (2.3)	
Marital status			
Never married	141 (1.8)	17 (0.4)	<0.001
Married	7617 (89.4)	7474 (81.6)	
Separated/divorced	137 (2.3)	89 (1.1)	
Widowed	505 (6.6)	1345 (16.9)	
Region location			
Eastern China	2562 (36.6)	2716 (35.6)	0.1541
Middle China	3132 (34.0)	3302 (34.2)	
Western China	2707 (29.5)	2910 (30.2)	

Categorical variables presented as n (%), with n being unweighted frequency and % being weighted column percentage.
P values are for χ^2 tests.
Missing data: education 27, marriage status 4.

RESULTS

After excluding 379 participants with data missing on sex, health status and/or individual weights, a total of 17 309 individuals (8401 men and 8928 women) were included in our analysis. Missing data across confounding variables are presented in online supplementary table S1.

Sociodemographic characteristics of study participants in the CHARLS 2011 are shown in table 1. There was no association of sex with age and region location in China. Compared with women, a greater proportion of men reported living in rural areas. Women were more likely to report a lower level of formal education than men, and a larger proportion of women reported having no formal education. Most men and women were married, but a larger proportion of men than women reported never being married, while a larger proportion of women than men reported being widowed.

Table 2 shows sex differences in health-related behaviours among Chinese men and women for middle-aged and elderly groups. Compared with men, women aged 45–64 years were more likely to report engaging in walking. In contrast, in both age groups women were less likely to report engaging in vigorous physical activities than men. Self-reported tobacco smoking and alcohol consumption were substantially higher in men than in women. In addition, women were less likely to report consuming two meals or fewer per day than men in the middle-aged group, while the opposite was observed for the ≥65 years age group.

Sex differences in self-reported health outcomes by age group are presented in table 3. In both age groups, men reported better overall health than women. The prevalence of heart disease and arthritis was higher among women than men. The prevalence of cancer was higher in women than in men for the middle-aged group only. In contrast, the prevalence of chronic lung disease was higher among men than women for both age groups. No sex difference was observed in the prevalence of hypertension, dyslipidaemia and stroke for either age group.

We also explored age-adjusted sex differences in NCD treatment among men and women (see online supplementary table S2). Women reported higher use of both Chinese traditional and Western modern treatments for

Table 2 Prevalence of self-reported health-related behaviours among men and women in the CHARLS 2011

		45–64 years			≥65 years		
		Men	Women		Men	Women	
		n=5747	n=6302	P value	n=2654	n=2626	P value
Vigorous physical activity		986 (15.1)	867 (11.9)	<0.001	287 (8.6)	174 (5.1)	<0.001
Moderate physical activity		1246 (19.9)	1651 (25.2)	<0.001	495 (16.4)	418 (13.6)	0.0063
Walking		1683 (28.4)	2139 (34.2)	<0.001	830 (29.5)	756 (27)	0.054
Smoking		3091 (57.1)	304 (4.1)	<0.001	1236 (44.3)	213 (7.8)	<0.001
Alcohol consumption		3469 (60.4)	750 (12.2)	<0.001	1208 (45.8)	296 (10.5)	<0.001
Number of meals per day	≤2	1335 (25.0)	1204 (19.8)	<0.001	584 (23.6)	627 (27.1)	0.0488
	≥3	4412 (75.0)	5098 (80.2)		2070 (76.4)	1999 (72.9)	

Categorical variables presented as n (%), with n being unweighted frequency and % being weighted percentage.
Differences in categorical variables explored by χ^2 test.
Missing data: smoking status 689, alcohol consumption 44.

Table 3 Prevalence of self-reported health outcomes among men and women in the CHARLS 2011

		45–64 years			≥65 years		
		Men	Women		Men	Women	P alue
		n=5747	n=6302	P value	n=2654	n=2626	
Reported health	Very good	604 (12.4)	392 (7.2)	<0.001	155 (6.0)	110 (5.3)	<0.001
	Good	1282 (22.8)	1088 (19.0)		456 (18.5)	349 (13.6)	
	Fair	2863 (49.2)	3294 (52.2)		1313 (48.3)	1236 (46.5)	
	Poor	984 (15.7)	1514 (21.7)		722 (27.1)	914 (34.6)	
Hypertension		1179 (20.8)	1384 (21.9)	0.3094	825 (36.3)	986 (38.6)	0.227
Dyslipidaemia		498 (9.1)	551 (9.6)	0.5086	240 (10.8)	291 (12.4)	0.2981
Heart disease		427 (7)	776 (11.5)	<0.001	401 (15.8)	472 (19.1)	0.0414
Stroke		100 (1.8)	100 (1.7)	0.6874	115 (5.1)	94 (3.8)	0.0995
Diabetes		270 (5.1)	360 (5.9)	0.321	172 (7.1)	189 (7.8)	0.5405
Chronic lung disease		639 (11.1)	521 (7.7)	<0.001	520 (19.1)	376 (15)	0.008
Cancer		34 (0.5)	83 (1.2)	<0.001	26 (1)	33 (1.2)	0.549
Arthritis		1598 (25.8)	2211 (32.7)	<0.001	830 (31.4)	1077 (39.4)	<0.001

Categorical variables presented as n (%), n, unweighted frequency; %, weighted percentage.
Differences in categorical variables were explored by χ^2 test.

arthritis and chronic lung diseases. Also, compared with men, women were more likely to report receiving no treatment for diabetes.

Table 4 shows the association (OR and relevant CI) between sex and chronic NCDs stratified by age group. In the crude model, relative odds of heart disease and

Table 4 Results of logistic regression models describing the association between sex and self-reported health outcomes among participants in the CHARLS 2011

	OR (95% CI) for men vs women					
	45–64 years (n=12 049)			≥65 years (n=5280)		
	Model A	Model B	Model C	Model A	Model B	Model C
Hypertension	0.94	0.91	1.08	0.91	0.85**	1.13
	(0.83 to 1.06)	(0.79 to 1.04)	(0.91 to 1.29)	(0.77 to 1.06)	(0.73 to 1.00)	(0.95 to 1.36)
Dyslipidaemia	0.94	0.88	1.05	0.86	0.60***	0.86
	(0.78 to 1.13)	(0.74 to 1.05)	(0.85 to 1.29)	(0.65 to 1.14)	(0.43 to 0.84)	(0.60 to 1.23)
Heart disease	0.58***	0.57***	0.65***	0.80**	0.65***	0.82
	(0.50 to 0.68)	(0.48 to 0.66)	(0.52 to 0.80)	(0.64 to 0.99)	(0.51 to 0.83)	(0.63 to 1.06)
Stroke	1.07	1.13	1.66**	1.35	1.63**	2.12***
	(0.77 to 1.49)	(0.79 to 1.60)	(1.09 to 2.52)	(0.94 to 1.92)	(1.08 to 2.46)	(1.36 to 3.30)
Diabetes	0.87	0.92	1.39	0.91	0.69**	1.06
	(0.66 to 1.15)	(0.72 to 1.18)	(0.96 to 2.02)	(0.66 to 1.24)	(0.51 to 0.93)	(0.73 to 1.53)
Chronic lung disease	1.49***	1.66***	1.51***	1.34***	1.39**	1.43**
	(1.23 to 1.81)	(1.37 to 2.01)	(1.21 to 1.89)	(1.08 to 1.66)	(1.08 to 1.80)	(1.09 to 1.88)
Cancer	0.41***	0.42***	0.65	0.84	0.51**	0.74
	(0.27 to 0.64)	(0.26 to 0.68)	(0.33 to 1.27)	(0.48 to 1.48)	(0.27 to 0.97)	(0.36 to 1.52)
Arthritis	0.72***	0.76***	0.70***	0.71***	0.68***	0.66***
	(0.63 to 0.81)	(0.66 to 0.87)	(0.58 to 0.84)	(0.61 to 0.82)	(0.57 to 0.80)	(0.54 to 0.80)

Binary logistic regression: Model A: crude model (no adjustment); Model B: adjusted for education, marital status, region in China and urban residence; Model C: adjustment as for model B with the addition of physical activity (doing any PA vs not doing any PA), smoking behaviour, alcohol consumption, and diet. Doing PA refers to doing any vigorous PA and/or moderate PA and/or walking.
*P<0.1; **P<0.05; ***P<0.01

arthritis were lower in men than in women, while those of chronic lung diseases were higher in men for both middle-aged and elderly groups. Odds of cancer were lower in men than in women in the middle-aged group. Adjustment for education, marital status, region in China and urban residence did not affect the abovementioned relationships between sex and health outcomes, and it additionally uncovered higher odds of stroke and lower odds of hypertension, dyslipidaemia, diabetes and cancer in elderly men compared with elderly women. In fully adjusted models, where models were additionally adjusted for health-related behaviours including physical activity, smoking status, alcohol consumption and diet, relative odds (middle-aged group/elderly group) of stroke (1.66 (95% CI 1.09 to 2.52)/2.12 (95% CI 1.36 to 3.30)) and chronic lung disease (1.51 (95% CI 1.21 to 1.89)/1.43 (95% CI 1.09 to 1.88)) were higher while those of arthritis (0.70 (95% CI 0.58 to 0.84)/0.66 (95% CI 0.54 to 0.80)) were lower in men compared with women in both middle-aged and elderly groups. However, the odds of heart disease (0.65 (95% CI 0.52 to 0.80)) remained lower in men compared with women among middle-aged study participants only.

DISCUSSION

We observed marked sex differences in self-reported NCD prevalence among Chinese adults aged 45 years and older who participated in the CHARLS nationally representative study in 2011. In both middle-aged and elderly sub-groups, odds of arthritis were lower while those of stroke and chronic lung disease were higher in men than in women. However, odds of heart disease were lower in men than in women, but only in the group of individuals aged 45–64 years. These associations were independent of age, education, marital status, region in China, urban residence, physical activity, smoking, alcohol consumption and number of meals eaten each day. The present study provides a better understanding of sex differences in NCDs in middle-aged and older adults in China. Identifying and targeting groups at high risk for NCDs may improve healthcare delivery and help with planning approaches for primary and secondary prevention of NCDs in middle-aged and older adults in China.

Our study found that women were more likely than men to report worse self-rated health and having arthritis and less likely to report a history of stroke and chronic lung diseases. These findings are in line with previous similar research in several regions and countries including Latin America, China and India. The prevalence of rheumatoid arthritis was five times higher in women than in men in Latin America,[18] while Zhong *et al* reported that the prevalence of COPD was higher in men (12.4%) than in women (5.1%) among 20 245 participants aged 40 years or older in seven provinces/cities in China.[19] Similar to our findings, investigators from India have also reported worse health in women compared with men.[20]

The sex differences in tobacco smoking and alcohol consumption observed in our study are also consistent with previous research. Chen *et al* conducted two nationwide prospective studies 15 years apart and found that only 2% of Chinese women smoked compared with over 60% of their male counterparts.[21] Furthermore, the tobacco-attributed proportion of mortality is higher among men than among women. It is estimated that smoking will cause about 20% of all adult male deaths in China during the decade starting in 2010.[21 22] Similar to the findings in our study, the prevalence of male and female current alcohol drinking was 55.6% and 15.0% in another nationally representative study of Chinese men and women from 31 provinces in China in 2007.[23]

Sex differences in the prevalence of hypertension, diabetes and heart disease observed in our study were not always consistent with findings from previous studies.[24–28] For example, Yang W *et al*[27] reported that the prevalence of diabetes among Chinese adults aged 20 years or older was 9.7%, which is higher than that in our study (5–8%), and male sex was significantly associated with an increased risk of diabetes. We observed odds of diabetes that were lower in men than in women for individuals aged 65 years or older. The discrepancy in the results may have been due to differences in the age of the studied population and the way diabetes was determined. In the study by Yang *et al*, study participants were on average younger and diabetes diagnosis was defined by a blood glucose level and not self-reported. Our results also contrast with the results of the study of Yang L *et al*[28] who reported that the prevalence of hypertension was higher in men than in women aged 15 or older in China. There was a difference in the age distribution of the populations between the studies that may contribute to the discrepancy in the findings. In addition, many potential confounding variables such as physical activity and diet were not adjusted for in the study by Yang L *et al*.[28]

The results of our study indicate that women were more likely to report having heart disease than men, which was consistent with the results reported in some low- and middle-income countries, but not in most high-income countries.[29–31] This may be a result of lower healthcare seeking by women than by men, as it has been reported that, in developing countries, men use health services more frequently than women.[32] Indeed, in a study exploring gender differences in the use of healthcare in China, there was a greater use of healthcare in men than in women.[33] Men also tended to have a longer duration of hospitalisation and to spend more on hospitalisation than women, while greater use of healthcare in women compared with men was observed only during women's childbearing years.[33] Chinese cultural gender norms and values mean that preferential treatment is often given to male family members because of their greater economic contribution.[33 34] Additionally, women in China often tend to postpone their own health-seeking behaviour until really necessary in order to preserve the family's funds, which may result in a detrimental effect on their health and longevity.[35]

It is frequently observed that women have poorer self-reported health than men.[22 36–38] In our study, we also found that women were more likely to report certain NCDs and poorer self-rated health than men. One potential explanation is that women have a higher prevalence of degenerative but non-fatal conditions such as arthritis and other painful conditions, hypertension and/or vision problems than men, while men may experience more severe NCDs.[36] A mix of biological factors and societal gender inequalities have been proposed as major contributing factors to gender gaps in self-reported measures of health.[37] Previous research has also demonstrated that widowed women have much higher risks of reporting poor self-rated health than married women.[39] In our study, it is notable that a larger proportion of women than men reported being widowed, which may have also contributed to gender disparities.

Socioeconomic status may also have contributed to the differences in health between women and men. The association between educational attainment and health outcomes has been well established.[40] It has been found that better educated individuals report better health and have fewer chronic diseases than those with lower levels of formal education.[41] Therefore, in our study the lower education attainment of women compared with men may have contributed to women reporting worse overall health. However, it is important to note that marriage motivates couples to share health resources, exchange knowledge about prevention and treatment of illnesses,[42] and share lifestyle and attitudes.[43] In a recent study that examined the association between spousal education and self-rated health among married men and women in the USA, being married to a highly educated person was associated with lower odds of reporting fair or poor health.[44] Similarly, in a Norwegian study[42] that explored the relationship between the educational achievements of family members and mortality, the education of the spouse was negatively associated with mortality. Interestingly, the investigators observed that the education of spouses had a weaker effect on health than individuals' own education, both for men and women.[42] In addition, there are also gender inequalities in earnings whereby women get paid less than men, even for equivalent work; and girls and women lag behind in education and employment opportunities, which continue to damage the health of millions of girls and women worldwide.[21 45 46] It is therefore possible that the proportion of each NCD that is undiagnosed is greater in women than men as a result of these socioeconomic and cultural norms in healthcare seeking. The sex difference in the combined prevalence of both diagnosed and undiagnosed disease ('true prevalence') of conditions that we have found to be more common in women may have been underestimated, but sex differences in the true prevalence of conditions that we have found to be less common in women may have been overestimated by using self-reported outcomes.

There are several limitations to the study. This study is cross-sectional, and is therefore simply descriptive and may be influenced by survival bias. Longitudinal studies are needed to determine whether the sex differences persist or change over time and whether they differ for younger and older population groups. The study is representative of people from China aged 45 years and older; however, the findings may not apply to younger population groups. Furthermore, sociodemographic characteristics and health-related behaviours were self-reported and hence prone to recall bias, which may affect men and women differently. Health outcomes were also self-reported and may differ from those noted in medical records. This discrepancy could be due to recall bias and may differ between men and women. This discrepancy may also be due to poor communication between a patient and a health professional, health literacy of the patient, and patients may also report conditions for which they have been tested but not diagnosed, or they may self-diagnose if they were not satisfied with the doctor's explanation for their health complaint.[47] Multiple statistical tests were performed, which may have led to false positive results, and the large sample size may give statistically significant results that are not clinically important. The analyses were adjusted for several potential confounding factors; however, the results may still be confounded by other known and unknown factors. The strengths of the study lie in the use of a nationally representative sample of adults aged 45 years or older, multiple reported health outcomes and consideration of multiple factors that can potentially confound or mediate the relationship between sex and health.

CONCLUSIONS

In our study, in both middle-aged and elderly subgroups, the odds of self-reported arthritis were lower in men than in women while the odds of stroke and chronic lung disease were higher in men than in women. The odds of heart disease were also lower in men than in women, but only in the group of individuals aged 45–64 years. We argue for a greater focus on sex differences in common health problems and a gendered approach to monitoring, policy and intervention in the control of NCDs.

Contributors YL conceptualised and designed the study, analysed and interpreted data, drafted the manuscript, critically revised the manuscript for important intellectual content and approved the final manuscript as submitted. GL conceptualised and designed the study, acquired and analysed data, drafted the manuscript and approved the final manuscript as submitted. HW conceptualised and designed the study, drafted the manuscript and approved the final manuscript as submitted. WJ and SW conceptualised and designed the study, critically revised the manuscript for important intellectual content and approved the final manuscript as submitted. DG conceptualised and designed the study, interpreted data, drafted the manuscript, critically revised the manuscript for important intellectual content and approved the final manuscript as submitted. All authors read and approved the final manuscript.

Competing interests None declared.

Patient consent Obtained.

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