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Parity and the metabolic syndrome in older Chinese women: The Guangzhou Biobank Cohort Study

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Summary

Objective: To examine whether parity or gravidity contributes to the development of the metabolic syndrome (MS).

Methods: The first phase of the Guangzhou Biobank Cohort Study recruited 7352 women and 3065 men aged 50 to 93 years in 2003-4. Data on the number of live births and pregnancies, and other reproduction associated factors, socioeconomic and lifestyles factors were collected by standardized interview. The MS components were determined through physical examination and measurement of fasting blood samples. MS was identified if waist circumferences were ≥90cm for men, or ≥80cm for women, plus any two of: a) raised TG level: 1.7 mmol/L, or specific treatment for this lipid abnormality; b) reduced HDL-cholesterol: <1.03 mmol/L in males or <1.29 mmol/L in females, or specific treatment for this lipid abnormality; c) raised blood pressure: systolic or diastolic blood pressure ≥130 or ≥85 mm Hg, or hypertension therapy; d) raised fasting glucose ≥5.6 mmol/L, or previously diagnosed Type 2 diabetes.

Results: Before adjustment for potential confounders, there were associations between the number of births and lifestyle and socioeconomic factors in both sexes. However, in women, but not in men, BMI, waist-hip ratio, triglyceride and glucose were positively associated with the number of birth after adjusting for a range of potential confounders. The age-adjusted prevalent MS increased with the higher number of birth and pregnancy in women, but the gradient for birth was steeper than that for pregnancies [odds ratio change per birth: 1.16 (95% CI: 1.11-1.22), p<0.001; odds ratio change per pregnancy: 1.11 (95% CI: 1.06-1.16), p<0.001], although attenuating the associations adjustment did not affect the significance of these findings. There was no association in men for the number of their partners' live births given the same analysis and similar shared living background with the women.

Conclusion: Higher parity or gravidity was associated with a consistent increase in the risk of MS in Chinese women. As the association persisted after adjustment for lifestyle factors and there was no association between the risk of MS and the number of births associated with the partners of the males, the association in women may represent a biological response to pregnancy.

Introduction

The dramatic alterations in the hormonal milieu and body morphology during pregnancy among women, and other concomitant changes, may have detrimental effects on the body, promoting increases in the vascular risk factors associated with the metabolic syndrome (MS) in later life, including weight gain, increased blood pressure, insulin resistance, and dyslipidemia.[1-8] Additional pregnancies, socioeconomic status, and lifestyle factors may also influence development of these risk factors.[9,10] By examining the effects of live births in women and those associated with the partners of the men, we aimed to establish whether parity or gravidity is associated with the development of the metabolic syndrome (MS).

Methods

Guangzhou Biobank Cohort Study

The Guangzhou Biobank Cohort Study is a collaboration between the Guangzhou Number 12 Hospital, Guangzhou, China and, the Universities of Hong Kong, Hong Kong and Birmingham, UK. We plan to recruit about 30,000 older participants aged 50 or above from 2003-2007 and to follow them up to examine environmental and genetic determinants of common chronic diseases in an older southern Chinese population. The hospital where the study is conducted has all the facilities of a general medium-sized hospital and an infrastructure for occupational health surveillance for workers of many factories and employees of some service industry. Guangzhou is the major city in southern China with a population of 7.25 million.

In developing countries such as China, the infrastructure，such as a client registration list of family physician, to facilitate cohort studies is not available. However, a community social and welfare association, “The Guangzhou Health and Happiness Association for the Respectable

Elders", aligned with the Guangzhou government was chosen as a sampling frame, because it is a large association with branches throughout Guangzhou and its membership is open to anyone for a nominal, discretionary fee of 48 Yuan (US$ 6) per month. It has a city-wide network with around 100,000 members, approximately 9% of the Guangzhou older population.

The male and female participants were randomly recruited from the association's membership list of eligible subjects. About 5% of eligible subjects refused to participate, with less than 1% of females, and about 10% of males refusing. The males generally refused because of a cultural unwillingness of Chinese males to give blood due to the belief in an associated loss of 'shung qi' or 'life energy', and because of job commitments. There were also more women than men in the older population due to the longer life expectancy. Generally however most of the subjects were keen to participate as they could receive free health examinations. We only included those who were ambulatory, and not receiving treatment modalities which if omitted may result in immediate life threatening risk, such as chemotherapy or radiotherapy for cancer, and dialysis for renal failure. Those with less immediate risk, such as those with a history of vascular disease or associated risk factors including diabetes and hypertension were not excluded from the study. The first phase 10417 participants were recruited during 2003-4. The study has received ethical approval from the Guangzhou Medical Ethics Committee of the Chinese Medical Association, Guangzhou, China. All participants gave written, informed consent prior to participating in the study.

Measurements

Six full time trained nurses interviewed the participants, with all questions being computerized and the information collected and entered directly into the computer. Parity refers to the number of biological live births for women and, for men refers to their children, i.e. to the live births of their

partners. Gravidity is defined as the number of pregnancies, including lost pregnancies and still births. Information on other reproduction associated factors (age at menarche, age at menopause, age at first pregnancy, history of miscarriage, pregnancy terminations, breast feeding, and use of contraceptive pills or hormone therapy) was collected in the women. In addition, information on socioeconomic factors (education, occupation, household income), lifestyle factors (smoking, alcohol drinking, physical activity) was collected.

Participant recruitment began on September 1, 2003. In June 2004, with 200 randomly selected participants were invited back to the hospital and re-interviewed with the same questionnaire for validation. We used the kappa value and Intraclass Correlation Coefficient (ICC) to assess the reliability for categorical and continuous variables respectively. The kappa values of parity and gravidity were 0.93 and 0.79 respectively. The kappa values for other categorical variables involved in this paper were: smoking (0.96 and 0.88 for the two questions on smoking status), drinking (0.60), physical activity (0.58), education (0.90), occupation (0.80), household income (0.60), and use of contraceptive pills (0.67), and the ICC for continuous variables were: age at menarche (0.92), age at menopause (0.70) and age at first pregnancy (0.50).

Seated blood pressure was measured three times, one minute apart, after a 3 minute rest, using the Omron 705CP sphygmomanometer. The average of the last two readings was used in the analysis. Weight and height were measured with light indoor clothing and without shoes. Body mass index (BMI) was calculated as the weight in kilogram (kg) divided by the square of height in meters. Waist circumference was measured horizontally around the smallest circumference between the ribs and iliac crest. For obese participants with no natural waistline, waist circumference was measure at the level of the navel. Hip circumference was taken around the maximal girth of the hips. Total serum cholesterol, LDL-, and HDL-cholesterol, triglycerides (TG), and glucose levels were

determined by Shimadzu CL-8000 Automatic Chemical Analyzer in the hospital laboratory. Blood samples were drawn using a vacutainer tube in the morning after an overnight fast. The interview and all examinations above were conducted in Guangzhou No. 12 Hospital according to the "Guangzhou Biobank Cohort Study" standard operating procedures prepared by the collaborators.

The International Diabetes Federation (IDF) metabolic syndrome definition (April, 2005) was used to diagnose MS.[11] Participants were classified as having the MS if their waist circumference was ≥90cm for men, or ≥80cm for women, plus any two of the following four factors: a) raised TG level: 1.7 mmol/L, or specific treatment for this lipid abnormality; b) reduced HDL-cholesterol: <1.03 mmol/L in males or <1.29 mmol/L in females, or specific treatment for this lipid abnormality; c) raised blood pressure: systolic BP ≥130 mm Hg, or diastolic BP ≥85 mm Hg, or treatment of previously diagnosed hypertension; d) raised fasting plasma glucose ≥5.6 mmol/L, or previously diagnosed type 2 diabetes.

Statistical analyses

ANCOVA was used to compare age-adjusted means of continuous variables. Linear regression was used to assess the linear trend. The regression coefficient per unit increase was used to assess the change in the dependent variable for 1 live birth or pregnancy. Logistic regression was used to estimate odds ratios and adjusted prevalence for dichotomous variables. In the multivariate model, adjustments were made for the following variables: age; socioeconomic factors including education (no formal school, primary school, junior middle school, senior school, senior technical school, university or above), occupation (agriculture & related workers, factory worker, administrator, sales & service worker, professional, military/disciplined services, house wife/ husband, unemployed), marital status (married, separated/divorced, widowed, never married) and household income (RMB

Yuan <5000, 5000-9999, 10000-19999, 20000-29999, 30000-49999, >50000); lifestyle factors including smoking status (never, ever), drinking status (never, ever), and moderate physical activity (no activity, ≤30 minutes/day, 31-60 minutes/day, ≥60 minutes/day); other reproduction associated factors including age at menarche, age at menopause, age at first pregnancy, use of contraceptive pills (never, ever). For the models which included the adjustment of reproduction associated factors (age at first pregnancy), the single birth or pregnancy group was treated as the reference group instead of zero birth group or zero pregnancy group, because the variable age at first pregnancy was not available for most participants in the zero birth group and all participants in the zero pregnancy group. Triglyceride and glucose levels were log normally distributed. Their geometric means were presented in the tables, and natural log values were used in the regression models. Stata 8.2 for Windows was used for all analysis.

Results

A total of 7352 women and 3065 men aged 50 to 93 years were recruited, of whom 10370 (99.5%) had data describing their reproductive history or for males that of their partner(s) included in this analysis, and the mean (SD) age was 63.97 (6.04) and 66.19 (5.78) years, respectively. In women, the median, and mean (SD) number of births was 3 and, 2.92 (1.37) with a range of 0 to 10 births, and the median, and mean number of pregnancies (SD) was 4 and, 4.29 (1.86) with a range of 0 to 19 pregnancies. In men, the mean (SD) number of live births was 2.64 (1.27) with a range of 0 to 10 births. The distribution of births for both women and men were similar. Nulliparous women (135) constituted 1.84% and no pregnancy group (125) formed 1.66% of women. Thirty nine (1.28%) men were childless. 89.07% of women and 85.19% of men had 2 or more children. A total of 2.38% of women had never breast fed their children; 24.81% women had miscarriage and 69.92% women

had termination of pregnancy; 16.66% women had used contraceptive pills and 33 women had used hormone replacement therapy. A total of 2301 (31.62%) women and 475 (15.6%) men were diagnosed as having the MS. Prevalences of relevant morbidities, such as hypertension and diabetes, were similar to recent, representative samples in China, with hypertension being present in 42.1% of men and 43.2% of women aged 55-64 years in the cohort compared with 40.7% and 38.9% in the same age group nationally in urban areas.[12] Similarly, diabetes was present in 11.9% of men and 14.7% of women aged 55-64 years in the cohort compared with 12.1% and 12.9% in the same age group nationally.[13] The demographic characteristics of the participants are shown in table 1.

Socioeconomic and lifestyle factors

Increasing births were significantly associated with education and occupation (all p values <0.001). Participants with primary level education and manual occupation tended to have a greater number of births in both women and men (Tables 2 and 3). Similar associations between gravidity and the socioeconomic factors were found in the women (data not shown).

In women, there was a linear association between the number of births and smoking (p <0.001), but no significant association was identified for drinking (p=0.49). Both prevalence of smoking and drinking increased with an increasing number of pregnancies (p<0.001 and p=0.004). In men, both prevalence of smoking and drinking increased with a higher number of births (p<0.001 and p=0.021 respectively). Births and pregnancies were not associated with moderate physical activity in either gender (Tables 2 and 3).

Reproduction associated factors

Increasing births were associated with older age of menarche, younger age at first pregnancy, more

pregnancy terminations and longer duration of breast feeding (p values range from <0.001 to 0.019), but were not associated with age at menopause, miscarriage or use of contraception pills (table 2). Gravidity had a strong linear association with all reproduction associated factors (p values ranged from <0.001 to 0.0018).

Metabolic syndrome component risk factors

In women, age-adjusted systolic and diastolic blood pressures had strong linear associations with increasing pregnancies and births, but the association was not significant after full adjustment. Regarding the risk of obesity, increasing pregnancies and births were associated higher age-adjusted BMI, and waist-to-hip ratio (all p<0.001). There was no association between BMI and pregnancy after full adjustment, while other associations remained significant. Age-adjusted total, HDL-, LDL-cholesterol were negatively and triglycerides were positively associated with pregnancies and births (p values ranged from <0.001 to 0.040). Except for triglycerides, the other associations were not significant after full adjustment (Tables 2 and 4), whereas age-adjusted fasting glucose was not significantly associated with births, but was significant after full adjustment. In men, only age-adjusted mean BMI and systolic blood pressure were associated with the number of births, but they disappeared after adjusting for other factors. No significant associations were found between other metabolic risk factors and births (Tables 3 and 4). The age-adjusted means, prevalence of MS risk factors and potential confounders by gravidity in women were similar to those described in table 2 for parity (data not shown).

Prevalent MS

The age-adjusted and fully adjusted prevalence of MS by pregnancies and births are shown in figure

1. In women, there was an ascending linear trend between pregnancies and births [odds ratio change per birth 1.16 (95%CI 1.11-1.22), <0.001] and age-adjusted prevalent MS, but the gradient for births was steeper than that for pregnancies [odds ratio change per birth 1.11 (95%CI 1.06-1.16), <0.001], which was consistent with those for the other risk factors described above. After adjustment for a range of potential confounding factors including age, socioeconomic factors, lifestyle and other reproductive factors the odds ratios of prevalent MS for pregnancies and births remained significant, as shown in table 4. Even after additional adjustment for BMI, the relationship remained significant for both (Table 4 and figure 1). In men, the relationship between their partner's births and MS was less evident [odds ratio change per birth 1.07 (95%CI 0.97-1.17), p=0.16] and was not significant.

Discussion

To our knowledge, this is the first study assessing the association between prevalent MS and the number of live births. We found some consistent associations between pregnancies and births with the MS and associated cardiovascular risk factors in Chinese women. Women with a higher number of pregnancies and births had a higher prevalence of the MS, with the association of births being stronger than that for pregnancy. Adjustment for socioeconomic and lifestyle factors had little effect on the odds ratios. As MS components are well documented risk factors for cardiovascular disease,[14] and people with MS are more likely to develop cardiovascular disease,[15-18] our results are consistent with most large studies describing the association between births and cardiovascular disease.[9,10,19,20]

Most previous studies found a modest relationship between births and BMI, and an increased trend of greater upper body fat distribution with an increasing number of births in women.[1,3] Our

findings are consistent with these results, and show that increasing births results in increased BMI and this may, in part, explain the increase in prevalent MS. The extent of the increase in obesity with the number of births varies in different ethnic groups, with Lawlor et al reporting that age-adjusted BMI increased by 0.36 with per child increase in British women, which is greater than that in our women (0.24). Similarly, each live birth in our women was associated with 0.45 kg, which was quite similar to that in US women who gained 0.55 kg per live birth.[21] However, central obesity appeared more closely associated with births in the current study than that in Lawlor's study (waist-hip ratio 0.0063 vs 0.003 per child).[9] The associations between births and blood pressure, and lipids in our study are consistent with most previous studies.[2,4,5,7,8] The relationship between births and glucose level is less clear,[5,22,23] although in the current study, after adjustment, the association was significant. However, weight gain does not account for all the association as even after adjustment for BMI, a relationship exists between births and prevalent MS, suggesting additional changes may have occurred. The presence of gestational diabetes or preeclampsia may contribute to the development of components of the metabolic syndrome.[24] However, data regarding the status of these conditions in the subjects during pregnancy are not available.

Although we aimed to study the association between pregnancies and births and MS in Chinese women, a crucial issue is whether the observed relationship between the syndrome and reproduction was due to biological processes initiated by conception, or whether other mechanisms are involved,[25] such as sociodemographic or lifestyle factors in response to the pregnancy or upbringing of children. Our results showed that lower education and occupation was associated with a greater number of pregnancies and births in women and men for the latter. These socioeconomic factors were also associated with increased smoking and alcohol consumption, apart from the latter in females, which therefore correlated with a higher number of pregnancies and births. However,

adjustment for these factors did not change the association between pregnancies and births and the MS. It is difficult to discount entirely the role of unmeasured confounding factors. Socioeconomic status may not have been adequately controlled for by statistical adjustment for education and income.[5] The same problems may apply to lifestyle risk factors. We analyzed the data describing the men in the same way and found no relationship between births and MS and associated vascular risk factors, despite the broadly similar living background shared with the women in the study. The women showed greater effect of births than pregnancies on MS. Although births were highly correlated with pregnancies, theses two factors are not interchangeable as the latter included abortions. The duration of childbearing and the intensity of the hormonal effects of pregnancy would be less than that for a completed birth, and may explain the weaker effect of pregnancies on MS compared to that for live births. These results strongly suggest that there are some biological reproductive effects influencing MS and associated cardiovascular risks which persist in later life in Chinese women. The effect was unlikely due to lifestyle or sociodemographic factors.

Conclusions drawn from our cross-sectional design may be limited by possible biases. Survival bias (if those with a greater number of pregnancies and births had increased risk of premature death) would lead to underestimation of the strength of association between pregnancies or births and MS. Self-reporting of pregnancies or births could be subject to recall error. Some pregnancy losses are clinically unrecognized and not recalled.[5] However, live births are more likely to be fully recalled than pregnancies. The similarity of the distribution of the number of children for men and women, and the similar results by pregnancies and births, suggest that recall error would not have substantially biased our results. Our subjects are unlikely to be completely representative of the older population of Guangzhou, and in common with any older study population in a developing country they are survivors. Thus, caution is needed to infer population prevalences from this study.

However investigation of relationships within the study will only be biased if the probability of inclusion within the study varies according to the outcome of interest within levels of a predictor, which is unlikely, and there is no reason to think that any of these groups would have been more or less susceptible to the effects of parity or gravidity on vascular risk factors. Moreover, if survivorship were an issue we might expect different relationships in the older than the younger subjects, which was not apparent. The strengths of our study included: a) the large sample size; b) the criteria of MS were determined by physical and laboratory measurements and not by self-reporting; c) the comparison of MS-pregnancy association with MS-births in women and d) the analysis of the birth data in men showing that the result is more likely due to biology than lifestyle.

In the present study, the no births and infertility rate were 1.84% and 1.66% respectively in our Chinese women, and the childlessness rate in our Chinese men was 1.28%, which are lower than those of other populations (3%) with little disease.[26] These are consistent with the strong Chinese culture preference for marriage and childbearing and the societal stigma associated with childlessness, and are supported by Liu et al's report of primary infertility overall in Chinese being 1.3%,[27] and the 1997 National Population and Reproductive Health Survey which showed that zero parity and zero gravidity rates were 2.23% and 1.56% respectively among women (urban) aged 45-49 years.[28]

We did not include miscarriage, termination of pregnancy and the duration of breast feeding in the multivariate model. Obviously increasing pregnancies and births will increase these factors and there seems to be no biological mechanisms to suggest that they are associated with the MS. Including these variables would result in over adjustment and under-estimation of the association between reproduction and the MS and associated cardiovascular risk factors. Further studies to examine the effect of lost pregnancy and breast feeding on the MS may be warranted.

In summary, higher pregnancies or births was associated with a consistent increase in the risk of MS in Chinese women even after adjustment for a range of potential confounders. As no association was found in men between births and the MS, the association with MS in women is likely to represent a biological response to pregnancy. Since 1980s, the Chinese government had implemented the one child policy strictly and the proportion of single birth women should have been increasing quickly. It should be interesting to assess whether such changes in reproduction pattern have any effect on the MS in the near future. Moreover, further research on whether parity could be an explanation for variation in MS in women and in sex ratio of MS in different populations is warranted.

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Table 1 Demographic characteristics of the Guangzhou Biobank Cohort Study participants

	Male (n=3052)		Female (n=7318)		Total (n=10370)	
	Frequency	%	Frequency	%	Frequency	%
Age(years)						
50-59	494	16.2	2242	30.7	2736	26.4
60-69	1713	56.1	3827	52.3	5540	53.4
70+	845	27.7	1249	17.1	2094	20.2
Education						
No formal school	84	2.7	1246	17.0	1336	12.8
Primary school	891	29.2	2950	40.3	3841	37.0
Junior middle school	882	29.0	1619	22.1	2501	24.1
Senior/ middle technical/ technical	632	20.7	1097	15.0	1729	16.7
Senior technical school / college	261	8.6	233	3.2	494	4.8
University	301	9.8	173	2.4	474	4.6
Occupation*						
Agriculture & related workers	145	4.8	926	12.7	1071	10.3
Factory worker	1154	37.8	3619	49.5	4773	46.0
Administrator / manager	882	28.9	917	12.6	1799	17.4
Sales & service workers	548	18.0	847	11.6	1395	13.5
Professional / technical	134	4.4	618	8.4	752	7.3
Military / disciplined services	69	2.3	7	0.1	76	0.7
House wife / husband	0	0	74	1.0	74	0.7
Other	120	3.9	310	4.2	430	4.2
Marital status						
Married	2821	92.5	5194	71.0	8015	77.3
Separated / divorced	28	0.9	107	1.5	135	1.3
Widowed	194	6.4	1989	27.2	2183	21.1
Never married	8	0.3	26	0.4	34	0.4
Household income (Yuan; US$1=8.01Y)						
<5,000	22	1.0	98	2.1	120	1.8
5,000-9,999	100	4.6	497	10.6	597	8.7
10,000-19,999	457	20.8	1100	23.4	1557	22.6
20,000-29,999	695	31.7	1275	27.1	1970	28.6
30,000-49,999	535	24.4	1034	21.9	1569	22.8
≥50,000	383	17.5	698	14.8	1081	15.7
Smoking (Ever, %)	1762	57.8	388	5.3	2150	20.7
Drinking (Ever, %)	2193	71.9	2685	36.6	4878	47.0
Moderate activity						
≤30minutes/day	813	26.7	1871	25.5	2684	25.9
31-60 minutes/day	445	14.6	1648	22.5	2093	20.2
≥60 minutes /day	362	11.9	1165	15.9	1527	14.7
Body mass index (kg/m^2)						
<18.5	170	5.6	340	4.7	510	4.9
18.5 ≤BMI <23	1168	38.4	2572	35.2	3740	36.2
23 ≤BMI <25.0	752	24.7	1797	24.6	2549	24.7
≥25.0	943	31.3	2590	35.5	3543	34.3
Central obesity	667	22.5	3695	50.1	4362	42.6
Hypertension	1443	47.5	3486	47.7	4929	47.6
Diabetes	398	13.1	1165	16.0	1563	15.1
Metabolic syndrome§	475	15.6	2301	31.6	2776	26.9

* Longest held occupation; central obesity: waist circumference was ≥90cm for men, or ≥80cm for women; hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or drugs for hypertension; diabetes: fasting blood glucose ≥7.0 mmol/L or drugs for diabetes; § IDF definition (April, 2005)

Table 2 Age-adjusted demographic, reproductive parameters, vascular risk factors and components of MS by parity in Chinese women.

	Number of births						Difference per increase of 1 birth*	P for trend
	0	1	2	3	4	≥5		
n	135	665	2365	2035	1221	897		
Age (years)	65.7(64.8,66.3)	60.1(59.7, 60.5)	61.3(61.1,61.5)	64.5(64.2,64.7)	66.8(66.5,67.1)	68.7(68.4,69.1)	2.1(2.0,2.2)	<0.001
Education (>primary, %)	42.3(34.1,50.9)	68.6(64.8,72.2)	56.1(54.0,58.3)	41.1(38.9,43.2)	22.4(20.1,24.9)	11.9(9.8,14.3)	0.6(0.5,0.6)	<0.001
Occupational (non-manual job, %)	35.9(28.0,44.5)	55.5(51.5,59.5)	45.4(43.2,47.7)	33.5 (31.4,35.6)	22.7(20.4,25.2)	12.4 (10.4,14.8)	0.6 (0.6,0.7)	<0.001
Single/ separated (%)	22.2(15.8,30.3)	1.4 (0.8,2.4)	1.5(1.1,2.0)	0.9 (0.6,1.4)	1.0(0.6,1.8)	1.5(0.9,2.8)	0.6(0.5,0.7)	<0.001
Smoking status (ever, %)	4.1 (1.9,8.5)	2.2(1.3, 3.9)	3.7(2.9,4.6)	4.8(3.9,5.8)	5.9(4.7,7.3)	8.0(6.4,9.9)	1.3(1.2,1.4)	<0.001
Drinking status (ever, %)	34.6(27.1, 43.0)	37.9(34.3,41.6)	36.6(34.7,38.6)	36.8(34.7,38.9)	35.0(32.3,37.8)	35.2(32.1,38.4)	1.0(1.0,1.1)	0.49
Moderate activity (%)	54.9(46.4, 63.2)	65.5(61.7,69.1)	65.2(63.1,67.2)	64.5 (62.4,66.5)	63.5(60.7,66.2)	61.3(58.0,64.6)	1.0(0.9,1.0)	0.35
Systolic blood pressure (mm Hg)	133(129,137)	131(130,133)	132(131,133)	133(132,134)	134(133,135)	137(135,138)	1.0(0.5,1.4)	0.001
Diastolic blood pressure (mm Hg)	74(72,75)	72(72,73)	73(73, 74)	74(73, 74)	74(74, 75)	76(75, 77)	0.6(0.4,0.9)	<0.001
Body mass index (kg/m^2)	23.3(22.7,23.8)	23.4(23.1,23.7)	23.8(23.6,23.9)	24.0(23.9,24.2)	24.3(24.1,24.5)	24.3(24.1,24.6)	0.2(0.2,0.3)	<0.001
Waist-to-hip ratio	0.86(0.85,0.87)	0.85(0.85,0.86)	0.86(0.86,0.86)	0.87(0.86,0.87)	0.88(0.87,0.88)	0.88(0.87,0.88)	0.0063(0.0049,0.0076)	<0.001
Weight gain since 18 years (kg)	9.3(7.9,10.7)	9.9(9.3,10.6)	10.7(10.4,11.1)	11.0(10.7,11.4)	11.6(11.2,12.1)	11.7(11.2,12.3)	0.45(0.3,0.6)	<0.001
Total cholesterol (mmol/L)	6.05(5.61,6.49)	6.31(6.10,6.51)	5.98(5.87,6.09)	5.92(5.81,6.04)	5.92(5.77,6.07)	5.93(5.75,6.10)	-0.058(-0.11,-0.0039)	0.036
Triglyceride (mmol/L) †	1.35(1.25,1.48)	1.39(1.32,1.45)	1.42(1.39,1.45)	1.48(1.45,1.51)	1.48(1.43,1.52)	1.51(1.45,1.55)	0.020(0.0098,0.031)	<0.001
HDL-cholesterol (mmol/L)	1.77(1.71,1.83)	1.74(1.71,1.77)	1.75(1.73,1.76)	1.72(1.71,1.74)	1.72(1.70,1.74)	1.72(1.69,1.74)	-0.0085(-0.016,-0.0013)	0.021
LDL-cholesterol (mmol/L)	3.13(3.01,3.24)	3.09(3.04,3.14)	3.09(3.03,3.09)	3.06(3.03,3.09)	3.05(3.01,3.09)	3.03(2.98,3.07)	-0.018(-0.032,-0.0044)	0.0093
Glucose (mmol/L) †	5.87(5.64,6.11)	5.93(5.81,5.99)	5.87(5.81,5.99)	5.93(5.87,5.99)	5.93(5.87,6.05)	5.99(5.87,6.11)	0.0040(-0.00085,0.0089)	0.11
Age at menarche (yrs)	15.4(15.1,15.8)	15.0(14.8,15.1)	14.9(14.8,15.0)	15.5(15.4,15.6)	15.8(15.7,15.9)	16.0(15.9,16.2)	0.3(0.3,0.3)	<0.001
Age at menopause (yrs)	48.6(47.9,49.3)	48.9(48.6,49.2)	49.4(49.2,49.6)	49.2(49.0,49.4)	49.5(49.2,49.7)	49.4(49.2,49.7)	0.1(0.01,0.2)	0.24
Age at first pregnancy (yrs)	27.6(26.3,28.9)	28.2(28.0,28.5)	25.0(24.8,25.1)	23.4(23.3,23.6)	22.5(22.3,22.7)	21.5(21.3,21.7)	-1.45(-1.52,1.38)	<0.001
Miscarriage (ever, %)	59.8(37.7,78.5)	26.59(23.1,30.4)	25.0(23.2,26.9)	23.5(21.7,25.4)	25.8(23.4,8.3)	25.5(22.7,28.5)	1.0(0.9,1.0)	0.57
Termination of pregnancy (ever %)	14.2(4.6,36.1)	58.5(54.3,62.5)	69.8(67.8,71.8)	73.5(71.5,75.4)	72.0(69.4,74.4)	65.6(62.3,68.7)	1.1(1.0,1.1)	0.019
Duration of breast feeding (months)	-	8.3(7.3,9.3)	20.3(19.8,20.8)	33.8(33.3,34.4)	46.9(46.2,47.7)	62.4(61.5,63.3)	13.6(13.3,13.8)	<0.001
Ever use of pills (%)	1.4(0.4, 5.6)	10.2(8.2,12.5)	18.0(16.4,19.7)	16.0(14.5,17.7)	13.9(12.0,16.1)	13.0(10.7,15.6)	1.0(1.0,1.1)	0.43

Values are means and prevalence (95% confidence intervals). All means, prevalence, regressions coefficients and odds ratios are age-adjusted, except for age. *Difference per increase of one birth: for continuous variables, regression coefficients of unit increase in the variables per increase of one birth; for dichotomous variables, odds ratio for increase in one birth. † Geometric means presented: regression coefficients represent increase in logged variable per increase of one birth.

Table 3 Age-adjusted demographic, vascular risk factors and components of MS by parity in Chinese men.

	Number of births						Difference per birth increase*	P for trend
	0	1	2	3	4	≥ 5		
n	39	413	1162	797	390	251		
Age (years)	67.3(65.6,68.9)	62.0(61.5,62.5)	64.7(64.4,65.0)	67.8(67.5,69.5)	69.0(68.5,69.5)	70.2(69.6,70.9)	2.0(1.8,2.2)	<0.001
Education (> primary school, %)	53.9(38.3,68.7)	79.6(75.4,83.3)	76.8(74.3,79.1)	67.4(63.9,70.7)	53.4(48.1,58.6)	35.7(29.7,42.1)	0.6(0.6,0.7)	<0.001
Occupation (non-manual job, %)	36.6(22.7,53.3)	59.4(54.3,64.3)	56.0(53.0,59.0)	54.3(50.4,58.1)	41.4(36.2,46.8)	32.3(26.5,38.7)	0.8(0.7,0.9)	<0.001
Single/ separated (%)	20.3(10.3,36.1)	1.7(0.8,3.6)	0.5(0.2,1.1)	1.1(0.6,2.2)	1.3(0.5,3.1)	0.4(0.05,2.80)	0.53(0.38,0.75)	<0.001
Smoking status (ever, %)	65.1(49.1,78.4)	51.2(46.3,56.1)	56.7(53.8,59.5)	61.0(57.4,64.4)	61.8(56.7,66.6)	71.3(65.3,76.6)	1.1(1.1,1.3)	<0.001
Drinking status (ever, %)	55.4(39.8,70.1)	69.7(64.9,74.0)	73.9(71.3,76.3)	73.0(68.6,75.1)	72.2(67.4,76.5)	79.5(74.0,74.1)	1.1(1.0,1.2)	0.021
Moderate activity (%)	62.9(46.8,76.6)	48.7(43.8,53.7)	53.9(51.1,56.8)	55.3(50.1,60.5)	55.3(50.1,60.5)	48.4(41.9,54.9)	1.0(0.9,1.1)	0.76
Systolic blood pressure (mm Hg)	137(130,144)	134(132,136)	134(133,136)	135(134, 137)	137(135,139)	138(135,141)	0.98(0.23,1.72)	0.010
Diastolic blood pressure (mm Hg)	77(73,80)	76.4(75,78)	77(76,78)	77(76,78)	78(76,79)	78(77,80)	0.37(-0.023,0.77)1	0.065
Body mass index (kg/m^2)	24.1(23.1,25.1)	23.5(23.14,23.78)	23.4(23.3,23.63)	23.5(23.3,23.8)	23. 5(23.1,23. 8)	23.8(23.4,24.3)	0.045(-0.062,0.15)	0.041
Waist-to-hip ratio	0.93(0.91,0.95)	0.90(0.89,0.91)	0.90(0.90,0.90)	0.90(0.90,0.91)	0.91(0.90,0.91)	0.91(0.90,0.92)	0.0023(0.0000079,0.0045)	0.050
Weight gain since 18 years (kg)	10.7(8.1,13.3)	10.7(9.9,11.6)	10.6(10.2,11.1)	10.2(9.6,10.8)	9.7(8.8,10.5)	11.3(10.2,12.4)	-0.08(-0.4,0.2)	0.60
Total cholesterol (mmol/L)	5.66(5.32,6.00)	5.56(5.45,5.67)	5.56(5.50,5.62)	5.49(5.41,5.56)	5.44(5.33,5.55)	5.54(5.40,5.68)	-0.026(-0.063,0.011)	0.16
Triglyceride (mmol/L) †	1.51(1.27,1.77)	1.36(1.30,1.45)	1.31(1.27,1.35)	1.34(1.28,1.38)	1.34(1.26,1.41)	1.35(1.26,1.43)	-0.0039(-0.022,0.014)	0.67
HDL-cholesterol (mmol/L)	1.56(1.45,1.67)	1.54(1.51,1.58)	1.59(1.57,1.61)	1.56(1.53,1.58)	1.57(1.53,1.60)1	1.55(1.51,1.60)	-0.0025(-0.015,0.0095)	0.68
LDL-cholesterol (mmol/L)	2.80(2.61,2.99)	2.86(2.80,2.92)	2.85(2.82,2.89)	2.80(2.76,2.84)	2.78(2.72,2.84)	2.85(2.78,2.93)	-0.012(-0.033,0.0077)	0.23
Glucose (mmol/L) †	6.11(5.76,6.55)	5.81(5.70,5.93)	5.81(5.76,5.87)	5.87(5.81,5.93)	5.87(5.70,5.99)	5.70(5.59,5.87)	-0.0029(-0.0098,0.004)	0.41

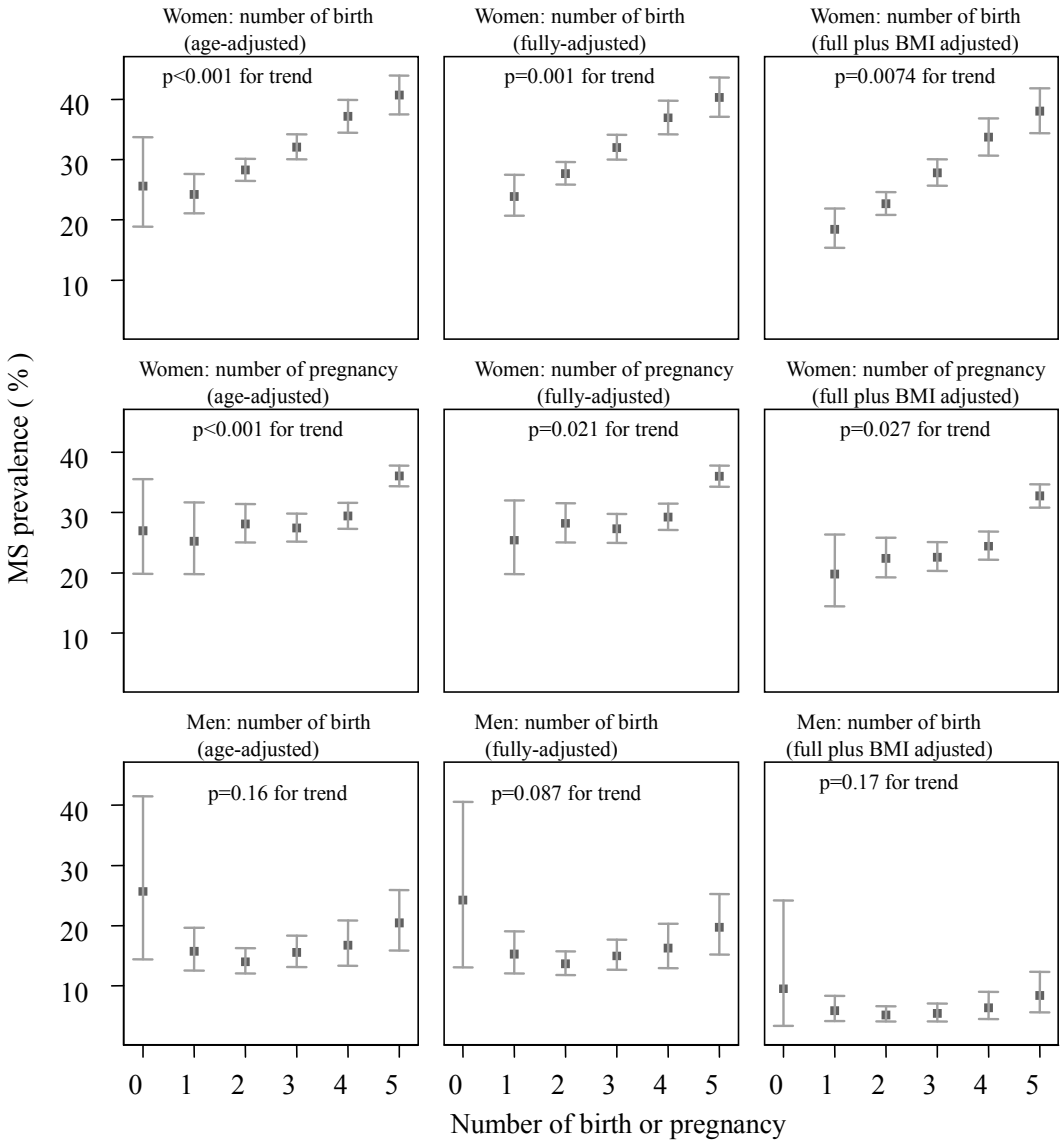
Values are means and prevalence (95% confidence intervals). All means, prevalence, regressions coefficients and odds ratios are age-adjusted, except for age. *Difference per increase of one birth: for continuous variables, regression coefficients of unit increase in the variables per increase of one birth; for dichotomous variables, odds ratio for increase in one birth. †Geometric means presented: regression coefficients represent increase in logged variable per increase of one birth.

Table 4 Association between MS and its component risk factors and pregnancies and births after fully adjusting confounders* in Chinese

	Women						Men		
	n†	Difference per increase of 1 birth**	*P* for trend	n†	Difference per increase of 1 pregnancy**	*P* for trend	n†	Difference per increase of 1 birth**	*P* for trend
Systolic blood pressure (mm Hg)	6915	0.25 (-0.36,0.87)	0.42	6920	-0.022 (-0.54,0.50)	0.56	3019	0.66 (-0.14,1.47)	0.11
Diastolic blood pressure (mm Hg)	6915	0.17 (-0.14, 0.49)	0.29	6920	0.055 (-0.21,0.32)	0.69	3017	0.22 (-0.21, 0.65)	0.31
Body mass index (kg/m^2)	6912	0.11 (0.02, 0.21)	0.018	6917	0.060 (-0.02,0.14)	0.14	3019	0.076 (-0.039, 0.19)	0.20
Waist-to-hip ratio	6914	0.0035 (0.0017, 0.0053)	<0.001	6919	0.0026 (0.0011, 0.0041)	0.001	3018	0.0016 (-0.00089, 0.0040)	0.21
Triglyceride‡ (mmol/L)	6925	0.017 (0.0024, 0.030)	0.021	6930	0.022 (0.010, 0.034)	<0.001	3025	-0.00031 (-0.019, 0.019)	0.97
HDL-cholesterol (mmol/L)	6925	-0.0042 (-0.014, 0.0055)	0.39	6930	-0.0084 (-0.017, -0.00019)	0.045	3025	-0.00076 (-0.012, 0.014)	0.91
Glucose‡ (mmol/L)	6925	0.0069 (0.00052, 0.013)	0.034	6930	0.0042 (-0.0013, 0.0096)	0.132	3025	-0.00025 (-0.0078, 0.0073)	0.95
Metabolic syndrome*	6865	1.11 (1.05,1.18)	0.001	6891	1.06 (1.01,1.12)	0.021	3014	1.09 (0.99,1.21)	0.087
Metabolic syndrome§	6859	1.10 (1.03,1.18)	0.0074	6885	1.07 (1.01,1.14)	0.027	3014	1.09 (0.96,1.25)	0.17

*adjusted variables for women include: age, socioeconomic factors (education, occupation, house income and marital status), lifestyle factors (smoking, drinking and physical activity), reproduction associated factors (age at menarche, age at menopause, age at first pregnancy, use of contraceptive pills). Adjust variables for men include: age, socioeconomic factors (education, occupation, house income and marital status), lifestyle factors (smoking, drinking and physical activity). §Adjusted for the above factors and BMI. †Number of participants with complete data on all variables included in the fully adjusted model. ‡Regression coefficients represent increase in logged variable per increase of one pregnancy or birth. ** Difference per increase of one birth (pregnancy): for MS components, regression coefficients of unit increase in the variables per increase of one birth (pregnancy); for the MS, odds ratio for increase in one birth (pregnancy).

Figure 1 Age-adjusted and fully-adjusted MS prevalence (95% confidence intervals) by births and pregnancies in Chinese females and births from partners of the males.


Women: number of birth
(age-adjusted)
p<0.001 for trend
Women: number of birth
(fully-adjusted)
p=0.001 for trend
Women: number of birth
(full plus BMI adjusted)
p=0.0074 for trend
Women: number of pregnancy
(age-adjusted)
p<0.001 for trend
Women: number of pregnancy
(fully-adjusted)
p=0.021 for trend
Women: number of pregnancy
(full plus BMI adjusted)
p=0.027 for trend
Men: number of birth
(age-adjusted)
p=0.16 for trend
Men: number of birth
(fully-adjusted)
p=0.087 for trend
Men: number of birth
(full plus BMI adjusted)
p=0.17 for trend
MS prevalence (%)
10
20
30
40
0 1 2 3 4 5
Number of birth or pregnancy