



BMJ Open Association between leisure sedentary behaviour and uterine fibroids in non-menopausal women: a population-based study

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ABSTRACT

Objective Sedentary behaviour is associated with a variety of adverse health outcomes, including obesity, oestrogen metabolism and chronic inflammation, all of which are related to the pathogenesis of uterine fibroids (UFs). This study aimed to explore the relationship between leisure sedentary time (LST) and UFs.

Design Cross-sectional.

Setting We conducted a cross-sectional analysis of data from patients from the Yunnan region in the China Multi-Ethnic Cohort Study.

Participants A total of 6623 non-menopausal women aged 30–55 years old were recruited. Menstrual status was self-reported. Participants who lacked a unique national identity card, suffered from serious mental illness, did not have a clear diagnosis of UFs, or provided incomplete information were excluded.

Primary and secondary outcome UFs were diagnosed by abdominal B-ultrasound. Leisure sedentary behaviour was assessed by using a face-to-face questionnaire interview. Logistic regression and restricted cubic spline were employed to explore the relationship between LST and UFs.

Results A total of 562 participants had UFs, with a prevalence rate of 8.5% (7.8%, 9.2%). Multivariate adjusted logistic regression analysis showed that the risk of UFs in women with LST \geq 6 hour/day was 2.008 times that in women with LST<2 hour/day (95% CI 1.230 to 3.279). The restricted cubic spline results showed that there was a linear dose–response relationship between LST and UFs (p for non-linearity>0.05). According to the results of the stratified analysis for menstrual status and body mass index (BMI), there was a correlation between LST and the prevalence of UFs only in women with a BMI<24 kg/m² or perimenopause.

Conclusion LST was independently associated with the prevalence of UFs, and a linear dose–response relationship was observed. Our study provides evidence on the factors influencing UFs, and further research is needed to propose feasible measures for UFs prevention.

INTRODUCTION

Uterine fibroids (UFs) are the most common benign tumours in women of childbearing

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The large sample size and good quality control are strengths of the study.
- ⇒ The cross-sectional design of the study prevented us from explaining causality, which is one of the limitations of this study.
- ⇒ The information was collected based on face-to-face questionnaires, so recall bias is inevitable.
- ⇒ Although we adjusted for potential confounding factors as much as possible, it is inevitable that there are unadjusted confounders that affected the results.

age. They are composed of smooth muscle and connective tissue and are also called uterine leiomyomas. A literature review indicates that the prevalence of UFs varies from 4.5% to 68.8%.¹ Patients with UFs may be asymptomatic² or may exhibit abnormal bleeding, pain in the pelvic and abdominal organs, adverse reproductive outcomes of infertility, and so on, which have a moderate to severe impact on women's quality of life.^{3–6} UF is still the main indication for hysterectomy in Chinese women, which not only causes damage to the human body but also places economic burdens on people.⁷

The incidence of UFs varies in different age groups, with the highest incidence of UFs in the 40–50 years old age group.⁸ Obesity and weight gain after the age of 18 are risk factors for UFs.^{9–11} However, the risk of UFs can be reduced by a late age at menarche, late age at first birth, parity, oral contraceptives, etc.^{12–14} Although existing studies have shown that physical activity (PA) can reduce the risk of UFs,^{5 6} sedentary time is now recognised as not only as the absence of PA but also as a distinct set of behaviours. The health implications of sedentary behaviour are distinct

from those related to a lack of exercise.^{15 16} Sedentary behaviour damages the metabolism and increases the risk of all-cause death. At the same time, sedentary behaviour is also associated with oestrogen-dependent tumours, such as endometrial cancer,¹⁷ ovarian cancer^{18 19} and breast cancer.²⁰ UFs are also oestrogen-dependent tumours.²¹ Recent findings suggest that television (TV) viewing time (a subdomain of leisure sedentary behaviour) may be independently associated with adverse health outcomes, such as a higher prevalence of diabetes, cardiovascular disease and all-cause mortality, even after adjusting for PA.^{22 23} At present, the relationship between UFs and leisure sedentary behaviour is unclear. Yunnan Province is located in southwest China, with a unique geographical environment and multiethnic characteristics. Ethnic groups represent not only a diversity of genes but also diverse characteristics of the daily lifestyle. Therefore, it is necessary to explore the relationship between UFs and leisure sedentary behaviour.

MATERIALS AND METHODS

Study population and participant selection

The data were taken from the baseline survey of the Yunnan cohort of the China Multi-Ethnic Cohort Study, which is a prospective community-based cohort study in southwest China. A detailed description of the study design, sampling strategy and baseline characteristics on the cohort has been published previously.²⁴ In short, 99 556 participants from five provinces (including Tibet, Sichuan, Yunnan, Guizhou and Chongqing) in Southwest China were recruited. The sample in this study was obtained from community-based populations in the Yunnan Province by using a multistage stratified cluster sampling method. In the first phase, four ethnic minority settlements (Wuding, Yongren, Heqing and Yongsheng counties) were selected as our study sites, mainly including the Yi, Bai, and Han ethnic groups. In the second phase, we selected 2–8 communities in each region based on community size. Finally, participants who met the inclusion and exclusion criteria were invited to participate in our study. The inclusion criteria: (a) non-menopausal women aged 30–55 years on the day of the survey and (b) being a resident of the survey site for generations and able to complete the baseline survey as well as the follow-up study. Exclusion criteria: (a) unable to provide a unique national ID card; (b) suffering from severe mental illness (such as schizophrenia and bipolar disorder) and (c) refusing to comply with the study requirements.

A total of 7224 non-menopausal women aged 30–55 years in Yunnan Province were initially included. We further excluded 327 participants for the following reasons: failure to undergo normal B-ultrasound examination, B-ultrasound examination indicating an unclear uterus or hysterectomy, failure to achieve a clear diagnosis (including possible/suspected UFs) and B-ultrasound examination indicating pregnancy. In addition, 15 people who lacked information about leisure sedentary time

(LST) were also excluded. Finally, people with unreasonable dietary intake (energy intake <600 or >3500 kcal/day (n=139)) or lack of information about other covariates (n=120) were excluded. The final sample consisted of 6623 participants, and more details are shown in online supplemental figure 1.

Measurements

Trained investigators collected basic information such as social demographics, menstrual history, birth history, contraceptive use, leisure sedentary behaviour, PA and diet through face-to-face interviews with the participants using electronic questionnaires. After the questionnaire was completed, a physical examination (height, weight) and abdominal B-ultrasound examination (gynaecological examination requiring holding urine) were carried out. These examinations were completed by doctors who had obtained the qualification certificate of licensed doctors and received standardised training to ensure the accuracy of the data. When measuring height and weight, participants were required to wear light clothes without socks and shoes, and the results were accurate to 0.1 cm and 0.1 kg, respectively.

Definition of UFs

The patients included in this study were defined as those with UFs based on a joint diagnosis using B-ultrasound results conducted by two experienced doctors who specialise in the field. Additionally, individuals diagnosed as UFs by health institutions at township level or above were also included. However, those who had undergone hysterectomy were excluded because we were unable to ascertain whether their hysterectomy was due to UFs, as they were not specifically asked about the reasons for undergoing hysterectomy during the survey. We used the B-ultrasound diagnosis results to define UFs because numerous studies have demonstrated that ultrasound is the primary imaging examination method for UFs, offering high sensitivity and specificity in diagnosing leiomyomas.^{13 25 26} During B-ultrasound examination, UFs typically appear as well-defined solid, concentric, hypoechoic masses that can cause varying degrees of acoustic shadowing. However, depending on the level of calcification and/or the amount of fibrous tissue present, UFs may exhibit different echogenicity, usually being hyperechogenic or isoechoic.²⁵

Leisure sedentary behaviour assessment

Sedentary behaviour refers to awake behaviour characterised by energy consumption ≤ 1.5 metabolic equivalent task (MET) when sedentary, reclining or lying down. Screen time and sedentary time are usually the two main indicators used to quantify sedentary behaviour time.²⁷ We used questionnaires to collect the time spent by participants in activities such as chess, mobile phones, tablets, TV, books, newspapers, knitting and other activities and used the results to quantify the time spent in leisure sedentary behaviour, which was defined as LST. Then the

participants were divided into four groups according to LST: <2 hour/day, 2–3.99 hour/day, 4–5.99 hour/day and ≥6 hour/day.

Covariates

We identified the following covariates: age (30–39 years, 40–49 years, ≥50 years old), occupation (farmer, non-farmer), marital status (married/cohabiting, widowed, separated/divorced), education level (primary school and below, middle school, college and above), menstrual status (premenopause, perimenopause), age at menarche (≤12 years, 13–16 years, ≥17 years), number of live births (1, ≥2), age at first live birth (<20 years, 20–24 years, ≥25 years), time since last live birth (≤12 years, 13–17 years, 18–22 years and ≥23 years), and contraceptive use (whether the participants took contraceptives at all times before the survey). Premenopause includes regular and irregular menstruation. Regular menstruation is a periodic activity with an average of approximately 28 days during the menstrual period. The general blood output is 20–60 mL, and the cycle lasts for 2–8 days. Irregular menstruation is an abnormal menstrual disorder. Perimenopause refers to the period within 1 year after a woman's last menstrual period.

The types and duration of activities related to work, commuting, housework and leisure time exercise of participants in the past year were collected by a developed questionnaire. We divided PA into professional PA, traffic PA, leisure PA and housework PA. We used the MET value for a given type of PA multiplied by the hours spent on that activity per day and summed the results for all activities to calculate the metabolic equivalent of 1 day of PA. Participants were divided into three groups according to PA (MET-hour/day): <27.35 MET-hour/day, 27.35–44.98 MET-hour/day and ≥44.99 MET-hour/day. The semiquantitative food frequency questionnaire was used to collect dietary information, including the quantity and frequency of intake of each food group, as well as information on edible oil and salt, and then the total energy intake per day was estimated according to the China Food Exchange list and the 2018 China Food Composition Table. Body mass index (BMI) was calculated by dividing weight (kg) by height (m²). BMI was divided into two groups: <24 kg/m² (normal weight) and ≥24 kg/m² (overweight or obesity).

Statistical analysis

Classification variables were expressed as frequencies and percentages, and continuous variables that did not conform to a normal distribution were expressed as M (P₂₅, P₇₅). The χ^2 test was used to analyse whether the prevalence of UFs was different among different basic characteristics. At the same time, univariate logistic regression was carried out to determine which factors were associated with UFs. Multivariable adjusted logistic regression was used to analyse the relationship between LST and UFs. According to the literature, potential covariates were selected, and three models were constructed. In model

1, no adjustment was made. Model 2 was adjusted for age, marital status, education level, occupation, BMI and ethnicity. Model 3 was further adjusted for age at first live birth, age at menarche, number of live births, time since last live birth, menstrual status, use of contraceptives and PA. The ORs and its 95% CI were used to estimate the correlation strength. The dose–response relationship between LST (hour/day) and UFs was explored with a restricted cubic spline, also adjusted for the covariates included in model 3. At the same time, because BMI and menstrual status are important confounding factors, stratified analysis was conducted to compare the relationship between LST and UFs in different BMI groups and different menstrual status groups. After excluding 165 patients who reported that they had been diagnosed with hypertension, diabetes or hyperlipidaemia by doctors, we conducted a sensitivity analysis. Since the time interval between their first diagnosis and the investigation was less than or equal to 1 year, their lifestyle may have been significantly changed due to these chronic diseases, such as increasing exercise and reducing sedentary time, which would have an impact on the research results.

All analyses were performed using IBM SPSS V.26.0 and R V.4.2.1 software. A two-tailed $p \leq 0.05$ was considered statistically significant.

Patient and public involvement

Patients and the public were not involved in the design of the study, the conduct of the study or the dissemination of the findings.

RESULTS

A total of 6623 participants aged 30–55 years were included in this study, 562 of whom suffered from UFs, with a prevalence rate of 8.5% (7.8%, 9.2%). Among the 6623 women, the proportions of those aged 40–49, married/cohabiting, with a primary school education and below and farmers were 58.5%, 96.1%, 63.0% and 69.6%, respectively. In addition, the proportions of participants with normal BMI, those not taking contraceptives and those in premenopause were 62.4%, 90.1% and 86.6%, respectively. The age at first live birth and age at menarche of most participants were in the 20–24 age group (72.1%) and the 13–16 age group (73.9%), respectively, and 82.4% of the participants had more than two live births. For LST, most participants were in the 2–3.99 hour/day group (60.8%) (table 1).

The χ^2 test was used to compare the prevalence of UFs among different demographic characteristics, and the results showed that the prevalence of UFs only varied among the different age groups. The prevalence of UFs increased with age, and the prevalence rate was the highest in the ≥50 years group, followed by the 40–49 years group and the 30–39 years group ($p < 0.017$) (table 2). The univariate logistic regression analysis showed that BMI, number of live births, menstrual status, time since last live birth, PA and LST were correlated with the prevalence

Table 1 Basic characteristics of the study population

Variables	Group	Han (n=2954)	Yi (n=1887)	Bai (n=1782)	All participants (n=6623)
Age group (years)	30–39	687 (23.3)	503 (26.7)	332 (18.6)	1522 (23.0)
	40–49	1748 (59.2)	1050 (55.6)	1077 (60.4)	3875 (58.5)
	≥50	519 (17.6)	334 (17.7)	373 (20.9)	1226 (18.5)
Marital status	Married/cohabiting	2832 (95.9)	1810 (95.9)	1720 (96.5)	6362 (96.1)
	Separated/divorced	55 (1.9)	32 (1.7)	29 (1.6)	116 (1.8)
	Widowed	67 (2.3)	45 (2.4)	33 (1.9)	145 (2.2)
Education level	Primary school and below	1727 (58.8)	1128 (59.8)	1320 (74.1)	4175 (63.0)
	Middle school	1059 (35.8)	688 (36.5)	438 (24.6)	2185 (33.0)
	College and above	168 (5.7)	71 (3.8)	24 (1.3)	263 (4.0)
Occupation	Farmer	1893 (64.1)	1454 (77.1)	1265 (71.0)	4612 (69.6)
	Non-farmer	1061 (35.9)	433 (22.9)	517 (29.0)	2011 (30.4)
BMI (kg/m ²)	<24	2013 (68.1)	941 (31.9)	1099 (61.7)	4136 (62.4)
	≥24	941 (31.9)	863 (45.7)	683 (38.3)	2487 (37.6)
Age at first live birth (years)	<20	131 (4.4)	264 (14.0)	64 (3.6)	459 (6.9)
	20–24	1916 (64.9)	1300 (68.9)	1558 (87.4)	4774 (72.1)
	≥25	907 (30.7)	323 (17.1)	160 (9.0)	1390 (21.0)
Age at menarche (years)	≤12	428 (14.5)	129 (6.8)	225 (12.6)	782 (11.8)
	13–16	2248 (76.1)	1360 (72.1)	1284 (72.1)	4892 (73.9)
	≥17	278 (9.4)	398 (21.1)	273 (15.3)	949 (14.3)
No of live births	1	748 (25.3)	279 (14.8)	138 (7.7)	1165 (17.6)
	≥2	2206 (74.7)	1608 (85.2)	1644 (92.3)	5458 (82.4)
Contraceptive use	No	2657 (89.9)	1634 (86.6)	1678 (94.2)	5969 (90.1)
	Yes	297 (10.1)	253 (13.4)	104 (5.8)	654 (9.9)
LST (hour/day)	<2	701 (23.7)	496 (26.3)	472 (26.5)	1669 (25.2)
	2–3.99	1779 (60.2)	1197 (63.4)	1054 (59.1)	4030 (60.8)
	4–5.99	388 (13.1)	168 (8.9)	210 (11.8)	766 (11.6)
Menstrual status	≥6	86 (2.9)	26 (1.4)	46 (2.6)	158 (2.4)
	Premenopause	2558 (86.6)	1678 (88.9)	1501 (84.2)	5737 (86.6)
	Perimenopause	396 (13.4)	209 (11.1)	281 (15.8)	886 (13.4)
Time since last live birth (years)	≤12	782 (26.5)	531 (28.1)	361 (20.3)	1647 (25.3)
	13–17	598 (20.2)	334 (17.7)	422 (23.7)	1354 (20.4)
	18–22	808 (27.4)	490 (26.0)	451 (25.3)	1749 (26.4)
	≥23	766 (25.9)	532 (28.2)	548 (30.8)	1846 (27.9)

Continued

Table 1 Continued

Variables	Han (n=2954)	Yi (n=1887)	Bai (n=1782)	All participants (n=6623)
PA (MET-hour/day)				
<27.35	861 (29.1)	452 (24.0)	870 (48.8)	2183 (33.0)
27.35–44.98	1027 (34.8)	716 (37.9)	509 (28.6)	2252 (34.0)
≥44.99	1066 (36.1)	719 (38.1)	403 (22.6)	2188 (33.0)
Energy (kcal/day)	1857.2 (1510.4, 2245.4)	1454.9 (1164.2, 1783.6)	1893.5 (1553.9, 2268.6)	1746.3 (1407.7, 2152.9)

Data are presented as numbers (%) for categorical variables or M (P25, P75) for continuous variables. BMI, body mass index; LST, leisure sedentary time; PA, physical activity; MET, metabolic equivalent task.

Table 2 Prevalence of UFs in rural Yunnan Province, China

Variables	UFs			P value
	n (N)	%	95% CI	
Age group (years)				
30–39	53 (1522)	3.5	(2.6 to 4.4)	<0.001
40–49*	359 (3875)	9.3	(8.4 to 10.2)	
≥50*†	150 (1226)	12.2	(10.4 to 14.0)	
Marital status				
Married/cohabiting	532 (6362)	8.4	(7.7 to 9.1)	0.172
Separated/divorced	12(116)	10.3	(4.8 to 15.8)	
Widowed	18(145)	12.4	(7.0 to 17.8)	
Education level				
Primary school and below	365 (4175)	8.7	(7.8 to 9.6)	0.564
Middle school	174 (2185)	8	(6.9 to 9.1)	
College and above	23(263)	8.7	(5.3 to 12.1)	
Occupation				
Farmer	371 (4612)	8	(7.2 to 8.8)	0.051
Non-farmer	191 (2011)	9.5	(8.2 to 10.8)	
Ethnicity				
Han	238 (2954)	8.1	(7.1 to 9.1)	0.491
Yi	170 (1887)	9	(7.7 to 10.3)	
Bai	154 (1782)	8.6	(7.3 to 9.9)	

Data are presented as numbers (%) for categorical variables. P values were derived from χ^2 tests.
 *Indicates that there was a difference between the prevalence rate compared with the 30–39 years group.
 †Indicates that there was a difference between the prevalence rate compared with the 40–49 years group.

of UFs. However, no correlation was found with the remaining factors. The specific ORs (95% CIs) are shown in online supplemental table 1.

The ORs and 95% CIs of leisure sedentary behaviour for UFs for all participants are presented in figure 1. In model 1, compared with women with LST<2 hour/day, the ORs (95% CIs) of women with LSTs of 2 to 3.99 hour/day, 4–5.99 hour/day and ≥6 hour/day were 1.013 (0.822 to 1.249), 1.215 (0.903 to 1.636) and 1.936 (1.203 to 3.116), respectively. The adjusted analysis of potential covariates in model 3 showed that LST was positively correlated with the risk of UFs. The risk of UFs in women with LST≥6 hour/day was 2.008 times that in women with LST<2 hour/day (95% CI 1.230 to 3.279). Figure 1 shows that the ORs (95% CIs) of UFs in women aged 40–49 and ≥50 years were 1.875 (1.264 to 2.782) and 2.419 (1.507 to 3.885), respectively, compared with the 30–39 years group. Compared with one live birth, the OR (95% CI) of UFs with ≥2 live births was 0.684 (0.551 to 0.849). Compared with ≤12 years since last live birth, the ORs (95% CIs) of UFs from 13 to 17 years, 18–22 years and ≥23 years since last live birth were 1.756 (1.193 to 2.585), 1.854 (1.246 to 2.760) and 1.972 (1.291 to 3.014), respectively. More details are shown in figure 1.

The restricted cubic spline method found no significant nonlinear relationship between LST and UFs risk in either the rough model or the adjusted model (p for

Variables	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
LST (hour/day)			
<2	Ref.	Ref.	Ref.
2-3.99	1.013(0.822,1.249)	1.022(0.828,1.261)	1.000(0.810,1.235)
4-5.99	1.215(0.903,1.636)	1.223(0.905,1.653)	1.196(0.884,1.618)
≥6	1.936(1.203,3.116)	1.981(1.219,3.221)	2.008(1.230,3.279)
Age group (years)			
30-39		Ref.	Ref.
40-49		2.913(2.166,3.916)	1.875(1.264,2.782)
≥50		4.041(2.917,5.598)	2.419(1.507,3.885)
BMI (kg/m²)			
<24		Ref.	
≥24		1.198(1.004,1.430)	
Occupation			
Farmer		Ref.	
Non-farmer		1.269(1.051,1.532)	
Number of live births			
1			Ref.
≥2			0.684(0.551,0.849)
Time since last live birth (years)			
≤12			Ref.
13-17			1.756(1.193,2.585)
18-22			1.854(1.246,2.760)
≥23			1.972(1.291,3.014)
PA (MET-hour/day)			
<27.35			Ref.
27.35-44.98			1.028(0.836,1.266)
≥44.99			0.783(0.626,0.980)

Figure 1 The relationship between the prevalence of UFs and LST (n=6623). Model 1: no covariates were adjusted; model 2: adjusted for age, marital status, education level, occupation, ethnicity and BMI; model 3: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first live birth, age at menarche, number of live births, time since last live birth, menstrual status, contraceptive use and PA. BMI, body mass index; LST, leisure sedentary time; MET, metabolic equivalent task; PA, physical activity; UFs, uterine fibroids.

non-linearity>0.05), although there was a linear dose-response relationship between them (figure 2).

Stratified analysis of different menstrual statuses showed that LST was not associated with the prevalence of UFs in premenopausal women but was associated with the prevalence of UFs in perimenopausal women. In perimenopausal women, compared with LST<2 hour/day, the ORs (95% CIs) of UFs in women with LSTs of 2–3.99 hour/day, 4–5.99 hour/day and ≥6 hour/day were 0.882 (0.527 to 1.475), 0.773 (0.349 to 1.712) and 5.432 (1.799 to 16.406), respectively. In the stratified analysis of BMI, women with a BMI<24 kg/m² and LST≥6 hour/

day had 2.152 times the risk of UFs compared with women with LST<2 hour/day. However, in women with a BMI≥24 kg/m², there was no correlation between UFs and LST (table 3).

A similar result was observed in the sensitivity analysis as in the main analysis, with an OR (95% CI) of UFs in women with LST≥6 hour/day of 2.049 (1.247 to 3.368) compared with those with LST<2 hour/day (online supplemental figure 2). The restricted cubic spline also showed that there was a linear dose-response relationship between LST and the risk of UFs (p for non-linearity=0.2051) (online supplemental figure 3). Similarly, there was a

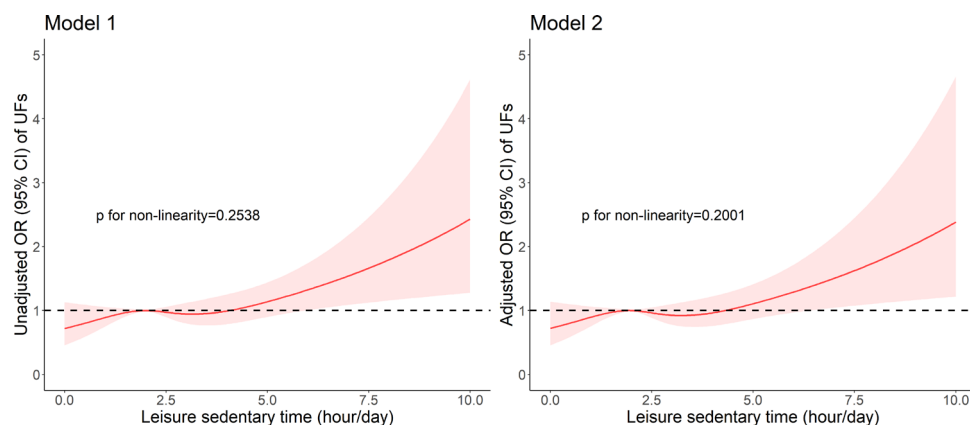


Figure 2 Linear relationship between LST and UFs in the participants (n=6623). Model 1: no covariates were adjusted; model 2: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first live birth, age at menarche, number of live births, time since last live birth, menstrual status, contraceptive use and PA. The OR is shown with the red solid line, and 95% CIs are shown with the shaded area. The black horizontal short dashed line represents the reference line y=1. BMI, body mass index; LST, leisure sedentary time; PA, physical activity; UFs, uterine fibroids.

Table 3 Stratified analysis of the relationship between LST and UFs in different menstrual status and BMI groups

Group		Model 1	Model 2
Premenopause (n=5737)			
LST (hour/day)	<2	Ref.	Ref.
	2–3.99	1.036 (0.823, 1.304)	1.020 (0.808, 1.288)
	4–5.99	1.285 (0.930, 1.774)	1.271 (0.913, 1.770)
	≥6	1.542 (0.885, 2.687)	1.558 (0.875, 2.771)
Perimenopause (n=886)			
LST (hour/day)	<2	Ref.	Ref.
	2–3.99	0.923 (0.558, 1.526)	0.882 (0.527, 1.475)
	4–5.99	0.909 (0.419, 1.969)	0.773 (0.349, 1.712)
	≥6	5.852 (2.045, 16.743)	5.432 (1.799, 16.406)
BMI<24 kg/m ² (n=4136)			
LST (hour/day)	<2	Ref.	Ref.
	2–3.99	1.046 (0.791, 1.382)	1.043 (0.786, 1.384)
	4–5.99	1.391 (0.944, 2.050)	1.412 (0.947, 2.106)
	≥6	1.938 (1.010, 3.716)	2.152 (1.091, 4.244)
BMI≥24 kg/m ² (n=2487)			
LST (hour/day)	<2	Ref.	Ref.
	2–3.99	0.983 (0.716, 1.349)	0.927 (0.672, 1.279)
	4–5.99	1.003 (0.630, 1.596)	0.923 (0.574, 1.487)
	≥6	1.895 (0.942, 3.813)	1.845 (0.888, 3.834)

Model 1: no covariates were adjusted.

Model 2: adjusted for age, marital status, education level, occupation, BMI (menstrual status only), ethnicity, age at first live birth, age at menarche, number of live births, time since last live birth, contraceptive use, menstrual status (BMI only) and PA.

BMI, body mass index; LST, leisure sedentary time; PA, physical activity; UFs, uterine fibroids.

positive correlation between LST and the risk of UFs only in perimenopausal women or women with BMI<24 kg/m², while no statistical correlation between UFs and LST was found in premenopausal women or women with BMI≥24 kg/m² (online supplemental table 2).

DISCUSSION

In this study, the results showed that LST was independently related to the prevalence of UFs, and the restricted cubic spline showed a linear dose–response relationship between LST and the risk of UFs. Stratified analysis of menstrual status and BMI showed that the influence of LST on UFs was different under different menstrual statuses and BMI conditions.

Although there are no studies on LST and UFs to date, we found many articles about exploring sedentary behaviour and oestrogen-dependent tumours (ovarian cancer, endometrial cancer) by consulting literature. For example, studies in China and Japan have found that an increase in TV watching time was related to an increased risk of ovarian cancer.^{28 29} A recent study also showed that leisure sedentary behaviour, such as watching TV, had an independent causal association with the risk of endometrial cancer, breast cancer and ovarian cancer.³⁰ Since UFs are also known to be oestrogen-dependent tumours,

the finding in our study provides evidence for future exploration of the correlation between LST and UFs. Although the relevant mechanism is still unclear, there are several possible assumptions. One possible cause is that sedentary behaviour is related to obesity, and studies have shown that obesity is a risk factor for UFs.⁹ Both sedentary behaviour and obesity increase the oestrogen level in the body, thus promoting the formation and development of UFs. Another potential mechanism lies in the association between sedentary behaviour and metabolic disorders, as well as the link between sedentary behaviour and chronic inflammation. Prolonged sedentary time is related to more serious chronic inflammation and insulin resistance.³¹ Prolonged sedentary time also leads to an increase in the levels of free insulin-like growth factor and tumour necrosis factor in the body,³² which in turn promotes the occurrence of UFs. The final possible assumption is that sedentary behaviour also leads to a decrease in vitamin D in the body.³³ Previous studies have shown that vitamin D deficiency is a risk factor for UFs. Vitamin D regulates cell growth and differentiation and inhibits the proliferation of leiomyoma cells.^{34 35} Therefore, sedentary behaviour will reduce the level of vitamin D in the body, thus promoting the occurrence of UFs.



The correlation between LST and prevalence of UFs was observed only in women with BMI<24 kg/m². This suggests that in overweight or obese individuals, other factors may influence the development of UFs, thereby attenuating the impact of sedentary behaviour. Consequently, sedentary behaviour is no longer independently associated with UFs. In multivariable adjusted logistic regression, BMI could be included in the model when only demographic characteristics-related were considered (model 2). However, when we included additional factors such as the number of live births, age at first live birth, age at menarche (model 3), there was no statistically significant association between BMI and UFs. This result partially supports the aforementioned reasons. Our study is cross-sectional and more prospective studies are needed to explore the underlying mechanisms.

Similarly, a correlation between LST and UFs was found only in perimenopausal women. This may be attributed to the fact that perimenopausal women generally have older age compared with than premenopausal women, resulting in a longer duration of oestrogen exposure. In short, the finding revealed the association between sedentary behaviour and oestrogen metabolism. Some studies also revealed that the association between sedentary behaviour and oestrogen metabolism was found only in postmenopausal women, and sedentary behaviour was associated with higher levels of postmenopausal oestrogens/oestrogen metabolites.^{36 37} Generally, changes in endocrine, biological and clinical manifestations associated with menopause occur during both perimenopause and menopause. During the perimenopause, the hormone levels in women's bodies drop suddenly, which easily causes hormone disorders and increases blood pressure levels and insulin resistance levels.³⁸ Sedentary behaviour may stimulate the occurrence of UFs by aggravating metabolic disorders during perimenopause.

This study is the first to investigate the relationship between LST and UFs, and adjust for as many potential confounding factors as possible. In addition, the research data are based on the southwest natural population cohort, with a large sample size. The quality of the data has been strictly reviewed, and the quality control is good.

However, our research also has some shortcomings: First, this is a cross-sectional study, which cannot determine the causal relationship between LST and UFs. Second, LST and most of the covariates were self-reported, so we cannot avoid memory bias. However, for some data, such as LST, we only collected information from the year prior to the survey. Third, although we adjusted for as many potential confounding factors as possible, we cannot guarantee that there are other unadjusted confounding factors affecting the results. Finally, our research is based on the data of women in Yunnan Province, a population whose occupation is predominantly farmers, so this result may not be generalisable to populations outside Yunnan, especially women who are not farmers. Although our study contains some limitations, taken together, the results show a relatively clear relationship between leisure

sedentary behaviour and UFs, and this study can provide information for exploring the aetiology of UFs in the future.

CONCLUSION

This cross-sectional study based on the natural population showed that LST has a linear positive correlation with UFs, indicating that LST may be an independent risk factor for UFs. Both BMI and menstrual status played a role in the association between LST and UFs. LST was related to the prevalence of UFs in women with a BMI<24 kg/m². Similarly, LST was only related to the prevalence of UFs in perimenopausal women. Therefore, more attention should be given to leisure sedentary behaviour of women with BMI<24 kg/m² and perimenopausal women.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Medical Ethical Review Board of Kunming Medical University (KMMU2020MEC078). Participants gave informed consent to participate in the study before taking part.

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Data availability statement Data are available on reasonable request. Anonymous datasets are available from the corresponding author (mengqiong2006@163.com).

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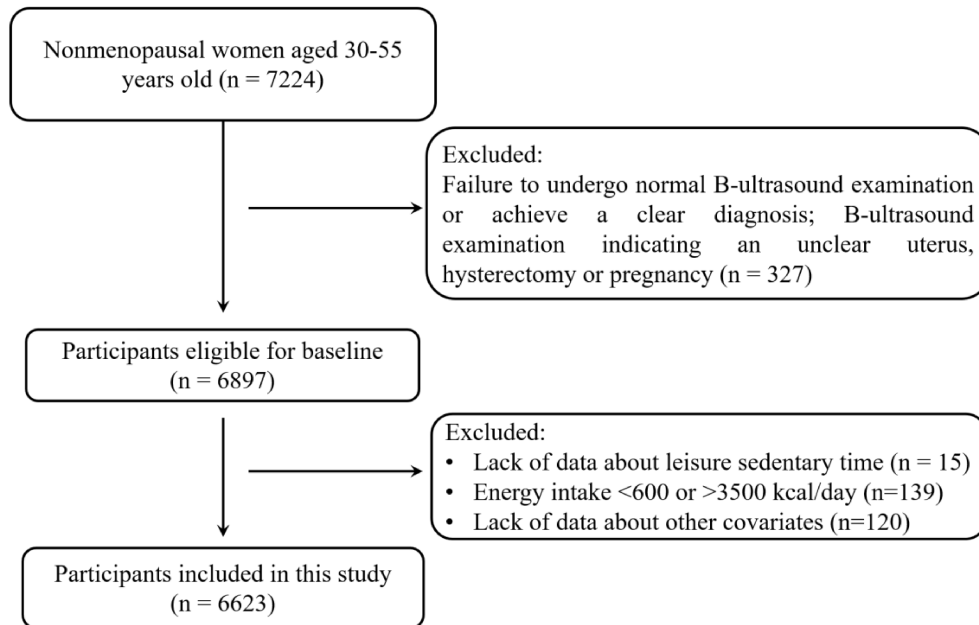
Appendices

Article title

Association between leisure sedentary behaviour and uterine fibroids in nonmenopausal women: a population-based study

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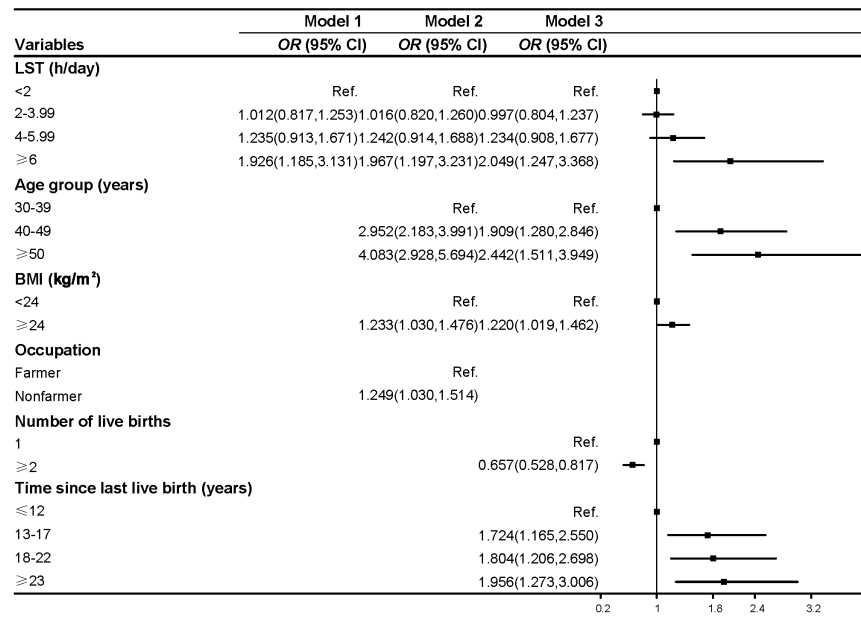
Supplemental Figure 1 Flowchart of participants recruitment and study inclusion.

Supplemental Table 1 Single-factor logistic regression analysis of different variables and UFs

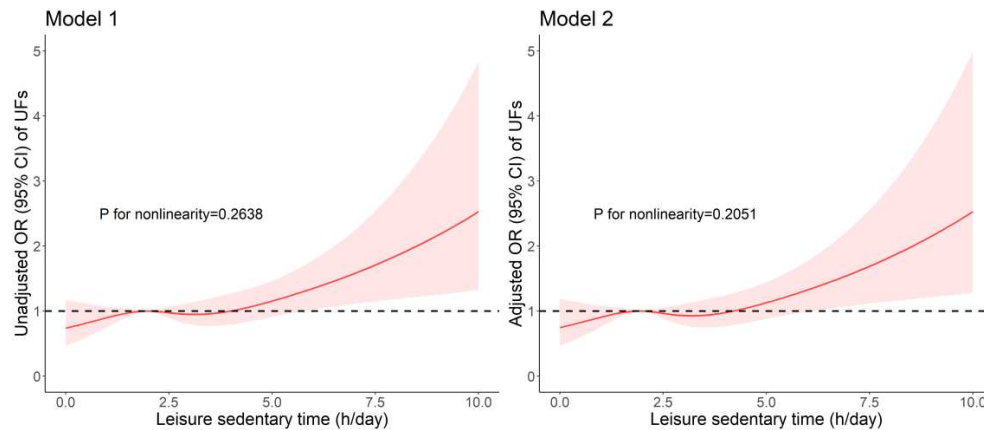
Variables	UFs			OR (95% CI)
	n(N)	%	95% CI	
BMI (kg/m²)				
<24	322(4136)	7.8	(7.0,8.6)	Ref.
≥24	240(2487)	9.7	(8.5,10.9)	1.265(1.062,1.507)
Age at first live birth (years)				
<20	34(459)	7.4	(5.0,9.8)	Ref.
20-24	415(4774)	8.7	(7.9,9.5)	1.190(0.827,1.712)
≥25	113(1390)	8.1	(6.7,9.5)	1.106(0.742,1.648)
Age at menarche (years)				
≤12	64(782)	8.2	(6.3,10.1)	Ref.
13-16	418(4892)	8.5	(7.7,9.3)	1.048(0.796,1.379)
≥17	80(949)	8.4	(6.6,10.2)	1.033(0.733,1.456)
Number of live births				
1	130(1165)	11.2	(9.4,13.0)	Ref.
≥2	432(5458)	7.9	(7.2,8.6)	0.684(0.556,0.842)
Contraceptive use				
No	516(5969)	8.6	(7.9,9.3)	Ref.
Yes	46(654)	7.0	(5.0,9.0)	0.800(0.585,1.093)
LST (h/day)				
<2	135(1669)	8.1	(6.8,9.4)	Ref.
2-3.99	330(4030)	8.2	(7.4,9.0)	1.013(0.822,1.249)
4-5.99	74(766)	9.7	(7.6,11.8)	1.215(0.903,1.636)
≥6	23(158)	14.6	(9.1,20.1)	1.936(1.203,3.116)
Menstrual status				
Premenopause	467(5737)	8.1	(7.4,8.8)	Ref.
Perimenopause	95(886)	10.7	(8.7,12.7)	1.355(1.074,1.711)
Time since last live birth (years)				
≤12	60(1674)	3.6	(2.7,4.5)	Ref.
13-17	116(1354)	8.6	(7.1,10.1)	2.512(1.830,3.472)
18-22	173(1749)	9.9	(8.5,11.3)	2.953(2.184,3.993)
≥23	213(1846)	11.5	(10.0,13.0)	3.509(2.613,4.711)
PA (MET-h/day)				
<27.35	207(2183)	9.5	(8.3,10.7)	Ref.
27.35-44.98	203(2252)	9.0	(7.8,10.2)	0.946(0.772,1.159)
≥44.99	152(2188)	6.9	(5.8,8.0)	0.713(0.573,0.887)
Energy (kcal/day)		1751.9(1419.4,2132.4)		1.000(1.000,1.000)

Data are presented as *M* (*P25*, *P75*) for continuous variables or number (%) for categorical variables.

BMI, body mass index; LST, leisure sedentary time; PA, physical activity; MET, metabolic equivalent task.



Supplemental Figure 2 Sensitivity analysis of the relationship between the prevalence of UFs and LST (n=6458). Model 1: no covariates were adjusted; Model 2: adjusted for age, marital status, education level, occupation, ethnicity and BMI; Model 3: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first live birth, age at menarche, number of live births, time since last live birth, menstrual status, contraceptive use and PA. BMI, body mass index; LST, leisure sedentary time.



Supplemental Figure 3 Sensitivity analysis of the linear relationship between LST and UFs in the participants (n=6458). Model 1: no covariates were adjusted; Model 2: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first live birth, age at menarche, number of live births, time since last live birth, menstrual status, contraceptive use and PA. The odds ratio is shown with the red solid line, and 95% confidence intervals are shown with the shaded area. The black horizontal short dashed line represents reference line $y = 1$.

Supplemental Table 2 Sensitivity analysis: stratified analysis of the relationship between LST and UFs in different menstrual status and BMI groups

Group		Model 1	Model 2
Premenopause (n=5601)			
LST (h/day)	<2	Ref.	Ref.
	2-3.99	1.037(0.820,1.311)	1.018(0.802,1.292)
	4-5.99	1.303(0.938,1.810)	1.289(0.920,1.806)
	≥6	1.512(0.853,2.678)	1.544(0.853,2.794)
Perimenopause (n=857)			
LST (h/day)	<2	Ref.	Ref.
	2-3.99	0.912(0.546,1.523)	0.863(0.510,1.458)
	4-5.99	0.936(0.430,2.040)	0.792(0.355,1.763)
	≥6	5.833(2.032,16.747)	5.485(1.808,16.640)
BMI <24 kg/m ² (n=4067)			
LST (h/day)	<2	Ref.	Ref.
	2-3.99	1.014(0.763,1.346)	1.007(0.755,1.342)
	4-5.99	1.393(0.941,2.062)	1.425(0.951,2.134)
	≥6	2.006(1.044,3.856)	2.248(1.137,4.446)
BMI ≥24 kg/m ² (n=2391)			
LST (h/day)	<2	Ref.	Ref.
	2-3.99	1.019(0.737,1.411)	0.957(0.688,1.333)
	4-5.99	1.035(0.643,1.665)	0.942(0.578,1.534)
	≥6	1.793(0.866,3.713)	1.720(0.803,3.684)

Model 1: no covariates were adjusted.

Model 2: adjusted for age, marital status, education level, occupation, BMI (menstrual status only), ethnicity, age at first live birth, age at menarche, number of live births, time since last live birth, contraceptive use, menstrual status (BMI only) and PA.

BMI, body mass index; LST, leisure sedentary time.

BMJ OPEN

Externally peer reviewed? Yes

Evidence type: Observational

Subjects: Women

6+ hours/day of sedentary leisure time linked to doubling in fibroids risk

Risk seems to be linear in women who've not yet gone through the menopause

Clocking up 6 or more hours of sedentary leisure time every day may double a woman's risk of uterine fibroids before she's gone through the menopause, suggests research published in the open access journal **BMJ Open**.

The risk of these benign, but potentially large and painful, womb growths seems to rise in tandem with the amount of time spent sitting or lying down during the day, the findings suggest.

Uterine fibroids are the most common benign tumours in women of childbearing age, varying in prevalence from 4.5% to 69%, say the researchers.

These growths may not produce any symptoms, but they may also be associated with abnormal bleeding, pelvic and abdominal pain, and infertility, among other things, they add.

Sedentary behaviour is associated with tumours that rely on the female hormone oestrogen, such as endometrial, ovarian, and breast cancers; uterine fibroids are also fuelled by oestrogen.

The researchers therefore wanted to find out if there might be a link between extensive sedentary leisure time and the risk of uterine fibroids.

They drew on the Yunnan cohort of the China Multi-Ethnic Cohort Study, which is a prospective community-based long term study in southwest China, involving 99,556 participants from five provinces.

The final study sample included 6623 women aged 30 to 55 who had not yet gone through the menopause.

Basic background information was collected from each of the women. This included menstrual/reproductive history, number of children and age at first birth, contraceptive use, sedentary leisure time, physical activity, diet, height and weight.

The average ages when periods first started and when giving birth for the first time were 13-16 and 20-24, respectively, and nearly 84% had more than two children.

Sedentary behaviour was classified as 1.5 or fewer metabolic equivalent of task (MET) hours/day when sitting or lying down. METs express how much energy in calories is expended per hour of physical activity.

Participants were asked to specify how much time they spent playing board games, on screen time, reading, knitting and other similar activities and were then divided into four sedentary leisure time groups: under 2 hours/day; 2–3.99 hours/day; 4–5.99 hours/day; and 6 or more hours/day.

Around 6 out of 10 (61%) of the women clocked up 2–3.99 hours/day of sedentary leisure time.

In all, 562 (8.5%) of the women had uterine fibroids, the prevalence of which increased with age. Rates were highest (2.5 times higher) among those aged 50 and older.

Weight (BMI), number of live births (more than 2), menstrual status, time since last live birth (13-17 years onwards), physical activity and sedentary leisure time were all associated with uterine fibroids.

But the more sedentary leisure time spent, the greater the risk of uterine fibroids seemed to be. And after accounting for potentially influential factors, sedentary leisure time of 6 or more hours a day was associated with a risk twice that of women who clocked up fewer than 2.

While sedentary leisure time wasn't associated with the prevalence of fibroids in premenopausal women, it was associated with the prevalence of fibroids in perimenopausal women: the risk was 5 times higher among those who clocked up 6 or more sedentary leisure hours a day than it was in those who clocked up fewer than 2 hours.

This is an observational study, and as such, can't establish causal factors. And the study relied on subjective assessment for many of the factors, point out the researchers.

But one possible explanation for the observed associations might be that sedentary behaviour is related to obesity, which is a risk factor for uterine fibroids, say the researchers. Both sedentary behaviour and obesity increase the body's oestrogen level.

Other possible explanations include the known associations between sedentary behaviour and metabolic disorders, chronic inflammation, and vitamin D deficiency, they suggest.

"This cross-sectional study, based on the natural population, showed that [sedentary leisure time] has a linear positive correlation with [uterine fibroids], indicating that [it] may be an independent risk factor," they conclude.