BMJ Open

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

Yunrui Sun,[1] Xiaoyu Han,[2] Zhongxin Hou,[1] Haoyuan Deng,[3] Nan Cheng,[4] Nishang Zhang,[5] Jianghui Zhang,[6] Yi Li,[1] Qian Wang,[1] Jianzhong Yin ,[1,5] Qiong Meng [1]

To cite: Sun Y, Han X, Hou Z, *et al*. Association between leisure sedentary behaviour and uterine fibroids in non-menopausal women: a population-based study. *BMJ Open* 2023;**13**:e073592. doi:10.1136/bmjopen-2023-073592

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2023-073592).

YS and XH contributed equally. JY and QM contributed equally.

YS and XH are joint first authors.

Received 13 March 2023
Accepted 20 October 2023

For numbered affiliations see end of article.

Correspondence to
Qiong Meng; mengqiong2006@163.com and Jianzhong Yin; yinjianzhong2005@sina.com

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≥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/m^2 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.

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.

INTRODUCTION

Uterine fibroids (UFs) are the most common benign tumours in women of childbearing 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 asymptomatic[2] 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 isoechogenic.[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 (m^2). BMI was divided into two groups: <24 kg/m^2 (normal weight) and ≥24 kg/m^2 (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 (P_{25}, P_{75}). 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≤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)
	≥6	86 (2.9)	26 (1.4)	46 (2.6)	158 (2.4)
Menstrual status	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	Group	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 OR (95% CI)	Model 2 OR (95% CI)	Model 3 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)

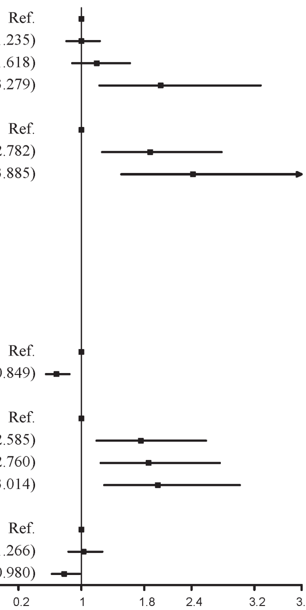

Figure 1 The relationship between the prevalence of UFs and LST (n=6623). Model 1: no covariates were adjusted; model 2: adjusted for age, marital status, education level, occupation, ethnicity and BMI; model 3: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first 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/m^2 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/m^2, 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

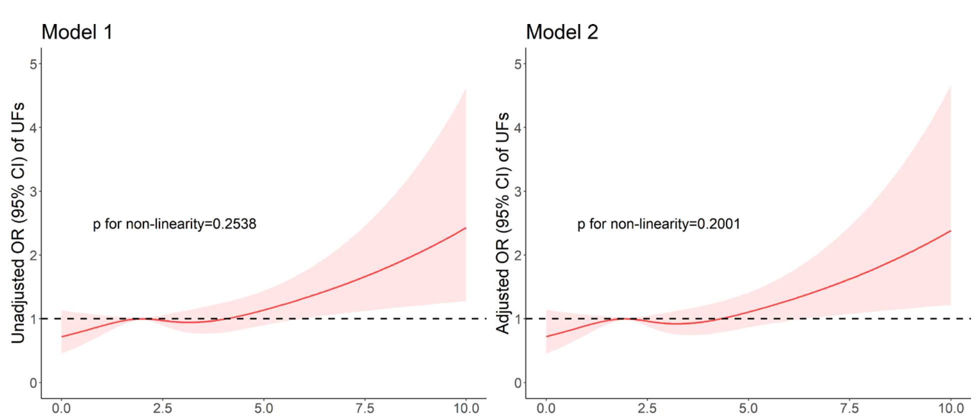

Figure 2 Linear relationship between LST and UFs in the participants (n=6623). Model 1: no covariates were adjusted; model 2: adjusted for age, marital status, education level, occupation, ethnicity, BMI, age at first live birth, age at menarche, number of live births, time since last live birth, menstrual 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.

Sun Y, *et al*. *BMJ Open* 2023;**13**:e073592. doi:10.1136/bmjopen-2023-073592

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/m^2, while no statistical correlation between UFs and LST was found in premenopausal women or women with BMI≥24 kg/m^2 (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 oertrogen 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/m^2.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/m^2. 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/m^2 and perimenopausal women.

Author affiliations
[1]School of Public Health, Kunming Medical University, Kunming, China
[2]Institute for Acute Communicable Disease Prevention and Control, Yunnan Provincial Center for Disease Control and Prevention, Kunming, Yunnan, China
[3]Medical Department, The First Affiliated Hospital of Kunming Medical University, Kunming, China
[4]Department of Public Health, Wuhan Mental Health Center, Wuhan, China
[5]Baoshan College of Traditional Chinese Medicine, Baoshan, China
[6]AIDS Care Center, Yunnan Provincial Hospital of Infectious Disease, Kunming, China

Acknowledgements We gratefully acknowledge the staff of various health institutions in Yunnan Province and the undergraduates of Kunming Medical University who conducted the site survey. We are grateful to all survey respondents for their participation in this work.

Contributors YS and XH, joint first authors, analysed and interpreted the data and drafted the manuscript, which was critically revised by all others. ZH, HD, NC, NZ, JZ, YL and QW contributed to the data collection and data analysis. QM and JY contributed to the design of the study and the supervision of the statistical analysis. QM revised the manuscript and had primary responsibility for the overall content as the guarantor. All authors have read and agreed to the published version of the manuscript.

Funding This study was funded by the National Natural Science Foundation of China (No. 81960617) and National Key R&D Program of China (2017YFC0907302)

Disclaimer The study funder had no influence on the study design, collection, management, analysis, and interpretation of data, writing of the report, or decision to submit the report for publication.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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.

Provenance and peer review Not commissioned; externally peer reviewed.

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

ORCID iDs
Jianzhong Yin http://orcid.org/0000-0002-1876-387X
Qiong Meng http://orcid.org/0000-0002-2498-9816

REFERENCES

1 Stewart EA, Cookson CL, Gandolfo RA, *et al*. Epidemiology of uterine Fibroids: a systematic review. *BJOG* 2017;124:1501–12.
2 Hasselrot K, Lindeberg M, Konings P, *et al*. Investigating the loss of work productivity due to symptomatic Leiomyoma. *PLoS One* 2018;13:e0197958.
3 Babalola O, Gebben D, Tarver ME, *et al*. Patient preferences regarding surgical treatment methods for symptomatic uterine Fibroids. *Ther Innov Regul Sci* 2023;57:976–86.
4 Hervé F, Katty A, Isabelle Q, *et al*. Impact of uterine Fibroids on quality of life: a national cross-sectional survey. *Eur J Obstet Gynecol Reprod Biol* 2018;229:32–7.
5 He Y, Zeng Q, Dong S, *et al*. Associations between uterine Fibroids and lifestyles including diet, physical activity and stress: a case-control study in China. *Asia Pac J Clin Nutr* 2013;22:109–17.
6 Baird DD, Dunson DB, Hill MC, *et al*. Association of physical activity with development of uterine Leiomyoma. *Am J Epidemiol* 2007;165:157–63.
7 Liu F, Pan Y, Liang Y, *et al*. The Epidemiological profile of hysterectomy in rural Chinese women: a population-based study. *BMJ Open* 2017;7:e015351.
8 Pavone D, Clemenza S, Sorbi F, *et al*. Epidemiology and risk factors of uterine Fibroids. *Best Pract Res Clin Obstet Gynaecol* 2018;46:3–11.
9 Qin H, Lin Z, Vásquez E, *et al*. Association between obesity and the risk of uterine Fibroids: a systematic review and meta-analysis. *J Epidemiol Community Health* 2021;75:197–204.
10 Sun K, Xie Y, Zhao N, *et al*. A case-control study of the relationship between visceral fat and development of uterine Fibroids. *Exp Ther Med* 2019;18:404–10.
11 Yang Q, Ciebiera M, Bariani MV, *et al*. Comprehensive review of uterine Fibroids: developmental origin. *Endocr Rev* 2022;43:678–719.
12 Song S, Park S, Song BM, *et al*. Risk of uterine Leiomyomata with Menstrual and reproductive factors in premenopausal women: Korea nurses' health study. *BMC Womens Health* 2023;23:305.
13 Wu B-J, Wei W, Hu C-Y, *et al*. Investigation on factors related to uterine Fibroids in rural women of northern Anhui province. *J Obstet Gynaecol Res* 2021;47:3279–87.
14 Kwas K, Nowakowska A, Fornalczyk A, *et al*. Impact of contraception on uterine Fibroids. *Medicina (Kaunas)* 2021;57:717.
15 Mahmood B, Nettlefold L, Ashe MC, *et al*. Device-worn measures of sedentary time and physical activity in South Asian adults at high risk for type 2 diabetes in Metro-Vancouver, Canada. *PLoS One* 2022;17:e0266599.
16 Boursiquot BC, Bellettiere J, LaMonte MJ, *et al*. Sedentary behavior and atrial fibrillation in older women: the OPACH study. *J Am Heart Assoc* 2022;11:e023833.
17 Yuan L, Ni J, Lu W, *et al*. Association between domain-specific sedentary behaviour and endometrial cancer: a systematic review and meta-analysis. *BMJ Open* 2023;13:e069042.
18 Biller VS, Leitzmann MF, Sedlmeier AM, *et al*. Sedentary behaviour in relation to ovarian cancer risk: a systematic review and meta-analysis. *Eur J Epidemiol* 2021;36:769–80.
19 Buras AL, Wang T, Whiting J, *et al*. Prospective analyses of sedentary behavior in relation to risk of ovarian cancer. *Am J Epidemiol* 2022;191:1021–9.
20 Jochem C, Wallmann-Sperlich B, Leitzmann MF. The influence of sedentary behavior on cancer risk: epidemiologic evidence and potential molecular mechanisms. *Curr Nutr Rep* 2019;8:167–74.
21 Afrin S, El Sabeh M, Miyashita-Ishiwata M, *et al*. Simvastatin reduces plasma membrane Caveolae and Caveolin-1 in uterine Leiomyomas. *Life Sci* 2022;304:120708.
22 Imran TF, Ommerborn M, Clark C, *et al*. Television viewing time, physical activity, and mortality among African Americans. *Prev Chronic Dis* 2018;15:E10.
23 Werneck AO, Oyeyemi AL, Collings PJ, *et al*. Physical activity can attenuate, but not eliminate, the negative relationships of high TV viewing with some chronic diseases: findings from a cohort of 60 202 Brazilian adults. *J Public Health (Oxf)* 2021;43:e7–15.
24 Zhao X, Hong F, Yin J, *et al*. Cohort profile: the China multi-ethnic cohort (CMEC) study. *Int J Epidemiol* 2021;50:721–721l.
25 Bajaj S, Gopal N, Clingan MJ, *et al*. A pictorial review of Ultrasonography of the FIGO classification for uterine Leiomyomas. *Abdom Radiol (NY)* 2022;47:341–51.
26 Wesselink AK, Rosenberg L, Wise LA, *et al*. A prospective cohort study of ambient air pollution exposure and risk of uterine Leiomyomata. *Hum Reprod* 2021;36:2321–30.
27 Thivel D, Tremblay A, Genin PM, *et al*. Physical activity, inactivity, and sedentary behaviors: definitions and implications in occupational health. *Front Public Health* 2018;6:288.
28 Zhang M, Xie X, Lee AH, *et al*. Sedentary Behaviours and epithelial ovarian cancer risk. *Cancer Causes Control* 2004;15:83–9.
29 Ukawa S, Tamakoshi A, Mori M, *et al*. Association between average daily television viewing time and the incidence of ovarian cancer: findings from the Japan collaborative cohort study. *Cancer Causes Control* 2018;29:213–9.
30 Chen J, Yang K, Qiu Y, *et al*. Genetic associations of leisure sedentary behaviors and the risk of 15 site-specific cancers: A Mendelian randomization study. *Cancer Med* 2023;12:13623–36.
31 León-Latre M, Moreno-Franco B, Andrés-Esteban EM, *et al*. Sedentary lifestyle and its relation to cardiovascular risk factors, insulin resistance and inflammatory profile. *Rev Esp Cardiol (Engl Ed)* 2014;67:449–55.
32 Ciavattini A, Di Giuseppe J, Stortoni P, *et al*. Uterine Fibroids: pathogenesis and interactions with Endometrium and Endomyometrial junction. *Obstet Gynecol Int* 2013;2013:173184:173184.:.
33 Joh HK, Lim CS, Cho B. Lifestyle and dietary factors associated with serum 25-Hydroxyvitamin D levels in Korean young adults. *J Korean Med Sci* 2015;30:1110–20.
34 Li S, Chen B, Sheng B, *et al*. The associations between serum vitamin D, calcium and uterine Fibroids in Chinese women: a case-controlled study. *J Int Med Res* 2020;48:300060520923492.
35 Vergara D, Catherino WH, Trojano G, *et al*. Vitamin D: mechanism of action and biological effects in uterine Fibroids. *Nutrients* 2021;13:597.
36 Dallal CM, Brinton LA, Matthews CE, *et al*. Association of active and sedentary behaviors with postmenopausal estrogen metabolism. *Med Sci Sports Exerc* 2016;48:439–48.
37 Oh H, Arem H, Matthews CE, *et al*. Sitting, physical activity, and serum oestrogen metabolism in postmenopausal women. *The Women's Health Initiative Observational Study Br J Cancer* 2017;117:1070–8.
38 Marlatt KL, Pitynski-Miller DR, Gavin KM, *et al*. Body composition and Cardiometabolic health across the Menopause transition. *Obesity (Silver Spring)* 2022;30:14–27.