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Physical activity and sedentary time in relation to semen quality in healthy men screened as potential sperm donors

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STUDY QUESTION: Is physical activity or sedentary time associated with semen quality parameters?

SUMMARY ANSWER: Among healthy men screened as potential sperm donors, higher self-reported physical activity was associated with increased progressive and total sperm motility.

WHAT IS KNOWN ALREADY: Despite the claimed beneficial effect of moderate physical activity on semen quality, results from epidemiological studies have been inconclusive. Previous studies were mostly conducted among endurance athletes or male partners of couples who sought infertility treatment.

STUDY DESIGN, SIZE, DURATION: Healthy men screened as potential sperm donors were recruited at the Hubei Province Human Sperm Bank of China. Between April 2017 and July 2018; 746 men completed the long-form International Physical Activity Questionnaire (IPAQ) and provided repeated semen samples ($n = 5252$) during an approximately 6-month period.

PARTICIPANTS/MATERIALS, SETTING, METHODS: Total metabolic equivalents (METs), moderate-to-vigorous METs and sedentary time were abstracted from the IPAQ. Sperm concentration, total sperm count, progressive motility and total motility in repeated specimens were determined by trained clinical technicians. Mixed-effect models were applied to investigate the relationships between physical activity and sedentary time and repeated measures of semen quality parameters.

MAIN RESULTS AND THE ROLE OF CHANCE: After adjusting for multiple confounders, total METs and moderate-to-vigorous METs were both positively associated with progressive and total sperm motility. Compared with men in the lowest quartiles, those in the highest quartiles of total and moderate-to-vigorous METs had increased progressive motility of 16.1% (95% CI: 6.4, 26.8%) and 17.3% (95% CI: 7.5, 27.9%), respectively, and had increased total motility of 15.2% (95% CI: 6.2, 24.9%) and 16.4% (95% CI: 7.4, 26.1%), respectively. Sedentary time was not associated with semen quality parameters.

LIMITATIONS, REASONS FOR CAUTION: The IPAQ was reported only once from study participants; measurement errors were inevitable and may have biased our results. Furthermore, although we have adjusted for various potential confounders, the possibility of unmeasured confounding cannot be fully ruled out.

WIDER IMPLICATIONS OF THE FINDINGS: Our findings suggest that maintaining regular exercise may improve semen quality parameters among healthy, non-infertile men. Specifically, we found that higher self-reported total and moderate-to-vigorous METs were associated with improved sperm motility, which reinforces the existing evidence that physical activity may improve male reproductive health.

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Introduction

Moderate physical activity is widely recognized as an important component of a healthy lifestyle, which has been associated with reduced risks of diabetes (Aune et al., 2015), cardiovascular diseases (Lee, 2010), certain cancers (Rezende et al., 2018) and depression (Mammen and Faulkner, 2013), potentially by reducing endogenous oxidative stress and changing endogenous sexual hormone secretion. The World Health Organization (WHO) has ranked physical inactivity as the fourth leading risk factor of global mortality (WHO 2010a). However, whether moderate physical activity has any beneficial effect on male fertility remains inconclusive.

Several epidemiologic studies have revealed a positive association between physical activity and sperm concentration, progressive motility and percent of normal morphology (Vaamonde et al., 2012; Li et al., 2013; Gaskins et al., 2014). In contrast, Gebreegziabher et al. (2004) found that distance cyclists had a significantly higher percentage of abnormal spermatozoa than the controls; an early intervention study conducted among five normal human volunteers reported reduced total sperm count and serum testosterone levels after a 3-month overtraining (Roberts et al., 1993). Meanwhile, a lack of convincing association between physical activity and markers of semen quality was also reported (Minguez-Alarcon et al., 2014; Jozkow et al., 2017). The controversial findings may be due in part to imprecise risk estimation driven by limited sample size (mostly less than 100 men) and non-uniform measures to characterize individuals' physical activity patterns. More importantly, all previous studies collected semen samples at a single time point, which may have resulted in measurement error due to the high within-individual variability in semen quality parameters (Chiu et al., 2017).

In the present study, we recruited 746 healthy men screened as potential sperm donors who provided repeated semen samples ($n = 5252$) over an approximately 6-month period. We applied a validated long-form International Physical Activity Questionnaire (IPAQ) to determine participants' physical activity patterns and sedentary time and assessed associations with repeated measures of semen quality parameters.

Materials and Methods

Study population

We recruited healthy men who volunteered as potential sperm donors at the Hubei Province Human Sperm Bank. Participants were eligible if they fulfilled the following criteria: (i) aged between 22 to 45 years; (ii) had a high school degree or above; (iii) had no sexually transmitted diseases or genetic diseases (e.g. chlamydia, gonorrhoea, HIV, hepatitis, syphilis, thalassemia and karyotype); and (iv) no history of chemical and radioactive exposure (Ping et al., 2011). Overall, 1487 men were enrolled between April 2017 and July 2018. Each volunteer completed a baseline questionnaire, underwent a physical examination and provided a semen sample at enrollment. Donor semen quality at screening should meet the following criteria: (i) fresh semen should have a liquefaction time < 60 min, sperm concentration $\geq 60 \times 10^6$/mL, progressive motility $\geq$60% and percentage of normal morphology $>$30% and (ii) post-thaw semen should have a motility $\geq$40%, number of motile sperm per vial $\geq 12 \times 10^6$ and frozen-thaw survival rate $\geq$ 60% (Ping et al., 2011). All participants who met the donation criteria were requested to provide certain amounts of semen specimens within 6 months; those who did not meet the criteria were asked to provide a sample for further screening. Height and weight were measured by a digital weight and height scale; waist circumference and hip circumference were measured by a flexible rule at recruitment. We administrated five questionnaires at recruitment and during the follow-up visits (1–15, 16–31, 32–63 and $\geq$64 days since recruitment) to collect participants' demographic information (e.g. age, marital status and income), medical history, medication use and lifestyle factors (e.g. smoking and alcohol consumption). Among 1487 men who consented to donate their sperm samples, 102 men were excluded at baseline due to physician-diagnosed medical conditions that may affect reproductive health (e.g. thalassemia, chromosome abnormalities and HBV infection). The long-form IPAQ was administrated at 16–31 days following recruitment. A total of 630 men did not complete the IPAQ either because of a lack of time ($n = 183$; 13.2%) during this specific period or due to the loss to follow-up ($n = 447$; 32.3%). We further excluded nine men due to incomplete IPAQ data. Finally, a total of 746 men were included in our current analysis. No significant differences were observed in demographic characteristics among participants included and excluded in our current analysis, as well as the overall eligible study population ($n = 1385$; 102 were excluded; Supplementary Table SI).

Ethical approval

This study was approved by the Ethics Committee of the Reproductive Medicine Center, Tongji Medical College, Wuhan, China. All donors were fully aware of the donation process and provided signed informed consent before participation.

Physical activity

Self-reported time spent in different types of the Reproductive Medicine Center, physical activities (work-related activity, transportation activity, domestic activity and recreational activity) and sedentary behavior over the past week was abstracted from the long-form IPAQ, which has been validated in a Chinese population (Qu and Li, 2004; Macfarlane et al., 2011). The IPAQ items evaluated the frequency and time (at least 10 min) spent in the abovementioned specific activities each day. Weekly physical activity (metabolic equivalents; MET-min/week) was calculated by multiplying total minutes by activity-specific MET score (3 for domestic activities; 3.3 for walking; 4 for moderate-intensity physical activity; 5.5 for vigorous physical activity in the garden or yard; 6 for cycling; and 8 for vigorous physical activity). We defined total METs as the sum MET scores of walking, moderate-intensity activity and vigorous activity. We defined moderate-to-vigorous METs as the sum scores of moderate-intensity and vigorous activity. Sedentary activity was the sitting time (in minutes) on a typical weekday and weekend. In our validation analysis, we invited 10 participants to complete the same IPAQ questionnaire twice over the study period (time interval range: 7–130 days). The results showed high intra-class correlation coefficients (range: 0.84–0.97) for repeated measures of total and moderate-to-vigorous METs and sedentary time, indicating good test–retest reliability.

Semen collection and analysis

Semen samples were obtained by masturbation in a private room at the sperm bank after an abstinence period of no less than 48 h. After collection, the samples were immediately liquefied at 37°C and then analyzed by professional technicians according to the guideline of the WHO laboratory manual for semen examination (WHO 2010b). Ejaculation volume was estimated by semen weight (assuming a density of 1.0 g/mL). Sperm concentration, progressive motility and total motility were evaluated by placing 10 μL of well-mixed semen in a clean Makler chamber using a microscope, as described previously (Rao et al., 2015). Total sperm count was calculated by multiplying semen volume by concentration. Semen samples were analyzed by three well-trained laboratory technologists using the same apparatus; internal quality control was performed to ensure that the within-day and between-day variations were less than 10%.

Statistical analysis

The participants were classified into quartiles based on their total METs, moderate-to-vigorous METs and sedentary time. The differences in demographic characteristics across the quartile of total METs were assessed using Chi-square tests or Kruskal–Wallis test where appropriate. We log-transformed sperm motility, concentration and total count to normalize their distributions. Mixed-effect models with a subject-specific random intercept were used to evaluate the associations of total METs, moderate-to-vigorous METs and sedentary time quartiles with repeated measures of each semen quality parameter. An unstructured variance–covariance structure was chosen by comparing the model fit based on Akaike's information criterion (AIC) and Schwart's Bayesian criterion (BIC) (AIC or BIC with the lowest scores were considered the best fit models). Regression coefficient (β) was converted into %change using the following formula: %change = $(10^{\beta} - 1) \times 100$ (Ma et al., 2019). Tests for trend across the quartiles of MET scores and sedentary time were assessed by modeling median values within each quartile as a continuous value. To test the robustness of our findings, we further modeled physical activity and sedentary time as continuous values instead of categorical variables.

Inclusion of covariates in the multivariable models was based on statistical and biological–causal considerations (Kleinbaum et al., 1988). We only included the covariate with a P value <0.20 in the preliminary bivariate analysis; the covariate with a P value >0.15 for all tested semen quality parameters was removed from further consideration. The final models were adjusted for age (years), BMI (kg/m^2), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<2000, 2000–10 000 or >10 000 Yuan) and sampling season (spring, summer, autumn or winter).

Stratified analyses were conducted to assess if the associations were consistent across BMI categories (<24 or ≥24 kg/m^2) and age groups (<28 or ≥28 years), and the significance of the potential interaction was tested by including a cross-product term in the final model. In a sensitivity analysis, we also calculated the average sperm quality parameters across visits for each participant and used this average as the outcome to assess the associations with quartiles of MET scores and sedentary time using general linear models. SAS version 9.4 (SAS Institute, Cary, NC, USA) was applied for all data analyses.

Results

The characteristics of participants in our analyses stratified by quartiles of total METs are presented in Table I**.** In total, 746 men provided 5252 semen samples (mean frequency: 7.0). The mean (SD) age was 28.4 (5.4) years, and the mean (SD) BMI was 22.9 (3.2) kg/m^2, respectively. The mean (SD) abstinence time was 6.2 (3.0) days. Most participants were non-smokers (57.8%) and had a household income of 2000–10 000 yuan per month (64.3%). Men who had higher total METs were less likely to be current or former smokers. The proportion of semen samples collected during spring, summer, autumn and winter differed across quartiles of total METs.

Semen quality parameters stratified by physical activity and sedentary time are presented in Table II**.** Compared with subjects in the first quartile, the multivariable-adjusted analyses showed that progressive and total sperm motility were significantly higher among individuals in the second, third and fourth quartiles of total and moderate-to-vigorous METs (all P for trend <0.05). Sperm concentration and total sperm count were not related to self-reported physical activities.

The associations between MET scores and semen quality parameters based on crude and adjusted models were similar (Table III). Positive dose–response relationships were observed between total and moderate-to-vigorous METs and progressive and total sperm motility (all P for trend <0.005). In the multivariable mixed-effect models, men in the highest versus lowest quartiles of total and moderate-to-vigorous METs had increased progressive motility of 16.1% (95% CI: 6.4, 26.8%) and 17.3% (95% CI: 7.5, 27.9%), respectively, and increased total motility of 15.2% (95% CI: 6.2, 24.9%) and 16.4% (95% CI: 7.4, 26.1%), respectively. Dose–response relationships remained when modeling total and moderate-to-vigorous METs as continuous variables (Supplementary Table SII). The abovementioned relationships were further confirmed by the within-subject average sperm parameters based on general linear models (Supplementary Table SIII). We did

Table I Demographic characteristics of study participants by quartiles of total metabolic equivalent (MET) scores.

Characteristics	Overall population	Stratified by total METs			
		Q1	Q2	Q3	Q4
	n = 746	*n* = 183	*n* = 189	*n* = 189	*n* = 185
Total METs (min/week), median	2245.5	526.5	1584	3168.0	7082.3*
Age (years), mean ± SD	28.4 ± 5.4	28.5 ± 5.4	28.0 ± 5.4	28.5 ± 5.3	28.4 ± 5.6
BMI (kg/m ^{2}), mean ± SD	22.9 ± 3.2	22.7 ± 3.4	22.8 ± 3.2	23.0 ± 3.0	23.3 ± 3.2
Abstinence time (days), mean ± SD	6.2 ± 3.0	6.2 ± 3.5	6.2 ± 2.6	6.1 ± 2.8	6.3 ± 3.2
Marital status, *N* (%)					
Married	244 (32.7)	71 (38.8)	53 (28.0)	61 (32.3)	59 (31.9)
Unmarried	476 (63.8)	108 (59.0)	128 (67.7)	121 (64.0)	119 (64.3)
Divorced	26 (3.5)	4 (2.2)	8 (4.2)	7 (3.7)	7 (3.8)
Smoking status, *N* (%)					
Current smoker	261 (35.0)	78 (42.6)	63 (33.3)	61 (32.3)	59 (31.9)
Former smoker	54 (7.2)	17 (9.3)	17 (9.0)	10 (5.3)	10 (5.4)
Non-smoker	431 (57.8)	88 (48.1)	109 (57.7)	118 (62.4)	116 (62.7)*
Drinking habit, *N* (%)					
Current drinker	86 (11.5)	23 (12.6)	19 (10.1)	24 (12.7)	20 (10.8)
Former drinker	7 (0.9)	3 (1.6)	1 (0.5)	1 (0.5)	2 (1.1)
Occasional drinker	448 (60.1)	105 (57.4)	122 (64.6)	107 (56.6)	114 (61.6)
Non-drinker	205 (27.5)	52 (28.4)	47 (24.9)	57 (30.2)	49 (26.5)
Tea consumption, *N* (%)					
Yes	212 (28.4)	44 (24.0)	59 (31.2)	52 (27.5)	57 (30.8)
No	534 (71.6)	139 (76.0)	130 (68.8)	137 (72.5)	128 (69.2)
Income, yuan/month, *N* (%)					
< 2000	108 (14.5)	22 (12.0)	31 (16.4)	35 (18.5)	20 (10.9)
2000–10 000	479 (64.3)	123 (67.2)	112 (59.3)	113 (59.8)	131 (71.2)
> 10 000	158 (21.2)	38 (20.8)	46 (24.3)	41 (21.7)	33 (17.9)
Sampling season, *N* (%)					
Spring	1271 (24.2)	316 (24.4)	313 (23.6)	346 (26.4)	296 (22.5)
Summer	1854 (35.3)	429 (33.1)	434 (32.7)	493 (37.6)	498 (37.8)
Autumn	1388 (26.4)	348 (26.8)	377 (28.4)	309 (23.6)	354 (26.9)
Winter	739 (14.1)	204 (15.7)	204 (15.4)	163 (12.4)	168 (12.8)*

Demographic characteristics across quartiles of total MET scores were compared using Kruskal–Wallis analyses or χ^2 tests where appropriate.
The participants were classified into quartiles based on their total MET (metabolic equivalents). Q1, the first quartile; Q2, the second quartile; Q3, the third quartile; Q4, the fourth quartile.
* $P < 0.05$, sampling season and smoking status have significant differences across quartiles of total METs.

not observe any notable associations between sedentary time and semen quality parameters (Table III).

The associations of physical activities in relation to progressive and total sperm motility stratified by BMI and age are shown in Figure 1. Positive associations of total and moderate-to-vigorous METs with progressive and total sperm motility were exhibited only among men whose BMI was less than 24 kg/m^2 or age less than 28 years (all *P* for trend <0.05), although there was no evidence of interaction (*P* for interaction = 0.72 and 0.43, respectively). For other semen quality parameters, we only observed dose–response relationships for total METs and sperm concentration among men who were less than 28 years of age (*P* for trend <0.05; Supplementary Table SIV).

Discussion

Among 746 healthy Chinese men screened as potential sperm donors, we observed positive dose–response relationships for total and moderate-to-vigorous METs and progressive and total sperm motility. In the stratified analyses, these dose–response relationships were only confirmed among leaner (BMI <24 kg/m^2) or younger (<28 years) men. No significant associations were observed between sedentary activity and semen parameters.

In support of our findings, several epidemiologic studies have revealed that physically active men had apparently higher sperm motility compared with the more sedentary participants (Vaamonde et al.,

Table II Semen quality parameters by quartiles of MET scores and sedentary time.

Adjusted means (95% CI)[a]	Quartiles of MET scores or sedentary time				
	Q1	Q2	Q3	Q4	*P* for trend[b]
Total METs (min/week)					
Median [range]	**526.5 [0, 1039.5]**	**1584 [1039.5, 2247]**	**3168 [2247, 4365]**	**7082.25 [4365, 36 960]**	-
Number of men	183	189	189	185	-
Number of semen samples	1297	1328	1311	1316	-
Progressive motility, %	54.97 (52.7, 57.2)	55.9 (53.7, 58.1)	55.8 (53.5, 58.0)	57.5 (55.3, 59.8)	**0.02**
Total motility, %	58.2 (56.0, 60.4)	59.1 (57.0, 61.3)	59.2 (57.0, 61.4)	60.7 (58.5, 63.0)	**0.02**
Sperm concentration, $\times 10^6$/mL	51.3 (46.2, 56.3)	52.2 (47.1, 57.2)	52.0 (46.9, 57.0)	53.5 (48.4, 58.6)	0.69
Total sperm count, 10^6	152.1 (132.9, 171.3)	150.4 (131.4, 169.4)	145.3 (126.0, 164.6)	157.5 (138.1, 176.9)	0.39
Moderate-to-vigorous activity (min/week)					
Median [range]	**0 [0, 210]**	**452.5 [210, 735]**	**1260 [735, 2190]**	**4110 [2190, 36 960]**	-
Number of men	194	176	197	179	-
Number of semen samples	1297	1314	1324	1317	-
Progressive motility, %	54.6 (52.3, 56.8)	56.4 (54.2, 58.6)	55.9 (53.7, 58.2)	57.4 (55.2, 59.7)	**0.006**
Total motility, %	57.8 (55.6, 59.9)	59.7 (57.5, 61.9)	59.2 (57.0, 61.4)	60.7 (58.4, 62.9)	**0.004**
Sperm concentration, $\times 10^6$/mL	50.3 (45.3, 55.3)	53.9 (48.9, 58.9)	52.4 (47.3, 57.5)	52.0 (46.9, 57.2)	0.29
Total sperm count, 10^6	151.5 (132.5, 170.6)	156.0 (137.0, 175.1)	143.2 (123.8, 162.6)	151.9 (132.3, 171.4)	0.32
Sedentary activity (min/week)					
Median [range]	**960 [70, 1320]**	**1650 [1320, 2070]**	**2460 [2070, 2940]**	**3480 [2940, 7140]**	-
Number of men	181	178	202	185	-
Number of semen samples	1244	1340	1324	1344	-
Progressive motility, %	56.1 (53.8, 58.4)	56.2 (53.9, 58.4)	56.1 (54.0, 58.3)	55.3 (53.0, 57.6)	0.69
Total motility, %	59.3 (57.0, 61.6)	59.4 (57.2, 61.6)	59.5 (57.4, 61.7)	58.4 (56.2, 60.7)	0.53
Sperm concentration, $\times 10^6$/mL	53.2 (48.0, 58.4)	52.3 (47.2, 57.3)	51.2 (46.3, 56.1)	52.7 (47.5, 57.8)	0.73
Total sperm count, 10^6	151.0 (131.3, 170.7)	159.1 (139.9, 178.3)	146.4 (127.7, 165.1)	149.0 (129.5, 168.5)	0.32

[a]The marginal means were adjusted for age (years), BMI (kg/m^2), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<2000, 2000–10 000 or >10 000 yuan) and sampling season (spring, summer, autumn or winter).
[b]Tests for trend across quartiles of MET scores and sedentary time were assessed by modeling median values within each quartile as a continuous value.

Table III Estimated percent change (95% CIs) of semen quality parameters in relation to quartiles of MET scores and sedentary time[a].

	Quartiles of MET scores or sedentary time				
	Q1	Q2	Q3	Q4	*P* for trend[b]
Total METs					
Progressive motility					
Crude model	0	7.1 (−2.0, 16.9)	6.9 (−2.1, 16.7)	15.5 (5.7, 26.2)	**0.003**
Adjusted model	0	7.6 (−1.4, 17.4)	6.5 (−2.4, 16.2)	16.1 (6.4, 26.8)	**0.002**
Total motility					
Crude model	0	6.7 (−1.6, 15.8)	6.9 (−1.4, 16.0)	14.4 (5.5, 24.2)	**0.002**
Adjusted model	0	7.3 (−1.0, 16.3)	6.8 (−1.5, 15.7)	15.2 (6.2, 24.9)	**0.002**
Sperm concentration					
Crude model	0	3.4 (−19.1, 32.2)	13.6 (−11.1, 45.2)	21.1 (−5.4, 55.0)	0.10
Adjusted model	0	2.7 (−19.6, 31.0)	11.3 (−12.8, 42.0)	20.6 (−5.7, 54.3)	0.10
Total sperm count					
Crude model	0	5.1 (−22.7, 42.8)	5.3 (−22.5, 43.1)	18.6 (−12.9, 61.5)	0.27
Adjusted model	0	0.4 (−26.1, 36.3)	−1.0 (−27.0, 34.4)	12.3 (−17.5, 52.8)	0.41
Moderate-to-vigorous activities					
Progressive motility					
Crude model	0	9.8 (0.5, 19.9)	8.9 (−0.1, 18.7)	17.0 (7.1, 27.7)	**0.002**
Adjusted models	0	11.6 (2.3, 21.7)	9.2 (0.2, 18.9)	17.3 (7.5, 27.9)	**0.003**
Total motility					
Crude model	0	9.4 (0.9, 18.7)	8.5 (0.2, 17.5)	15.9 (6.9, 25.6)	**0.002**
Adjusted models	0	11.2 (2.6, 20.5)	8.9 (0.7, 17.8)	16.4 (7.4, 26.1)	**0.002**
Sperm concentration					
Crude model	0	22.7 (−4.1, 57.0)	19.5 (−6.0, 51.9)	15.8 (−9.4, 48.0)	0.57
Adjusted models	0	16.7 (−8.6, 49.1)	15.7 (−8.9, 46.9)	11.3 (−12.9, 42.1)	0.71
Total sperm count					
Crude model	0	12.9 (−17.0, 53.6)	1.3 (−25.0, 36.7)	5.8 (−22.1, 43.8)	0.93
Adjusted models	0	6.4 (−21.7, 44.5)	−7.1 (−31.1, 25.3)	−4.4 (−29.60 29.9)	0.65
Sedentary activities					
Progressive motility					
Crude model	0	0.4 (−8.3, 9.8)	1.98 (−6.6, 11.3)	−1.4 (−9.8, 7.8)	0.82
Adjusted models	0	−1.4 (−9.8, 7.7)	−1.3 (−9.6, 7.7)	−5.2 (−13.5, 3.8)	0.27
Total motility					
Crude model	0	0.5 (−7.5, 9.2)	2.7 (−5.2, 11.4)	−1.8 (−9.6, 6.6)	0.74
Adjusted models	0	−1.1 (−8.9, 7.3)	−0.3 (−8.1, 8.0)	−5.4 (−13.0, 2.9)	0.22
Sperm concentration					
Crude model	0	−9.6 (−29.6, 16.1)	−15.2 (−33.5, 8.1)	−14.2 (−33.0, 9.9)	0.21
Adjusted models	0	−10.1 (−29.8, 15.2)	−14.1 (−32.6, 9.5)	−11.7 (−31.5, 13.8)	0.34
Total sperm count					
Crude model	0	−3.7 (−29.5, 31.5)	−18.9 (−40.2, 9.8)	−8.9 (−33.1, 24.1)	0.40
Adjusted models	0	−5.5 (−30.6, 28.8)	−18.4 (−39.7, 10.6)	−11.6 (−35.7, 21.4)	0.34

[a]Models were adjusted for age (years), BMI (kg/m2), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<2000, 2000–10 000 or >10 000 yuan) and sampling season (spring, summer, autumn, or winter).
[b]Tests for trend across the quartiles of MET scores and sedentary time were assessed by modeling median values within each quartile as a continuous value.

2012; Lalinde-Acevedo et al., 2017); a randomized controlled trial demonstrated an improvement in semen quality among 419 infertile patients following moderate aerobic exercise over 24 weeks (Hajizadeh Maleki and Tartibian, 2017). In contrast, a decline in sperm motility was also reported among male volunteers who attended high-intensity training (Safarinejad et al., 2009; Hajizadeh Maleki and Tartibian, 2015). To our knowledge, only two previous studies have assessed the associations between levels of exercise intensity and semen quality

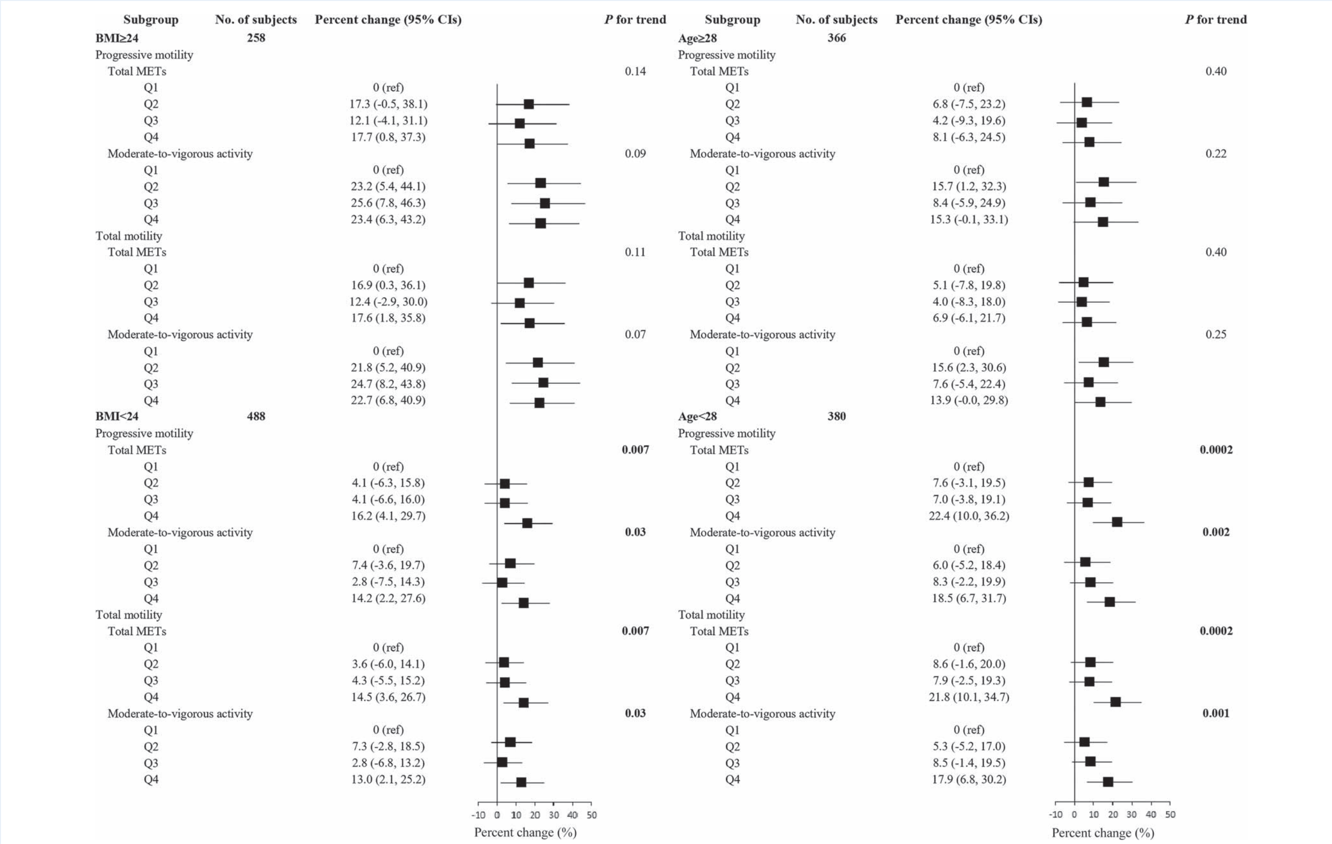

Figure 1 Percent change (95% CIs) in progressive and total sperm motility in relation to quartiles of MET scores and sedentary time, stratified by BMI and age. Models were adjusted for age (years), BMI (kg/m^2), abstinence period (days), marital status (married, unmarried or divorced), smoking (never, former or current), drinking (never, occasional, former or current), tea consumption (yes or no), monthly income (<2000, 2000–10 000 or >10 000 yuan) and sampling season (spring, summer, autumn or winter). Tests for trend across quartiles of MET scores were assessed by modeling median values within each quartile as a continuous value. Physical activities were categorized according to quartiles of total METs or moderate-to-vigorous METs. METs, metabolic equivalents.

(Wise et al., 2011; Gaskins et al., 2015). Inconsistent with our findings, they did not find any evidence of associations between total METs or moderate-to-vigorous METs and semen quality. Also, we did not observe any associations between sedentary time and semen quality parameters, again contrasting with a previous study of 2517 men from fertility centers (Stoy et al., 2004). The inconsistency in findings across studies may be due in part to the differences in study population, including selections of endurance athletes (Safarinejad et al., 2009; Hajizadeh Maleki and Tartibian, 2015), male partners of infertile couples (Wise et al., 2011) and healthy men (Vaamonde et al., 2012; Gaskins et al., 2015; Hajizadeh Maleki et al., 2017; Lalinde-Acevedo et al., 2017). Additionally, chance findings in previous studies cannot be fully ruled out due to sample size (most of which had fewer than 100 men) and application of unstandardized questionnaires to characterize levels of exercise intensity. Most importantly, previous studies relied on only one semen sample per participant, which may inadequately represent a man's reproductive function at any given time (Amann, 2009; Chiu et al., 2017).

In our stratified analyses, the positive dose–response relationships between total and moderate-to-vigorous METs and sperm motility were only observed among leaner men (BMI < 24 kg/m^2) or younger men (those aged <28 years). It is well-documented that overweight/obesity is associated with impaired semen quality (Eisenberg et al., 2014; Ma et al., 2019). Obesity can disrupt sex hormone balance and induce inflammation and oxidative stress, leading to hypogonadism, testicular dysfunction and impaired semen quality (Liu and Ding, 2017). Similarly, numerous studies have reported age-related declines in semen volume, sperm motility and sperm morphology (Kidd et al., 2001; Kühnert and Nieschlag, 2004), potentially because of increased oxidative stress levels and upregulated inflammatory processes (Tremellen, 2008; Aitken et al., 2014; Frungieri et al., 2018). We, therefore, hypothesized that the protective association of physical activity may have been confounded by other factors related to obesity and advancing age.

The mechanisms underlying the association between physical activity and semen quality are unclear. However, previous studies have shown that regular exercise can reduce oxidative stress by promoting antioxidant enzyme activity and upregulating endogenous antioxidant defense (Higuchi et al., 1985; Ji et al., 1988; Pingitore et al., 2015; Powers et al., 2016). Meanwhile, high-intensity activities (e.g. athlete training) were also found to disrupt the oxidant/antioxidant equilibrium (Vaamonde et al., 2009; Gomes et al., 2015), leading to a wide range of reproductive disorders (Redman, 2006). In addition, the hypothalamic–pituitary–gonadal (HPG) axis, which stimulates secretion of pituitary follicle-stimulating hormone (FSH), luteinizing hormone (LH) and testosterone (Lucia et al., 1996), may also play a role (Safarinejad et al., 2009; Parn et al., 2015). Vaamonde et al. (2012) found that moderate-to-high intensity exercise (e.g. endurance activities, except bicycling) was associated with increased plasma concentrations of FSH, LH and testosterone, synergistically with higher semen quality.

Our findings have important public health implications. Physical inactivity is increasing rapidly in many countries and has become a global pandemic (Sallis et al., 2016). In China, total physical activity was around 399 MET hours/week for adults in 1991, which fell to 213 MET hours/week by 2009, largely due to declines in occupational, domestic and travel physical activity (Ng and Popkin, 2012). Physical inactivity is the fourth leading cause of death worldwide (WHO 2010a), which represents a major threat to global health. Meanwhile, some authors have noted evidence of the decline in semen quality during the 20th century coincided with simultaneous changes in lifestyle and environmental factors (Carlsen et al., 1992; Centola et al., 2016). Physical inactivity could be one of the contributing factors, but the exact causal relation cannot be established. In this study, we found that higher levels of total and moderate-to-vigorous physical activity were associated with increased progressive and total sperm motility, strengthening previous evidence that physical activity may improve male reproductive health.

A major strength of our study was that we collected repeated within-individual semen samples at different time points over a 6-month period, given well-documented evidence of substantial within-subject variability in sperm parameters (Stokes-Riner et al., 2007; Chiu et al., 2017). Additionally, we recruited healthy men screened as potential sperm donors from a sperm bank who were likely more representative than previous study populations recruited from athletes or infertile couples. Our study also had several limitations. First, we only measured physical activity once over a 6-month period. Although our validation analysis showed excellent intra-class correlation coefficients for repeated measures of total and moderate-to-vigorous METs and sedentary time (range: 0.84–0.97), measurement error cannot be fully ruled out. Nevertheless, the measurement errors were more likely to be non-differential (i.e. unrelated to the semen quality parameters) and thus would attenuate our risk estimations rather than induce them. Second, the IPAQ questionnaire did not collect data on specific types of physical activity (e.g. cycling or running), making it impossible to compare the effects of different exercises on semen quality. Third, although we adjusted for various potential confounders, the potential for unmeasured confounding (e.g. related to diet or environmental pollutants) to still influence our results cannot be ruled out (Wang et al., 2017; Wang et al., 2019). Fourth, the recruited sperm donors in our study were typically healthy, and the generalizability of study results to the overall population or to men with fertility concerns should be cautioned. Finally, assumptions of causality are unjustified; our present findings need to be confirmed through other study designs, including randomized trials where a more causal interpretation is possible.

In summary, our findings suggest that maintaining regular exercise may improve semen quality parameters among health, non-infertile men. Specifically, we found that higher levels of total and moderate-to-vigorous METs were associated with better total and progressive sperm motility in a dose-dependent manner. These associations tended to be stronger among younger and non-obese men. Our findings reinforce the existing evidence that physical activity may improve male reproductive health. However, additional intervention studies are needed to confirm the role of physical activity in male reproductive health, especially among men with fertility problems.

Authors' roles

All authors fulfill the criteria for authorship. A.P., Y.-X.W. and C.-L.X. designed the study and revised the manuscript. B.S. and Z.-H.S. conducted the statistical analysis, summarized the results and drafted the manuscript. H.-G.C., P.D., Y.-J.C., P.W., L.W., T.-Q.M. and Q.W. collected the clinical data, and C.M., M.A. and J.E.C. critically appraised and revised the manuscript for intellectual content.

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Conflict of interest

None declared.

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