Association between maternal physical exercise and the risk of preterm birth: a case-control study in Wuhan, China

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**What is already known on this topic**?

• Maternal physical activity is generally considered to be beneficial to pregnant women and reduce the risk of preterm birth, yet the quantitative relationship between maternal physical exercise and the risk of preterm birth is not clear.

• Previous evidence on the association between physical activity and preterm birth recruited preterm birth cases based on respondents’ willingness to participate, age, or chronic diseases; however, these studies are subject to bias of selecting preterm birth cases.

**What this study adds**?

• The Bayesian generalized additive mixed model in this study showed a “U-shaped” nonlinear relationship between physical exercise and preterm birth probability.

• Our study adds to the evidence that more maternal physical exercise is associated with lower risk of preterm birth, but overwhelming physical exercise (more than 150 minutes per day) may increase the risk of preterm birth.

**Abstract**

**Background:** To examine the association between physical exercise during pregnancy and preterm birth (PTB) risk via quantitative measures.

**Methods:** We conducted a case-control study. Cases included 2,393 pregnant women who experienced PTB in Wuhan, China from 2011 to 2013. Controls included 4,263 women who experienced full-term births and were matched to cases based on the day of delivery. Self-reported measures of maternal physical exercise were collected. A Bayesian hierarchical logistic regression and a generalized additive mixed model (GAMM) were used.

**Results:** Compared to women not involved in any physical activity, those who participated in physical exercise 1-2 times, 3-4 times, and over five times per week had 21% (aOR: 0.79, 95% CI: 0.68-0.91), 31% (aOR: 0.69, 95% CI: 0.59-0.81) and 33% (aOR: 0.67, 95% CI: 0.59-0.77) lower odds of PTB, respectively. The Bayesian GAMM showed the probability of experiencing PTB decreased as physical exercise increased from zero to about 150 minutes per day. However, the association became positive once physical exercise exceeded 150 minutes per day.

**Conclusion:** Physical exercise during pregnancy, at a moderate amount and intensity, may be associated with lower PTB risk. More data from pregnant women with high participation in physical exercise are needed to confirm this relationship.

**keywords**: preterm birth, physical exercise, pregnancy, Bayesian, nonlinear, Wuhan

1. **Introduction**

Preterm births (PTB), defined as births that occurred at a gestational age of less than 37 weeks, accounted for approximately 35% of deaths among newborn babies globally in 2016.[1](#ref-goldenberg2008epidemiology)–[3](#ref-chawanpaiboon2019global) Even though over 50% of preterm neonates survive, they face substantially higher risks of short-term and long-term morbidity and mortality.[4](#ref-simmons2010preventing),[5](#ref-qian2016ambient) Common complications of PTB, including respiratory distress syndrome, bronchopulmonary dysplasia, and sepsis, were the leading causes of death in children less than five years old in 2016.[3](#ref-chawanpaiboon2019global) Even though PTB poses a significant threat to healthcare, social security, and the economy, few evidence-based strategies have been developed to effectively reduce the incidence of PTB.[5](#ref-qian2016ambient)–[7](#ref-frey2016epidemiology)

It is generally recommended that pregnant women maintain an adequate level of physical exercise. The Department of Health and Human Services in the United States advises pregnant women to participate in at least two and a half hours of aerobic activity per week with moderate-intensity.[8](#ref-UShealthservice) The British Nutrition Foundation suggests that being physically active is beneficial to both the pregnant woman and the baby.[9](#ref-BritishNutrition) Health departments and media in Norway, Denmark, China, and other countries have also provided similar recommendations.[6](#ref-juhl2008physical),[10](#ref-PeopleDaily) Although being physically active is recommended for pregnant women, health authorities do not explicitly claim that physical activity is directly associated with a decreased risk of PTB.

Biologically, physical exercise produces higher levels of adrenaline, noradrenaline, and catecholamines, which can induce preterm birth via uterine contractions or intrauterine growth restriction.[6](#ref-juhl2008physical),[11](#ref-barakat2015exercise),[12](#ref-di2016exercise) However, physical exercise can also improve placental vascularization and decrease oxidative stress in pregnant women, both of which may reduce the risk of PTB.[11](#ref-barakat2015exercise),[13](#ref-boscaglia2003changes) Empirically, some randomized controlled trials (RCTs) and observational studies have reported that aerobic exercise was associated with a reduction in the incidence of PTB.[6](#ref-juhl2008physical),[12](#ref-di2016exercise),[14](#ref-domingues2008leisure)–[17](#ref-huang2019maternal) But other studies reported a null association between physical activity and the risk of preterm birth.[18](#ref-barakat2014exercise),[19](#ref-tinloy2014exercise) Therefore, there is no consensus in theoretical mechanisms or scientific research on the association between maternal physical activity and PTB risk.

Although some of the studies mentioned above were RCTs, they did not have very high external validity, since the study samples were relatively small and based on the respondents’ willingness to participate,[15](#ref-guendelman2013association),[18](#ref-barakat2014exercise),[19](#ref-tinloy2014exercise) age,[19](#ref-tinloy2014exercise) or chronic disease.[17](#ref-huang2019maternal) Other studies used a limited number of cases and controls or even national cohorts, but only a certain percent of pregnant women were recruited and not all PTB cases were included. For example, 60% of the invited women in the Danish National Birth Cohort study agreed to participate in their study while 40% refused.[6](#ref-juhl2008physical) Moreover, these previous studies did not report a nonlinear relationship between physical exercise and PTB. Considering the possibility of a nonlinear relationship is crucial since the conclusion may not be simply bidirectional, as in the presence or absence of physical activity. Instead, this association depends on the amount and intensity of exercise.

It is estimated China had the second largest proportion of PTB internationally in 2014, only behind India.[3](#ref-chawanpaiboon2019global),[20](#ref-chen2018epidemiology) Additionally, only 11% of pregnant women in China meet the international guidelines for physical activity during pregnancy, a significantly lower proportion than that in Western countries.[21](#ref-guelfi2015comparison) Understanding the association between physical exercise and PTB may help reduce the prevalence of PTB and create substantial social value in China. The current study attempts to address some of the main gaps in the literature around the association between exercise during pregnancy and the risk of PTB, including case selection bias and potential nonlinear relationships. Utilizing survey data from all preterm births in Wuhan, China from June 2011 to June 2013, the purpose of this study is to examine the association between maternal physical activity and PTB and to evaluate the dose-response shape of the relationship.

1. **Methods**
   1. **Study population**

Wuhan, the capital city of Hubei Province, is known as the largest city in central China and serves as a transportation hub. There are approximately 10 million people in Wuhan, and over 60% of them reside in seven core, urban districts: Jiangan, Jianghan, Qiaokou, Hanyang, Wuchang, Qingshan, and Hongshan.[22](#ref-cyearbook2017) Wuhan, which is known as an “oven city” in China, has a subtropical and humid climate with temperatures exceeding 40 degrees Celsius during the summer.[5](#ref-qian2016ambient)

We conducted a case-control study to evaluate the relationship between physical exercise and PTB.[5](#ref-qian2016ambient) Cases were defined as all pregnant women who delivered preterm or low birth weight babies in the seven core, urban districts of Wuhan from June 9, 2011 to June 10, 2013. Controls were pregnant women who had full-term delivery and were randomly selected from the same district in the same period as cases. Controls were selected three times per month: on the 10th, 20th, and the last day of each month. We sampled births from the 1st to the 10th day of the month on the 20th day; births from the 11th to 20th days were sampled on the last day of the month; and births after the 20th day were sampled on the 10th day of the following month. Cases and controls were matched based on birth date within a 10-day window to account for potential effects of weather and environmental exposures.[5](#ref-qian2016ambient) In total, 6,656 pregnant women agreed to participate in the study: 2,393 PTB cases and 4,263 full-term birth controls. All study participants were administered a questionnaire in their homes by trained interviewers.

* 1. **Outcome and exposure measurement**

The outcome, PTB, was dichotomized as full-term birth (38 to 42 weeks of gestation) and PTB (less than 37 completed weeks of gestation).[5](#ref-qian2016ambient)

We measured maternal physical activity using two questions: “How many times did you exercise regularly, for 30 to 40 minutes per week, during the late gestational period (after seven gestational months)?” and “How much time did you spend on outdoor sports per day during your pregnancy?” The first question created a five-level variable, including “none” (reference group), “1 to 2 times,” “3 to 4 times,” “more than 5 times,” and “a doctor or nurse advised you not to exercise.”.[5](#ref-qian2016ambient) The second question produced a continuous variable that measured the number of minutes the women spent participating in outdoor sports per day during their pregnancy.

* 1. **Covariates**

Based on the risk factors identified in previous literature and on data availability,[5](#ref-qian2016ambient),[23](#ref-meis1998preterm),[24](#ref-chen2017prevalence) we identified a set of sociodemographic, genetic, maternal comorbidity and parity, environmental, and pathophysiological factors as independent variables. Maternal age (less than or equal to 21, 22-28, and >28 years of age), education (less than high school, high school or occupational school, college, and graduate school), and household income (1,000-2,999 RMB as low, 3,000-6,999 RMB as middle, and more than 6,999 RMB as high income, with 1 USD equaling around 6.5 RMB at the time of this study) were included as socioeconomic variables. Family history of premature or low birth weight newborns and newborn gender were used as proxies of genetics. Maternal comorbidity was dichotomized as no disease or having one of the following: diabetes, thyroid disease, hepatitis, hypertension, heart disease, renal disease, anemia, epilepsy, asthma, depression, anxiety, or others. Maternal parity was dichotomized as first baby or at least one prior live birth. Body mass index prior to pregnancy (classified as less than or equal to 18.5, 18.5-24 and >24), weight gain during pregnancy in kilograms, and colporrhagia during pregnancy (yes or no) were included as pathophysiological variables. Air pollution (no abnormal smells versus noticeable smell in the residence) was included as an environmental variable.

* 1. **Data analyses**

This is a matched case-control study where cases and controls were loosely matched by time of delivery. Given the relatively unstructured nature of the matching, the analysis utilized a standard (unconditional) statistical modeling strategy. This meant negligible loss in testing and estimation but much faster estimation speed and better statistical precision.[25](#ref-pearce2016analysis),[26](#ref-kuo2018unconditional) For the five-level, physical exercise predictor, we performed a Bayesian hierarchical logistic regression that included a random intercept for each of the seven districts to account for geographic clustering in the data. Similarly, we conducted a conditional logistic regression model, which included the same predictors as a sensitivity test.

To detect any possible nonlinear relationships, we also conducted a Bayesian generalized additive mixed model (GAMM) with random intercepts for the seven inner-city districts.[27](#ref-baayen2017cave) The number of basis functions was set at 10 to capture any potential nonlinear relationship, and the smoothing parameters were selected using the package’s default optimizing algorithm.[28](#ref-carpenter2017stan),[29](#ref-goodrich2018) Since 1,926 (28.9%) respondents failed to fill out the question about continuous physical activity (the response rate 71.1%, however, was still higher than the 65% threshold recommended by the Pregnant Risk Assessment Monitoring System[30](#ref-CDCPRAMS)), either because a doctor or nurse advised them not to exercise or for other reasons, we included only respondents with non-missing values on physical activity. The distribution of the outcome and covariates did not change substantially before or after deleting these observations. We did not perform a conditional GAMM as a sensitivity test since no applicable software package could perform that model. As recommended by the package developers, we assigned weakly informative priors to the parameters as follows: Normal for intercept parameters, Normal for all non-intercept parameters, and Gamma for scale (standard deviation) parameters. To ensure that the Markov chain Monte Carlo (MCMC) algorithm converged, we set four chains with 2,000 warm-up (burn-in) and 5,000 iteration steps for each chain. We used Gelman-Rubin statistics,[31](#ref-gelman1992inference) posterior trace plots, and the number of effective sample sizes as diagnostic statistics.[32](#ref-muth2018user) Adjusted odds ratios (aORs) and 95% credible intervals (CIs) were reported. All data manipulation, visualization, and statistical modeling were carried out using the statistical computing environment R 3.5.2.[33](#ref-citingr)

1. **Results**

An overview and case-control comparisons of socioeconomic characteristics and PTB risk factors for the study population are summarized in Table 1. Mothers who experienced PTB tended to participate in significantly less physical exercise during pregnancy compared to those who did not experience PTB. In addition, a significantly higher percentage of mothers that experienced PTB were young (35.5% versus 25.7%) and overweight (11.8% versus 9.3%), experienced colporrhagia (34% versus 20%), had a family history of PTB (7% versus 3%) and maternal comorbidity (19% versus 15%), and gave birth to male babies (59.6% versus 53.3%). We found no significant statistical differences between cases and controls regarding education and income.

**Table 1**: Characteristics of the study population overall and by birth term in Wuhan, China from June 9, 2011, to June 10, 2013

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Variables | Overall  (n = 6656) | Full-term  (n = 4263) | Preterm  (n = 2393) | P-values |
| Exercise frequency per week (%) |  |  |  | <0.001 |
| 0 | 1881 (28.3) | 1107 (26.0) | 774 (32.3) |  |
| 1-2 | 1285 (19.3) | 834 (19.6) | 451 (18.8) |  |
| 3-4 | 1179 (17.7) | 802 (18.8) | 377 (15.8) |  |
| >5 | 2170 (32.6) | 1476 (34.6) | 694 (29.0) |  |
| Advised against | 141 (2.1) | 44 (1.0) | 97 (4.1) |  |
| Exercise per day, in minutes (mean (sd)) | 43.39 (24.30) | 44.02 (24.61) | 42.13 (23.64) | 0.012 |
| Maternal age (%) |  |  |  | <0.001 |
| <22 | 1944 (29.2) | 1094 (25.7) | 850 (35.5) |  |
| 22-28 | 3880 (58.3) | 2604 (61.1) | 1276 (53.3) |  |
| >28 | 832 (12.5) | 565 (13.3) | 267 (11.2) |  |
| Education (%) |  |  |  | 0.112 |
| Less than high school | 1279 (19.2) | 825 (19.4) | 454 (19.0) |  |
| High school or occupational school | 1917 (28.8) | 1262 (29.6) | 655 (27.4) |  |
| College | 3131 (47.0) | 1960 (46.0) | 1171 (48.9) |  |
| Graduate school | 329 (4.9) | 216 (5.1) | 113 (4.7) |  |
| Income (%) |  |  |  | 0.058 |
| Middle income | 4482 (67.3) | 2910 (68.3) | 1572 (65.7) |  |
| Low income | 626 (9.4) | 379 (8.9) | 247 (10.3) |  |
| High income | 1548 (23.3) | 974 (22.8) | 574 (24.0) |  |
| Family history (mean (sd)) | 0.04 (0.21) | 0.03 (0.17) | 0.07 (0.26) | <0.001 |
| Baby's gender = male (%) | 3699 (55.6) | 2273 (53.3) | 1426 (59.6) | <0.001 |
| Maternal disease (mean (sd)) | 0.17 (0.37) | 0.15 (0.36) | 0.19 (0.39) | <0.001 |
| Parity = more than one (%) | 1119 (16.8) | 682 (16.0) | 437 (18.3) | 0.02 |
| BMI before (%) |  |  |  | 0.005 |
| Underweight | 1325 (19.9) | 869 (20.4) | 456 (19.1) |  |
| Normal | 4651 (69.9) | 2996 (70.3) | 1655 (69.2) |  |
| Overweight/Obesity | 680 (10.2) | 398 (9.3) | 282 (11.8) |  |
| Weight gain, in kilograms (mean (sd)) | 14.28 (3.95) | 14.53 (4.00) | 13.82 (3.82) | <0.001 |
| Colporrhagia (mean (sd)) | 0.25 (0.43) | 0.20 (0.40) | 0.34 (0.47) | <0.001 |
| Noticeable air pollution (%) | 1060 (15.9) | 671 (15.7) | 389 (16.3) | 0.605 |

Parameter estimates of the two Bayesian hierarchical models had over 3,000 effective sample sizes in MCMC draws, and their associated Gelman-Rubin statistics were all less than 1.1. The four chains were well-mixed without any divergent chains or significant auto-correlation (Appendix 1 and 2). All evidence indicated that the MCMC algorithms converged and that the estimates were valid and trustworthy.

We observed a consistent and considerable inverse association between the three physical exercise groups and PTB (Table 2). Compared to mothers who never participated in physical exercise, those who participated in physical exercise 1 to 2 times a week (aOR: 0.79, 95% CI: 0.68-0.91), 3 to 4 times a week (aOR: 0.69, 95% CI: 0.59-0.81), and more than 5 times a week (aOR: 0.67, 95% CI: 0.59-0.77) all had considerably lower chances of experiencing PTB. The mothers who were advised against physical exercise by their doctors or nurses (aOR: 2.50, 95% CI: 1.72-3.69) had significantly higher chances of experiencing PTB compared to those who did not conduct any physical exercise. To account for the nature of the matched case-control study design, we also performed a conditional logistic regression as a sensitivity test. These results are summarized in Table 3. The parameter estimates for physical exercise in the conditional logistic model were consistent with those estimated using the Bayesian unconditional logistic models.

**Table 2**: Estimated ORs and 95% credible intervals using Bayesian hierarchical logistic regression for PTB in Wuhan, China from June 9, 2011, to June 10, 2013

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | aOR | 95% CI left | 95% CI right |
| (Intercept) | 1.11 | 0.81 | 1.51 |
| Exercise frequency per week (Reference: zero) | | | |
| 1-2 | 0.79 | 0.68 | 0.91 |
| 3-4 | 0.69 | 0.59 | 0.81 |
| >5 | 0.67 | 0.59 | 0.77 |
| Advised against | 2.5 | 1.72 | 3.69 |
| Maternal age (Reference: < 22) | | | |
| 22-28 | 0.66 | 0.59 | 0.75 |
| >28 | 0.68 | 0.57 | 0.83 |
| Education (Reference: less than high school) | | | |
| High school or occupational school | 0.97 | 0.82 | 1.13 |
| College | 1.14 | 0.97 | 1.34 |
| Graduate school | 0.95 | 0.72 | 1.26 |
| Income (Reference: middle) | | | |
| Low income | 1.21 | 1.01 | 1.46 |
| High income | 1.05 | 0.93 | 1.19 |
| Family history | 2.31 | 1.81 | 2.94 |
| Baby's gender (Reference: female) | 1.28 | 1.15 | 1.43 |
| Maternal disease | 1.25 | 1.09 | 1.43 |
| Parity (more than one) | 0.96 | 0.81 | 1.12 |
| BMI before pregnancy (Reference: underweight) | | | |
| Normal | 0.96 | 0.84 | 1.09 |
| Overweight/Obesity | 1.12 | 0.92 | 1.37 |
| Weight gain, in kilograms | 0.96 | 0.94 | 0.97 |
| Colporrhagia | 1.85 | 1.65 | 2.09 |
| Noticeable air pollution | 0.96 | 0.83 | 1.11 |

**Table 3**: Estimated ORs and 95% credible intervals using conditional logistic regression for PTB in Wuhan, China from June 9, 2011, to June 10, 2013

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | aOR | 95% CI left | 95% CI right |
| Exercise frequency per week (Reference: zero) | | | |
| 1-2 | 0.85 | 0.75 | 0.96 |
| 3-4 | 0.79 | 0.69 | 0.9 |
| >5 | 0.79 | 0.71 | 0.89 |
| Advised against | 1.51 | 1.19 | 1.92 |
| Maternal age (Reference: < 22) | | | |
| 22-28 | 0.77 | 0.7 | 0.85 |
| >28 | 0.78 | 0.66 | 0.91 |
| Education (Reference: less than high school) | | | |
| High school or occupational school | 0.97 | 0.85 | 1.11 |
| College | 1.06 | 0.93 | 1.21 |
| Graduate school | 0.91 | 0.72 | 1.15 |
| Income (Reference: middle) | | | |
| Low income | 1.15 | 0.99 | 1.33 |
| High income | 1.02 | 0.91 | 1.13 |
| Family history | 1.5 | 1.26 | 1.78 |
| Baby's gender (Reference: female) | 1.16 | 1.06 | 1.26 |
| Maternal disease | 1.13 | 1.01 | 1.26 |
| Parity (more than one) | 0.96 | 0.84 | 1.09 |
| BMI before pregnancy (Reference: underweight) | | | |
| Normal | 0.99 | 0.88 | 1.1 |
| Overweight/Obesity | 1.09 | 0.93 | 1.28 |
| Weight gain, in kilograms | 0.97 | 0.96 | 0.98 |
| Colporrhagia | 1.43 | 1.31 | 1.57 |
| Noticeable air pollution | 0.98 | 0.87 | 1.1 |

The parameter estimates of the Bayesian GAMM are summarized in Table 4. The parameter estimates (aORs) for variables other than physical exercise in minutes are generally consistent with those in Table 2. Figure 1 demonstrates the relationship between physical activity in minutes (x-axis) and the probability of PTB (y-axis) controlling for other covariates, with 95% credible interval (CI) bands wrapping around the point estimates. Interestingly, there seems to be a “U-shaped” relationship between physical exercise and PTB probability. As physical exercise increased from zero to about 150 minutes, the probability of experiencing PTB went down. However, once the physical exercise exceeded 150 minutes per day, the probability of PTB stopped decreasing and had a moderate increase with more physical exercise. It should be noted that the credible intervals of physical exercise more than 150 minutes were wide, as there were few participants that exercised more than 150 minutes per day during pregnancy.

**Table 4**: Estimated ORs and 95% credible intervals using Bayesian hierarchical generalized additive mixed models for PTB in Wuhan, China from June 9, 2011, to June 10, 2013

|  |  |  |  |
| --- | --- | --- | --- |
| Variable | aOR | 95% CI left | 95% CI right |
| (Intercept) | 0.81 | 0.56 | 1.16 |
| Smoothing splines |  |  |  |
| s(Exercise).1 | 0.99 | 0.07 | 9 |
| s(Exercise).2 | 0.99 | 0.08 | 7.82 |
| s(Exercise).3 | 0.99 | 0.08 | 8.43 |
| s(Exercise).4 | 1.08 | 0.14 | 18.44 |
| s(Exercise).5 | 1.36 | 0.32 | 21.77 |
| s(Exercise).6 | 0.91 | 0.19 | 6.12 |
| s(Exercise).7 | 0.88 | 0.06 | 2.34 |
| s(Exercise).8 | 1.64 | 0.57 | 43.57 |
| s(Exercise).9 | 0.74 | 0.03 | 2.63 |
| Maternal age (Reference: < 22) | | | |
| 22-28 | 0.62 | 0.54 | 0.72 |
| >28 | 0.69 | 0.54 | 0.88 |
| Education (Reference: less than high school) | | | |
| High school or occupational school | 0.98 | 0.8 | 1.19 |
| College | 1.13 | 0.93 | 1.38 |
| Graduate school | 0.79 | 0.56 | 1.12 |
| Income (Reference: middle) | | | |
| Low income | 1.09 | 0.86 | 1.35 |
| High income | 1.07 | 0.92 | 1.25 |
| Family history | 2.22 | 1.67 | 2.94 |
| Baby's gender (Reference: female) | 1.28 | 1.13 | 1.45 |
| Maternal disease | 1.16 | 0.99 | 1.37 |
| Parity (more than one) | 0.97 | 0.8 | 1.18 |
| BMI before pregnancy (Reference: underweight) | | | |
| Normal | 0.97 | 0.83 | 1.14 |
| Overweight/Obesity | 1.19 | 0.94 | 1.5 |
| Weight gain, in kilograms | 0.96 | 0.95 | 0.98 |
| Colporrhagia | 1.76 | 1.53 | 2.02 |
| Noticeable air pollution | 0.94 | 0.79 | 1.11 |

1. **Discussion**

We found maternal physical exercise 1-2 times, 3-4 times, and over 5 times per week was associated respectively with 21% (aOR = 0.79, 95% CI: 0.68-0.91), 31% (aOR = 0.69, 95% CI: 0.59-0.81), and 33% (aOR = 0.67, 95% CI: 0.59-0.77) lower odds of PTB, respectively, when compared to women who were not involved in any physical activity. In addition, we observed a “U-shaped” relationship between physical exercise in minutes and the probability of PTB in the Bayesian GAMM. The probability of PTB decreased as physical exercise increased from zero to 150 minutes per day but began to increase as physical exercise exceeded over 150 minutes per day. Our study supports the previous literature that found a relationship between PTB and physical activity,[6](#ref-juhl2008physical),[12](#ref-di2016exercise),[15](#ref-guendelman2013association)–[17](#ref-huang2019maternal) with the striking nuance that, while lower levels of physical activity are associated with reduced risk for PTB, higher levels of physical activity are associated with an increased risk for PTB.

Although the underlying mechanism between physical exercise and PTB is not entirely clear, several hypotheses can potentially explain the generally inverse relationship. First, maternal physical exercise can improve the mother’s psychological well-being, lowering the chances of depression during pregnancy and, thereby, preventing PTB.[34](#ref-bouras2015preterm),[35](#ref-staneva2015effects) Additionally, insulin sensitivity can be increased with physical exercise and contribute to reducing inflammatory response, which is reported to be a significant risk factor for PTB.[15](#ref-guendelman2013association),[36](#ref-goldenberg2005prepregnancy) Other physiological pathways by which physical exercise helps prevent PTBs, such as exercise improving placental vascularization and reducing oxidative stress and gestational diabetes mellitus, have been suggested by other cohort studies and RCTs.[37](#ref-clapp1992effect)–[39](#ref-wang2017randomized)

Previous investigations have generally yielded consistent conclusions with our logistic regression results. For example, Juhl et al. reported an adjusted hazard ratio of 0.82 (95% confidence interval: 0.76-0.86) in exercising pregnant women compared with non-exercising pregnant women based on a Danish birth cohort.[6](#ref-juhl2008physical) Guendelman et al. conducted a case-control study based on pregnant women in Southern California and reported an inverse association between moderate exercise in the second trimester and PTB (aOR: 0.90, 95% confidence interval: 0.84-0.96).[15](#ref-guendelman2013association) Compared to these studies, our study yielded point estimates of greater magnitude (aOR all less than 0.80), which may be explained by Chinese pregnancy culture. In traditional Chinese medicine and culture, pregnancy is a vulnerable period when the mother needs to recuperate and remain sedentary and is often associated with numerous antenatal taboos.[40](#ref-lee2009antenatal) It is reported that pregnant women in China have much less physical exercise than pregnant women in Western countries.[21](#ref-guelfi2015comparison) Therefore, the magnitude of exercise effect among the Chinese population may be higher than that among Western populations. This is supported by another Chinese study on the association between maternal exercise and PTB, which found adjusted OR point estimates for low, medium, and high exercise frequency all less than 0.70 and all statistically significant.[17](#ref-huang2019maternal)

The two models in our study reached similar conclusions that physical exercise is negatively associated with PTB risk. However, the Bayesian GAMM model suggested that the risk of PTB increased as pregnant women engaged in more than 150 minutes of exercise per day, which was different to the results from the Bayesian logistic regression model. The two predictors were measuring maternal physical activity from different perspectives: the predictor in Bayesian GAMM measured the amount of physical exercise time per day in minutes, while the predictor in Bayesian logistic regression measured the frequency of exercise per week as a categorical variable. The results from the two regression models suggest that pregnant women should engage in frequent physical activity of moderate intensity and length to reduce the risk of PTB but should not exercise for overwhelming amount of time.

Compared with previous studies, ours has several strengths. First, we included all PTBs in the urban districts of Wuhan, China from June 2011 to June 2013. Therefore, the PTB selection bias from previous studies is minimized in ours. In addition, the participants in this study were recruited from all seven core, urban districts of a large metropolitan city in the same period in China. In this way, unmeasured potential confounders like prenatal care quality and geographic distance to high-quality health care facilities are minimized since there is less variability in these potential confounders among the study population.[5](#ref-qian2016ambient) We also used a Bayesian GAMM to detect the nonlinear relationship between maternal exercise and risk of PTB. Previous investigations have used either a dichotomous or a multi-category variable to measure physical exercise, which could have led to exposure misclassification bias. By contrast, the Bayesian GAMM and quantitative measurement of exercise in this study demonstrated a “U-shaped” relationship between maternal physical exercise and PTB.

Despite these strengths, this study also possesses some limitations. First, our key exposure variable, maternal physical exercise, was self-reported and subject to recall bias in terms of both quantity and quality of exercise. The desire to be active may have led participants to over-report.[15](#ref-guendelman2013association) Second, the quantitative measure of physical activity has a fair amount of missing values (28.9%), and we conducted the Bayesian GAMM based on the complete data. However, we did not find substantial differences in the distribution of outcome and covariates before and after deleting the observations with missing values. It is unlikely that these missing values were informative. Third, since this is a case-control study, we are not able to capture all confounders, such as whether PTB was spontaneous or medically induced, spousal support, and physical exercise in different trimesters. Fourth, the observed association between maternal exercise and PTB does not necessarily establish causality since this is a observational case-control study.

In conclusion, our study adds to the evidence that more maternal physical exercise is associated with lower risk of PTB, but overwhelming physical exercise may increase the risk of PTB. Pregnant women are suggested to engage in frequent, moderate intensity and length physical exercise. Further study is needed to substantiate the positive association at higher levels of physical exercise and determine the threshold of physical exercise that leads to an increasing risk of PTB. A clearer understanding of the frequency and quality of recommended exercise can help nations around the globe recommend appropriate levels of physical activity for pregnant women.

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