The association between prenatal yoga and the administration of ritodrine hydrochloride during pregnancy: an adjunct Study of Japan Environment and Children's Study.

(妊娠中のヨガ(マタニティ・ヨガ)実践と、塩酸リトドリン投与 との関連に関する研究:子どもの健康と環境に関する全国調査にお ける追加調査)

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27 ABSTRACT

Background: While the beneficial effects of prenatal yoga have been reported in recent 28years, little is known about its effectiveness in pregnant Japanese women. Despite 29several adverse effects, ritodrine hydrochloride is frequently prescribed to suppress 30 preterm labor in Japan, and its usage may therefore indicate cases of preterm labor. This 31study aimed to clarify the association between prenatal yoga and ritodrine hydrochloride 32use during pregnancy. 33 Methods: An observational study was conducted as an adjunct study by the Hokkaido 34unit of the Japan Environment and Children's Study. Information on prenatal yoga 35practice was collected using a self-questionnaire between March 21, 2012 and July 7, 36 2015 targeting women who had recently delivered. Ritodrine hydrochloride use was 3738identified from medical records. A total of 2,692 women were analyzed using logistic regression models that adjusted for possible confounders. 39**Results:** There were 567 (21.1%) women who practiced prenatal yoga, which was 40 associated with a lower risk of ritodrine hydrochloride use (adjusted odds ratio [OR] 41 0.77; 95% CI 0.61-0.98). This was especially evident in women with a total practice 4243duration that exceeded 900 minutes throughout their pregnancy (adjusted OR 0.54; 95% CI 0.38-0.76). A sensitivity analysis that excluded patients with threatened abortion 44

45	during the study period produced similar results.
46	Conclusions: Prenatal yoga was associated with a lower risk of ritodrine hydrochloride
47	use, particularly in women with more than 900 minutes of practice time over the course
48	of their pregnancy. Prenatal yoga may be a beneficial option for pregnant women in the
49	selection of alternative therapies.
50	
51	Keywords: yoga; pregnancy; preterm; ritodrine; JECS

53 INTRODUCTION

Yoga is a mental and physical practice with origins in ancient Indian philosophy¹. 54Previous research based on randomized controlled trials (RCTs) have suggested that 55yoga may reduce low back pain,² improve vitality in breast cancer patients, and reduce 56inflammatory cytokines³. In recent years, prenatal yoga has also been reported to reduce 57psychiatric stress and anxiety,^{4, 5} low back pain,⁶ pregnancy complications in high-risk 58patients (such as those with obesity or advanced age),⁷ and the duration of labor in 59healthy pregnant women⁸. The beneficial effects of prenatal yoga have been previously 60 summarized elsewhere⁹. 61 Two RCTs have also investigated the effects of yoga on neonatal prematurity: a study 62 from the US reported significantly longer mean gestational durations before delivery in 63 women who practiced yoga (yoga group, mean (SD) 38.6 (1.9) weeks; non-yoga group, 64 36.7 (2.6) weeks)¹⁰. Similarly, a study from India observed a significantly lower 65 prevalence of preterm births (yoga group, 20.7%; control group, 45.7%) among women 66 with high-risk factors such as history of obstetric complications, obesity, or advanced 67 age⁷. However, studies have yet to examine the effects of prenatal yoga on prematurity 68 or tocolytic drug use in pregnant Japanese women,⁹ and there is currently little evidence 69 to support the practice of prenatal yoga in Japan. 70

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71	Preterm birth is a major contributing factor to perinatal morbidity and mortality ^{11, 12} .
72	Drugs such as β 2-agonists are frequently administered throughout the world to treat
73	preterm labor, ¹³ which if left untreated can lead to spontaneous preterm birth. Despite
74	evidence supporting the effectiveness of betamimetics in reducing the number of
75	women in preterm labor who gave birth within 48 hours, these drugs have not been
76	observed to actually reduce the number of preterm births ¹³ . Due to the relatively high
77	risk of adverse effects and the lack of effectiveness in preventing preterm births, the
78	usage of betamimetics tends to be avoided, particularly among developed countries ^{13, 14} .
79	The proportion of preterm births in Japan is among the lowest in the world ¹⁵⁻¹⁷ . The
80	key drug for treating preterm labor in Japan is ritodrine hydrochloride, which is a
81	β -agonist ¹⁸⁻²⁰ . While the Japanese Ministry of Health, Labour and Welfare approved
82	another tocolytic agent (magnesium sulfate) for the treatment of preterm labor in 2008,
83	its use is restricted to cases that are unresponsive to ritodrine hydrochloride. As a result,
84	ritodrine hydrochloride remains the de facto first-line drug for preterm labor in Japan ¹⁹ .
85	Despite its widespread use, ritodrine hydrochloride places a substantial burden on the
86	cardiovascular system ²¹ and may also result in other adverse effects, ²²⁻²⁵ indicating that
87	it should only be administered when necessary. Hence, identifying alternative options
88	that may contribute to a decrease in ritodrine hydrochloride use would be beneficial for

- 89 pregnant women. In this study, we investigated the use of prenatal yoga as a possible
- 90 alternative to reduce preterm labor in pregnant women.

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- 91 This observational study aimed to clarify the association between prenatal yoga and
- 92 the use of ritodrine hydrochloride during pregnancy.

93 **METHODS**

94 Study Participants

- 95 The Japan Environment and Children's Study (JECS)²⁶ is an ongoing large-scale
- 96 prospective birth cohort study, and its protocol has been previously described in detail²⁷.
- Women are recruited in the early stages of pregnancy, and a total of 103,106 women
- throughout Japan participated in this study between January 1, 2011 and March 31,
- 99 2014^{28} . The Hokkaido unit (e Appendix 1) is one of 15 regional centers of the JECS,
- and had recruited 8,362 pregnant women at the time of the study.
- 101 This study was conducted as an Adjunct Study outlined in the JECS protocol paper²⁷.
- 102 The study protocol was approved by the Ministry of the Environment, Japan. This
- adjunct study on the effects of prenatal yoga was performed on JECS Hokkaido unit
- 104 participants using self-questionnaires. Participants provided written informed consent
- 105 before inclusion in the study. Explanatory materials and self-questionnaires regarding
- 106 prenatal yoga were sent to eligible study participants after delivery, and the
- 107 questionnaires were collected between March 21, 2012 and July 7, 2015.
- 108 The sample selection flow diagram is shown in Figure 1. Of the possible 8,362 study
- 109 participants, we sent the self-questionnaire to 7,571 participants after their delivery. The
- 110 791 participants who were not sent questionnaires were excluded due to miscarriages,

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111	stillbirths, participation withdrawal, or for other reasons. A total of 5,468 agreed to
112	participate in the study, indicating a response rate of 72.2%.
113	The questionnaire data on yoga were then merged with a second dataset provided by
114	the JECS Hokkaido unit. This second dataset included participants who gave birth on or
115	before September 30, 2013, and was released in June 2015. After merging the data, the
116	sample included 3,387 women who had corresponding data in both datasets. We
117	excluded those with multiple pregnancies ($n = 55$), missing birth data ($n = 10$), and
118	uncertain gender ($n = 1$). An outlier who experienced weight gain of 30 kg or more
119	during pregnancy $(n = 1)$ and participants with errors/missing data in any of the
120	covariates ($n = 628$) were also excluded. The final study sample for analysis comprised
121	2,692 women.
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123	Ethical Issues
124	This adjunct study of the JECS was approved by the Institutional Ethics Boards for
125	Epidemiological Studies at Asahikawa Medical University, the Hokkaido University

126 Center for Environment and Health Sciences, and the Japan Red Cross Hokkaido

127 College of Nursing.

129 **Exposure Variable**

The exposure variable analyzed in this study was the practice of prenatal yoga during 130the index pregnancy period. A self-questionnaire was sent to each participant after 131132delivery. The median period between delivery and response to the questionnaire was approximately 3 months (mean 2.7 months; range 0–26). The main question in the 133self-questionnaire was "Did you practice prenatal yoga during this pregnancy period?" 134If the answer was "Yes", the participant was categorized into the "prenatal yoga group"; 135if the answer was "No" or "I tried to, but was stopped by the physician", the participant 136 was categorized into the "non-prenatal yoga group". Respondents in the prenatal yoga 137group were then directed to answer additional questions that addressed practice methods 138(use of instructor or self-study by DVDs or books), practice frequency (duration of 139140practice in gestational weeks, frequency of practice per week, and duration of practice in minutes per exercise session), and the specific components of yoga (inclusion or 141 non-inclusion of physical posture, breathing techniques, and meditation practice). 142143

144 **Outcome Variable**

The outcome variable analyzed in this study was the use of ritodrine hydrochloride. The
use of ritodrine hydrochloride once or more during the index pregnancy period was

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148	coordinators after delivery.
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150	Covariates
151	We collected information on various potential confounding factors of preterm
152	delivery ²⁹⁻³¹ and prenatal yoga. Using a self-questionnaire sent to the participants
153	between 12 and 16 weeks of gestation, we collected data on marital status, employment
154	status, physical activity level before pregnancy (metabolic equivalents
155	[METS]×min/day), ^{32, 33} and malformation of uterus, if any.
156	Using another self-questionnaire sent to the participants between 22 and 28 weeks of
157	gestation, we collected data on smoking, alcohol consumption and maternal education.
158	In the post-delivery self-questionnaire that addressed prenatal yoga, we additionally
159	collected data on whether each participant had intended to practice prenatal yoga at
160	approximately 15 weeks of gestation and whether they had undertaken any
161	complementary therapies during pregnancy. These factors were analyzed due to the
162	assumption that people with interest in prenatal yoga may have higher health
163	consciousness and engage in other activities that they perceive to be healthy.
164	The following information were also collected from medical records: maternal age at

ascertained from medical records by physicians, midwives, or JECS research

165	delivery, prenatal care hospital, parity, pre-pregnancy body mass index (BMI), infertility
166	treatment, history of preterm delivery, history of spontaneous abortion, chronic
167	hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune
168	disease, gender of offspring, use of iron preparations during pregnancy, and threatened
169	abortion during pregnancy. In addition, hospitals that offered in-hospital prenatal yoga
170	classes were identified either through their websites or phone calls during the study
171	period.
172	
173	Statistical Analysis
174	Analyses were performed using IBM SPSS Statistics 23.0 for Windows (SPSS Inc.,
175	Chicago, IL, USA). Baseline characteristics were calculated and presented as numbers
176	and percentages or means and standard deviations, where applicable. Chi-square tests or
177	Fisher's exact tests were performed to assess differences in baseline characteristics for
178	categorical variables and the Mann-Whitney U test was used for continuous variables.
179	Odds ratios (ORs) with 95% confidence intervals (CIs) for ritodrine hydrochloride use
180	according to the practice of prenatal yoga were estimated using logistic regression
181	models. We developed 3 multivariate logistic regression models for conducting
182	adjustments using the forced entry method. Model 1 adjusted for maternal age at

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183	delivery, participation area, parity, marital status, smoking, alcohol consumption,
184	maternal education, pre-pregnancy BMI, employment status, physical activity level
185	before pregnancy, intention to practice prenatal yoga at around 15 weeks of gestation,
186	and prenatal yoga classes held at the prenatal care hospital as the baseline covariates.
187	Model 2 adjusted for the same variables in Model 1, as well as infertility treatment,
188	history of preterm delivery, history of spontaneous abortion, malformation of uterus,
189	chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, and
190	autoimmune disease as covariates of complications or medical history. Model 3 adjusted
191	for the same variables in Model 2, as well as practice of alternative therapies other than
192	prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and
193	threatened abortion during pregnancy as covariates of information obtained during
194	pregnancy.
195	In order to further explore the exposure-response relationship, we analyzed the
196	prenatal yoga group based on the following 3 practice frequency factors: number of
197	practice weeks, number of practice sessions, and total practice duration in minutes.
198	Participants in the prenatal yoga group were allocated into 2 groups for each of these
199	factors based on their respective median values. Next, the OR for each of these
200	dichotomous variables was then calculated using a logistic regression model that

201 included the covariates described in Model 3.

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202	We also divided the prenatal yoga group into 4 subgroups based on the combination of
203	the start point of yoga in gestational weeks (divided according to the median value in
204	gestational weeks) and total practice duration (divided according to the median value in
205	minutes) to explore the following two possibilities: the first possibility is that
206	participants who had started prenatal yoga earlier may demonstrate the net effect of this
207	practice because they could be interpreted as having physically similar states to the
208	non-prenatal yoga group with regard to experiencing uterine contractions (due to
209	statistical adjustment for threatened abortion in the multivariate analysis). The second
210	possibility is that participants who had started prenatal yoga later were in better
211	condition to practice yoga due to a lack of uterine contractions. Furthermore, we
212	conducted sensitivity analyses and exploratory subanalyses (e Appendix 2). Statistical
213	significance was set at $P < 0.05$ for all analyses.
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215 **RESULTS**

during their pregnancy period. The comparison of the baseline characteristics between
the prenatal yoga group and the non-prenatal yoga group is shown in Table 1.
After adjusting for covariates (Table 2), the practice of prenatal yoga had a
significantly lower OR for the use of ritodrine hydrochloride (adjusted OR, 0.77; 95%)

A total of 567 (21.1%) women in the study sample reported taking part in prenatal yoga

221 CI, 0.61–0.98).

In an analysis of practice frequency types (Table 3), the ORs for ritodrine

223 hydrochloride use were significantly lower for higher numbers of practice weeks

224 (adjusted OR, 0.67; 95% CI, 0.48–0.93), higher numbers of practice sessions (adjusted

OR, 0.62; 95% CI, 0.44–0.86), and higher total practice duration in minutes (adjusted

OR, 0.54; 95% CI, 0.38–0.76) relative to the non-prenatal yoga group.

As shown in Table 4, there was a marginally significantly lower risk of ritodrine

hydrochloride use in the group that started prenatal yoga at 21 weeks of gestation or

earlier and had a total practice duration of more than 900 minutes (adjusted OR, 0.69;

230 95% CI, 0.46–1.03). The group that started prenatal yoga at 22 weeks or later and had a

- total practice duration time of 900 minutes or less showed no significant relationship
- with ritodrine hydrochloride use (adjusted OR, 0.94; 95% CI, 0.64–1.38); in contrast,

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233	the group that started prenatal yoga at 22 weeks or later and had a total practice duration
234	of more than 900 minutes showed a significantly lower risk for ritodrine hydrochloride
235	use (adjusted OR, 0.34; 95% CI, 0.19–0.62).
236	The sensitivity analysis that excluded cases with threatened abortion during pregnancy
237	produced results that were similar to those of the main analysis (e-Table 1). The other
238	sensitivity analysis (which excluded cases who tried to do prenatal yoga but were
239	stopped by their physician) did not show any significant relationship between prenatal
240	yoga and ritodrine hydrochloride use (e-Table 2); however, the subanalysis stratified by
241	both the start point of prenatal yoga and total practice duration indicated a significant
242	exposure-response relationship between prenatal yoga and ritodrine hydrochloride use,
243	which was similar to the findings of the main analysis. The exploratory analysis of
244	practice methods, breathing technique, and meditation (e-Table 3) showed few
245	differences in ritodrine hydrochloride use among the different practice methods and the
246	use or non-use of meditation. Practice methods, the median values for practice
247	frequency, and components of prenatal yoga are shown in e-Table 4.
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249 **DISCUSSION**

After adjusting for a diverse range of covariates, the practice of prenatal yoga was found 250to be significantly associated with reduced ritodrine hydrochloride administration in 251pregnant women. Furthermore, the stratified analysis showed that a total practice 252duration of more than 900 minutes had a significantly protective OR with respect to 253ritodrine hydrochloride use. The group that started prenatal yoga at 21 weeks of 254gestation or earlier and had a total practice duration of more than 900 minutes also 255showed a marginally significant relationship with reduced ritodrine hydrochloride use . 256To the best of our knowledge, there has yet to be a study that reported the effects of 257prenatal yoga on the use of tocolytic drugs. However, 3 interventional studies have 258previously analyzed the effects of prenatal yoga on prematurity,^{7, 10, 34} and found that 259260subjects who practiced yoga had significantly lower incidences of preterm births and longer gestational periods when compared with subjects who had not practiced yoga. 261One of these studies was not an RCT³⁴ and the study subjects were selected for 262interventions based on the distance of their residence to the hospital, which may have 263led to the introduction of selection bias. As a result, the differences in the effects of 264265prenatal yoga between that study and our findings could not be directly compared. Of the remaining 2 studies, one was an RCT conducted in the US that focused on pregnant 266

267	women who also had prenatal depression, ¹⁰ and the other was an RCT conducted in
268	India that investigated pregnant women with high-risk factors that included obesity,
269	history of obstetric complications, and advanced age ⁷ . These characteristics may limit
270	the generalizability of those findings. Although this present analysis was conducted as
271	an observational study, the study subjects were pregnant women from the general
272	population in Japan, thereby providing a relatively higher level of generalizability to our
273	results. In contrast to the previous studies that focused on prematurity, the outcome
274	measure of our study was ritodrine hydrochloride use, which may be indicative of a
275	pregnant woman's experience of any uterine contractions ²⁴ . On the other hand, a
276	previous observational study ³⁵ showed no significant association between yoga and
277	preterm birth, and a non-RCT study ³⁶ was similarly unable to detect an association
278	between yoga and the number of gestational weeks before delivery (yoga group, 38.8
279	weeks; control group, 38.8 weeks). While the results are not conclusive, this study
280	conducted a multifaceted analysis that adjusted for many covariates, and our findings
281	indicate that prenatal yoga has possible preventive effects on ritodrine hydrochloride
282	use.
283	Although the mechanism underlying the reduction of ritodrine hydrochloride use
284	through prenatal yoga remains unclear, uterine contractions induced by the

285	inflammatory process may be a possible cause. Bacterial infection has been documented
286	to be one of the main causes of spontaneous preterm delivery ³⁷⁻³⁹ . Furthermore, the
287	roles for the pro-inflammatory cytokines interleukin (IL)-1 β , IL-6, IL-8, and tumor
288	necrosis factor alpha (TNF- α) are evident in both full-term and preterm delivery, and
289	have been shown to be independent of the presence of infections ^{38, 40, 41} . This indicates
290	that the inflammatory process, regardless of bacterial infections, may result in uterine
291	contractions that lead to preterm labor. The beneficial role of yoga has also been
292	demonstrated in non-pregnant women, where an RCT study of breast cancer survivors
293	showed a significant dose-response decrease in serum IL-1 β and IL-6 in those who
294	practiced yoga ³ . It is possible that a reduction in the inflammatory response in the
295	prenatal yoga group was able to suppress uterine contractions, and as a result, reduce the
296	need for ritodrine hydrochloride prescriptions.
297	The strengths of this study are 1) a substantially large sample size, 2) demonstration of
298	the existence of an exposure-response relationship between prenatal yoga and ritodrine
299	hydrochloride use, 3) the examination of medical records to ascertain ritodrine
300	hydrochloride use and numerous covariates, 4) statistical adjustment of many potential
301	confounders, 5) provision of relatively detailed insight into the benefits of prenatal yoga,
302	and 6) production of comparatively generalizable results for pregnant Japanese women.

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303	On the other hand, there were also limitations in this study. First, there is the
304	possibility of reverse causality, where participants in the prenatal yoga group may have
305	been able to exercise only because they were not impeded by uterine contractions. In
306	fact, the OR for ritodrine hydrochloride use was lower in the group that started prenatal
307	yoga at 22 weeks or later and had a total practice duration of more than 900 minutes
308	when compared with the group that started prenatal yoga at 21 weeks of gestation or
309	earlier and had a total practice duration of more than 900 minutes. However, we
310	demonstrated that the latter group had a marginally significant lower risk for ritodrine
311	hydrochloride use, and the sensitivity analysis models also indicated a significant
312	exposure-response relationship. These findings therefore strongly indicate the reduction
313	of ritodrine hydrochloride use by prenatal yoga. Second, the information on prenatal
314	yoga was collected retrospectively after delivery (mean: 2.7 months post-delivery), and
315	the reliability and validity of the original questionnaire were not examined. There may
316	have been some pregnant women who practiced prenatal yoga up until delivery, and
317	information acquisition should therefore have ideally been conducted at the time of
318	admission for delivery. Despite this limitation, we were able to carry out the survey at a
319	relatively close time frame after delivery. Third, some participants in the prenatal yoga
320	group may have practiced yoga after having received ritodrine hydrochloride, which

321	may have led to an underestimation of the potential benefits of yoga and prevented the
322	observation of statistically significant associations in several aspects of the analyses.
323	Fourth, the use of ritodrine hydrochloride includes both oral administration and infusion.
324	Despite these differences in administration routes, both these methods are likely to
325	reflect the participants' experience of uterine contractions ²⁴ , which may be an indicator
326	of preterm labor. Fifth, the use of ritodrine hydrochloride is dependent on the discretion
327	of each obstetrician, which may have introduced a degree of bias into the study.
328	However, this analysis adjusted for variations in participation regions and for prenatal
329	yoga classes that were held in the prenatal care hospital. Sixth, the number of excluded
330	participants from this analysis was 695 from the original 3387 (20.5%) patients, and the
331	majority of these cases were excluded due to missing values. However, a supplementary
332	analysis showed that the proportions of patients who practiced prenatal yoga and were
333	administered ritodrine hydrochloride did not differ between these excluded subjects and
334	subjects who were included in the final analysis (data not shown). Seventh, the outcome
335	in this analysis was not preterm birth or threatened preterm labor, which could not be
336	analyzed due to low statistical power. However, we intend to analyze these outcomes in
337	the future with a larger sample size after improvements have been made to all of the
338	JECS participants' data.

339	The main finding of this study was that prenatal yoga was associated with a lower risk
340	of ritodrine hydrochloride use in pregnant Japanese women, especially those with a total
341	practice duration that exceeded 900 minutes. This result suggests that performing
342	prenatal yoga for a cumulative total of more than 900 minutes during pregnancy may
343	counter the onset of uterine contractions that necessitates the use of ritodrine
344	hydrochloride. Prenatal yoga may therefore be a viable and beneficial option for
345	pregnant women in the selection of alternative therapies.
346	
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353	The findings and conclusions of this article are solely the responsibility of the authors
354	and do not represent the official views of the Ministry of the Environment, Japan.
355	Conflicts of interest: None declared.
356	

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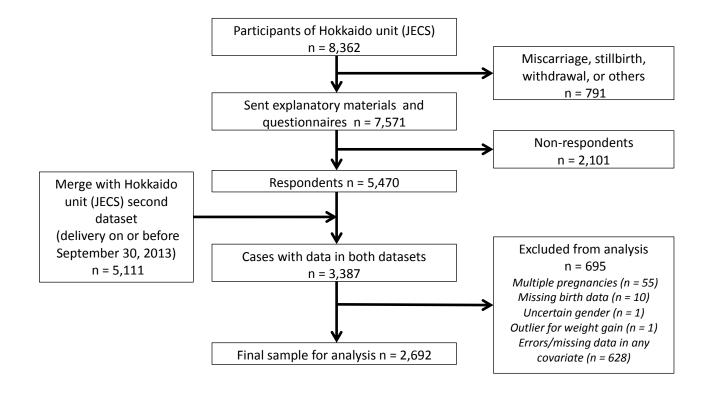


Figure 1. The sample selection flow diagram

	No Prenatal Yoga (n = 2125)	Prenatal Yoga (n = 567)	
Variable	N (%)	N (%)	P value
Maternal age at delivery (y)			0.248
≤24	137 (6.4)	24 (4.2)	
25-29	569 (26.8)	160 (28.2)	
30-34	800 (37.6)	213 (37.6)	
≥35	619 (29.1)	170 (30.0)	
Participation area			0.927
Sapporo	1155 (54.4)	312 (55.0)	
Asahikawa	496 (23.3)	128 (22.6)	
Kitami	474 (22.3)	127 (22.4)	
Parity			<0.001
0	819 (38.5)	375 (66.1)	
1	940 (44.2)	148 (26.1)	
2	309 (14.5)	36 (6.3)	
≥3	57 (2.7)	8 (1.4)	
Marital status	. ,		0.119
Married	2039 (96.0)	552 (97.4)	0
Single (Unmarried, divorced, or widowed)	86 (4.0)	15 (2.6)	
Smoking at the second trimester			< 0.001
Never smoked	1108 (52.1)	351 (61.9)	-0.00
Ex-smokers who quit before pregnancy	623 (29.3)	155 (27.3)	
Ex-smokers who quit after pregnancy	302 (14.2)	56 (9.9)	
Current smokers	92 (4.3)	5 (0.9)	
Alcohol consumption at the second trimester		0.0)	< 0.00
Never drank	569 (26 7)	107 (18 0)	<0.00
	568 (26.7) 242 (16.1)	107 (18.9)	
Ex-drinkers who quit before pregnancy	343 (16.1)	91 (16.0)	
Ex-drinkers who quit after pregnancy Current drinkers	1134 (53.4)	357 (63.0)	
	80 (3.8)	12 (2.1)	
Maternal education			<0.00
Junior high school	83 (3.9)	15 (2.6)	
High school Junior college, vocational school, or	674 (31.7)	112 (19.8)	
	935 (44.0)	259 (45.7)	
specialized vocational high school University or graduate school	433 (20.4)	181 (31.9)	
Pre-pregnancy BMI (kg/m ²)	400 (20.4)	101 (01.0)	<0.001
	352 (16.6)	108 (19.0)	~0.00
18.5–24.9	1522 (71.6)	427 (75.3)	
≥25	251 (11.8)	32 (5.6)	
	231 (11.8)	32 (3.0)	0.027
Employment status	016 (42.1)	217 (28 2)	0.02
Housewife	916 (43.1) 687 (33.3)	217 (38.3)	
Regular employee or self-employed Temporary staff, part-time staff, or commissioned staff	687 (32.3) 447 (21.0)	206 (36.3)	
		113 (19.9)	
Unemployed or others Physical activity level before pregnancy (IPAQ)	75 (3.5)	31 (5.5)	
······································	400.4 (705.0)		
METS × min/day (Mean [SD])	403.1 (705.0)	374.5 (636.7)	0.39
Intention to do prenatal yoga at around	1205 (05 0)		< 0.00
15 weeks of gestation	1395 (65.6)	539 (95.1)	
Prenatal yoga classes were held in prenatal care hospital	1458 (68.6)	437(77.1)	<0.00
Infertility treatment			0.13
None (Spontaneous pregnancy)	1986 (93.5)	521 (91.9)	
Ovulation induction or AIH	100 (4.7)	38 (6.7)	
ART	39 (1.8)	8 (1.4)	
History of preterm delivery ^a	57 (4.4)	7 (3.6)	0.640
History of spontaneous abortion ^b	417 (27.1)	101 (36.3)	0.00
Malformation of uterus	10 (0.5)	1 (0.2)	0.47
	38 (1.8)		0.36
Chronic hypertension	· · ·	7 (1.2)	
Diabetes mellitus	29 (1.4)	5 (0.9)	0.360
Psychiatric illness	8 (0.4)	1 (0.2)	0.694
Hypothyroidism	16 (0.8)	12 (2.1)	0.004
Autoimmune disease	10 (0.5)	2 (0.4)	1.00
Practice of alternative therapies other than prenatal yoga ^c	383 (18.0)	195 (34.4)	< 0.00
Gender of offspring (Male)	1121 (52.8)	292 (51.5)	0.595
Use of iron preparations during pregnancy	611 (28.8)	178 (31.4)	0.220
Threatened abortion during pregnancy	128 (6.0)	22 (3.9)	0.048
Use of ritodrine hydrochloride	651 (30.6)	139 (24.5)	0.004

^aOnly among women with parity \geq 1 (n = 1,498) ^bOnly among women with gravida \geq 1 (n = 1,815).

^cIncludes Lamaze technique, sophrology, aromatherapy, maternity swimming, maternal aerobics, massage, acupuncture, Qigong, Tai Chi, meditation, hypnotherapy, or autogenic training. dχ2 test. eFisher's exact test. fMann-Whitney U test.

BMI, Body Mass Index; SD, Standard Deviation; IPAQ, International Physical Activity Questionnaire

AIH, Artificial insemination with husband's sperm; ART, Assisted reproduction technology

Table 2 Adjusted odd ratios for ritodrine hydrochloride use

		,	
	OR	95%CI	P value
No prenatal yoga	1 (Ref)		
Prenatal yoga (Crude)	0.74 (0.60 to 0.91) 0.005
(Model 1)	0.77 (0.61 to 0.97) 0.030
(Model 2)	0.78 (0.62 to 0.99) 0.041
(Model 3)	0.77 (0.61 to 0.98) 0.034

Model 1 adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, and prenatal yoga classes held at the prenatal care hospital.

Model 2 adjusted for the variables in Model 1, as well as infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, and autoimmune disease.

Model 3 adjusted for the variables in Model 2, as well as practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy.

	OR	95%(CI	P value	P value for trend
Number of practice weeks					
No prenatal yoga (n = 2125)	1 (Ref)				0.016
Prenatal yoga ≤13 weeks (n = 294)	0.86 (0.63 to	1.17)	0.332	
Prenatal yoga >13 weeks (n = 251)	0.67 (0.48 to	0.93)	0.019	
Number of practice sessions					
No prenatal yoga (n = 2125)	1 (Ref)				0.007
Prenatal yoga ≤17 sessions (n = 279)	0.92 (0.67 to	1.25)	0.581	
Prenatal yoga >17 session (n = 264)	0.62 (0.44 to	0.86)	0.005	
Total practice duration in minutes					
No prenatal yoga (n = 2125)	1 (Ref)				0.002
Prenatal yoga ≤900 min (n = 269)	1.04 (0.76 to	1.42)	0.804	
Prenatal yoga >900 min (n = 267)	0.54 (0.38 to	0.76)	<0.001	

Table 3 Adjusted odd ratios for ritodrine hydrochloride use stratified by the number of yoga practice weeks, number of practice sessions, and total practice duration in minutes

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy. OR, odds ratio; CI, confidence intervals

	OR	95%(CI	P value	P value for trend
Number of practice weeks					
No prenatal yoga (n = 2125)	1 (Ref)				0.016
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Prenatal yoga >13 weeks (n = 251)	0.67 (0.48 to	0.93)	0.019	
Number of practice sessions					
No prenatal yoga (n = 2125)	1 (Ref)				0.007
Prenatal yoga ≤17 sessions (n = 279)	0.92 (0.67 to	1.25)	0.581	
Prenatal yoga >17 session (n = 264)	0.62 (0.44 to	0.86)	0.005	
Total practice duration in minutes					
No prenatal yoga (n = 2125)	1 (Ref)				0.002
Prenatal yoga ≤900 min (n = 269)	1.04 (0.76 to	1.42)	0.804	
Prenatal yoga >900 min (n = 267)	0.54 (0.38 to	0.76)	<0.001	

Table 3 Adjusted odd ratios for ritodrine hydrochloride use stratified by the number of yoga practice weeks, number of practice sessions, and total practice duration in minutes

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy. OR, odds ratio; CI, confidence intervals

Table 4 Adjusted odd ratios for ritodrine hydrochloride use stratified by the start of yoga in gestational weeks and total practice duration in minutes

	OR	95%0	CI	P value	P value for trend
Start of yoga in gestational weeks and total practice					
duration in minutes					
No prenatal yoga (n = 2125)	1 (Ref)				0.001
Prenatal yoga ≤21 weeks and ≤900 min (n = 102)	1.21 ((0.76 to	1.92)	0.413	
Prenatal yoga ≥22 weeks and ≤900 min (n = 167)	0.94 ((0.64 to	1.39)	0.770	
Prenatal yoga ≤21 weeks and >900 min (n = 167)	0.69 ((0.46 to	1.03)	0.069	
Prenatal yoga ≥22 weeks and >900 min (n = 100)	0.34 ((0.19 to	0.62)	<0.001	

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy.

e Appendix 1

The Hokkaido unit administrates participants from 3 areas: Sapporo area (Kita-ward and Toyohira-ward of Sapporo city; total population, 497,000), Asahikawa area (Asahikawa city; population, 346,000) and Kitami area (Kitami city, Okedo town, Kunneppu town, Tsubetsu town, and Bihoro town; total population, 155,000).

e Appendix 2

We conducted sensitivity analyses using restricted samples comprising 2,542 cases (excluding 150 threatened abortion cases) and 2,632 cases (excluding 60 cases who had attempted to do prenatal yoga but were stopped by their physician). Finally, as an exploratory subanalysis on practice methods and the components of yoga, we divided the prenatal yoga group into 4 subgroups based on combinations of 3 patterns: categorization according to practice methods (instructor or self-study) and the median of total practice duration in minutes, categorization according to breathing technique use and the median of total practice duration in minutes.

e-Table 1. Adjusted odd ratios for ritodrine hydrochloride use among women without threatened abortion

	OR		95	%C	l	P value	P value for trend
No prenatal yoga (n = 1997)	1 (Ref)						
Prenatal yoga (n = 545)	0.79	(0.62 t	to	1.01)	0.065	
Number of practice weeks							
No prenatal yoga (n = 1997)	1 (Ref)						0.052
Prenatal yoga ≤13 weeks (n = 282)	0.85	(0.62 t	to	1.16)	0.295	
Prenatal yoga >13 weeks (n = 244)	0.73	(0.52 t	to	1.03)	0.072	
Number of practice sessions							
No prenatal yoga (n = 1997)	1 (Ref)						0.024
Prenatal yoga ≤17 sessions (n = 267)	0.90	(0.66 t	to	1.24)	0.529	
Prenatal yoga >17 sessions (n = 257)	0.67	(0.48 t	to	0.95)	0.022	
Total practice duration in minutes							
No prenatal yoga (n = 1997)	1 (Ref)						0.010
Prenatal yoga ≤900 min (n = 258)	1.01	(0.74 t	to	1.39)	0.955	
Prenatal yoga >900 min (n = 259)	0.60	(0.43 t	to	0.85)	0.004	
Start of yoga in gestational weeks and total practice							
duration in minutes							
No prenatal yoga (n = 1997)	1 (Ref)						0.003
Prenatal yoga ≤21 weeks and ≤900 min (n = 99)	1.17	(0.73 t	to	1.88)	0.508	
Prenatal yoga ≥22 weeks and ≤900 min (n = 159)	0.92	(0.62 t	to	1.37)	0.669	
Prenatal yoga ≤21 weeks and >900 min (n = 161)	0.77	(0.51 t	to	1.15)	0.201	
Prenatal yoga ≥22 weeks and >900 min (n = 98)	0.39	(0.22 t	to	0.69)	0.001	

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, and use of iron preparations during pregnancy.

	OR		95%	CI	P value	P value for trend
No prenatal yoga (n = 2065)	1 (Ref)					
Prenatal yoga (n = 567)	0.86	(0.67 to	1.09)	0.213	
Number of practice weeks						
No prenatal yoga (n = 2065)	1 (Ref)					0.113
Prenatal yoga ≤13 weeks (n = 294)	0.95	(0.70 to	1.30)	0.754	
Prenatal yoga >13 weeks (n = 251)	0.75	(0.53 to	1.05)	0.093	
Number of practice sessions						
No prenatal yoga (n = 2065)	1 (Ref)					0.058
Prenatal yoga ≤17 sessions (n = 279)	1.02	(0.74 to	1.39)	0.918	
Prenatal yoga >17 sessions (n = 264)	0.69	(0.49 to	0.97)	0.031	
Total practice duration in minutes						
No prenatal yoga (n = 2065)	1 (Ref)					0.021
Prenatal yoga ≤900 weeks (n = 269)	1.16	(0.85 to	1.58)	0.353	
Prenatal yoga >900 weeks (n = 267)	0.60	(0.43 to	0.85)	0.004	
Start of yoga in gestational weeks and total practice						
duration in minutes						
No prenatal yoga (n = 2065)	1 (Ref)					0.006
Prenatal yoga ≤21 weeks and ≤900 min (n = 102)	1.37	(0.86 to	2.17)	0.186	
Prenatal yoga ≥22 weeks and ≤900 min (n = 167)	1.05	(0.71 to	1.54)	0.819	
Prenatal yoga ≤21 weeks and >900 min (n = 167)	0.77	(0.52 to	1.16)	0.214	
Prenatal yoga ≥22 weeks and >900 min (n = 100)	0.37	(0.21 to	0.67	0.001	

e-Table 2. Adjusted odd ratios for ritodrine hydrochloride use among women with the exclusion of those who attempted to start prenatal yoga but were stopped by their physician

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy.

e-Table 3 Adjusted odd ratios for ritodrine hydrochloride use stratified by practice methods, breathing technique use, meditation	
use, and total practice duration in minutes	
	_

	OR		95%CI		P value	P value for trend
Practice methods and total practice duration in minutes						
No prenatal yoga (n = 2125)	1 (Ref)					0.003
Self-study and ≤900 min (n = 108)	1.07	(0.68 to	1.67)	0.777	
Instructor and ≤900 min (n = 160)	1.04	(0.70 to	1.54)	0.861	
Self-study and >900 min (n = 109)	0.45	(0.26 to	0.76)	0.003	
Instructor and >900 min (n = 157)	0.61	(0.40 to	0.93)	0.022	
Breathing technique use and total practice duration in minutes						
No prenatal yoga (n = 2125)	1 (Ref)					0.001
Without breathing techniques and ≤900 min (n = 68)	1.14	(0.66 to	1.99)	0.639	
With breathing techniques and ≤900 min (n = 199)	0.99	(0.69 to	1.42)	0.959	
Without breathing techniques and >900 min (n = 30)	0.76	(0.31 to	1.87)	0.548	
With breathing techniques and >900 min (n = 237)	0.52	(0.36 to	0.74)	<0.001	
Meditation use and total practice duration in minutes						
No prenatal yoga (n = 2125)	1 (Ref)					0.002
Without meditation and ≤900 min (n = 177)	0.99	(0.68 to	1.43)	0.950	
With meditation and ≤900 min (n = 90)	1.13	(0.68 to	1.86)	0.644	
Without meditation and >900 min (n = 134)	0.47	(0.29 to	0.77)	0.002	
With meditation and >900 min ($n = 133$)	0.61	(0.39 to	0.96)	0.032	

Adjusted for maternal age at delivery, participation area, parity, marital status, smoking, alcohol consumption, maternal education, pre-pregnancy BMI, employment status, physical activity level before pregnancy, intention to do prenatal yoga at around 15 weeks of gestation, prenatal yoga classes held at the prenatal care hospital, infertility treatment, history of preterm delivery, history of spontaneous abortion, malformation of uterus, chronic hypertension, diabetes mellitus, psychiatric illness, hypothyroidism, autoimmune disease, practice of alternative therapies other than prenatal yoga, gender of offspring, use of iron preparations during pregnancy, and threatened abortion during pregnancy.

e Table 4. Practice methods, practice frequency, and the components of

prenatal yoga	·
Prenatal Yoga Factors	N (%)
Practice methods (n = 565)	
Instructor	341 (60.4)
Self-study using DVDs or books	224 (39.6)
Practice frequency (median [SD])	
Start of yoga in gestational weeks (n = 551)	22.0 (7.1)
End of yoga in gestational weeks (n = 545)	37.0 (5.9)
Frequency per week (n = 561)	1.0 (1.7)
Duration of practice in minutes per session (n = 555)	60.0 (29.9)
Components of prenatal yoga (n = 565)	
Physical posture	553 (97.9)
Breathing technique	465 (82.3)
Meditation	236 (41.8)
SD. Standard Deviation	

SD, Standard Deviation