Received: 15 February 2023 | Accepted: 11 June 2023

DOI: 10.1111/jog.15722

ORIGINAL ARTICLE

Changes in preterm and extremely preterm birth rates in Japan after the introduction of obstetrical practice guidelines in 2008

Satoshi Shimano[1] | Takashi Yamada[2] | Kazutoshi Cho[3] | Kazuo Sengoku[4] | Tasuku Mariya[5] | Tsuyoshi Saito[5]

[1]Department of Obstetrics and Gynecology, Nakashibetsu Municipal Hospital, Nakashibetsu, Hokkaido, Japan

[2]Department of Obstetrics and Gynecology, JCHO Hokkaido Hospital, Sapporo, Hokkaido, Japan

[3]Department of Pediatrics, JCHO Hokkaido Hospital, Sapporo, Hokkaido, Japan

[4]Mori Obstetrical and Gynecological Hospital, Asahikawa, Hokkaido, Japan

[5]Department of Obstetrics and Gynecology, Sapporo Medical University, School of Medicine, Sapporo, Hokkaido, Japan

Correspondence
Satoshi Shimano, Department of Obstetrics and Gynecology Nakashibetsu Municipal Hospital, Nakashibetsu, W 10-jo, S 9-Chome, Nakashibetsu-Cho, Hokkaido 086-1110, Japan.
Email: shima722@beach.ocn.ne.jp

Abstract

Aim: Obstetrical guidelines were established in Japan in 2008, and obstetrical diagnoses and treatments were subsequently standardized nationally. We examined changes in the preterm birth rate (PTBR) and extremely preterm birth rate (EPTBR) following the introduction of such guidelines.

Methods: Information on 50 706 432 live births in Japan between 1979 and 2021, including Japanese reproductive medicine, the childbearing age of pregnant women, and the employment status of reproductive-age women between 2007 and 2020, were obtained from the Japanese government and academic societies. Regression analysis was used to compare chronological changes nationally and those of eight Japanese regions. Regional and national average PTBRs and EPTBRs from 2007 to 2020 were compared by using a repeated measures analysis of variance.

Results: From 1979 to 2007, PTBRs and EPTBRs in Japan increased significantly. However, from 2008, the national PTBR and EPTBR decreased until 2020 ($p < 0.001$) and 2019 ($p = 0.02$), respectively. From 2007 to 2020, overall PTBR and EPTBR were 5.68% and 0.255%, respectively. A significant difference in the PTBR and EPTBR existed between the eight Japanese regions. During this period, the number of pregnancies using assisted reproductive technology increased from 19 595 to 60 381, pregnant women became older, the employment rate of those of reproductive age increased, and nonregular employment was 54%, which was 2.5 times higher than for men.

Conclusions: In Japan, after obstetrical guidelines were enacted in 2008, PTRBs decreased significantly even under the pressure of increasing preterm births. Countermeasures may be necessary for regions showing high PTBRs.

KEYWORDS
assisted reproductive technology, bacterial vaginosis, Japan, obstetrical guidelines, preterm birth rates

INTRODUCTION

In Japan, evidence-based medicine has been recommended since the 2000s. In 2008, clinical practice guidelines in obstetrics were created.[1] Since then, the guidelines have been revised every 3 years to 2020.[2–5] In obstetrics, we anticipated that the implementation of such guidelines would lead to a reduction in the preterm birth rate (PTBR). In particular, the following four clinical items in the guidelines were thought to have the greatest impact on the PTBR:

First, CQ301 (cervical insufficiency): In 2008, if cervical insufficiency was suspected in a previous pregnancy, careful follow-up or a prophylactic cervical cerclage was performed. For an existing pregnancy, careful follow-up or a therapeutic cervical cerclage was performed. In 2017, a change was made such that if follow-up was selected and cervical shortening observed, a therapeutic cervical cerclage was required. However, if signs of infection were found, in principle, treatment of the infection was given priority.[6] In addition, although a retrospective study, a paper described the effect of therapeutic cervical cerclage on the prolongation of pregnancy in cases of prolapsed fetal membranes.[7] Progesterone therapy has been described since 2014. However, the therapy is not covered by health insurance in Japan and, therefore, it was rarely implemented up to 2020.[8]

Second, CQ302 (preterm labor): Attention has been drawn to chorioamnionitis. As for tocolytic agents, ritodrine hydrochloride has been used from April 1986, magnesium sulfate from 2006, and nifedipine from 2017.[4]

Third, CQ303 (PROM): Pregnant women <34 gestational weeks (GWs) were managed with antibiotics between 2008 and 2020. Since 2011, if clinical chorioamnionitis is diagnosed at ≧26 GWs labor and delivery should be attempted within 24 h without waiting for a natural labor otherwise a cesarean section is then performed.[2]

Finally, CQ601 (bacterial vaginosis: BV): It was consistently stated that no evidence existed that BV screening and the subsequent treatment of all pregnant women prevented preterm births from 2008 to 2020.[9–11] In 2008, the treatment of pregnant women with symptomatic BV using antibiotics was recommended.[1] In 2011, BV testing was promoted for all women with known high-risk factors for preterm delivery, such as a previous preterm delivery, and patients with BV were to be treated using antibiotics as soon as possible.[2] In addition, our papers are cited, in which it was reported that the prevalence of BV during pregnancy exceeded 20% in 2000,[2,12] as well as that the risk of therapeutic cervical cerclage was low in facilities providing screening and treatment for all pregnant women with BV.[2,13] In 2017, if BV screening and treatment were performed to prevent preterm births, it was required to be done before 20 GWs; those who were found to be positive were treated with antibiotics.[4,14] In other words, room has existed for the screening and treatment of all pregnant women with BV to prevent preterm birth at the physician's discretion since 2008.

In addition to the development of obstetrical guidelines, it has been pointed out that factors affecting the premature birth rate in Japan include an increase in births in older mothers, an increase in part-time workers (nonregular workers), and an increase in assisted reproductive technology (ART).[15–17] The premature birth rate for multiple pregnancies was high,[16–18] such that in April 2008, the Japan Society of Obstetrics and Gynecology (JSOG) decided that the number of embryos to be transferred in ART should be only one on principle to prevent multiple pregnancies.[19] To examine these effects, we investigated the aging of pregnant women, the employment rate of women of reproductive age, and the increase in ART.

With the development and enforcement of these obstetrical guidelines, and with regard to late childbearing, women's social advancement, and the development of ART, has the PTBR really decreased? We examined chronological changes in the PTBR and extremely preterm birth rate (EPTBR) in Japan from 1979 to 2021 and compared their frequencies with those in other countries. We also report on whether a difference in the PTBR and EPTBR from 2007 to 2020 exists in the eight regions of Japan.

MATERIALS AND METHODS

Data

Data for examining the PTBR and EPTBR over the 43 years from 1979 to 2021 in Japan were obtained from a database found on a website of the Japanese Ministry of Health, Labour and Welfare (JMHLW).[20] The PTBR and EPTBR in the eight regions of Japan for the 14 years from 2007 to 2020 were analyzed by order-made tabulation provided by the JMHLW.[21–23] We defined a PTBR as <37 GWs/live birth, and an EPTBR as <28 GWs/live birth.[24,25]

The average ages at which mothers gave birth to their first, second, and third children,[26] the birth rates by five-year age group at reproductive age[27] and data on the employment rate and status of women[28,29] were obtained from the websites of the JMHLW and Japanese Ministry of Internal Affairs and Communications (JMIAC). Data on ART were obtained from the JSOG website.[30]

Statistical analysis

A regression coefficient method was used to test chronological changes in the whole country between 1979 and 2021, and in each of the eight regions and the national average between 2007 and 2020. A general linear model by repeated measures analysis of variance (RM-ANOVA) was used to compare PTBRs and EPTBRs of the eight regions and the national average from 2007 to 2020. Comparisons between each region and the national average were adjusted by Tukey's multiple comparison method.

For statistical analyses, SPSS Statistics 25 (IBM Corporation) was used for a general linear model by RM-ANOVA, and EZR (Saitama Medical Center, Jichi Medical University) was used for an analysis of covariance to test slopes of the regression equation and Fisher's exact test. Microsoft Excel 2019 was used to draw graphs.

Approval by institutional review board

No ethics approval was necessary because studies were conducted for public health purposes using publicly available national surveillance data from JMHLW, JMIAC, and JSOG.

RESULTS

Chronological changes in the national PTBR and EPTBR between 1979 and 2021

Total live births from 1979 to 2021 were 50 706 432. The average PTBR was 4.96% and the average EPTBR was 0.206% (Table 1). The PTBR significantly increased by 2%, from 3.8% to 5.8%, from 1979 to 2007 ($p < 0.001$). From 2008, the PTBR decreased significantly until 2020 ($p < 0.001$) but increased in 2021 (Figure 1a). The EPTBR significantly increased by over twofold from 0.114% to 0.263% from 1979 to 2007 ($p < 0.001$); however, this showed a significant decrease from 2008 until 2019 ($p = 0.02$) but then increased in 2020 (Figure 1b). Thus, PTBRs and the EPTBR significantly decreased over the subsequent 13 years since the 2008 obstetrical guidelines were developed.

Chronological changes and differences in PTBR and EPTBR in the eight regions and the national average between 2007 and 2020

The total number of live births in Japan between 2007 and 2020 was 13 997 363. Excluding foreigners with unknown birthplaces and cases with unknown delivery weeks, target cases were 13 992 420 (Table S1). A breakdown of births in the eight regions is as follows: 515 054 in the Hokkaido region, 892 528 in the Tohoku region, 4 680 334 in the Kanto region, 2 398 903 in the Chubu region, 2 489 997 in the Kinki region, 834 170 in the Chugoku region, 401 394 in the Shikoku region, and 1 780 040 in the Kyushu region (Table S2).

The PTBRs and EPTBRs for each year in the eight regions are shown in Tables 2a and 2b, respectively (Tables S3a and S3b). Figure 2a,b shows chronological changes in the PTBR and EPTBR for the average of the whole country and the eight regions of Japan. The national PTBR in Japan decreased significantly from 2007 to 2020 as determined using regression coefficients ($p < 0.001$). With respect to the eight regions, Kanto, Chubu, Kinki, Shikoku, and Kyushu showed significant regression lines ($p = 0.007$, $p = 0.013$, $p = 0.002$, $p = 0.002$, and $p = 0.002$, respectively); PTBRs were significantly decreased.

The national EPTBR in Japan showed a significant decrease ($p = 0.02$) from 2007 to 2019 but increased in 2020. Therefore, the 14-year regression curve became nonsignificant ($p = 0.084$) and the significant downward trend in EPTBR did not continue. Of the eight regions, only Kinki showed a significant decrease ($p = 0.003$).

The average PTBR for the last 14 years in Japan was 5.68% (Table 2a). Table 3a shows the results of multiple comparisons using Tukey's method and a general linear model by RM-ANOVA for the PTBR over time in each

TABLE 1 PTBR and EPTBR in Japan between 1979 and 2021.

Year	Live births	PTBs	PTBR (%)	EPTBs	EPTBR (%)
1979	1 642 580	62 654	3.81	1878	0.114
1980	1 576 889	64 889	4.12	1957	0.124
1981	1 510 447	55 963	3.71	1872	0.124
1982	1 496 397	55 691	3.72	1941	0.130
1983	1 508 687	62 467	4.14	2440	0.162
1984	1 489 780	64 733	4.35	2455	0.165
1985	1 431 577	59 795	4.18	2292	0.160
1986	1 382 946	57 784	4.18	2221	0.161
1987	1 346 658	56 988	4.23	2234	0.166
1988	1 314 006	58 683	4.47	2193	0.167
1989	1 246 802	54 574	4.38	2134	0.171
1990	1 221 585	55 231	4.52	2312	0.189
1991	1 223 245	55 405	4.53	2275	0.186
1992	1 208 989	56 530	4.68	2390	0.198
1993	1 188 282	54 806	4.61	2316	0.195
1994	1 238 328	59 015	4.77	2617	0.211
1995	1 187 064	58 293	4.91	2384	0.201
1996	1 206 555	60 321	5.00	2341	0.194
1997	1 191 665	59 356	4.98	2409	0.202
1998	1 203 147	61 036	5.07	2461	0.205
1999	1 177 669	60 806	5.16	2496	0.212
2000	1 190 547	64 006	5.38	2540	0.213
2001	1 170 662	62 200	5.31	2589	0.221
2002	1 153 855	62 289	5.40	2663	0.231
2003	1 123 610	62 143	5.53	2874	0.256
2004	1 110 721	62 936	5.67	2868	0.258
2005	1 062 530	60 377	5.68	2667	0.251
2006	1 092 674	62 318	5.70	2817	0.258
2007	1 089 818	63 113	5.79	2869	0.263
2008	1 091 156	62 819	5.76	2824	0.259
2009	1 070 036	60 989	5.70	2717	0.254
2010	1 071 305	61 315	5.72	2782	0.260
2011	1 050 807	60 285	5.74	2667	0.254
2012	1 037 232	59 514	5.74	2671	0.258
2013	1 029 817	59 235	5.75	2630	0.255
2014	1 003 609	56 909	5.67	2580	0.257
2015	1 005 271	56 147	5.59	2544	0.253
2016	977 242	54 610	5.59	2439	0.250
2017	946 146	53 561	5.66	2241	0.237
2018	918 400	51 732	5.63	2357	0.257
2019	865 239	48 538	5.61	2163	0.250
2020	840 835	46 102	5.48	2174	0.259
2021	811 622	46 347	5.71	2065	0.254
Total	50 706 432	2 512 505	4.96	104 359	0.206

Abbreviations: EPTBR, extremely preterm birth rate; PTBR, preterm birth rate.

region and nationally. Considering the overall data from 2007 to 2020, the PTBR in Hokkaido was significantly higher than those of the other seven regions and the

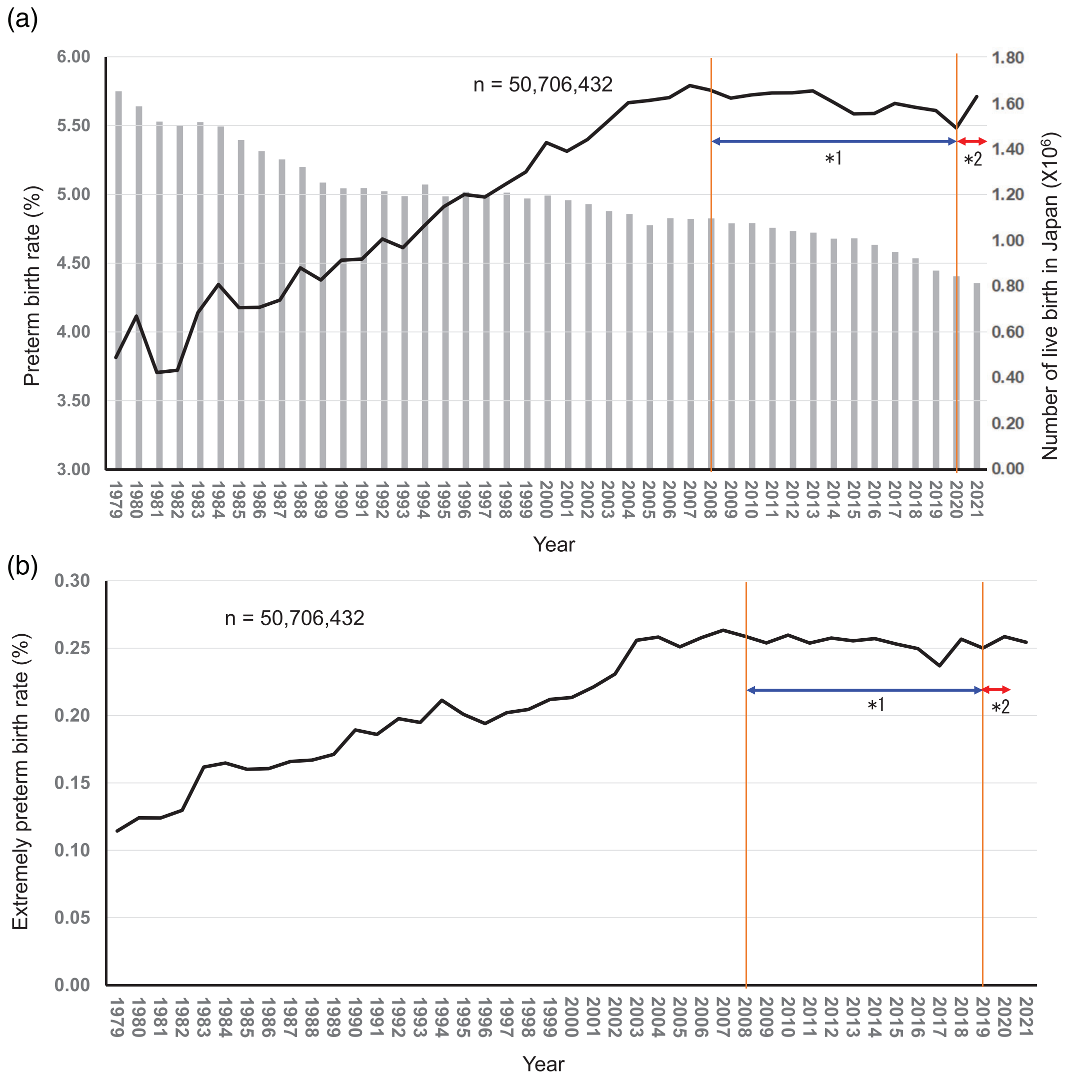

FIGURE 1 (a) The number of live births was 50 706 432. Chronological change in preterm birth rate (PTBR; line graph) and total live births (bar graph) every year in Japan between 1979 and 2021. The PTBR decreased significantly from 2008 until 2020*[1] ($p < 0.001$) but increased in 2021*[2]. (b) Chronological change in extremely preterm birth rate (EPTBR; line graph) in Japan between 1979 and 2021. The EPTBR significantly decreased from 2008 until 2019*[1] ($p = 0.02$) but then increased in 2020*[2].

national average ($p < 0.001$ for all). The PTBR in Kyushu was also significantly higher than the national average ($p = 0.002$), and the rates in Chugoku and Shikoku were significantly lower than the national average ($p < 0.001$ for each).

The average EPTBR for the last 14 years in Japan was 0.255% (Table 2b). Table 3b shows the results of multiple comparisons of EPTBRs over time in each region and nationwide. The EPTBRs in Tohoku and Kyushu were significantly higher than the national average and those of the other six regions ($p < 0.001$ for all).

Thus, both the PTBR and EPTBR decreased nationally between 2007, and 2020 or 2019, respectively. The PTBRs in Hokkaido and Kyushu and the EPTBRs in Tohoku and Kyushu were significantly higher than the national averages.

Maternal aging between 2007 and 2020

Maternal age at birth of first, second, or third child

Figure 3a shows the average maternal age at the birth of the first, second, or third child (Table S4a). From 2007 to 2020, the age of the mother for her first child's birth increased from 29.4 to 30.7 years; the average ages for second and third children's births also increased.

Birth rate according to 5-year age groups for reproductive age

Figure 3b shows changes in the birth rate in six categories of 5-year age groups for reproductive age (Table S4b).

TABLE 2A The preterm birth rates in eight regions of Japan from 2007 to 2020.

	Hokkaido (%)	Tohoku (%)	Kanto (%)	Chubu (%)	Kinki (%)	Chugoku (%)	Shikoku (%)	Kyushu (%)	Nationwide (%)
2007	6.29	5.80	5.55	5.85	5.94	5.49	5.61	6.16	5.79
2008	6.20	5.74	5.62	5.83	5.86	5.32	5.62	6.02	5.76
2009	6.01	5.72	5.57	5.84	5.67	5.43	5.57	5.95	5.70
2010	6.22	5.68	5.59	5.74	5.76	5.53	5.45	6.04	5.73
2011	6.61	5.54	5.65	5.67	5.88	5.66	5.39	5.82	5.74
2012	6.49	5.72	5.69	5.80	5.65	5.40	5.45	5.92	5.74
2013	6.65	5.88	5.60	5.76	5.81	5.43	5.72	5.91	5.75
2014	6.42	5.71	5.56	5.75	5.72	5.28	5.32	5.83	5.67
2015	6.10	5.55	5.41	5.72	5.57	5.56	5.34	5.82	5.58
2016	6.08	5.61	5.46	5.75	5.60	5.32	5.31	5.74	5.59
2017	6.36	5.63	5.45	5.73	5.77	5.54	5.29	5.94	5.66
2018	5.76	5.83	5.52	5.70	5.67	5.39	5.40	5.82	5.63
2019	5.94	5.76	5.51	5.71	5.54	5.32	5.24	5.89	5.61
2020	5.93	5.39	5.32	5.76	5.41	5.29	5.27	5.71	5.48
Average	6.23	5.69	5.54	5.76	5.71	5.43	5.44	5.90	5.68

TABLE 2B The extremely preterm birth rates in eight regions of Japan from 2007 to 2020.

	Hokkaido (%)	Tohoku (%)	Kanto (%)	Chubu (%)	Kinki (%)	Chugoku (%)	Shikoku (%)	Kyushu (%)	Nationwide (%)
2007	0.267	0.319	0.258	0.239	0.267	0.213	0.277	0.294	0.263
2008	0.261	0.309	0.229	0.250	0.286	0.243	0.232	0.296	0.259
2009	0.254	0.288	0.251	0.232	0.250	0.199	0.266	0.304	0.254
2010	0.254	0.300	0.240	0.259	0.258	0.252	0.214	0.310	0.260
2011	0.249	0.255	0.240	0.228	0.253	0.254	0.279	0.320	0.254
2012	0.220	0.334	0.252	0.215	0.256	0.218	0.251	0.325	0.258
2013	0.291	0.322	0.237	0.239	0.244	0.236	0.323	0.292	0.255
2014	0.262	0.340	0.237	0.233	0.262	0.208	0.213	0.326	0.257
2015	0.245	0.284	0.225	0.251	0.268	0.226	0.326	0.292	0.253
2016	0.245	0.326	0.236	0.255	0.238	0.260	0.192	0.268	0.250
2017	0.214	0.310	0.226	0.215	0.240	0.190	0.200	0.290	0.237
2018	0.224	0.347	0.245	0.257	0.228	0.230	0.248	0.305	0.257
2019	0.255	0.333	0.240	0.247	0.239	0.221	0.205	0.280	0.250
2020	0.241	0.322	0.232	0.275	0.237	0.228	0.262	0.328	0.259
Average	0.249	0.312	0.239	0.242	0.253	0.227	0.250	0.302	0.255

From 2007 to 2020, the birth rate for 15- to 19-year-old, 20- to 24-year-old, and 25- to 29-year-old mothers decreased, while those of 30- to 34-year-old and 35- to 39-year-old mothers increased from 2007 to 2017 and decreased from 2018 to 2020. The birth rate for 40- to 44-year-old mothers increased linearly. Relatively, the birth rate shifted to an older age group of 30 years and above.

Employment rate and form according to reproductive age

Figure 3c shows the employment rate according to reproductive age (Table S4c). From 2007 to 2020, the employment rate of 15- to 44-year-old women increased, meaning more women entered the workforce. From 2007 to 2020, the nonregular employment rate for women was 53.5%–54.4%, and that for men was 18.3%–22.1%. Women had a higher proportion of nonregular workers than men.[29]

Number of births and multiple births due to ART from 2007 to 2020

Table 4a shows the total number of live births, number of multiple births, multiple birth rates, and the PTBR and EPTBR for multiple births. The PTBR and EPTBR for multiple births were 54.0% and 2.19%, respectively, in

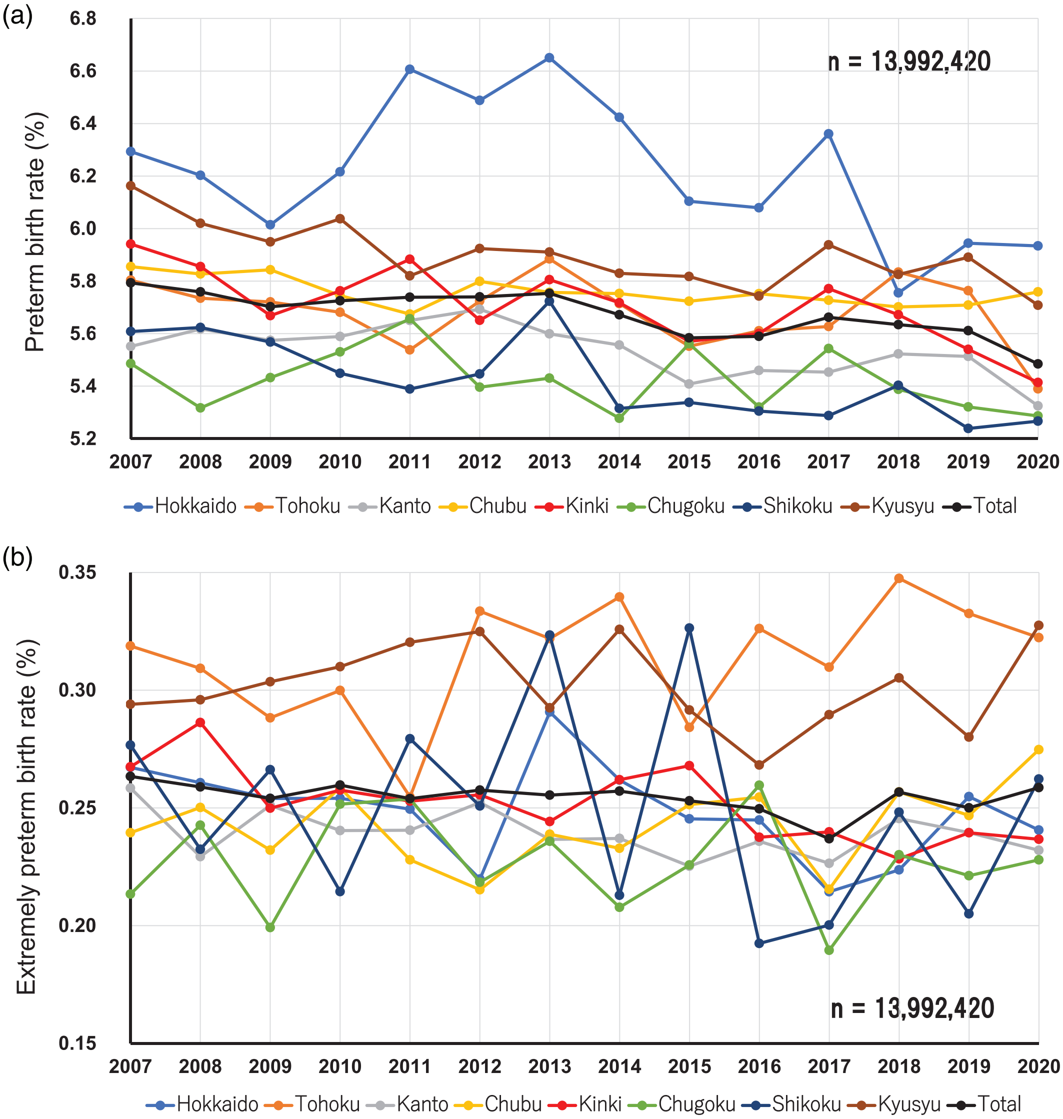

FIGURE 2 (a) Preterm birth rates in the eight regions and the whole of Japan from 2007 to 2020. (b) Extremely preterm birth rates in the eight regions and whole of Japan from 2007 to 2020.

TABLE 3A *P* values of Tukey's pairwise multiple comparisons using RM-ANOVA for preterm births.

Regions	Hokkaido	Tohoku	Kanto	Chubu	Kinki	Chugoku	Shikoku	Kyushu	Nationwide
Hokkaido	–								
Tohoku	<0.0001	–							
Kanto	<0.0001	0.1407	–						
Chubu	<0.0001	0.898	0.002	–					
Kinki	<0.0001	1	0.0563	0.9821	–				
Chugoku	<0.0001	0.0001	0.4864	<0.0001	<0.0001	–			
Shikoku	<0.0001	0.0001	0.4998	<0.0001	<0.0001	1	–		
Kyushu	<0.0001	0.0035	<0.0001	0.197	0.012	<0.0001	<0.0001	–	
Nationwide	<0.0001	1	0.2053	0.8209	0.9998	0.0003	0.0003	0.0019	–

Note: The significant level was set at $p < 0.05$.
Abbreviation: RM-ANOVA, repeated measures analysis of variance.

Japan from 2007 to 2020. From 2007 to 2020 in Japan, the PTBR in multiple pregnancies was 9.5 (54.0/5.68) times higher than that for singleton pregnancies. The EPTBR in multiple pregnancies was 8.6 (2.19/0.255) times higher than that for singleton births. The multiple birth rate decreased significantly from 2.21% in 2007 to

TABLE 3B *P* values of Tukey's pairwise multiple comparisons using RM-ANOVA in extremely preterm births.

Regions	Hokkaido	Tohoku	Kanto	Chubu	Kinki	Chugoku	Shikoku	Kyushu	Nationwide
Hokkaido	–								
Tohoku	<0.0001	–							
Kanto	0.9673	<0.0001	–						
Chubu	0.9979	<0.0001	1	–					
Kinki	1	<0.0001	0.8448	0.9682	–				
Chugoku	0.1829	<0.0001	0.8532	0.6237	0.0733	–			
Shikoku	1	<0.0001	0.9511	0.9957	1	0.153	–		
Kyushu	<0.0001	0.9035	<0.0001	<0.0001	0.0001	<0.0001	<0.0001	–	
Nationwide	0.9984	<0.0001	0.6426	0.8658	1	0.0281	0.9993	<0.0001	–

Note: The significant level was set at $p < 0.05$.
Abbreviation: RM-ANOVA, repeated measures analysis of variance.

1.87% in 2011 ($p = 0.012$) but then significantly increased up to 2020 ($p < 0.001$).

The total number of live and multiple births, total number of births and multiple births produced by in vitro fertilization, and ART birth rates and multiple birth rates are shown in Table 4b. The number of ART births increased linearly from 19 595 in 2007 to 60 598 in 2019 (Table 4b). The ART birth rate increased linearly from 1.80% in 2007 to 7.18% in 2020 (Table 4b). The ART multiple birth rate decreased significantly from 16.3% to 11.9% from 2007 to 2008 ($p < 0.01$) and remained below the 2007 level of 16.3% until 2014. It exceeded that in 2015 and rose to 19.4% in 2020 (Figure 4, Table 4b). More notably, the increase in single births with ART increased 3.7-fold from 15 681 in 2007 to 57 382 in 2019. As a result, ART singleton births increased sharply from 2007 to 2019. The ART multiple birth rate has exceeded that in 2007 since 2015 and increased up to 2020.

DISCUSSION

It was postulated that the implementation of obstetrical guidelines would lead to a reduction in the PTBR and EPTBR. In Japan, the PTBR and EPTBR increased significantly from 1979 to 2007.[31,32] This is despite the total number of yearly births decreasing by half, from 1.64 million to 810 000, over the 43-year period.[20] Notably, when obstetrical guidelines were introduced in 2008, both the national PTBR and EPTBR started to decrease, with the PTBR significantly decreasing until 2020 and the EPTBR significantly decreasing until 2019. It is therefore surmised that the creation and enforcement of obstetrical guidelines contributed to the reduction in the PTBR and EPTBR in Japan. In addition, it may be that the increase observed in the PTBR in 2021 and the increase in the EPTBR in 2020 may be due to the onset of the COVID-19 pandemic. However, several reports[33] concluded that COVID-19 increased the rate of preterm delivery, while others concluded that it had no effect.[34] In fact, according to a US report, the PTBR and EPTBR in 2019 and 2020 decreased from 10.23% and 0.66% to 10.09% and 0.64%, respectively.[35] It will be interesting to see the results of live births in 2021 and 2022, when COVID-19 infections increased in Japan.

With respect to the rest of the world, the PTBR of Japan is lower than that of the United States (Table S5 and Figure S1)[35,36] and also the accurately estimated PTBRs of other world regions (Figure S2a).[37] In addition, an increased chronological change was noted for the PTBRs of neighboring countries and regions such as Taiwan (from 3.33% to 5.11% [2004–2013])[38] and Guangzhou, China (from 5.1% to 5.9% [2001–2016]).[39] However, in the United States, it fell from 10.44% in 2007 to 9.57% in 2014. It then rose to 10.23% in 2019.[35,36] The PTBR in Japan ranged from 5.79% to 5.48% (2007–2020), which is a significant decrease. Japan's PTBR is much lower than that of the United States and has not increased like those of Taiwan and China.

A comparison of the PTBR in Japan as a whole and in the eight regions showed significantly higher PTBRs in Hokkaido and Kyushu (Figure 2a), meaning the potential existed for these to be reduced. In particular, the average PTBR was 6.23% in Hokkaido, which was significantly higher than that of the other seven Japanese regions and the overall average of 5.68% in Japan. We first obtained data from 2007 to 2014. The PTBR in Hokkaido was much higher than that in other regions and we theorized this might be due to the low population density of this region. The Hokkaido region occupies 22.1% of Japan's area; however, it has only 4.2% of the population. The population density is 64 people/m^2 in Hokkaido, the lowest compared to the Japanese average of 331 people/m^2 and is less than 1/20 of that of the Kanto region (Figure S3). We postulate that the long distances required for traveling to maternity examinations and delivery, and the inconvenience of transportation due to snow during the winter, made medical treatment inconvenient and therefore caused the high PTBR in Hokkaido. However, in 2018, the PTBR dropped to 5.76%, which was not significantly different

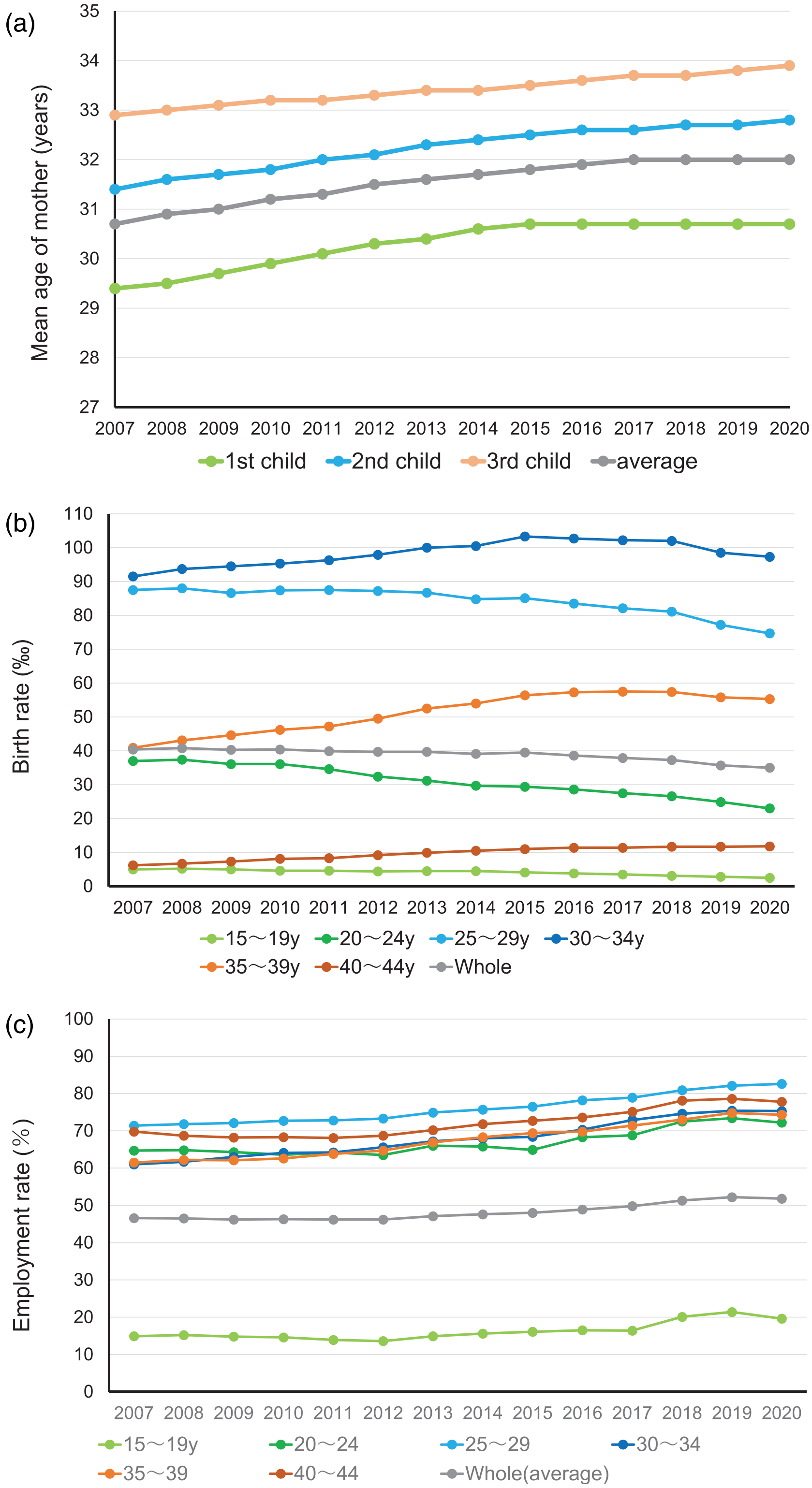

FIGURE 3 (a) Trends in mean age of mother by live birth order in Japan. (b) Birth rate by female age (5-year groups) 2007–2020 (per 1000 Japanese female population). (c) Employment rate by female age (5-year groups) and the whole of Japan (percentage).

when compared with the national average (Fisher's exact test, $p = 0.353$). This suggests that the above postulated cause of a high PTBR was no longer a contributing factor. The decreased PTBR may be a result of our presentations at the 15th and 16th Hokkaido Perinatal Congress (HPC; July 29, 2017, August 18, 2018, respectively) and the 54th Annual Congress of Japan Society of Perinatal and Neonatal Medicine (July 10, 2018) on the high PTBR of Hokkaido up to 2014 in Figure 2a. It is very likely that clinical practice will improve in future with the study of past clinical statistics.

Comparing the EPTBR of Japan with those of other countries, it is notably lower than that of the United States (Table S5 and Figure S1)[35,36] as well as the

TABLE 4A Multiple birth rate, PTBR, and EPTBR in multiple births in Japan.

Year	Total live births	Total multiple births	TMBs/ TLBs (%)	PTB of MBs	PTBR of MBs (%)	EPTB of MBs	EPTBR of MBs (%)
2007	1 089 286	24 079	2.21	13 661	56.7	576	2.39
2008	1 090 564	22 357	2.05	13 002	58.2	544	2.43
2009	1 069 549	20 891	1.95	11 954	57.2	466	2.23
2010	1 070 847	20 198	1.89	11 619	57.5	460	2.28
2011	1 050 359	19 612	1.87	11 151	56.9	427	2.18
2012	1 036 863	20 067	1.94	11 112	55.4	465	2.32
2013	1 029 512	20 006	1.94	10 887	54.4	445	2.22
2014	1 003 308	19 490	1.94	10 214	52.4	378	1.94
2015	1 005 447	19 468	1.94	10 084	51.8	468	2.40
2016	976 977	19 367	1.98	9784	50.5	440	2.27
2017	945 907	19 041	2.01	9667	50.8	345	1.81
2018	918 162	18 739	2.04	9613	51.3	369	1.97
2019	865 023	17 402	2.01	8749	50.3	327	1.88
2020	840 616	17 146	2.04	8660	50.5	380	2.22
Total	13 992 420	277 863	1.99	150 157	54.0	6090	2.19

Abbreviations: EPTBR, extremely preterm birth rate; MB, multiple birth; PTBR, preterm birth rate; TLBs, total live births; TMBs, total multiple births.

TABLE 4B Birth rate for ART and the rate of ART MBs in TMBs.

Year	TLBs of ART	TLBs	TLBs of ART/TLBs (%)	MBs in ART	SBs in ART	TMBs	TMBs in ART/TMBs (%)
2007	19 595	1 089 286	1.80	3914	15 681	24 079	16.3
2008	21 704	1 090 564	1.99	2670	19 034	22 357	11.9
2009	26 680	1 069 549	2.49	2727	23 953	20 891	13.1
2010	28 945	1 070 847	2.70	2802	26 143	20 198	13.9
2011	32 426	1 050 359	3.09	2702	29 724	19 612	13.8
2012	37 953	1 036 863	3.66	3102	34 851	20 067	15.5
2013	42 554	1 029 512	4.13	2985	39 569	20 006	14.9
2014	47 322	1 003 308	4.72	3034	44 288	19 490	15.6
2015	51 001	1 005 447	5.07	3186	47 815	19 468	16.4
2016	54 110	976 977	5.54	3476	50 634	19 367	17.9
2017	56 617	945 907	5.99	3439	53 178	19 041	18.1
2018	56 979	918 162	6.21	3153	53 826	18 739	16.8
2019	60 598	865 023	7.01	3216	57 382	17 402	18.5
2020	60 381	840 616	7.18	3318	57 063	17 146	19.4
Total	596 865	13 992 420	4.27	3123	553 141	19 847	15.7

Abbreviations: ART, assisted reproductive technology; MB, multiple birth; MBR, multiple birth rate; SB, single birth; TLB, Total live birth; TMB, Total multiple birth.

accurately estimated EPTBRs of other regions of the world (Figure S2b).[37] Even if low, the EPTBR in Hokkaido rose to 0.291% and the PTBR was highest at 6.65% in 2013, the year we conducted a questionnaire survey on uterine cervical cancer (UCC), *Chlamydia trachomatis* (CT) and BV screening rates of pregnant women in this region in February. This was also when we collected detailed information on the time of BV screening and diagnostic methods used. In 2012, UCC and CT screening rates reached 100%, as per guidelines. Bacterial vaginosis was universally screened for in 75.4% of 28 956 eligible cases; however, 7944 patients (27.4%) adopted a Nugent score in the screening before 20 weeks of gestation.[40] The therapeutic effect was not expected. Screening before 12 weeks of gestation and adoption of a Nugent score were then encouraged. These actions were taken as countermeasures against the high PTBRs in 2013. The results of this questionnaire survey were reported at the 11th HPC on August 17, 2013, and published in a paper in 2016.[40]

Comparing EPTBRs in Japan as a whole and in the eight regions, the average EPTBRs of 0.312% in Tohoku

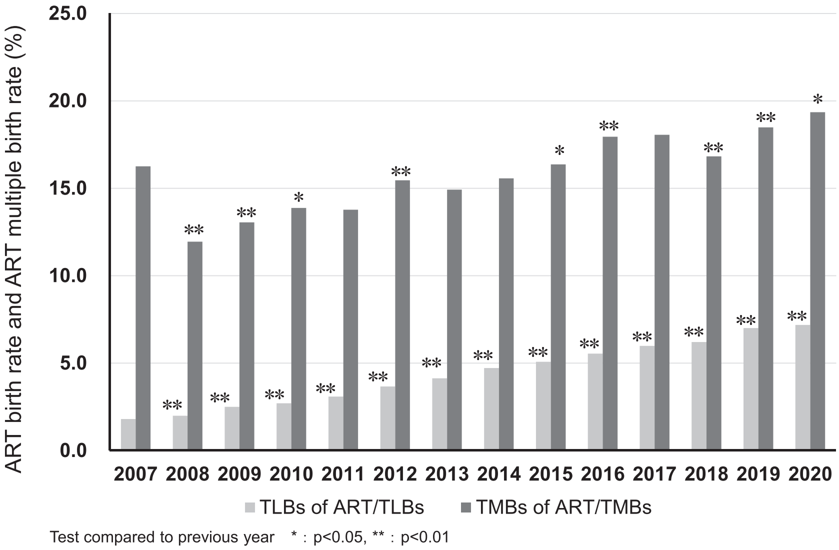

FIGURE 4 Chronological change in ART birth rate and ART multiple birth rate in Japan between 2007 and 2020. ART, assisted reproductive technology; TLB, total live birth; TMB, total multiple live birth.

and 0.302% in Kyusyu were significantly higher than those of the other six regions and the overall average of 0.255% in Japan. It may be possible to reduce the EPTBR in these regions.

From 2007 to 2020, the increase in childbearing age was marked. The PTBR increased with increasing age compared to pregnant women who gave birth for the first time when between 20 and 24 years of age. The PTBR increased (odds ratio [OR], 1.63; 95% confidence interval [CI], 1.35–1.98) among those aged between 35 and 39 years.[41] Looking at birth rates in reproductive age groups, the relative birth rate shifted to an older age group of 30 years and above. Thus, these findings suggest that the aging of pregnant women means they are more likely to give birth prematurely due to the many complications of pregnancy.[16,42]

A rise in the employment rate from 2007 to 2020 was observed for the reproductive age range from 15 to 44 years. The nonregular employment rate for women was about 2.5 times higher than men,[29] and they were more likely to give birth prematurely.[17]

In April 2008, we investigated the effects of reducing the number of fertilized eggs returned to the uterus to one during in vitro fertilization.[19] Importantly, PTBRs were similar for multiple births (Relative risk, 1.07; 95% CI, 1.02–1.13) when comparing ART pregnancies to natural conception; however, these doubled for singleton births.[43] The proportion of multiple births produced by in vitro fertilization as a percentage of all multiple births significantly decreased from 2007 to 2008, increased from 2015 more than that in 2007, and then rose gradually until 2020. This is because ART pregnancies increased sharply from 2007 to 2019.

Looking at single pregnancies in ART, an increase of 32 134 births from 2007 to 2015 was noted. The PTBR of singleton pregnancies in ART was twice that of natural conception.[44,45] Preterm births increased by 1796 ($1796 = 32\,134 \times 0.0559$) in 2015. Converting this to the PTBR, this was a 0.18% ($1796/100\,5271 \times 100\% = 0.18\%$) increase. Reducing the number of fertilized eggs returned to the uterus to just one was effective in reducing preterm births from 2007 to 2008; however, the preterm birth pressure due to ART increased every year thereafter. The PTBR in 2015 decreased by 0.20% ($0.20\% = 5.79\% - 5.59\%$) compared to 2007. These are some of the reasons why the PTBR has decreased by 0.38%.

From 2007 to 2019, the aging of pregnant women, increase in the employment rate at reproductive age, and increase in pregnant women using ART have brought about pressures on the number of premature births. However, the PTBR and EPTBR showed a significant decline up to 2019 after peaking in 2007 suggesting obstetrical guidelines influenced these rates.

However, despite the enforcement of obstetrical guidelines, a significant difference in the PTBR and EPTBR was noted between the eight regions of Japan. In areas where the PTBR and EPTBR were found to be high, investigating the cause and taking countermeasures may be the key to further reducing the premature birth rate in Japan.

This paper has limitations. The factors affecting preterm births are many, including medical causes.[46,47] In addition, economic and social factors,[48,49] as well as other factors such as anxiety,[50] have been implicated in preterm births. We have not considered these elements and believe that further examinations are necessary in the future.

In summary, although the PTBR and EPTBR in Japan showed a significant increase from 1979 to 2007, the introduction of obstetrical guidelines in 2008 was followed by a reduction in these rates. We therefore suspect that such guidelines contributed to reductions observed in the PTBR and EPTBR, despite pressures on premature births such as the aging of women of childbearing age, an increase in the employment rate of women of reproductive age, and an increase in pregnant women due to ART.

AUTHOR CONTRIBUTIONS

Tsuyoshi Saito was a supervisor of the study; Takashi Yamada, Kazutoshi Cho, Kazuo Sengoku, and Tasuku Mariya were responsible for the acquisition of data and statistical analysis. Satoshi Shimano designed this study and was also the chief investigator. All authors contributed to the writing of the final manuscript and have approved the final article.

ACKNOWLEDGMENTS

The authors are grateful to Dr Shigeaki Ohtsuki for his thoughtful suggestions on statistical analysis and Dr Yasuaki Tamura from the Department of Pathology, Sapporo Medical University, School of Medicine for his thoughtful contributions on this manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interests for this article.

DATA AVAILABILITY STATEMENT

Secondary use of the data we obtained from the Japanese Ministry of Health, Labour and Welfare (JMHLW) cannot be shared publicly, because of Statistics Act in Japan. Therefore, the custom-made tabulated data from 2007 to 2020 used here cannot be shared publicly. Other data (Table 1, Figures 1a,b and 3a–c, and Tables S4a, S4b, S4c) can be obtained from the website of the JMHLW and Japanese Ministry of Internal Affairs and Communications (JMIAC) can be shared publicly. If you want to know the vital, social, and economic statistics of Japan, you can contact the JMHLW and JMIAC (Tel: +81-3-5253-1111).

ORCID

Satoshi Shimano https://orcid.org/0000-0002-9661-2305
Takashi Yamada https://orcid.org/0000-0001-6865-6960
Kazutoshi Cho https://orcid.org/0000-0003-2742-4084
Kazuo Sengoku https://orcid.org/0000-0002-0405-4976
Tasuku Mariya https://orcid.org/0000-0002-7110-980X
Tsuyoshi Saito https://orcid.org/0000-0002-9148-1609

REFERENCES

1. Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetrical and Gynecologists (JAOG). Guidelines for obstetrical practice in Japan. 2008 edition; 2008: 1–193 (in Japanese).
2. Minakami H, Hiramatsu Y, Koresawa M, Fujii T, Hamada H, Iitsuka Y, et al. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG) 2011 edition. J Obstet Gynaecol Res. 2011;37:1174–97.
3. Minakami H, Maeda T, Fujii T, Hamada H, Iitsuka Y, Itakura A, et al. Guidelines for obstetrical practice in Japan: Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG): 2014 edition. J Obstet Gynaecol Res. 2014;40(6):1469–99.
4. Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG). Guidelines for obstetrical practice in Japan. 2017 edition. 2017: 1–449 (in Japanese).
5. Japan Society of Obstetrics and Gynecology (JSOG) and Japan Association of Obstetricians and Gynecologists (JAOG). Guidelines for obstetrical practice in Japan. 2020 edition. 2020: 1–384 (in Japanese).
6. Sakai M, Shiozaki A, Tabata M, Sasaki Y, Yoneda S, Arai T, et al. Evaluation of effectiveness of prophylactic cerclage of a short cervix according to interleukin-8 in cervical mucus. Am J Obstet Gynecol. 2006;194:14–9.
7. Aoki S, Ohnuma E, Kurasawa K, Okuda M, Takahashi T, Hirahara F. Emergency cerclage versus expectant management for prolapsed fetal membranes: a retrospective, comparative study. J Obstet Gynaecol Res. 2014;40(2):381–6.
8. Otsuki K. Trend of preventive management of preterm birth. J Jpn Soc Perin Neon Med. 2020;56(1):1–22. (in Japanese).
9. McDonald HM, Brocklehurst P, Gordon A. Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev. 2007;(1):CD000262.
10. Brocklehurst P, Gordon A, Heatley E, Milan SJ. Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev. 2013;(1):CD000262.
11. Subtill D, Brabant G, Tilloy E, Devos P, Canis F, Fruchart A, et al. Early clindamycin for bacterial vaginosis in pregnancy (PREMEVA): a multicentre, double-blind, randomised controlled trial. Lancet. 2018;392(10160):2171–9.
12. Shimano S, Nishikawa A, Sonoda T, Kudo R. Analysis of the prevalence of bacterial vaginosis and *Chlamydia trachomatis* infection in 6083 pregnant women at a hospital in Otaru, Japan. J Obstet Gynaecol Res. 2004;30:230–6.
13. Shimano S, Kawamura M, Sonoda T, Minakami H. Possible association between screening BV at the prenatal visit and reduced cervical cerclage: multi-center questionnaire in Hokkaido, Japan. J Obstet Gynaecol Res. 2009;35:262–70.
14. Sangkomkamhang US, Lumbiganon P, Prasertcharoensuk W, Laopaiboon M. Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery. Cochrane Database Syst Rev. 2015;2015(2):CD006178.
15. Oba T, Sekizawa A. The trend of preterm birth in Japan. Clin Obstet Gynaecol. 2015;69:274–9. (in Japanese).
16. Tamura N, Hanaoka T, Ito K, Araki A, Miyashita C, Ito S, et al. Different risk factors for very low birth weight, term-small-for-gestational-age, or preterm birth in Japan. Int J Environ Res Public Health. 2018;15(2):369.
17. Shiozaki A, Yoneda S, Nakabayashi M, Takeda Y, Takeda S, Sugimura M, et al. Multiple pregnancy, short cervix, part-time worker, steroid use, low educational level and male fetus are risk factors for preterm birth in Japan: a multicenter, prospective study. J Obstet Gynaecol Res. 2014;40(1):53–61.
18. Jakobsson M, Gissler M, Paavonen J, Tapper AM. The incidence of preterm deliveries decreases in Finland. BJOG. 2008;115(1): 38–43.
19. Views on prevention of multiple pregnancies in assisted reproductive technology by the Japan Society of Obstetrics and Gynecology. Acta Obst Gynaec Jpn 2008; 60: 1159 (in Japanese).
20. e-Stat. Portal site of official statistics of Japan [cited 2022 Dec 18]. Available from: https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00450011&tstat=000001028897&cycle=7&tclass1=000001053058&tclass2=000001053061&tclass3=000001053064&tclass4val=0
21. List of custom-made tabulation usage records; 2019 [cited 2022 Dec 18]. Available from: https://www.mhlw.go.jp/toukei/itaku/order03.html

22. List of custom-made tabulation usage records; 2020 [cited 2022 Dec 18]. Available from: https://www.e-stat.go.jp/microdata/jisseki/order/30045020200001
23. List of custom-made tabulation usage records; 2021 [cited 2022 Dec 18]. Available from: https://www.e-stat.go.jp/microdata/jisseki/order/30045020210001
24. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379:2162–72.
25. Vogel JP, Chawanpaiboon S, Watananirun K, Lumbiganon P, Petzold M, Moller AB, et al. Global, regional and national levels and trends of preterm birth rates for 1990 to 2014: protocol for development of World Health Organization estimates. Reprod Health. 2016;13(1):76.
26. Ministry of Health Labour and Welfare. Vital Statistics of Japan Final data Natality yearly 2021 Tables 4–19. Trends in mean age of mother by live birth order: Japan [cited 2023 Apr 1] Available from: https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00450011&tstat=000001028897&cycle=7&year=20210&month=0&tclass1=000001053058&tclass2=000001053061&tclass3=000001053064&result_back=1&tclass4val=0
27. Ministry of Internal Affairs and Communications [Tables 2–17 Number of births and birth rate by female age (5-Year Group) 1925–2020] [cited 2023 Apr 1]. Available from: https://www.stat.go.jp/data/nihon/02.html
28. Statistics Bureau, Ministry of Internal Affairs and Communications of Japan. Historical data 3 (3) Employed person and employment rate by age group – Whole Japan; 2022 [cited 2023 Apr 1]. Available from: http://www.stat.go.jp/data/roudou/longtime/03roudou.htm
29. Ministry of Health Labour and Welfare. The actual situation of working women in 2021 Changes in the ratio of non-regular staff/employees [cited 2023 Apr 1]. Available from: https://www.mhlw.go.jp/bunya/koyoukintou/josei-jitsujo/dl/21fu-all.pdf
30. Summary report of ART online registry from 2007 to 2020 by the Ethics Committee of the Japan Society of Obstetrics and Gynecology [cited 2023 Apr 1]. Available from: https://www.jsog.or.jp/modules/committee/index.php?content_id=12
31. Sakata S, Konishi S, Ng CFS, Watanabe C. Preterm birth rates in Japan from 1979 to 2014: analysis of national vital statistics. J Obstet Gynaecol Res. 2018;44(3):390–6.
32. Saito S. Prevention of preterm birth (2) bacterial vaginosis: actual condition and countermove. Boshi Hoken Joho. 2010;61:12–6. (in Japanese).
33. Piekos SN, Roper RT, Hwang YM, Sorensen T, Price ND, Hood L, et al. The effect of maternal SARS-CoV-2 infection timing on birth outcomes: a retrospective multicentre cohort study. Lancet Digit Health. 2022;4(2):e95–104.
34. Mullin AM, Handley SC, Lundsberg L, Elovitz MA, Lorch SA, McComb EJ, et al. Changes in preterm birth during the COVID-19 pandemic by duration of exposure and race and ethnicity. J Perinatol. 2022;42(10):1346–52.
35. Osterman M, Hamilton B, Martin JA, Driscoll AK, Valenzuela CP. Births: final data for 2020. Natl Vital Stat Rep. 2021;70(17):1–50.
36. Barfield WD. Public health implications of very preterm birth. Clin Perinatol. 2018;45(3):565–77.
37. Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health. 2019;7(1):e37–46.
38. Chang YK, Tseng YT, Chen KT. The epidemiologic characteristics and associated risk factors of preterm birth from 2004 to 2013 in Taiwan. BMC Pregnancy Childbirth. 2020;20(1):201.
39. Lu J, Wei D, Shen S, Xia X, He J, Sun Y, et al. Increasing trends in incidence of preterm birth among 2.5 million newborns in Guangzhou, China, 2001 to 2016: an age-period-cohort analysis. BMC Public Health. 2020;20(1):1653.
40. Shimano S, Yamada T, Sonoda T, Yamaguchi T, Mizunuma M, Morikawa M, et al. Clinical screening strategies for cervical cancer, *Chlamydia trachomatis* infection, and bacterial vaginosis in pregnant women in Hokkaido between 2004 and 2012: a retrospective study. Int J Women's Health Care. 2016;1:1–5.
41. Kyozuka H, Fujimori K, Hosoya M, Yasumura S, Yokoyama T, Sato A, et al. The effect of maternal age at the first childbirth on gestational age and birth weight: the Japan Environment and Children's Study (JECS). J Epidemiol. 2019;29(5):187–91.
42. Matsuda Y, Kawamichi Y, Hayashi K, Shiozaki A, Satoh S, Saito S. Impact of maternal age on the incidence of obstetrical complications in Japan. J Obstet Gynaecol Res. 2011;37(10):1409–14.
43. Helmerhorst FM, Perquin DA, Donker D, Keirse MJ. Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies. BMJ. 2004;328(7434):261.
44. Jackson RA, Gibson KA, Wu YW, Croughan MS. Perinatal outcomes in singletons following in vitro fertilization: a meta-analysis. Obstet Gynecol. 2004;103(3):551–63.
45. McDonald SD, Murphy K, Beyene J, Ohlsson A. Perinatal outcomes of singleton pregnancies achieved by in vitro fertilization: a systematic review and meta-analysis. J Obstet Gynaecol Can. 2005;27(5):449–59.
46. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. Lancet. 2008;371(9606):75–84.
47. Manuck TA, Esplin MS, Biggio J, Bukowski R, Parry S, Zhang H, et al. The phenotype of spontaneous preterm birth: application of a clinical phenotyping tool. Am J Obstet Gynecol. 2015;212(4):487.e11.
48. Li X, Sundquist J, Kane K, Jin Q, Sundquist K. Parental occupation and preterm births: a nationwide epidemiological study in Sweden. Paediatr Perinat Epidemiol. 2010;24(6):555–63.
49. McHale P, Maudsley G, Pennington A, Schlüter DK, Barr B, Paranjothy S, et al. Mediators of socioeconomic inequalities in preterm birth: a systematic review. BMC Public Health. 2022;22(1):1134.
50. Rose MS, Pana G, Premji S. Prenatal maternal anxiety as a risk factor for preterm birth and the effects of heterogeneity on this relationship: a systematic review and meta-analysis. Biomed Res Int. 2016;2016:8312158.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Shimano S, Yamada T, Cho K, Sengoku K, Mariya T, Saito T. Changes in preterm and extremely preterm birth rates in Japan after the introduction of obstetrical practice guidelines in 2008. J Obstet Gynaecol Res. 2023. https://doi.org/10.1111/jog.15722