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The association between interpregnancy intervals and preterm birth: a systematic review and meta-analysis

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Abstract

Background Research has shown a relationship between interpregnancy intervals (IPIs) and preterm birth, but a comprehensive understanding remains elusive. The aim of this systematic review and meta-analysis was to examine the effect of different IPIs on the risk of preterm birth

Methods Systematic searches were conducted in PubMed, Cochrane, Web of Science, and Embase up to June 2, 2023. Studies included in the review provided data on IPIs and preterm birth outcomes, assessed via the NOS quality scale. A Bayesian network meta-analysis was performed to evaluate the association between IPIs and preterm birth.

Results From 34 studies and 8,646,679 individuals, the optimal IPIs were found to be 24-29 months, showing significantly lower risks of preterm birth at less than 32 weeks of gestation [OR=0.55 (95%CI: 0.50 - 0.62)]and at less than 37 weeks of gestation[OR=0.61 (95%CI: 0.59 - 0.63)]compared to IPIs less than 5 months.

Conclusions IPIs of 24-29 months significantly reduce the risk of preterm birth, suggesting a potential target range for family planning and clinical recommendations.

Trial registration Not applicable.

Keywords Interpregnancy intervals, Preterm birth, Systematic review, Meta-analysis

Background

The World Health Organization (WHO) defines preterm birth as deliveries occurring before 37 weeks of gestation. In terms of survival and quality of life, preterm birth stand as the most crucial factor contributing to adverse outcomes in infants [1]. The *Born Too Soon* report, released by the World Health Organization in 2012, reported an average preterm birth incidence of 10% [2], and there were 15 million preterm birth cases each year. Preterm birth are the primary cause of neonatal mortality and the second leading cause of mortality in children under 5 years of age [3]. In countries with high population density, preterm birth pose a significant social challenge. For instance, in China, the incidence of preterm birth has been steadily rising, increasing from 4%−5% in the 1990s to the current range of 7%−10% [4]. The World Health Organization highlighted in the *Born Too Soon* report that the adjusted incidence of preterm birth in China in 2010 was 7.1%. The standardized mortality rate of preterm neonates in China is higher than that of Western Europe (14.57/100,000) and lower than that of North

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America (32.61/100,000) [5]. Consequently, exploring controllable strategies for the reasonable prevention of preterm birth is currently a significant challenge for obstetric professionals.

Teresa Cobo et al. conducted a comprehensive review analysis to categorize risk factors associated with preterm birth into demographic, obstetric and gynecologic, and current pregnancy-related factors [6]. Numerous large-scale population studies have identified a short interpregnancy interval (IPI) as a risk factor for adverse perinatal outcomes [7–12]. IPI is defined as the time between a previous live birth and a subsequent conception [13]. However, it remains unclear whether this is an independent risk factor or if the association is influenced by other reproductive risk factors. Similarly, little is known about the correlation between long intervals and perinatal outcomes [14].

There is a lack of evidence-based support regarding the risk of preterm birth associated with different IPIs. Therefore, we conducted a systematic review and meta-analysis to investigate the impact of various IPIs on the risk of preterm birth. Our goal was to determine whether IPIs can serve as a controllable risk factor for preterm birth, providing a foundation for the prevention of preterm birth. This information is significant for enhancing collaborative decision-making between healthcare providers and women planning another pregnancy.

Materials and methods

Study registration

This study was conducted in accordance with the reporting guidelines for systematic reviews and meta-analyses (PRISMA-2020, Supplementary File 1) and was prospectively registered on the PROSPERO platform (ID: CRD42022344131).

Search strategy

In this study, we used the terms "preterm" and "birth interval" to comprehensively search four databases, namely PubMed, Cochrane, Web of Science, and Embas, from the databases' inception to April 12, 2022. To avoid missing any relevant studies, we additionally searched the references and related literature of the included studies on June 30, 2023, to supplement the included literature and identify potentially relevant studies. (Supplementary File 2).

Eligibility criteria

Inclusion criteria

P (Populations) Patients were multiparae with a documented IPI.

E (Exposure) The exposure factor was long IPI or short IPI, with IPI defined as the length of time between a previous live birth and a subsequent conception.

C (Control) The reference IPI level was defined based on the included studies.

O (Outcome) The outcomes were odds ratio (OR), relative risk (RR), and hazard ratio (HR), reflecting the association between IPI and preterm birth after adjusting for other confounding factors, or directly calculated RR value in propensity score matching studies.

S (Study design) Cohort studies, case-control studies, and cross-section studies.

Exclusion criteria

P (Populations) Studies with inaccurate calculation of IPI or controversial definitions of preterm birth.

E (Exposure) Studies with serious flaws in defining IPI.

C (Control) None.

O (Outcome) In cohort, case-control, or cross-section studies, only univariate analysis of the association between IPI and ASD was conducted.

S (Study design) Conference abstracts without full text, dissertations, etc.

Literature screening

We imported the retrieved literature into EndnoteX9 software, eliminated duplicate publications, and initially filtered the primary studies that met the criteria by reviewing their titles and abstracts. Subsequently, we downloaded and thoroughly examined the full texts of the primarily eligible studies. Finally, we selected the primary studies that satisfied the inclusion criteria for this systematic review.

Data extraction

A standard data extraction spreadsheet was created in advance of data extraction. The extracted content encompassed title, first author, publication year, study design, author's country, patient source, sampling time, IPI definition, exposure factors, sample size for each exposure factor group, preterm birth numbers in each exposure

factor group, total number, statistical methods, control of confounding factors, and outcome indicators.

The literature screening and data extraction were independently conducted by two researchers, with a cross-check afterwards. If there was any disagreement, a third researcher was involved in the discussion for a final decision.

Quality assessment of literature

The Newcastle-Ottawa Scale (NOS) was utilized to assess the quality of the included literature [16]. The scale comprises three main sections, totaling 8 items and 9 scoring points. It is designed to evaluate cohort studies and cross-section studies, focusing specifically on study population selection, comparability between groups, and exposure or outcome measurement. The NOS employs a semi-quantitative principle with a star rating system, allowing for a maximum score of 9 stars. The comparability between groups in these 8 items can receive up to 2 stars, while the highest score for each remaining item is 1 star. In this study, literature that received a score of 5 stars or more was considered high-quality, whereas literature with a score of less than 5 stars was categorized as low-quality. The evaluation of literature quality was independently conducted by two researchers, followed by a cross-check upon completion. Disputes, if any, were resolved by discussing with a third researcher.

Data analysis methods

This network meta-analysis employed a Bayesian random effects model to compare the effects of interventions. The modeling utilized the Markov chain Monte Carlo method with 4 chains running concurrently. Annealing times were set at 20,000 iterations, with 50,000 simulation iterations. To evaluate model fit and overall consistency, the Deviance Information Criterion (DIC) was employed. In cases of a closed-loop network, the node-splitting method was applied to analyze local consistency. Additionally, interventions are ranked based on Surface Under the Cumulative Ranking (SUCRA) values, and a league table was generated to compare differences in the effect between interventions. To visually represent heterogeneity among studies, a funnel plot was utilized. The analyses are conducted using Stata 15.0 (Stata Corporation, College Station, TX) and R4.2.0 (R Development Core Team, Vienna, http://www.R-project.org). A statistically significant difference is defined as $P<0.05$.

Result

Literature screening results

After conducting a comprehensive search across the PubMed, Cochrane, Web of Science, and Embase databases, a total of 14,212 pieces of literature were identified. The literature was then imported into the EndNote software for management. Following the removal of duplicate entries, 596 articles remained. Upon reviewing the titles and abstracts of the articles, 132 articles were primarily selected. Subsequently, we retrieved and carefully read the full texts of these 132 articles and excluded empirical summaries, duplicate publications, reviews, and case reports, resulting in a final set of 36 pieces of literature. These 36 selected pieces were thoroughly reviewed and analyzed in adherence to the established inclusion and exclusion criteria. Two pieces of literature were excluded due to discrepancies in outcome indicators, a lack of control for confounding factors, and inaccurate content data. As a result, a total of 34 pieces of literature [10, 11, 13–44] were eligible and included. The detailed screening process is visually presented in Figure 1.

Basic characteristics of the included literature

Among the 34 pieces of literature included, there were approximately 8,646,679 cases, including around 418,104 cases of preterm birth. The sampling time of cases in the included literature ranged from 1985 to 2020, which could be divided into four periods: ≤3 years [3, 16, 26, 28–30, 34, 36, 39, 43], 3–5 years [20, 22, 23, 31, 32, 35, 38, 41, 44], 6–10 years [10, 11, 14, 15, 18, 21, 24, 27, 33, 37, 42], and >10 years [17, 19, 25, 40]. These cases mainly came from population databases in various countries or regions, and some also came from local hospitals. The included sample sizes (N) could mainly be divided into five categories: N≤10,000 in nine studies [10, 16, 23, 27, 30, 36, 38, 43, 44], 1<N≤10,000 in 8 studies [14, 15, 19, 22, 24, 31, 34, 39], 10<N≤500,000 in 9 studies [11, 13, 18, 20, 21, 29, 32, 33, 35, 37, 41], 50<N<1,000,000 in 4 studies [25, 26, 28, 42], ≥1,000,000 in 2 studies [17, 40].

The researchers of the included literature mainly came from 12 countries and organizations, specifically the United States (14 studies), China (6 studies), Canada (2 studies), Brazil (2 studies), Tanzania (2 studies), the Netherlands (2 studies), Japan (1 study), Argentina (1 study), Israel (1 study), Colombia (1 study), Saudi Arabia (1 study), and the United Nations (1 study).

As illustrated in Table 1, among the 34 pieces of literature included, there were 31 cohort studies (CS) and 3 case-control studies (CCS). IPI was defined as the duration between a previous live birth and a subsequent conception. Two calculation methods were employed: ① From the time of the previous delivery to the menstrual cycle date of the next pregnancy; ② From the time of the previous delivery to the next delivery, minus the gestational age of the second child.

Out of the 34 pieces of literature included, 9 articles from the United States, Brazil, Japan, Canada, and the

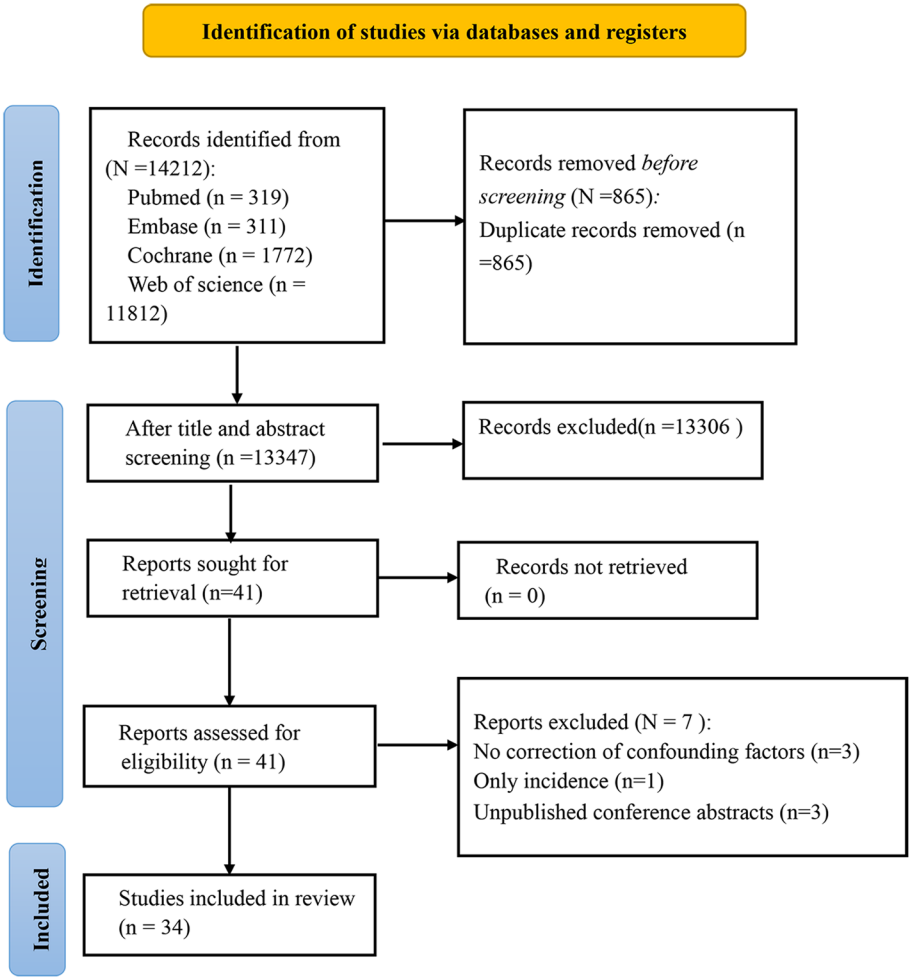

Fig. 1 Literature Screening Process and Results

United Nations addressed extremely preterm birth (delivery at 20–28 weeks of gestation) within the classification of pregnancy outcomes [13, 15, 18, 23, 26, 34, 35, 37, 40]. The majority of the other studies did not provide a detailed classification of preterm birth.

There were numerous confounding factors (Cf) that can contribute to preterm birth, including maternal age at childbirth (Cf −1), maternal education level (Cf −2), race or ethnicity (Cf −3), lifestyle choices (e.g., smoking or alcohol consumption, Cf −4), physical condition (e.g., obesity, chronic diseases, uterine abnormalities or conditions, Cf −5), method of conception (Cf −6), socio-economic status (Cf −7), marital status (Cf −8), and others (Cf −9). Among these, 29 pieces of literature controlled for age factors [10, 11, 13, 14, 16–23, 27–30, 32–38, 40–43, 45, 46]. In addition, the majority of studies controlled for other diversifying confounding factors.

Quality assessment of the included literature

The (NOS was used to assess the quality of the included literature. The results are illustrated in Table 2.

(1) In the 3 case-control studies [10, 16, 24], the case definition was sufficient, and the cohort was representative; community control was used, and the control was defined as having no medical history. In terms of comparability, one study [24] received a score of 0 for not controlling confounding factors. There were reliable records, and the exposure of cases and controls was determined using the same method, with no description of non-response rate.
(2) In the 31 cohort studies, the exposure cohort effectively represented the average population of the community. The non-exposure cohort was selected from the same community as the exposure cohort, and reliable records on ascertainment of exposure were provided, except for one study [34]. No out-

Table 1 Basic features of the included literature

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
1 PMID: 9702144 1998	Cs	Obstetric automatic recording system 1980–1990	IPI-1	<3 3–6 ≥6	106 332 762 1178 2022	24 59 122 164 262	4400	< 37	Cf-1, Cf-3, Cf-9	Multiple logistic regression	7
2 PMID: 10029642 1999	Cs	Utah's recorded life statistics 1989–1996	IPI-1	0–5 6–11 12–17 18–23 24–59 60–119 ≥120	9311 2370029081 25655 65944 16374 3140	/	173205	< 32w 32 - 36w 37 - 38w	Cf-1 - Cf-9	Separate logistic regression model	9
3 PMID: 10711549 2000	Cs	/ 1991.01– 1991.09	IPI-1	<6 6–11 12–17 18–23 24–29 30–35 36–47 48–59 >59	26022 41454 39390 32172 26568 21111 30874 21301 50950	4311 6322 5857 4134 3435 2814 4279 2914 8050	289842	< 23 23 - 32 33 - 37	Cf-1, Cf-3, Cf-9	Multivariate logistic regression	8
4 PMID: 12907483 2003	Cs	Scottish Obstetrics and Gynecology Hospital 1992–1998	IPI-1	1–5 6–11 12–17 18–23 24–59	3282 8999 12220 11793 32761	152 264 328 282 922	89143	< 37w	Cf-3, Cf-4, Cf-7	Multivariate logistic regression analysis	8
5 PMID: 15255877 2004	Cs	Three maternal and child health centers in three different areas of Alexandria, Egypt 2001.10– 2002.07	IPI-1	<12 12–36 37–48 49–60 >60	103 552 182 120 245	8 54 19 14 18	1202	< 37	Cf-1, Cf-2, Cf-4	Stepwise logistic regression	7

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
6 PMID: 16055588 2005	Cs	Perinatal Information System Database of Uruguayan Montevideo Latin American Center for Perinatology and Human Development 1985–2004	IPI-1	< 6 6–11 12–17 18–23 24–59 ≥ 60	34888 165438 169940 150807 395026 209331	8408 18529 16484 14477 38318 24910	1125430	< 37 <32	Cf-1, Cf-2, Cf-5, Cf-8, Cf-9	Multiple logistic regression	9
7 PMID: 17826413 2007	Cs	Missouri Department of Health 1989–1997	IPI-1	<6 6–12 12–18 >18	15200 27405 27523 86202	2083 2380 1816 5382	156330	< 35 32 - 35 28 - 32 20 - 28	Cf-1, Cf-2, Cf-3, Cf-4, Cf-5, Cf-8, Cf-9	Logistic regression analysis	9
8 PMID: 17551822 2008	Cs	Obstetric Information System of Women's Comprehensive Health Center 1986–2000	IPI-1	< 6 6–11 12–17 18–23 24–59 >60	1038 1919 2204 1141 5505 3123	102 156 161 75 400 238	14930	< 37	Cf-1, Cf-2, Cf-4, Cf-8, Cf-9	Logistic regression	9
9 PMID: 19913144 2009	Cs	Israeli Population Registry 2000–2005	IPI-3	0–5, 6–11, 12–23, 24–59 ≥60	36020 77899 124152 158636 44131	2141+407 3479+627 5660+1040 7966+1394 2889+548	440838	< 37 < 33	Cf-1, Cf-3, Cf-9	Multivariate logistic regression	8
10 PMID: 21288503 2011	Cs	Netherlands Obstetric Registration Office 2000.01.01–2007.12.31	IPI-2	0–5 6–11 12–17 18–23 ≥ 24	10211 31614 45148 43093 127814	1236 2425 2876 2805 10532	263142	< 37	Cf-1, Cf-2, Cf-7	Univariate and multivariate logistic regression analysis	8
11 PMID: 24893887 2014	Cs	Ohio Department of Health 2006–2011	IPI-2	<12 12–18 ≥18	9808 48788 396120	1969 4998 30405	45716	< 37	Cf-1, Cf-2, Cf-3, Cf-4, Cf-7, Cf-8, Cf-9	Multiple logistic regression	9
12 PMID: 26311118 2015	Cs	Level III Perinatal Center at Osaka University 2008–2012	IPI-1	<12 ≥12	71 476	19 70	547	< 32w 32 - 36w < 37w	Cf-1 - Cf-9	Multiple logistic regression model	8

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
13 PMID: 26412012 2015	RTCs	REDCap electronic data capture tool is hosted by the University of Utah 2002–2012	IPI-1	≤18	1353	743	35983	22 - 27 28 - 33 34 - 36	/	Multivariate logistic regression analysis	6
14 PMID: 26399217 2015	Cs	Perinatal Information System Database of Uruguayan Montevideo Latin American Center for Perinatology and Women's Reproductive Health 1990–2009	IPI-1	3–11 12–23 24–35 36–47 48–59 60–71 72–83 84–95 96–107 108–119	/	/	894476	< 37	/	Logistic regression analysis	9
15 PMID: 27367283 2016	Cs	Netherlands Obstetric Registration Office 1999–2009	IPI-1	0 - 5 6 –11 12 - 17 18 - 23 24 –59 ≥60	432 1015 1014 796 1399 93	127 178 121 103 236 24	2361	< 37 < 32	Cf-1, Cf-3, Cf-7	Univariate and multivariate conditional logistic regression analysis	8
16 PMID: 27268015 2016	Cs	Kilimanjaro Communication Management Consultants (KCMC) Birth Registration 2000–2010	IPI-1	<24 24 - 36 37–59 ≥60	3309 5774 5509 2442	416 554 489 248	17030	< 37	Cf-1, Cf-2, Cf-4, Cf-9	Multivariate logistic regression analysis Generalized Additive Models (GAMs)	9
17 PMID: 27903080 2016	Cs	Tennessee Birth Statistical Document 2012.01.01–2014.12.31	IPI-1	<6 6–12 12–18 18–60	/	/	101912	< 37 < 34	Cf-1, Cf-2, Cf-3, Cf-4, Cf-5, Cf-8, Cf-9	Multivariate logistic regression model	9

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
18 PMID: 27565663 2016	Cs	Office of Statewide Health Planning and Development (OSHPD) in California 2007–2009	IPI-1	<6 6–17 18–51	36143 213557 395829	1012 3203 5542	645529	< 34	Cf-1, Cf-2, Cf-3, Cf-5, Cf-7	Trend test is Cochran-Armitage two-sided linear trend test.	8
19 PMID: 27405702 2016	Cs	Office of Statewide Health Planning and Development, California 2007–2010	IPI-4	<6 6–11 12–17 18–23 24–29 30–35 36–47 48–59 ≥60	54083 113057 130515 110229 89485 72266 109041 77532 215003	5414 7781 7771 6236 5124 4352 6869 5199 17100	971211	< 37	Cf-1, Cf-2, Cf-4, Cf-5, Cf-8, Cf-9	Logistic regression	9
20 PMID: 28421614 2017	Cs	Xiangya Hospital of Central South University, Second Xiangya Hospital, and Third Xiangya Hospital in Hunan Province, China 2015–2016	IPI-3	7–24 25–48 49–72 73–96 ≥97	300 863 791 632 723	18 78 76 72 11	3309	< 37	Cf-1, Cf-2, Cf-5, Cf-8, Cf-9	Univariate and multivariate logistic regression model	9
21 PMID: 28742654 2017	RTCs	Perinatal Data Registry of British Columbia 2000–2015	IPI-1	0–5 6–11 12–17 18–23 24–59 ≥60	3242 14607 16772 12069 24541 5125	232+227 714+650 707+607 501+505 1024+1305 244+371	38178	< 37	Cf-4, Cf-7, Cf-9	Logistic regression and unconditional (unmatched) logistic regression	8
22 PMID: 30006251 2018	Cs	National Vital Statistics System, National Center for Health Statistics 2016	IPI-1	0 - 5 6 –11 12 - 17 18 - 23 ≥24	2800 7894 11119 7960 16911	137 281 397 293 606	46684	< 28 28 - 32 32 - 37	Cf-1, Cf-2, Cf-3, Cf-4, Cf-5, Cf-8, Cf-9	Multinomial logistic regression	9

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
23 PMID: 29293278 2018	Cs	Guangzhou Perinatal Health Care and Delivery Monitoring System (gphcdss) 2000–2015	IPI-2	<6 6–12 12–18 18–24 24–30 30–36 36–60 60–120 ≥120	9230 28315 28498 23501 21875 18673 45508 49299 2460	642 1471 1343 1005 861 831 2032 2703 222	227352	< 37w	Cf-1, Cf-2, Cf-6	Poisson regression model with robust variance	8
24 PMID: 30383085 2018	Cs	Perinatal Data Registry of British Columbia (BC), Canada 2004–2014	IPI-1	<6 6–11 12–17 18–23 ≥24	8375 25085 33500 26534 55050	616 1568 1804 1452 3299	148 544	< 28 < 37	Cf-1, Cf-4, Cf-5, Cf-7, Cf-8, Cf-9	Logistic regression, robust variance	9
25 PMID: 31701403 2019	Cs	Electronic Medical Records of International Peace Maternity & Child Health Hospital of shanghai (IPMCH) 2014–2016	IPI-1	<12 12–23 24–59 60–119 ≥120 mon	412 1282 3776 3159 923	23 59 176 212 76	9552	< 37	Cf-1, Cf-4, Cf-5, Cf-6	Multivariate logistic regression	9
26 PMID: 31209276 2019	Cs	Maternal and Infant Discharge Data from the Office of Statewide Health Planning and Development (OSHPD), California 2007–2012	IPI-1	< 6 6–11 12–17 18–23 24–29 30–35 36–47 48–59 ≥ 60	White 16875 Black 6612 White 49736 Black 10775 White 66366 Black 9749 White 55756 Black 8321 White 41987 Black 6866 White 30323 Black 5740 White 39359 Black 9378 White 24207 Black 6912 White 61310 Black 22215	White 1533 Black 918 White 2897 Black 1182 White 3344 Black 916 White 2697 Black 754 White 2062 Black 593 White 1643 Black 521 White 2243 Black 912 White 1575 Black 696 White 4600 Black 2645	385919	20 - 36 20 - 23 24 - 31 32 - 36	Cf-1, Cf-2, Cf-4, Cf-5, Cf-6, Cf-7, Cf-9	Multivariate logistic regression	8

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
27 PMID: 32925974 2020	Cs	KCMC Medical Birth Registry 2000–2015	IPI-1	24–59 <24 >59	2805 1902 1049	281 227 130	5946	28 - 32 32 - 37	Cf-1, Cf-2, Cf-4, Cf-5	Multivariate log-binomial regression model	8
28 PMID: 33270912 2020	Cs	Perinatal Data Registry of British Columbia (BC), Canada 2004–2014	IPI-1	<6 6–11 12–17 18–23 ≥24	5469 20065 28594 22643 44380	616 1568 1803 1450 none	121 151	20 - 23 24 - 31 32 - 36	Cf-1, Cf-2, Cf-4, Cf-5, Cf-7	Log-binomial regression	8
29 PMID: 34234517 2021	Cs	Local hospitals in Shaanxi Province 2010–2013	IPI-1	<6 6–11 12–17 18–23 24–59 60–119 ≥120	1375 1242 1120 951 3876 3212 1455	38 31 34 24 91 90 60	13,231	24 - 32 33 - 36	Cf-1, Cf-2, Cf-4, Cf-7, Cf-8, Cf-9	Generalized linear model	9
30 PMID: 34854081 2021	Cs	Birth Cohort from the Center for Data and Knowledge Integration, Brazil National Live Birth Information System 2001–2015	IPI-1	<12 12–24 ≥24	/	/	1764025	< 28 28 - 31 32 - 36	Cf-1, Cf-2, Cf-3, Cf-9	Multivariate logistic regression analysis	8
31 PMID: 35260953 2022	Cs	California Health Care Access and Information Database 2007 - 2012	IPI-2	< 6 6–11 12–17 18–23	16903 40985 48710 38135	1462 2776 2943 2355	144733	<32 32–36 37–38	Cf-1, Cf-2, Cf-7, Cf-9	Multivariate logistic regression	8
32 PMID: 35696164 2022	Cs	Women and Children's Health Information System in Guangdong Province 2014.01.01–2020.12.31	IPI-1	<6 6–11 12–17 18–23 24–29 30–35 ≥36	49485 174675 181172 122866 86842 55364 54988	3135 7801 7116 4678 3421 2219 2519	725392	< 37	Cf-1, Cf-3, Cf-7, Cf-9	Logistic regression model	8

Table 1 (continued)

References / year	Study type	Patient source and sampling time	IPI definition	Exposure factors				Outcome indicators / month	Control confounding factors	Statistical methods	Quality assessment
				Interval / month	Sample size	Preterm birth cases	The total				
33 PMID: 37141470 2023	Cs	Medical College of Wisconsin (MCW) in Milwaukee, Wisconsin 2015–2018	IPI-2	<6 6–11 12–17 ≥18	80 181 223 978	12 8 13 61	1462	< 37	Cf-1, Cf-2, Cf-3, Cf-4, Cf-7, Cf-9	Logistic regression	8
34 PMID: 37099258 2023	Cs	Health Commission of Luzhou City 2015.10.01–2020.10.31	IPI-1	<12 12–23 24–59 ≥60	350 945 2544 3830	82 161 371 680	7669	< 37	Cf-1, Cf-5, Cf-9	Logistic regression model	9

Table 2 NOS scale for quality assessment of the included literature

No	Author	Year	v1	v2	v3	v4	v5	v6	v7	v8	Total score
1	Lorraine V. Klerman	1998	1	1	1	1	1	1	1	0	7
2	BAO-PING ZHU	1999	1	1	1	1	2	1	1	1	9
3	ELENA FUENTES-AFFLICK	2000	1	1	1	1	1	1	1	1	8
4	Gordon C S Smith	2003	1	1	1	1	1	1	1	1	8
5	Mostafa A. Arafa	2004	1	1	1	1	1	1	1	0	7
6	Agustin Conde-Agudelo,	2005	1	1	1	1	2	1	1	1	9
7	Emily A. DeFranco	2007	1	1	1	1	2	1	1	1	9
8	Jose´ G. Cecatti	2008	1	1	1	1	2	1	1	1	9
9	Sorina Grisaru-Granovsky	2009	1	1	1	1	1	1	1	1	8
10	Frederike J. de Weger	2011	1	1	1	1	1	1	1	1	8
11	EA DeFranco	2014	1	1	1	1	2	1	1	1	9
12	Michiko Yamashita	2015	1	1	0	1	2	1	1	1	8
13	LF Wong	2015	1	1	1	1	0	1	1	0	6
14	LE Mignini	2015	1	1	1	1	2	1	1	1	9
15	Bouchra Koullali	2016	1	1	1	1	1	1	1	1	8
16	Michael J. Mahande	2016	1	1	1	1	2	1	1	1	9
17	Shyama Appareddy	2016	1	1	1	1	2	1	1	1	9
18	Flojaune Griffin Cofer	2016	1	1	1	1	1	1	1	1	8
19	BZ Shachar,	2016	1	1	1	1	2	1	1	1	9
20	Chunxiang Qin	2017	1	1	1	1	2	1	1	1	9
21	Gillian E. Hanley	2017	1	1	1	1	1	1	1	1	8
22	Timothy O. Ihongbe	2018	1	1	1	1	2	1	1	1	9
23	Lifang Zhang	2018	1	1	1	1	1	1	1	1	8
24	Laura Schummers	2018	1	1	1	1	2	1	1	1	9
25	Jing Lin	2019	1	1	1	1	2	1	1	1	9
26	Julia A. Lonhart	2019	1	1	1	1	1	1	1	1	8
27	Nathaniel Halide Kalengo	2020	1	1	1	1	2	0	1	1	8
28	Laura Schummers	2020	1	1	1	1	1	1	1	1	8
29	Guoshuai Shi	2021	1	1	1	1	2	1	1	1	9
30	Aline S. Rocha	2021	1	1	1	1	2	0	1	1	8
31	Jayme L Congdon	2022	1	1	1	1	1	1	1	1	8
32	Ting Xu	2022	1	1	1	1	1	1	1	1	8
33	Elizabeth Panther	2023	1	1	1	1	1	1	1	1	8
34	Yan Ma	2023	1	1	1	1	2	1	1	1	9

(1) In the quality assessment process for case-control studies, the table above includes the following criteria: v1 - Is the case definition sufficient? v2 - Representativeness of the case v3 - Selection of controls v4 - Control definition v5 - Comparability (adjustment for confounding factors) v6 - Basis for exposure determination v7 - Whether the case and control exposures were determined using the same method v8 - Non-response rate

(2) In the process of assessing the quality of cohort studies, the table above includes the following criteria: v1 - Representativeness of the exposure cohort v2 - Selection of the non-exposure cohort v3 - Basis for exposure determination v4 - Absence of outcome events in the study population before the study commencement v5 - Comparability (adjustment for confounding factors) v6 - Assessment of outcome events v7 - Adequacy of follow-up for observing outcome events v8 - Completeness of follow-up

come events were observed in the study subjects prior to the commencement of the study. Out of the cohort comparability achieved through design or analysis, 19 articles controlled for age factors and other confounding variables, such as pregnancy and delivery history, and pregnancy complications. Two pieces of literature [38, 40] did not describe the assessment of outcome events and were assigned a score of 0. Adequate follow-up was conducted to

observe the occurrence of outcomes, and all participants completed the follow-up.

Results of meta-analysis

Association of different interpregnancy intervals with preterm birth at <37 weeks

(1) Relationship between different IPI levels

Thirty-four studies investigated the correlation between various IPI levels and preterm birth occurring before 37 weeks of gestation. The analysis included 34 distinct IPI levels, which could be classified into <6 months (up to 5 months), 6–11 months (6 to 11 months), 12–17 months (12 to 17 months), 12–23 months (12 to 23 months), 18–23 months (18 to 23 months), 24–29 months (24 to 29 months), 24–59 months (24 to 59 months), and ≥60 months (60 months and beyond). Additionally, a limited number of studies (only one article) reported alternative IPI levels such as 6–17 months (6 to 17 months), ≥17 months (more than 17 months), and 48–71 months (48 to 71 months). The detailed IPI associations are depicted in Figure 2A.

(2) Network meta-analysis results

The network meta-analysis showed that compared to an IPI of < six months, most other IPI levels appeared to reduce the risk of preterm birth at <37 weeks [IPI of 6–11 months: OR=0.75 (95%CI: 0.74 - 0.77), 12–17 months: OR=0.69 (95%CI: 0.68 - 0.71), 18–23 months: OR=0.64 (95%CI: 0.63 - 0.65), 24–29 months: OR=0.61 (95%CI: 0.59 - 0.63), 30–35 months: OR=0.66 (95%CI: 0.64 - 0.68), 36–47 months: OR=0.72 (95%CI: 0.70 - 0.74), 48–59 months: OR=0.72 (95%CI: 0.70 - 0.74), 60–71 months: OR=0.72 (95%CI: 0.68 - 0.75), 72–83 months: OR=0.75 (95%CI: 0.71 - 0.78), 84–95 months: OR=0.78 (95%CI: 0.75 - 0.82), 96–107 months: OR=0.83 (95%CI: 0.78 - 0.89), 108–119 months: OR=0.87 (95%CI: 0.82 - 0.93), and 120 months: OR=0.94 (95%CI: 0.86 - 1.0)].

At the same time, the risk of preterm birth was similar between some IPI levels and the IPI of < six months [IPI of 12–35 months: OR=1.20 (95%CI: 0.66 - 2.3), 24–47 months: OR=1.30 (95%CI: 0.79 - 2.20), 48–71 months: OR=1.50 (95%CI: 0.91 - 2.60), less than 23 months: OR=0.98 (95%CI: 0.88 - 1.10). In addition, compared to an IPI of < six months, the IPI levels of less than 11 months [OR=1.1 (95%CI: 1.00 - 1.10) and over 96 months [OR=1.7 (95%CI: 1.40 - 2.00)] were associated with a higher risk of preterm birth. These IPI levels were only reported in a very small number of studies, so more studies are needed to validate such results. The detailed results are illustrated in Figure 3A.

(3) Ranking of various IPIs for preterm birth (<37 weeks)

Bayesian network meta-analysis ranks each IPI using posterior probabilities, with higher probabilities indicating better effects. In the primary IPI levels, the posterior probabilities were 0.18 for less than 6 months, 0.45 for 6–11 months, 0.69 for 12–17 months, 0.38 for 12–23 months, 0.85 for 18–23 months, 0.89 for 24–29

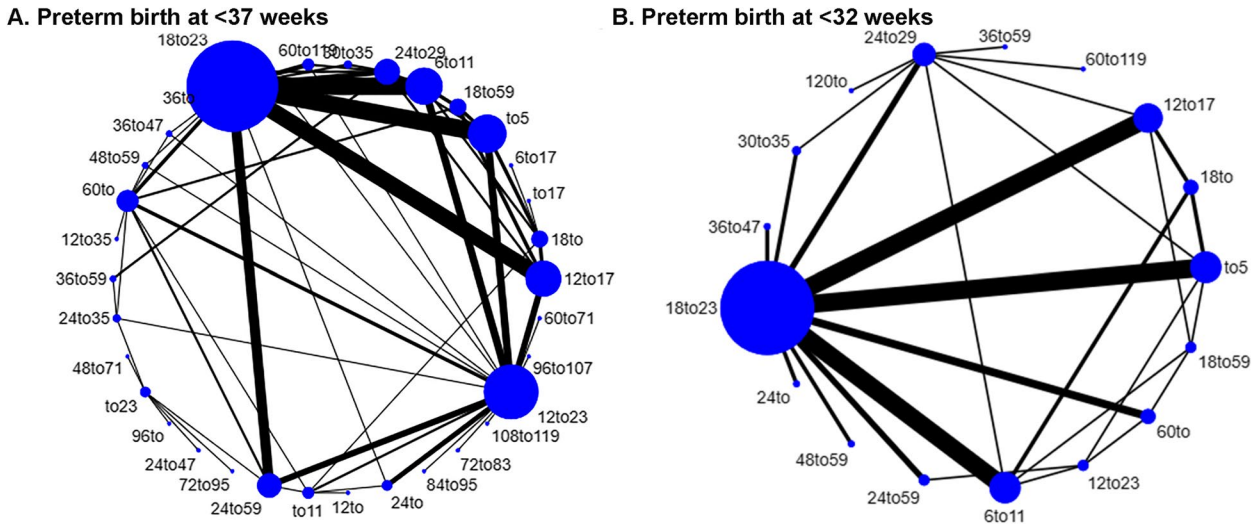

Fig. 2 The association between different IPI levels and preterm birth (Note: (1) **A**-The association between different IPI levels and preterm birth at <37 weeks. **B**-The association between different IPI levels and preterm birth at <32 weeks. (2) The nodes in the above figure represent IPI levels, and the lines between the nodes indicate direct comparisons in the included primary studies; the thicker the line is, the more primary studies it includes; (3) The larger the node is, the more studies it covers)

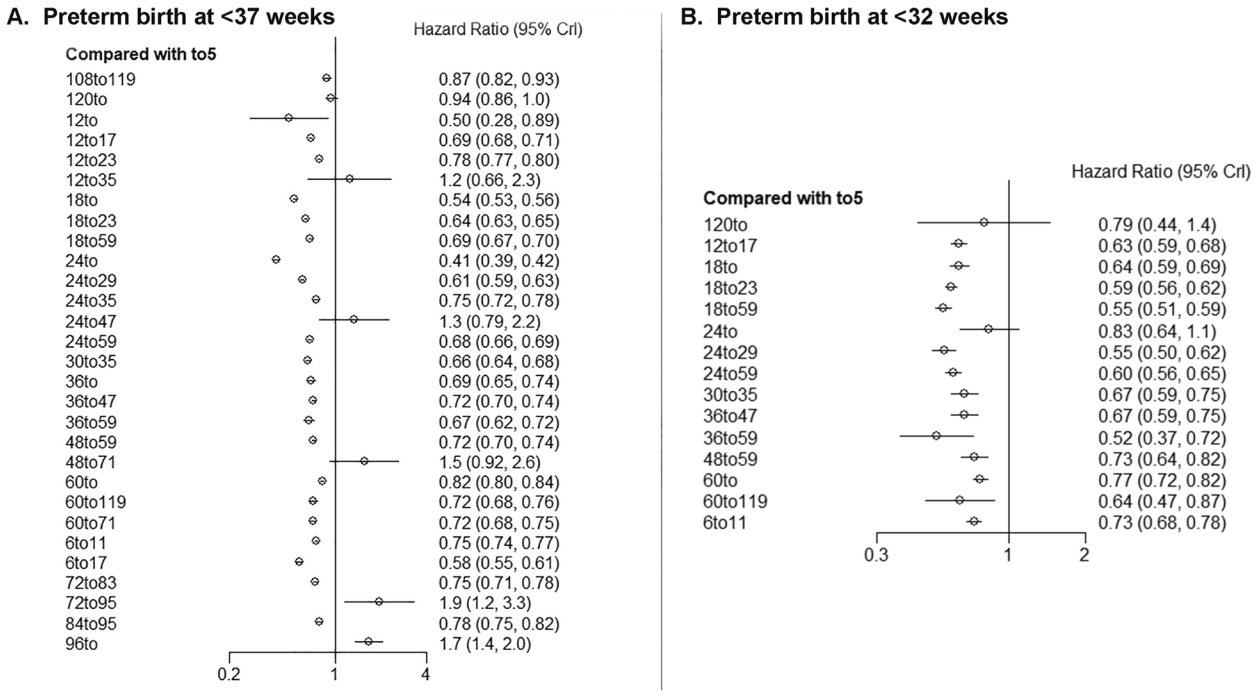

Fig. 3 Forest map for the association between the risk of preterm birth and interpregnancy intervals, (Note: **A** Forest map for the association between the risk of preterm birth (<37 weeks) and interpregnancy intervals, with an interpregnancy interval of <6 months as the reference level; **B** Forest map for the association between the risk of preterm birth (<32 weeks) and interpregnancy intervals, with an interpregnancy interval of <6 months as the reference level)

months, 0.76 for 24–59 months, and 0.32 for 60 months or longer. Our findings suggested that the optimal IPI fell within the range of 24–29 months.

(4) Comparison of preterm birth at different IPI levels

An important advantage of network meta-analysis is that it can provide pair comparison results. The results are illustrated in the league Table S1 (Supplementary Material 3).

Association of different interpregnancy intervals with preterm birth at <32 weeks

(1) Relationship between different IPI levels

Ten studies investigated the correlation between various IPI levels and preterm birth at <32 weeks. These studies encompassed 17 distinct IPI levels, which could be classified into <6 months (up to 5), 6–11 months (6 to 11), 12–17 months (12 to 17), 18–23 months (18 to 23), and 24–29 months (24 to 29). Additionally, a minimal number of studies (only 1 article) reported findings for alternative IPI levels, such as ≥24 months (up to 24), 36–47 months (36 to 47), 48–59 months (48 to 59), 60–119 months (60 to 119), and ≥120 months (up to 120). The detailed associations between IPI and preterm birth are visually presented in Figure 2B.

(2) Network meta-analysis results

The network meta-analysis showed that compared to an IPI of <6 months, almost other IPI levels can reduce the risk of preterm birth (<32 weeks) [IPI of 6–11 months: OR=0.73 (95%CI: 0.68 - 0.78), 12–17 months: OR=0.63 (95%CI: 0.59 - 0.68), 18–23 months: OR=0.59 (95%CI: 0.56 - 0.62), 24–29 months: OR=0.55 (95%CI: 0.50 - 0.62), 30–35 months: OR=0.67 (95%CI: 0.59 - 0.75), 36–47 months: OR=0.67 (95%CI: 0.59 - 0.75), 48–59 months: OR=0.73 (95%CI: 0.64 - 0.82), greater than 60 months: OR=0.77 (95%CI: 0.72 - 0.82)].

Meanwhile, the risk of preterm birth was similar between some IPI levels and the IPI of < six months[IPI of > 24 months: OR=0.83 (95%CI: 0.64 - 1.1), IPI of > 120 months: OR=0.79 (95%CI: 0.44 - 1.4). These IPI levels were only reported in a very small number of studies, so more studies are needed to validate such results. The detailed results are illustrated in Figure 3B.

(3) Ranking of various IPIs for preterm birth (<32 weeks)

Bayesian network meta-analysis ranks each IPI using posterior probabilities. The higher the probability, the more favorable the effect. In terms of main IPI levels, the posterior probabilities were 0.02 for less than 6 months, 0.29 for 6–11 months, 0.57 for 12–17 months, 0.77 for 18–23 months, 0.89 for 24–29 months, 0.46 for 30–35 months, 0.88 for 36–59 months, 0.57 for 60–119 months, and 0.30 for 120 months or longer. Our analysis suggested that the optimal IPI fell within the range of 24 to 29 months.

(4) Comparison of preterm birth at different IPI levels

An important advantage of network meta-analysis is that it can provide pair comparison results. The results are detailed in the league Table S1 (Supplementary Material 3).

Discussion

It was discovered that the primary IPI levels were <6 months (0 to 5), 6–11 months (6 to 11), 12–17 months (12 to 17), 12–23 months (12 to 23), 18–23 months (18 to 23), 24–29 months (24 to 29), 24–59 months (24 to 59), and ≥60 months (60 to). This study revealed that compared to an IPI of less than 5 months, the IPI of 24–29 months was associated with a lower risk of preterm birth at 32 and 37 weeks of gestation.

Several previous studies have examined the relationship between IPI and preterm birth risk.Wanze Ni, Maryam Asgharnia, and Naoko Kozuk [46–48] posited that the risk of preterm birth in women with an IPI of 18–23 months is low, suggesting potential benefits of this IPI range. Hanna Mühlrad [49] contends that an IPI of less than 24–29 months correlates with a decrease in maternal morbidity incidence but does not impact the neonatal morbidity rate. Conversely, an IPI exceeding 24–29 months is linked to an increased risk of maternal and neonatal morbidity. Due to variations in reference levels of IPI across existing studies, we employed a traditional meta-analysis approach to investigate the preterm birth risk associated with different IPIs. Subsequently, we utilized the Bayesian network meta-analysis method to further explore this association.

Controllable factors contributing to the risk of preterm birth [50] encompass lifestyle and behavioral adjustments, such as ceasing smoking, refraining from alcohol and drug use, and effectively managing stress. Adequate prenatal care and the proper management of health conditions, such as hypertension and diabetes, are crucial during pregnancy. Nutritional status plays a significant role; addressing inadequate or excessive weight before pregnancy through diet and exercise is recommended. Furthermore, in terms of the work environment, avoiding extended working hours and prolonged standing is beneficial. Additionally, minimizing exposure to environmental pollutants is advised. Our study reveals that IPI is a modifiable risk factor for preterm birth. Subsequently, we strive to incorporate more controllable factors into our investigation, exploring the intricate relationship between IPIs and the occurrence of preterm birth.

Advanced maternal age and IVF pregnancies have been linked to heightened risks of preterm birth (PTB) due to various factors, including biological changes, increased comorbidities, and complications related to pregnancy. Advanced maternal age, typically defined as 35 years or older, is recognized for raising the risk of PTB, whereas IVF pregnancies, particularly those that involve multiple gestations or ovarian hyperstimulation, may lead to both iatrogenic and spontaneous PTB [51]. These insights indicate that delaying a second pregnancy in these circumstances may be intricate, as the potential advantages of allowing maternal recovery and lowering preterm risk must be balanced against the declining ovarian reserve and rising obstetric complications tied to postponed pregnancies. Future investigations should examine whether a customized approach to interpregnancy intervals (IPIs) can reduce these risks, considering the distinct challenges associated with advanced maternal age and IVF.

In addition to preterm birth, IPI was also reported to be associated with preeclampsia and low birth weight infants [14, 52]. Notably, a relatively short IPI (<2 years) did not increase the risk of recurrent preeclampsia, while longer intervals (>4 years) appeared to elevate the risk. Both short intervals (<24 months) and long intervals (37–59 months or longer) are linked to an increased risk of preterm birth and low birth weight, while short intervals are also associated with a higher risk of perinatal death. A moderate IPI is optimal for minimizing adverse pregnancy and childbirth outcomes. Very short intervals (less than 6–12 months) are linked to an increased risk of preterm birth and other neonatal complications, particularly in low- and middle-income countries. On the other hand, very long intervals (over 60 months) also pose risks, including a heightened likelihood of maternal complications. Moderate intervals, typically between 18–23 months, seem to strike a balance, minimizing risks for both mother and child. However, it is crucial to note that these recommendations may vary based on individual circumstances, including the health of pregnant women, previous birth outcomes, and socio-economic factors.

Recent studies have emphasized the intricate nature of preterm birth, suggesting a functional taxonomy that classifies preterm birth into separate phenotypes

according to etiological factors [53]. This structure underscores the necessity for a more refined methodology, given that various preterm birth phenotypes may exhibit distinct correlations with risk factors. While our existing data do not permit phenotype-specific analyses, subsequent research should incorporate these classifications to enhance our comprehension of how diverse IPIs affect particular preterm birth phenotypes.

Limitations of this study

This study also has some limitations. First, IPI is a potentially modifiable risk factor for adverse birth outcomes. However, outcomes may be varied among different groups, leading to biased results. These broader differences can be attributed to variances in healthcare, industrial development, and the characteristics of pregnant women. Therefore, conducting studies in different locations contributes to a comprehensive understanding of how IPIs affect adverse birth outcomes. Second, IPI is linked to numerous potential confounding factors, including the mother's age, race, and socio-economic status. Most studies on IPIs and adverse birth outcomes are traditional retrospective cohort studies, without adjustments for certain unmeasured confounding factors. Failure to account for these factors may lead to an underestimation or overestimation of the association between IPIs and corresponding birth outcomes. The extent to which this association can be attributed to unmeasured confounding factors remains unclear.

The significance of this study on the prevention of preterm birth

Based on the comprehensive analysis and summary of the evidence of various IPI levels, this study sheds light on the impact of long and short IPI levels on the risk of preterm birth. Our findings indicate that the optimal IPI falls within the range of 24–29 months. This information serves as a valuable reference for clinical obstetrics and gynecology practice.

Abbreviations

IPIs	Interpregnancy intervals
WHO	World Health Organization
OR	Odds ratio
RR	Relative risk
HR	Hazard ratio
DIC	Deviance Information Criterion
SUCRA	Surface Under the Cumulative Ranking
CCS	Case-control studies
Cf	Confounding factors

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-07259-y.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

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Not applicable.

PROSPERO platform

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Authors' contributions

All authors contributed to the study conception and design. Writing - original draft preparation: [XW, PZ, SW]; Writing - review and editing: [XW, WL, JZ]; Conceptualization: XW, WL, JZ]; Methodology: [XW, WL, JZ]; Formal analysis and investigation: [XW, SW]; Funding acquisition: [WL, JZ]; Resources: [XW, YW, PZ]; Supervision: [JZ], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

Declarations

Ethics approval and consent to participate

All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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