

A systematic review of prediction models for spontaneous preterm birth in singleton asymptomatic pregnant women with risk factors

Chunmei Yan^{a,1}, Qiuyu Yang^{b,c,1}, Richeng Li^{a,*}, Aijun Yang^d, Yu Fu^e, Jieneng Wang^f, Ying Li^{b,c}, Qianji Cheng^{b,c}, Shasha Hu^g

^a Department of Gynaecology and Obstetrics, Hospital of Lanzhou Jiaotong University, Lanzhou, China

^b Department of Social Medicine and Health Management, School of Public Health, Lanzhou University, Lanzhou, China

^c Evidence Based Social Science Research Center, School of Public Health, Lanzhou University, Lanzhou, China

^d Department of Gynaecology and Obstetrics, Gansu Provincial Maternity and Child-Care Hospital, Lanzhou, China

^e Department of Prenatal Diagnosis Center, Gansu Provincial Maternity and Child-Care Hospital, Lanzhou, China

^f Department of Cardiovascular Surgery, First Hospital of Lanzhou University, Lanzhou, China

^g Department of Obstetrics and Gynecology, First Hospital of Lanzhou University, Lanzhou, China

ARTICLE INFO

Keywords:

Prediction model
Spontaneous preterm birth
Singleton pregnancy
Risk factor
Systematic review

ABSTRACT

Backgrounds: Spontaneous preterm birth (SPB) is a global problem. Early screening, identification, and prevention in asymptomatic pregnant women with risk factors for preterm birth can help reduce the incidence and mortality of preterm births. Therefore, this study systematically reviewed prediction models for spontaneous preterm birth, summarised the model characteristics, and appraised their quality to identify the best-performing prediction model for clinical decision-making.

Methods: PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure, China Biology Medicine disc, VIP Database, and Wanfang Data were searched up to September 27, 2021. Prediction models for spontaneous preterm births in singleton asymptomatic pregnant women with risk factors were eligible for inclusion. Six independent reviewers selected the eligible studies and extracted data from the prediction models. The findings were summarised using descriptive statistics and visual plots.

Results: Twelve studies with twelve developmental models were included. Discriminative performance was reported in 11 studies, with an Area Under the Curve (AUC) ranging from 0.75 to 0.95. The AUCs of the seven models were greater than 0.85. Cervical length (CL) is the most commonly used predictor of spontaneous preterm birth. A total of 91.7% of the studies had a high risk of bias in the analysis domain, mainly because of the small sample size and lack of adjustment for overfitting.

Conclusion: The accuracy of the models for spontaneous preterm births in singleton asymptomatic women with risk factors was good. However, these models are not widely used in clinical practice because they lack replicability and transparency. Future studies should transparently report methodological details and consider more meaningful predictors with new progress in research on preterm birth.

* Corresponding author. Hospital of Lanzhou Jiaotong University, Lanzhou, 730070, China.

E-mail address: lricheng09@163.com (R. Li).

¹ Chunmei Yan and Qiuyu Yang contributed equally to this work.

<https://doi.org/10.1016/j.heliyon.2023.e20099>

Received 10 July 2023; Received in revised form 11 September 2023; Accepted 12 September 2023

Available online 13 September 2023

2405-8440/© 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

The World Health Organization defines preterm births as babies born alive before 37 completed gestational weeks [1], including spontaneous and iatrogenic preterm births. Across countries, the estimated preterm birth rate ranged from 4% to 10.6% in 2020, with an estimated 13.4 million live preterm births [1]. Approximately two-thirds of all preterm births occur spontaneous preterm birth [2]. Preterm birth complications are the leading causes of death in children under 5 years of age and were responsible for approximately 900 000 babies dying in 2019 [1,3]. However, many survivors are at greater risk of a range of long-term morbidities or lifetime disabilities, including chronic kidney disease, hypertension, diabetes, ischaemic heart disease, lower sleep quality, learning disabilities, and visual and hearing problems [1,4–8]. In summary, preterm births, particularly spontaneous births, are a global problem. Therefore, developing and implementing key interventions to prevent spontaneous preterm birth is essential.

More attention should be paid to asymptomatic women with risk factors for preterm birth. Early screening, identification, and prevention in asymptomatic pregnant women with risk factors for preterm birth can help reduce the incidence and mortality of preterm births. Many studies have shown that implementing adequate programs to prevent preterm birth is desirable [9–12]. This prediction model is a promising approach for identifying risk factors and estimating the probability of preterm birth. Therefore, this systematic review aimed to review existing prediction models for spontaneous preterm birth, summarise model characteristics, appraise their quality, and identify the best-performing prediction model for clinical decision-making.

2. Methods

Our systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. The study protocol was registered in PROSPERO (CRD42022329721).

2.1. Search strategy

We systematically searched seven databases, including PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure, VIP Database, China Biology Medicine Disk, and Wanfang Data, for articles published up to September 27, 2021. The search strategy is presented in [Table S1](#). In addition, we manually searched for the references of eligible studies and relevant systematic reviews.

2.2. Eligibility criteria

Studies were eligible for this systematic review based on the following inclusion criteria: (1) developing and/or validating a prediction model for spontaneous preterm birth; (2) studies focused on singleton asymptomatic pregnant women with risk factors for preterm birth who did not have symptoms of threatened preterm labour and abortion but had at least one risk factor for spontaneous preterm birth, such as previous spontaneous preterm birth, previous late miscarriage, previous cervical surgery, cervical length measuring <25 mm in the current pregnancy, previous uterine surgery, maternal age >35 years, and assisted reproductive technology (ART) in the current pregnancy; and (3) the prediction model included 2 or more predictors. Reviews, conference abstracts, and letters were also excluded.

2.3. Study selection and data extraction

The six reviewers (YCM, YQY, LRC, LY, CQJ, and YAJ) were divided into three groups, each responsible for screening 1/3 of the literature. Each group independently screened the titles and abstracts of the identified articles and selected the articles for full-text review. Disagreements were resolved by a third reviewer (HSS). Each group independently extracted data from eligible articles based on a critical appraisal and data extraction checklist for systematic reviews of prediction modelling studies (CHARMS) checklist [14]. From each eligible study, the first author, publication year, country, data source, study design, data collection period, age, number of participants, number of events, risk factors for spontaneous preterm birth, number of predictors retained in the final model, the definition of spontaneous preterm birth, modelling method, handling of continuous predictors and missing data, selection of predictors, and model performance measures were extracted.

2.4. Assessment of risk of bias

Six reviewers (YCM, YQY, LY, CQJ, FY, and WJN) were divided into three groups, with each group responsible for 1/3 of the included studies. Each group was independently assessed for risk of bias in the included studies using the PROBAST tool [15]. Disagreements were resolved by a third reviewer (HSS). The PROBAST tool consists of 20 signalling questions across four domains: participants, predictors, outcomes, and analysis. Signalling questions were answered with yes, probably yes, no, probably no, or no information. The risk of bias in each domain was rated as low, high, or unclear risk of bias. The overall assessment of the risk of bias was rated as low risk if all domains were judged to be low risk, high risk if at least one domain was judged to be high risk, unclear risk if at least one domain was judged to be at unclear risk, and all other domains were judged to be low risk.

2.5. Data synthesis

The results were summarised and reported using descriptive statistics. If more than one model for the same predicted outcome was used in a study, we chose the maximum C-statistic or AUC (used to describe the discriminatory ability of the model) to represent that outcome. If more than one predicted outcome (e.g., spontaneous delivery at <37 and < 34 weeks) was included in the study, we presented the results for each outcome separately. Meta-analyses were not performed as the included studies were heterogeneous.

3. Results

The search identified 10299 studies from seven databases. A total of 8573 records were excluded after title and abstract screening, and 93 studies were eligible for full-text review. Based on the selection criteria, 12 articles on 12 developmental models were included [16–27]. A flowchart of the study selection process is shown in Fig. 1. A list of excluded studies is provided in Table S2.

3.1. Characteristics of included studies

The characteristics of the included studies are summarised in Table 1. The 12 included studies were published between 2003 and 2021, mainly in Europe and East Asia. More than half of the studies ($n = 9$) were retrospective cohort studies, and three prospective cohort studies were included. The risk factors for spontaneous preterm birth in asymptomatic pregnant women in the included studies are shown in Table 1. The most common risk factors were previous miscarriage, preterm birth, and a short cervix. Seven studies [19,21,22,24–27] constructed prediction models for specific pregnant women (e.g., cervical insufficiency, short cervix, history of cervical conization, and cervical cerclage).

3.2. Characteristics of prediction models

Table 2 summarises the modelling methods and model performance. Most models ($n = 9$) were developed using a logistic regression analysis. The area under the curve (AUC) of the prediction model is shown in Fig. 2. Of the 12 models, 11 had AUC ranging from 0.75 to 0.95. Moreover, five studies used the Hosmer-Lemeshow test to report calibration, and one study used a calibration scatter plot. The AUCs of the seven prediction models were greater than 0.85 [17–21,24,26], and the sensitivity and specificity of the five models were good. In addition, only seven models provided calculation formulae. Of these models with an AUC >0.85, only five provided full formulas to calculate the probability of spontaneous preterm birth.

Table 3 lists the predictors included in the models. The number of predictors in each model varied from 2 to 8. While some common variables were included in most studies, such as cervical length, history of preterm birth, and cervical dilatation, many other variables were included in only one or a few studies. Cervical length was the most consistent predictor of spontaneous preterm birth.

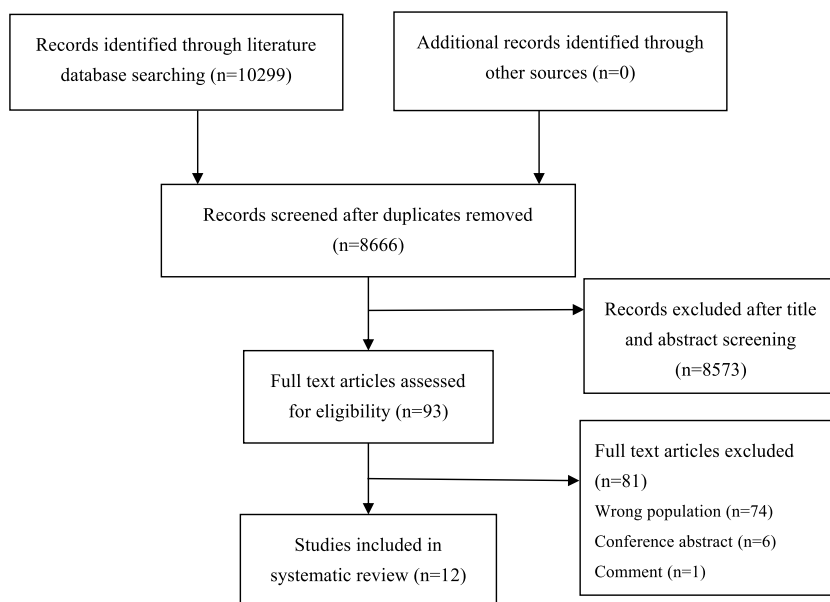


Fig. 1. Selection of studies for inclusion in review.

Table 1
Characteristics of included studies (n = 12).

Study	Country	Multicenter	Recruitment dates	Study design	Sample size (Total/case)	Age (Mean years)	High-risk factor for spontaneous preterm birth	Predicted outcome (Weeks)
Gioan, 2018 ¹⁶	France	Yes	Jul 2007 to Apr 2012	Prospective cohort	764/220	29.4	Short cervix (a cervical length <25 mm measured by transvaginal ultrasound) and/or an obstetric history: history of preterm birth and/or late miscarriage	<37
Fuchs, 2012 ¹⁷	France	No	Jan 1994 to Dec 2006	Retrospective cohort	85/37	31.5	spontaneous expulsion of a pregnancy ≥ 14 and < 22 weeks	<32
Kuhr, 2016 ¹⁸	UK	Yes	Oct 2010 to Jul 2014	Prospective cohort	624/94	33	Previous second-trimester pregnancy losses, previous preterm births, in utero exposure to diethylstilbestrol (e.g. when the pregnant women' mother was pregnant with them) or surgery for a uterine malformation	<37
Lee, 2016 ¹⁹	Korea	No	Sep 2004 to Apr 2014	Retrospective cohort	57/37	31.7	Previous spontaneous preterm birth or previous preterm prelabor rupture of membranes <37 weeks, previous late miscarriage (16–23 + 6 weeks), previous cervical surgery or cervical length measuring <25 mm in the current pregnancy	<34
Odibo, 2003 ²⁰	USA	No	1996 to 2002	Retrospective cohort	256/51	30.5	Cervical insufficiency	<32
Park, 2020 ²¹	Korea	No	Sep 2004 to Feb 2015	Retrospective cohort	80/39	31.6	One or more spontaneous preterm delivery (14–34 weeks), two or more dilatation and curettages for voluntary first-trimester abortion, Mullerian anomaly, cone biopsy, and diethylstilbestrol exposure	<32
Rawashdeh, 2020 ²²	Australia	No	Jan 2003 to Dec 2014	Retrospective cohort	274/26	15–51 ^a	Premature cervical dilation or a short cervix (≤ 25 mm)	<37
Vogel, 2007 ²³	Denmark	No	Over a 2-year period ^b	Retrospective cohort	62/20	24	Cervical cerclage	<35
Yoo, 2017 ²⁴	Korea	No	Sep 2009 to Dec 2015	Retrospective cohort	62/25	32.2	At least one prior spontaneous birth (16–30 weeks), short cervical length (≤ 25 mm)	<32
Boelig, 2020 ²⁵	USA	Yes	Jan 2012 to Dec 2018	Retrospective cohort	108/29	29.3	Cervical insufficiency or a short cervix (≤ 25 mm)	<34
Lou, 2018 ²⁶	China	No	Jan 2008 to Mar 2018	Retrospective cohort	118/44	30.3	Short cervix (≤ 20 mm)	≥ 28 and <37
Anumba, 2021 ²⁷	UK	No	Jan 2014 to Aug 2016	Prospective cohort	365/43	30.1	Cervical conization	<37
							History of sPTB	<37

a = Values were given as the ranges; b = Not reported recruitment dates; sPTB = spontaneous preterm birth; mm = millimeter.

3.3. Risk of bias assessment

Eleven studies had a high risk of bias. Details of the risk of bias assessment are shown in Fig. 3. All studies were at low risk of bias for the outcome and participant domains, 25% of studies (n = 4) were at low risk of bias for the predictor domain, and 75% of studies (n = 8) had an unclear risk of bias because there was no information on whether predictors were assessed without knowledge of the outcome. A total of 91.7% of the studies (n = 11) had a high risk of bias in the analysis domain, mainly because of the small sample size with events per predictor and the lack of adjustment for overfitting.

4. Discussion

We systematically reviewed prediction models for spontaneous preterm births in singleton asymptomatic pregnant women with risk factors for preterm births. Twelve studies were included in the systematic review. The AUC of the models ranged from 0.75 to 0.95. The most common predictor for most prediction models was cervical length. Overall, most studies had a high risk of bias, with the analysis domain being most commonly rated as having a high risk of bias.

A clinical prediction model was originally constructed to predict diseases using a small number of predictors that are easy to collect and inexpensive to detect [28,29]. In this systematic review, we found that cervical length was the most commonly used predictor was

Table 2
Modelling method and model performance of prediction models.

Study	Modelling method	Full model presented	Discrimination (AUC)	Calibration	Classification metrics
Gioan, 2018 ¹⁶	Logistic regression	Yes	0.77 (95% CI 0.72–0.81)	Good calibration	Se: 0.74 (95% CI 0.63–0.84); Sp: 0.73 (95% CI 0.67–0.78); PLR: 2.7 (95% CI 2.20–3.50); NLR: 0.35 (95% CI 0.20–0.50); PPV: 0.45 (95% CI 0.36–0.53); NPV: 0.91 (95% CI 0.86–0.94)
Fuchs, 2012 ¹⁷	Logistic regression	Yes	0.88 (95% CI 0.81–0.95)	NR	NR
Kuhr, 2016 ¹⁸	Parametric survival model	Yes	<37weeks: 0.78; <34weeks: 0.83; <30weeks: 0.88	NR	<37weeks: Se:0.78 (95% CI 0.68–0.85); Sp: 0.64 (95% CI 0.59–0.68); PLR: 2.20 (95% CI 1.80–2.50); NLR: 0.40 (95% CI 0.20–0.50); PPV: 0.28 (95% CI 0.22–0.33); NPV: 0.94 (95% CI 0.91–0.96) <34weeks: Se: 0.78 (95% CI 0.65–0.89); Sp: 0.80 (95% CI 0.76–0.83); PLR: 3.50 (95% CI 2.90–4.30); NLR: 0.30 (95% CI 0.20–0.50); PPV: 0.24 (95% CI 0.17–0.31); NPV: 0.97 (95% CI 0.96–0.99) <30weeks: Se: 0.63 (95% CI 0.42–0.81); Sp: 0.90 (95% CI 0.88–0.93); PLR: 6.60 (95% CI 4.50–9.70); NLR: 0.40 (95% CI 0.30–0.70); PPV: 0.23 (95% CI 0.14–0.34); NPV: 0.98 (95% CI 0.97–0.99)
Lee, 2016 ¹⁹	Logistic regression	No	0.95 (95% CI 0.89–1.00)	0.37*	Se: 0.92 (95% CI 0.78–0.98); Sp: 0.90 (95% CI 0.68–0.99); PLR: 9.19 (95% CI 2.50–34.30); NLR: 0.09 (95% CI 0.03–0.30)
Odibo, 2003 ²⁰	Logistic regression	No	0.91	NR	Se: 0.80; Sp: 0.96; PPV: 0.82; NPV: 0.95
Park, 2020 ²¹	Logistic regression	Yes	0.90 (95% CI 0.83–0.97)	0.28*	Se: 0.89 (95% CI 0.76–0.97); Sp: 0.80 (95% CI 0.64–0.91); PLR: 4.50 (95% CI 2.40–8.40); PLR: 0.10 (95% CI 0.10–0.30)
Rawashdeh, 2020 ²²	LWL, GP, K*, LR, RF	No	RF ^a : 0.75	Calibration scatter plot	NR
Vogel, 2007 ²³	Generalized linear	No	NR	NR	Se: 0.69; Sp: 0.95; PPV: 0.82; NPV: 0.91; PLR: 14.2
Yoo, 2017 ²⁴	Logistic regression	Yes	0.91 (95%CI 0.83–0.99)	0.31*	Se: 0.96 (95% CI 0.79–0.99); Sp: 0.76 (95% CI 0.59–0.88); PLR: 3.95 (95% CI 3.20–4.80); PLR: 0.05 (95% CI 0.01–0.40)
Boelig, 2020 ²⁵	Logistic regression	Yes	0.76 (95%CI 0.67–0.86)	NR	Se: 0.79; Sp: 0.75; PPV: 0.54; NPV: 0.91
Lou, 2018 ²⁶	Logistic regression	Yes	Training set: 0.93 (95%CI 0.87–0.99) Testing set: 0.94 (95% CI 0.86–1.00)	0.993*	Training set: Se: 0.92; Sp: 0.82; PPV: 0.69; NPV: 0.96 Testing set: Se: 0.93; Sp: 0.90; PPV: 0.81; NPV: 0.96
Anumba, 2021 ²⁷	Logistic regression	No	0.80 (95% CI 0.72–0.87)	NR	Se: 0.80 (95% CI 0.44–0.98); Sp: 0.85 (95% CI 0.77–0.92)

AUC=Area Under Curve, NR=Not report; RF=Random forest; Se = sensitivity; Sp = specificity; PLR = positive likelihood ratio; NLR = negative likelihood ratio; PPV = positive predictive value; NPV = negative predictive value; 95% CI = 95% confidence interval; a = correlation coefficient, * = p-value of Hosmer-Lemeshow goodness of fit test.

cervical length. Other common predictors were a history of preterm birth and cervical dilatation. These predictors are easily available and do not require invasive laboratory tests. However, with the development of the economy and the advancement of technology, the costs of data collection and storage have been greatly reduced, and data analysis technology is improving. Therefore, clinical prediction models should also break through the inherent concept by applying larger amounts of data to serve doctors, patients, and medical decision-makers with more accurate results [29]. The aetiopathogenesis of spontaneous preterm birth is multifactorial; therefore, holistic generalized prediction models should be constructed to cover all or most of the etiologic mechanisms of preterm birth [2,30]. In our study, some risk factors associated with preterm birth were not included in the final model, such as ART [31–34], gestational diabetes mellitus [35,36], gestational hypertension [37,38]. Studies have shown that pregnant women conceived through ART are more likely to have spontaneous preterm birth, which may be related to their older age, endometriosis, polycystic ovary syndrome or other unexplained infertility [39,40]. Previous studies have also indicated that pregnant women with gestational diabetes mellitus have a direct effect on preterm birth, possibly through hyperglycemia-induced endothelial dysfunction, oxidative stress, and impaired vasodilation [36,41]. Studies have shown that the pathophysiological mechanisms linking pregnancy-induced hypertension to preterm birth include inflammation, oxidative stress and endocrine disruption [42–44].

Researchers often use automatic screening software (such as logistic regression and Cox regression in IBM SPSS) to determine whether the factors should be included [29]. They performed a univariate analysis of every variable individually or a multivariate analysis based on the results of the univariate analysis. Factors with *P* values less than 0.1 will be included in the model (here, the *P*

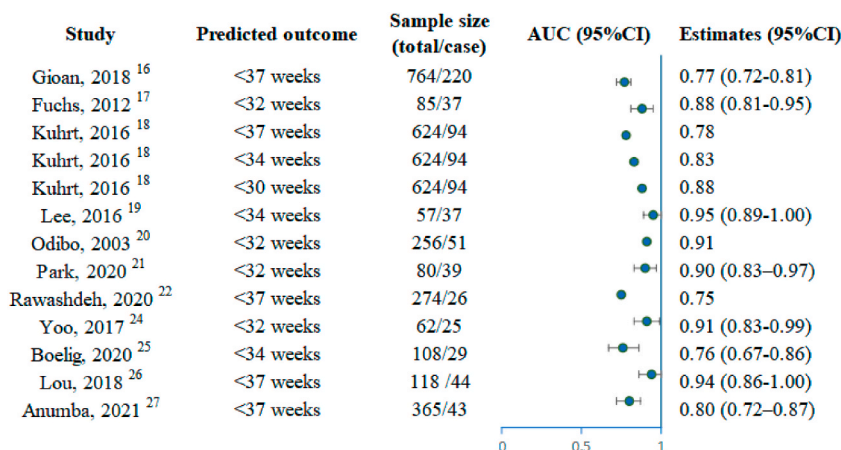


Fig. 2. AUCs of prediction models for spontaneous preterm birth.

Table 3

Predictors included in the prediction models for spontaneous preterm birth.

Predictors	Study ^a										
	Gioan, 2018 ¹⁶	Fuchs, 2012 ¹⁷	Kuhr, 2016 ¹⁸	Lee, 2016 ¹⁹	Odibo, 2003 ²⁰	Park, 2020 ²¹	Vogel, 2007 ²³	Yoo, 2017 ²⁴	Boelig, 2020 ²⁵	Lou, 2018 ²⁶	Anumba, 2021 ²⁷
Gestational age	✓								✓		
Maternal age				✓							✓
Smoking during pregnancy	✓										
History of cone biopsy					✓						
History of preterm birth	✓		✓								✓
History of miscarriage	✓	✓									
Daily walk time	✓										
Cervical dilatation		✓		✓		✓		✓			
Cervical length	✓		✓		✓		✓		✓		✓
Membranes bulging into the vagina		✓									
Infection ^b		✓									
Emergency cerclage					✓						
AF MMP-1				✓							
AF MMP-8				✓							
Plasma IL-6						✓					
C3a levels						✓					
TNF-α							✓				
sIL-6Rα							✓				
Bacterial vaginosis	✓										
Use of corticosteroid								✓			
Cervicovaginal fluid VDBP								✓			
fFN concentration			✓								✓
PROM	✓		✓								
Cervical ESI											✓

a = one of the included studies (Rawashdeh, 2020) did not report predictor; b = WBC ≥ 13600 × 10⁶ L⁻¹ and/or C-reactive protein >15 mg L⁻¹; ✓ = variable included in each model; AF = amniotic fluid; MMP = matrix metalloproteinase; IL-6 = interleukin-6; TNF-α = tumor necrosis factor-alpha; sIL-6Rα = soluble IL-6 receptor alpha; VDBP = vitamin D binding protein; fFN = fetal fibronectin; PROM = premature rupture of membranes; ESI = electrical impedance spectroscopy

value could be less than 0.05 or 0.2). Notably, this statistical screening method may sometimes exclude factors associated with preterm birth as disqualifying factors. Other factors screening methods included the Akaike information criterion [30] and clinical experience [29]. Choosing a better method for identifying risk factors is important for prediction models, and, importantly, there are no standard rules. Therefore, for future studies, we recommend a combination of statistical analysis and a clinical perspective to determine which factors should be considered.

Domain		Author (year)											
		Anumba, 2021	Fuchs, 2012	Gioan, 2018	Kuhr, 2016	Lee, 2016	Odibo, 2003	Park, 2020	Rawashdeh, 2020	Vogel, 2007	Yoo, 2017	Boelig, 2020	Lou, 2018
Participants	Item 1	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 2	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Predictors	Item 1	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 2	Green	Yellow	Green	Green	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
	Item 3	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Outcome	Item 1	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 2	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 3	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 4	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 5	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 6	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
Analysis	Item 1	Green	Red	Green	Green	Red	Red	Red	Red	Red	Red	Red	Red
	Item 2	Green	Yellow	Yellow	Green	Red	Yellow	Yellow	Yellow	Yellow	Green	Green	Red
	Item 3	Green	Green	Red	Green	Green	Green	Green	Red	Green	Green	Green	Green
	Item 4	Green	Green	Green	Green	Green	Green	Green	Green	Green	Yellow	Yellow	Green
	Item 5	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Red
	Item 6	Green	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow	Yellow
	Item 7	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Item 8	Green	Red	Green	Green	Red	Yellow	Red	Yellow	Yellow	Yellow	Yellow	Red
	Item 9	Yellow	Green	Yellow	Yellow	Green	Green	Green	Red	Green	Green	Green	Green

	Yes/probably yes
	No/probably no
	No information

Fig. 3. Risk of bias assessment of included studies.

Currently, few models of spontaneous preterm birth have been applied in clinical practice [45,46]. This may be attributed to multiple reasons. First, the reporting and methodological quality of the prediction model was unclear [47]. For example, in our review, approximately half of the models did not provide calculation formulae, indicating that their clinical use would not be possible. Second, clinicians may question the accuracy of the models because they may not include well-known predictors [45]. Third, these models are too complex for daily use in clinical settings. Another important reason is that many models have not been validated in other populations, making their generalisability unclear [47]. In our review, only the results of one study by Kurht et al. [18] were translated into an application (QUIPP, Quantitative Instrument for the Prediction of Preterm birth) and applied in clinical practice to help clinicians make clinical decisions. However, this application lacks transparency in certain aspects related to model development and proper validation [48], which precludes transportation to settings with other treatment policies or other countries.

No study had an overall low risk of bias, according to the PROBAST, reflecting some methodological shortcomings in the included studies. The analysis domain was most commonly rated as having a high risk of bias in the included studies, mainly because of the small sample size with events per predictor and the lack of adjustment for overfitting. The limited effective sample sizes likely led to overfitting and underfitting of the model, which yielded biased estimates of the apparent model predictive performance [15].

This systematic review has several strengths. We conducted a comprehensive search, independently screened the literature by six reviewers, and extracted data on the key characteristics of prediction models for spontaneous preterm birth, including the population, predictors, and predicted outcomes. Additionally, we assessed the quality of the included studies using the PROBAST tool. However, this study had several limitations. One limitation of our study is that we did not perform a meta-analysis because the included studies were heterogeneous. The main sources of heterogeneity may include differences in clinical settings, patient characteristics, and time points used to estimate the risk of spontaneous preterm birth across studies. Additionally, we only included studies that focused on singleton pregnancies with risk factors, but the results from studies on multiple pregnancies or pregnant women without risk factors may be informative. Future studies should explore whether there are significant differences in the results of preterm birth prediction models between pregnant women with and without risk factors.

5. Conclusion

In conclusion, we included 12 prediction models for spontaneous preterm births in singleton asymptomatic women with risk factors and found that the accuracy of these models was good. However, these models are not widely used in clinical practice because they lack replicability and transparency. Future studies should transparently report the methodological details of the model construction and validation to ensure replicability and transparency. Furthermore, prediction models should consider more meaningful predictors in future research.

Funding

Project Supported by the Gansu Natural Science Foundation (22JR5RA366).

Author contribution statement

Chunmei Yan; Qiuyu Yang; Richeng Li: Conceived and designed the experiments.

Chunmei Yan; Qiuyu Yang; Aijun Yang; Yu Fu; Jieneng Wang; Ying Li; Qianji Cheng; Shasha Hu: Performed the experiments; Analyzed and interpreted the data.

Chunmei Yan; Qiuyu Yang: Wrote the paper.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2023.e20099>.

References

- [1] Who, Preterm birth (2023). <https://www.who.int/en/news-room/fact-sheets/detail/preterm-birth>.
- [2] R.L. Goldenberg, J.F. Culhane, J.D. Iams, R. Romero, Epidemiology and causes of preterm birth, *Lancet* 371 (9606) (2008) 75–84, [https://doi.org/10.1016/S0140-6736\(08\)60074-4](https://doi.org/10.1016/S0140-6736(08)60074-4).
- [3] J. Perin, A. Mullick, D. Yeung, F. Villavicencio, G. Lopez, K.L. Strong, D. Prieto-Merino, S. Cousens, R.E. Black, L. Liu, Global, regional, and national causes of under-5 mortality in 2000–19: an updated systematic analysis with implications for the Sustainable Development Goals, *Lancet Child Adolesc. Health* 6 (2) (2022) 106–115, [https://doi.org/10.1016/S2352-4642\(21\)00311-4](https://doi.org/10.1016/S2352-4642(21)00311-4).
- [4] C. Crump, J. Sundquist, M.A. Winkleby, K. Sundquist, Preterm birth and risk of chronic kidney disease from childhood into mid-adulthood: national cohort study, *BMJ* 365 (2019) 11346, <https://doi.org/10.1136/bmj.11346>.
- [5] C. Crump, J. Sundquist, K. Sundquist, Risk of hypertension into adulthood in persons born prematurely: a national cohort study, *Eur. Heart J.* 41 (16) (2020) 1542–1550, <https://doi.org/10.1093/eurheartj/ehz904>.
- [6] C. Crump, J. Sundquist, K. Sundquist, Preterm birth and risk of type 1 and type 2 diabetes: a national cohort study, *Diabetologia* 63 (3) (2020) 508–518, <https://doi.org/10.1007/s00125-019-05044-z>.
- [7] C. Crump, E.A. Howell, A. Stroustrup, M.A. McLaughlin, J. Sundquist, K. Sundquist, Association of preterm birth with risk of ischemic heart disease in adulthood, *JAMA Pediatr.* 173 (8) (2019) 736–743, <https://doi.org/10.1001/jamapediatrics.2019.1327>.
- [8] S.S.M. Visser, W.J.M. van Diemen, L. Kervezee, A. van den Hoogen, O. Verschuren, S. Pillen, et al., The relationship between preterm birth and sleep in children at school age: a systematic review, *Sleep Med. Rev.* 57 (2021), 101447, <https://doi.org/10.1016/j.smrv.2021.101447>.
- [9] A. Care, S.J. Nevitt, N. Medley, S. Donegan, L. Good, L. Hampson, et al., Interventions to prevent spontaneous preterm birth in women with singleton pregnancy who are at high risk: systematic review and network meta-analysis, *BMJ* 376 (2020), e064547, <https://doi.org/10.1136/bmj-2021-064547>.
- [10] R.A. Rahman, I.K. Atan, A. Ali, A.M. Kalok, N.A.M. Ismail, Z.A. Mahdy, et al., Use of the Arabin pessary in women at high risk for preterm birth: long-term experience at a single tertiary center in Malaysia, *BMC Pregnancy Childbirth* 21 (1) (2021) 368, <https://doi.org/10.1186/s12884-021-03838-x>.
- [11] A. Conde-Agudelo, R. Romero, E. Da Fonseca, J.M. O'Brien, E. Cetingoz, G.W. Creasy, et al., Vaginal progesterone is as effective as cervical cerclage to prevent preterm birth in women with a singleton gestation, previous spontaneous preterm birth, and a short cervix: updated indirect comparison meta-analysis, *Am. J. Obstet. Gynecol.* 219 (1) (2018) 10–25, <https://doi.org/10.1016/j.ajog.2018.03.028>.
- [12] EPPPIC Group, Evaluating progesterone for preventing preterm birth international collaborative (EPPPIC): meta-analysis of individual participant data from randomised controlled trials, *Lancet* 397 (10280) (2021) 1183–1194, [https://doi.org/10.1016/S0140-6736\(21\)00217-8](https://doi.org/10.1016/S0140-6736(21)00217-8).
- [13] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, *BMJ* 372 (2021) n71, <https://doi.org/10.1136/bmj.n71>.
- [14] K.G. Moons, J.A. de Groot, W. Bouwmeester, Y. Vergouwe, S. Mallett, D.G. Altman, et al., Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist, *PLoS Med.* 11 (2014), e1001744, <https://doi.org/10.1371/journal.pmed.1001744>.
- [15] K.G.M. Moons, R.F. Wolff, R.D. Riley, P.F. Whiting, M. Westwood, G.S. Collins, et al., PROBAST: a tool to assess risk of bias and applicability of prediction model studies: explanation and elaboration, *Ann. Intern. Med.* 170 (1) (2019) W1–W33, <https://doi.org/10.7326/M18-1377>.
- [16] M. Gioan, F. Fenollar, A. Loundou, J.P. Menard, J. Blanc, C. D'Ercole, et al., Development of a nomogram for individual preterm birth risk evaluation, *J Gynecol Obstet Hum Reprod* 47 (10) (2018) 545–548, <https://doi.org/10.1016/j.jogoh.2018.08.014>.
- [17] F. Fuchs, M.V. Senat, H. Fernandez, A. Gervaise, R. Frydman, J. Bouyer, Predictive score for early preterm birth in decisions about emergency cervical cerclage in singleton pregnancies, *Acta Obstet. Gynecol. Scand.* 91 (6) (2012) 744–749, <https://doi.org/10.1111/j.1600-0412.2012.01386.x>.
- [18] K. Kuhlert, E. Smout, N. Hezelgrave, P.T. Seed, J. Carter, A.H. Shennan, Development and validation of a tool incorporating cervical length and quantitative fetal fibronectin to predict spontaneous preterm birth in asymptomatic high-risk women, *Ultrasound Obstet. Gynecol.* 47 (1) (2016) 104–109, <https://doi.org/10.1002/uog.14865>.
- [19] S.M. Lee, K.H. Park, E.Y. Jung, S.H. Cho, A. Ryu, Prediction of spontaneous preterm birth in women with cervical insufficiency: comprehensive analysis of multiple proteins in amniotic fluid, *J. Obstet. Gynaecol. Res.* 42 (7) (2016) 776–783, <https://doi.org/10.1111/jog.12976>.
- [20] A.O. Odibo, C. Farrell, G.A. Macones, V. Berghella, Development of a scoring system for predicting the risk of preterm birth in women receiving cervical cerclage, *J. Perinatol.* 23 (8) (2003) 664–667, <https://doi.org/10.1038/sj.jp.7211004>.

- [21] H. Park, S. Hong, H.N. Yoo, Y.M. Kim, S.J. Lee, K.H. Hoon Park, The identification of immune-related plasma proteins associated with spontaneous preterm delivery and intra-amniotic infection in women with premature cervical dilation or an asymptomatic short cervix, *J Korean Med Sci* 35 (7) (2020) e26, <https://doi.org/10.3346/jkms.2020.35.e26>.
- [22] H. Rawashdeh, S. Awawdeh, F. Shannag, E. Henawi, H. Faris, N. Obeid, et al., Intelligent system based on data mining techniques for prediction of preterm birth for women with cervical cerclage, *Comput. Biol. Chem.* 85 (2020), 107233, <https://doi.org/10.1016/j.compbiolchem.2020.107233>.
- [23] I. Vogel, A.R. Goepfert, P. Thorsen, K. Skogstrand, D.M. Hougaard, A.H. Curry, et al., Early second-trimester inflammatory markers and short cervical length and the risk of recurrent preterm birth, *J. Reprod. Immunol.* 75 (2) (2007) 133–140, <https://doi.org/10.1016/j.jri.2007.02.008>.
- [24] H.N. Yoo, K.H. Park, E.Y. Jung, Y.M. Kim, S.Y. Kook, S.J. Jeon, Non-invasive prediction of preterm birth in women with cervical insufficiency or an asymptomatic short cervix (≤ 25 mm) by measurement of biomarkers in the cervicovaginal fluid, *PLoS One* 12 (7) (2017), e0180878, <https://doi.org/10.1371/journal.pone.0180878>.
- [25] R.C. Boelig, M.N. Naert, N.S. Fox, S. Hennessy, I. Chervoneva, V. Berghella, et al., Predictors of early preterm birth despite vaginal progesterone therapy in singletons with short cervix, *Am. J. Perinatol.* 37 (13) (2020) 1289–1295, <https://doi.org/10.1055/s-0040-1710008>.
- [26] Y.L. Lou, Y.M. Zhou, H. Lu, W.G. Lv, Establishment of a prognostic model for preterm delivery in women after cervical conization, *J. Zhejiang Univ.* 47 (4) (2018) 351–356, <https://doi.org/10.3785/j.issn.1008-9292.2018.08.04>.
- [27] D.O.C. Anumba, V. Stern, J.T. Healey, S. Dixon, B.H. Brown, Value of cervical electrical impedance spectroscopy to predict spontaneous preterm delivery in asymptomatic women: the ECCLIIPP prospective cohort study, *Ultrasound Obstet. Gynecol.* 58 (2) (2021) 293–302, <https://doi.org/10.1002/uog.22180>.
- [28] H.Q. Gu, Z.R. Zhou, Z.H. Zhang, Q. Zhou, Clinical prediction models: basic concepts, application scenarios, and research strategies, *Chin J Evid Based Cardiovasc Med* 10 (12) (2018) 1454–1456, <https://d.wanfangdata.com.cn/periodical/zgxxxyxzz201812005>.
- [29] Z.R. Zhou, W.W. Wang, Y. Li, K.R. Jin, X.Y. Wang, Z.W. Wang, et al., In-depth mining of clinical data: the construction of clinical prediction model with R, *Ann. Transl. Med.* 7 (23) (2019) 796, <https://doi.org/10.21037/atm.2019.08.63>.
- [30] P.A. Della Rosa, C. Miglioli, M. Caglioni, F. Tiberio, K.H.H. Mosser, E. Vignotto, et al., A hierarchical procedure to select intrauterine and extrauterine factors for methodological validation of preterm birth risk estimation, *BMC Pregnancy Childbirth* 21 (1) (2021) 306, <https://doi.org/10.1186/s12884-021-03654-3>.
- [31] P. Cavoretto, M. Candiani, V. Giorgione, A. Inversetti, M.M. Abu-Saba, F. Tiberio, et al., Risk of spontaneous preterm birth in singleton pregnancies conceived after IVF/ICSI treatment: meta-analysis of cohort studies, *Ultrasound Obstet. Gynecol.* 51 (1) (2018) 43–53, <https://doi.org/10.1002/uog.18930>.
- [32] N. Jančar, B. Mihevc Ponikvar, S. Tomšič, E. Vrtačnik Bokal, S. Korošec, Is IVF/ICSI an independent risk factor for spontaneous preterm birth in singletons? A population-based cohort study, *BioMed Res. Int.* 2018 (2018), 7124362, <https://doi.org/10.1155/2018/7124362>.
- [33] G. Esposito, S. Cipriani, S. Noli, M. Franchi, G. Corrao, F. Parazzini, et al., The changing impact of assisted reproductive techniques on preterm birth during the period 2007–2020 in Lombardy, Northern Italy, *Eur. J. Obstet. Gynecol. Reprod. Biol.* 278 (2022) 51–56, <https://doi.org/10.1016/j.ejogrb.2022.09.003>.
- [34] P.I. Cavoretto, V. Giorgione, A. Sotiriadis, P. Viganò, E. Papaleo, A. Galdini, et al., IVF/ICSI treatment and the risk of iatrogenic preterm birth in singleton pregnancies: systematic review and meta-analysis of cohort studies, *J. Matern. Fetal Neonatal Med.* 35 (10) (2022) 1987–1996, <https://doi.org/10.1080/14767058.2020.1771690>.
- [35] M.M. Hedderson, A. Ferrara, D.A. Sacks, Gestational diabetes mellitus and lesser degrees of pregnancy hyperglycemia: association with increased risk of spontaneous preterm birth, *Obstet. Gynecol.* 102 (4) (2003) 850–856, [https://doi.org/10.1016/s0029-7844\(03\)00661-6](https://doi.org/10.1016/s0029-7844(03)00661-6).
- [36] G. Li, Y. Xing, G. Wang, Q. Wu, W. Ni, N. Jiao, et al., Does recurrent gestational diabetes mellitus increase the risk of preterm birth? A population-based cohort study, *Diabetes Res. Clin. Pract.* 199 (2023), 110628, <https://doi.org/10.1016/j.diabres.2023.110628>.
- [37] X. Cao, D. Zu, Y. Liu, Effects of interaction between gestational hypertension and history of preterm birth on the risk of preterm birth: an analysis based on the national vital statistics system database, *Med Sci Monit* 28 (2022), e935094, <https://doi.org/10.12659/MSM.935094>.
- [38] H. An, M. Jin, Z. Li, L. Zhang, H. Li, Y. Zhang, et al., Impact of gestational hypertension and pre-eclampsia on preterm birth in China: a large prospective cohort study, *BMJ Open* 12 (9) (2022), e058068, <https://doi.org/10.1136/bmjopen-2021-058068>.
- [39] S. Vannuccini, V.L. Clifton, I.S. Fraser, H.S. Taylor, H. Critchley, L.C. Giudice, et al., Infertility and reproductive disorders: impact of hormonal and inflammatory mechanisms on pregnancy outcome, *Hum. Reprod. Update* 22 (1) (2016) 104–115, <https://doi.org/10.1093/humupd/dmv044>.
- [40] T. Premru-Srsen, E. Bokal Vrtačnik, T. Bizjak, I. Verdenik, S. Korošec, H. Ban Frangež, Preterm delivery risk in infertile women who conceived after reproductive surgery: natural conception versus IVF/ICSI, *Hum. Reprod.* 36 (6) (2021) 1630–1639, <https://doi.org/10.1093/humrep/deaa380>.
- [41] B.H. Sudasinghe, C.N. Wijeyaratne, P.S. Ginige, Long and short-term outcomes of Gestational Diabetes Mellitus (GDM) among South Asian women - a community-based study, *Diabetes Res. Clin. Pract.* 145 (2018) 93–101, <https://doi.org/10.1016/j.diabres.2018.04.013>.
- [42] J.M. Catov, C.E. Lewis, M. Lee, M.F. Wellons, E.P. Gunderson, Preterm birth and future maternal blood pressure, inflammation, and intimal-medial thickness: the CARDIA study, *Hypertension* 61 (3) (2013) 641–646, <https://doi.org/10.1161/HYPERTENSIONAHA.111.00143>.
- [43] M.R. Sutherland, M. Bertagnolli, M.A. Lukaszewski, F. Huyard, C. Zyzdorzcyk, T.M. Luu, et al., Preterm birth and hypertension risk: the oxidative stress paradigm, *Hypertension* 63 (1) (2014) 12–18, <https://doi.org/10.1161/HYPERTENSIONAHA.113.01276>.
- [44] E.S.D.S. Magalhães, M.D.B.B. Méio, F.M. Peixoto-Filho, S. Gonzalez, A.C.C. da Costa, M.E.L. Moreira, Pregnancy-induced hypertension, preterm birth, and cord blood adipokine levels, *Eur. J. Pediatr.* 179 (8) (2020) 1239–1246, <https://doi.org/10.1007/s00431-020-03586-8>.
- [45] C.E. Kleinrouweler, F.M. Cheong-See, G.S. Collins, A. Kwee, S. Thangaratinam, K.S. Khan, et al., Prognostic models in obstetrics: available, but far from applicable, *Am. J. Obstet. Gynecol.* 214 (1) (2016) 79–90, <https://doi.org/10.1016/j.ajog.2015.06.013>, e36.
- [46] K.G. Moons, D.G. Altman, Y. Vergouwe, P. Royston, Prognosis and prognostic research: application and impact of prognostic models in clinical practice, *BMJ* 338 (2009) b606, <https://doi.org/10.1136/bmj.b606>.
- [47] W. Bouwmeester, N.P. Zuithoff, S. Mallett, M.I. Geerlings, Y. Vergouwe, E.W. Steyerberg, et al., Reporting and methods in clinical prediction research: a systematic review, *PLoS Med.* 9 (5) (2012) 1–12, <https://doi.org/10.1371/journal.pmed.1001221>.
- [48] I. Dehaene, J. Steen, G. Vandewiele, K. Roelens, J. Decruyenaere, The web-based application "QUIPP v.2" for the prediction of preterm birth in symptomatic women is not yet ready for worldwide clinical use: ten reflections on development, validation and use, *Arch. Gynecol. Obstet.* 306 (2) (2022) 571–575, <https://doi.org/10.1007/s00404-022-06418-2>.