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REVIEW ARTICLE

Placental alpha microglobulin-1 (PartoSure) test for the prediction of preterm birth: a systematic review and meta-analysis

Reihaneh Pirjani[a], Ashraf Moini[a], Amir Almasi-Hashiani[b], Maryam Farid Mojtahedi[a], Samira Vesali[c], Ladan Hosseini[d] and Mahdi Sepidarkish[e]

[a]Department of Obstetrics and Gynecology, Arash Women's Hospital, Tehran University of Medical Sciences, Tehran, Iran; [b]Department of Epidemiology, School of Health, Arak University of Medical Sciences, Arak, Iran; [c]Department of Epidemiology and Reproductive Health, Reproductive Epidemiology Research Center, Royan Institute for Reproductive Biomedicine, ACECR, Tehran, Iran; [d]Research Development Center, Arash Women's Hospital, Tehran University of Medical Sciences, Tehran, Iran; [e]Department of Biostatistics and Epidemiology, Babol University of Medical Sciences, Babol, Iran

ABSTRACT

Objectives: To assess the accuracy of the placental alpha microglobulin-1 (PAMG-1) to predict preterm birth (PB) in women with symptoms of PB through use of formal methods for systematic reviews and meta-analytic techniques.

Methods: We performed a comprehensive search of medical bibliographic databases to identify observational studies that reported on the predictive accuracy of PAMG-1 for PB. Two investigators independently assessed studies, assessed quality of studies, and extracted data. Summary receiver operating characteristic (SROC) curves, pooled sensitivities, specificities, likelihood ratios (LR), and diagnostic odds ratio (DOR) were generated.

Results: Seventeen studies involving 2590 women met the inclusion criteria. Meta-analysis of 15 studies (including 1906 women) revealed a pooled sensitivity of 66.2% (95% CI: 59.1, 72.7) and specificity of 96.1% (95% CI: 95.1, 97.0) with the SROC equal to 0.97 (95% CI: 0.95, 0.98) for prediction of delivery within 7 d of testing. The summary estimates were 15.26 (95% CI: 11.80, 19.75) for LR + and 0.31 (95% CI: 0.17, 0.55) for LR − for prediction of delivery within 7 d of testing. Pooled estimate of DOR for predicting delivery within 7 d of testing was 55.13 (95% CI: 35.32, 86.06). The sensitivity, specificity and the SROC of PAMG-1 pooled from 10 studies (including 1508 women) for prediction of delivery within 14 d of testing were 64.4% (95% CI: 56.8, 71.5), 96.9% (95% CI: 95.8, 97.7) and 0.97 (95% CI: 0.95, 0.98). The overall pooled LR + and LR − of PAMG-1 for predicting delivery within 14 d of testing among the included studies were 16.72 (95% CI: 12.03, 23.23) and 0.42.1 (95% CI: 0.31, 0.56), respectively. The pooled DOR of the PAMG-1 for prediction delivery within 14 d of testing was equal to 44.65 (95% CI: 26.30, 75.78).

Conclusion: Cervical PAMG-1 had a high accuracy to predict PB within 7 and 14 d of testing in symptomatic pregnant women.

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Biomarker; placental alpha macroglobulin-1; predictive value; prematurity; preterm labor

Introduction

Preterm birth defined as delivery at the pregnancy age 23–37 completed weeks is a major cause of neonatal mortality and morbidity worldwide; its prevalence is 6–10% [1]. The annual cost of the preterm birth (PB) would impose heavy expenses on the health economics of each country in addition to neurodevelopmental impairments among surviving babies [2]. On the other hand, unnecessary admission of pregnant women with false PB, even if it does not result in any intervention, would cause financial burden [3]. A reliable test that helps diagnose true PB would, therefore, reduce additional costs. There are several tests of various accuracies for predicting spontaneous PB used in women who present with symptoms suggestive of spontaneous PB such as biophysical markers (digital cervical exam for evaluating cervical dilation and transvaginal ultrasound for measuring cervical length) and biomarkers including quantitative and qualitative fetal fibronectin (fFN) in vaginal secretions and phosphorylated insulin-like growth factor binding protein 1 (phIGFBP-1) [4]. Lee et al. reported that positive placental alpha microglobulin-1 (PAMG-1) in cervicovaginal discharge of patients with clinically intact

CONTACT Mahdi Sepidarkish Mahdi.sepidarkish@gmail.com Department of Biostatistics and Epidemiology, Babol University of Medical Sciences, PO Box 16635148, Ganjafroz Street, Babol 47176-47745, Iran

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membranes (sterile speculum) could predict reliably the delivery within 7 d of initial test in women presented with suspicious membrane rupture [3–5].

Current practice regarding tests for predicting spontaneous PB varies widely. We also encounter lacking consensus about the best testing policy [6]. In 2014, Nikolova et al. reported that the inflammatory processes associated with impending labor and delivery allow trace amounts of PAMG-1, or levels of PAMG-1 less than those typically associated with the visual presence of amniotic fluid in the vaginal cavity, to pass in to the vaginal cavity through microperforations or preexisting pores in the amniotic membranes [7]. A newly developed bedside test kit optimized for PAMG-1 detection in this scenario has been made commercially available under the trade name PartoSure^{TM} time-to-delivery (TTD) test [8]. PAMG-1 in cervical secretions could identify symptomatic women at risk of PB. Since then, several authors have reported that cervical PAMG-1 can accurately predict PB in women with an episode of PB and intact membranes and compared to cervicovaginal fFN, it is not affected by recent sexual intercourse or contamination with urine, have lower costs and faster testing [7,9–12]. There was no consensus about cervical PAMG-1 and PB, and there has not been a systematic review in its current practice. So, we carried out a systematic review to assess the accuracy of cervical PAMG-1 to predict PB in women with symptoms of PB.

Materials and methods

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and in accordance with recommended methods for systematic reviews of diagnostic test accuracy [13].

Selection criteria for studies

The review included diagnostic epidemiologic (cohort and cross-sectional) studies that reported the accuracy of the PAMG-1 to predict imminent spontaneous PB in patients with threatened PB. The reference standard outcomes considered delivery within 7 and 14 d of testing in symptomatic women. Studies were excluded if any of the following applied: (1) they were case-control, reviews, case series, case report, editorials, or letters to editor, (2) they assessed PAMG-1 in women with suspected or established preterm premature rupture of membranes, (3) they predicted PB in women with twin or more gestation, (4) they did not report sufficient information to calculate accuracy test estimates or did not allow construction of 2×2 contingency tables. If there were duplicate publications, the most complete version or the paper with the highest number of subjects would be included. There were no language restrictions.

Literature search

We undertook a comprehensive search for all published original articles and abstracts on PAMG-1 for the prediction of PB using the Embase, PubMed, Scopus and Web of Science bibliographic databases. Our search was restricted to the time period 1 October 2014 to 15 October 2019, since the first study about accuracy of PAMG-1 was introduced in October 2014. We also checked the citation lists of relevant publications and included studies. We hand-searched references of identified selected articles for additional relevant citations. In addition, we contacted investigators and specialists in the field for possible unpublished research on the topic and additional relevant citations. No further limitations were made in order to be as sensitive as possible. The search was modified for Web of Science, Embase, and Scopus using their subject headings instead of the MeSH subject headings. Search details are available in Appendix S1 in the supplementary material.

Study selection and data extraction

All citations identified by bibliographic databases were downloaded in to Endnote software version 19 (the Thompson Corporation, New York, NY). The citations were organized, duplicates deleted, and each citation was assigned by a unique identification number. Initially, two investigators (MS and AAH) independently assessed titles and abstracts to select potentially relevant citations. The studies were scrutinized using predefined eligibility criteria (see aforementioned text). Any citation identified by either review author was selected for full-text review. Discrepancies were resolved through discussion between the review authors or arbitration by a third review author (RP). All selected articles were read and abstracted by the two review authors (MS and AAH) using a prepiloted structured data extraction specifically created for this systematic review and crosschecked to ensure accuracy. Studies that did not report sufficient information to calculate accuracy-test estimates were excluded if no further information was acquired after two attempts to contact the study's authors. The following data

were extracted from each article: (i) general characteristics of the study, such as authors, setting, publication year, population, sample size and design; (ii) inclusion/exclusion criteria for patients entering study; (iii) test characteristics (gestational age at testing, laboratory methods used); (iv) reference standard outcomes; and (v) data to calculate accuracy estimates (true positive, false positive, true negative, and false negative). When accuracy estimates data were not reported, we recalculated them from the reported results.

Assessment of methodological quality

Included studies were critically appraised by two review authors (MS and AAH) using *a priori* criteria based on a modified version of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 tool, a validated tool for diagnostic studies [14]. A description of the items and the interpretation in the context can be found in Appendix S2 in the supplementary material.

Statistical analysis and data synthesis

Data from included studies were synthesized for symptomatic women with threatened PB and stratified according to the reference standard outcomes considered delivery within 7 and 14 d of testing. Data abstracted from each included study were arranged in 2×2 contingency table included true positive, false positive, true negative, and false negative. Accuracy for each study was determined by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive or negative likelihood ratios (LR) and diagnostic odds ratio (DOR) with 95% confidence intervals (CIs). Accuracy estimates with 95% CIs were pooled using bivariate random-effects models (Metandi package in Stata) [15]. Summary and individual estimates were also presented graphically with the 95% CIs and prediction region by summary receiver operating characteristic (SROC) curves for each predefined reference standard outcome (delivery within 7 and 14 d of testing). The results of the included studies were tested for statistical heterogeneity by visual examination of both forest plots and SROC plots, and by means of the quantity I^2. Statistical heterogeneity was considered substantial I^2 value exceeded 40%. The statistical analyses were performed using Stata/SE 13.0 for Windows (Stata Corporation, College Station, TX) and Meta-DiSc for Windows package.

Results

Selection, characteristics, and quality of studies

A total of 252 potentially relevant records were identified through database searching (89 from PubMed, 70 from Embase, 59 from Scopus, and 34 from Web of Science) and 11 additional records were identified through other sources (Figure 1). After removing 73 duplicate records, the titles and abstracts for 173 remained records were assessed for eligibility. In the first screening (abstracts/titles), 128 citations were excluded, and 45 underwent full-text evaluation. After excluding 28 records based on full-text articles, 17 studies involving 2590 women were included in the systematic review. Table 1 shows the main characteristics of the 17 studies included [7–12,16–27]. There were 16 prospective [7–11,16–20,23–28] and one retrospective cohort studies [21]. Four of the studies were performed in Russia [9,11,16,17], one in Macedonia [10], two in Macedonia and Russia [7,8], one in Macedonia, Russia and Finland [26], one in Turkey [19], one in United Arab Emirates [24], two in Belgium [18,23], one United Kingdom [20], one in USA [28], one in Thailand [27] and one in Spain [21]. The sample sizes varied from 35 [18] to 635 [28] symptomatic women. All studies were limited to women with singleton gestation and intact membranes. All studies used a concentration $\geq 1\,\mu g/l$ to indicate an abnormal test result. Ten studies (58.82%) reported data for more than one reference standard outcome. Many studies did not report all factors that could affect methodological quality. Nevertheless, most of studies were classified as low risk of bias. The most prevalent shortcomings were the method of sampling of patients, the lack of information regarding blinding of outcome assessor and withdrawal of patients.

PAMG-1 in symptomatic women for prediction of delivery within 7 d of testing

Fifteen studies were included in the bivariate random-effects models; with a total of 1906 samples that included 198 (10.38%) confirmed delivery within 7 d of testing. Meta-analysis revealed a pooled sensitivity of 66.2% (95% CI: 59.1, 72.7; Figure 2(A)) and specificity of 96.1% (95% CI: 95.1, 97.0; Figure 2(B)) with an area under the SROC curve equal to 0.97% (95% CI: 0.95, 0.98; Figure 2(C)). Results were largely homogenous, with a small proportion of studies being outliers (Sensitivity $\chi^2 = 21.19$, $p = .096$, inconsistency $I^2 = 33.9\%$; Specificity $\chi^2 = 18.7$, $p = .170$, inconsistency $I^2 = 25.8\%$). The summary estimates were 15.26 (95%

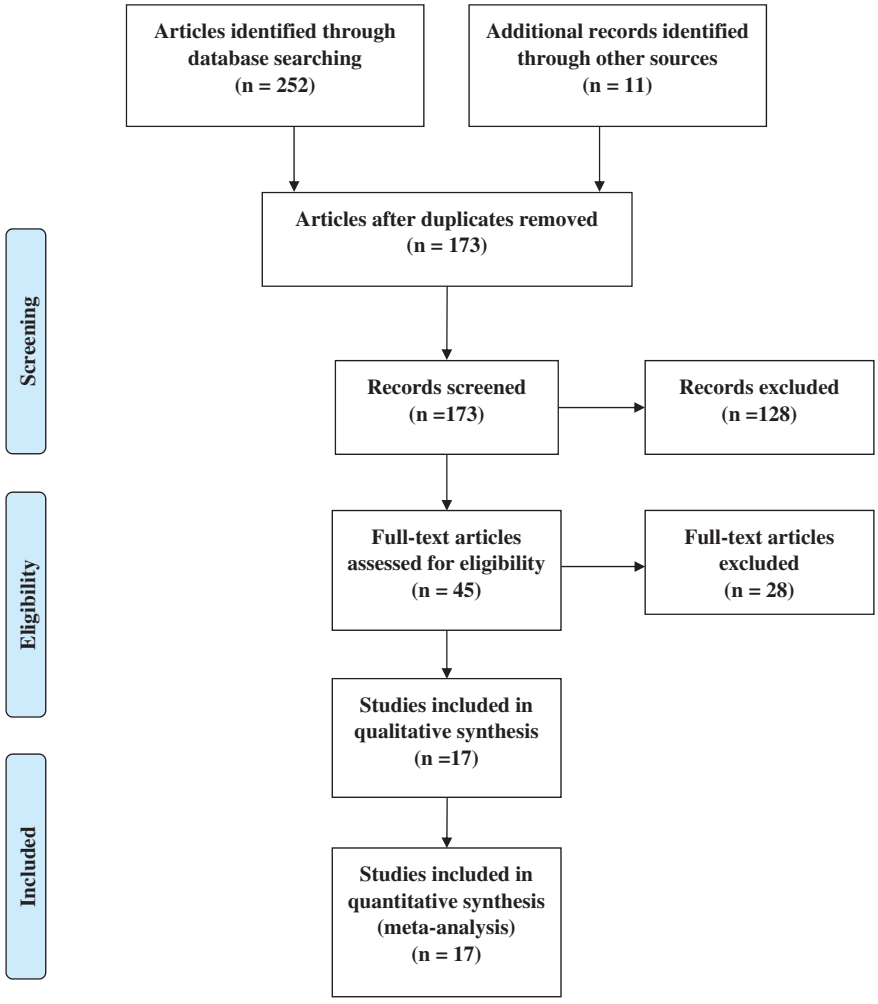


Figure 1. Study flow diagram.

CI: 11.80, 19.75) for LR + and 0.31 (95% CI: 0.17, 0.55) for LR− (Figure 2(D,E)). Pooled estimate of DOR of cervical PAMG-1 for delivery within 7 d of testing was 55.13 (95% CI: 35.32, 86.06). There was no graphical and statistical heterogeneity and inconsistency of DOR between the studies (DOR $\chi^2 = 8.45$, $p = .864$, inconsistency $I^2 = 0\%$; Figure 2(F)).

PAMG-1 in symptomatic women for prediction of delivery within 14 d of testing

Ten studies were included in the bivariate random-effects models; with a total of 1508 samples that included 174 (11.53%) confirmed delivery within 14 d of testing. The sensitivity and specificity of PAMG-1 pooled from 10 studies were 64.4% (95% CI: 56.8, 71.5; Figure 3(A)) and 96.9% (95% CI: 95.8, 97.7; Figure 3(B)). Heterogeneity was high for the pooled sensitivity ($\chi^2 = 27.9$, $p = .001$, inconsistency $I^2 = 67.7\%$) and low for the pooled specificity ($\chi^2 = 8.39$, $p = .495$, inconsistency $I^2 = 0\%$). The overall pooled LR + and LR − of PAMG-1 for predicting delivery within 14 d of testing among the included studies were 16.72 (95% CI: 12.03, 23.23) and 0.42.1 (95% CI: 0.31, 0.56), respectively (Figure 3(C,D)). However, moderate heterogeneity was observed for LR− ($\chi^2 = 15.82$, $p = .071$, inconsistency $I^2 = 43.1\%$), but there was no statistically significant heterogeneity between studies with respect to LR+ ($\chi^2 = 6.79$, $p = .659$, inconsistency $I^2 = 0\%$). As shown in Figure 3(E), the pooled DOR of the PAMG-1 for delivery within 14 d of testing was equal to 44.65 (95% CI: 26.30, 75.78; $\chi^2 = 10.29$, $p = .327$, inconsistency $I^2 = 12.6\%$). The SROC curves showed that the cervical PAMG-1 had a noticeable predictive ability for delivery within 14 d of testing (0.97, 95% CI: 0.95, 0.98; Figure 3(F)).

Discussion

Our review on 17 studies showed that the cervical PAMG-1 has a very high specificity, LR + and DOR to predict PB within 7 and 14 d of testing. For the

Table 1. Characteristics of studies included in the systematic review.

Study	Country	Study design	No. of women	Inclusion criteria	Exclusion criteria	Maternal age	Gestational age at testing (weeks)	Reference standard outcome
Nikolova et al. [7]	Macedonia and Russia	Prospective cohort	101	Singleton pregnancies with symptoms of PB, clinically intact amniotic membranes, and minimal cervical dilatation (≤3 cm)	Overt rupture of fetal membranes, advanced cervical dilatation, suspected placenta previa, a cervical cerclage in place, or who were under the age of 18	28 (range: 18, 43)	(20–36/6)	Spontaneous PB within 7 and 14 d of testing
Nikolova et al. [8]	Macedonia and Russia	Prospective cohort	203	Singleton pregnancies with symptoms of PB, clinically intact membranes, and cervical dilatation of ≤3 cm	Overt rupture of fetal membranes, advanced cervical dilatation, suspected placenta previa, a cervical cerclage in place, or who were under the age of 18	27 (range: 18, 43)	(20/7–36/6)	Spontaneous PB within 7 and 14 d of testing
Caroline and Annick [18]	Belgium	Prospective cohort	35	Pregnant women clinically intact membranes, cervical dilation <3 cm, and cervical length <30 mm	Not reported	30	(22–34)	Spontaneous PB within 7 and 14 d of testing
Bolotskikh and Borisova [16]	Russia	Prospective cohort	49	Pregnant women with the symptoms of spontaneous PB (10 contractions per hour median, IQR: 5–13)	Not reported	Not reported	(29/7–34/6)	Spontaneous PB within 14 d of testing
Lou and Ajay [20]	UK	Prospective cohort	65	Singleton pregnancies with symptoms of preterm labor, clinically intact membrane and cervical dilatation <4 cm	Vaginal bleeding, cervical cerclage in place, digital examination prior to specimen collection and recent sexual intercourse in the last 24 h.	Not reported	(24–34/6)	Spontaneous PB within 7 d of testing
Van Holsbeke et al. [23]	Belgium	Prospective cohort	50	Pregnant women clinically intact membranes, cervical dilation <3 cm, And cervical length <30 mm	Not reported	29	(22–34)	Spontaneous PB within 7 d of testing
Konoplyannikov et al. [11]	Russia	Prospective cohort	71	Clinically intact membranes and cervical dilation 53 cm	Overt rupture of fetal membranes, advanced cervical dilatation, suspected placenta previa, a cervical cerclage in place, or	Not reported	(20–37)	Spontaneous PB within 7 d of testing
Fatkullin et al. [9]	Russia	Prospective cohort	45	Pregnant women clinically intact membranes, minimal cervical dilation	Not reported	Not reported	(24–34/6)	Spontaneous PB within7 and 14 d of testing
Melchor et al. [21]	Spain	Retrospective cohort	367	Patients with singleton gestations with symptoms of early PB, clinically intact membranes, and cervical dilation <3 cm, who did not have a medically-indicated PB within 14 d of testing	Vaginal bleeding, placenta previa, or a cervical cerclage in place at the time of testing	32.47±(5.89)	(24–34/6)	Spontaneous PB within7 and 14 d of testing
Bolotskikh and Borisova [17]	Russia	Prospective cohort	99	Aged ≥ 18 years with single pregnancy presenting with selfreported signs, symptoms, or complaints suggestive of PB	Use of tocolytic medications cervical dilatation >3 cm suspected placenta previa gestational age of <22 + 0 or ≥ 37 weeks overt rupture of the fetal membranes heavy vaginal bleeding	25 (23, 38) (median, IQR)	(22–36/6)	Spontaneous PB within7 and 14 d of testing
Hadzi-Lega et al. [10]	Macedonia	Prospective cohort	57	Singleton gestation, symptoms of PB intact membranes and a minimal cervical dilatation of ≤3 cm	Multiple pregnancies, ruptured membranes, antepartum hemorrhage, active labor, or cervical cerclage	27 (range: 23, 30.5)	(22–35)	Spontaneous PB within7 and 14 d of testing
Çekmez et al. [19]	Turkey	Prospective cohort	72	Pregnant women with singleton pregnancies at	Active bleeding, multiple pregnancies, growth	26±(2.6)	(24–34)	Spontaneous PB within7 and 14 d of testing

(*continued*)

Table 1. Continued.

Study	Country	Study design	No. of women	Inclusion criteria	Exclusion criteria	Maternal age	Gestational age at testing (weeks)	Reference standard outcome
				least four contractions in 60 min based on external cardiotocography,cervical dilation of >1 cm to <3 cm, effacement of >50%, and a cervical length of <30	restriction, fetal anomalies, placental anomalies, history of coitus within 24 h, history of PB, preeclampsia or signs of any infection			
Wing et al. [28]	USA	Prospective cohort	635	Pregnant women presented with signs and symptoms of PB	Ruptured membranes or cervical dilatation 3 cm or greater	28.26±(5.8)	(24.0–34.9)	Spontaneous PB within 7 and 14 d of testing
Lotfi et al. [24]	United Arab Emirates	Prospective cohort	132	Patients with PB symptoms, cervical dilatation ≤3 cm, no intercourse within 24 h, and clinically intact membranes	Suspected placental previa, digital exam prior to specimen collection, previous tocolytic treatment, cervical dilatation greater than 3 cm, and overt rupture of fetal membranes	Not reported	(24.7–34/6)	Spontaneous PB within 7 and 14 d of testing
Nikolova et al. [26]	Macedonia, Finland and Russia	Prospective cohort	383	Patients with intact amniotic membranes and cervical dilation ≤3 cm, without recent intercourse or cerclage	Multiple gestations, overt rupture of fetal membranes, advanced cervical dilation (>3 cm), a symptom not associated with idiopathic threatened PB (e.g. trauma), tocolytic medications for treatment of threatened PB before the collection of the cervicovaginal specimens or cervical length measurements and enrollment in a tocolytic study, heavy vaginal bleeding, suspected placenta previa, cervical cerclage or pessary in place, intercourse within 24 hours, or <18 years old	Not reported	(20–36/6)	Spontaneous PB within 7 and 14 d of testing
Santipap and phupong [27]	Thailand	Prospective cohort	154	Singleton pregnant women presenting with the signs and symptoms of PB	Preterm premature rupture of membranes, cervical dilatation >3 cm, multiple pregnancies, fetal growth restriction, antepartum hemorrhage, fetal chromosomal or congenital anomalies, a nonreassuring fetal heart rate and fetal adrenal gland	37.3±(1.7)	(22–36/6)	Spontaneous PB within 7 d of testing
Ravi et al. [25]	United Arab Emirates	Prospective cohort	72	Patients presenting with singleton pregnancies, signs of PB, intact membranes, no coitus within 24 h, and cervical dilation ≤3 cm.	Previous vaginal examination, sexual intercourse (within 24 h), cervical dilation of more than 3 cm, frank vaginal bleeding, placenta previa, rupture of membranes (on speculum examination), multiple gestations, gestational age below 23 weeks or above 35 weeks	28.5 (range: 19, 42)	(23–35/6)	Spontaneous PB within7 and 14 d of testing

PB: preterm birth; IQR: inter quartile range.

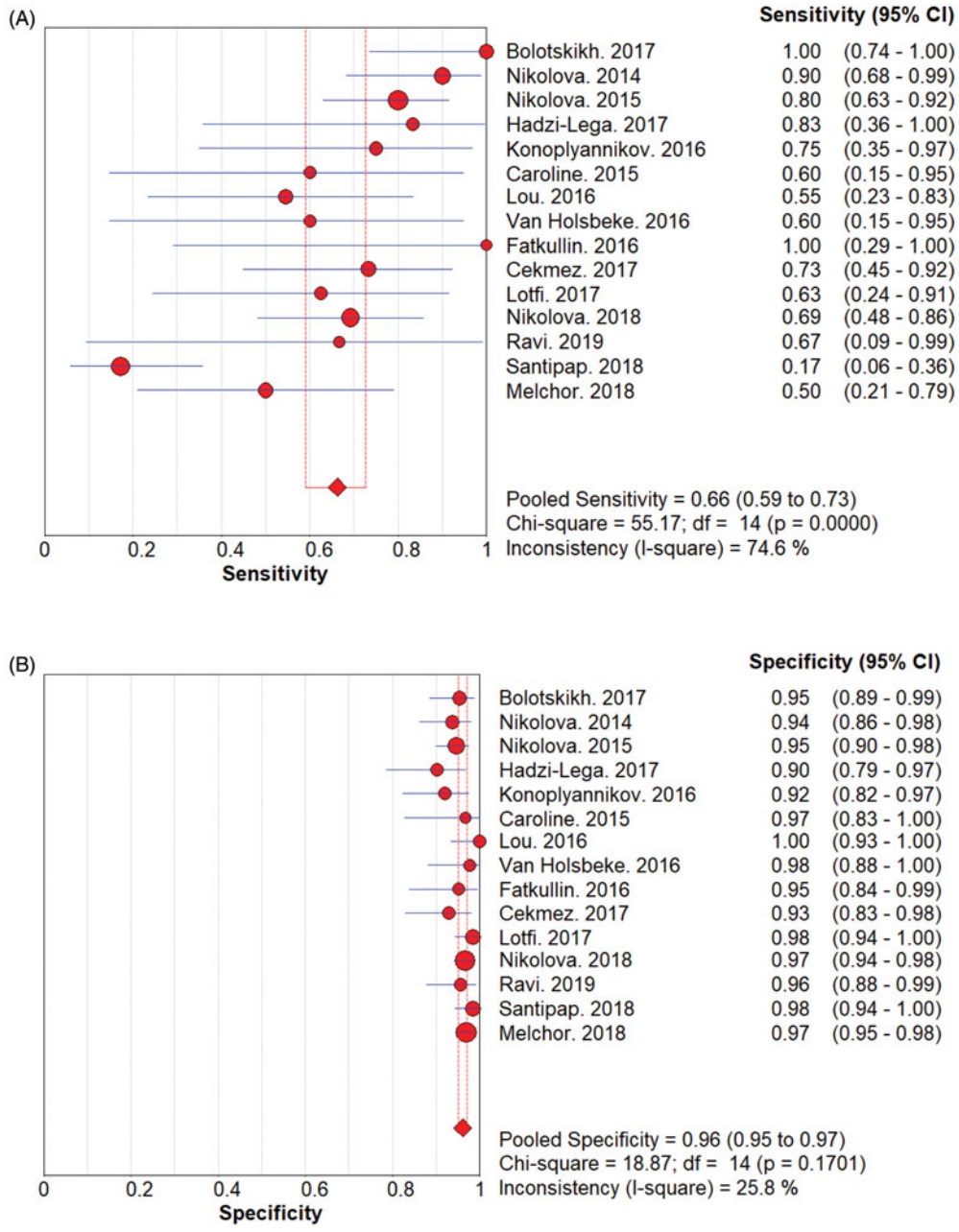


Figure 2. Pooled estimates of diagnostic indices for predicting spontaneous preterm birth within 7 d of testing using placental alpha microglobulin-1 (PAMG-1); (A) sensitivity, (B) specificity, (C) summary receiver operating characteristic curve, (D) positive likelihood ratio, (E) negative likelihood ratio, (F) diagnostic odds ratio.

detection of PB within 7 d of testing, pooled bivariate analyses from 1906 samples (198 confirmed deliveries) demonstrated a sensitivity of 66.2% (95% CI: 59.1, 72.7), specificity of 96.1% (95% CI: 95.1, 97.0), LR + of (95% CI: 11.80, 19.75), and DOR of 55.13 (95% CI: 35.32, 86.06). For the detection of PB within 14 d of testing, pooled bivariate analyses from 1508 samples (174 confirmed deliveries) demonstrated a sensitivity of 64.4% (95% CI: 56.8, 71.5), specificity of 96.9% (95% CI: 95.8, 97.7), LR + of 16.72 (95% CI: 12.03, 23.23), and DOR of 44.65 (95% CI: 26.30, 75.78). A meta-analysis in 2016 evaluated the effect of fetal fibronectin test in the prevention of PB in singleton pregnancies and concluded that fetal fibronectin testing was not associated with the prevention of PB or improvement in perinatal outcome and even is associated with higher costs [29]. The question now arises is that it is not time to put fetal fibronectin out? Based on the conclusion of George A, continued use of fetal fibronectin in women with threatened PB is not reasonable [30].

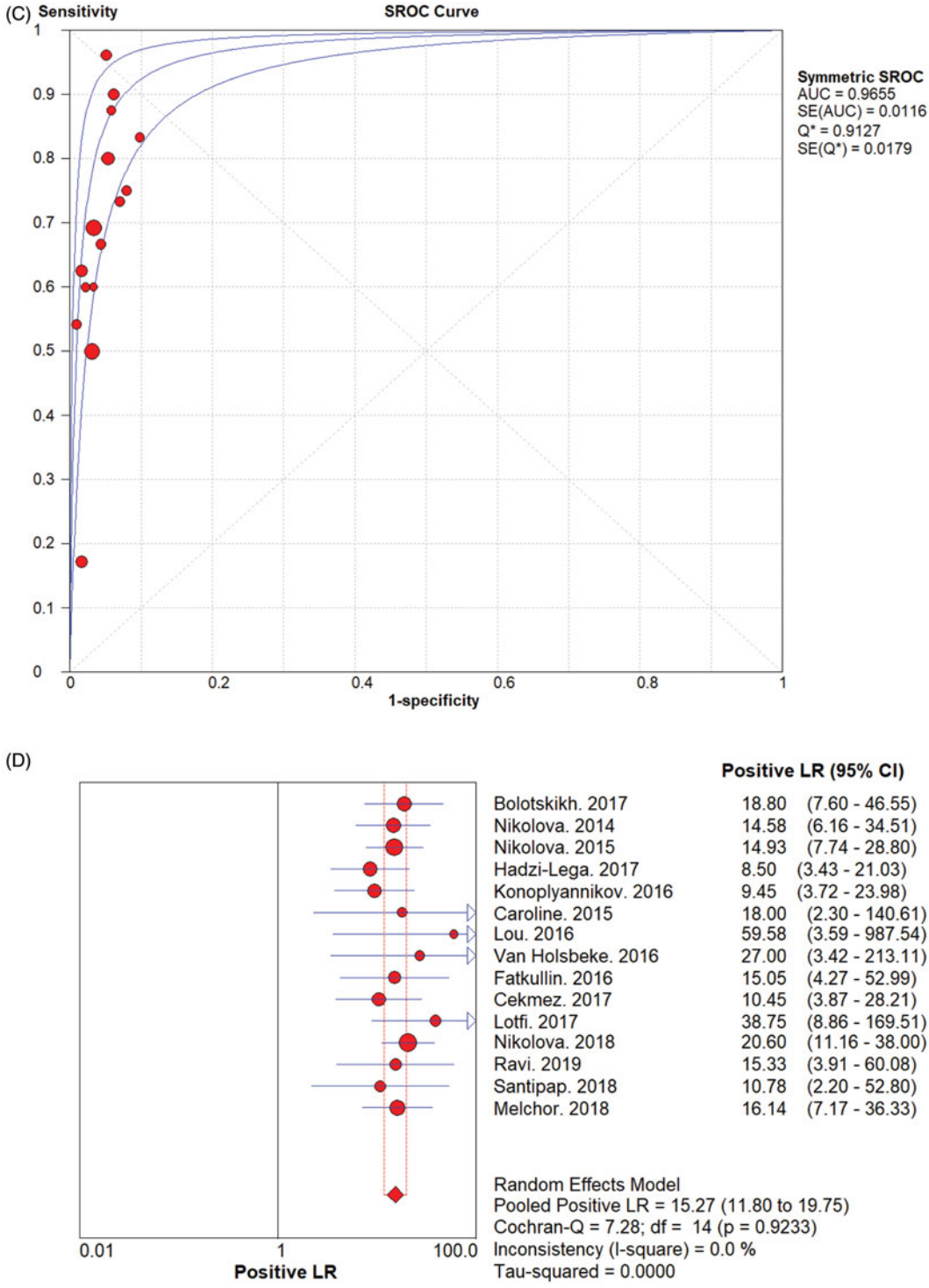
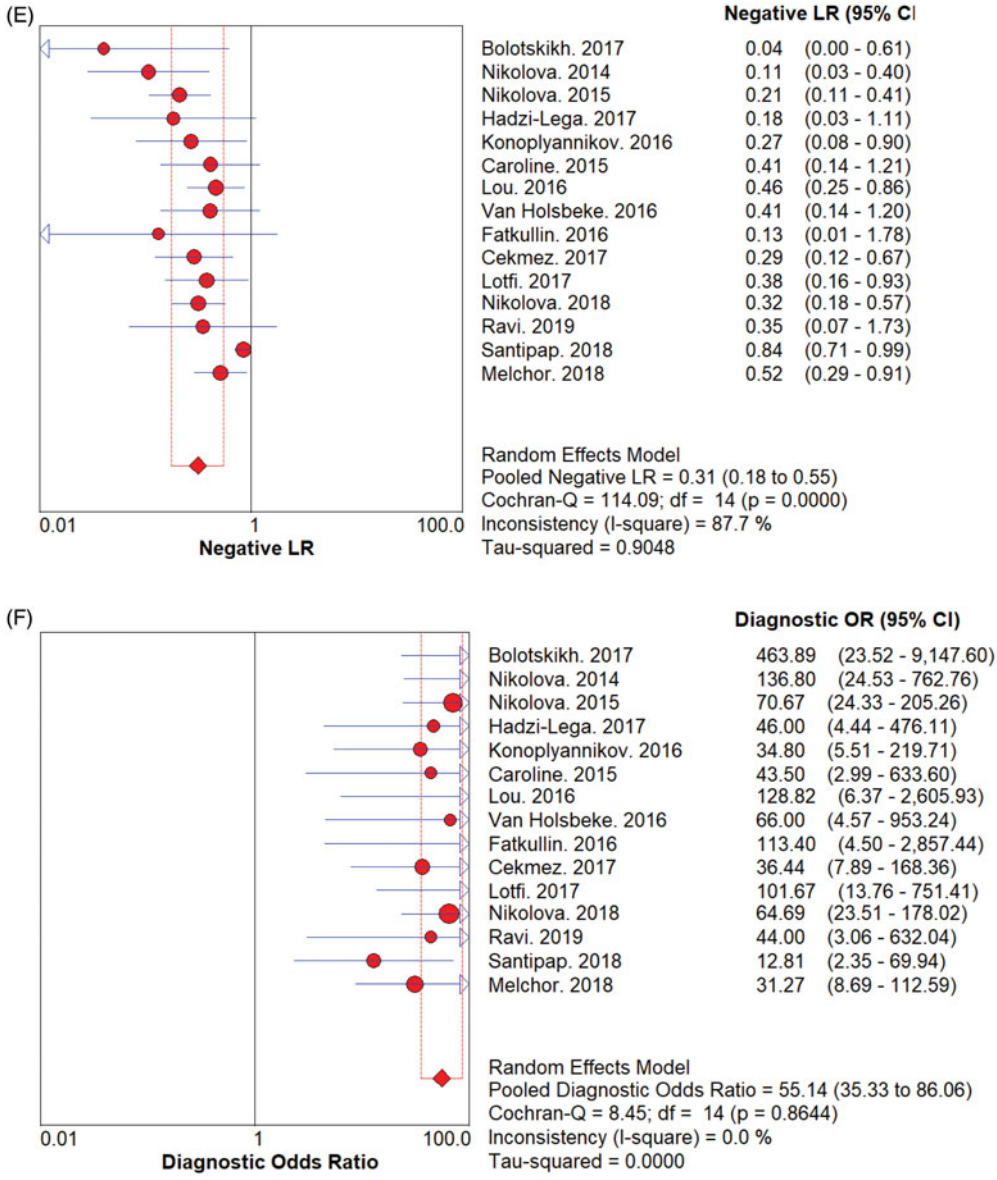


Figure 2. Continued.

In the meta-analysis that was performed on cervical phosphorylated insulin-like growth factor binding protein-1 (phIGFBP-1) test in 2017, it was found the overall predictive ability of phIGFBP-1 test for the identification of women at risk for PB is limited and according to available literature they mentioned that there was no sufficient evidence to recommend the routine clinical use of cervical phIGFBP-1 test in women with or without symptoms of PB [6]. Contrary to above meta-analysis that found FFN and phIGFBP-1 can be disappointing, our study suggests that PAMG-1 is an accurate predictor of PB. In our opinion, in the future this test may be known as a bedside, noninvasive and accurate test for predicting PB.

So far, the number of studies conducted on other markers (FFN and phIGFBP-1) is high, and those



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markers have been studied in both symptomatic and asymptomatic individuals. However, the number and variety of studies on PAMG-1 are low. In our opinion, PAMG-1 should also be evaluated in asymptomatic women who are high risk for spontaneous PB. It seems that doing this test will not be cost-effective in all asymptomatic low-risk pregnant women. However, use of the test in women who are considered to be at high risk for PB according to other criteria, such as a previous history of PB and uterine fibroids, accurate prediction of PB and timely admission and interventions, will prevent neonatal morbidity and mortality. Anyway, future studies should focus on dispensable costs associated with evaluation of PB in both high risk and low-risk women. As described by Romero, inflammatory process is one of the mechanisms that lead to leakage of PAMG-1 into cervicovaginal secretions duo to weakness or micro-perforation in membrane [5]. Although the prevalence of infections and inflammation in women with spontaneous PB is higher, all women who have inflammation and infection will not get PB; thus, the positive test in these women may reduce the PPV of the test. The other possible mechanism is transudation of amniotic fluid secondary to increase intrauterine pressure [5]. Considering this mechanism, some factors such as polyhydramnios and station of fetal head may affect the result of PAMG-1 test.

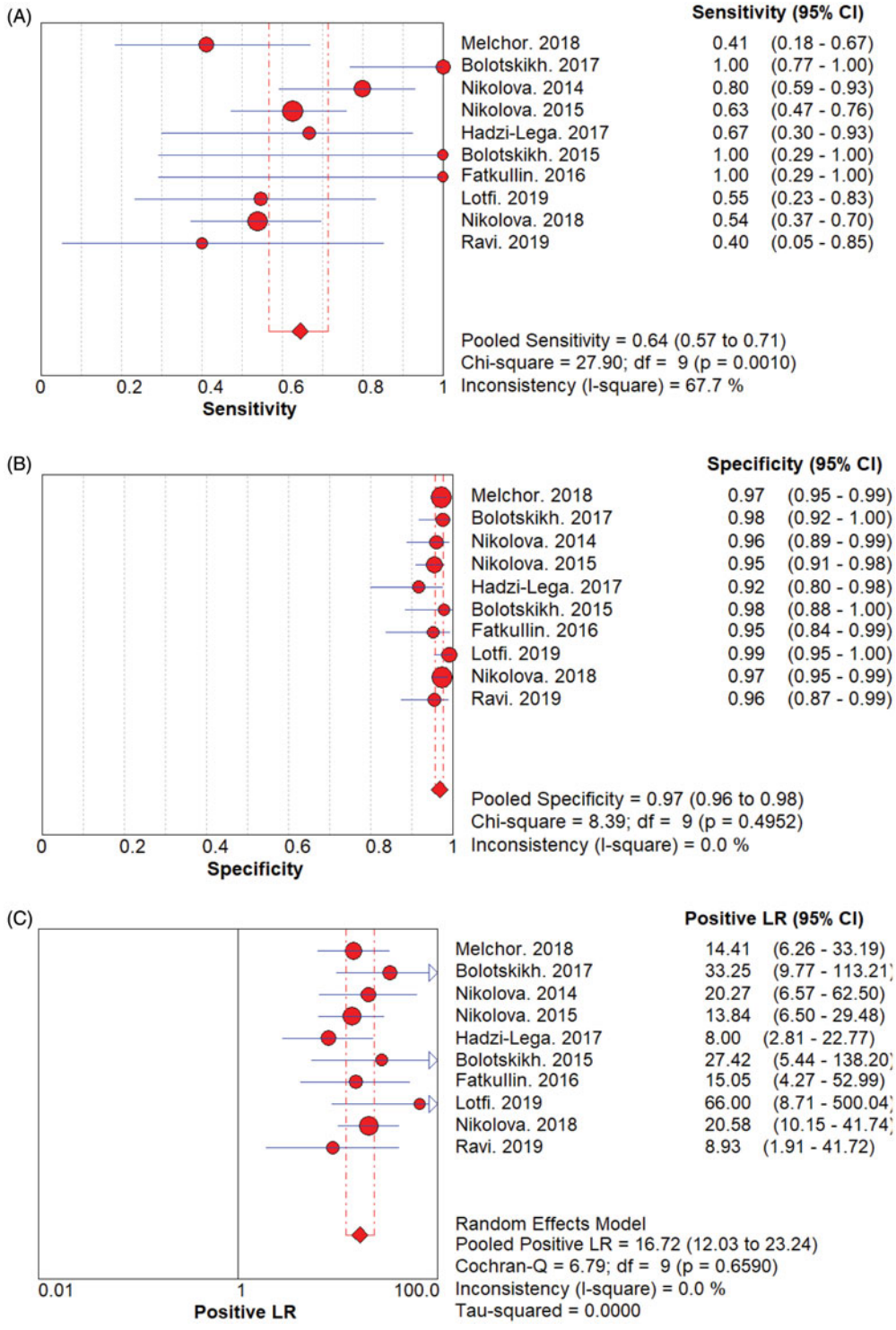

Figure 3. Pooled estimates of diagnostic indices for predicting spontaneous preterm birth within 14 d of testing using placental alpha microglobulin-1 (PAMG-1); (A) sensitivity, (B) specificity, (C) positive likelihood ratio, (D) negative likelihood ratio, (E) diagnostic odds ratio, (F) summary receiver operating characteristic curve.

Strengths and limitations

The strengths of our study were as follows: (1) Valid guidelines were used for conducting and reporting of systematic reviews of predictive test accuracy; (2) an extensive literature search was carried out without language restrictions and contacts were established with field experts; (3) overall, studies included for the assessment of diagnostic accuracy were fairly homogeneous; (4) all studies evaluated symptomatic women with intact amniotic membrane and all studies considered the same outcome; (5) the strict study quality

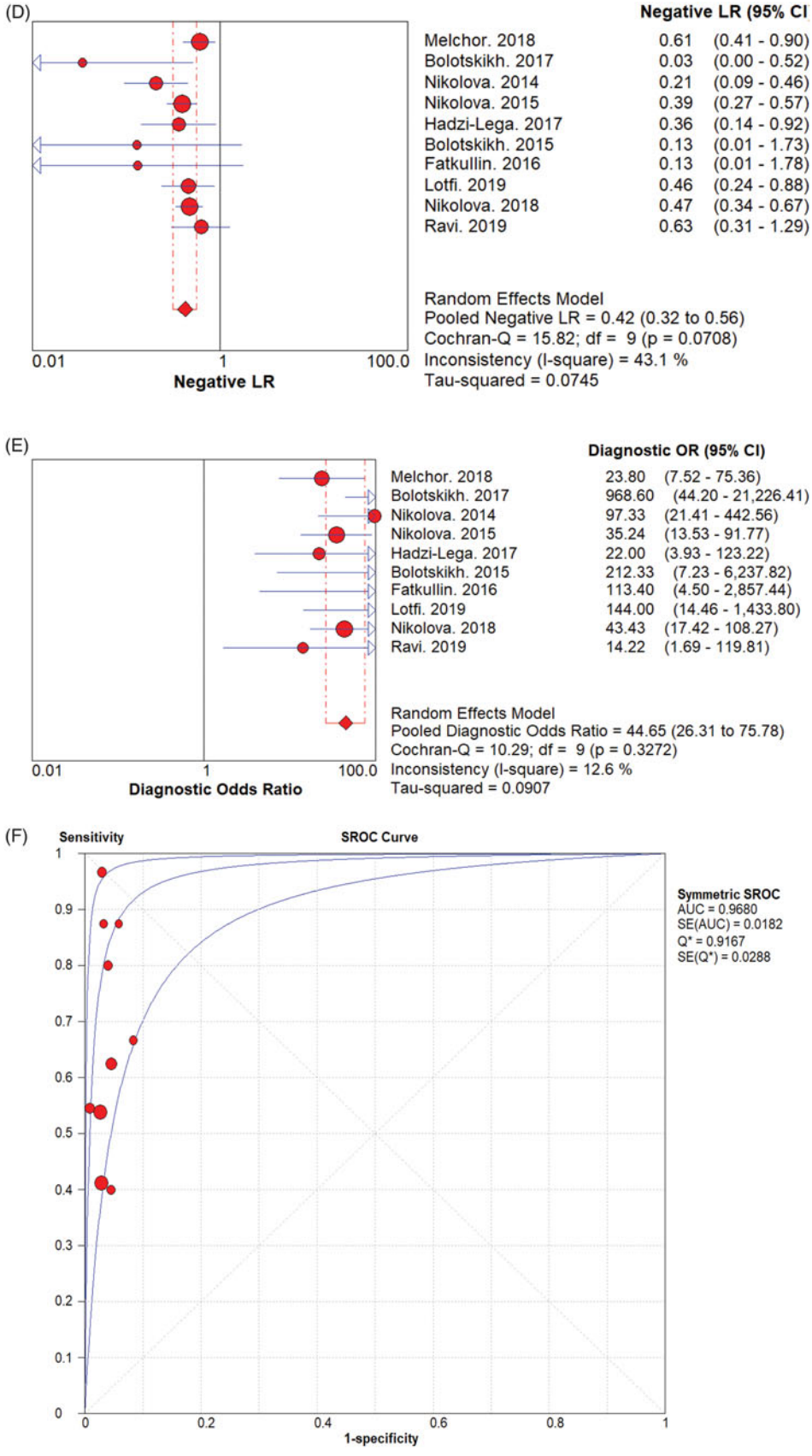

Figure 3. Continued.

assessment was done using a modified version of QUADAS-2; (6) the rigorous statistical methods were used to obtain summary measures of predictive accuracy. The limitations of our study were: (1) despite the fact that in all reviewed studies the inclusion criteria were well-defined, a number of studies did not list the exact exclusion criteria; (2) though it seems that all studies evaluated spontaneous (not iatrogenic) PB, but some studies have not exactly mentioned iatrogenic PB as an exclusion criterion; (3) there was no detailed information on the type of therapeutic interventions such as tocolytic drugs, magnesium sulfate and betamethasone in women who had positive tests. These interventions could affect the outcomes; (4) in all the reviewed studies, prediction of spontaneous PB within 7 and 14 d of testing was evaluated while they did not consider PB before 37 and 34 weeks except one study.

Conclusions

Our review showed that the cervical PAMG-1 had a high specificity and relatively high sensitivity to predict PB within 7 and 14 d of testing in symptomatic pregnant women.

Disclosure statement

There are no financial, personal or other influences for any author that may affect the objectivity of this manuscript.

ORCID

Reihaneh Pirjani http://orcid.org/0000-0002-4102-7475
Ashraf Moini http://orcid.org/0000-0002-5074-2286
Amir Almasi-Hashiani http://orcid.org/0000-0003-4434-561X
Maryam Farid Mojtahedi http://orcid.org/0000-0002-4417-1181
Samira Vesali http://orcid.org/0000-0003-0005-8045
Ladan Hosseini http://orcid.org/0000-0003-4982-4070
Mahdi Sepidarkish http://orcid.org/0000-0003-4732-6684

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