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ORIGINAL ARTICLE

Predictive factors of preterm delivery in French Guiana for singleton pregnancies: definition and validation of a predictive score

Malika Leneuve-Dorilas[a], Pierre Buekens[b], Anne Favre[a], Gabriel Carles[c], Alphonse Louis[a], Gerard Breart[d] and Mathieu Nacher[a]

[a]Cayenne Hospital Center, Cayenne, French Guiana; [b]Department of Epidemiology, School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA, USA; [c]Hospital Center of Saint-Laurent du Maroni, French Guiana; [d]INSERM, National Institute of Health and Medical Research, Paris, France

ABSTRACT

Objective: Given the high rate of premature birth in French Guiana (13.5%), and its stability in time, the aim of the present study was to define a predictive score for preterm birth in women with a unique pregnancy in order to help prioritize health resources in the local context.

Methods: A retrospective study was conducted on all deliveries of unique pregnancies in French Guiana collected between 1 January 2013 and 31 December 2014 in the Registre d'Issue de Grossesse Informatisé (RIGI), a registry that collects data on live births over 22 weeks of amenorrhea on the territory. Statistically significant predictors ($p < .05$) of preterm delivery were included in a logistic regression model. The selected variables were chosen to be available during the first trimester. Coefficients were used to establish a score which was categorized and prospectively validated using data from 2015.

Results: Seven explanatory variables, all measurable during the first trimester of pregnancy, were significantly associated with preterm birth. The predictive score divided in deciles allowed to establish sensitivity and specificity thresholds. Overall, depending on the chosen threshold the score sensitivity was low and the specificity was high. Lowering the threshold identified half of women as "at risk" for preterm birth.

Conclusion: This first trimester score was insufficiently sensitive to identify individual women at risk for preterm delivery.

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KEYWORDS
French Guiana; prediction; preterm birth; risk factors

Introduction

Preterm birth is a serious neonatal complication of single or multiple pregnancies. Premature newborns have an increased risk of death, long-term neurological complications and developmental disorders. Preterm birth is the first cause of neonatal death and the second cause of death in children aged <5 years worldwide [1,2]. The prematurity rate is thus considered as a major health indicator for a given country.

Preterm birth is defined by birth before 37 completed weeks of amenorrhea. Every year, there are 15 million preterm births worldwide, with important differences regarding the incidence rates [3]. The highest incidence rates are reported in low-income countries (12.5%), relative to medium income (8.8%) or high-income countries (7.5%). It is highest in Southern and East Africa (17.5–14.3%), in South and Southeast Asia (11.1–11.4%). In North America, preterm birth rates are estimated at 10.6%, in Europe 6.2% ranging from 5% to 10%, in Central America, it is 9.1%, in the Caribbean 6.7%, and in South America 7.9% [3–5]. French Guiana, a French territory in South America, has the highest fertility rate in Latin America (3.5%) and also has a high prematurity rate at 13.5% versus 7% in mainland France and 7.9% in South America. French Guiana's prematurity rates are high and have remained so despite efforts to improve care for pregnant women [6,7].

Multiple maternal factors have been associated with preterm birth and measures such as cervical cerclage and/or progesterone have proven to be effective in some cases. The goal of prognostic studies is not necessarily to better understand the pathophysiology of a disease but to use multiple variables to predict the risk of future outcomes with as much accuracy as possible. Many prognostic models have been developed in medicine but few are formally

CONTACT Malika Leneuve-Dorilas malika.leneuve@hotmail.fr Centre Hospitalier Andrée Rosemon de Cayenne, Avenue des flamboyants, Cayenne 97306, Guyane française/French Guiana

Supplemental data for this article can be accessed here.

validated in new patients, and even fewer are evaluated for their impact on decision making and patient outcome, and therefore, in practice, few models are actually used.

Given the stagnation of the high prematurity rate in French Guiana, and the heterogeneity of pregnant women, we aimed to better predict preterm birth in order to try to improve prevention. Using data from the deliveries registry of French Guiana, our aim in the present study was to identify the main predictors of preterm birth using unambiguous variables that are easily available during the first trimester of pregnancy. This aimed to focus health and social resources on women most at risk of preterm delivery. Hence, the predictors were routinely available and did not require invasive or subjective measures, or waiting for laboratory results, which could lead to follow up interruption. More specifically, given the reported unreliability of predictive scores between different populations, we aimed to develop and then prospectively validate a score derived from the available data in order to formalize decision making in the specific context of French Guiana.

Materials and methods

Particularities of French Guiana

French Guiana is the largest French overseas territory, situated between Brazil and Suriname. Although its area is 83,846 km^2, there are only 260,000 inhabitants mostly along the coastal region, the rest of the territory being mostly covered by primary Amazonian forest [8,9]. In these remote areas, a network of health centers care for the population. French Guiana has the highest GDP *per capita* but also the highest birth rate in Latin America. The socioeconomic inequalities are important with nearly 30% of the population being immigrants. The health system is the French System, but there are some gaps with mainland France in terms of infrastructure and health professional density. French Guiana is facing an epidemiological transition from the burden of tropical diseases toward chronic diseases. During the first study period in 2013–2014, 331 pregnancies were multiple and 12,652 were single pregnancies. In 2015, there were 195 multiple pregnancies and 6719 single pregnancies.

Type of study

This multicentric study took place in all maternities of French Guiana. The RIGI (Registre d'Issue de Grossesse Informatisé) compiles all births using a centralized platform at the perinatal health professionals' regional network. The information on pregnancies is entered in a registry at the time of delivery according to the patient's medical and obstetrical history (medical records and interview).

Variables recorded in the registry

The variables recorded in this registry are as follows: residence area, place of birth, health insurance coverage, age, family situation (in a couple or not), profession, gravidity, parity, scarred uterus, number of previous cesarean sections, type of pregnancy, number of ultrasounds, surveillance mode (gynecologist–obstetrician, midwife, general practitioner, mother and child care), the trimester at first visit, prenatal interview, preparation for birth, crude number of consultations before birth, anesthesiologist consultation, *in utero* transfer, serologic anomalies, alcohol, drugs, and tobacco consumption. The existence of a cardiopathy, chronic hypertension, diabetes, sickle cell disease, or obesity is also recorded. Other pathologies associated with pregnancy are also reported pregnancy-induced hypertension, preeclampsia, gestational diabetes, a context of preterm labor, prematurely ruptured membranes. Finally, the place of birth (home, hospital), term of birth, the mode of labor initiation, and the motive of labor induction if labor was induced, the duration of membrane rupture, the color of amniotic fluid, delivery mode (normal vaginal spontaneous, vaginal with instrumentation, cesarean section and motive), obstetrical extraction maneuvers, presentation, type of delivery, if it was associated with postpartum hemorrhage, lesions perineal lesions, type of anesthesia if there was any for the mother. The RIGI mentions sex, weight, height, cranial perimeter, trophicity, Apgar score at 1 and 5 minutes of life, lactate measurement, resuscitation, emergency procedures, congenital malformations, child outcome (if deceased, transfer), type of feeding. The history of preterm delivery, vaginal swab results are not part of the variables routinely recorded in the RIGI. All viable births occurring after 22 weeks of amenorrhea were included.

Study variables

From the list of variables that are routinely recorded in the registry, the study only used variables that could be obtained at the end of the first trimester: age, place of birth, residence area, family situation, profession, health insurance coverage, gravidity, parity, scarred uterus, prenatal interview, and preparation for birth.

The variables profession, place of birth, residence area were not used because they had many modalities and were not usable in practice. The variable preparation for birth was also not retained because it is often only performed during the second trimester.

Analysis

A descriptive analysis of data from 2013–2014 was performed and was stratified according to the outcome: preterm birth or no preterm birth.

Bivariate analysis looked for explanatory variables that were significantly associated with preterm birth. We used variables that were easily available during the first trimester in order to aim for early prediction of preterm delivery. All significant variables ($p < .05$) were then included in a multiple logistic regression model. Hosmer–Lemeshow's goodness-of-fit test was used to assess the fit of the model.

The coefficients from the final model were used to predict each individual's probability of premature delivery from the different values of the explanatory variables of this patient. The score was categorized (min/first decile, first quartile, median, third quartile ninth decile, 95% and maximum value) and was then prospectively validated using the data set from the RIGI for the year 2015. Predicted probabilities were calculated from the individual risk score using the formula $P = 1/(1 + \text{e-risk score})$. Observed and predicted preterm births were tabulated. Sensitivity and specificity, predictive values, were calculated for different values of the score. The performance of the model to predict preterm births in both datasets was evaluated using ROC curves. Data analysis was performed using R and Stata software.

We could not compare our score with other scores such as the Creasy score or the Nova Scotia score because some of the variables used in these scoring systems were not available in the registry.

Regulatory and ethical aspects

The database has been approved since 1992 by the Commission Nationale Informatique et Libertés, the French Structure that overseas medical research data and projects.

Results

The analysis of the 2013–2014 data allowed to identify the variables associated with preterm delivery. The logistic model is presented in Table 1. Age <18 years or ≥40 years were independently associated with a greater risk of preterm delivery relative to women aged 18–34 years. Single women or women for whom the information was not available there were independently more likely to give birth prematurely relative to women living in a couple. Women with no health insurance were at greater risk of preterm delivery than women with standard health insurance, whereas those with government insurance for persons with limited resources had a lower risk of preterm delivery than women with standard health insurance, perhaps reflecting the fact that those with standard health insurance work, which may have affected the risk of preterm delivery, or the fact that poorer women attend public structures specialized in maternal care, whereas those who work go to private general practice, which may be less specialized. Multigestity, and multiparity were independently associated with preterm delivery relative to primigestous and primiparous women. A history of scarred uterus was independently associated with preterm delivery. Finally, Table 1 shows that the prenatal interview was associated with a lower risk of preterm delivery.

Prematurity risk score

The risk score values taken by each woman were obtained by multiplying the beta coefficients established using the 2013–2014 model by the observed values of each variable either in 2013–2014 or in 2015 for the temporal validation study.

Validation of the score with 2015 data

Between 1 January 2015 and 31 December 2015, there were 6914 live births (after 22 weeks of amenorrhea).

Using the same logistic model gave similar results (Table 2). Figure 1 shows the similar lack of discrimination power for ROC curves for the training data set and the 2015 validation set. Figure 2 shows the evolution of sensitivity and specificity for different values of the computed score. Ultimately, a sensitivity of 50% would require a threshold that would identify half of the women as at risk for preterm delivery (Figure 3). Figure 4 shows the quantitative distribution of the score in women who ultimately delivered prematurely and those who did not, showing a bell-shaped curve.

Discussion

Scoring systems are often used in obstetrics to choose the type of delivery, to evaluate the fetus' or the newborn's condition [10–14]. There have also been various predictive scores in order to identify women at risk for

Table 1. Sociodemographic and medical factors and their link to premature delivery in French Guiana between January 2013 and December 2014.

	Number (% proportion of premature births)	OR [95%CI] adjusted	*p* value
Age (Years)			
< 18	123/797 (15.4%)	1.4 [1.1–1.8]	.003*
[18–34]	1110/9598 (11.6%)	1	
[34–40]	225/1648 (13.7%)	1.1 [0.9–1.3]	.4
≥ 40	95/575 (16.5%)	1.3 [1–1.6]	.05*
Family situation			
Living in a couple	1087/9516 (11.4%)	1	
Single	397/2767 (14.3%)	1.2 [1.1–1.4]	.002*
No information	73/369 (19.8%)	1.7 [1.3–2.2]	.0001*
Health coverage			
General health insurance	846/7226 (11.7%)		
Universal coverage (CMU)	195/1907 (10.2%)	0.8 [0.7–0.9]	.006*
State Insurance (« *Aide Médicale d'Etat* »)	109/1211 (9%)	0.6 [0.5–0.8]	.0001*
No Health Insurance	185/1191 (15.5%)	1.2 [1–1.5]	.01*
No Information	222/1117 (19.9%)	1.7 [1.4–2]	.0001*
Gestity			
Primigestity	290/2526 (11.5%)	1	
Second gestity	279/2466 (11.3%)	1.4 [1.1–1.7]	.008*
Multigestity [3–4]	402/3538 (11.4%)	1.4 [1.1–1.8]	.02*
Great multigestity [5–9]	477/3468 (13.8%)	1.6 [1.2–2.2]	.003*
Gestity >9	109/654 (16.7%)	2 [1.3–3.1]	.001*
Parity			
Primiparity	436/3585 (12.2%)	1	
Second parity	288/2827 (10.2%)	0.7 [0.5–0.8]	.001*
Multiparity Parity [3–4]	418/3386 (12.3%)	0.8 [0.6–1]	.04*
Parity [5–9]	370/2581 (14.3%)	0.8 [0.6–1.2]	.1
Parity >9	45/273 (16.5%)	0.7 [0.4–1.2]	.2
Scarred uterus			
Yes	255/1610 (15.8%)	1	
No	1302/11042 (11.8%)	0.7 [0.6–0.8]	.0001*
Prenatal interview			
Yes	18/423 (4.3%)	0.3 [0.2–0.5]	.0001*
No	1539/12229 (12.6%)	1	

The (*) sign marks statistical significance for alpha = 5%.

Table 2. The sensitivity specificity and proportion correctly classified by the prematurity score used on the 2013–2014 training data set, and the 2015 external validation set.

Risk score	Sensitivity (%)	Specificity (%)	Correctly classified (%)	VPP (%)	VPN (%)	Predicted preterm delivery (%)	Observed preterm delivery (%)	Cumulated observed preterm delivery (%)
2013–2014								
1 (Min)	100.00	0.00	12.31	5.0	10.4	9.8	6.3 (78/1232)	6.3
2 (10ème p)	94.98	10.43	20.84	16.2	22.3	21.6	9.2 (251/2723)	15.5
3 (25ème p)	78.82	32.77	38.44	14.7	17.7	17.3	10.4 (228/2188)	25.9
4 (Médiane)	64.13	50.49	52.17	27.6	26.1	26.3	12.9 (428/3316)	38.8
5 (75ème p)	36.57	76.59	71.67	18.7	14.5	15	15.3 (290/1897)	54.1
6 (90ème p)	17.90	91.12	82.10	8.3	4.5	4.9	20.5 (129/630)	74.6
7 (95ème p)	9.59	95.64	85.05	9.6	4.3	5	23.6 (149/631)	98.2
8 (Max)	0.00	100.00	87.69					
2015								
1 (Min)	100.00	0.00	11.45	8.3	10.3	5.2	9.4 (64/678)	9.4
2 (10ème p)	91.67	10.34	19.65	12.2	14.9	10.1	9.6 (94/978)	19
3 (25ème p)	79.43	25.22	31.43	21.6	26.1	14.6	9.7 (166/1714)	28.7
4 (Médiane)	57.81	51.28	52.03	24.3	24.4	25.6	11.4 (187/1637)	40.1
5 (75ème p)	33.46	75.69	70.86	21.5	14.6	24.4	16.01 (165/1030)	56.1
6 (90ème p)	11.98	90.25	81.29	8.9	4.3	15.4	21.3 (69/324)	77.4
7 (95ème p)	2.99	94.55	84.06	2.9	5.5	.8	6.6 (23/347)	84
8 (Max)	0.00	100.00	88.55					

preterm delivery [15]. The Creasy scoring system was developed in New Zealand with a sensitivity ranging from 18.2% to 62.2% and a positive predictive value ranging from 16% to 38.2%. But the use of the Creasy score in homogenous, often underprivileged, populations showed little predictive interest suggesting the poor portability of this score to different populations from the population used to establish the score. This

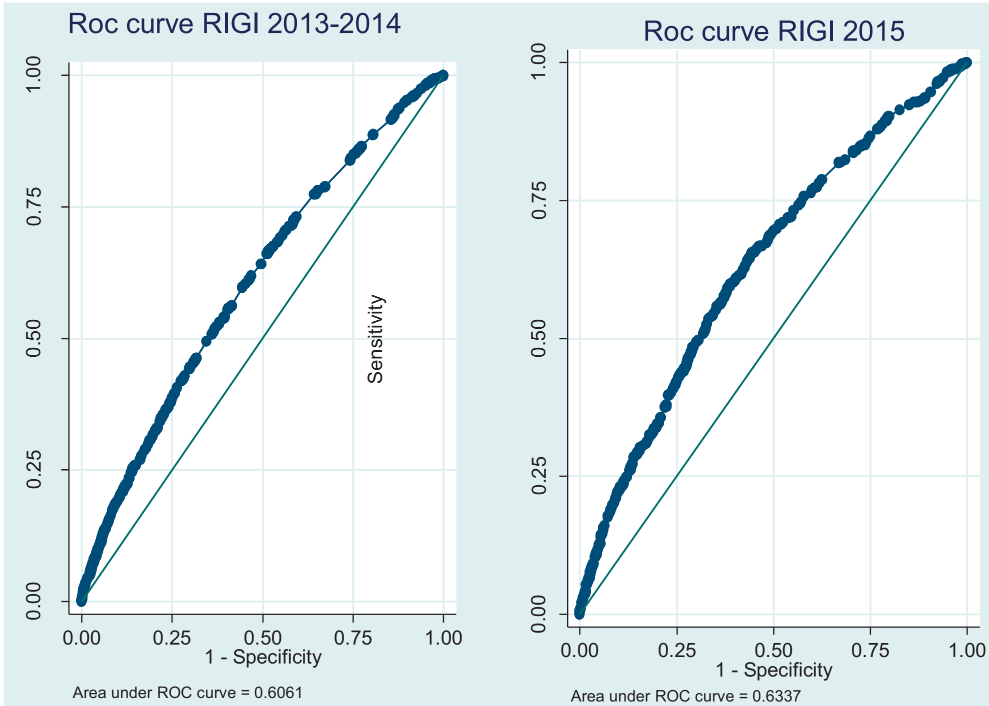

Figure 1. ROC curve for the logistic regression model using 2013–2014 data. ROC curve for the logistic regression model using 2015 data.

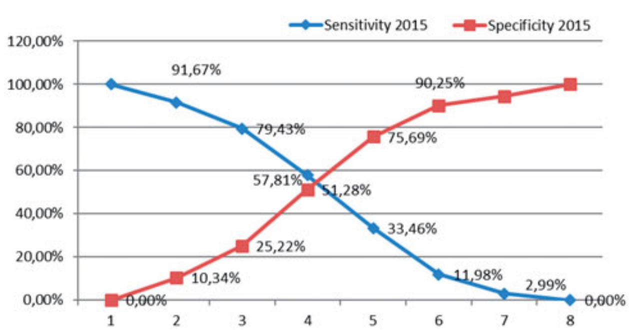

Figure 2. Evolution of sensitivity and specificity for different values of the computed score used on the 2013–2014 training data set, and the 2015 external validation set.

score in fact seemed to distinguish between at risk socioeconomic classes in New Zealand rather than between the predictive values of the variables themselves beyond New Zealand [16]. For this reason, in North America, another score was used, the Nova Scotia score, which had a sensitivity of 30.8% and a positive predictive positive value of 14.4%. More recent studies, looked at more complex predictors (serum pregnancy-associated plasma protein-A, free β-human chorionic gonadotrophin (β-hCG) and uterine artery pulsatility index) and maternal characteristics, which allowed identifying up to 38.2% of very preterm deliveries in women with previous pregnancies, and 18.4% in those without a previous pregnancy [17]. Another cohort using simple maternal variables was able to identify 23.3% percent of premature deliveries. A model combining maternal data and cervical length in the first trimester (11–13 weeks) was able to predict 54.8% of very preterm deliveries (<34 weeks of gestation (WG)). The different studies attempting to develop new scoring systems suggest that all these scoring systems are disappointing and difficult to transpose in different populations. Scores are thus often not externally validated and impact studies looking at interventions in clinical practice are lacking.

Our scoring system relied on noninvasive, low-tech variables that are available as soon as the pregnancy is known. Our aim was to identify women with no known risk factor for an increased risk of preterm birth; therefore, we excluded multiple pregnancies, a known risk factor preterm birth from the analysis. These variables are also immediately available; the women do not need to wait for biological results, or appointments, which in our territory is important given irregular follow-up. The sensitivity of the logistic model was very low, which implied that most women who eventually had preterm delivery were not identified. Depending on the threshold chosen, the categorical score was able to correctly identify over 50% of the preterm (37WG) deliveries. Our model's c index was 0.64, which is not a very high discriminative capacity.

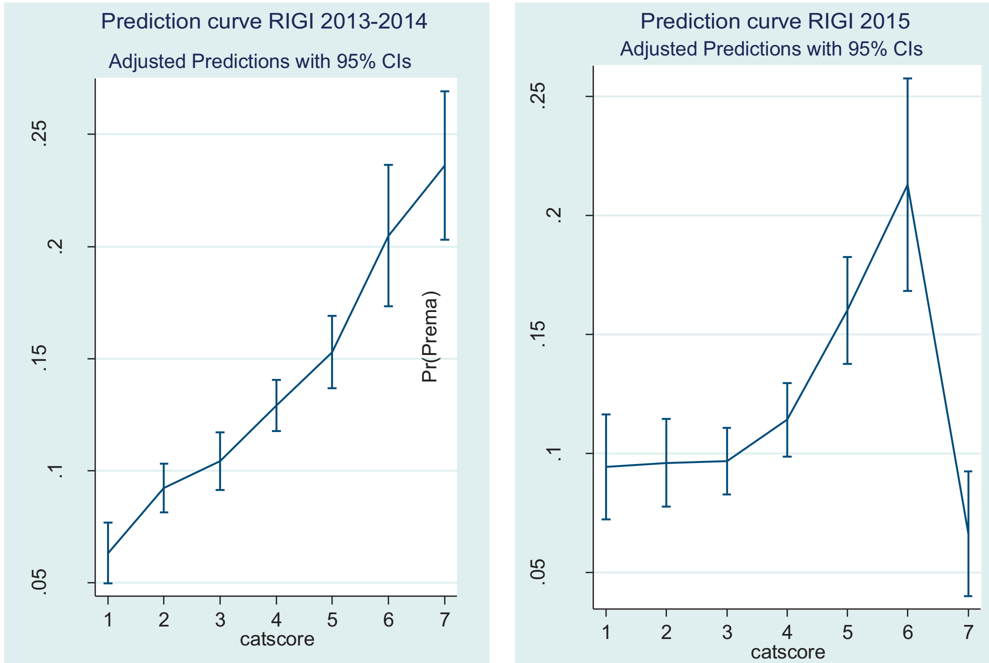

Figure 3. Predicted probability of preterm delivery using a logistic model with preterm delivery as outcome variable and the risk score as explanatory variable (indicator variables with 1 as reference) used on the 2013–2014 training data set, and the 2015 external validation set.

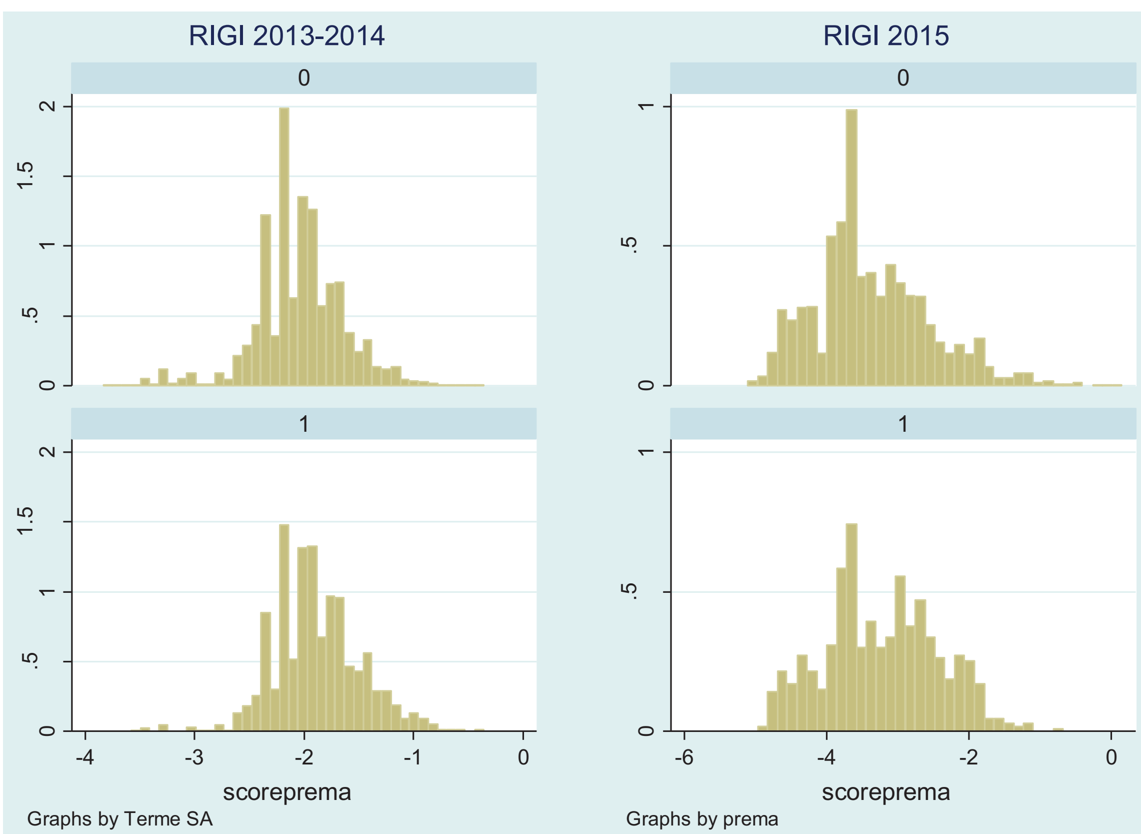

Figure 4. The quantitative distribution of the score in women who ultimately delivered prematurely and those who did not used on the 2013–2014 training data set, and the 2015 external validation set. "0" correspond to births at term and "1" correspond to preterm birth (prema).

However, when trying to increase sensitivity, the specificity of the model and of the related score dropped, leading to labeling nearly half of the population as "at risk" for preterm birth. Given the relative disappointing impact of specific medical interventions to prevent preterm birth, and their potential adverse effects, such a score could put women at risk for excessive interventionism with methods without proven benefits. This lack of sensitivity drastically compromises the usefulness of such a score in practice for individual patients. The very low sensitivity observed is consistent with the debates emphasizing that the different risk factors for preterm birth are widespread in the community and that the risk scores follow a bell curve distribution, where most women fall in the intermediate risk range. The plot of our predicted probabilities showed exactly this. This suggests that interventions should be community-wide rather than individual based. There are two reasons for this: the concentration of resources on women with the highest risk only identifies a minority of the preterm births and given the poor efficacy of interventions to prevent preterm birth, it is not very likely to significantly reduce preterm birth; actually helping most women with intermediate risks with simple social interventions may actually yield a greater reduction in the number of preterm births as observed in French cohorts following the laws on maternity leave.

There have been past debates between schools of thought refusing the fatality of preterm birth, computing risk scores leading to increased interventionism with unproven and nonharmless methods, and schools emphasizing that risk is bell shaped, multifactorial and incompletely understood; risk is thus hard to evaluate for individual patients, and interventions have adverse effects and limited efficacy [18].

However, beyond individual women, what has shown a positive impact is social interventions aiming to improve the social conditions of pregnancy in the most vulnerable social groups, a situation that is very frequent present in French Guiana, where the newborns of immigrant and uninsured mothers end up in pediatric ICU much more frequently than other groups. Single mothers, teenagers, women without health insurance, situations that are frequent in French Guiana, were here at greater risk of preterm delivery. These groups could be bridged with the help of local NGOs and health mediators working with these communities.

Conclusion

Our objective was first to identify a score focused on the population of French Guiana, which still has a high preterm delivery rate. A score was computed to try to identify women at risk for preterm delivery at the end of the first trimester. The score's performance was stable in a prospective temporal validation study. However, the low sensitivity limits its usefulness for individual pregnant women. At best, the prediction score could correctly identify 55% of preterm births during the first trimester but with a marked reduction in specificity. The limited efficacy of individual interventions aiming to prevent preterm birth combined with the low sensitivity of the score are another illustration of the elusive goal of a magic bullet like score that would allow to drastically reduce preterm birth.

Disclosure statement

The authors declare no conflict of interest regarding this study.

Availability of data and materials

The database will not be shared because it is the property of the different centers of French Guiana and the perinatal association of the country.

References

[1] Frey HA, Klebanoff MA. The epidemiology, etiology, and costs of preterm birth. Semin Fetal Neonat Med. 2016;21(2):68–73.

[2] Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832): 2162–2172.

[3] Koullali B, Oudijk MA, Nijman TAJ, et al. Risk assessment and management to prevent preterm birth. Semin Fetal Neonat Med. 2016;21(2):80–88.

[4] Blencowe H, Cousens S, Chou D, et al. Born Too Soon: the global epidemiology of 15 million preterm births. Reprod Health. 2013;10(Suppl 1):S2.

[5] Beck S, Wojdyla D, Say L, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ. 2010;88(1):31–38.

[6] Direction de la Recherche. des études. de l'évaluation et des Statistiques (DREES). La situation périnatale en France en 2010 - Premiers résultats de l'enquête nationale périnatale, Etude et résultats. 2011.

[7] Cardoso T, Carles G, Patient G, et al. Périnatalité en Guyane française: evolution de 1992 à 1999. J Gynecol Obstet Biol Reprod. 2003;32(4):345–355.

[8] Montabo B. Le Grand livre de l'histoire de la Guyane: de 1848 à nos jours. Orphie. 2004;2:384.

[9] Institut National de la Statistique et des Etudes Economiques. Tableaux economiques régionaux Guyane [National Institute of Statistics and Studies in

Economics. Regional Economic Tables French Guiana, Cayenne, French Guiana]. 2009;2010.

[10] Droulez A, Girard R, Dumas AM, et al. Prédiction de la réussite du déclenchement du travail. Comparaison entre le score de bishop et le dosage de la fibronectine foetale. J Gynecol Obstet Biol Reprod. 2008;37(7): 691–696.

[11] Pitkin RM. Commentary on pelvic scoring for elective induction: bishop EH. Pelvic scoring for elective induction. Obstet Gynecol. 2003;101(5, part 1):266–268.

[12] Schreyer P, Caspi E, Natan NB, et al. The predictive value of fetal breathing movement and bishop score in the diagnosis of "true" preterm labor. Am J Obstet Gynecol. 1989;161(4):886–889.

[13] Manning FA, Snijders R, Harman CR, et al. Fetal biophysical profile score. VI. Correlation with antepartum umbilical venous fetal pH. Am J Obstet Gynecol. 1993;169(4):755–763.

[14] Eun S, Lee JM, Yi DY, et al. Assessment of the association between Apgar scores and seizures in infants less than 1 year old. Seizure. 2016;37:48–54.

[15] Papiernik E, Grangé G. Prenatal screening with evaluated high risk scores. J Perinat Med. 1999;27(1): 21–25.

[16] Owen J, Goldenberg RL, Davis RO, et al. Evaluation of a risk scoring system as a predictor of preterm birth in an indigent population. Am J Obstet Gynecol. 1990;163(3):873–879.

[17] Sananes N, Meyer N, Gaudineau A, et al. Prediction of spontaneous preterm delivery in the first trimester of pregnancy. Eur J Obstet Gynecol Reprod Biol. 2013; 171(1):18–22.

[18] Papiernik E. Preventing preterm birth – is it really impossible?: a comment on the IOM report on preterm birth. Matern Child Health J. 2007;11(5):407–410.