Predictive modeling of emergency cesarean delivery

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Abstract

Objective
To increase discriminatory accuracy (DA) for emergency cesarean sections (ECSs).

Study design
We prospectively collected data on and studied all 6,157 births occurring in 2014 at four public hospitals located in three different autonomous communities of Spain. To identify risk factors (RFs) for ECS, we used likelihood ratios and logistic regression, fitted a classification tree (CTREE), and analyzed a random forest model (RFM). We used the areas under the receiver-operating-characteristic (ROC) curves (AUCs) to assess their DA.

Results
The magnitude of the LR+ for all putative individual RFs and ORs in the logistic regression models was low to moderate. Except for parity, all putative RFs were positively associated with ECS, including hospital fixed-effects and night-shift delivery. The DA of all logistic models ranged from 0.74 to 0.81. The most relevant RFs (pH, induction, and previous C-section) in the CTREEs showed the highest ORs in the logistic models. The DA of the RFM and its most relevant interaction terms was even higher (AUC = 0.94; 95% CI: 0.93–0.95).

Conclusion
Putative fetal, maternal, and contextual RFs alone fail to achieve reasonable DA for ECS. It is the combination of these RFs and the interactions between them at each hospital that make it possible to improve the DA for the type of delivery and tailor interventions through prediction to improve the appropriateness of ECS indications.
Introduction

A worrisome issue in obstetrics is the longstanding increase in cesarean section rates, as well as the unjustified variations in these rates in clinical practice across public and private hospitals worldwide[1–3]. This is particularly important in the case of emergency (i.e., unscheduled) cesarean section (ECS) rates, assuming that the appropriateness of indications for scheduled C-sections is reasonably acceptable and much higher than that for ECSs [4–11]. Heterogeneity in clinical decision-making should always be investigated when unjustified variations are suspected. Knowing the fetal, maternal, and contextual factors that drive the decision to perform an ECS at each hospital is paramount to designing and implementing hospital-tailored interventions specifically aimed at improving the appropriateness of indications for ECSs in order to avoid unnecessary ECSs and the associated complications and costs [12–22].

Few current clinical guidelines and interventions target these objectives [23–29]. Those that do are neither based on a comprehensive set of proven fetal and maternal risk factors (RFs) with high discriminant accuracy (DA) nor designed to take into account contextual factors that have been shown to be associated with both an increased rate of unnecessary ECSs and unjustified variations in clinical practice. Furthermore, most RFs for ECSs should be considered putative, since they have mainly been selected by means of logistic regression models that usually lack information regarding both their goodness-of-fit and their DA [30–38]. Traditional measures of association alone are inappropriate to discriminate between who will suffer a given outcome and who will not. Therefore, interventions based on average risk estimates for people both exposed and unexposed to spurious RFs could be ineffective, inefficient, and even potentially harmful [12–22].

To our knowledge, very few studies have sought to improve the ability to predict which women are at higher risk of ECS. Those that do are limited to nulliparas, include only a few of the putative RFs, and report no measures of either calibration or DA of the statistical models developed [30–38]. Our objective is not to build an explanatory model of the decisions to perform an ECS, but to increase the predictive accuracy regarding this type of delivery in order to provide more validated information with the ultimate view to improving the appropriateness of indications for ECS and thus preventing unnecessary C-sections.

Material and methods

The present study is part of a large multifaceted intervention intended to improve the appropriateness of the indications for ECSs in 22 public hospitals of the Spanish National Health Service launched by the Spanish Ministry of Health. Of those 22 participating hospitals, four (A, B, C, and D) were included in this study because their databases were the most reliable in terms of consistency and coverage to ensure that robust predictive models of ECSs could be built. In size and complexity, the obstetric services of these four hospitals belong to level II (out of III) of the Spanish National Hospital Catalogue. They can be considered representative of about 42% of all obstetrics services of the Spanish National Health Service that belong to this level, since they all have a very similar case mix, and attend pregnant women with similar obstetric risk.

The study population consisted of all 6,157 singleton births, with no exclusions, occurring in 2014 at four public hospitals located in three different autonomous communities of Spain. According to the Spanish National Institute of Statistics, these 6,157 births account for 1.5% of all yearly births in Spain (around 420,000/year). Hospitals A and B account for 26.5% of all births occurring yearly in the Autonomous Community of the Balearic Islands, Hospital C for 12.6% of those occurring in Galicia, and Hospital D for 2.0% of those occurring in Valencia (https://www.datosmacro.com/demografia/natalidad/espana-comunidades-autonomas).
Data were collected prospectively over 2014 and registered in a specifically designed database that included the fetal, maternal, and contextual independent variables (Table 1 and S1 Tables). All presentations were included in the analysis. All variables put forth in the medical literature as predictive variables (putative PFs) of the type of delivery were in principle considered in the study with few exceptions. Since birth weight is a post-delivery variable, it cannot be predictive of the type of delivery. The estimated preterm fetal weight could be considered a potential predictive variable. However, it is barely used given that its measurement is very imprecise ($\pm 400$ g) [1, 4, 6–10].

Unlike other predictive models published, we additionally included hospital fixed-effects and night-shift delivery as potentially predictive contextual independent variables. They are unobserved effects of hospital (contextual) characteristics that are not captured by any of the independent variables included in the models. They may be predictive of the type of delivery, account for a certain fraction of the medical variations (total variance) of ECSs often found in small area analysis, and modify the strength of the associations of the independent RFs and the

Table 1. Fetal, maternal, and contextual covariate definition and categorization.

| Covariates                  | Covariate categorization                  |
|-----------------------------|------------------------------------------|
| Age                         | $< 35$ or $\geq 35$ years                |
| Mother’s weight             | $> 90$ kg                                |
| Mother’s height             | $\leq 1.5$ μ                             |
| Mother’s Body Mass Index (BMI) | $\leq 35$ op $> 35$                      |
| Gestational age             | $\leq 36$ weeks                          |
| Previous pregnancies        | No (0) or Yes ($\geq 1$)                |
| Smoker                      | Yes or No                                |
| Previous C-section          | 0 or $\geq 1$                            |
| Comorbidity$^1$             | Yes ($\geq 1$) or No                     |
| Obstetric risk$^2$          | Yes or No                                |
| Labor induction$^3$         | Used or Not used                          |
| Intrapartum (scalp) pH      | $< 7.20$ or $\geq 7.20$                 |
| Night-shift delivery        | Yes (C-section initiated between 9 p.m. and 4 a.m.) or No (initiated between 4 a.m. and 9 p.m.) |
| Fetus gender                | Male (0) female (1)                      |

$^1$Defined as having one or more of the following comorbidities during pregnancy: anaemia, asthma, heart disease, coagulopathy, type I and II diabetes in pregnancy, treated autoimmune disease, treated epilepsy, treated mental disease, treated neurological disease, treated renal disease, hemiplegia, treated liver disease, treated hyper and hypotriiodism, HIV infection, chronic hypertension, idiopathic thrombocytopenic purpura, malignant tumor, hepatitis C and B virus, amniocentesis, corial biopsy, cordocentesis, cannabis, cocaine, heroin, other drugs, disseminated intravascular coagulation, colestasys, corioamnionitis, pathological Doppler result, chronologically prolonged pregnancy, fetal death, stained amniotic fluid, pathological non-stress test, oligoamnios, small for gestational age, pre-eclampsia, premature rupture of membranes, prolonged pregnancy.

$^2$Defined as the presence during pregnancy of one or more of the following factors that increase the chance of an adverse pregnancy outcome: cholestasis, chorioamnionitis, diabetes insulin and non-insulin dependent, chronologically prolonged pregnancy, multiple pregnancy, hellp syndrome, hypertension, isoimmunization in pregnancy, stained amniotic fluid, fetal malformation, uterine malformation, fetal malposition, myomectomy, oligoamnios, previous preterm labor, placenta praevia, polyhydramnios, preeclampsia, premature rupture of membranes, siphylis, toxoplasmosis, previous c-section, repeated abortions, previous miscarriages, anteparturm alteration of fetal wellbeing.

$^3$All labors started by administering oxytocin or prostaglandins when indicated.

https://doi.org/10.1371/journal.pone.0191248.t001
type of delivery. They are not explanatory of the type of delivery, but their association with it may be indicative of different entrenched, difficult to measure clinical practices across hospitals that are likely to influence the decision regarding the type of delivery and therefore they warrant further investigation. Night-shift delivery was also included as an additional potentially predictive contextual independent variable, since it has been shown to be both a good predictor of the delivery mode, and an appropriate instrumental variable to infer causal associations between the average treatment effect of non-medically indicated cesarean sections (compared with vaginal delivery) on newborn’s health outcomes [39].

Descriptive statistics were calculated for all fetal, maternal, and contextual variables. Scheduled, emergency, and overall (both scheduled and emergency) C-sections were estimated for the whole population and for each hospital with their corresponding 95% CI.

The first step in our analytical approach to identify RFs for ECS was to calculate the prevalence of each putative RF in the overall population and in mothers delivering both by vaginal birth and by ECS, as well as their 95% CI. We then estimated the prevalence ratios of each RF (by dividing the prevalence of the RF by the prevalence of ECS). Finally, we estimated the positive likelihood ratios (LR+) of each RF and their 95% CIs. (A LR+ >10 is considered high enough to rule in the outcome, 5–10 is considered moderate, and 2–5 is considered low [40–47].

The second step was to build a logistic regression model for each of the four hospitals included in the study (A, B, C, and D), as well as a logistic model for the overall sample to find out which fetal, maternal, and contextual RFs (independent variables) were associated with the outcome (delivery type: vaginal or ECS), as well as the strength of the associations found. Model specification was performed based on stepwise top-bottom variable selection, and taking into consideration the clinical relevance of each variable. Crude and adjusted ORs were obtained, as well as their 95% CIs. The models’ goodness-of-fit was compared by means of the -2log-likelihood ratios and the Akaike information criterion (AIC). Their DA was assessed through their areas under the receiver-operating-characteristic (ROC) curves (AUCs) along with their 95% CI.

We then fitted a classification tree (CTREE or conditionally unbiased inference classification tree), a relatively new and useful predictive technique for studying RFs and outcomes based on the unbiased recursive splitting of the study population sample into subgroups according to the independent variables [48]. The underlying mathematical algorithm chooses which independent to split, their discriminatory value, and the order in which the splitting occurs. Outcome discrimination can thus be maximized at each step, making it possible to account for complex relationships between variables and their interactions and preventing both over-fitting and biased variable selection. The process develops a hierarchical tree structure that enables such simultaneous analyses and presents them in a clinically useful format [48–50].

Unlike CART models, CTREE can handle datasets with both categorical and numerical variables without producing biased splits, and the interpretation of both odds ratios and likelihood ratios is straightforward. Therefore, we used dichotomous variables to enable comparisons with other published studies despite a small potential loss of information. All births were included in the analysis, and anonymity was preserved. A database was constructed by two computer engineers, who also managed the transfer of data. Database quality was periodically audited and was considered reliable in terms of consistency, coverage, and agreement. The database is available upon request. The Spanish Ministry of Health approved this study under the Strategy for Assistance at Normal Childbirth in the National Health System (PI/01445).

We also developed a random forest model (RFM) that fits n classification trees by randomly selecting predictors for each tree. CTREE was used as the base learner, and 500 different trees were created by bootstrapping, rendering more accurate predictions than a single tree analysis.
This algorithm allows to estimate the relative importance of each independent variable in the model (i.e. the contribution of each independent variable to the predictive power of the random forest). The methodology to compute relative importance of each variable (known as conditional permutation importance), and more information regarding CART, CTREE, and RFM can be found elsewhere [48–50]. We also compared the models’ discriminatory performance by means of their corresponding ROC curves. Goodness-of-fit analysis across the abovementioned models was performed using in-sample (n = 6,157) data with ROC curves. The statistical analyses were performed using R Statistical Software (Foundation for Statistical Computing, Vienna, Austria) [49, 50].

**Results**

ECS rates varied from 8 to 15% across hospitals, whereas overall C-section rates were higher (12–21%) (Table 2). Descriptive population statistics are shown in Table 3. Mothers delivering by ECS were slightly older, had higher BMIs and weight, were more likely to have had a previous C-section, had more comorbidity, presented greater obstetric risk, more often underwent labor induction and delivered during the night shift, and had a slightly lower gestational age, and intrapartum (scalp) pH than those who had eutocic deliveries. No differences were found regarding smoking during pregnancy (Table 4).

The prevalence of the putative RFs for ECS in the overall population, as well as in eutocic and ECS deliveries, is shown in Table 5. In the overall population, the RFs with the highest prevalence (over 40%) were previous pregnancies, night delivery, BMI ≥ 25, and obstetric risk. The prevalence of all RFs except smoking and parity was higher in women delivering by ECS.

### Table 2. Emergency and overall (scheduled and emergency) cesarean rates by hospital.

|          | Number | Emergency rate (%) | 95% CI | Overall rate (%) | 95% CI |
|----------|--------|--------------------|--------|------------------|--------|
| Hosp. A  | 1,923  | 8                  | 7–9    | 14               | 13–15  |
| Hosp. B  | 893    | 9                  | 8–10   | 12               | 11–13  |
| Hosp. C  | 2,458  | 15                 | 14–16  | 21               | 20–22  |
| Hosp. D  | 883    | 11                 | 10–12  | 15               | 14–16  |
| Total    | 6,157  | 11                 | 11     | 17               | 17     |

https://doi.org/10.1371/journal.pone.0191248.t002

### Table 3. Descriptive population statistics.

| Numeric Variables              | Mean    | Std. Dev |
|--------------------------------|---------|----------|
| Mother’s age (years)           | 31.89   | 5.41     |
| Mother’s weight (kg)           | 66      | 13.7     |
| Mother’s height (m)            | 1.62    | 0.06     |
| Previous pregnancies (No.)     | 1.23    | 1.25     |
| Gestational age (weeks)        | 39.2    | 1.78     |
| Categorical Variables          | Percentage | Number   |
| Smoker (Yes, No)               | 12.2    | 6,157    |
| Previous C-section (Yes, No)   | 11.3    | 6,157    |
| Comorbidity (Yes, No)          | 17.4    | 6,157    |
| Obstetric risk (Yes, No)       | 40.6    | 6,157    |
| Labor induction (Yes, No)      | 22.7    | 6,157    |
| Scalp pH < 7.20                | 9.3     | 6,157    |
| Night-shift delivery (Yes, No) | 45.3    | 6,157    |
| Fetus gender (male)            | 52.1    | 6,157    |

https://doi.org/10.1371/journal.pone.0191248.t003
than in those with eutocic deliveries according to their 95% CI. All prevalence ratios were 6% or lower, and the LR+ of all individual RFs were low (4.14 or lower).

The gender of the fetus was neither associated with the type of delivery nor improved either the calibration (-2 log likelihood ratios, AIC) or the discriminant accuracy (C statistic) of the final models. Therefore, it was excluded from the final logistic models. BMI was finally

### Table 4. Distribution of fetal, maternal, and contextual variables by delivery type.

| Independent variables          | Vaginal birth | Emergency C-sections | p-value |
|--------------------------------|--------------|----------------------|---------|
| Age (years)                    | 31.46        | 32.83                | <0.001  |
| Weight (kg)                    | 65.7         | 67.9                 | <0.001  |
| Height (m)                     | 1.63         | 1.61                 | <0.001  |
| BMI                            | 23.96        | 26.66                | <0.001  |
| Gestational age (weeks)        | 39.3         | 38.8                 | <0.001  |
| Fetus gender (%)               | 51.5         | 55.3                 | 0.065   |
| Previous pregnancies (mean)    | 1.125        | 1.257                | <0.001  |
| Smoker (%)                     | 11.9         | 13.4                 | 0.256   |
| Previous C-sections (%)        | 10.1         | 22.4                 | <0.001  |
| Comorbidity (%)                | 17           | 25                   | 0.014   |
| Obstetric risk (%)             | 35           | 58                   | <0.001  |
| Labor induction (%)            | 20           | 43                   | <0.001  |
| Intrapartum pH                 | 7.296        | 7.245                | <0.001  |
| Night-shift delivery (%)       | 44           | 55                   | <0.001  |

https://doi.org/10.1371/journal.pone.0191248.t004

### Table 5. Prevalence ratios and positive likelihood ratios of the putative risk factors for emergency C-sections.

|                          | Overall prevalence | 95% CI | Prevalence eutocic deliveries | 95% CI | Prevalence emergency C-sections | 95% CI | Prevalence ratio | LR+ | 95% CI |
|--------------------------|--------------------|--------|-------------------------------|--------|---------------------------------|--------|-----------------|-----|--------|
| Smoker                   | 12                 | 12,12  | 12                            | 12,12  | 13                              | 12,14  | 1.104           | 1.08| 1–1.16 |
| Previous C-section       | 11                 | 11,11  | 10                            | 10,10  | 22                              | 20–24  | 1.028           | 2.2 | 2–2.4  |
| Comorbidity              | 17                 | 17–17  | 17                            | 16–18  | 25                              | 23–27  | 1.585           | 1.47| 1.38–1.56 |
| Obstetric risk           | 41                 | 40–42  | 38                            | 37–39  | 58                              | 56–60  | 3.69            | 1.52| 1.47–1.57 |
| Previous pregnancies     | 68                 | 67–69  | 69                            | 68–70  | 68                              | 66–70  | 6.221           | 0.98| 0.95–1.01 |
| Induction                | 23                 | 22–24  | 20                            | 19–21  | 43                              | 41–45  | 2.062           | 2.15| 2.05–2.25 |
| Scalp pH                 | 9                  | 9,9    | 7                             | 7,7    | 29                              | 27–31  | 2.636           | 4.14| 3.85–4.42 |
| Night-shift delivery     | 45                 | 44–46  | 45                            | 44–46  | 55                              | 53–57  | 4.114           | 1.22| 1.17–1.26 |
| Mother’s weight (> 90kg) | 3                  | 3,3    | 5                             | 5,6    | 9                               | 8,10   | 1.08            | 1.03| 1.01–1.06 |
| Mother’s height (< 1.50 m)| 3                  | 3,3    | 3                             | 3,3    | 5                               | 4,6    | 1.14            | 1.03| 1.01–1.04 |
| Gestational age (≤ 36 weeks) | 6              | 5,6    | 5                             | 4,6    | 15                              | 13–17  | 1.22            | 1.11| 1.06–1.13 |
| BMI ≥ 25                 | 41                 | 40–42  | 37                            | 35–39  | 51                              | 49–53  | 3.611           | 1.37| 1.32–1.43 |
| Age ≥ 35                 | 27                 | 26–28  | 26                            | 25–27  | 34                              | 32–36  | 2.441           | 1.3 | 1.23–1.38 |

https://doi.org/10.1371/journal.pone.0191248.t005
included since it did not make any difference to include height and weight separately or BMI in terms of both the calibration (AIC) and the discriminant accuracy (C statistic) of the models. We did choose the most parsimonious models as the final ones. Gestational age was also excluded from the final logistic models due to its high collinearity with the rest of the independent variables that remained in the model for each hospital, and because its inclusion led to biased intercept estimates of these logistic models.

According to the final logistic regression model for the overall population (Table 6), all RFs except for the number of previous pregnancies were positively associated with ECS. The strongest associations were those found for scalp pH (OR = 5.56), Hospital C (OR = 2.69), induction (OR = 2.32), and previous ECS (OR = 2.28). The remaining ORs were lower than 1.5, although the lower limits of their 95% CI were greater than 1.0. The only inverse association found was that between parity and ECS (OR = 0.87). With regard to the contextual variables, hospital fixed-effects and night-shift delivery were also positively associated with ECS. The strongest association was found with Hospital C, what is consistent with its substantial relative importance found in the random forest (Table 7).

The strength of the positive associations was relatively similar in the models for each of the four hospitals and in the model for the overall population. Although pH, induction, and previous ECS appear to be the RFs with the highest ORs, and age and BMI those with the lowest, their relative magnitude at each hospital varied slightly, except for pH, which was substantially higher at one hospital (OR = 7.17). Parity was positively associated with ECS at only one hospital, whereas obstetric risk was positively associated with it at only two.

The logistic model for the overall population and those for each hospital fit the data well, as indicated by both the -2log-likelihood ratio and the Akaike criterion.
the population model increased notably when hospital fixed-effects were included. The DA of all five models was notably high, with AUCs ranging from 0.74 to 0.81 (Table 6).

Of the two recursive partitioning models (CTREE and Random Forest), CTREE was used as the base learner for the Random Forest algorithm (n = 500). Fig 1 depicts the tree structure of the trained CTREE. The first split \( p < 0.001 \) is scalp pH, followed by labor induction and previous ECS, for pH \( \geq 7.20 \) and pH \( < 7.20 \) respectively, meaning that if the pH \( \geq 7.20 \), the

Table 7. Relative importance of each putative risk factor for type of delivery according to the random forest.

| Variable          | Relative importance |
|-------------------|---------------------|
| Scalp pH          | 100                 |
| Previous C-section| 76.712              |
| Induction         | 31.755              |
| Hosp. C           | 29.895              |
| BMI               | 27.854              |
| Hosp. A           | 20.03               |
| Obs. risk         | 11.635              |
| Age               | 9.002               |
| Pregnancies       | 4.901               |
| Hosp. D           | 3.709               |
| Smoker            | 3.194               |

https://doi.org/10.1371/journal.pone.0191248.t007

Fig 1.

https://doi.org/10.1371/journal.pone.0191248.g001
next split is birth induction ($p < 0.001$), whereas if the pH $< 7.20$, the next split is previous ECS ($p = 0.003$). The interpretation extends to the conditional nodes (splits) and leaves. By way of example of the meaning and utility of hospital effects, on the extreme right side of Fig 1 it can be seen that mothers whose fetuses had a scalp pH $> 7.20$ and had not had a previous ECS, in hospital D had a probability of almost 48% of having an ECS, whereas in the other hospitals (A, B, and C) this probability went down to 27%. The AUC mean value of the CTREE was 0.88 (95% CI: 0.84–0.92).

The RFM consisted of a set of $n = 500$ CTREEs with an optimal number of randomly selected variables = 2. Although random forest algorithms tend to be more of a black box in terms of their interpretation, their predictive power (AUC = 0.94; 95% CI: 0.93–0.95) provides reliable predictions even at an individual level. The relative variable importance of all variables included in the RFM is shown in Table 7. The three most relevant RFs (pH, induction, and previous ECS) also showed the strongest associations in the logistic models. Since the LR+ of all the interaction terms found in the RFM were lower than 10, as was the case for the individual RFs (Table 5), they failed to rule in the type of delivery.

**Discussion**

The strength of the associations between some putative RFs and ECS, their prevalence, their prevalence ratios, and their LR+ in the overall population were low to moderate, indicating, as in other studies, that single RFs alone offer only a low DA for most outcomes, such as ECS [40–47].

With the exception of scalp pH, the magnitude of the strength of these associations was low and similar across the four hospitals. Likewise, all were positive except for the number of pregnancies, which showed an inverse association. Heterogeneity did not seem to play a relevant role in the study population solely on the basis of this initial analysis. Moreover, only the number of pregnancies seemed to increase the odds of a vaginal delivery, as would be expected.

In the final logistic model for the overall population both contextual variables (hospital fixed-effects and night-shift delivery) were positively associated with ECS and increased goodness-of-fit. These variables were associated with higher ECS rates and may thus favor the indication of ECS over vaginal deliveries. Regardless of maternal and fetal characteristics, and as indicated in a number of studies, different entrenched practices across hospitals seem to influence the decision regarding delivery type, similar to how physicians’ desire for night-time leisure influences the decision to perform an ECS at the start of the night shift [4–11, 39].

No single 100% accurate predictive model of the type of delivery has been published to date. In fact, only a few have been published all showing a low predictive and discriminant accuracy. All these contextual (hospital) factors that may contribute both to predict and explain variations in both the type of delivery and in the appropriateness of the c-section’s indications (as shown by the high variability of rates of c-sections in several published atlases of variations in medical practice) remain unobserved and unknown. The only available way to account for them is by including hospital fixed-effects in logistic models and in random forests as contextual variables (which are tantamount of the second level variables in multilevel analyses). Moreover, their inclusion in the models reduced the biases in the estimates of the measures of strength of the associations without resulting in overfitting, and increase their discriminant accuracy because they account for the abovementioned unobserved predictive factors [4–11, 39].

These results illustrate the usefulness of this analytic approach because they suggest that some hospital characteristics (i.e., method of payment and other incentives, physicians’ desire for night-time leisure, established non-evidence-based practices such as to perform a c-section
to mothers having had a previous c-section) may explain unjustified variations and inappropriateness of some indications for c-sections that warrant further investigation.

Consequently, all fetal, maternal, and contextual factors alone failed to achieve a reasonable DA for ECS rates in different population subgroups at each hospital even after they were controlled for in these models. This is consistent with the well-known fact that the decision regarding the type of delivery hinges not only on different combinations of these RFs and the interactions between them, but also to some extent on variations across individual hospital practices and even individual clinicians’ practices. It can thus be the product of unjustified non-evidence-based clinical practices, which has long been shown in studies of variations in clinical practice with regard to CS using small area analysis [4–11].

Measures of association alone are insufficient to discriminate between those individuals who will develop a given outcome and those who will not (a strong association is not tantamount to high DA given that the false positive and false negative fractions of the population are low) [40–43]. It is the set of independent variables included in the final logistic models that could make it possible to achieve acceptable DA, as shown by their high AUC (0.75–0.81). To our knowledge, no logistic regression model published to date has achieved an AUC similar to those reported here.

The AUCs of the RFM (0.93–0.95) and the CTREE (0.84–0.92) offer a considerably improved additional analytical approach to the same issue due to the nature of their optimization algorithm, maximum likelihood for logistic and unbiased recursive partitioning for CTREE. Their incremental DA is notably higher than that of logistic models due to the unsupervised detection of interactions in the CTREE model and 500 such CTREEs in the RFM. The reasons for this improvement in DA are mainly twofold. First, it results from detecting associations and interactions among the combinations of RFs used in clinical decision-making regarding the type of delivery at each hospital that are not captured by logistic models. Second, the model also captures heterogeneity (the trees’ branches), among both the hospitals and the clinicians’ decision-making frameworks, that logistic models likewise cannot capture.

In terms of implications for clinical practice, we found some medically unjustified differences in ECS rates for hospital D compared to the other hospitals, e.g., in induced births between 11 p.m. and 3 a.m. in which the scalp pH was above 7.20 (nodes 2, 16, and 20). Moreover, in the subgroups of deliveries with pH above 7.20 and at least one previous C-section (nodes 25 and 26), the ECS rates climbed to 50% and almost 60%, respectively. The utility of these results lies in that, despite they are neither explanatory not confirmatory, they suggest potential sources of inappropriate ECSs in Hospital D (contextual factors) that should be further investigated (i.e., changes in payment methods, lack of updated clinical guidelines, lack of utilization management, demand side issues).

One of the main limitations of this study is that only 4 out 22 obstetrics services were included as explained in the Introduction. These four hospitals could be considered representative of up the 42% of hospitals within the Spanish National Health Service in terms of obstetric case mix, obstetric risk, and number of births and CS rates. However, it is to be expected that studies intended to build a predictive model for the type of delivery fail to have a high external validity with regard to the specific RFs for ECS. As already noted, it is the combination of RFs (fetal, maternal, and contextual) at each particular hospital and the interactions between them what makes it possible to improve the DA for the type of delivery. The more the clinical practice varies across centers and clinicians, the more different RF-combination subgroups can be expected to appear in the CTREES given their higher ability to capturing them; hence, the more hospital-specific the combination of RFs and interactions between them yielding the highest DA will be. Given that we performed a 10-fold cross-validation using randomly
allocated 90/10% training/test sample sizes, the chances of the RFM being overfitted and the AUCs being overestimated are very low.

Another limitation of the study is that scalp pH is a very proximate measure likely linked to fetal distress, so it is not a surprise that it is highly predictive. We did not include cord pH because it is a post-delivery endpoint and as such cannot be considered a predictive variable of the type of delivery. We could agree that scalp pH is linked to fetal distress and can be highly predictive. However, we have included it in the models as a predictive variable for several reasons: i) scalp pH is an intrapartum variable, not a final endpoint. Variations in the cut-off points actually used in clinical practice may explain both variations in the diagnosis of fetal distress, and in the fraction of appropriate and inappropriate indications for ECSs across hospitals (as it have been shown is studies of the appropriateness of the different types of emergency ECSs indications, in this particular case, fetal distress); ii) it has also been shown that both the clinical management of intrapartum (scalp) pH and thus of fetal distress varies across hospitals, and that it accounts for a considerable fraction of inappropriateness of ECSs for this specific indication, what could make scalp pH a predictive variable for some but not all ECSs; and iii) tenfold cross validation performed in the CTREE model prevented from obtaining overfitted estimates when including this variable.

Therefore, this study’s main contribution is that the information provided by the combination of logistic regressions and CTREES can provide more accurate information than either method alone to help clinicians and managers find the sources of heterogeneity and unjustified variations in ECSs, design and implement hospital-tailored interventions intended to improve the appropriateness of their indications, and reduce unnecessary ECS and their avoidable complications and costs. This comprehensive and complementary statistical methodology, combined with robust data collection and audit processes, makes it possible to analyze an intricate medical decision-making problem with higher discriminant capacity than previous studies.

In conclusion, fetal, maternal, and contextual factors alone fail to achieve a reasonable discriminatory accuracy for type of cesarean delivery. We have met our objective by simultaneously considering these factors at each particular hospital by using both logistic regressions and the CTREES for the following reasons. First, this analytical strategy has improved the final discriminatory accuracy of the models for the type of delivery compared with that of the predictive models published to date. Second, the discriminatory accuracy of these models has been validated in our study by means of ten-fold cross-validation. Third, the results allow for further investigating sources of variability and inappropriateness of ECSs. Finally, based on this information, they also allow for tailoring hospital-specific interventions intended to discriminatory accuracy improve the appropriateness of indications for ECS.

Supporting information

S1 Tables. Database that includes the fetal, maternal, and contextual independent variables of hospitals A, B, C, and D. (XLSX)

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References
1. Zhang J, Troendle J, Reddy UM, Laughton SK, Branch DW, Burkman R, et al. Contemporary cesarean delivery practice in the United States. Am J Obstet Gynecol 2010; 203: 326.e1–326.e10.
2. Brandy E, Hamilton E, Martin JA, Osterman MJK, Curtin SC, Mathews TJ. Births: Final Data for 2014. Nat Vital Stat Rep 2015; 64: 1–64.
3. Instituto Nacional de Estadística. Distribución de la actividad obstétrica realizada en los hospitales según la finalidad de los mismos. Madrid: INE; 2014.
4. Gregory KD, Korst LM, Platt LD. Variation in elective primary cesarean delivery by patient and hospital factors. Am J Obstet Gynecol 2001; 184: 1521–1534. PMID: 11408876
5. García-Armesto S, Angulo-Pueyo E, Martínez-Lizaga N, Comendeiro-Maaløe M, Serai-Rodríguez M, Bernal-Delgado E. Methodology Medical Practice Variations in the utilization of low-value interventions. Zaragoza, Spain: Health Sciences Research Institute; 2016.
6. Fantini MP, Stivanello E, Frammartino B, Barone A, Fusco D, Dalilolo L, et al. Risk adjustment for inter-hospital comparison of primary cesarean section rates: need, validity and parsimony. BMC Health Serv Res 2006; 6: 100. https://doi.org/10.1186/1472-6963-6-100 PMID: 16911770
7. DiGiuseppe DL, Aron DC, Payne SM, Snow RJ, Dierker L, Rosenthal GE. Risk adjusting cesarean delivery rates: a comparison of hospital profiles based on medical record and birth certificate data. BMC Health Serv Res 2001; 36: 959–977.
8. Kritchevsky SB, Braun B, Gross PA, Newcomb CS, Kelleher CA, Simmons BP. Definition and adjustment of Cesarean section rates and assessments of hospital performance. Int J Qual Health Care 1999; 11: 283–291. PMID: 10501598
9. Dhillon BS, Chandhiok N, Bhatia S, Koyaji KJ, Das MC. Vaginal birth after cesarean section (VBAC) versus emergency repeat cesarean section at teaching hospitals in India: an ICMR task force study. Int J Reprod Contraception Obstet Gynecol 2014; 50: 584–592.
10. Librero J, Péiró S, Calderón SM. Inter-hospital variations in caesarean sections. A risk adjusted comparison in the Valencia public hospitals. J Epidemiol Community Health 2000; 54: 631–636. https://doi.org/10.1136/jech.54.8.631 PMID: 10890876
11. Bailit JL, Dooley SL, Peaceman AN. Risk Adjustment for Interhospital Comparison of Primary Cesarean Rates. Obstet Gynecol 1999; 93: 1025–1030. PMID: 10362175
12. Calvo Pérez A, Cabeza Vengoechea PJ, Campillo Artero C, Agüera Ortiz J. Idoneidad de las indicaciones de cesárea. Una aplicación en la gestión de la práctica clínica. Progresos Obstet Ginecol 2007; 50: 584–592.
13. Calvo A, Campillo C, Juan M, Roig C, Hermoso JC, Cabez a PJ. Effectiveness of a multifaceted strategy to improve the appropriateness of cesarean sections. Acta Obstet Gynecol Scand 2009; 88: 842–845. https://doi.org/10.1080/0001634090315313 PMID: 19488884
14. Chaillet N, Dumont A. Evidence-based strategies for reducing cesarean section rates: a meta-analysis. Birth 2007; 34: 53–64. https://doi.org/10.1111/j.1523-5366.2006.00146.x PMID: 17324180
15. Ecker JL, Frigoletto FD. Cesarean Delivery and the Risk–Benefit Calculus. N Engl J Med 2007; 356: 885–888. https://doi.org/10.1056/NEJMoa068290 PMID: 17329693
16. Althabe F, Belizán JM, Villar J, et al. Mandatory second opinion to reduce rates of unnecessary caesarean sections in Latin America: A cluster randomised controlled trial. Lancet 2004; 363: 1934–1940. https://doi.org/10.1016/S0140-6736(04)16406-4 PMID: 15194292
17. Walker R, Turnbull D, Wilkinson C. Strategies to address global cesarean section rates: A review of the evidence. Birth 2002; 29: 28–39. PMID: 11943787
18. Chaillet N, Dumont A, Abrahamowicz M, Pasquier JC,Audibert F,Monnier P, et al. A Cluster-Randomized Trial to Reduce Cesarean Delivery Rates in Quebec. N Engl J Med 2015; 372: 1710–1721. https://doi.org/10.1056/NEJMoa1407120 PMID: 25923551
19. Sanchez-Ramos L, Kaunitz AM, Peterson HB, Martinez-Schnell B, Thompson RJ. Reducing cesarean sections at a teaching hospital. Am J Obstet Gynecol 1990; 163: 1081–1088. PMID: 2403133

20. Robson MS, Scudamore IW, Walsh SM. Using the medical audit cycle to reduce cesarean section rates. Am J Obstet Gynecol 1996; 174: 199–205. PMID: 8572006

21. Myers SA, Gleicher N. The Mount Sinai cesarean section reduction program: An update after 6 years. Soc Sci Med 1993; 37: 1219–1222. PMID: 8272900

22. Myers SA, Gleicher N. A Successful Program to Lower Cesarean-Section Rates. N Engl J Med 1988; 319: 1511–1516. https://doi.org/10.1056/NEJM198812083192304 PMID: 3185675

23. Bloomfield T. Caesarean section, NICE guidelines and management of labour. J Obstet Gynaecol 2004; 24: 485–490. https://doi.org/10.1080/0144361042331271052 PMID: 15369924

24. Chittithavorn S, Pinjaroen S, Suwanrath C, Soonthornpun K. Clinical practice guideline for cesarean section due to Cephalopelvic Disproportion. J Med Assoc Thailand 1993; 37: 1219–1222. PMID: 8272900

25. Lomas J, Enkin M, Anderson GM, Hanna WJ, Vayda E, Singer J. Opinion leaders vs audit and feedback to implement practice guidelines: Delivery after previous cesarean section. JAMA 1991; 265: 2202–2207. PMID: 12907101

26. Kominiarek MA, VanVeldhuisen P, Hibbard J, Learman L, et al. The maternal body mass index: A strong association with delivery route. Am J Obstet Gynecol 2010; 203: 264e1–264e7.

27. Lynch CM, Sexton DJ, Hession M, Morrison JJ. Obesity and Mode of Delivery in Primigravid and Multigravid Women. Am J Perinatol 2008; 25: 163–167. https://doi.org/10.1055/s-2008-1061496 PMID: 18300188

28. Pickhardt MG, Martin JN, Meydrech EF, Blake PJ, Martin RW, Perry KG, et al. Vaginal birth after cesarean delivery: Are there useful and valid predictors of success or failure? Am J Obstet Gynecol 1992; 166: 1811–1819. PMID: 1615990

29. Wilkes PT, Wolf DM, Kronbach DW, Kunze M, Gibbs RS. Risk factors for cesarean delivery at presentation of nulliparous patients in labor. Obstet Gynecol 2003; 102: 1352–1357. PMID: 14662226

30. Costa-Ramón A-M, Rodríguez-González A, Serra-Burriel M, Campillo-Artero C. Cesarean Sections and Newborn Health Outcomes. Barcelona: Center for Research in Health and Economics, University Pompeu Fabra; 2016. (CRES-UPF Work Paper No. 201610(94): 1–30.)

31. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. BMJ 2004; 329: 168–169. https://doi.org/10.1136/bmj.329.7458.168 PMID: 15258077

32. Eden KB, McDonagh M, Denman MA, Marshall N, Emes c, Fu R, et al. New Insights on Vaginal Birth After Cesarean: Can It Be Predicted? Obstet Gynecol 2010; 116: 967–981. https://doi.org/10.1097/AOG.0b013e3181f2de49 PMID: 20859163

33. Grimes DA, Schulz KF. Epidemiology 3: Refining clinical diagnosis with likelihood ratios. Lancet 2005; 365: 1500–1505. https://doi.org/10.1016/S0140-6736(05)66422-7 PMID: 15850636
43. Juárez SP, Wagner P, Merlo J. Applying measures of discriminatory accuracy to revisit traditional risk factors for being small for gestational age in Sweden: a national cross-sectional study. BMJ Open 2014; 4: 1–11.

44. Khoury MJ, Iademarco MF, Riley WT. Precision Public Health for the Era of Precision Medicine. Am J Prev Med 2016; 50: 398–401. https://doi.org/10.1016/j.amepre.2015.08.031 PMID: 26547538

45. Merlo J, Mulinari S. Measures of discriminatory accuracy and categorizations in public health: a response to Allan Krasnik’s editorial. Eur J Public Health 2015; 25: 910–910. https://doi.org/10.1093/eurpub/ckv209 PMID: 26604325

46. Pepe MS, Janes H, Longton G, Leisenring W, Newcomb P. Limitations of the odds ratio in gauging the performance of a diagnostic, prognostic, or screening marker. Am J Epidemiol 2004; 159: 882–890. PMID: 15105181

47. Wald NJ, Hackshaw AK, Frost CD. When can a risk factor be used as a worthwhile screening test? BMJ 1999; 319: 1562–1565. PMID: 10591726

48. Strobl C, Boulesteix AL, Zeileis A, Hothorn T. Bias in random forest variable importance measures: illustrations, sources and a solution. BMC Bioinformatics 2007; 8: 25. https://doi.org/10.1186/1471-2105-8-25 PMID: 17254353

49. Breiman L. Random forests. Mach Learn 2001; 45: 5–32.

50. R Development Core Team. R: A language and environment for statistical computing. Vienna: Foundation for Statistical Computing; 2011.