

# Risk calculator for advanced neonatal resuscitation

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## ABSTRACT

In order to predict which newborns will require advanced resuscitation (ANR), we developed an ANR risk calculator (calculator.) using a bootstrap sample size of 52 973 from a case-control study of newborns  $\geq 34$  weeks gestation. Multivariable logistic regression coefficients were obtained for the 10 original risk factors and two interaction terms. The area under the receiving-operating characteristic curve predicting ANR was 0.9243. ANR prediction is improved by accounting for perinatal variables, beyond factors known prenatally. Prospective validation of this model is warranted in a clinical setting.

## INTRODUCTION

Very few newborns will require advanced neonatal resuscitation (ANR) procedures, such as tracheal intubation or emergency vascular access, at birth.<sup>1 2</sup> If ANR procedures are required, they must be initiated without delay.<sup>3</sup> Currently, there is little information allowing providers to estimate the risk of requiring ANR.<sup>4</sup> Isolated risk factors do not accurately predict the risk of ANR.<sup>3</sup>

Based on Berazategui's original data set, we sought to construct a prediction model that could be incorporated into a user-friendly tool to help providers to better estimate this risk of ANR.<sup>5</sup>

## METHODS

Using data from Berazategui,<sup>5</sup> we implemented bootstrap resampling to generate an empirical data distribution reflective of the population prevalence of ANR. We focused on infants born  $\geq 34$  weeks gestational age. All cases were kept in the new distribution, while control subjects were resampled with replacement until the distribution reached a prevalence of 0.37%. Ten risk factors identified by Berazategui<sup>5</sup> were used as variables in a similar multivariable logistic regression model, along with two interaction terms (Fetal Bradycardia\*Emergency C-section and Abrupton\*Emergency C-section), fitted to the bootstrap sample data. Results were validated by leaving out one case and recalculating the model coefficients to assess their stability, while also

using the left-out case for computation of sensitivity and specificity. Analyses were performed using R software V.3.5.0 (Vienna, Austria).

## RESULTS

All cases were sampled (n=196), while the controls (n=784) were sampled with replacement to obtain a bootstrap sample size of n=52 973, thus ensuring a prevalence of ANR in the data set (196/52 973=0.0037) equal to the population prevalence cited in the reference study. **Table 1** reports descriptive statistics from the original study along with those of the bootstrap sample. Multivariable logistic regression coefficients were obtained for the 10 original risk factors and two interaction terms on the bootstrap data. Leave-one-out cross-validation confirmed that the model coefficient estimates were stable across the resampled values (SD of log odds estimates of the leave-one-out models were all less than 0.18). **Figure 1** displays the receiving-operating characteristic curve showing the sensitivity and specificity at various cut-off points for the computed probability.

## PATIENT AND PUBLIC INVOLVEMENT

Neither patients nor public were involved in this study's development.

## DISCUSSION

We created a risk calculator that may be useful for resource allocation in the delivery room. Although individual risk factors are not useful for identifying newborns at risk of ANR, combining a small number of variables provides a more precise prediction.

While the original case-control study could not estimate an individual newborn's risk, our model used a resampling method to construct a large bootstrap sample that was reflective of the original population. Although the bootstrap sample may exacerbate bias from the original controls due to extensive resampling, this bias will primarily affect the model's specificity. Bias is



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**Table 1** Descriptive statistics of the original and bootstrap data sets

Variable(s)*	Original sample				Bootstrap sample			
	N	ANR no, n=784†	ANR yes, n=196†	P value‡	N	ANR no, n=52 777†	ANR yes, n=196†	P value‡
Gestational age 34–37 weeks	980	130 (17%)	63 (32%)	<0.001	52 973	8790 (17%)	63 (32%)	<0.001
Growth restriction	980	12 (1.5%)	11 (5.6%)	0.002	52 973	788 (1.5%)	11 (5.6%)	<0.001
Gestational diabetes	975	13 (1.7%)	4 (2.1%)	0.8	52 769	849 (1.6%)	4 (2.1%)	0.6
Meconium stained amniotic fluid	980	38 (4.8%)	72 (37%)	<0.001	52 973	2598 (4.9%)	72 (37%)	<0.001
Forceps or vacuum delivery	980	10 (1.3%)	13 (6.6%)	<0.001	52 973	673 (1.3%)	13 (6.6%)	<0.001
Chorioamnionitis	980	4 (0.5%)	6 (3.1%)	0.006	52 973	301 (0.6%)	6 (3.1%)	0.001
Fetal bradycardia	980	14 (1.8%)	54 (28%)	<0.001	52 973	1004 (1.9%)	54 (28%)	<0.001
Placental abruption	980	5 (0.6%)	24 (12%)	<0.001	52 973	323 (0.6%)	24 (12%)	<0.001
General anaesthesia	980	6 (0.8%)	23 (12%)	<0.001	52 973	465 (0.9%)	23 (12%)	<0.001
Emergency caesarean section	980	26 (3.3%)	64 (33%)	<0.001	52 973	1816 (3.4%)	64 (33%)	<0.001
Fetal bradycardia*Emergency c-section	980	7 (0.9%)	31 (16%)	<0.001	52 973	524 (1.0%)	31 (16%)	<0.001
Abruption*Emergency c-section	980	2 (0.3%)	22 (11%)	<0.001	52 973	131 (0.2%)	22 (11%)	<0.001

\*Ten covariates from the original cohort including three antepartum and seven intrapartum factors, along with last two interaction terms which were not included in the original cohort.

†n (%).

‡Pearson's  $\chi^2$  test; Fisher's exact test.

ANR, advanced neonatal resuscitation.

unlikely to affect the model's sensitivity. As a screening tool, sensitivity is most relevant to users who must determine when to call a team with ANR skills to the delivery room.

This study confirmed the previously validated logistic regression model, but the risk calculation needs to be validated clinically. We developed a prototype mobile app that

allows users to choose the local ANR prevalence and calculate a newborn's ANR risk by clicking each variable and selecting the appropriate option. (View the calculator by clicking here: calculator.) Once validated in a clinical setting, the app may help providers to determine their local threshold for allocating skilled personnel to the delivery room.

In conclusion, we demonstrated feasibility of developing an ANR risk calculator that may allow more rational allocation of delivery room personnel. A clinical validation study is planned.

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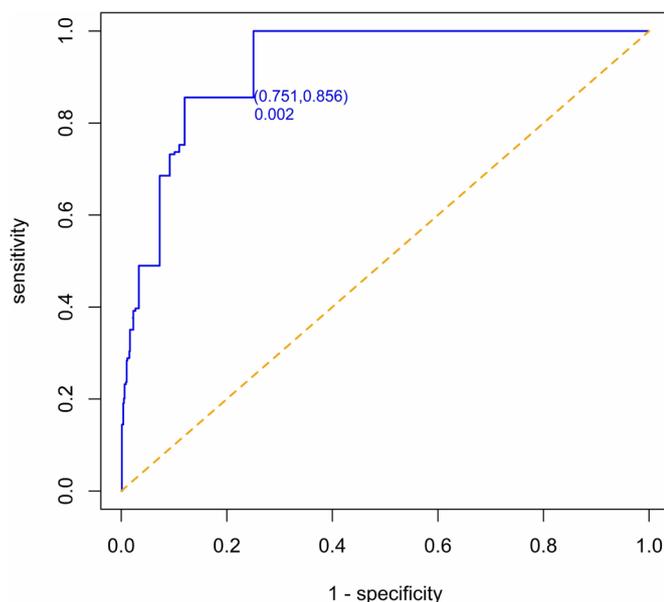
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**Figure 1** ROC curve of infants needing ANR from the multivariable logistic regression model based on the bootstrapped data set. Illustrated in the figure is a threshold value of 0.002 for the computed risk of ANR using the model that yields a sensitivity of 0.856 and a specificity of 0.751. ANR, advanced neonatal resuscitation; ROC, receiving-operating characteristic.



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