A Prognostic Model for Tracheostomy and Mortality in Infants with Severe Bronchopulmonary Dysplasia at Different Stages

Monica Colon-Vargas

Fall 2023

Objective: This study aims to construct predictive models at three crucial stages in infants with sBPD: Birth, 36 weeks, and 44 weeks, while comparing the performance of a mixed model with StepAIC and a LASSO model.
Methods: This study employs two statistical techniques for each dataset, initially fitting a generalized mixed model to account for the nested data structure. Variable selection is carried out using the stepwise Akaike Information Criterion (stepAIC) algorithm. This process is repeated independently for each training imputed dataset, ensuring a comprehensive approach. Subsequently, a Lasso logistic known for reliable predictions and feature selection, is applied. Cross-validation determines the optimal penalization parameter, and the final model is derived by pooling coefficients from each training imputed dataset. This methodology is systematically applied across six distinct models for a comprehensive comparative analysis.
Conclusions: Both methods performed well across the three stages, with maternal ethnicity consistently significant. Prenatal corticosteroid use emerged significantly in all six models. Notably, the 36-week model highlighted the importance of variables at that time, including weight, ventilation support, and medication for pulmonary hypertension. The 44-week mixed model exhibited sparsity, while the LASSO model, despite its selection ability, was less sparse post-StepAIC. Model selection prioritized AUC scores, leading to recommendations based on distinct model strengths at different time points.The mixed model is recommended for predicting tracheostomy outcomes at birth and 44 weeks, while the LASSO model is suggested for predictions at 36 weeks.

1 Introduction

The optimal criteria and timing for tracheostomy placement in neonates with severe bronchopulmonary dysplasia (sBPD) remain uncertain. Some studies propose potential benefits in growth with earlier tracheostomy placement. Previous examinations of extensive databases have demonstrated accurate prediction of tracheostomy placement or mortality based on baseline demographics and clinical diagnoses. However, these analyses have not incorporated detailed respiratory parameters and have not offered predictions at different postmenstrual ages (PMA). A precise prediction of the likelihood of tracheostomy at early PMA could significantly influence counseling for families and the timing of tracheostomy placement, a topic currently under active debate in the context of sBPD.

The primary objective of this study is to develop a regression model with the aim of predicting the composite outcome of tracheostomy or death. The overarching goal is to contribute valuable insights that can guide the establishment of indication criteria and inform decisions regarding the optimal timing for tracheostomy placement in neonates with severe sBPD. This model seeks to elevate the accuracy of prognostic assessments, ultimately enabling healthcare professionals to make more informed clinical decisions in managing the patient population with sBPD.

2 Data and Methodology

The study participants were selected from the BPD Collaborative Registry, which is a collaborative initiative comprising interdisciplinary BPD programs in the United States and Sweden. The registry specifically includes infants born with a gestational age of less than 32 weeks and diagnosed with severe bronchopulmonary dysplasia (sBPD) based on the 2001 NHLBI criteria. In the registry, standard demographic and clinical data are collected at four-time points: birth, 36 weeks PMA, 44 weeks PMA and discharge.The data consists of individuals with BPD and comprehensive growth data recorded from January 1 to July 19, 2021 from 10 BPD Collaborative centers.

Data inaccuracies were identified, including instances of repeated identification, which were subsequently rectified by eliminating duplications. Additionally, due to the limited number of individuals in centers 20 and 21, they were consolidated into a unified category for analysis. Due to discrepancies in the levels of the maternal race, the variable `mat_race` was excluded from the analysis.

Table 1 presents a comprehensive set of summary statistics for the dataset, with a focus on the two response variables, namely Tracheostomy and Death. It is essential to dissect these statistics within the context of various aspects related to the data. First and foremost, the data appears to originate from ten different medical centers. It is noteworthy that center 20 (class containing both centers 20 and 21) contains relatively fewer cases, suggesting that they might be smaller facilities, in contrast to center 2, which evidently stands out as a larger center. Furthermore, center 2 is notably the primary provider of tracheostomies, closely followed by centers 12, 1, and 4. A similar trend is observed for the occurrence of deaths, with centers 2, 12, and 1 featuring more. The analysis of mothers' ethnicity reveals a balanced distribution across both outcomes. A noticeable trend in the data is the lower birth weight of infants who either died or underwent a tracheostomy, which may indicate that low birth weight is a risk factor for these outcomes. Additionally, a majority of these births occurred through cesarean section. Furthermore, it is worth highlighting that males appear to be more affected, with a higher number of deaths and tracheostomies. This gender disparity warrants a more in-depth analysis to understand the underlying factors contributing to this observed difference in outcomes between males and females.

This study is structured into three distinct segments. Initially, we construct a predictive model for the composite outcome in newborn babies, utilizing a subset of the dataset that exclusively incorporates variables measured at birth (Birth-model). Subsequently, we develop a second model to forecast the necessity of a tracheotomy, taking into account variables assessed at the 36-week stage of the pregnancy (36-week model). In developing this model, we restrict our analysis to patients who possess at least one recorded measurement within the 36-week window. Lastly, the third model encompasses the complete dataset and is designed to predict the occurrence of tracheotomies at the 44-week (44-week model). Consistent with the previous model, this dataset includes patients who have at least one recorded measurement within the 44-week window. This approach ensures that the models are developed and validated based on a comprehensive and appropriate population. The primary aim is to construct a predictive model designed to assess the probability of tracheostomy necessity at three distinct temporal moments in a patient's early life—specifically, at birth, 36 weeks, and 44 weeks. This predictive framework seeks to furnish anticipatory insights into the potential requirement for tracheostomy intervention across these critical time points.

For each dataset utilized in constructing an individual model, two statistical techniques are employed. Given the nested structure of the data, where each patient is nested within a center, a generalized mixed model is initially fitted, incorporating random intercepts with the center acting as a random effect. Considering the correlations among variables, such as the high correlation between birth weight (`bw`), birth

length (`blength`), and birth head circumference (`birth_hc`), variable selection becomes imperative. The stepwise Akaike Information Criterion (stepAIC) algorithm is applied for this purpose, aiming to minimize the stepAIC value and determine the optimal set of features. This algorithm is executed independently for each training imputed dataset (totaling 5), and the frequency of variable selection is recorded. Selecting all variables that have been chosen at least once for fitting compromised the model's ability to accurately capture the genuine significance of the variables. To avoid this, we adopt a criterion where only variables selected in more than 50% of instances are retained. Subsequently, the model is fitted to each training imputed dataset using the selected variables, and the resulting coefficients are aggregated through averaging. This rigorous process ensures that the final model captures the genuine significance of the selected variables while accommodating the nuances of the data structure. Subsequently, a Lasso logistic model is applied to the dataset, maintaining the center as a fixed effect. Despite the inherent limitation of not explicitly accommodating the nested structure of the data, this approach is pursued to facilitate a comparative analysis. The choice to employ Lasso in this context is grounded in its established reputation for delivering reliable predictions and its feature selection. To determine the optimal penalization parameter, cross-validation is performed independently on each training imputed dataset. Following the selection of coefficients for each training imputed dataset, pooling together these coefficients we derive the final model. It is noteworthy to highlight that the described methodology is systematically reiterated for each individual model, culminating in a comparative assessment encompassing a total of six distinct models.

For model evaluation, we present results encompassing metrics such as the Area Under the Receiver Operating Characteristic Curve (AUC), Brier score, sensitivity, and specificity. These metrics collectively provide a nuanced evaluation of the models' discriminative ability, calibration, and performance in correctly identifying true positive and true negative instances.

Table 1: Summary Statistics Grouped by Response Outcome

		Death				Tracheostomy		
Death	**N**	**Overall**, N = 993	**No**, N = 939	**Yes**, N = 54	**N**	**Overall**, N = 995	**No**, N = 849	**Yes**, N = 146
center	983				985			
1		55.00 (5.60%)	48.00 (5.17%)	7.00 (12.96%)		55.00 (5.58%)	32.00 (3.80%)	23.00 (16.20%)
2		628.00 (63.89%)	599.00 (64.48%)	29.00 (53.70%)		629.00 (63.86%)	565.00 (67.02%)	64.00 (45.07%)
3		57.00 (5.80%)	56.00 (6.03%)	1.00 (1.85%)		57.00 (5.79%)	56.00 (6.64%)	1.00 (0.70%)
4		59.00 (6.00%)	58.00 (6.24%)	1.00 (1.85%)		60.00 (6.09%)	49.00 (5.81%)	11.00 (7.75%)
5		40.00 (4.07%)	38.00 (4.09%)	2.00 (3.70%)		40.00 (4.06%)	35.00 (4.15%)	5.00 (3.52%)
7		32.00 (3.26%)	32.00 (3.44%)	0.00 (0.00%)		32.00 (3.25%)	31.00 (3.68%)	1.00 (0.70%)
12		69.00 (7.02%)	55.00 (5.92%)	14.00 (25.93%)		69.00 (7.01%)	34.00 (4.03%)	35.00 (24.65%)
16		38.00 (3.87%)	38.00 (4.09%)	0.00 (0.00%)		38.00 (3.86%)	37.00 (4.39%)	1.00 (0.70%)
20		5.00 (0.51%)	5.00 (0.54%)	0.00 (0.00%)		5.00 (0.51%)	4.00 (0.47%)	1.00 (0.70%)
Unknown		10	10	0		10	6	4
mat_ethn	936				938			
1		74.00 (7.91%)	71.00 (8.02%)	3.00 (5.88%)		74.00 (7.89%)	66.00 (8.23%)	8.00 (5.88%)
2		862.00 (92.09%)	814.00 (91.98%)	48.00 (94.12%)		864.00 (92.11%)	736.00 (91.77%)	128.00 (94.12%)
Unknown		57	54	3		57	47	10
bw	993	806.20 (296.98)	811.12 (288.99)	720.69 (406.03)	995	806.10 (296.77)	813.82 (295.25)	761.21 (302.58)
ga	993	25.77 (2.14)	25.77 (2.14)	25.83 (2.13)	995	25.77 (2.14)	25.76 (2.14)	25.84 (2.13)
blength	915	32.49 (3.82)	32.60 (3.75)	30.32 (4.37)	917	32.49 (3.82)	32.56 (3.80)	31.97 (3.94)
Unknown		78	71	7		78	48	30
birth_hc	916	23.19 (2.76)	23.24 (2.71)	22.34 (3.54)	918	23.19 (2.76)	23.22 (2.71)	22.99 (3.07)
Unknown		77	72	5		77	46	31
del_method	990				992			
1		284.00 (28.69%)	274.00 (29.27%)	10.00 (18.52%)		285.00 (28.73%)	254.00 (29.99%)	31.00 (21.38%)
2		706.00 (71.31%)	662.00 (70.73%)	44.00 (81.48%)		707.00 (71.27%)	593.00 (70.01%)	114.00 (78.62%)
Unknown		3	3	0		3	2	1
prenat_ster	958	832.00 (86.85%)	788.00 (86.69%)	44.00 (89.80%)	960	834.00 (86.88%)	711.00 (85.77%)	123.00 (93.89%)
Unknown		35	30	5		35	20	15
com_prenat_ster	922	607.00 (65.84%)	573.00 (65.56%)	34.00 (70.83%)	924	609.00 (65.91%)	523.00 (65.05%)	86.00 (71.67%)
Unknown		71	65	6		71	45	26
mat_chorio	931	160.00 (17.19%)	153.00 (17.37%)	7.00 (14.00%)	933	160.00 (17.15%)	138.00 (17.27%)	22.00 (16.42%)
Unknown		62	58	4		62	50	12
gender	989				991			
Female		407.00 (41.15%)	390.00 (41.71%)	17.00 (31.48%)		408.00 (41.17%)	348.00 (41.18%)	60.00 (41.10%)
Male		582.00 (58.85%)	545.00 (58.29%)	37.00 (68.52%)		583.00 (58.83%)	497.00 (58.82%)	86.00 (58.90%)
Unknown		4	4	0		4	4	0
sga	978				980			
Not SGA		775.00 (79.24%)	747.00 (80.84%)	28.00 (51.85%)		777.00 (79.29%)	677.00 (80.79%)	100.00 (70.42%)
SGA		203.00 (20.76%)	177.00 (19.16%)	26.00 (48.15%)		203.00 (20.71%)	161.00 (19.21%)	42.00 (29.58%)
Unknown		15	15	0		15	11	4
any_surf	561	460.00 (82.00%)	432.00 (81.66%)	28.00 (87.50%)	562	460.00 (81.85%)	394.00 (80.90%)	66.00 (88.00%)
Unknown		432	410	22		433	362	71
weight_today.36	901	2,120.08 (413.67)	2,132.66 (397.30)	1,826.46 (633.79)	903	2,120.90 (413.58)	2,131.91 (410.26)	2,023.88 (432.03)
Unknown		92	75	17		92	38	54
ventilation_support_level.36	963				965			
0		116.00 (12.05%)	114.00 (12.46%)	2.00 (4.17%)		117.00 (12.12%)	111.00 (13.25%)	6.00 (4.72%)
1		588.00 (61.06%)	581.00 (63.50%)	7.00 (14.58%)		588.00 (60.93%)	559.00 (66.71%)	29.00 (22.83%)
2		259.00 (26.90%)	220.00 (24.04%)	39.00 (81.25%)		260.00 (26.94%)	168.00 (20.05%)	92.00 (72.44%)
Unknown		30	24	6		30	11	19
inspired_oxygen.36	901	0.34 (0.15)	0.33 (0.13)	0.52 (0.25)	903	0.34 (0.15)	0.32 (0.13)	0.49 (0.20)
Unknown		92	76	16		92	37	55
p_delta.36	865	5.28 (9.75)	4.85 (9.37)	17.14 (12.70)	867	5.27 (9.74)	4.26 (8.87)	15.13 (12.13)
Unknown		128	104	24		128	63	65
peep_cm_h2o_modified.36	876	6.34 (2.91)	6.31 (2.93)	7.13 (2.25)	878	6.33 (2.91)	6.20 (2.90)	7.50 (2.79)
Unknown		117	95	22		117	59	58
med_ph.36	963				965			
0		898.00 (93.25%)	860.00 (93.99%)	38.00 (79.17%)		899.00 (93.16%)	797.00 (95.11%)	102.00 (80.31%)
1		65.00 (6.75%)	55.00 (6.01%)	10.00 (20.83%)		66.00 (6.84%)	41.00 (4.89%)	25.00 (19.69%)
Unknown		30	24	6		30	11	19
weight_today.44	550	3,646.12 (682.09)	3,674.90 (662.68)	3,222.71 (822.51)	550	3,646.12 (682.09)	3,667.21 (665.21)	3,550.07 (750.40)
Unknown		443	424	19		445	398	47
ventilation_support_level_modified.44	572				572			
0		269.00 (47.03%)	268.00 (50.28%)	1.00 (2.56%)		269.00 (47.03%)	262.00 (56.83%)	7.00 (6.31%)
1		146.00 (25.52%)	141.00 (26.45%)	5.00 (12.82%)		146.00 (25.52%)	128.00 (27.77%)	18.00 (16.22%)
2		157.00 (27.45%)	124.00 (23.26%)	33.00 (84.62%)		157.00 (27.45%)	71.00 (15.40%)	86.00 (77.48%)
Unknown		421	406	15		423	388	35
inspired_oxygen.44	548	0.34 (0.15)	0.33 (0.13)	0.53 (0.23)	548	0.34 (0.15)	0.32 (0.13)	0.44 (0.19)
Unknown		445	426	19		447	397	50
p_delta.44	548	7.62 (14.19)	6.44 (13.12)	26.75 (17.10)	548	7.62 (14.19)	4.80 (12.01)	21.10 (15.99)
Unknown		445	423	22		447	396	51
peep_cm_h2o_modified.44	550	4.30 (4.46)	4.03 (4.40)	8.78 (2.71)	550	4.30 (4.46)	3.37 (4.06)	8.69 (3.59)
Unknown		443	421	22		445	395	50
med_ph.44	572				572			
0		473.00 (82.69%)	458.00 (85.93%)	15.00 (38.46%)		473.00 (82.69%)	413.00 (89.59%)	60.00 (54.05%)
1		99.00 (17.31%)	75.00 (14.07%)	24.00 (61.54%)		99.00 (17.31%)	48.00 (10.41%)	51.00 (45.95%)
Unknown		421	406	15		423	388	35
hosp_dc_ga	870	52.79 (26.54)	52.44 (26.66)	58.90 (23.75)	871	52.78 (26.53)	48.93 (23.63)	79.94 (29.94)
Unknown		123	116	7		124	86	38
Trach	993	146.00 (14.70%)	129.00 (13.74%)	17.00 (31.48%)				
Death					993	54.00 (5.44%)	37.00 (4.37%)	17.00 (11.64%)
Unknown						2	2	0

[1] n (%); Mean (SD)

2.1 Outcome Variable

The objective of this study is to create a predictive model for the combined outcomes of tracheotomy and death. This model will aid in determining when and for whom tracheotomy placement is appropriate, thus improving clinical decision-making in patient care. The initial step in this study involves the construction of a composite outcome variable. To delineate this composite outcome, the following approach is adopted: Patients who have undergone a tracheotomy, without consideration of their subsequent survival status, are categorized into the "tracheotomy" group. Likewise, patients who did not receive a tracheotomy but subsequently deceased are also classified under the "tracheotomy" category. This particular categorization serves the purpose of recognizing cases where death might have been averted if a tracheotomy had been performed. Conversely, individuals who neither underwent a tracheotomy nor succumbed to mortality are categorized under the "no tracheotomy" group. This approach allows us to create a comprehensive analysis of the combined outcome involving tracheotomies and deaths. By considering cases where tracheotomies might have prevented deaths, we can gain a fuller understanding of the clinical decisions and preventive actions needed in this scenario. Following the specification of our outcome variable, the dataset exhibits a class imbalance with 810 instances in the negative class and 183 instances in the positive class. Given this imbalanced distribution, it is anticipated that the optimal threshold in probability for prediction will be constrained to lower values. This adjustment aims to achieve a balanced trade-off between sensitivity and specificity in the predictive model.

2.2 Missing Data

The dataset exhibits a notable issue with missing data, where approximately 15% of cases lack complete information. From Table 1, this discrepancy is primarily observed in variables collected at the 44-week mark, with a similar pattern evident in the variable denoting whether the baby received surfactant treatment within the first 72 hours of life `any_surf`. Notably, variables measured at 36 weeks also display substantial rates of missing data. Figure 1 illustrates the pattern of missing values in relation to the hospital discharge timing of patients. Notably, patients discharged prior to the 44-week mark exhibit a higher prevalence of missing values in variables collected at that specific time point. In contrast, patients discharged after the 44th week demonstrate a comparatively lower incidence of missing values in the same variables.

The three dataset utilized for constructing the three models exhibit a significant prevalence of missing values. To enhance the model's quality and robustness, the adoption of a technique to address this issue becomes imperative. Multiple imputation is deployed across the three datasets, resulting in the creation of five complete datasets for each, aggregating to a total of 15 complete datasets. Subsequently, models are fitted to these complete datasets, yielding model estimates which are subsequently pooled, culminating in the derivation of three final model (one for each dataset).

Variable	n	%	Variable	n	%
inspired_oxygen	447	44.92	birth_hc	77	7.74
p_delta.44	447	44.92	com_prenat_ster	71	7.14
weight_today.44	445	44.72	mat_chorio	62	6.23
peep_cm_h2o_modified.44	445	44.72	mat_ethn	57	5.73
any_surf	433	43.52	prenat_ster	35	3.52
ventilation_support_level_modified.44	423	42.51	ventilation_support_level.36	30	3.02
med_ph.44	423	42.52	med_ph.36	30	3.02
p_delta.36	128	12.86	sga	15	1.51
hosp_dc_ga	124	12.46	center	10	1.01
peep_cm_h20_modified.36	117	11.76	gender	4	0.40
weight_today.36	92	9.25	del_method	3	0.30
inspired_oxygen.36	92	9.25	Death	2	0.20
blength	78	7.84	new_trach	2	0.20

Table 1: Missing Data per Variables

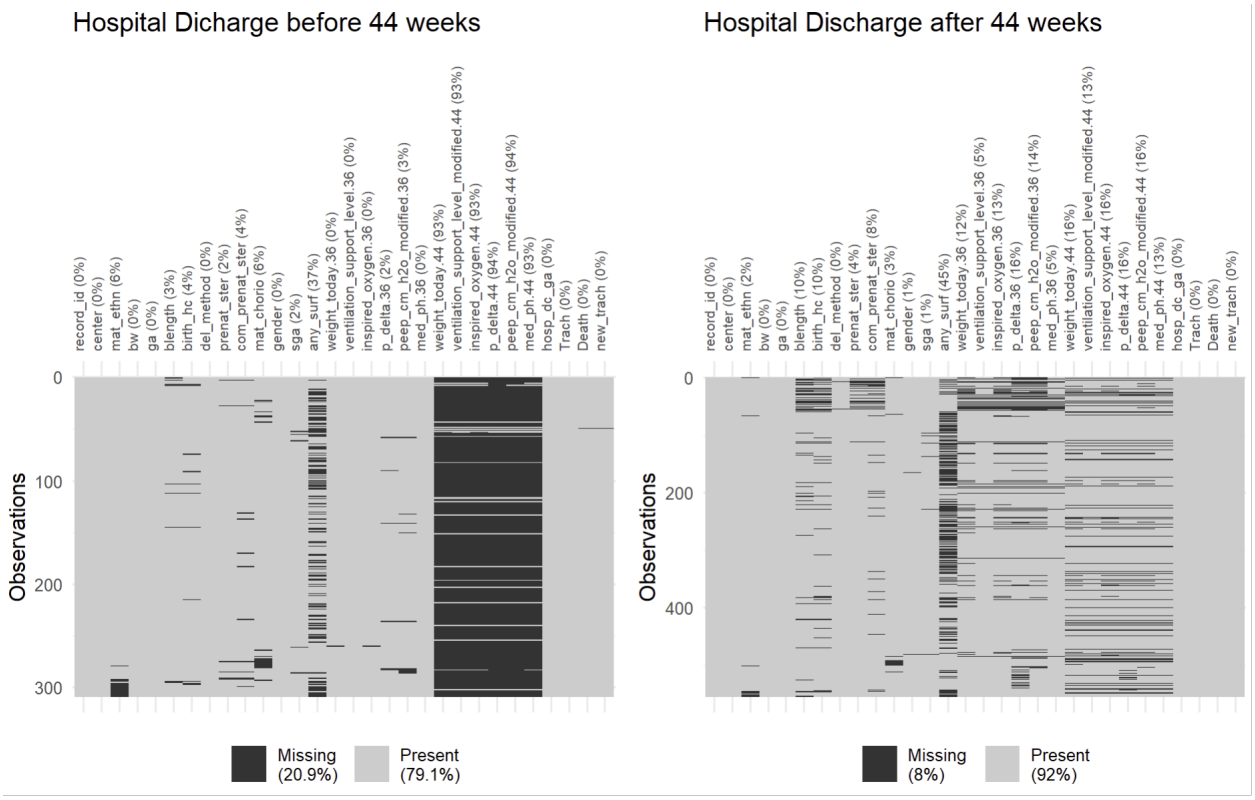

Figure 1: Missing Data

3 Results

The study employs three distinct models to discern predictive factors influencing patient outcomes across different stages of care. The Birth Model, encompassing the entire patient cohort, exclusively considers variables measured at birth. The 36-Week Model, focusing on patients with a hospital discharge occurring after at least 36 weeks, extends its analysis to include variables measured both at birth and at the 36-week

mark. Lastly, the 44-Week Model, limited to patients with a hospital discharge after a minimum of 44 weeks, integrates all available variables throughout the entire care timeline.

3.1 Birth Model

The coefficients for the birth model are presented in Table 2. The mixed model employed in this analysis incorporates essential covariates, ensuring a comprehensive examination of factors influencing outcomes at birth. After applying the StepAIC criterion, the model considers ethnicity, gestational age, birth length, the use of prenatal steroids, an indicator for infants categorized as small for gestational age, and an indicator denoting whether the infant received surfactant. Each coefficient in the table signifies the change in the log-odds of the response variable associated with a one-unit change in the corresponding predictor variable, holding all other variables constant. Infants considered small for gestational age, infants who received a surfactant, and infants whose model received a course of corticosteroids have positive coefficients implying they are more likely to have a tracheostomy. In the context of the LASSO model, it is noteworthy that the majority of coefficients exhibit smaller magnitudes compared to the coefficients from other models. However, we can emphasize that the signs of the coefficients align, enabling consistent conclusions to be drawn.

Table 3 presents the performance metrics for both the LASSO model and the comparative model. Notably, both models demonstrate similar overall performance, with the LASSO model exhibiting a marginally higher AUC and Sensitivity. Despite the similarities, it is imperative to address the nuanced performance of the models in terms of Sensitivity. The recorded Sensitivity scores of 0.626 and 0.647, while indicative of reasonable performance, suggest a propensity for an increased likelihood of false negatives in the predictions. To enhance predictive accuracy, additional models at 36 weeks and 44 weeks have been incorporated, aiming to improve sensitivity and overall predictive capabilities. This strategic expansion across different time frames contributes to a comprehensive evaluation of predictive performance, refining the reliability of models in anticipating tracheotomies during the early stages of infant development.

	Mixed Model*	LASSO		
Coefficient	Estimate	Estimate	Coefficient	Estimate
intercept	-2.829	-0.992	center2	-1.416
mat_ethn2	0.715	0.465	center3	-2.230
bw	0	0	center4	-0.541
ga	0.066	0.020	center5	-1.127
blength	-0.072	-0.042	center7	-2.324
birth_hc	0	0.005	center12	0.821
del_method2	0	0.096	center16	-2.466
prenat_sterYes	0.606	0.371	center 20	-0.259
com_prenat_sterYes	0	0.036		
mat_chorioYes	0	0.118		
genderMale	0	0.007		
sgaSGA	0.556	0.586		
any_surfYes	0.546	0.379		

Table 2: Coefficients for Birth Model
**Note: Random Intercept for center are not shown.*

Metrics	Mixed Model	LASSO
AUC	0.763	0.759
Brier	0.126	0.126
Sensitivity	0.626	0.647
Specificity	0.806	0.750
Threshold	0.204	0.168

Table 3: Performance Metrics and Threshold for Predictions for the Generalized Mixed Model and LASSO Birth Model

3.2 36-Week Model

Table 4 presents the coefficients derived from both the mixed model, incorporating center as a random effect, and the lasso model, where center is treated as a fixed effect in the context of the 36-week models. Employing the StepAIC criterion in the mixed model resulted in the selection of predictors, including ethnicity, prenatal steroids, an indicator for surfactant, weight at 36 weeks, type of ventilation support at 36 weeks, the fraction of inspired oxygen at 36 weeks, and an indicator for medication for pulmonary hypertension at 36 weeks. As before the birth model, the presence of prenatal corticosteroids and the administration of surfactant emerge as factors associated with an increased likelihood of tracheostomy. Also, a higher weight at 36 weeks is linked to a decreased probability of undergoing tracheostomy. Additionally, the log odds indicate that patients with non-invasive positive pressure support exhibit lower odds compared to those with no support, while patients with invasive positive pressure support have higher odds. Furthermore, infants receiving medication for pulmonary hypertension at 36 weeks demonstrate elevated odds of tracheostomy. In the lasso model, similar to the mixed model, birth weight is not chosen as a significant variable. The consistent sign of coefficients indicates similar conclusions in the interpretation of coefficients between the two models.

Table 5 reveals an increase in performance metrics when predicting tracheostomy with data available at 36 weeks. The LASSO model demonstrates a slight increase in AUC and a lower Brier score, indicating improved discriminatory performance compared to the Mixed Model. Nevertheless, it is noteworthy that the Mixed Model exhibits higher sensitivity and specificity. While the LASSO model excels in overall predictive accuracy, the Mixed Model demonstrates superior sensitivity and specificity.

Coefficient	Mixed Model* Estimate	LASSO Estimate	Coefficient	Estimate
intercept	-4.696	-4.582	center2	-1.141
mat_ethn2	1.005	0.596	center3	-2.890
bw	0	0	center4	-0.271
ga	0	0.011	center5	-1.543
blength	0	0.019	center7	-2.547
birth_hc	0	0.014	center12	0.836
del_method2	0	-0.045	center16	-1.396
prenat_sterYes	1.224	0.842	center 20	-1.289
com_prenat_sterYes	0	0.182		
mat_chorioYes	0	0.133		
genderMale	0	0.017		
sgaSGA	0	0.276		
any_surfYes	0.556	0.484		
weight_today.36	-0.001	-0.001		
ventilation_support_level.361	-0.019	-0.106		
ventilation_support_level.362	1.784	1.256		
inspired_oxygen.36	3.384	2.755		
p_delta.36	0	0.025		
peep_cm_h2o_modified.36	0	0.007		
med_ph.361	0.702	0.481		

Table 4: Coefficients for 36-Week Model
**Note: Random Intercept for center are not shown.*

Metrics	Mixed Model	LASSO
AUC	0.897	0.900
Brier	0.100	0.099
Sensitivity	0.920	0.911
Specificity	0.784	0.757
Threshold	0.122	0.103

Table 5: Performance Metrics for the Generalized Mixed Model and LASSO 36-Week Model

3.3 44-Week Model

Table 6 presents coefficients of the mixed model with center as a random effect and LASSO with center as a fixed effect. Following the StepAIC criterion, the mixed model identified the use of prenatal corticosteroids, ventilation support at 36 weeks, fraction of inspired oxygen at 36 weeks, ventilation support at 44 weeks, positive and exploratory pressure at 44 weeks, and medication for pulmonary hypertension at 44 weeks as important variables. Notably, the significance of prenatal corticosteroids extends across all three models, while ventilation support and fraction of inspired oxygen at 36 weeks are also emphasized in the 36-week model. The model also highlights the importance of ventilation support at 44 weeks, indicating lower log odds for non-invasive positive pressure compared to no support and higher odds for invasive positive pressure compared to no support. Additionally, elevated positive and exploratory pressure at 44 weeks and medication for pulmonary hypertension are associated with increased odds of tracheostomy. The lasso model culminated in a sparser model when compared birth LASSO model and 36-week LASSO model. Still encompasses more variables than the StepAIC criterion. Notably, the lasso model excludes birth weight, gestational age, gender,

weight at 36 weeks, positive and exploratory pressure at 36 weeks, medication for pulmonary hypertension at 36 weeks, weight at 44 weeks, the second level of ventilation support (non-invasive positive pressure), and peak inspiratory pressure needed at 44 weeks. This outcome underscores a limitation of LASSO, as it tends to eliminate specific levels of a variable rather than the variable as a whole. This nuance highlights the need for careful consideration when interpreting and comparing variable selection outcomes between LASSO and alternative methods.

Table 7 illustrates the enhanced performance of this model in comparison to the birth and 36-week models. The mixed model exhibits marginally higher AUC scores and lower Brier scores, indicative of improved discriminatory ability and overall model accuracy. Additionally, the mixed model demonstrates higher specificity but slightly lower sensitivity. These findings contribute to a nuanced understanding of the model's strengths and trade-offs in predicting tracheostomy outcomes, emphasizing the importance of considering multiple performance metrics for a comprehensive evaluation.

	Mixed Model*	LASSO		
Coefficient	Estimate	Estimate	Coefficient	Estimate
intercept	-3.325	-3.812	center2	-0.331
mat_ethn2	0	0.023	center3	-0.658
bw	0	0	center4	-0.781
ga	0	0	center5	0
blength	0	0.010	center7	-0.247
birth_hc	0	0.015	center12	1.330
del_method2	0	0.039	center16	0.288
prenat_sterYes	1.241	0.502	center20	-0.064
com_prenat_sterYes	0	0.195		
mat_chorioYes	0	0.012		
genderMale	0	0		
sgaSGA	0	0.055		
any_surfYes	0	-0.024		
weight_today.36	0	0		
ventilation_support_level.361	-0.490	-0.283		
ventilation_support_level.362	0.327	0.330		
inspired_oxygen.36	2.189	1.497		
p_delta.36	0	0.006		
peep_cm_h2o_modified.36	0	0		
med_ph.361	0	0		
weight_today.44	0	0		
ventilation_support_level_modified.441	-1.043	0		
ventilation_support_level_modified.442	0.337	1.293		
inspired_oxygen.44	0	0.486		
p_delta.44	0	0		
peep_cm_h2o_modified.44	0.259	0.120		
med_ph.44	0.899	0.781		

Table 6: Coefficients for 44-Week Model
**Note: Random Intercept for center are not shown.*

Metrics	Mixed Model	LASSO
AUC	0.933	0.900
Brier	0.082	0.083
Sensitivity	0.872	0.904
Specificity	0.901	0.873
Threshold	0.336	0.295

Table 7: Performance Metrics for the Generalized Mixed Model and LASSO 44-Week Model

4 Conslusion

4.1 Discussion

In this study, the objective was to construct predictive models at three critical time points in an infant's life: Birth, 36 weeks, and 44 weeks. A comparative analysis between two statistical methodologies—namely, a mixed model incorporating center as a random effect and a LASSO model with center as a fixed effect—was conducted. Given variable correlations, a StepAIC criterion was applied to the mixed model to facilitate variable selection, while the LASSO model inherently performs this task. Across all time point models, both methodologies exhibit commendable performance in key metrics. Maternal ethnicity consistently emerges as a significant predictor, except in the 44-week mixed model. For the mixed models, the utilization of prenatal corticosteroids consistently proves significant across all six models. Notably, for predicting tracheostomy at birth, gestational age, birth length, and indicators for small gestational age and surfactant administration assume importance. The 36-week mixed model underscores the significance of variables measured at this juncture, including weight, ventilation support, fraction of inspired oxygen, and an indicator for medication for pulmonary hypertension in predicting tracheostomy outcomes at 36 weeks. The 44-week mixed model is characterized as a sparse model, featuring ventilation support and a fraction of inspired oxygen at 36 weeks, ventilation support, positive and exploratory pressure, and medication for pulmonary hypertension at 44 weeks. Intriguingly, across all three time points, the LASSO model does not exhibit the same degree of sparsity as the mixed model after applying the StepAIC criterion. This observation underscores that, despite the inherent variable selection capability of LASSO, the mixed model with StepAIC tends to yield a more sparsely parameterized model for this data.

Given that AUC is a comprehensive metric assessing the overall discriminatory ability of a model, our model selection criterion prioritizes higher AUC scores. Consequently, for predicting tracheostomy outcomes at birth and 44 weeks, we propose the use of the mixed model featuring center as a random intercept term with variable selection through the StepAIC criterion. However, for predicting tracheostomy at 36 weeks, our recommendation leans towards the LASSO model incorporating center as a fixed effect. This selection approach aligns with the distinctive strengths and performance characteristics demonstrated by each model variant at different time points in the predictive modeling process.

4.2 Limitations

Our work is subject to certain limitations. Notably, the dataset exhibits a substantial number of missing values, and the variable representing maternal race had to be excluded due to inconsistencies in the data. Furthermore, it is crucial to acknowledge the use of the StepAIC. It is important to recognize that stepAIC is implemented not primarily for the purpose of improving model performance, but rather to streamline

model complexity while mitigating the impact on performance. In this context, alternative techniques, such as forward best subsets, could be explored. Additionally, an alternative approach involves fitting a mixed-effects model with a LASSO penalty, incorporating center as a random intercept term instead of treating it as a fixed effect. These considerations underscore the need for a judicious exploration of alternative methodologies and the implications of specific choices in the modeling process.

5 Code Apendix

```r
#Set working directoty
setwd("C:/Users/monic/OneDrive/Desktop/PHP2050/Project 2/")

#Libraries
library(readr)
library(naniar)
library(gtsummary)
library(tableone)
library(dplyr)
library(ggplot2)
library(gtable)
library(kableExtra)
library(mice)
library(corrplot)
library(ggpubr)
library(lme4)
library(MASS)
library(pROC)
library(glmnet)

#Import Data
df <- read.csv("project2.csv")


#Exclude duplicates ID
df <- df %>% filter(record_id != 2000824)



#Change classes
df <- df %>%
  mutate_if(is.character,as.factor)
df <- df %>%
  mutate(center = factor(center),
         mat_race = factor(mat_race),
         mat_ethn = factor(mat_ethn),
         del_method = factor(del_method),
         ventilation_support_level.36 = factor(ventilation_support_level
             .36),
         ventilation_support_level_modified.44 = factor(ventilation_
             support_level_modified.44),
```

```
         Trach = factor(Trach)
  )
df <- df %>%
  mutate_if(is.integer, as.numeric)
df <- df %>%
  mutate(Trach = case_when(Trach == "0" ~ "No",
                           Trach == "1" ~ "Yes")) %>%
  mutate(Trach = as.factor(Trach))

#which(df$center==21)
df$center[806] <- 20

df <- df %>% dplyr::select(!mat_race) #droppin race because of coding
    error
df <- df %>%
  mutate(com_prenat_ster = case_when(prenat_ster == "No" ~ "No", TRUE ~ as
      .character(com_prenat_ster)))
df <- df %>% mutate(com_prenat_ster = as.factor(com_prenat_ster))
df <- df %>% droplevels()
```

```
#Summary Statistics
tab_death <- df %>% dplyr::select(!record_id) %>%
  tbl_summary(digits = list(everything() ~ c(2)),
                   statistic = list(all_continuous() ~ "{mean} ({sd})"),
                   by = Death) %>%
  add_overall() %>%
  add_n() %>%
  modify_header(label ~ "**Death**") %>%
  modify_spanning_header(c("stat_1", "stat_2") ~ "**Treatment Received**")
      %>%
  bold_labels()
tab_trach <- df %>% dplyr::select(!record_id) %>%
  tbl_summary(digits = list(everything() ~ c(2)),
              statistic = list(all_continuous() ~ "{mean} ({sd})"),
              by = Trach) %>%
  add_overall() %>%
  add_n() %>%
  modify_header(label ~ "**Death**") %>%
  modify_spanning_header(c("stat_1", "stat_2") ~ "**Treatment Received**")
      %>%
  bold_labels()

tbl_merge(
```

```
  tbls = list(tab_death, tab_trach),
  tab_spanner = c("**Death**", "**Tracheostomy**")) %>%
  as_kable_extra(booktabs = TRUE, caption = "Summary Statistics Grouped by Response Outcome") %>%
  kableExtra::kable_styling(latex_options = "scale_down")
```

```
#Composite Outcome
df <- df %>%
  mutate(new_trach = case_when( Trach == "Yes" ~ "Yes",
                          (Trach == "No" & Death == "Yes") ~ "Yes",
                          (Trach == "No" & Death == "No") ~ "No")
)
df$new_trach <- as.factor(df$new_trach)
```

```
 #Creating three data frames for the three models
df_birthmodel <- df[,c(1:14,30)]
df_36wkmodel <- df[,c(1:20,27,30)]
df_44wkmodel <- df %>% dplyr::select(!Trach & !Death)

#Impute
#Birthmodel
df_birthmodel_out <- mice(df_birthmodel[,-1], 5, pri=F, seed = 1)
df_imp_birthmodel <- vector("list",5)
for (i in 1:5){df_imp_birthmodel[[i]] <- mice::complete(df_birthmodel_out, i)}


#36-wk model
df_36wk_out <- mice(df_36wkmodel[,-1], 5, pri=F, seed = 1)
df_imp_36wk <- vector("list",5)
for (i in 1:5){df_imp_36wk[[i]] <- mice::complete(df_36wk_out,i)}
#select correct population
for (i in 1:5) {
  df_imp_36wk[[i]] <- df_imp_36wk[[i]] %>% filter(hosp_dc_ga > 36) %>% dplyr::select(!hosp_dc_ga)
}

#44-wk model
df_44wk_out <- mice(df_44wkmodel[,-1], 5, pri=F, seed = 1)
df_imp_44wk <- vector("list",5)
for (i in 1:5){df_imp_44wk[[i]] <- mice::complete(df_44wk_out,i)}
#select correct population
for (i in 1:5) {
```

```
  df_imp_44wk[[i]] <- df_imp_44wk[[i]] %>% filter(hosp_dc_ga > 44) %>%
      dplyr::select(!hosp_dc_ga)
}
```

```
#pct_complete_case(df)


#Creating Missing Values Table
missing_table <- df %>% dplyr::select(!record_id) %>%
  summarize(across(everything(), ~ sum(is.na(.)))) %>%
  t() %>%
  as.data.frame() %>%
  mutate(n=V1) %>%
  dplyr::select(n) %>%
  arrange(desc(n)) %>%
  mutate("%" = round(n/dim(df)[1],4)*100) %>%
  filter(n>0)


#kable(missing_table, caption = 'Missing Data per Variables', booktabs =
    TRUE) %>%
#  kable_styling(full_width=T, font_size = 8 ,latex_options = c('hold_
    position', 'scale_down'))

missing_table$Variable <- rownames(missing_table)
dd <- missing_table %>% dplyr::select(Variable, n, '%') #taking what we
    are going to separate
dd2 <- cbind(dd[1:13, ],dd[14:26,])#separating
kable(dd2,
      caption = "Missing Data per Variables",booktabs=T,row.names = F,
      align = "lrr") %>%
  kable_styling( font_size = 8,latex_options = c('scale_down'))


#Visualization for Missing Data
mis_vars <- missing_table %>% filter(n > 0) %>% rownames()

#vis_miss(df %>% select(all_of(mis_vars)))+theme(axis.text.x=element_text(
    size=rel(.9), angle = 90))
#vis_miss(df)+theme(axis.text.x=element_text(size=rel(.9), angle = 90))

missing_table_death_no <- df %>% filter(Death != "No") %>%
  summarize(across(everything(), ~ sum(is.na(.)))) %>%
```

```
  t() %>%
  as.data.frame() %>%
  mutate(n=V1) %>%
  dplyr::select(n) %>%
  arrange(desc(n)) %>%
  mutate("%" = round(n/dim(df %>% filter(Death != "No"))[1],4)*100)
missing_table_death_yes <- df %>% filter(Death != "Yes") %>%
  summarize(across(everything(), ~ sum(is.na(.x)))) %>%
  t() %>%
  as.data.frame() %>%
  mutate(n=V1) %>%
  dplyr::select(n) %>%
  arrange(desc(n)) %>%
  mutate("%" = round(n/dim(df %>% filter(Death != "Yes"))[1],4)*100)



#vis_miss(df)
p1 <- vis_miss(df %>% filter(hosp_dc_ga < 44))+theme(axis.text.x=element_
    text(size=rel(.8), angle = 90))+ggtitle("Hospital Dicharge before 44
    weeks")
p2 <- vis_miss(df %>% filter(hosp_dc_ga > 44))+theme(axis.text.x=element_
    text(size=rel(.8), angle = 90))+ggtitle("Hospital Discharge after 44
    weeks")
ggarrange(p1,p2,ncol = 2)
```

```
##########Divide each imputed dataset into testing and training
#BIRTHMODEL
training_sets_birthmodel <- list()
testing_sets_birthmodel <- list()

set.seed(1)

for (i in 1:5) {
  n <- nrow(df_imp_birthmodel[[i]])
  num_test <- ceiling(n * .25)

  test_indices <- sample(1:n, num_test)

  training <- df_imp_birthmodel[[i]][-test_indices, ]
  testing <- df_imp_birthmodel[[i]][test_indices, ]

  training_sets_birthmodel[[i]] <- training
```

```
  testing_sets_birthmodel[[i]] <- testing
}
#36-weekmodel
training_sets_36wk <- list()
testing_sets_36wk <- list()

set.seed(1)

for (i in 1:5) {
  n <- nrow(df_imp_36wk[[i]])
  num_test <- ceiling(n * .25)

  test_indices <- sample(1:n, num_test)

  training <- df_imp_36wk[[i]][-test_indices, ]
  testing <- df_imp_36wk[[i]][test_indices, ]

  training_sets_36wk[[i]] <- training
  testing_sets_36wk[[i]] <- testing
}

#44-weekmodel

training_sets_44wk <- list()
testing_sets_44wk <- list()

set.seed(1)

for (i in 1:5) {
  n <- nrow(df_imp_44wk[[i]])
  num_test <- ceiling(n * .25)

  test_indices <- sample(1:n, num_test)

  training <- df_imp_44wk[[i]][-test_indices, ]
  testing <- df_imp_44wk[[i]][test_indices, ]

  training_sets_44wk[[i]] <- training
  testing_sets_44wk[[i]] <- testing
}
```

```
#Variable Selection for Mixed Model
birth_model_var <- vector("list",5)
```

```
3
4  for (i in 1:5) {
5  xx <- training_sets_birthmodel[[i]][,-1] #not consider center(nested)
6  model <- glm(new_trach ~., data = xx, family = binomial) %>%
7    stepAIC(trace = FALSE)
8  ss <- summary(model)
9  ss$coefficients
10 birth_model_var[[i]] <- ss$coefficients
11 }
12
13
14 #Selected Variables for mixed model
15 #sapply(birth_model_var, function(df) rownames(df)[-1]) %>% table()
16 vars <- c(NA)
17 for (i in 1:5) {
18   vars <- c(vars,unlist(rownames(birth_model_var[[i]])))
19 }
20 vars <- table(vars[-1])
21 vars <- vars[vars>=3]
22 vars <- names(vars)
23
24 coef_birthmodel_mm <- matrix(NA,nrow = length(vars), ncol = 5)
25 rownames(coef_birthmodel_mm) <- vars
26 coef_center__birthmodel_mm <-  matrix(NA,nrow = 9, ncol = 5)
27 rownames(coef_center__birthmodel_mm) <- c("center1","center2","center3","
       center4","center5","center7","center12","center16","center20")
28 for (i in 1:5) {
29   mod <- glmer(new_trach ~ any_surf + blength + ga + mat_ethn + prenat_
         ster + sga +(1 | center),
30                data = training_sets_birthmodel[[i]] ,
31                family = binomial,
32                control=glmerControl(optimizer="bobyqa",
33                                     optCtrl=list(maxfun=2e5)))
34   k <- mod %>% summary() %>% coef()
35   coef_birthmodel_mm[,i] <- k[,1]
36   k <- ranef(mod)$center
37   coef_center__birthmodel_mm[,i] <- k$`(Intercept)`
38
39 }
40
41 coef_birthmodel_mm <- rowMeans(coef_birthmodel_mm)
42 coef_center__birthmodel_mm <- rowMeans(coef_center__birthmodel_mm)
43
```

```r

##Predict
auc_birthmodel_mm <- rep(NA,5)
brier_birthmodel_mm <- rep(NA,5)
sensitivity_birthmodel_mm <- rep(NA,5)
specificity_birthmodel_mm <- rep(NA,5)
threshold_birthmodel_mm <- rep(NA,5)

for (i in 1:5) {
x_new <- testing_sets_birthmodel[[i]]
x_new <- x_new %>% dplyr::select(any_surf, blength,ga,mat_ethn,prenat_ster
   ,sga, new_trach,center)
x_new <- cbind(1,x_new)
x_new <- model.matrix(new_trach ~ any_surf+blength+ga+mat_ethn+prenat_ster
   +sga + center, x_new,
                      contrasts.arg = list(center = contrasts( testing_
                         sets_birthmodel[[i]]$center,
                                                               contrasts =
                                                                  FALSE)))

pred <- x_new %*% c(coef_birthmodel_mm,coef_center__birthmodel_mm)
pred <- exp(pred)/(exp(pred)+1)

levels(testing_sets_birthmodel[[i]]$new_trach) = c(0,1)

roc1 <- roc(predictor = pred, response = testing_sets_birthmodel[[i]]$new_
   trach, levels = c(0,1), direction = "<")
#plot(roc1, print.thres=TRUE)

k <- coords(roc=roc1, x = "best")

#store metrics
auc_birthmodel_mm[i] <- auc(roc1)
brier_birthmodel_mm[i] <- mean((pred - (as.numeric(testing_sets_birthmodel
   [[i]]$new_trach)-1))^2)
sensitivity_birthmodel_mm[i] <- k$sensitivity
specificity_birthmodel_mm[i] <- k$specificity
threshold_birthmodel_mm[i] <- k$threshold
}

auc_birthmodel_mm_pooled <- mean(auc_birthmodel_mm)
brier_birthmodel_mm_pooled <- mean(brier_birthmodel_mm)
sensitivity_birthmodel_mm_pooled <- mean(sensitivity_birthmodel_mm)
```

```r
specificity_birthmodel_mm_pooled <- mean(specificity_birthmodel_mm)
threshold_birthmodel_mm_pooled <- mean(threshold_birthmodel_mm)
```

```r
#LASSO
lasso <- function(df) {
  #' Runs 10-fold CV for lasso and returns corresponding coefficients
  #' @param df, data set
  #' @return coef, coefficients for minimum cv error

  # Matrix form for ordered variables
  x.ord <- model.matrix(new_trach~., data = df)[,-1]
  y.ord <- df$new_trach

  k <- 10
  set.seed(1)
  folds <- sample(1:k, nrow(df), replace=TRUE)

  # Lasso model
  lasso_mod_cv <- cv.glmnet(x.ord, y.ord, nfolds = 10, foldid = folds,
                            alpha = 1, family = "binomial")
  lasso_mod <- glmnet(x.ord, y.ord, nfolds = 10, foldid = folds,
                            alpha = 1, family = "binomial",
                            lambda = lasso_mod_cv$lambda.min)
  # Get coefficients
  coef <- coef(lasso_mod)
  return(coef)
}

# Find average lasso coefficients over imputed datasets
lasso_coef1 <- lasso(training_sets_birthmodel[[1]])
lasso_coef2 <- lasso(training_sets_birthmodel[[2]])
lasso_coef3 <- lasso(training_sets_birthmodel[[3]])
lasso_coef4 <- lasso(training_sets_birthmodel[[4]])
lasso_coef5 <- lasso(training_sets_birthmodel[[5]])
lasso_coef <- cbind(lasso_coef1, lasso_coef2, lasso_coef3,
                    lasso_coef4, lasso_coef5)
avg_coefs_lasso_birthmodel <- apply(lasso_coef, 1, mean)


df_birthmodel_long_test <- bind_rows(testing_sets_birthmodel)

x_vars <- model.matrix(new_trach ~. , df_birthmodel_long_test) #get long
    data model matrix
```

```r

pred <- x_vars %*% avg_coefs_lasso_birthmodel #predict
pred <- exp(pred)/(1+exp(pred))


y <- df_birthmodel_long_test$new_trach
levels(y) = c(0,1)
roc1 <- roc(predictor = pred, response = y, levels = c(0,1), direction = "<")
#plot(roc1, print.thres=TRUE)
k <- coords(roc=roc1, x = "best")

#store metrics
auc_birthmodel_lasso <- auc(roc1)[1]
brier_birthmodel_lasso <- mean((pred - (as.numeric(y)-1))^2)
sensitivity_birthmodel_lasso <- k$sensitivity
specificity_birthmodel_lasso <- k$specificity
threshold_birthmodel_lasso <- k$threshold
```

```r
##################36wk model
#Variable Selection for Mixed Model
wk36_var <- vector("list",5)

for (i in 1:5) {
xx <- training_sets_36wk[[i]][,-1] #not consider center(nested)
model <- glm(new_trach ~., data = xx, family = binomial) %>%
  stepAIC(trace = FALSE)
ss <- summary(model)
ss$coefficients
wk36_var[[i]] <- ss$coefficients
}


#Selected Variables for mixed model
#sapply(birth_model_var, function(df) rownames(df)[-1]) %>% table()
vars <- c(NA)
for (i in 1:5) {
  vars <- c(vars,unlist(rownames(wk36_var[[i]])))
}
vars <- table(vars[-1])
vars <- vars[vars>=3]
vars <- names(vars)

```

```r
coef_36wk_mm <- matrix(NA,nrow = length(vars), ncol = 5)
rownames(coef_36wk_mm) <- vars
coef_center__36wk_mm <-  matrix(NA,nrow = 9, ncol = 5)
rownames(coef_center__36wk_mm) <- c("center1","center2","center3","center4","center5","center7","center12","center16","center20")
for (i in 1:5) {
  mod <- glmer(new_trach ~ blength + inspired_oxygen.36 + mat_ethn + med_ph.36 + prenat_ster +
                ventilation_support_level.36 + weight_today.36 + (1 | center),
              data = training_sets_36wk[[i]] ,
              family = binomial,
              control=glmerControl(optimizer="bobyqa",
                                   optCtrl=list(maxfun=2e5)))
  k <- mod %>% summary() %>% coef()
  coef_36wk_mm[,i] <- k[,1]
  k <- ranef(mod)$center
  coef_center__36wk_mm[,i] <- k$`(Intercept)`
  }

coef_36wk_mm <- rowMeans(coef_36wk_mm)
coef_center__36wk_mm <- rowMeans(coef_center__36wk_mm)


##Predict
auc_36wk_mm <- rep(NA,5)
brier_36wk_mm <- rep(NA,5)
sensitivity_36wk_mm <- rep(NA,5)
specificity_36wk_mm <- rep(NA,5)
threshold_36wk_mm <- rep(NA,5)

for (i in 1:5) {
x_new <- testing_sets_36wk[[i]]
x_new <- x_new %>% dplyr::select(blength, inspired_oxygen.36, mat_ethn, med_ph.36,  prenat_ster, ventilation_support_level.36, weight_today.36, new_trach,center)
#x_new <- cbind(1,x_new)
x_new <- model.matrix(new_trach ~ blength + inspired_oxygen.36 + mat_ethn + med_ph.36 + prenat_ster+ ventilation_support_level.36 + weight_today.36 + center, x_new,
                      contrasts.arg = list(center = contrasts( testing_sets_36wk[[i]]$center,
                                                               contrasts =
```

```
                                                                    FALSE)))

pred <- x_new %*% c(coef_36wk_mm,coef_center__36wk_mm)
pred <- exp(pred)/(exp(pred)+1)

levels(testing_sets_36wk[[i]]$new_trach) = c(0,1)

roc1 <- roc(predictor = pred, response = testing_sets_36wk[[i]]$new_trach,
    levels = c(0,1), direction = "<")
#plot(roc1, print.thres=TRUE)

k <- coords(roc=roc1, x = "best")

#store metrics
auc_36wk_mm[i] <- auc(roc1)
brier_36wk_mm[i] <- mean((pred - (as.numeric(testing_sets_36wk[[i]]$new_
   trach)-1))^2)
sensitivity_36wk_mm[i] <- k$sensitivity
specificity_36wk_mm[i] <- k$specificity
threshold_36wk_mm[i] <- k$threshold
}

auc_36wk_mm_pooled <- mean(auc_36wk_mm)
brier_36wk_mm_pooled <- mean(brier_36wk_mm)
sensitivity_36wk_mm_pooled <- mean(sensitivity_36wk_mm)
specificity_36wk_mm_pooled <- mean(specificity_36wk_mm)
threshold_36wk_mm_pooled <- mean(threshold_36wk_mm)

#Recal that we choose vars repeated 3 or more because if we include all
   selected, the model was not capturing true pvalues for borth birthmodel
    and 36wk model
```

```
# Find average lasso coefficients over imputed datasets
lasso_coef1 <- lasso(training_sets_36wk[[1]])
lasso_coef2 <- lasso(training_sets_36wk[[2]])
lasso_coef3 <- lasso(training_sets_36wk[[3]])
lasso_coef4 <- lasso(training_sets_36wk[[4]])
lasso_coef5 <- lasso(training_sets_36wk[[5]])
lasso_coef <- cbind(lasso_coef1, lasso_coef2, lasso_coef3,
                    lasso_coef4, lasso_coef5)
avg_coefs_lasso_36wk <- apply(lasso_coef, 1, mean)


```

```r
df_36wk_long_test <- bind_rows(testing_sets_36wk)

x_vars <- model.matrix(new_trach ~. , df_36wk_long_test) #get long data model matrix

pred <- x_vars %*% avg_coefs_lasso_36wk #predict
pred <- exp(pred)/(1+exp(pred))


y <- df_36wk_long_test$new_trach
levels(y) = c(0,1)
roc1 <- roc(predictor = pred, response = y, levels = c(0,1), direction = "<")
#plot(roc1, print.thres=TRUE)
k <- coords(roc=roc1, x = "best")

#store metrics
auc_36wk_lasso <- auc(roc1)[1]
brier_36wk_lasso <- mean((pred - (as.numeric(y)-1))^2)
sensitivity_36wk_lasso <- k$sensitivity
specificity_36wk_lasso <- k$specificity
threshold_36wk_lasso <- k$threshold
```