Posters

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Sepsis-induced Acute Lung Injury and the Development of Bronchopulmonary Dysplasia in Premature Infants

Jacob S. Ward

Hung-Wen Yeh

Megan Tucker

Venkatesh Sampath

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Jacob Ward, DO; Hung-Wen Yeh, PhD; Megan Tucker, MD; Venkatesh Sampath, MBBS, MRCPCH

Children's Mercy Hospital Kansas City, Missouri & University of Missouri Kansas City School of Medicine

Background

- Bronchopulmonary dysplasia **(BPD) is a common source of morbidity and mortality for premature infants** with several known risk factors.
- Our group recently showed inflammatory processes such **as late-onset-sepsis (LOS) and necrotizing enterocolitis (NEC) is associated with acute-lung injury (ALI)** as measured by pulmonary severity scores (PSS).
- We hypothesized that **LOS and associated ALI increases the likelihood of developing moderate to severe BPD.**
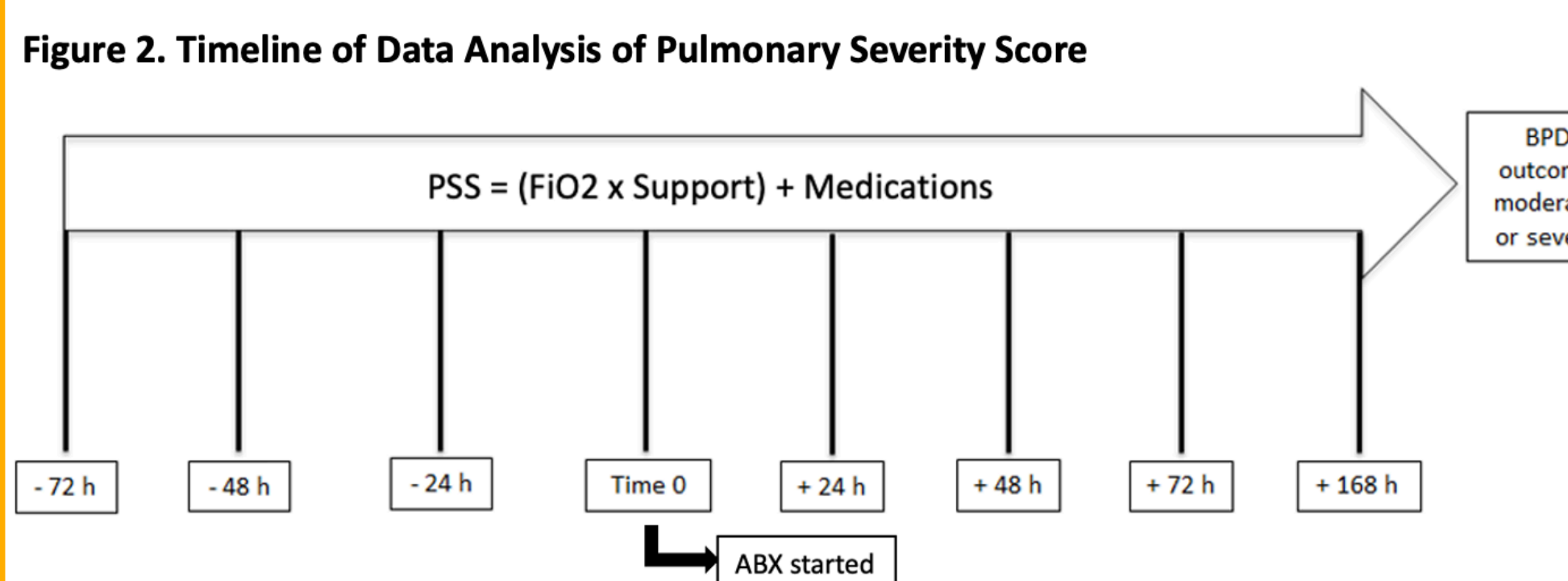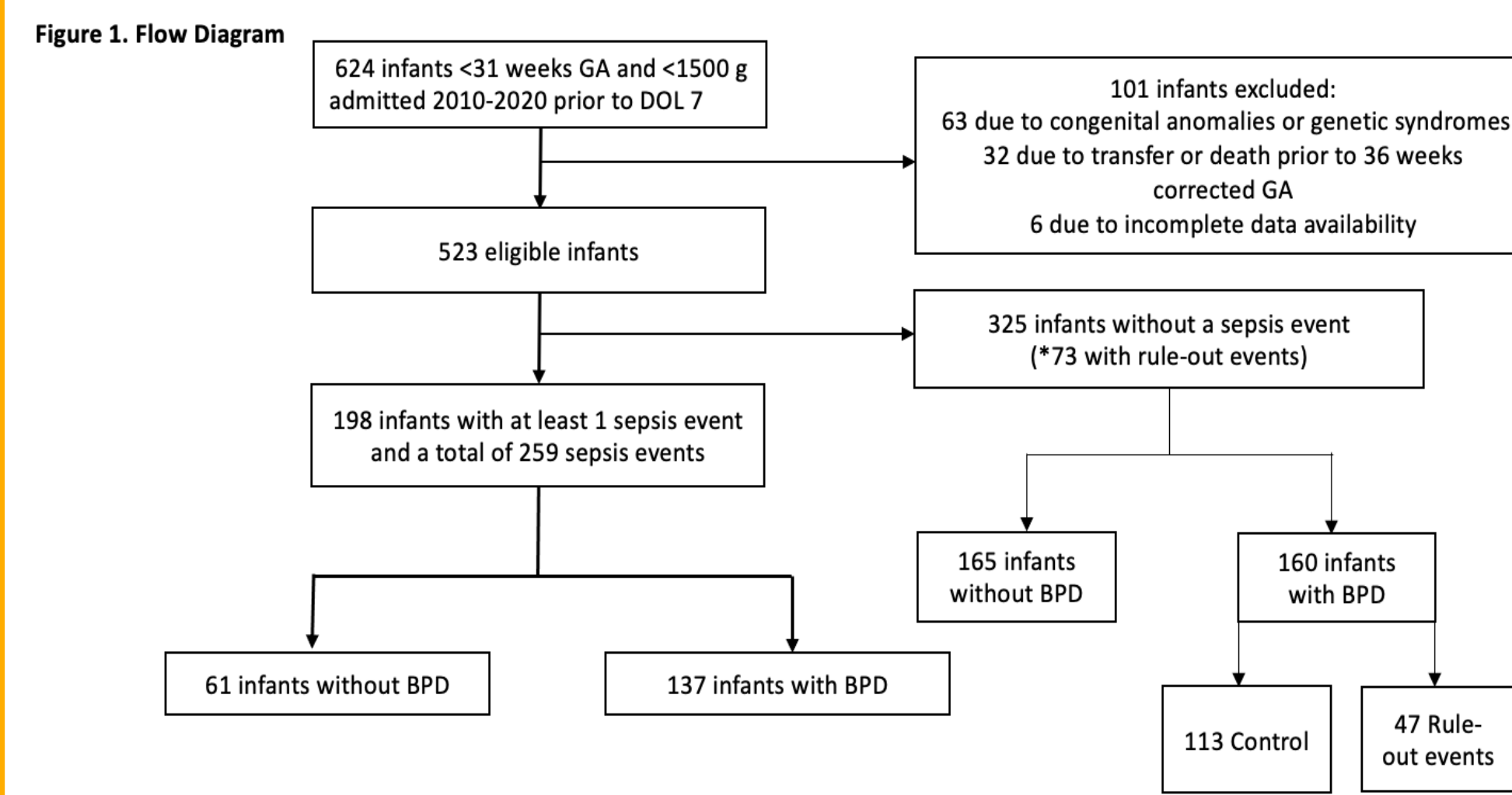
Objectives

1) Determine if LOS and number of LOS events increase risk of developing moderate to severe BPD.
2) Determine if LOS-induced ALI is more likely to result in moderate to severe BPD.

Design/Methods

- Retrospective case control study which included premature infants <31 weeks and <1500 (Fig. 1)
- Sepsis events defined per Table 1 and PSS calculated at different time points throughout event shown in Fig 2
- BPD classification per **NICHD 2000 consensus definition.**
- **3 models were built to predict BPD using different predictors**
  1. PSS profiles only.
  2. Demographic variables only. The stack ensemble of elastic net and conditional inference forest were used to predict BPD via 10-fold cross-validation with 10 replicates
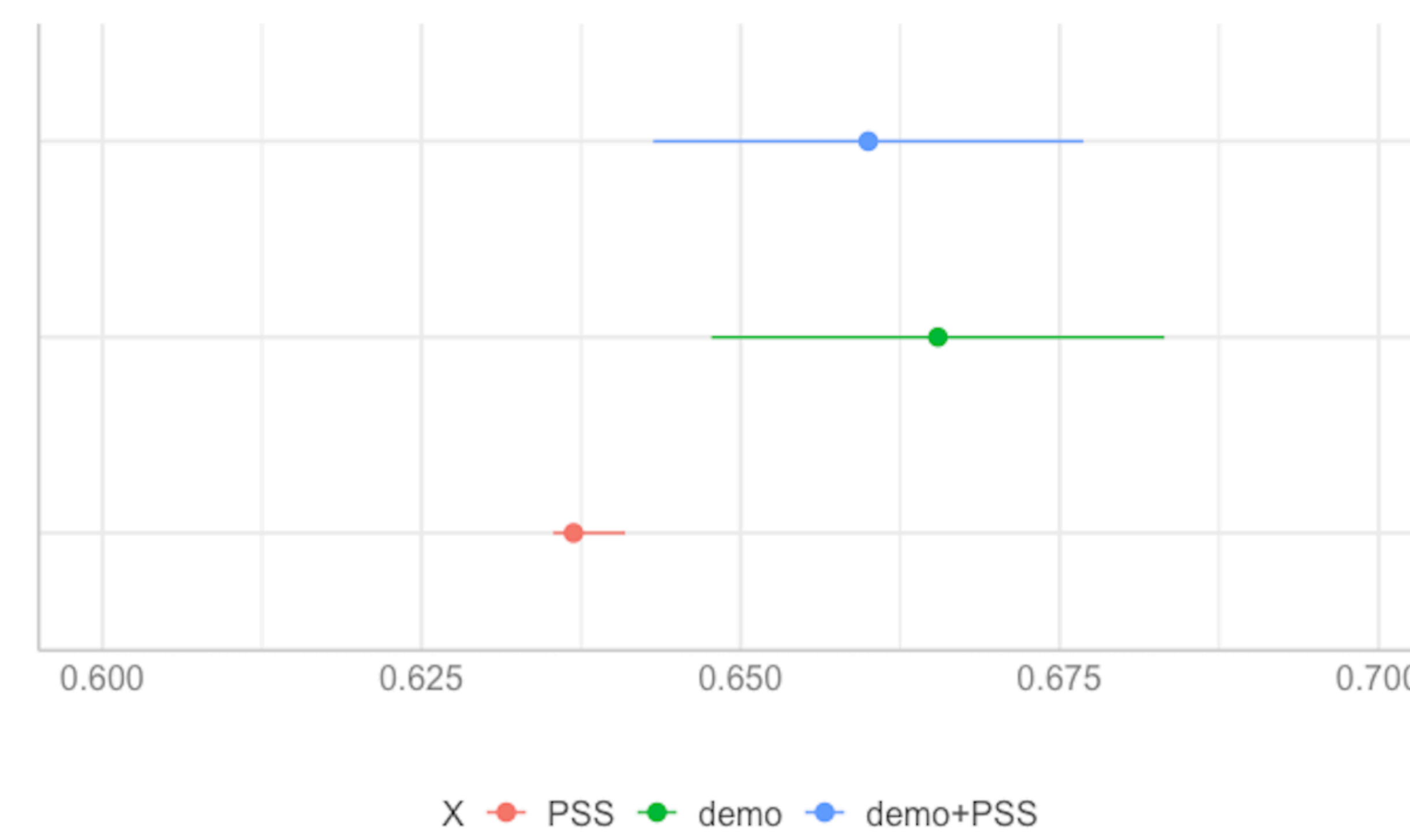 3. Demographic and PSS summary statistics (area under PSS curve and maximal PSS change). Same method as in 2.

Figure 1. Flow Diagram

624 infants <31 weeks GA and <1500 g admitted 2010-2020 prior to DOL 7 → 101 infants excluded: 63 due to congenital anomalies or genetic syndromes, 32 due to transfer or death prior to 36 weeks corrected GA, 6 due to incomplete data availability

523 eligible infants → 325 infants without a sepsis event (*73 with rule-out events)

198 infants with at least 1 sepsis event and a total of 259 sepsis events → 165 infants without BPD, 160 infants with BPD

61 infants without BPD, 137 infants with BPD

113 Control, 47 Rule-out events

Figure 2. Timeline of Data Analysis of Pulmonary Severity Score

PSS = (FiO2 x Support) + Medications

-72 h | -48 h | -24 h | Time 0 | +24 h | +48 h | +72 h | +168 h

ABX started

BPD outcome moderate or severe

Table 1. Classification of Sepsis Events

Culture positive sepsis	At least 1 positive blood culture and treated with antibiotics for greater than 6 consecutive days.
Necrotizing enterocolitis (NEC)/ Spontaneous intestinal perforation (SIP)	Infants diagnosed with stage II or greater NEC based on Bell's criteria or developed SIP as described in the medical record and who received antibiotics for greater than 6 days.
Urosepsis	Confirmed urinary tract infection (UTI) on catharized specimen who received antibiotics for greater than 6 days and met criteria for clinical sepsis.
Culture negative sepsis	Infants who received antibiotics for greater than 6 days for presumed sepsis and have 1 of following lab criteria: a. WBC < 5,000 b. WBC > 20,000 c. I:T ratio >/= 0.2 d. Platelet count < 100,000 e. CRP > 20mg/L (2.0 mg/dL)
Rule-out sepsis	Obtaining cultures and initiation of antibiotics for at least 48-72hr for concern of sepsis.

Results

Table 2. Bivariate Association of Sepsis with BPD

	no	yes	SMD
n	226	297	
Birth Weight (median)	**1000**	**840**	**0.20**
Gestational Age (median)	**27.5**	**26**	**0.26**
Race (%)			0.11
White	56.0	52.4	
Black	34.7	35.1	
Others	9.3	12.5	
Antenatal steroids = Yes (%)	30.3	44.8	0.30
Delivery mode = Vaginal (%)	38.5	30.0	0.18
Chorioamnionitis = Yes (%)	8.4	8.8	0.01
Sex = Female (%)	50.4	38.0	0.25
Multiple birth = Yes (%)	25.8	28.6	0.06
Apgar 5min (median)	7	6	0.07
# Sepsis episodes (median)	**0**	**0**	**0.21**
Sepsis = yes (%)	**27**	**46.1**	**0.41**

Table 3. Bivariate Associations of BPD with PSS

	no	yes	SMD
n	61	137	
Birth Weight	885	780	0.16
Gestational Age	26.3	25.4	0.24
Race (%)			0.27
White	50.8	45.4	
Black	42.4	39.4	
Others	6.8	15.2	
# sepsis	1	1	0.12
mPSS.auc	0.8	1.1	0.19
mPSS.chg	0.5	0.4	0.06
mPSS.d_3	0.7	0.9	0.16
mPSS.d0	0.8	1.1	0.15
mPSS.d1	0.9	1.0	0.12
mPSS.d2	**0.9**	**1.0**	**0.20**
mPSS.d3	**0.8**	**1.0**	**0.20**
mPSS.d7	**0.7**	**1.0**	**0.32**
mPSS.chg7	0.0	0.0	0.05

Tables 2 and 3: SMD - standardized mean difference or Cohen's D; bolded columns represent p<0.05.
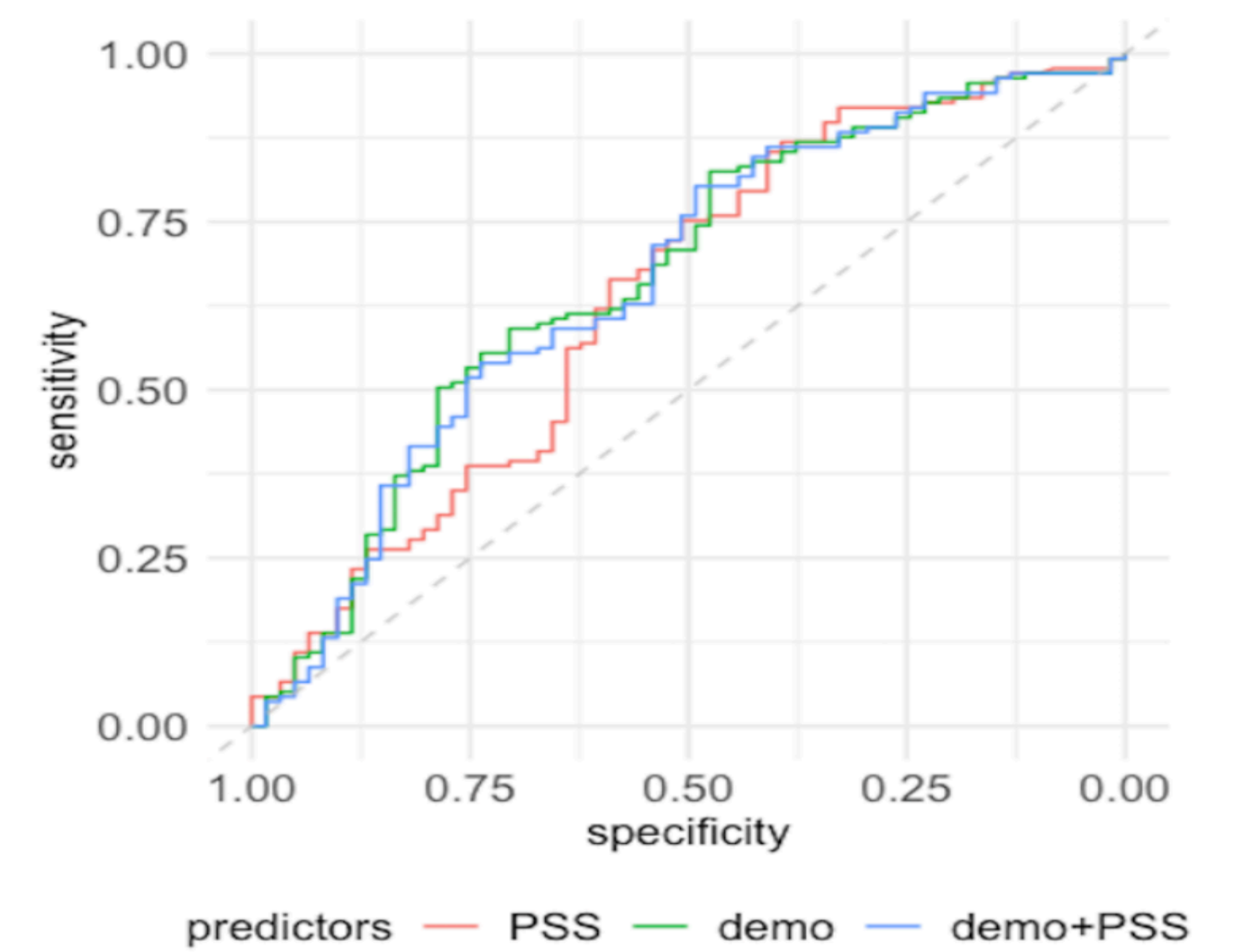
Figure 4. Area under ROC curves

Pulmonary Severity Score [PSS (alone)]	
Demographic variables [demo]	
demo+PSS	

Figure 3. Area under ROC curve and 95% CI

X — PSS — demo — demo+PSS

Pulmonary Severity Score [PSS (alone)]:	0.637 (0.635, 0.641)
Demographic variables [demo]:	0.665 (0.648, 0.683)
demo+PSS:	0.660 (0.643, 0.677)

Conclusions

- Our preterm cohort revealed a significant bivariate association of LOS, # LOS events, and PSS with BPD (Tab. 3 and Tab. 4).
- The **bivariate association of PSS and BPD**, showed **small associations** seen at time points **+48hr, +72hr,** and **+168hr** (Tab.3).
- **PSS can independently predict BPD**, however, when added to other demographic variables it does not enhance ability to predict BPD as area under ROC curve shows (Fig. 3 and Fig. 4)
- **Future work will hope to improve of prediction model by using additional parameters, such as CRP values.**
- We also hope to further examine the effect of sepsis-induced ALI on the development of severe BPD.

Acknowledgements

References

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Tucker, M. H., Yeh, H.-W., Oh, D., Shaw, N., Kumar, N., & Sampath, V. (2022). Preterm sepsis is associated with acute lung injury as measured by pulmonary severity score. Pediatric Research. https://doi.org/10.1038/s41390-022-02218-1