# Machine Learning Predicts Prolonged Acute Hypoxemic Respiratory Failure in Pediatric Severe Influenza 

## Supplemental Digital Content

Michaël S. Sauthier MD ${ }^{1,2,3}$, Philippe A. Jouvet MD PhD MBA ${ }^{3}$, Margaret M. Newhams MPH ${ }^{1}$, Adrienne G. Randolph MD MSc ${ }^{1,4}$ on behalf of the PALISI Pediatric Intensive Care Influenza (PICFLU) Network

1- Department of Anesthesiology, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, MA.
2- Department of Biomedical Informatics, Harvard Medical School, Boston, MA.
3- Departments of Pediatrics, Sainte-Justine Hospital, Montreal (Canada)
4- Departments of Anaesthesia and Pediatrics, Harvard Medical School, Boston, MA.

## Corresponding author:

Adrienne G. Randolph
Division of Critical Care Medicine, Bader 634, Boston
Children's Hospital, 300 Longwood Ave., Boston, MA 02115
adrienne.randolph@childrens.harvard.edu

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SDC 1: Performance of all models with $95 \%$ confidence interval. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated using probability cutoff of 0.5 .
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\begin{array}{|l|l|l|l|l|l|l|l|l|}\hline \text { Models } & \text { Timing } & \text { Algorithm } & \text { AUC } & \text { Sensitivity } & \text { Specificity } & \begin{array}{l}\text { Pos. pred. } \\
\text { value }\end{array}
$$ \& \begin{array}{l}Neg pred <br>

value\end{array} \& Accuracy\end{array}\right]\)| 0.74 |
| :--- |
| OI |
| Day 1 |
| OI |
| Day 1 |
| RF |


| OSI (all $\mathrm{SpO}_{2}$ ) | Day 2 | RF | $\begin{aligned} & \hline 0.78 \\ & (0.75-0.81) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.56 \\ & (0.44-0.67) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.92 \\ & (0.87-0.95) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.69 \\ & (0.59-0.8) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.86 \\ & (0.83-0.9) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.83 \\ & (0.79-0.86) \\ & \hline \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $\mathrm{SF}(\mathrm{all} \mathrm{SpO} 2)$ | Day 2 | LR | $\begin{aligned} & 0.79 \\ & (0.76-0.81) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.53 \\ & (0.36-0.64) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.77-0.94) \end{aligned}$ | $\begin{aligned} & 0.58 \\ & (0.46-0.67) \end{aligned}$ | $\begin{aligned} & 0.85 \\ & (0.8-0.88) \end{aligned}$ | $\begin{aligned} & 0.78 \\ & (0.74-0.81) \\ & \hline \end{aligned}$ |
| $\mathrm{SF}\left(\right.$ all $\mathrm{SpO}_{2}$ ) | Day 2 | RF | $\begin{aligned} & 0.75 \\ & (0.71-0.8) \end{aligned}$ | $\begin{aligned} & 0.43 \\ & (0.31-0.57) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.79-0.93) \end{aligned}$ | $\begin{aligned} & 0.54 \\ & (0.42-0.66) \end{aligned}$ | $\begin{aligned} & \hline 0.82 \\ & (0.79-0.86) \end{aligned}$ | $\begin{aligned} & 0.76 \\ & (0.72-0.8) \end{aligned}$ |
| Multivariables | Day 2 | LR | $\begin{aligned} & 0.86 \\ & (0.83-0.88) \end{aligned}$ | $\begin{aligned} & 0.61 \\ & (0.52-0.7) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.81-0.92) \end{aligned}$ | $\begin{aligned} & 0.62 \\ & (0.52-0.71) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.84-0.9) \end{aligned}$ | $\begin{aligned} & 0.81 \\ & (0.77-0.83) \end{aligned}$ |
| Multivariables | Day 2 | RF | $\begin{aligned} & 0.93 \\ & (0.89-0.95) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.69 \\ & (0.59-0.79) \end{aligned}$ | $\begin{aligned} & 0.94 \\ & (0.89-0.97) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.79 \\ & (0.68-0.88) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.9 \\ & (0.87-0.93) \end{aligned}$ | $\begin{aligned} & 0.88 \\ & (0.85-0.9) \end{aligned}$ |
| OI | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.81 \\ & (0.77-0.84) \end{aligned}$ | $\begin{aligned} & 0.66 \\ & (0.54-0.81) \end{aligned}$ | $\begin{aligned} & \hline 0.77 \\ & (0.69-0.88) \end{aligned}$ | $\begin{aligned} & \hline 0.74 \\ & (0.67-0.84) \end{aligned}$ | $\begin{aligned} & 0.71 \\ & (0.63-0.82) \end{aligned}$ | $\begin{aligned} & 0.72 \\ & (0.66-0.77) \end{aligned}$ |
| OI | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | RF | $\begin{aligned} & 0.82 \\ & (0.75-0.86) \end{aligned}$ | $\begin{aligned} & 0.71 \\ & (0.54-0.84) \end{aligned}$ | $\begin{aligned} & 0.79 \\ & (0.6-0.89) \end{aligned}$ | $\begin{aligned} & 0.76 \\ & (0.62-0.87) \end{aligned}$ | $\begin{aligned} & 0.74 \\ & (0.64-0.84) \end{aligned}$ | $\begin{aligned} & 0.75 \\ & (0.65-0.83) \end{aligned}$ |
| PF | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.73 \\ & (0.67-0.77) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.79 \\ & (0.68-0.9) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.52 \\ & (0.35-0.68) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.63 \\ & (0.54-0.72) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.71 \\ & (0.64-0.81) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.66 \\ & (0.6-0.72) \end{aligned}$ |
| PF | $\begin{aligned} & \hline \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.79 \\ & (0.73-0.85) \end{aligned}$ | $\begin{aligned} & 0.82 \\ & (0.64-0.96) \end{aligned}$ | $\begin{aligned} & \hline 0.63 \\ & (0.49-0.77) \end{aligned}$ | $\begin{aligned} & 0.7 \\ & (0.61-0.77) \end{aligned}$ | $\begin{aligned} & 0.79 \\ & (0.64-0.95) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.73 \\ & (0.65-0.8) \end{aligned}$ |
| OSI | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.82 \\ & (0.74-0.87) \end{aligned}$ | $\begin{aligned} & 0.79 \\ & (0.55-1) \end{aligned}$ | $\begin{aligned} & 0.63 \\ & (0.27-0.91) \end{aligned}$ | $\begin{aligned} & 0.7 \\ & (0.54-0.88) \end{aligned}$ | $\begin{aligned} & 0.77 \\ & (0.61-1) \end{aligned}$ | $\begin{aligned} & 0.71 \\ & (0.6-0.77) \end{aligned}$ |
| OSI | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | RF | $\begin{aligned} & 0.72 \\ & (0.61-0.8) \end{aligned}$ | $\begin{aligned} & 0.64 \\ & (0.44-0.83) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.59 \\ & (0.41-0.83) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.62 \\ & (0.51-0.77) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.61 \\ & (0.49-0.76) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.61 \\ & (0.52-0.71) \\ & \hline \end{aligned}$ |
| SF | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & \hline 0.82 \\ & (0.78-0.85) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.73 \\ & (0.58-0.86) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.74 \\ & (0.66-0.8) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.59 \\ & (0.52-0.64) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.85 \\ & (0.77-0.91) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.74 \\ & (0.7-0.76) \\ & \hline \end{aligned}$ |
| SF | $\begin{aligned} & \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.81 \\ & (0.76-0.85) \end{aligned}$ | $\begin{aligned} & 0.68 \\ & (0.47-0.86) \end{aligned}$ | $\begin{aligned} & 0.8 \\ & (0.7-0.9) \end{aligned}$ | $\begin{aligned} & 0.64 \\ & (0.54-0.75) \end{aligned}$ | $\begin{aligned} & 0.84 \\ & (0.75-0.92) \end{aligned}$ | $\begin{aligned} & 0.76 \\ & (0.71-0.81) \end{aligned}$ |
| OSI (all $\mathrm{SpO}_{2}$ ) | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.78 \\ & (0.75-0.8) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.51 \\ & (0.43-0.61) \end{aligned}$ | $\begin{aligned} & 0.94 \\ & (0.88-0.98) \end{aligned}$ | $\begin{aligned} & 0.75 \\ & (0.62-0.87) \end{aligned}$ | $\begin{aligned} & 0.85 \\ & (0.83-0.88) \end{aligned}$ | $\begin{aligned} & 0.83 \\ & (0.81-0.86) \end{aligned}$ |
| OSI (all $\mathrm{SpO}_{2}$ ) | $\begin{aligned} & \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.78 \\ & (0.75-0.81) \end{aligned}$ | $\begin{aligned} & \hline 0.58 \\ & (0.46-0.7) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.91 \\ & (0.87-0.95) \end{aligned}$ | $\begin{aligned} & \hline 0.69 \\ & (0.59-0.8) \end{aligned}$ | $\begin{aligned} & \hline 0.87 \\ & (0.83-0.9) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.83 \\ & (0.79-0.86) \end{aligned}$ |
| $\mathrm{SF}(\mathrm{all} \mathrm{SpO} 2)$ | $\begin{aligned} & \hline \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.8 \\ & (0.78-0.83) \end{aligned}$ | $\begin{aligned} & 0.62 \\ & (0.49-0.71) \end{aligned}$ | $\begin{aligned} & 0.82 \\ & (0.75-0.88) \end{aligned}$ | $\begin{aligned} & 0.53 \\ & (0.46-0.61) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.82-0.9) \end{aligned}$ | $\begin{aligned} & 0.77 \\ & (0.73-0.79) \end{aligned}$ |
| $\mathrm{SF}\left(\right.$ all $\mathrm{SpO}_{2}$ ) | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | RF | $\begin{aligned} & 0.83 \\ & (0.78-0.87) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.62 \\ & (0.48-0.76) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.86 \\ & (0.79-0.92) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.6 \\ & (0.51-0.71) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.83-0.91) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.8 \\ & (0.76-0.83) \\ & \hline \end{aligned}$ |
| Multivariables | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.86 \\ & (0.83-0.89) \end{aligned}$ | $\begin{aligned} & 0.64 \\ & (0.52-0.75) \end{aligned}$ | $\begin{aligned} & 0.86 \\ & (0.81-0.91) \end{aligned}$ | $\begin{aligned} & 0.61 \\ & (0.53-0.69) \end{aligned}$ | $\begin{aligned} & 0.88 \\ & (0.84-0.91) \end{aligned}$ | $\begin{aligned} & 0.81 \\ & (0.77-0.83) \\ & \hline \end{aligned}$ |
| Multivariables | $\begin{aligned} & \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.93 \\ & (0.9-0.95) \end{aligned}$ | $\begin{aligned} & 0.71 \\ & (0.6-0.82) \end{aligned}$ | $\begin{aligned} & \hline 0.93 \\ & (0.88-0.97) \end{aligned}$ | $\begin{aligned} & 0.78 \\ & (0.67-0.88) \end{aligned}$ | $\begin{aligned} & 0.91 \\ & (0.87-0.94) \end{aligned}$ | $\begin{aligned} & \hline 0.88 \\ & (0.85-0.91) \end{aligned}$ |
| Multivariables (reduced) | $\begin{aligned} & \text { Day } \\ & 1+2 \\ & \hline \end{aligned}$ | LR | $\begin{aligned} & 0.84 \\ & (0.81-0.87) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.59 \\ & (0.48-0.69) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.9 \\ & (0.85-0.94) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.68 \\ & (0.57-0.77) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.83-0.9) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.83 \\ & (0.79-0.85) \\ & \hline \end{aligned}$ |
| Multivariables (reduced) | $\begin{aligned} & \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.91 \\ & (0.88-0.94) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.72 \\ & (0.61-0.83) \end{aligned}$ | $\begin{aligned} & \hline 0.91 \\ & (0.86-0.96) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.74 \\ & (0.64-0.85) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.91 \\ & (0.87-0.94) \end{aligned}$ | $\begin{aligned} & 0.86 \\ & (0.83-0.89) \\ & \hline \end{aligned}$ |
| Multivariables (reduced+year) | $\begin{aligned} & \hline \text { Day } \\ & 1+2 \end{aligned}$ | LR | $\begin{aligned} & 0.84 \\ & (0.8-0.86) \end{aligned}$ | $\begin{aligned} & \hline 0.6 \\ & (0.48-0.71) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.9 \\ & (0.84-0.94) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.67 \\ & (0.55-0.76) \\ & \hline \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.83-0.9) \\ & \hline \end{aligned}$ | $\begin{aligned} & \hline 0.82 \\ & (0.78-0.85) \\ & \hline \end{aligned}$ |
| Multivariables (reduced+year) | $\begin{aligned} & \text { Day } \\ & 1+2 \end{aligned}$ | RF | $\begin{aligned} & 0.92 \\ & (0.88-0.94) \end{aligned}$ | $\begin{aligned} & 0.72 \\ & (0.61-0.84) \end{aligned}$ | $\begin{aligned} & 0.92 \\ & (0.87-0.97) \end{aligned}$ | $\begin{aligned} & 0.76 \\ & (0.66-0.87) \end{aligned}$ | $\begin{aligned} & 0.91 \\ & (0.87-0.94) \end{aligned}$ | $\begin{aligned} & 0.87 \\ & (0.84-0.9) \end{aligned}$ |

AUC: area under the ROC curve, RF: random forests, LR: logistic regression.

SDC 2: Importance of predictors in random forest models using the error rate classification after permutation of the predictors. MAwP: mean airway pressure.


