

## Supplementary Methods

We investigated overfitting of our models and report below the estimated percentage of overfitting for the models investigating the outcome **ICU admission** using the STATA package `overfit`. We follow the methods as per Harrell Jr FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Statistics in medicine*. 1996 Feb 29;15(4):361-87 and as described in detail in Copas JB. Regression, prediction and shrinkage. *Journal of the Royal Statistical Society: Series B (Methodological)*. 1983 Jul;45(3):311-35.

Exposure age

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	21.51	2.43	19.53
se	2.99	1.71	3.31

Exposure sex

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	19.17	1.79	17.68
se	2.92	1.66	3.06

Exposure country

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	19.17	1.79	17.68
se	2.92	1.66	3.06

Exposure WBC count on admission

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	23.42	1.77	22.01
se	3.05	2.07	3.40

Exposure platelets on admission

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	19.96	1.52	18.71
se	3.04	1.78	3.18

Exposure ferritin

Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	18.31	2.39	16.30

se	2.50	1.55	2.80
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Exposure gastro-intestinal involvement  
Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	20.57	1.83	19.07
se	2.98	1.68	3.14

Exposure mucocutaneous involvement  
Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	21.67	2.04	20.02
se	3.09	1.67	3.30

Exposure admission  
Shrinkage statistics (expressed in percent)

	out-of-sam~s	in-sample ~s	overfitting
estimate	19.17	1.79	17.68
se	2.92	1.66	3.06

The problem is described in the literature as the ‘small data bias’, i.e., the rule of thumb is that a minimum of 10 outcome events per predictor variable are required when using logistic regression. The article by Vittinghoff (Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. *Am J Epidemiol.* 2007 15;165(6):710-8. doi: 10.1093/aje/kwk052.) however specifically investigated this rule of thumb and concludes that this might be too conservative and that 5 to 9 outcomes per predictor variable result in acceptable levels of bias and coverage.

For a subset we also investigated overfitting as proposed in the book by Hosmer Jr DW & Lemeshow S. Applied logistic regression. Second edition (no changes in third edition). John Wiley & Sons; 2000 p134-135. We assessed goodness-of-fit and simplified our models further for comparison, which did not change our results. This is another solution, next to relaxing the rule of thumb and maintain reasonable caution in interpretation of the results.