Reply to: Consider the laboratory aspects in developing patient prediction models

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REPLYING TO J. Reeve & P. Twomey *Nature Machine Intelligence* <https://doi.org/10.1038/s42256-020-0221-2> (2020)

We agree with Reeve and Twomey that “pre-analytical and analytical issues need to be considered”¹. We summarize the details in the following paragraphs.

Tongji Hospital, where data were collected, is one of the most advanced hospitals in Wuhan and in China as a whole, and uses state-of-the-art equipment and protocols. In particular, it has strict procedures in place to minimize laboratory errors, including haemolysis. All samples are checked for errors. In the unlikely scenario that laboratory technicians find haemolysis in blood samples, they reject the samples and request new ones. If lower levels of haemolysis are not initially spotted, and are identified at the time of examination instead, the sample would then be marked as “Haemolysis+” or “+++”. A clinician may then request a second blood sample.

Regarding the LDH assay, Tongji Hospital uses the conversion of lactate to pyruvate ($L \rightarrow P$) with concomitant reduction of NAD^+ to NADH. The exact kit was lactate dehydrogenase acc.to IFCC ver.2 made by Roche diagnostics. Its Chinese Food and Drug administration (CFDA) number is 20162404206. According to the guidelines for this kit, the normal range for adults is $\leq 250 \text{ U l}^{-1}$ (ref.²).

Finally, Tongji Hospital only measures hs-CRP for COVID-19 patients. If new datasets with CRP data become available in the future, we can rerun our code³ to detect whether this is an important marker and compare it with hs-CRP. CRP and hs-CRP are expected to be highly correlated and an ideal dataset would contain both measurements, allowing a direct comparison to determine

which would be more informative (and whether they both contain the same information).

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Author contributions

All authors wrote the manuscript.

Competing interests

The authors declare no competing interests.

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