

## Reply to Russo et al

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## Conflict of Interest Information

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To the Editor,

We thank Dr. Russo and colleagues for taking the time to critically appraise and respond to our recent publication assessing clinical and laboratory characteristics of patients admitted to the Sechenov University hospital network in Moscow, Russia for suspected COVID-19 infection. We read about the findings of the RESILIENCY study [1] with great interest, as they are much in agreement with the results from our cohort. This further confirms the importance of appropriate clinical management of all admitted patients with suspected SARS-CoV-2 infection irrespective of the reverse transcription polymerase chain reaction (RT-PCR) result.

In their study, Russo et al [1] demonstrated that over half of the admitted patients did not have positive RT-PCR at the time of admission. The authors presented the clinical management protocol for all patients admitted to the emergency room (ER) with respiratory failure and/or fever who require management for suspected COVID-19. The findings are in line with the outcomes of our study, as 50.3% of patients admitted to hospital in our cohort did not have a single positive RT-PCR swab result. Likewise, the diagnostic and treatment strategies were based primarily on clinical and laboratory findings for all admitted patients, irrespective of the RT-PCR results.

A high false-negative rate of the RT-PCR tests, varying between 20 and 66%, depending on the day since symptom onset has been previously reported [2]. Although negative RT-PCR tests were found in almost half of patients in a few large cohort studies [3-5], including our own, patients with suspected COVID-19 infection were normally excluded from statistical analysis in the absence of the positive test result [3, 4, 6-9]. We would like to emphasise that most of the national and international data on COVID-19 cases and deaths are based exclusively on positive RT-PCR and may seriously underestimate the true prevalence and mortality of COVID-19. There is a pressing need to account for the number of patients with clinical features of COVID-19 and negative RT-PCR.

Russo et al. suggest that some clinical and laboratory features may help physicians discriminate cases of SARS-CoV-2 from other causes regardless of the RT-PCR results. We support authors in their initiative to develop reliable parameter sets to allow for early differentiation of patients at higher risk of unfavourable outcomes. This is very much in line with the national and international efforts to harmonise and collate data on clinical characteristics of COVID-19 and develop clinical algorithms and scoring systems. A recent multicentre study from the International Severe Acute Respiratory and emerging Infections Consortium Coronavirus Clinical Characterisation Consortium-(ISARIC-4C) resulted in the development of a very promising pragmatic risk score to predict mortality in patients admitted to hospital with COVID-19 [10], demonstrating an excellent negative predictive value. Future research should focus on the development and validation of reliable and user-friendly tools for use in routine clinical practice.

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