Clinical Infectious Diseases
CORRESPONDENCE

COVID-19: Find the Right Questions to be Answered

To the Editor—We read with great interest the article by Montejano and colleagues, which aimed to assess how the inclusion criteria of ongoing phase 2 and 3 clinical trials for coronavirus disease 2019 (COVID-19) treatment fit with the actual population of hospitalized individuals with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a teaching hospital in Madrid, Spain [1]. The authors found that most of individuals admitted to their hospital do not meet the inclusion criteria for recent trials and concluded that this was mainly due to discrepancies between the ideal trial population and the actual characteristics of COVID-19 hospitalized individuals, which are rapidly evolving.

Although we do agree that the characteristics of the hospitalized population change over time and might have led to the discrepancies observed, we would like to underline some inconsistencies in the methodology applied by the authors that could have led to an under estimation of eligible participants: (1) first of all the BEST [2] and DEFACOVID [3] trials, aimed to evaluate potential treatment for acute respiratory distress syndrome (ARDS). Because the authors excluded the "critically ill patients at the time of admission" from their analysed sample it is not surprising that most of the participants were not eligible for these 2 trials; (2) the author stated that "the initiation of COVID-19–specific treatment in 61% of patients" were among the most prevalent exclusion criteria. This statement would have only been true if the investigated trials would have been actively enrolling at the site when the retrospective eligibility assessment was carried out and all the individual would have had the possibility to be screened at the time of SARS-CoV-2 diagnosis/admission for the eligibility in these trials. Otherwise, considering that the observation of the authors was retrospective in nature, a prevalent user bias would have occurred and "potentially eligible individuals" at T0 (baseline) would have been wrongly identified as "non-eligible" because previously exposed to SARS-CoV-2 treatments [4].

Apart from these methodological concerns, we believe that the authors have raised an important issue. Although the COVID-19 pandemic is no longer considered a public health emergency of international concern by the World Health Organization (WHO) [5], it continues to challenge our everyday clinical practice; therefore, it remains crucial to identify residual unmet needs [6] in order to be able to pose the right causal questions [7]. In conclusion, because of the rapidly evolving clinical scenario, one important pitfall, not specifically mentioned by the authors, is that often, by the time the trial is completed, the original trial question is no longer relevant for clinical practice.

Note

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