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Fungal infections should be part of the core outcome set for COVID-19

In response to the needs of the rapidly evolving COVID-19 outbreak, the Clinical Characterisation and Management Working Group of the WHO Research and Development Blueprint programme, the International Forum for Acute Care Trialists, and the International Severe Acute Respiratory and Emerging Infections Consortium published a minimum set of common outcome measures for studies of COVID-19.¹ A core outcome set is crucial in the setting of an evolving research response to the COVID-19 pandemic and will greatly facilitate pooling of data across cohort studies and clinical trials.¹ The proposed minimal outcome set involves a broad range of parameters, including organ dysfunction, biochemical parameters, radiological findings, secondary infections, duration of intervention, quality of life, pregnancy outcomes, and resource use.¹ It is surprising that only bacterial and viral secondary infections are considered in the proposed set, without mention of fungal coinfections. There are indications that the frequency of bacterial coinfections in patients with COVID-19 might be low, whereas up to 30% of patients admitted to the intensive care unit (ICU) were reported to develop invasive pulmonary aspergillosis.²

Secondary infections with *Aspergillus* spp have emerged in association with influenza infection. Severe influenza was found to be an independent risk factor for invasive pulmonary aspergillosis.³ All-cause mortality of patients in the ICU with influenza-associated pulmonary aspergillosis was notably higher than in patients in the ICU with influenza only (51% vs 28%, $p < 0.001$),³ and some manifestations of influenza-associated pulmonary aspergillosis, such as invasive aspergillus tracheobronchitis, have been reported to have a mortality rate as high as 90%.⁴ The first data collected indicate that aspergillus disease manifestations are more heterogeneous in patients with COVID-19 than in those with influenza,⁵ which might be due to differences in the pathophysiology of the viral infection. Notably, serum galactomannan was frequently negative in patients with COVID-19-associated pulmonary aspergillosis (CAPA), whereas respiratory samples were aspergillus positive. Distinguishing between airway colonisation and invasive disease might prove difficult. Indeed, whereas patients with presumed CAPA can survive without antifungal therapy, cases of proven CAPA have been reported that were serum galactomannan negative.⁶ Given these diagnostic challenges and the lack of a CAPA case definition, clinical studies are urgently needed to gain more insight into the pathophysiology of CAPA, to identify host and risk factors, and to design diagnostic and treatment strategies. To benefit from data collected through

international clinical research studies of COVID-19, we believe that fungal infections should be part of the proposed core outcome set.

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