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- 4 Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis* 2020; published online Dec 14. [https://doi.org/10.1016/S1473-3099\(20\)30847-1](https://doi.org/10.1016/S1473-3099(20)30847-1).
- 5 Maertens J, Theunissen K, Verbeken E, et al. Prospective clinical evaluation of lower cut-offs for galactomannan detection in adult neutropenic cancer patients and haematological stem cell transplant recipients. *Br J Haematol* 2004; **126**: 852–60.

We read with interest the ECMM/ISHAM consensus criteria for COVID-19-associated pulmonary aspergillosis (CAPA), but noted with concern its limited applicability to resource-limited settings.<sup>1</sup> Multiple studies indicate that approximately 20% of severely ill patients with COVID-19 develop invasive aspergillosis if a diagnosis is actively sought.<sup>2</sup> Pakistan was among the first countries to report CAPA in critically ill patients with COVID-19 using AspICU criteria.<sup>3</sup> After an initial report of five putative CAPA cases from March to April, 2020, at our institute, within 2 months 12 more putative CAPA cases were identified. The largest series of CAPA cases include data from four low-income and middle-income countries (LMICs).<sup>4</sup> In these and other LMICs, very few clinical laboratories do fungal PCR or expensive serology-based tests such as galactomannan and  $\beta$ -D-glucan. Similarly, due to hazards related to aerosol production, bronchoscopic or non-bronchoscopic lavage procedures are rarely done. At our institute from July to December, 2020, 490 tracheal aspirates were sent for culture, compared with only two bronchial lavage samples from COVID-19 patients. Therefore, despite having substantial CAPA burden in our centre, none of the patients in retrospect could be categorised into any of the three grades of proven, probable, or possible, as suggested by Philipp Koehler and colleagues.<sup>1</sup>

A very restricted disease categorisation is concerning as it will lead to underrecognition of this important

complication in patients with COVID-19, not only for surveillance but also for their management. On the basis of better inclusivity of patients too hypoxic to undergo bronchoscopy and applicability to low-resource settings, we propose that endotracheal aspirates be added to the appropriate specimens for diagnosis. These may be cultured in high volume (0.5–1.0 mL) for better fungal yield<sup>5</sup> and in settings where galactomannan is available be validated for detecting the aspergillus antigen. High-volume culture on Sabouraud dextrose agar in our laboratory increased yield of moulds from 15% to 72% in 133 lower respiratory samples (tracheal aspirates, bronchial lavages, and sputa). However, cultures positive for *Aspergillus* spp must be interpreted strictly within each clinical context to prevent overdiagnosis. We have begun to validate aspergillus galactomannan in endotracheal aspirates for patients with CAPA. So far, in 15 patients with CAPA and 15 without, we have found a sensitivity and specificity of 93.3% and 60.0%, respectively, at a galactomannan index of 1.414 (appendix). These data, and those from a study by Roman-Montes and colleagues,<sup>6</sup> highlight the need for expanded datasets.

More flexible diagnostic criteria might be warranted for a common complication of a pandemic, incorporating simpler approaches on difficult-to-obtain samples, including high-volume culture and aspergillus antigen on tracheal aspirates.

DWD reports holding founder shares in F2G; acting as a consultant to Pulmatrix, Pulmocide, Zambon, iCo Therapeutics, Mayne Pharma, Biosergen, Bright Angel Therapeutics, Cipla, and Metis; being paid for talks on behalf of Dynamiker, Hikma, Gilead, Merck, Mylan, and Pfizer; and being a longstanding member of the Infectious Diseases Society of America Aspergillosis Guidelines group, the European Society for Clinical Microbiology, and Infectious Diseases Aspergillosis Guidelines group. All other authors declare no competing interests.

\*Kausar Jabeen, Joveria Farooqi, Muhammad Irfan, Syed Ahsan Ali, David W Denning  
kausar.jabeen@aku.edu

Aga Khan University, Karachi, Pakistan (KJ, JF, MI, SAA); Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK (DWD)

- 1 Koehler P, Bassetti M, Chakrabarti A, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis* 2020; published online Dec 14. [https://doi.org/10.1016/S1473-3099\(20\)30847-1](https://doi.org/10.1016/S1473-3099(20)30847-1).
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### Authors' reply

We thank Nitipong Permpalung and colleagues and Kausar Jabeen and colleagues for their thoughtful remarks on the 2020 ECMM/ISHAM consensus criteria on COVID-19-associated pulmonary aspergillosis (CAPA).<sup>1</sup> We acknowledge that the proposed definitions have shortcomings due to the recent and rapid emergence of CAPA limiting validation studies in this patient population. However, up to publication of these consensus definitions, CAPA cohort studies had used numerous case definitions, including EORTC/MSGERC (for immunocompromised patients), AspICU, modified AspICU, modified Influenza-Associated Pulmonary Aspergillosis (IAPA), and modified IAPA expert case definition, illustrating the urgent need for standardisation<sup>2</sup> and recognition of secondary fungal infections as an issue in future WHO COVID-19 clinical research recommendations.<sup>3</sup>

Despite reservations during the first COVID-19 wave about doing



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See Online for appendix