Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.

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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.[1] Multiple studies indicate that approximately 20% of severely ill patients with COVID-19 develop invasive aspergillosis if a diagnosis is actively sought.[2] Pakistan was among the first countries to report CAPA in critically ill patients with COVID-19 using AspICU criteria.[3] 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).[4] In these and other LMICs, very few clinical laboratories do fungal PCR or expensive serology-based tests such as galactomannan and β-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.[1]

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[5] 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,[6] 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.

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Authors' reply

We thank Nitipong Permpalung and colleagues and Kauser Jabeen and colleagues for their thoughtful remarks on the 2020 ECMM/ISHAM consensus criteria on COVID-19-associated pulmonary aspergillosis (CAPA).[1] 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[2] and recognition of secondary fungal infections as an issue in future WHO COVID-19 clinical research recommendations.[3]

Despite reservations during the first COVID-19 wave about doing

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bronchoscopy, this procedure remains the cornerstone of invasive aspergillosis diagnosis as it is a well validated procedure, it enables diagnosis of invasive tracheobronchitis, and bronchoalveolar lavage (BAL) fluid is validated for detection of galactomannan. During the first wave, bronchoscopy was already recommended in patients with COVID-19 to diagnose secondary infection, and the procedure can be done safely using WHO-style checklists, team timeouts, and safety precautions, including adequate personal protective equipment.[4] There is increasing evidence that infectious risk associated with bronchoscopy on intubated COVID-19 patients is indeed manageable.[5]

We agree that data are limited in relation to galactomannan performance and thresholds for the diagnosis of CAPA. However, thresholds identifying the optimal performance of galactomannan-EIA have been described in detailed studies across diverse populations, and consistent optimal thresholds have been determined, irrespective of patient population. Meta-analyses involving various patient populations have confirmed a high specificity (≥90%) when galactomannan-EIA is done with a threshold of ≥1·0, and on the basis of excellent meta-analytical performance (sensitivity 90%, specificity 94%) the 2019 American Thoracic Society guidelines support the use of galactomannan-EIA on BAL fluid in patients with suspected invasive fungal disease.[6] Furthermore, the thresholds provided are in line with those for the diagnosis of IAPA.

The CAPA consensus definitions accept non-directed bronchial lavage (NBL) galactomannan as a diagnostic criterion as NBL offers an opportunity to obtain material from the lower respiratory tract, with limited aerosolisation risk. Although NBL has not been validated for galactomannan detection, the thresholds we provided were based on existing evidence.[7,8] Furthermore, to acknowledge the scarcity of supporting evidence, we classified patients diagnosed through NBL galactomannan as possible CAPA, which highlights the reservation in relation to enrolling patients in clinical trials or registries but permits earlier therapy in the clinic through ease of sampling.

The diagnosis of CAPA remains challenging, and the comments by Jabeen and colleagues highlight the diagnostic difficulties encountered in resource-limited settings. The authors propose more flexible diagnostic criteria and advocate the use of endotracheal aspirates to diagnose CAPA. We believe that testing of upper respiratory tract specimens is insufficient to discriminate between aspergillus colonisation and invasive infection, and this specimen was therefore not considered a diagnostic criterion to classify CAPA cases. The positive predictive value of aspergillus culture of endotracheal aspirates was 20% in a study involving 56 CAPA cases and 156 controls (unpublished). Furthermore, our definition of CAPA relies not only on potentially restricted biomarkers, but also on conventional mycology, including microscopy and aspergillus culture, to fulfil microbiological diagnostic criteria, provided that lower respiratory tract specimens are obtained.

As highlighted by the conflicting opinions raised by Permpalung and colleagues and Jabeen and colleagues, we believe that the 2020 ECMM/ISHAM consensus definitions provide a solid base to standardise clinical CAPA research and enhance comparability of surveillance studies, in response to an urgent clinical need. As further evidence becomes available, our understanding of performance characteristics of diagnostic tests in various sample types will increase and will help to further refine the case definitions. Given the diagnostic challenges we encounter in CAPA, histopathological validation of diagnostic tests and the CAPA case definition is a crucial next step.

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What does 95% COVID-19 vaccine efficacy really mean?

It is imperative to dispel any ambiguity about how vaccine efficacy shown in trials translates into protecting individuals and populations. The mRNA-based Pfizer[1,2] and Moderna[3] vaccines were shown to have 94–95% efficacy in preventing symptomatic COVID-19, calculated as 100 × (1 minus the attack rate with vaccine divided by the attack rate with placebo). It means that in a population such as the one enrolled in the trials, with a cumulated COVID-19 attack rate over a period of 3 months of about 1% without a vaccine, we would expect roughly 0·05% of vaccinated people would get diseased. It does not mean that 95% of people are protected from disease with the vaccine—a general misconception of vaccine protection also found in a *Lancet Infectious Diseases* Editorial.[4] In the examples used in the Editorial, those protected are those who would have become diseased with COVID-19 had they not been vaccinated. This distinction is all the more important as, although we know the risk reduction achieved by these vaccines under trial conditions, we do not know whether and how it could vary if the vaccines were deployed on populations with different exposures, transmission levels, and attack rates.

Simple mathematics helps. If we vaccinated a population of 100 000 and protected 95% of them, that would leave 5000 individuals diseased over 3 months, which is almost the current overall COVID-19 case rate in the UK. Rather, a 95% vaccine efficacy means that instead of 1000 COVID-19 cases in a population of 100 000 without vaccine (from the placebo arm of the abovementioned trials, approximately 1% would be ill with COVID-19 and 99% would not) we would expect 50 cases (99·95% of the population is disease-free, at least for 3 months).

Accurate description of effects is not hair-splitting; it is much-needed exactness to avoid adding confusion to an extraordinarily complicated and tense scientific and societal debate around COVID-19 vaccines.

I declare no competing interests.

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Border screening is an essential component of COVID-19 testing strategies in Vanuatu

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In their Personal View, Belinda Hengel and colleagues[1] note that geographical dispersion of small populations across islands and other rural and remote settings presents a key barrier to COVID-19 testing access, and they present a decentralised COVID-19 point-of-care testing model based on in-community testing of suspected (symptomatic) cases. The model is based on point-of-care testing using a rapid, fully automated, self-contained, qualitative RT-PCR test for SARS-CoV-2 detection using single-use cartridges.[2] Hengel and colleagues note that several Pacific Island countries and territories already have GeneXpert platforms in use for tuberculosis management within provincial-level and national-level health services.[1] The proposed model is relevant to settings where there is widespread community transmission. However, it is less relevant in the absence of community transmission.

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The Pacific Island nation of Vanuatu (population 290 000, 83 islands), similar to many other Pacific Island countries and territories, has experienced border cases only—that is, cases identified in managed quarantine facilities—and has not experienced community transmission of SARS-CoV-2. COVID-19 testing via the GeneXpert platform became available in May, 2020.[3] Test procurement is through the regional Joint Incident Management Team (coordinated by the WHO Representative Office for the South Pacific), and test allocation to Vanuatu comprises approximately 3% of the population (8400 tests ordered).[4] Due to the limited number of tests available, and reflecting the epidemiological scenario of border cases only, Vanuatu has adopted a testing strategy that prioritises efficient and targeted resource use