

Protocol deviations

The following deviations from the original Invasive Fungal Diseases in Critically Ill Adult Patients in Intensive Care Unit (FUNDICU) protocol ¹ should be acknowledged:

- According to the protocol, the project was expected to be completed in 2019 ¹. After an initial delay related to the large amount of work required for the conduction of work package 1 (identification of the relevant literature), most of project activities were paused at the beginning of 2020 owing to the involvement of almost all panel members in the care of coronavirus disease 2019 (COVID-19) patients and resumed subsequently, with completion of the project in 2023.
- Based on the retrieved literature, the pre-defined systematic review on the use and performance of existing tests and definitions for the diagnosis of cryptococcosis was included in the systematic review on the use and performance of existing tests and definitions for other invasive fungal diseases ¹.
- The end of the literature search period was initially set at 31 December 2018 ¹, but subsequently expanded to 31 March 2022 in line with the delay in the project activities connected to the COVID-19 pandemic. Update results regarding invasive aspergillosis (IA) and invasive candidiasis (IC) have been published elsewhere^{2,3}. With regard to *Pneumocystis jirovecii* pneumonia (PJP), the update of the literature search, performed using the same methodology of the original search⁴, did not identify additional studies meeting inclusion criteria (of 382 papers retained after duplicates removal, 13 were eventually selected for full text evaluation based on title and abstract screening, and excluded for the following reasons: not conducted in the ICU [n = 8]; no isolated diagnostic performance for PJP [n = 4], single laboratory test used as diagnostic reference [n = 1]). No suitable studies were also retrieved when updating the previous literature search⁴ regarding invasive fungal diseases other than IC, IA, and PJP (of 379 papers initially retained after duplicates removal, 2 were eventually selected for full text evaluation based on title and abstract screening, and excluded for the following reason: not conducted in the ICU [n = 2]).
- After agreement between project chairs recognizing the expertise connected to the topic of the project, and before conduction of the project activities, an additional member (Joost Wauters) was added to the expert panel.
- The live meeting was conducted remotely via an online meeting platform owing to the changed timeline of the project and the difficulty in organizing a dedicated live event connected to the COVID-19 pandemic.
- A fourth round of remote voting was conducted in order to take into account reviewers' comments. This allowed to: (i) properly consider the weight of reviewers' suggestions against the already obtained provisional expert consensus by solid methodology (i.e., only proposed changes regarding points on which discussion were still protracted after the previous provisional consensus were considered for voting); (ii) guarantee the preservation of the rigorous methodology of voting process by expert panel members of any possible modifications of definitions. Eventually, besides minor text changes for fluency or clarification (without changes of meaning), the following two modifications were agreed during the final round of vote: (i) not to include serum BDG as mycological criterion for probable deep-seated candidiasis, pending further evidence (see the related discussion in the main manuscript); (ii) not to include multiorgan failure (MOF) as ICU host factor for probable invasive pulmonary aspergillosis (IPA) and probable tracheobronchial aspergillosis (TBA), since it could also represent a consequence of various other diseases/conditions in

critically ill patients (thus the risk of misclassification as IPA/TBA in presence of *Aspergillus* colonization and MOF due to other causes could be nonnegligible, leading to insufficient specificity for research definitions).

- Review from patients' representatives and from the European Federation of Pharmaceutical Industries and Associations (EFPIA) representatives and other stakeholders was not performed prior to submission for publication, as the panel eventually opted for an initial public version based on rigorous and exclusive evaluation by the involved scientific societies and groups. Nonetheless, post-publication review and inputs from patients' representatives and stakeholders are very welcome and we hope they will contribute to shape future updates of FUNDICU definitions.
- According to ESCMID rules, no public consultation was necessary prior to publication for this initiative of ESCMID study groups (ESGCIP and EFISG). However, as above, post-publication public review and inputs are very welcome and we hope they will contribute to shape future updates of FUNDICU definitions.
- Besides initially supporting international/European societies, endorsement of FUNDICU was also subsequently provided by the International Society of Antimicrobial Chemotherapy (ISAC) and the International Society for Human and Animal Mycology (ISHAM).
- Endorsement has also been provided by the following national scientific societies, acknowledged in the author byline: the Austrian Society for Medical Mycology (ÖGMM), the Italian Society of Anesthesia, Analgesia, Reanimation, and Intensive Care (SIAARTI), and the Italian Society of Anti-Infective Therapy (SITA).

References

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3. Bassetti M, Zuccaro V, Asperges E, Scudeller L, Giacobbe DR, investigators F. Performance of existing definitions and tests for the diagnosis of invasive aspergillosis in critically ill, non-neutropenic, adult patients: An update including COVID-19 data. *J Infect*. Nov 2022;85(5):573-607. doi:10.1016/j.jinf.2022.08.003
4. Giacobbe DR, Cortegiani A, Karaiskos I, et al. Performance of Existing Definitions and Tests for the Diagnosis of Invasive Fungal Diseases other than Invasive Candidiasis and Invasive Aspergillosis in Critically Ill, Adult Patients: A Systematic Review with Qualitative Evidence Synthesis. *Journal of fungi (Basel, Switzerland)*. Feb 28 2021;7(3)doi:10.3390/jof7030176