

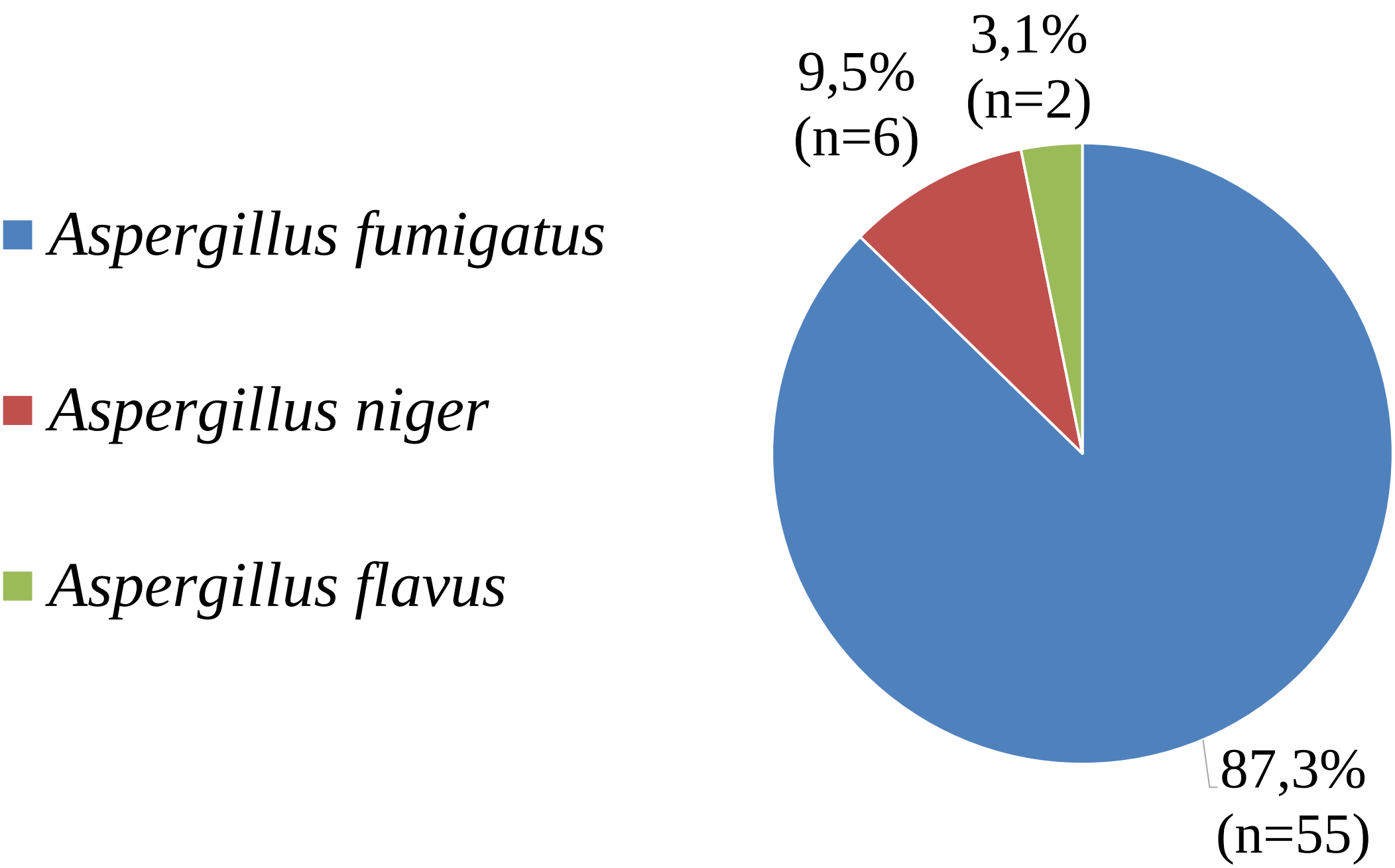
Introduction:

Aspergillosis is an infectious disease caused by inhaling *Aspergillus* mold spores from the environment. *Aspergillus fumigatus* is the most common causative agent of aspergillosis. In 2023, at the REUH laboratory, 63 *Aspergillus spp.* were isolated. Among these, *A. fumigatus* accounted for 87.3%, with other common non-fumigatus *Aspergillus* species including *A. flavus* (9.5%), *A. niger* (3.1%), and no *A. terreus*. Invasive pulmonary aspergillosis (IA) is the most severe form of infection for at-risk groups, including organ transplant recipients, patients with hematological malignancies and chronic lung diseases. First-line therapy for aspergillosis is voriconazole, a broad-spectrum triazole antifungal medication, along with other azoles. However, azole resistance is a growing global health issue, with rates ranging from 0% to 19% worldwide, average prevalence in Europe is ~3%.⁽¹⁾ The major resistance mechanisms involve point mutations in the coding sequence of *cyp51A* gene in combination with a 34-base pair (TR34/L98H) and 46-base pair (TR46/Y121F/T289A) tandemrepeat in the promoter region of this gene.⁽²⁾ The *cyp51A* gene is specific for both *A. fumigatus* wildtype and mutant strains.

Aims and Objectives:

The aim of the study was to analyse the prevalence of azole-resistant *Aspergillus fumigatus* and to improve diagnostics in Latvia.

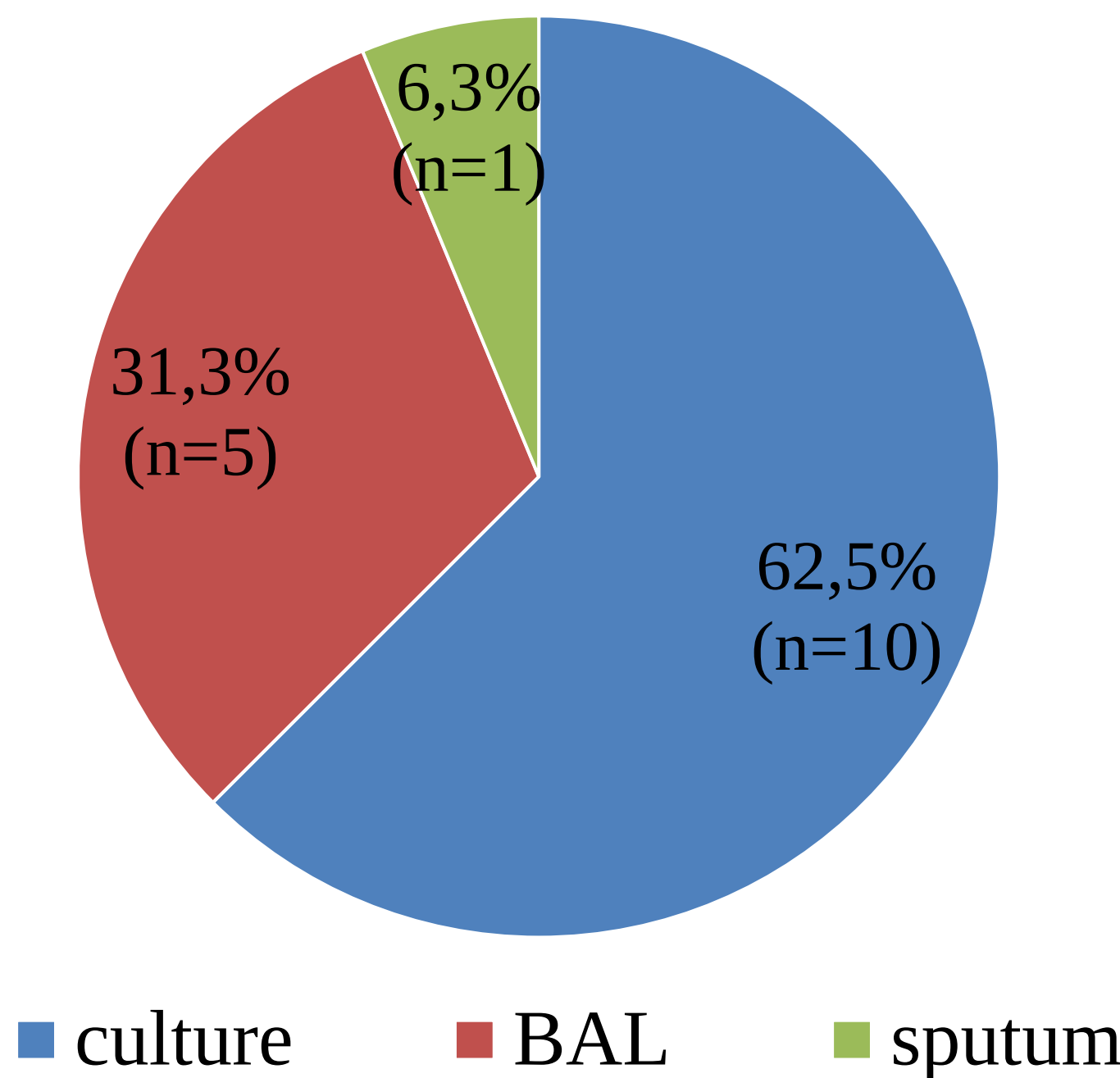
Aspergillus spp. species isolated in REUH in 2023



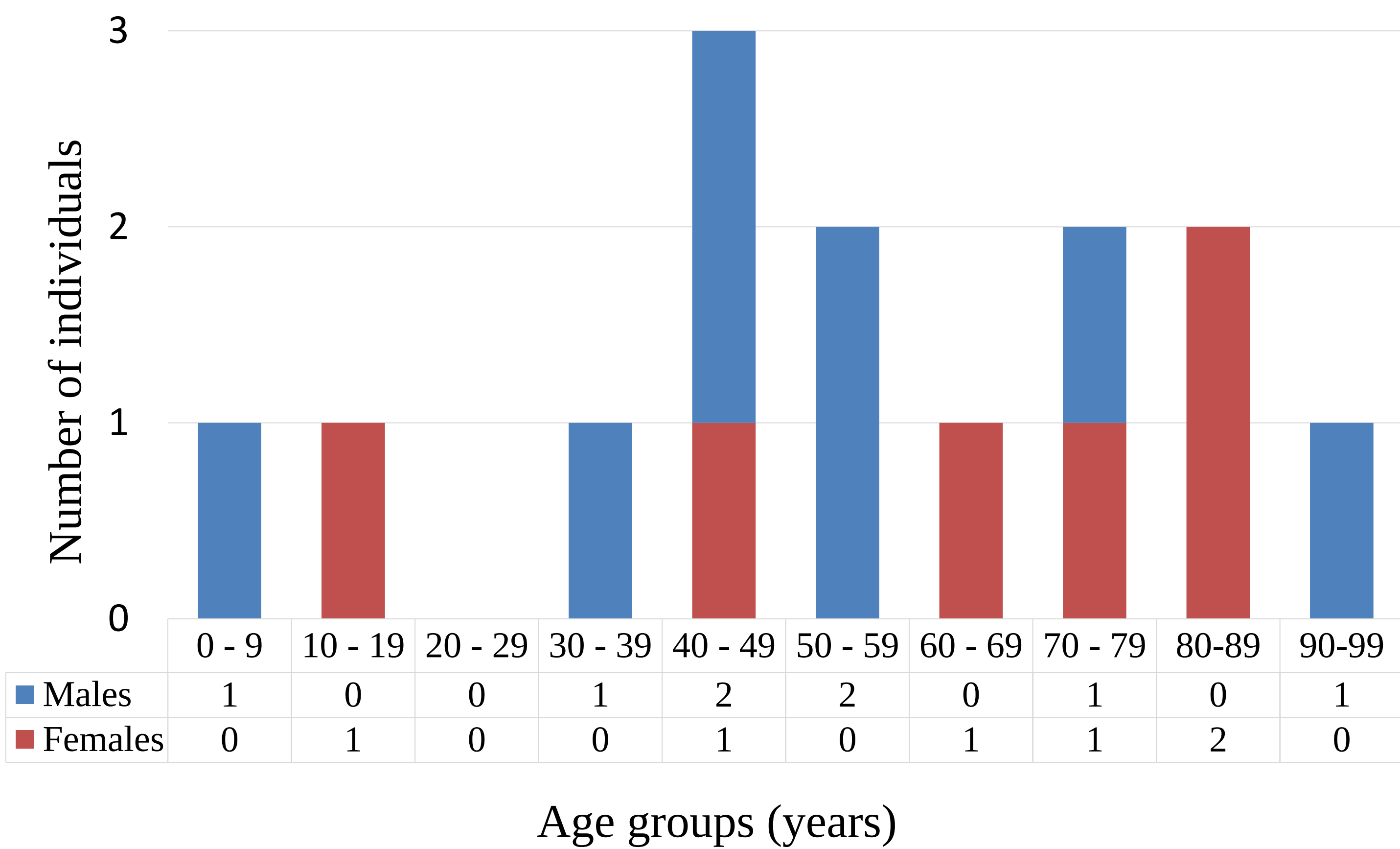
Materials and Methods:

From 01.12.2023 to 01.04.2024, 16 samples from 14 patients were tested at the NMRL of Latvia to detect *A. fumigatus cyp51A* gene, TR34, and TR46 mutations using the AsperGenius 2.0 Resistance TR Multiplex real-time PCR kit (PathoNostics, Netherlands). The sample materials were fungal culture (n = 10), bronchoalveolar lavage (BAL) (n = 5), and sputum (n = 1).

Tested specimen types



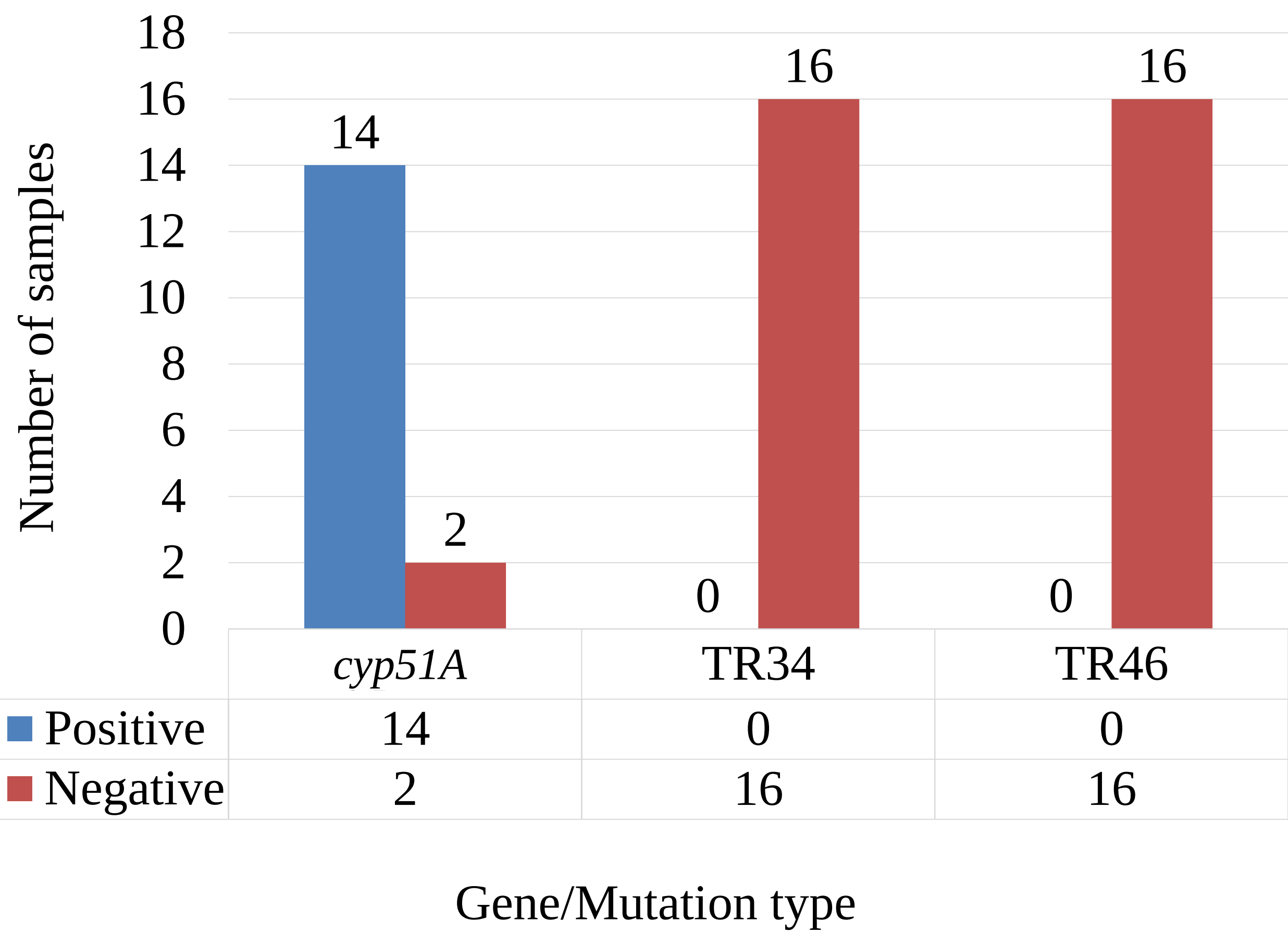
Age and Sex distribution



Results:

The analysis of data showed that the *A. fumigatus cyp51A* gene was found in 14 samples (from 12 patients) and was not found in two BAL samples (from 2 patients). TR34 and TR46 mutations were not detected in any of the 16 samples (from 14 patients). The male-to-female ratio was 8:6. The ages ranged from 1 month to 97 years, with a median age of 55 years. Of the total, 14.3% (2 out of 14) were children (1 month to 17 years) and 85.7% (12 out of 14) were adults (18 to 80 years).

Summary of *cyp51A* gene and TR34/TR46 mutation detection



Conclusions:

This test was applied for the first time in Latvia and found no TR34 and TR46-resistant strains. The PCR assay will help timely detect azole-resistant strains, initiate alternative therapy, and control the prevalence in Latvia. More samples are needed to thoroughly assess the prevalence in Latvia. Direct resistance detection via PCR simplifies and accelerates obtaining results.

References:

1. van der Linden JW, Arendrup MC, Warris A, Lagrou K, Pelloux H, Hauser PM, Chrysanthou E, Mellado E, Kidd SE, Tortorano AM, Dannaoui E, Gaustad P, Baddley JW, Uekötter A, Lass-Flörl C, Klimko N, Moore CB, Denning DW, Pasqualotto AC, Kibbler C, Arikian-Akdagli S, Andes D, Meletiadiis J, Naumiuk L, Nucci M, Melchers WJ, Verweij PE. Prospective multicenter international surveillance of azole resistance in *Aspergillus fumigatus*. *Emerg Infect Dis*. 2015 Jun;21(6):1041-4. doi: 10.3201/eid2106.140717. PMID: 25988348; PMCID: PMC4451897.

2. Jeanvoine A, Rocchi S, Bellanger AP, Reboux G, Millon L. Azole-resistant *Aspergillus fumigatus*: A global phenomenon originating in the environment? *Med Mal Infect*. 2020 Aug;50(5):389-395. doi: 10.1016/j.medmal.2019.07.014. Epub 2019 Aug 28. PMID: 31472992.