WHAT IS THE BURDEN OF ASPERGILLOSIS AND OTHER FUNGAL INFECTIONS IN PATIENTS WITH SEVERE INFLUENZA AND COVID-19 IN FIFE?

Jorge Menendez Lorenzo[1], Dr Devesh J Dhasmana[2]

[1]Medical Student Y3, [2]Consultant Respiratory Physician/Senior Lecturer

Respiratory Medicine, NHS Fife; School of Medicine, University of St Andrews, Fife

1. BACKGROUND

- Significant **Aspergillus co-infection** has been described in patients with severe COVID-19 and Influenza; this has been associated with major increased morbidity and mortality[1-2]

- Incidence reports of **IAPA (Influenza Associated Pulmonary Aspergillosis)** and **CAPA (COVID-19 Associated Pulmonary Aspergillosis)** have been varied in the literature; 4-35% and 16-23%, respectively[2-3]

- Securing the diagnosis of IAPA or CAPA is challenging, requires **clinical, radiological & microbiological markers** - fungal biomarkers (**Beta-D Glucan, Galactomannan, Aspergillus PCR**) are difficult/time-consuming to obtain

- The incidence of IAPA/CAPA in Fife is unknown. There are thought to be frequent positive fungal infections, however, whether these are **clinically significant infections and representing IAPA/CAPA** is not known

2. AIMS & OBJECTIVES

1) Identify the **number of patients admitted to ICU with Influenza or COVID-19** in NHS Fife over the last four years (April 2017 – Feb 2021).

2) Identify the **incidence of IAPA/CAPA** according to international guidelines

3) Assess the **burden of other fungal infections**

4) Review the **use of high-cost antifungal therapies**

5) Review the impact of these infections on **key admission outcomes** including ICU bed-days, length of stay, and survival

3. METHODS

- ICD-10 codes J10.0, J10.01, U07.1, U07.2 were used to identify the patients described above

- **Retrospective review** of clinical, microbiological and imaging data

- Data management and statistical analysis through Excel and R Stats

Figure 1. Methodology of project

4. RESULTS & DISCUSSION
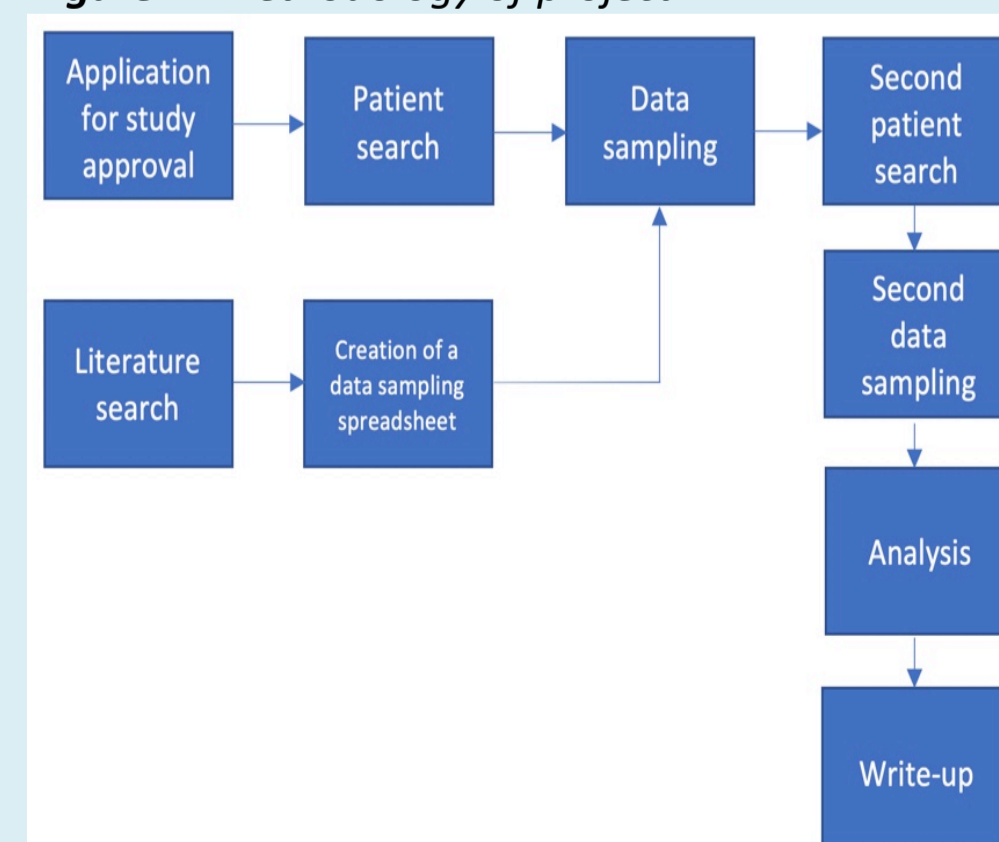
1) Nos. of ICU admissions

- **Cohort total = 89 (Influenza 27, COVID-19 62)**
- **NO** Influenza ICU admissions winter 2020/21.
- Similar trends nationally[4-5] *(Figure 2 and 3)*

Table 1. COVID-19 and Influenza admissions

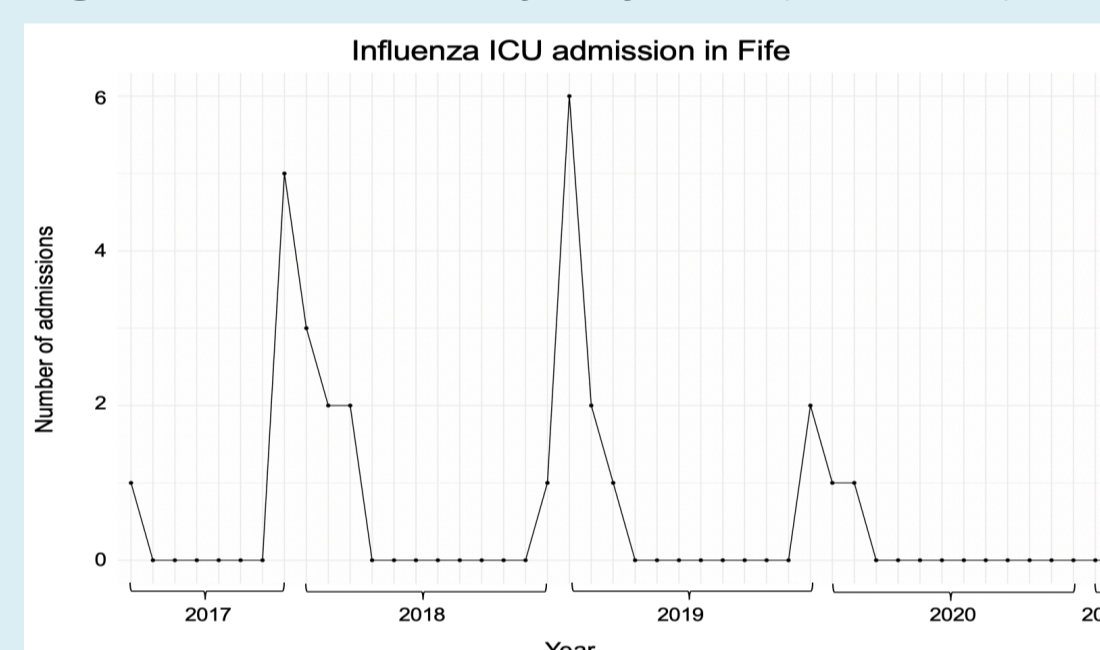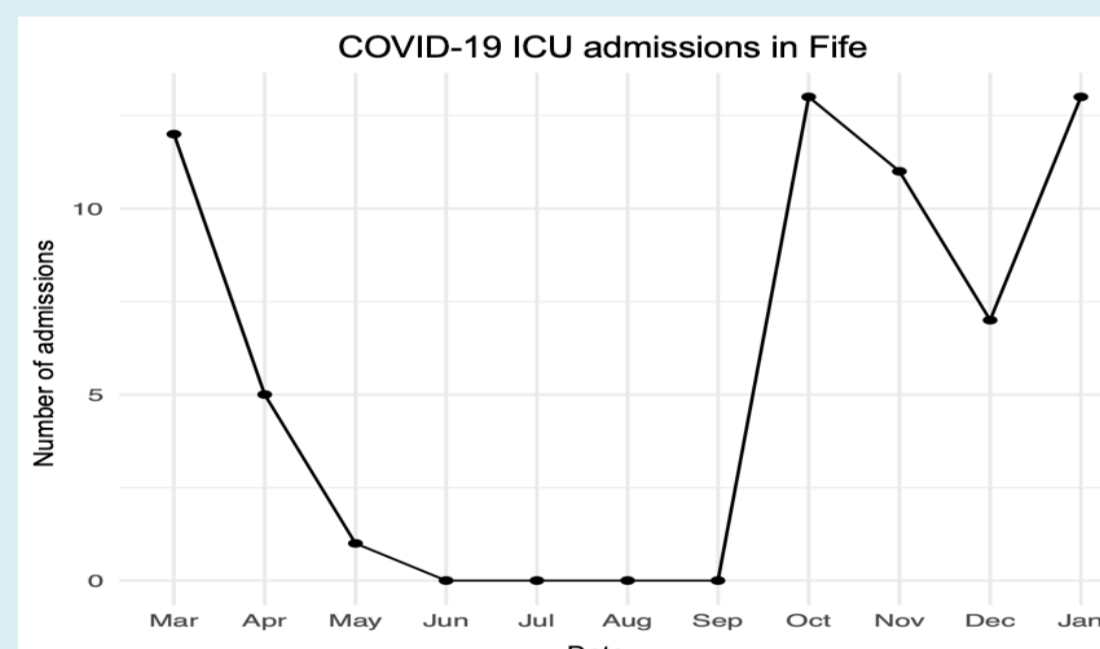|	Total	Male		Female		Age
		No.	%	No.	%	mean
COVID19	62	38	61.3%	24	38.7%	59.1
Influenza	27	15	55.6%	12	44.4%	53.3

Figure 2. ICU admissions for Influenza (2017-2021)

Figure 3. ICU admissions for COVID-19 (2020-2021)

2) Incidence of IAPA/CAPA

- **There were NO definite cases of IAPA or CAPA**
- *A.fumigatus* found in respiratory samples of 2 patients - neither met the criteria for CAPA/IAPA
- Only 3 patients underwent all diagnostic testing required for IAPA/CAPA classification *(Table 2)*

Table 2. Number of patients undergoing full diagnostic workup for IAPA/CAPA

	Number of Patients
Radiological Investigations	26 (29.2%)
Fungal Biomarker Testing	3 (3%)

3) Burden of fungal infections

- **44% (39/89) of patients had fungal infection** in the ICU: Candida (37), Aspergillus (2) *(Figure 4)*
- Multiple sites, **most common endotracheal (ET) samples at 54%** of all samples *(Figure 5)*
- However, Candida in ET has been described to be poorly indicative of underlying infection[6]

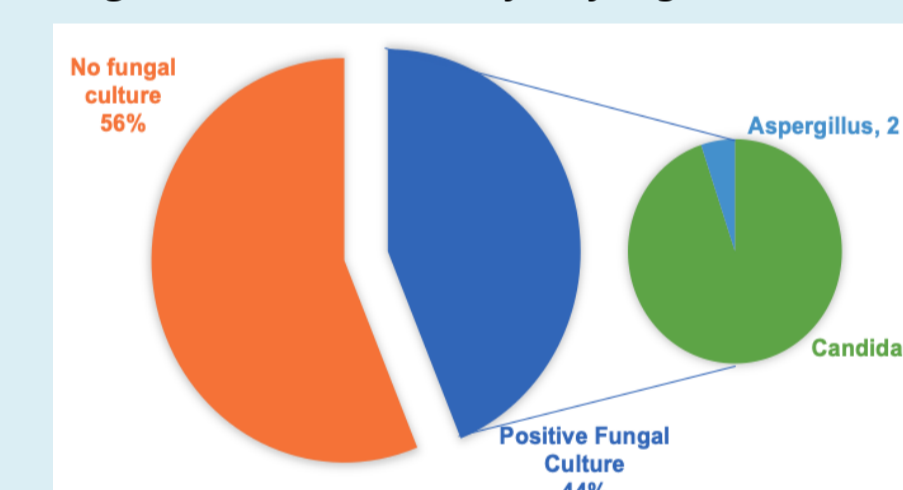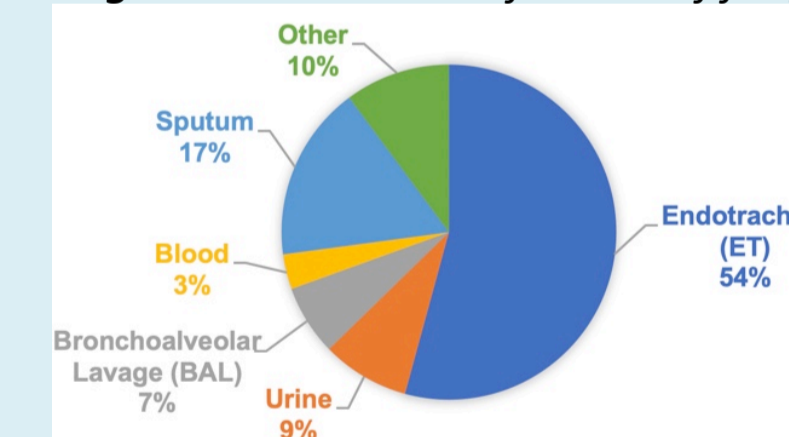*Figure 4. Breakdown of all fungal cultures*


Figure 5. Breakdown of source of fungal cultures

4) Costs of anti-fungal therapy

- Antifungal therapy was not commonly used (7/89)
- One of two patients with Candidemia underwent 10d caspofungin = drug cost ~£4,300
- **Retrospective data collection difficult** to work with; likely underestimate of antifungal use
- For same reasons, **difficult to judge clinical outcomes and therefore cost-efficiency**

5) Key admission outcomes

- Patients with fungal co-infection may show decreased survival, but low numbers, underpowered *(Figure 6)*
- Fungal co-infection was associated with **increased length of ICU and hospital stay**

Figure 6. Kaplan-Meier survival curve measuring survival for patients with and without fungal culture growth
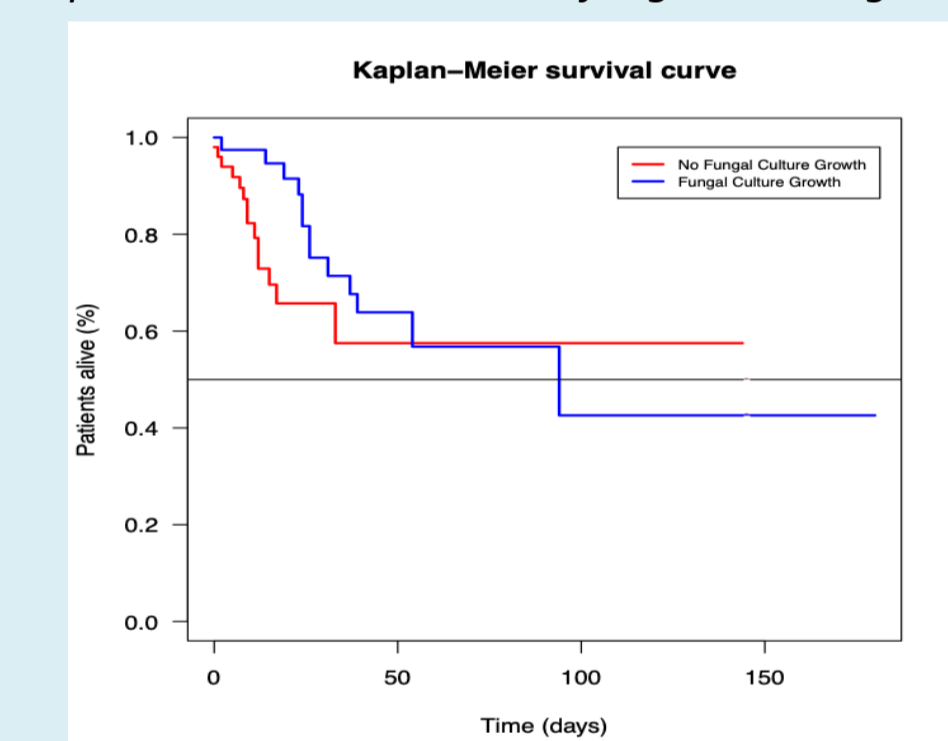
Study Limitations

- **Retrospective data sampling** → compromised data sets
- **Incomplete datasets** led to incomplete analysis; although, this was mainly an audit/service review looking at burden of fungal disease & appropriate investigations

5. CONCLUSIONS

- Our combined Influenza/COVID cohort comprised of 89 patients, the majority (62) presenting with COVID-19. ICU admissions for both groups mirrored national trends of incidence.

- N**o definite CAPA/IAPA** was seen in ICU, limited by the investigations that were carried out.

- **Fungal co-infection was frequent**; Candida the most common, but not necessarily pathogenic

- In our cohort **fungal co-infection was probably associated with worse clinical outcomes**– Increased length of hospital stay, ICU bed days and mortality

- **Further prospective research is necessary** to improve our understanding of IAPA/CAPA in Fife

REFERENCES

1. Machado M, Valerio M, Alvarez-Uria A, Olmedo M, Veintimilla C, Padilla B, et al. Invasive pulmonary aspergillosis in the COVID-19 era: An expected new entity. Mycoses. 2021;64(2):132-43.

2. Schauwvlieghe AFAD, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Van Tienen C, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. The Lancet Respiratory Medicine. 2018;6(10):782-92

3. Apostolopoulou A, Esquer Garrigos Z, Vijayvargiya P, Lerner AH, Farmakiotis D. Invasive Pulmonary Aspergillosis in Patients with SARS-CoV-2 Infection: A Systematic Review of the Literature. Diagnostics (Basel). 2020;10(10):807.

4. Coronavirus (COVID-19) in the UK: Gov.uk; 2021 [Available from: https://coronavirus.data.gov.uk/details/healthcare.

5. Influenza data and Statistics: World Health Organization; 2021 [Available from: https://www.euro.who.int/en/health-topics/communicable-diseases/influenza/data-and-statistics.

6. Meersseman W, Lagrou K, Spriet I, Maertens J, Verbeken E, Peetermans WE, et al. Significance of the isolation of Candida species from airway samples in critically ill patients: a prospective, autopsy study. Intensive Care Med. 2009;35(9):1526-31.

Jorge.menendezlorenzo@nhs.scot