

# Mycobacterium abscessus from respiratory and non-respiratory infections within Queensland

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## ABSTRACT

### BACKGROUND:

*Mycobacterium abscessus* group (*Mabs*) are rapidly growing nontuberculous mycobacteria (NTM), commonly found in a variety of water sources. *Mabs* consists of three subspecies including *abscessus*, *massiliense* and *bolletii*. They are opportunistic pathogens and can cause respiratory and non-respiratory infections. In Queensland, over the last 20 years, rates of NTM infection has increased, with *Mabs* being the third most common species reported (1). Clonal strains with increased virulence and antibiotic resistance have been recently identified, known as dominating circulating clones (DCCs). Bryant and colleagues (2016) described possible dissemination of DCCs distributed among cystic fibrosis (CF) populations globally, with person-to-person transmission implicated as a potential factor. However, transmission from or via environmental reservoirs is also thought to be the major driver of the increase in infections seen in the last 20 years. The prevalence and distribution of DCCs in CF and non-CF populations globally are highlighted in Figure 1.

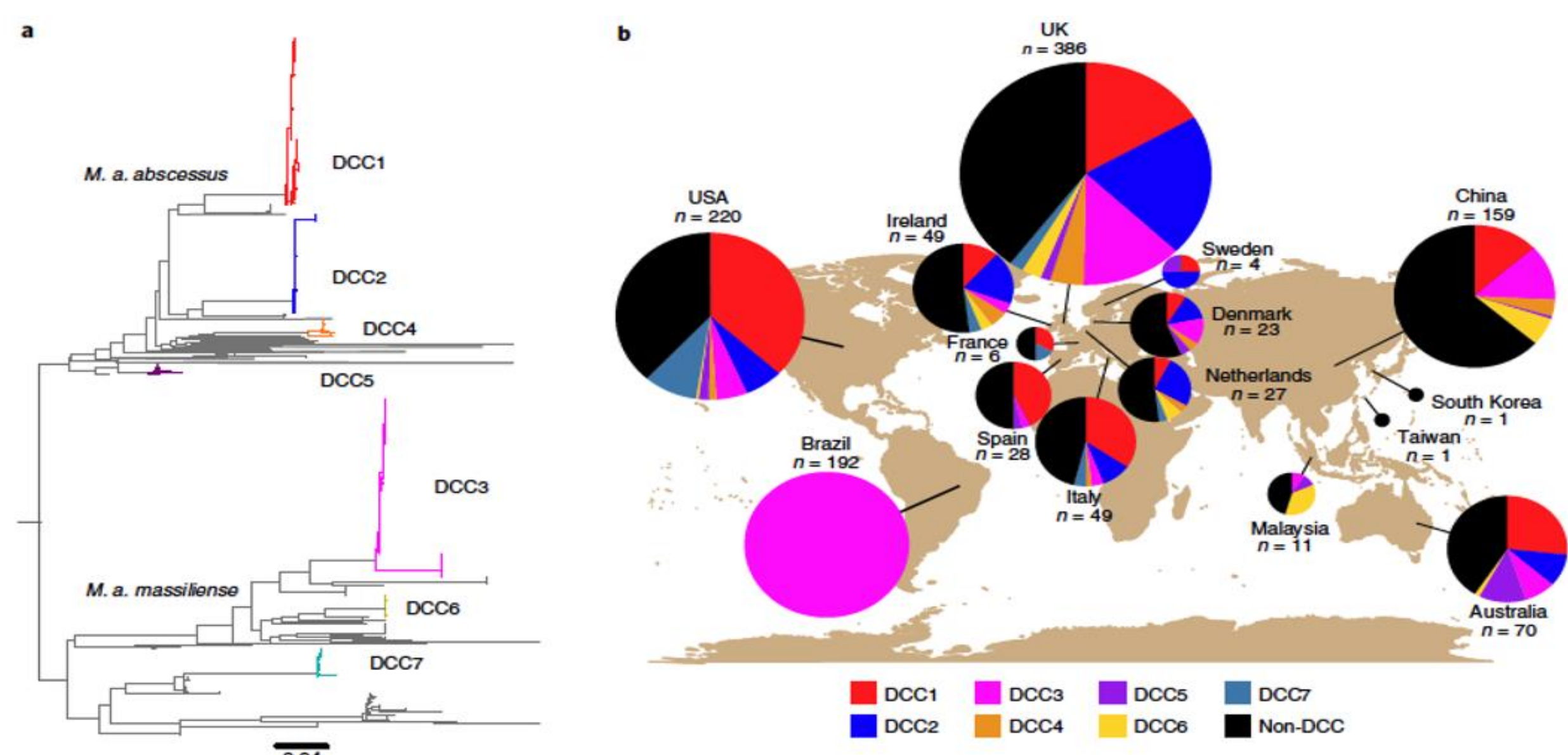


Figure 1. Global dissemination of DCCs (a. *Mabs* phylogenetic tree b. global prevalence DCCs) (Ruis et al. 2021)

We sought to determine the genomic relationship of *Mabs* in respiratory (non-CF) and non-respiratory infections over a 20-year period in the Queensland population.

### METHOD:

*Mabs* isolates cultured between 2000 and 2020 obtained from the QMRL included 85 respiratory (from 76 non-CF patients) and 74 non-respiratory (skin, soft tissue, fluid, blood) isolates (from 70 patients). Whole genome sequencing (WGS) has been performed on 80 isolates (24 non-CF respiratory; 46 non-respiratory) and phylogenetic trees constructed to assess the relationships between these isolates. Clonality is defined as <20 Single Nucleotide Polymorphism (2) differences from the core genome.

### RESULTS:

WGS identified 57 *M. abscessus* subsp *abscessus* (71.3%), 19 *M. abscessus* subsp *massiliense* (23.7%), and 4 *M. abscessus* subsp *bolletii* (5%) strains. Thirty-six of the 80 isolates clustered with previously identified DCCs. This included 16 isolates within DCC1 (7 respiratory, 9 non-respiratory) and 5 isolates within DCC3 (3 respiratory, 2 non-respiratory). Fifteen isolates (6 respiratory, 9 non-respiratory) were closely related to a previously identified South-East Queensland clonal cluster, now known to be part of DCC 5.

### CONCLUSION:

Forty-five percent of these isolates clustered with a DCC. This indicates that isolates belonging to DCCs are present in a range of clinical infections, although at a lower prevalence rate than in Qld CF patients. These results highlight the distribution and diversity of respiratory (non-CF) and non-respiratory *Mabs* infections in Queensland patients.

### KNOWLEDGE GAP:

Limited information on the prevalence and distribution of DCCs in NON-CF infections

### AIMS:

- To determine the genomic relationship of historical MABS in NON-CF respiratory and non-respiratory infections in QLD over 20 years
- To comment on the prevalence of DCCs in a range of clinical infections

### EXPECTED OUTCOMES:

Understand more about clonal dispersion, transmission routes and epidemiology

## METHODS

In collaboration with the QMRL isolate selection was based on the first *Mabs* isolate of the month where available, at 5 yearly increments between 2000-2020, with an extra collection year including 2019.

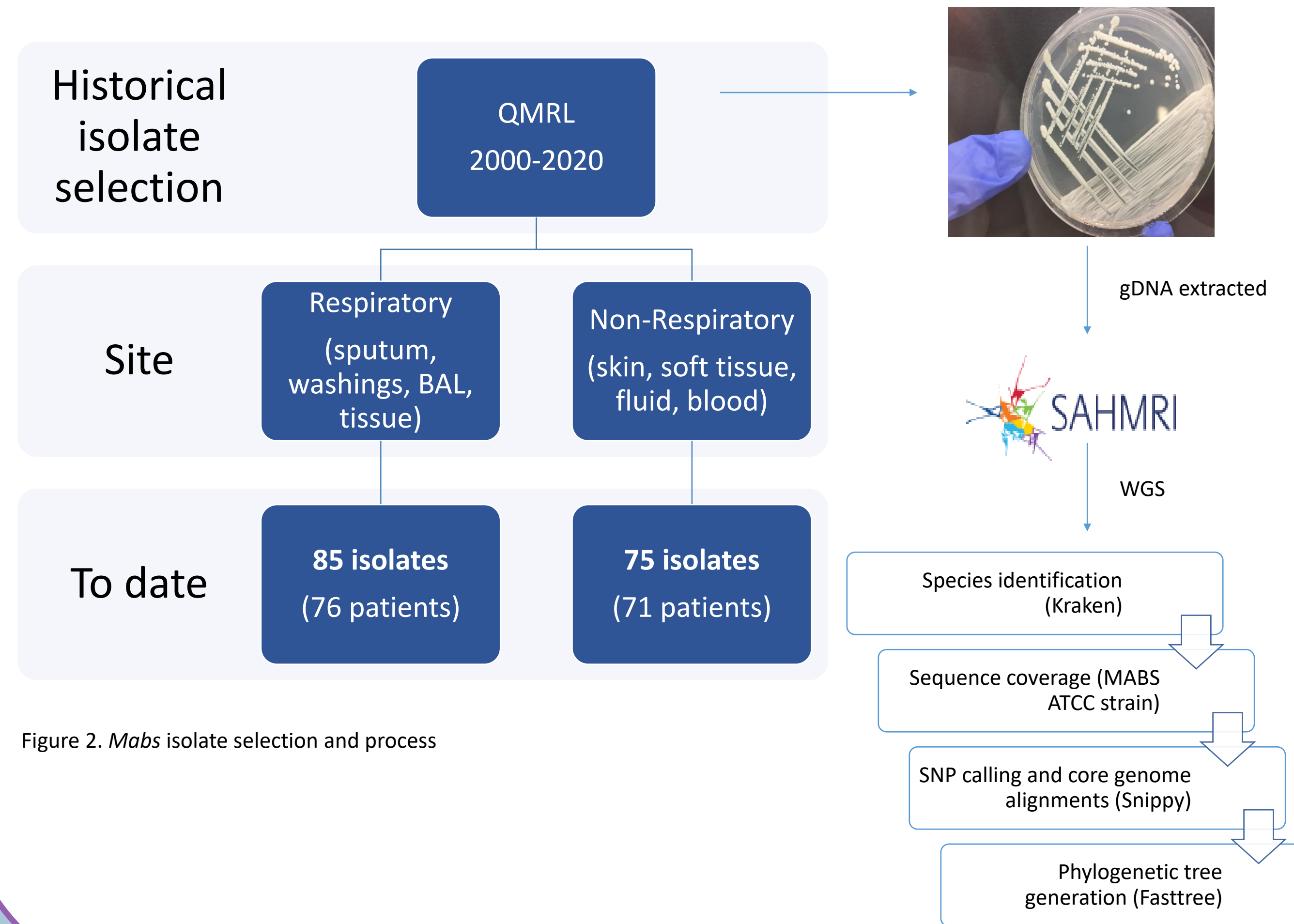


Figure 2. *Mabs* isolate selection and process

## RESULTS

Isolates were identified as:

- 71.3% subspecies *abscessus*
- 23.7% subspecies *massiliense*
- 5% subspecies *bolletii*

Table 1. Comparison between non-CF with CF respiratory isolates *Mabs* subspeciation

| <i>Mabs</i> subspecies   | NON-CF                       |                                  | CF Respiratory <sup>a</sup> |
|--------------------------|------------------------------|----------------------------------|-----------------------------|
|                          | Respiratory<br>n=34<br>n (%) | Non-Respiratory<br>n=46<br>n (%) | n=73*<br>n (%)              |
| <i>M. a. abscessus</i>   | 26 (76.5)                    | 31 (67.0)                        | 55 (73.3)                   |
| <i>M. a. massiliense</i> | 8 (23.5)                     | 11 (24.0)                        | 17 (22.6)                   |
| <i>M. a. bolletii</i>    | 0 (0.0)                      | 4 (9.0)                          | 2 (2.7)                     |

<sup>a</sup>Stockwell et al 2022, unpublished  
<sup>\*</sup>Includes >1 MABS subspecies n=2 (2.7%)

DCC results:

- 45% (36/80) clustered with a known DCC
- DCC 5 higher proportion in non-CF compared to CF

Table 2. Comparison between non-CF with CF respiratory isolates DCC clustering

| Clonal Cluster           | NON-CF                         |                                    | CF Respiratory <sup>a</sup> |
|--------------------------|--------------------------------|------------------------------------|-----------------------------|
|                          | Respiratory<br>(n=34)<br>n (%) | Non-Respiratory<br>(n=46)<br>n (%) | (n=73)<br>n (%)             |
| <i>M. a. abscessus</i>   |                                |                                    |                             |
| DCC1                     | 7 (20.5)                       | 9 (19.6)                           | 25 (34.2)                   |
| DCC5                     | 6 (17.6)                       | 9 (19.6)                           | 3 (4.1)                     |
| <i>M. a. massiliense</i> |                                |                                    |                             |
| DCC3                     | 2 (5.9)                        | 3 (6.5)                            | 5 (6.8)                     |

<sup>a</sup>Stockwell et al 2022, unpublished 73 CF patients (163 isolates)  
Two patients had >1 DCC (DCC1 & DCC3) and (DCC1 and unclustered)

### REFERENCES:

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- Bryant JM, Grogono PM, Rodriguez-Rincon D, Everall I, Brown KP et al. Emergence and spread of a human transmissible multidrug-resistant nontuberculous mycobacterium. *Science*; 2016. 354 (6316): 751-757.
- Ruis C, Bryant JM, Bell SC, Thomson R, Davidson RM, Hasan NA et al. Dissemination of *Mycobacterium abscessus* via global transmission networks. *Nat. Microbiol*; 2021. 6: 1279-1288.

## RESULTS

- DCC clustering of *Mabs* isolates within Queensland (Figure 3)
- Isolate alignment to reference strains (2)

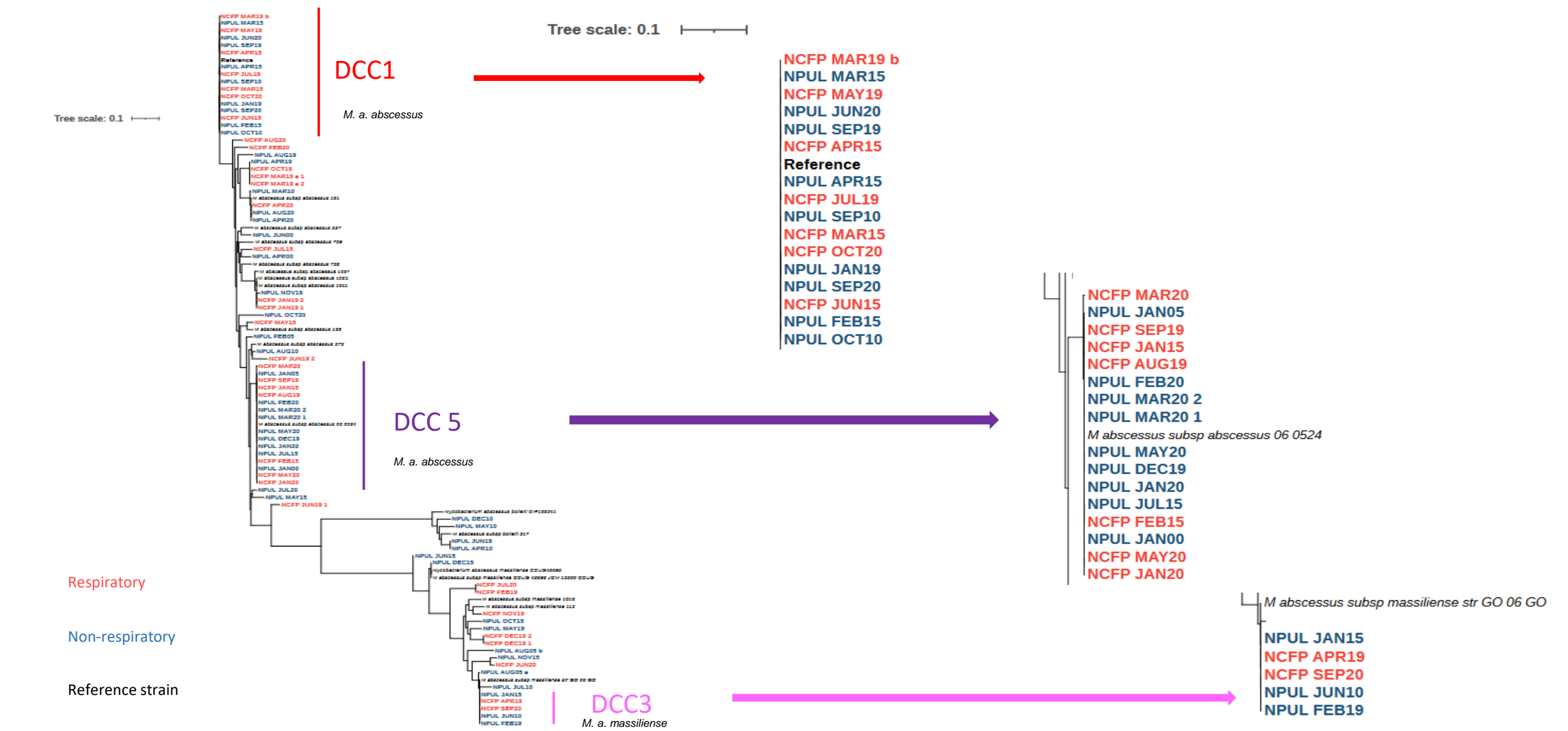


Figure 3. Phylogenetic tree of *Mabs* isolates from non-CF respiratory and non-respiratory origin (reference strain ATCC19977)

### Global comparison

- DCC1 subspecies *abscessus* is seen in higher proportion in Australia, Spain, and the US.
- DCC5 is less commonly seen globally and in the CF cohorts but higher in non-CF in Australia

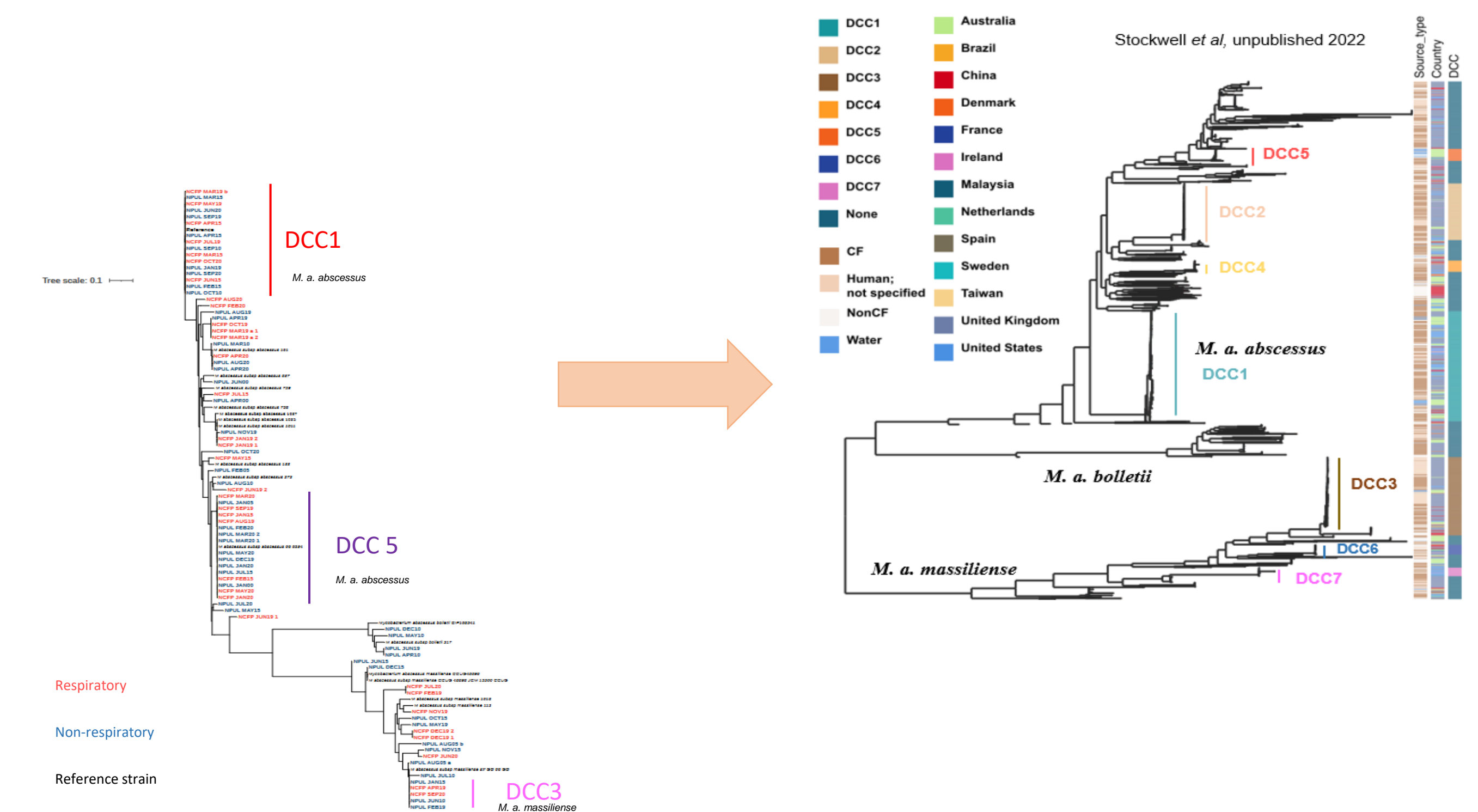


Figure 4. Phylogenetic tree of *Mabs* isolates from non-CF respiratory and non-respiratory origin (right) compared to global DCC distribution (left)

### SUMMARY

- M. a. abscessus* is the most predominant subspecies among CF and non-CF cohorts
- A proportion of non-CF respiratory and non-respiratory QLD strains belong to DCC1, 5 and 3
- DCCs belong to a range of clinical infections and are not limited to those with CF
- This work is contributing to understanding more about global distribution of DCCs in non-CF cohorts

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