

## BACKGROUND

Nontuberculous Mycobacterial (NTM) diseases involving implanted cardiac devices are extremely complex and difficult to manage due to the burden of potential device removal and uncertainties surrounding when to reimplant. Despite a considerable increase in knowledge about NTM disease, determining the optimal treatment approach for cardiac device-related NTM infection remains problematic and without standardization.

## OBJECTIVES

We performed a scoping review to explore the evidence for optimal management and outcomes of implantable cardiac device-related infection in NTM disease, including the requirement for device removal.

## METHODS

- Studies inclusion criteria:
  - Patients with cardiac device-related NTM infection and treated with any antibiotic treatment
  - All study designs that report NTM cases that involve implantable cardiac devices.
- We identified potentially eligible studies through an electronic search of 3 bibliographic databases from their inception to January 2022 (Ovid Medline, Scopus, and Embase)
- Studies were screened by pairs of two independent experts in the field of infectious diseases and all relevant data was extracted including patient characteristics, treatment, device removal, and reimplantation.
- We adapted The World Health Organization Tuberculosis outcome definitions for this scoping review (Table 1)
- Statistical analysis by Stata (StataCorp. 2015, v14 College Station, TX)

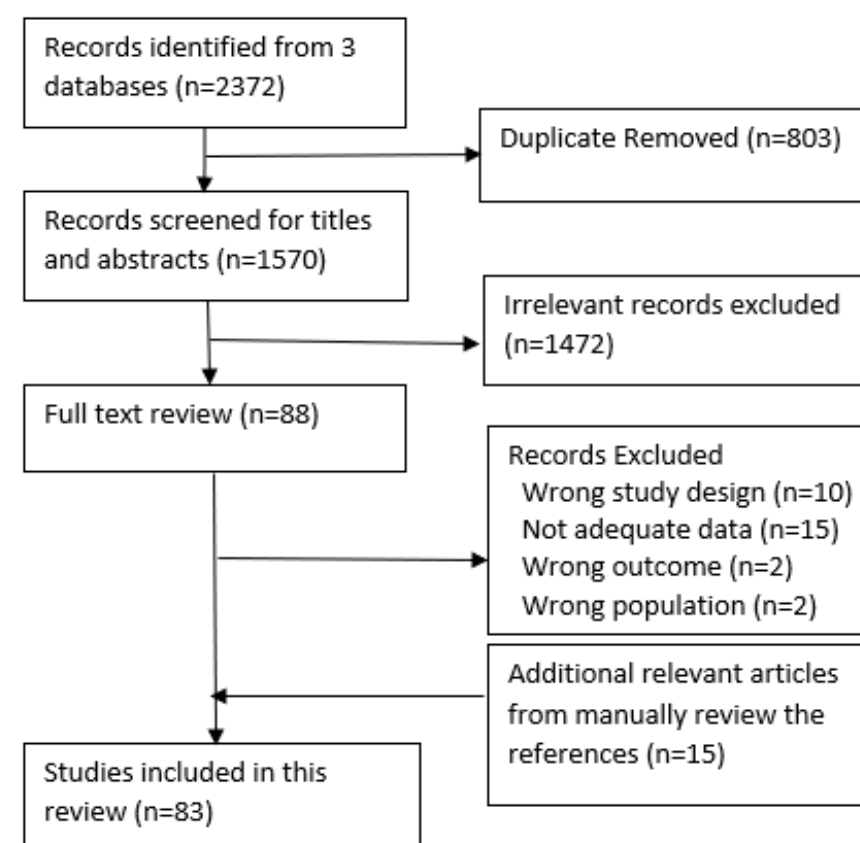
**Table 1 World Health Organization Tuberculosis Outcomes Definitions**

Outcome	Definition
Dies	A patient who died during the follow-up period
Failure	A patient who was shown to be culture positive in spite of optimized background regimen
Relapse	A patient with positive culture after evidence of clearing once complete antibiotic
Cured	A patient who was bacteriologically confirmed at the beginning of treatment, whose therapy was stopped and there was no evidence of bacteriologic disease at end of therapy or within 6 months of stopping therapy
Treatment complete	A patient who completed the treatment without follow up culture

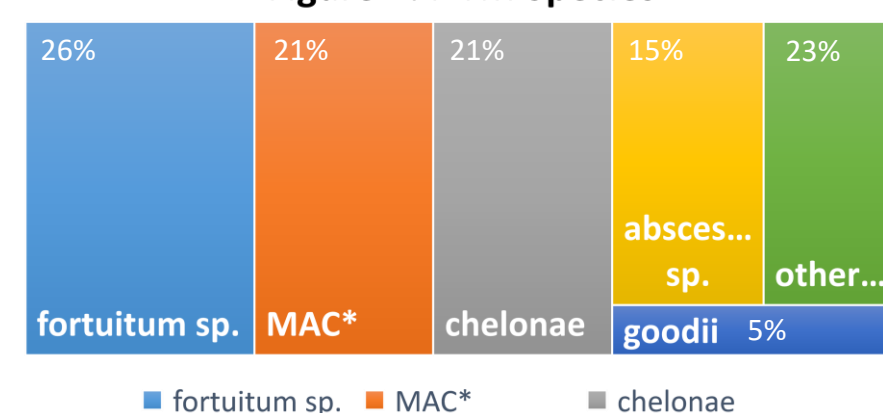
## RESULTS

We included a total of 122 patients from 83 studies (Figure 1). The average age was 60 years old (range 15-86 years old, standard deviation [SD] = 16). 65% of patients were male (N=79). Only 5% of patients (N=6) were documented to be immunocompromised.

**Figure 1: PRISMA Flow Diagram**



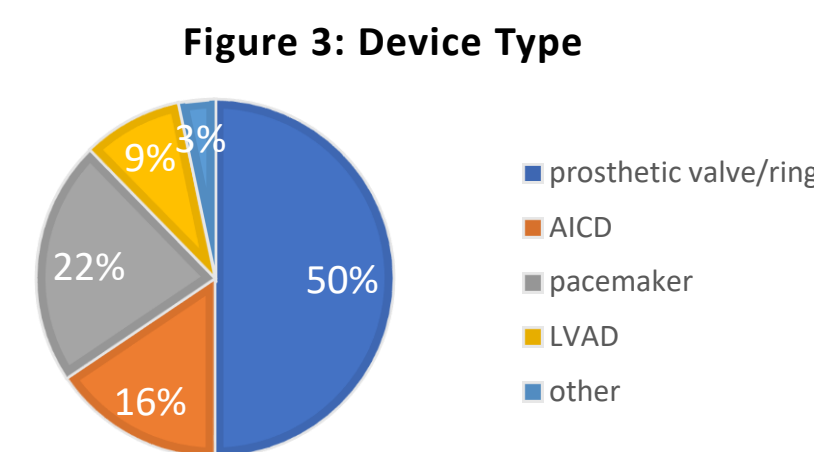
**Figure 2: NTM Species**



\*MAC (*Mycobacterium avium* complex): *M. chimera* 22 cases and *M. avium* 3 cases. \*\*Other NTM includes *M. mageritense* (n=3), *M. neonarum* (n=3), *M. wolinskyi* (n=3), *M. phlei* (n=1), *M. goodii* (n=3), and non-speciation (n=5)

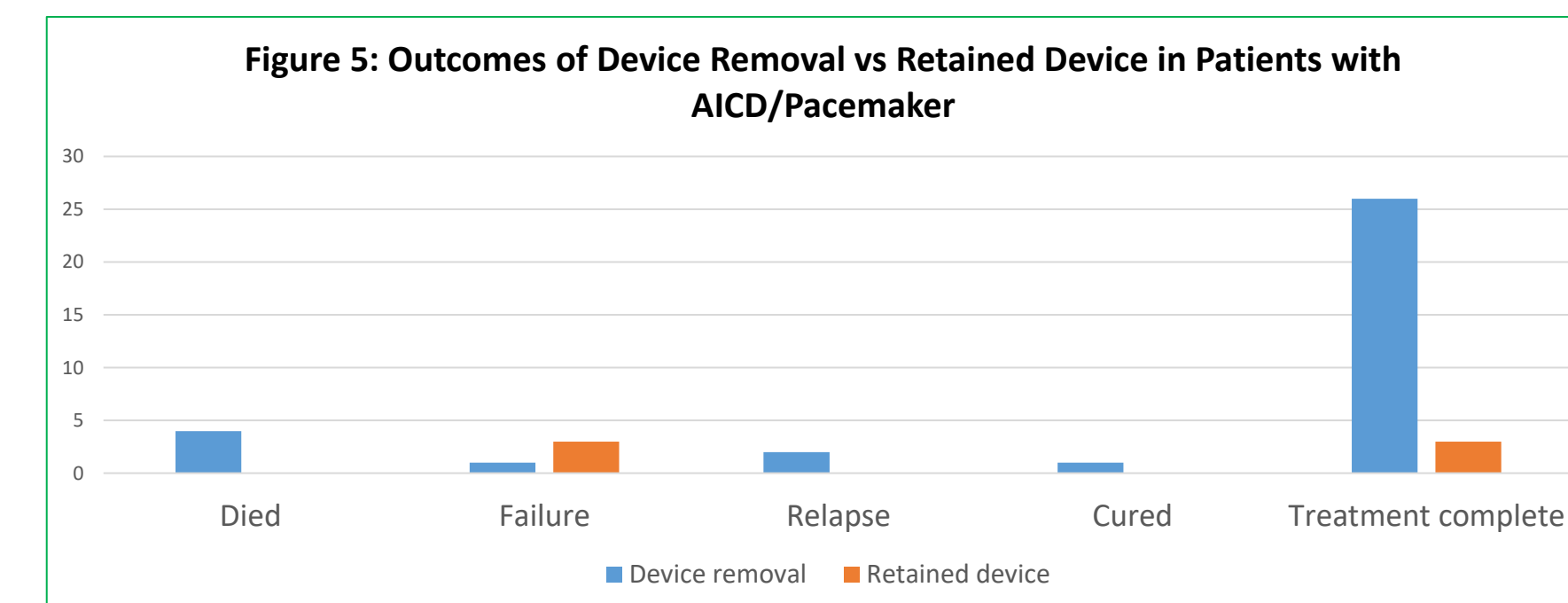
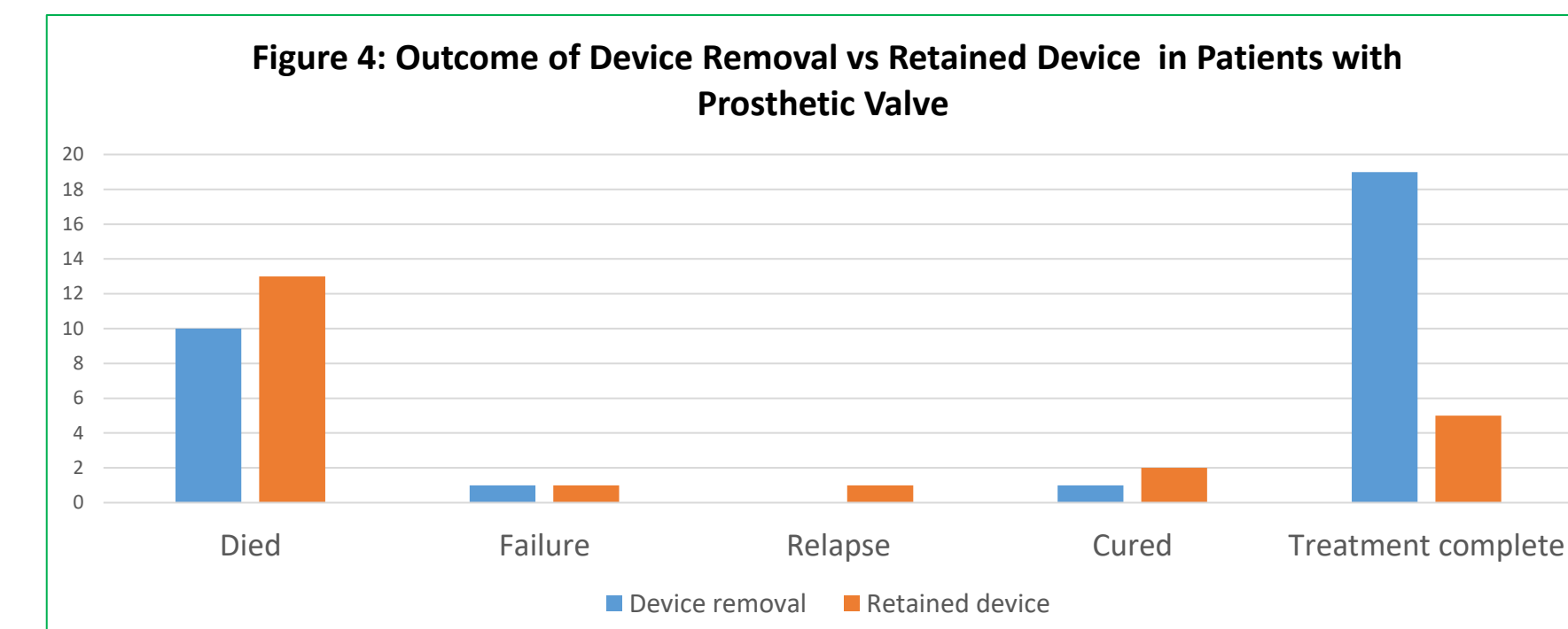
**NTM Species and Diagnosis:** The diagnosis of cardiac devices NTM-related infection was made by culture in 67% of patients (N=68) compared to 13% (N=16) that were exclusively diagnosed by 16s RNA from tissues. Blood cultures were reported to be positive in 43% (N=52) of all patients. Full susceptibilities were reported in 53% (N=63) of cases, with macrolide susceptibility in 58% (N=30) among those available reports.

**Treatments:** Of all patients, 60% received at least two antibiotics for target treatment; 43% included macrolide in their regimens (N=52). The duration of therapy was reported in 69% of patients (N=81) and ranged from two weeks to a lifelong suppression with a mean of 5.5 months (SD=5.4). Among 101 patients with available data on treatment duration, 56% of patients had treatment for at least six months (N=57).



**Table 2: Characteristics Of Patients Who Underwent Device Removal Vs Retained Device**

Variable	Device removal (n=47)	Retained device (n=75)
Age, mean (SD)	59 (17)	64 (14)
Male	45 (60%)	34(72%)
Cardiac Devices		
- Prosthetic valve	36 (48%)	25 (53%)
- Pacemaker/AICD	37 (49%)	9 (19%)
- LVAD	2 (3%)	9 (19%)
- Other	0	4 (9%)
NTM species		
- <i>M. fortuitum</i> spp.	22 (29%)	10 (21%)
- MAC	10 (13%)	15 (32%)
- <i>M. chelonae</i>	20 (27%)	5 (11%)
- <i>M. abscessus</i> spp.	8 (11%)	10 (21%)
- <i>M. goodii</i>	6 (8%)	0
- Other	9 (12%)	7 (15%)
Macrolide-based regimen	27 (36%)	25 (53%)
Outcomes		
- Died	16 (24%)	19 (50%)
- Failure	2 (3%)	5 (13%)
- Relapse	2 (3%)	2 (5%)
- Cured	2 (3%)	2 (5%)
- Treatment complete	45 (67%)	10 (26%)



**Outcomes:** Patients who underwent device removal had a better prognosis with “treatment complete” group (67% vs 26%) (Figure 3 and 4). In a multivariable logistic regression analysis adjusted for age, gender and cardiac devices, favorable outcomes with “treatment complete” and “cured” were found to be significantly associated with device removal (OR 5.17, 95%CI 2.08-12.82, p<0.01). Device removal was also found to be associated with a lower death rate in both univariable analysis (24% vs 50%, p<0.01) and multivariable logistic regression analysis adjusted for age, gender, and cardiac devices (OR 0.33, 95%CI 0.13-0.78, p=0.01)

## CONCLUSIONS

Reports of implantable cardiac device-related NTM infections were increasing, and suspicion should be high even for those without immunocompromising condition. Determining outcome was challenging and should be standardized to provide an evidence base for better management. In our analysis, patients who underwent device removal had improved survival, suggesting either that comorbidity precluded device removal and/or that removal may be an essential part of the management.

