

The Emerging Infections Network: Treatment of *Mycobacterium Abscessus* and the Use of Clofazimine

S.A. Novosad¹, K.L. Winthrop¹, P.M. Polgreen², S.E. Beekmann², A. Leitz¹, T. Vu¹
¹Oregon Health and Science University- Portland, OR/US, ²The University of Iowa - Iowa City/US

Introduction

- Pulmonary Nontuberculous Mycobacterial (NTM) Disease is being diagnosed more frequently
- M. abscessus* is an important cause of this disease
- M. abscessus* typically displays *in-vitro* resistance to most oral antibiotics, with the exception of clofazimine and macrolides
- Treatment involves multiple parenteral and oral antibiotics based upon susceptibility testing
- The optimal dosing and duration of such therapies is not well-defined

Figure one: Structure of clofazimine

- A fat-soluble riminophenazine dye approved by the FDA in 1986 for the treatment of lepromatous leprosy
- At present clofazimine is available in the United States through the FDA for individual patients via a Single Patient Investigational New Drug (SPIND)
- It is used in combination with other antimycobacterial drugs to treat mycobacterial infection in patients failing first line therapy
- Dosing and treatment duration are not currently defined

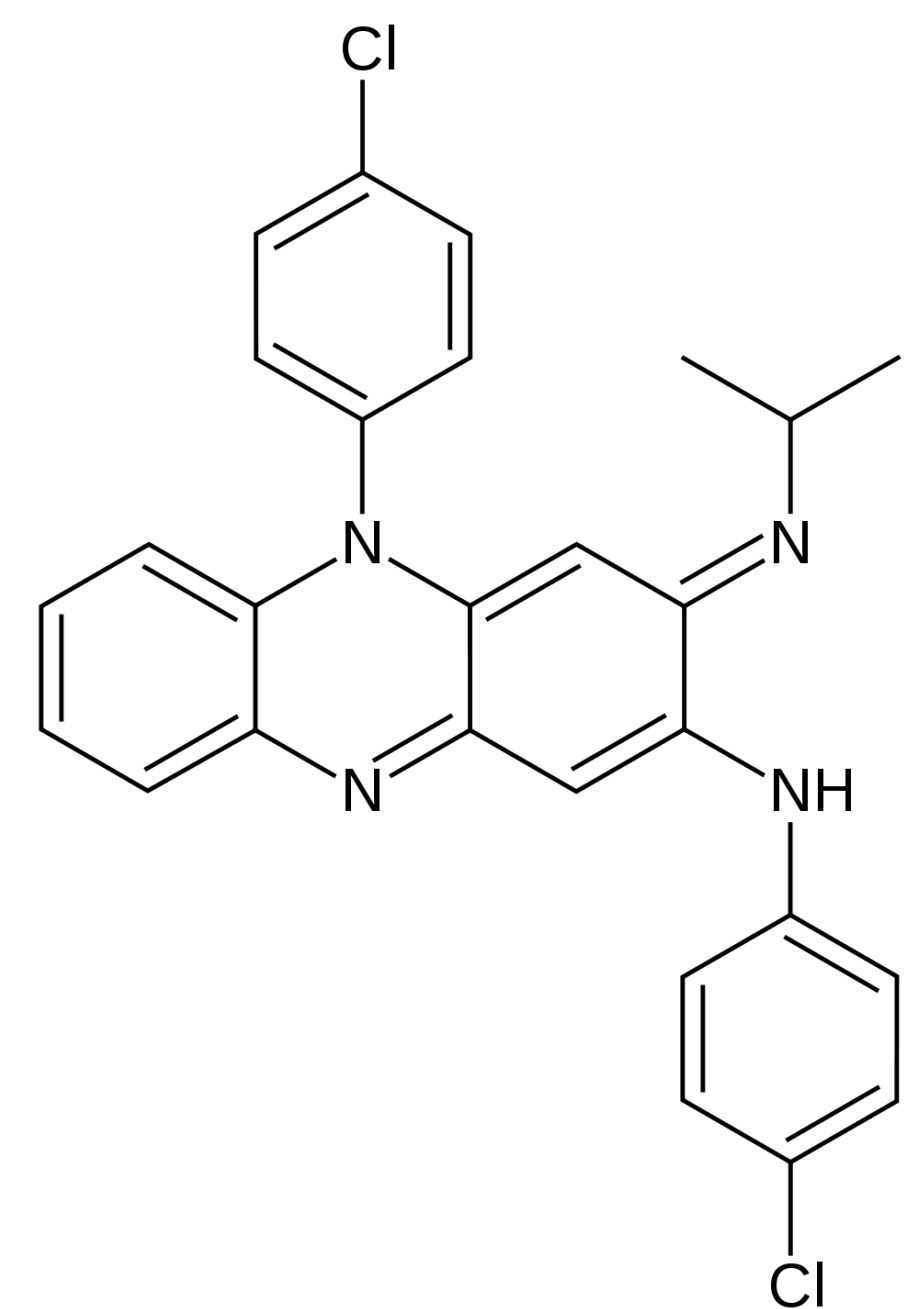


Figure two: Diagnosis treated with clofazimine, SPIND reports 2005-2011

Underlying diagnosis	Number (%)
<i>Mycobacterium avium complex</i> (MAC)	170 (79)
Multi-drug resistant tuberculosis	22 (10)
<i>Mycobacterium abscessus</i>	10 (4)
MAC and <i>M. abscessus</i>	4 (2)
<i>Mycobacterium simiae</i>	6 (3)
Other (<i>M. avium partuberculosis</i> , <i>M. haemophilum</i> , <i>M. fortuitum</i>)	4 (2)
Total	216

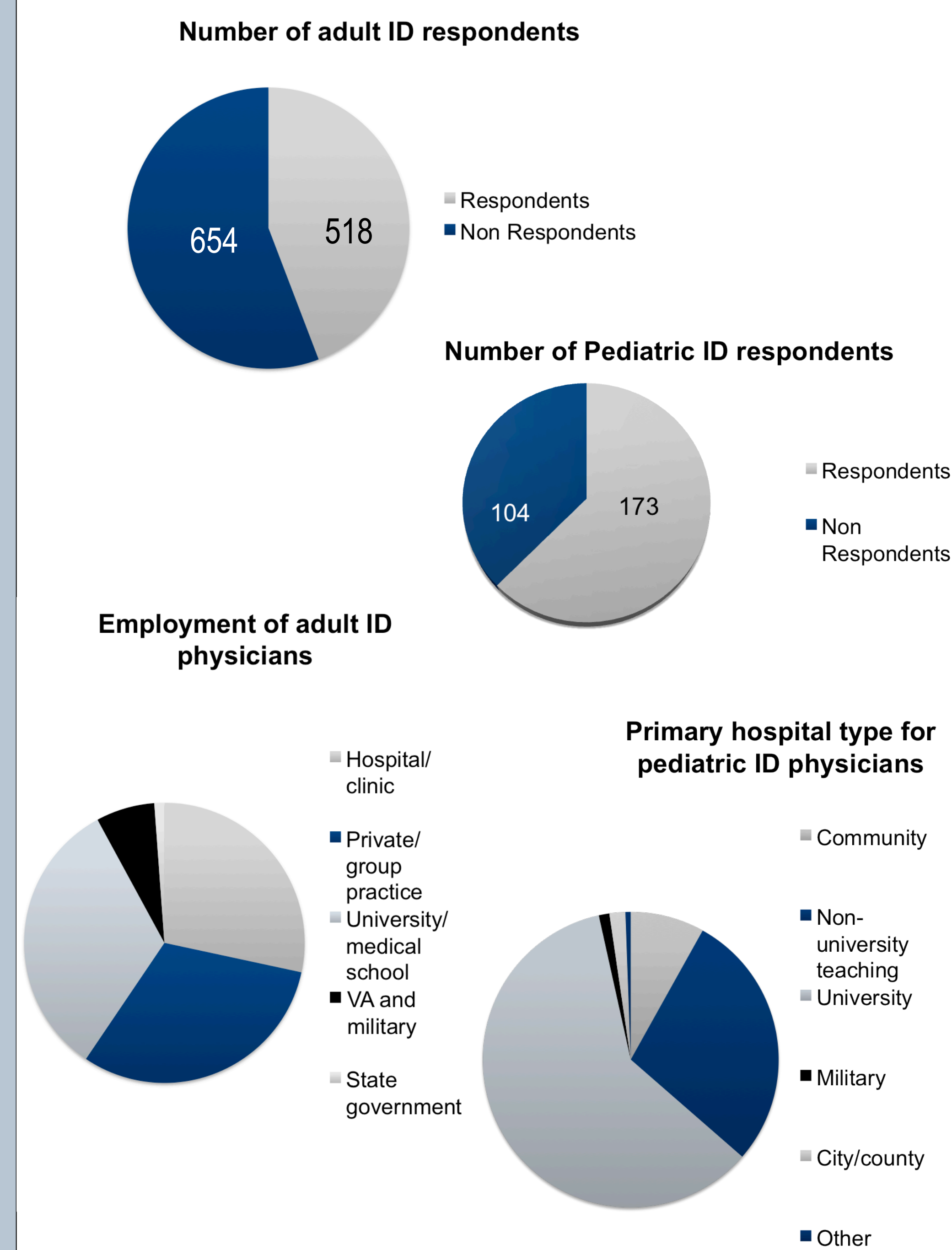
Objectives

- To better understand:
- How frequently do ID physicians encounter *M. abscessus*?
 - What medications are used to treat *M. abscessus*?
 - Response to therapy for *M. abscessus*
 - Physician awareness of clofazimine
 - Are physicians who want to use clofazimine able to obtain it?

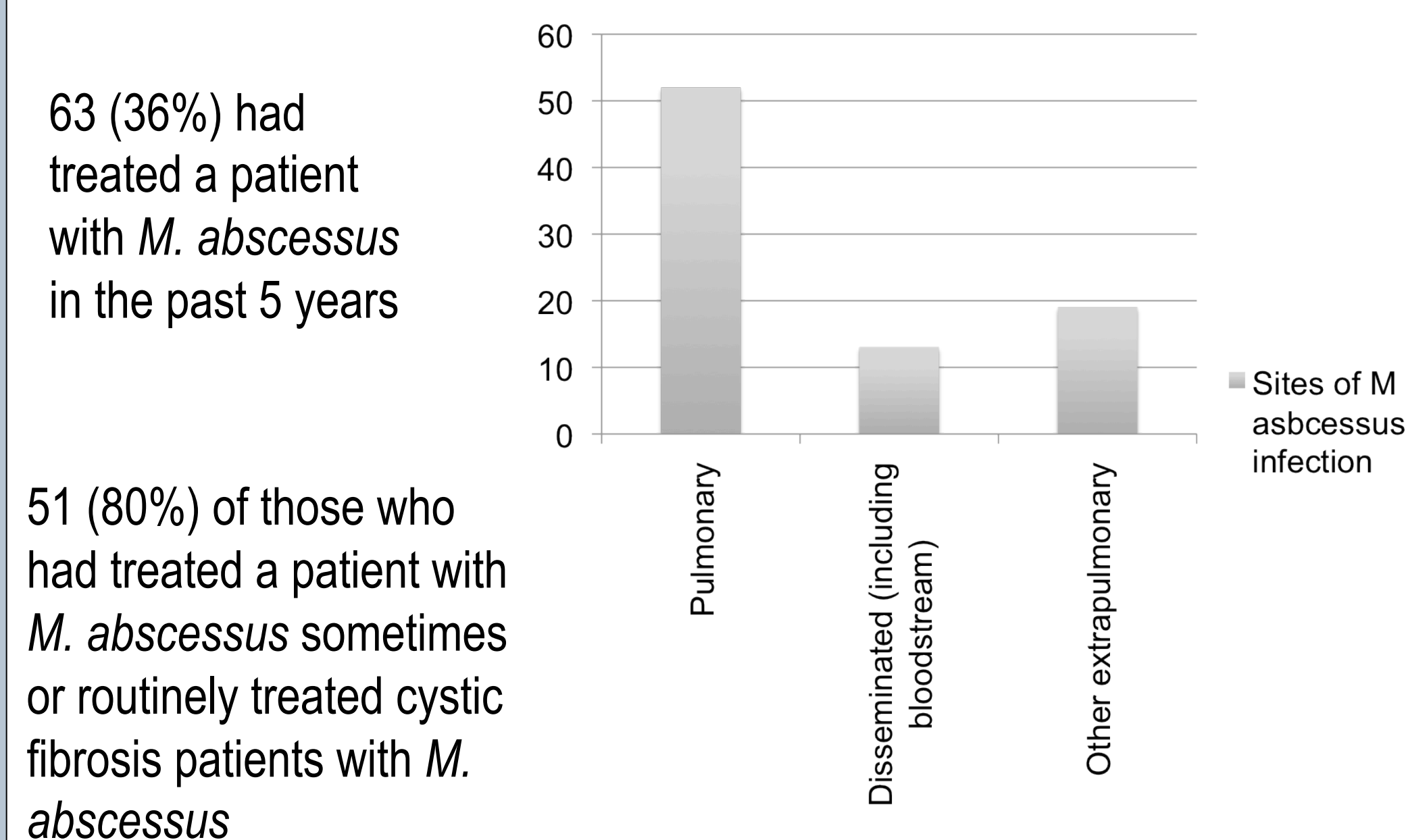
Methods

- Electronically surveyed members of the Infectious Diseases Society of America Emerging Infections Network (EIN)
- The survey was sent to 1172 ID physicians who practice adult infectious diseases with questions regarding *M. abscessus* and clofazimine
- A separate shorter survey was sent to ID physicians who practice pediatric infectious diseases with questions regarding *M. abscessus* and clofazimine

Figure three: ID physician respondents



Results from pediatric ID physicians: *M. abscessus*



Results from adult ID physicians: *M. abscessus*

- 202 (39%) reported treating at least one *M. abscessus* case over the last 5 years
- 104 (51%) reported their laboratories failed to speciate isolates beyond *M. chelonae-abscessus* complex
- 136 (68%) were pulmonary *M. abscessus* infections
- Physicians reported a variety of first-line therapy was used for pulmonary *M. abscessus*, including parenteral amikacin (73%), imipenem (69%), and cefoxitin (60%)
- Only 36 (18%) and 45 (22%) had used clofazimine or inhaled amikacin respectively
- 138 (78%) repeated sputum cultures after initiating therapy, but the timing was variable
- 45 (33%) were not sure what change in culture results would be considered sufficient to discontinue therapy
- 53 (36%) reported relapse of at least 50% of patients after discontinuation of therapy for pulmonary *M. abscessus*

Figure four: Perceived change in incidence of pulmonary NTM by adult ID physicians

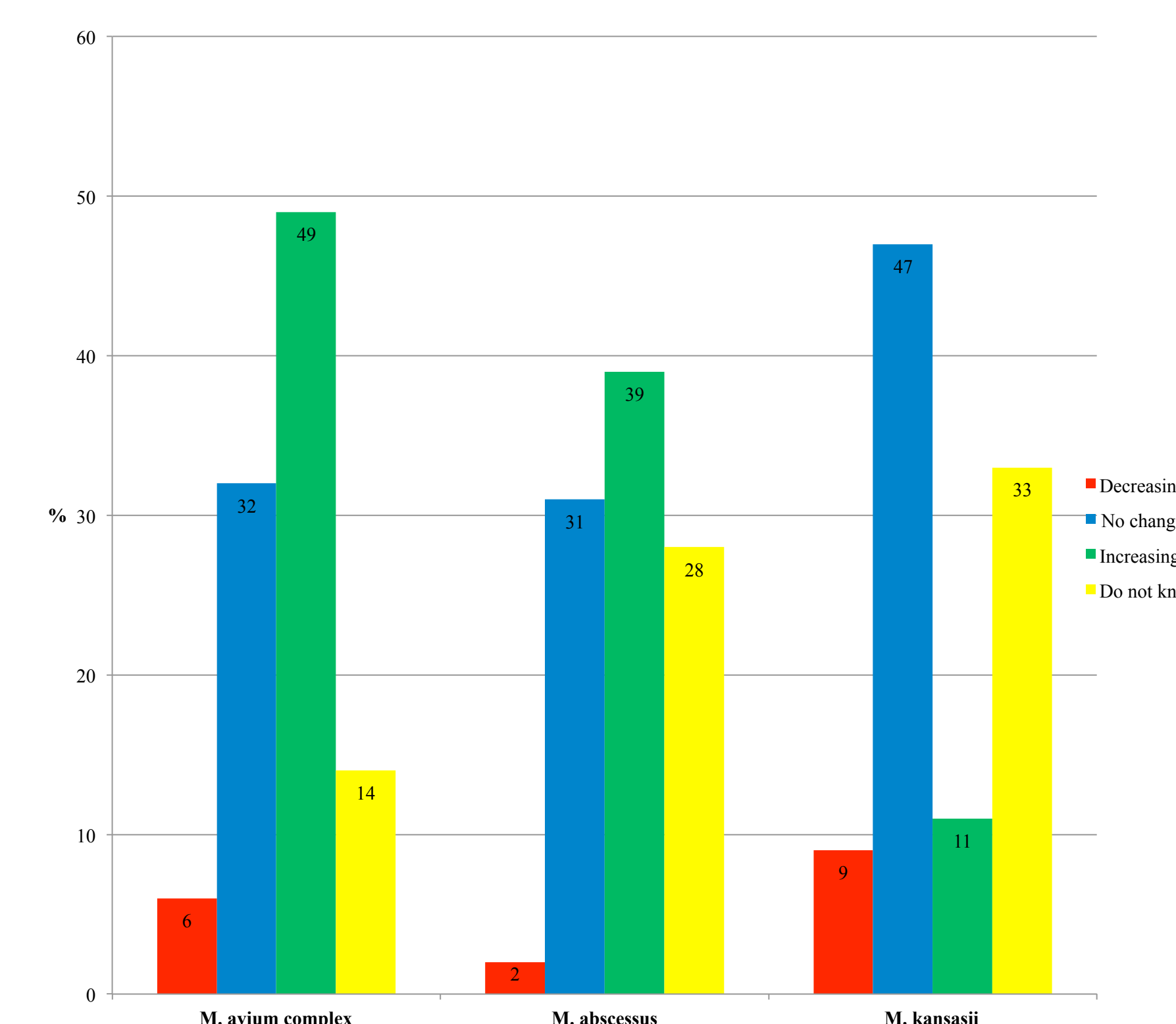
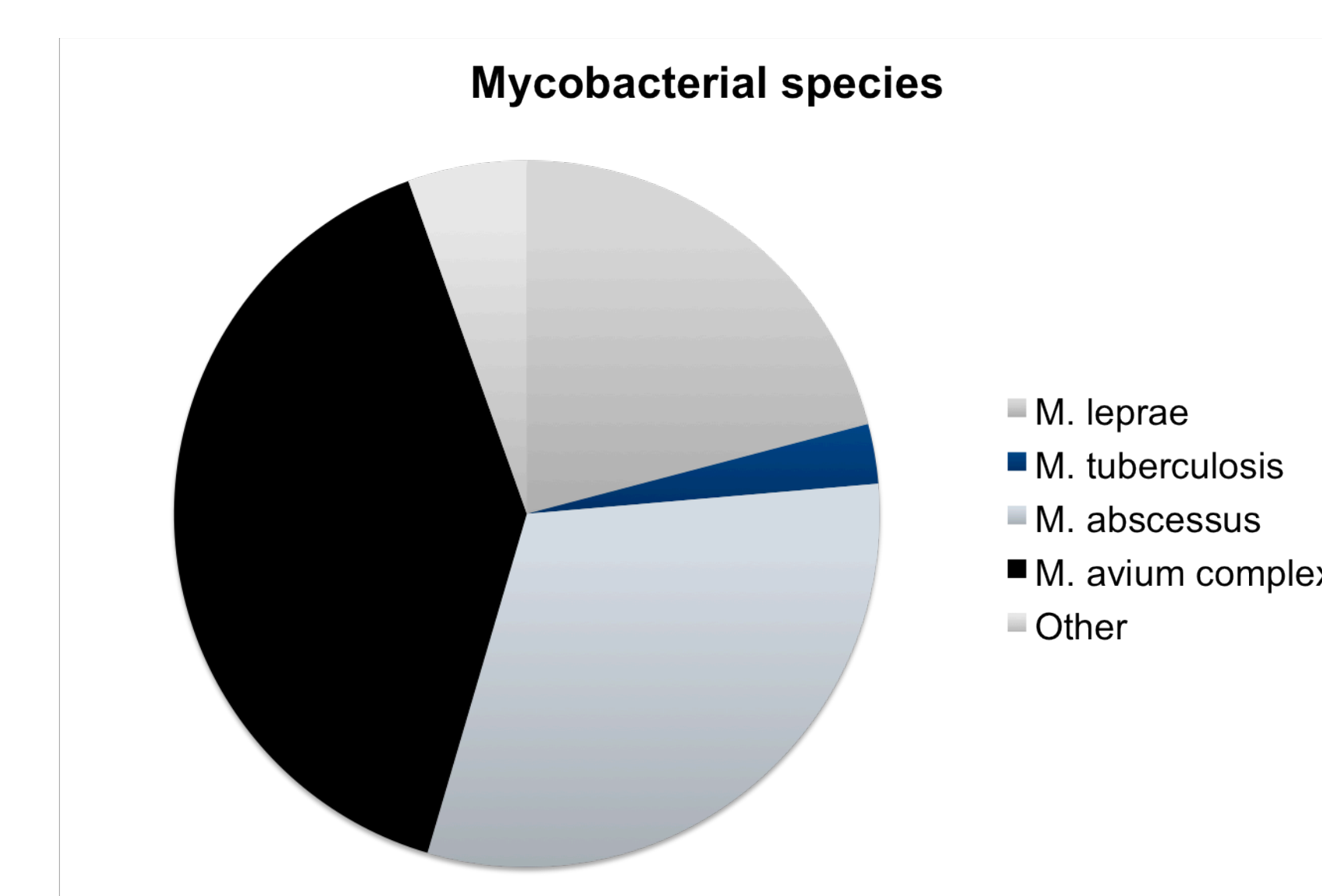


Figure five: Diagnosis associated with desire to use clofazimine by adult ID physicians



Results: Clofazimine

- Adults:
- 84% preferred to dose clofazimine at either 50 or 100 mg once daily
 - In the past 5 years, 434 (84%) of respondents did not try to obtain clofazimine 60 (12%) were successful in obtaining clofazimine on at least one occasion 26 (5%) wanted to used clofazimine but were not able to obtain it
- Pediatric:
- In the past 5 years, 161 (93%) of respondents had not wanted/or used clofazimine 9 (5%) had used clofazimine on at least one occasion 3 (2%) had wanted to use clofazimine but were unable to obtain it

Conclusions

- Adult ID physicians in the US believe *M. abscessus* and *M. avium complex* incidence is increasing
- Pediatric ID physicians in the US commonly treat pulmonary *M. abscessus* in cystic fibrosis patients
- Parenteral antibiotics instead of inhaled or oral antibiotics are commonly used to treat pulmonary *M. abscessus*
 - A high percentage of treating physicians relied on parenteral amikacin, imipenem, and cefoxitin
 - A small percentage used clofazimine or inhaled amikacin
- At least one half of physicians are not provided information on subspecies of *M. abscessus* on culture reports, which has important implications for therapy given the subspecies different resistance profiles
- Clofazimine is more commonly used to treat NTM rather than *M. tuberculosis* or *M. leprae* among adult ID physicians in the US
- Clofazimine is more commonly used by adult ID physicians than pediatric ID physicians

Future areas of research

- We are currently performing an expanded case series to learn more about the treatment of *M. abscessus*
- With specific questions regarding resistance profiles which antibiotics are selected outcomes of therapy side effects/toxicities associated with therapy
- We will perform a second case series to learn more about how clofazimine is utilized with particular attention to side effects and toxicities associated with therapy.

References

Vaidya P, O'Shaughnessy E, Mauer R, Rodgers A, et al. "Clofazimine use in patients with mycobacterial infections under single patient investigational new drug (SPIND)." Infectious Diseases Society of America, San Diego, Ca, 2012.