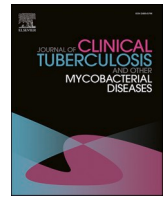




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# Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

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## Epidemiology, clinical characteristics, and outcomes of nontuberculous mycobacterial skin, soft tissue, and bone infections from a single center over a 10-year period

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## ABSTRACT

**Introduction:** Non-tuberculous mycobacteria (NTM) cause a wide variety of clinical syndromes. Data guiding diagnosis and treatment of NTM skin and soft tissue infections (SSTI) and bone infections are limited. We sought to better understand SSTI and bone infections caused by NTM.

**Methods:** All NTM clinical isolates recovered at Brooke Army Medical Center from 2012 to 2022 were screened; SSTI and bone isolates were included. Electronic health records were reviewed for epidemiologic, microbiologic, and clinical data. Infections were defined as recovery of one or more NTM isolate from skin, soft tissue, or bone cultures with a corresponding clinical syndrome.

**Results:** Forty isolates of skin, soft tissue, or bone origin from 29 patients were analyzed. Twenty (69 %) patients, majority female (14/20, 70 %), had infecting isolates, most commonly secondary to surgery (35 %) or trauma (35 %). Six of 20 (30 %) had bone infections. Time from symptom onset to isolate recovery was a median 61 days (IQR 43–95). Eight (40 %) had combined medical/surgical therapy, 8 (40 %) had surgery alone, and 4 (20 %) had medical therapy alone. *M. abscessus* was more frequently isolated from patients with true infections.

**Conclusions:** Data supporting diagnosis and treatment decisions in NTM SSTI/bone infections is sparse. In this study the majority of NTM isolated were true infections. We confirm that surgery and trauma are the most common routes of exposure. The delay between symptom onset and directed therapy and the wide variety of treatment regimens highlight a need for additional studies delineating criteria for diagnosis and treatment.

### 1. Introduction

Non-tuberculous mycobacteria (NTM) comprise more than 190 *Mycobacterium* species present in the environment, including in soil, water (both natural sources and municipal reservoirs), and animal reservoirs. [1,2] Infections with these organisms have become increasingly prevalent in recent years. In the 1980s, estimates in the United States reported the prevalence of NTM infection as 1.6 to 1.8 per 100,000 people, while a study from the early 2000s reported an increase to 14.1 per 100,000. [3] This may be due to several factors, including improved diagnostics, increased numbers of immunocompromised hosts, and a decrease of competing microorganisms in public water sources due to chlorination. [3,4] While most commonly the cause of pulmonary infections, NTM are known to cause a variety of extrapulmonary clinical

syndromes, including skin and soft tissue (SSTI) and bone infections. SSTI typically present as a nonspecific chronic, non-resolving, or relapsing ulcer, nodule, abscess, or cellulitis, often evolving over weeks to months. [1] NTM SSTI arise most frequently through hematogenous dissemination or direct inoculation from traumatic environmental exposure, surgery, or cosmetic procedures. [5,6].

NTM SSTIs are typically caused by the rapidly growing mycobacteria (RGM) species *M. abscessus*, *M. chelonae*, and *M. fortuitum*, although a variety of species have been implicated including slow-growing mycobacteria (SGM) species *Mycobacterium marinum* and *Mycobacterium avium* complex. [7] Diagnosis and subsequent treatment are often delayed for multiple reasons, including nonspecific clinical presentation, lack of suspicion for unusual organisms as the source of infection, and the fact that in the absence of suspicion, mycobacterial cultures are

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not often routinely performed for surgical wound infections. [6] Additionally, species identification often requires gene sequencing at reference laboratories leading to further delays. [1] Patients are frequently treated initially with antimicrobials used for standard bacterial SSTI, resulting in a relapse of infection or lack of response to medical therapy. Furthermore, because of their wide range of antimicrobial susceptibility patterns, identification of a clinical NTM isolate to species level is critical before consideration for antimicrobial treatment. Unfortunately, there are no randomized controlled trials to guide therapy of NTM SSTI and bone infections, and the most recent guidelines from 2007 are based on limited available literature and expert opinion.[7].

In this study, we sought to understand better SSTI and bone infections caused by NTM at our institution. We examined the clinical characteristics and presentation of patients with skin, soft tissue, or bone mycobacterial isolates. For patients with SSTI or bone isolates, we reviewed medical charts to identify their presenting symptoms, infection site, and exposure route. Given known difficulties with the diagnosis and treatment of these infections, we also examined the duration of symptoms prior to diagnosis and the variety of treatment regimens present in this cohort of patients.

## 2. Methods

### 2.1. Clinical

Brooke Army Medical Center (BAMC) is a 425-bed academic military treatment facility (MTF) located in San Antonio, Texas. Microbiology lab records were reviewed to identify all NTM clinical isolates recovered at BAMC from 2012 to 2022. These were initially screened, and isolates identified from a bone or skin and soft tissue culture were included. Corresponding electronic health records were reviewed retrospectively for epidemiologic, microbiologic, and clinical data. A standardized form was used to gather data including patient demographics, comorbid conditions, relevant exposures (alcohol or tobacco use, immunocompromising medications), clinical presentation (date of presumed exposure, date of symptom onset, and presenting symptom), microbiologic data, radiologic data, treatment regimen, and outcome of therapeutic intervention. There is no universally described definition for a skin, soft tissue, or bone infection with NTM; diagnosis typically relies on a combination of history taking, clinical presentation, and laboratory evaluation including microbiology and histopathology. For this paper we defined true infections as recovery of one or more NTM isolates of the same species cultured from skin, soft tissue, or bone and possessing a corresponding clinical syndrome such as abscess, draining sinus tract, or chronic wound. Patients were excluded if they had no follow-up within our healthcare system after NTM identification. Cure was defined as no signs or symptoms of NTM SSTI or bone infection at the end of medical therapy or after the last surgical procedure. This study was reviewed by the Human Research Protections Office at BAMC and was given a not research determination.

### 2.2. Microbiology

Isolates were cultured using liquid mycobacterial growth indicator tubes (BACTEC MGIT 960 system; Becton, Dickinson, and Company; Franklin Lakes, NJ) and solid Middlebrook 7H11 agar, both incubated for 6 weeks. Initial species identification was performed at BAMC using standard criteria, including growth rate, morphologic colony structure, high-performance liquid chromatography, and Gen-Probe/AccuProbe (Hologic, Inc.; Marlborough, MA). Definitive identification for non-MAC organisms was performed via gene sequencing (16S ribosomal RNA, *rpoB*, *erm*), and antimicrobial susceptibility testing for all organisms via broth microdilution, performed at reference laboratories (primarily University of Texas at Tyler Health Science Center with one isolate each sent to Labcorp and Focus Lab). Isolates were described as either susceptible, intermediate, or resistant to antimicrobials based on

Clinical and Laboratory Standards Institute (CLSI) guidelines.

### 2.3. Statistical analysis

Patients meeting described criteria for true NTM infection were compared with those who had colonizing isolates. Patient demographics including age, gender, race, and weight, as well as common or clinically significant comorbidities, route of exposure, and site of isolate recovery were summarized using descriptive statistics. For continuous variables the mean and interquartile ranges are shown, while categorical variables are reported as frequency (percentage).

## 3. Results

### 3.1. Clinical

A total of 1,442 mycobacterial isolates were reviewed from a 10-year period, and 40 isolates were identified as being from skin, soft tissue, or bone source. These isolates, from 29 corresponding patients, were analyzed with most patients (86 %, 25/29) having only one isolate. Isolates from 20 of the 29 met criteria for true infection, and most isolates (31 of 40, 78 %) were from these 20 patients (Table 1). The median age of patients with NTM SSTI or bone true infection was 51 [IQR 33–67] and 70 % were female. There was no statistically significant difference in the BMI of patients meeting true infection criteria (Median 26.6, [IQR 22.5–32.6]) versus those who did not meet infection criteria (median 26.5 [IQR 23.9–26.9]), nor was there a difference identified in comorbidities.

Every isolate not meeting infection criteria was from skin/soft tissue sources rather than bone. Five of the nine not meeting infection criteria

**Table 1**

Characteristics of Patients with Skin, Soft Tissue, and Bone Isolates.

Characteristic	All Patients with SSTI/Bone NTM Isolates	Patients Meeting Infection Criteria	Patients not Meeting Infection Criteria
Number, N	29	20 (69)	9 (31)
Age, median (IQR)	51 (31–66)	51 (33–67)	54 (33–64)
Gender, female	19 (65.5)	14 (70)	5 (55.6)
Ethnicity			
White	17 (58.6)	12 (60)	5 (55.6)
Black	3 (10.3)	1 (5)	2 (22.2)
Asian	2 (6.9)	2 (10)	0 (0)
Other/Unknown	7 (24.1)	5 (25)	2 (22.2)
Body Mass Index (BMI), median (IQR)	26.6 (22.7–30.2)	26.6 (22.5–32.6)	26.5 (23.9–26.9)
Comorbidities			
Hypertension	11 (37.9)	7 (35)	4 (44.4)
Cardiovascular disease	7 (24.1)	5 (25)	2 (22.2)
Diabetes mellitus	3 (10.3)	2 (10)	1 (11.1)
Solid organ malignancy	2 (6.9)	2 (10)	0 (0)
Autoimmune condition	6 (20.7)	4 (20)	2 (22.2)
Route of Exposure			
Trauma	10 (34.5)	7 (35)	3 (33.3)
Surgery	12 (41.4)	7 (35)	5 (55.6)
Suspected	2 (6.9)	2 (10)	0 (0)
Environmental Exposure			
Tattoo	1 (3.4)	1 (5)	0 (0)
Disseminated Infection	1 (3.4)	1 (5)	0 (0)
Unknown	3 (10.3)	2 (10)	1 (11.1)
Site of Isolate Recovery			
Skin/Soft Tissue	23 (79.3)	14 (70)	9 (100)
Bone	6 (20.7)	6 (30)	0 (0)

Data expressed as N (%) or Median (IQR).

were obtained via swab, two were aspirates of purulent material, one was a medical device culture (lacrimal duct stent), and one was a tissue biopsy. Three of nine patients had alternate pathogens identified, all were *Staphylococcus aureus*. For patients with true infections, routes of exposure were predominately surgery and traumatic injury with inoculation of significant environmental bioburden (Table 1). Fourteen of twenty true infecting isolates were skin and soft tissue infections, while the remaining 6 were bone infections. All bone isolates identified represented true infections, and 5 of 6 were associated with traumatic injury of extremities – 3 lower and 2 upper. RGM represented 100 % of bone isolates, with four of six bone infections being secondary to *M. abscessus*, and the remaining two secondary to *M. fortuitum* complex and *M. senegalense*, part of the *M. fortuitum* complex. [8].

Of the 20 patients with true infections, 4 received medical therapy alone, 8 received surgery alone, and 8 received combined medical and surgical therapy. All patients who received targeted antimicrobial therapy received an infectious disease consult, while 6 of the 8 patients who received surgical therapy alone had no consult. Time from symptom onset to isolate recovery was prolonged at a median of 61 days [IQR 43–95]. The time from isolate recovery to therapy was 34 days for patients who received medical therapy alone, and 33 days for patients who received combined surgical and medical therapy. Patients managed with surgery alone underwent a mean of 2.6 total surgeries, with a median of 1 surgical procedure prior to diagnosis and 1 surgical procedure post-diagnosis, with a median duration of follow-up of 11 months [IQR 3–30]. One patient underwent 7 total surgical procedures (4 prior to diagnosis and 3 after diagnosis). The 8 patients treated surgically had a wide variety of exposure routes: 3 with traumatic exposure, 4 with presumed surgical exposures, and 1 with an unknown exposure (Table 2). Surgical procedures performed for source control included extremity amputation (x1), wide excision of abscess/non-healing wounds (x3), multiple bone and soft tissue surgical debridement (x2), and irrigation and debridement with total hardware removal (x2).

All patients who received antimicrobial therapy were started on regimens with at least two antibiotics. Eight patients received a 3-drug regimen initially, with 4 patients receiving a 2-drug regimen (Table 2). Of the 7 patients with *M. abscessus* infections who received antimicrobials, four received regimens that included amikacin. Patients who received combined medical and surgical therapy received a median of 4 months of antimicrobial therapy (IQR 3–6), while patients who received antimicrobials alone had a median treatment length of 8.5 months (IQR 4.5–12.5). At the end of analysis, 15 of the 20 patients were cured of their NTM infections (Table 2). Of the 5 not cured, 3 died from underlying illnesses not related to their NTM infections. For the remaining 2 patients, care was transferred outside of our system, but at last follow-up treatment was ongoing without demonstration of cure.

### 3.2. Laboratory

Over 40 % (12/29) of the patients grew *M. abscessus* complex isolates, with 11 of 12 of these patients (91.7 %) meeting infection criteria (Table 3). The next most common isolates were MAC and *M. fortuitum*, isolated in 5 patients each, with 2 (40 %) and 3 (60 %) patients each meeting infection criteria, respectively. Seventeen of twenty (85 %) infections were due to RGM. Additional pathogens were identified in 4 of 20 patients – monomicrobial infections with *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Enterobacter cloacae*, and one polymicrobial infection with *Streptococcus anginosus*, *Streptococcus mitis*, and *Pseudomonas aeruginosa*. These 4 patients had primary surgical management and received antibiotics targeted solely at their typical bacterial pathogens. Nine of twenty patients had tissue cultures, allowing for the potential of concomitant histopathology; 8 had histopathology, 7 of which demonstrated granulomatous inflammation. For the 8 patients managed with surgery alone, only two had tissue cultures, both of which had histopathology demonstrating granulomatous inflammation.

Antimicrobial susceptibility testing was performed on 22 isolates

(Table 4). Susceptibility data was also included from two non-infecting *M. fortuitum* isolates. Of the 10 *M. abscessus* complex isolates tested, 6 were identified as subspecies *abscessus*, one as subspecies *massiliense*, and three were not sub-speciated. Overall, *M. abscessus* complex isolates demonstrated significant antimicrobial resistance. All 10 isolates were susceptible to amikacin, with the next highest susceptibilities to linezolid (60 %), and clarithromycin (30 %). The majority (90 %) were intermediately susceptible to cefoxitin and imipenem. In contrast, all *M. fortuitum* group isolates tested were susceptible to amikacin, ciprofloxacin, linezolid, and moxifloxacin, with 5 of 6 (83 %) demonstrating susceptibility to imipenem and trimethoprim/sulfamethoxazole (TMP/SMX).

## 4. Discussion

In this retrospective study, we describe the clinical characteristics, treatment course, and microbiology of patients with SSTIs and bone infections at a tertiary care facility in South Texas. We found that the majority of the 20 true infections occurred in women (70 %) with a median age of 51. This is consistent with most prior studies reviewed, which noted infections in majority females with median ages ranging from 47 to 62. [9–12] Unlike NTM lung disease, which typically occurs in patients with lower BMIs, our patients had a median BMI of 26.6. [13] We identified no differences in comorbidities when comparing patients with infecting isolates and non-infecting isolates, likely because most of these patients had a traumatic or surgical inoculation rather than predisposing underlying pathophysiology. The clinical characteristics of our patient group emphasize the differences between NTM lung disease and skin, soft tissue, and bone infections.

Our findings were consistent with published literature which notes that most SSTIs and bone infections due to NTM occur either via surgery or traumatic inoculation. Of the patients with bone infections, 5 of 6 were due to significant trauma, likely allowing for direct inoculation of NTM into the bone. Although the interval from symptom onset to diagnosis was prolonged at 61 days (IQR 43–95), this time period is shorter than prior studies, which report a range of 3 to 5 months. [10,12] There are multiple possibilities for this shorter interval, including the surgical and traumatic routes of exposure causing patients to seek care earlier than they might have otherwise, and a study population comprised of patients from a single healthcare system who tend to receive all their care within this system. This prolonged duration from symptom onset to diagnosis highlights the need for clinicians to maintain suspicion for NTM infections in patients with significant environmental trauma.

While the 2007 American Thoracic Society/Infectious Disease Society of America statement summarizes the expert consensus on the management of NTM infections, including SSTIs and bone infections, the 2020 update provides guidance only for NTM pulmonary disease. [7,15] The 2007 statement recommends at least 4 months of combination therapy for skin and soft tissue infection and at least 6 months for bone infections, with the understanding that surgery is generally required to obtain source control. In our study, patients who received medical therapy alone had a median treatment duration of 8.5 months, compared to a median duration of 4 months for patients who received combined medical and surgical therapy. While not definitive, this finding suggests the importance of adjunctive surgery in shortening antimicrobial duration.

The variety in antimicrobial regimens in this study emphasizes the need for standardized regimens, as no two patients received the same treatment. Of the 12 patients who received a course of NTM-directed antimicrobials, 5 received regimens that included at least one parenteral agent at the start. All 5 patients who received a parenteral antimicrobial had infections with an *M. abscessus* complex organism, likely representing the lack of treatment options for these infections given the significant antimicrobial resistance of this organism. Due to variable antimicrobial susceptibility, combination therapy often includes at least

**Table 2**  
Summary of 20 patients with Skin, Soft Tissue, and Bone infections 2012 to 2022.

Age/sex	Site	Presenting symptom	Involvement	Exposure	Duration of symptoms prior to diagnosis (d)	Mycobacterial species	Initial targeted antibiotic regimen	Duration of therapy (mo)	ID consult	Treatment	Outcome
56/M	Hand	Abscess	SSTI	Laceration exposed to environment	59	<i>M. abscessus</i> complex	Azithromycin, Imipenem, Linezolid	8	Yes	Combined	Cure
18/F	Lower extremity	Abscess	Bone and SSTI	MVC with tibial plateau fracture	65	<i>M. abscessus</i> complex	None	N/A	No	Surgical	Cure
32/M	Lower extremity	Abscess	SSTI	Spider bite	63	<i>M. abscessus</i> complex	Clarithromycin, Linezolid	3	Yes	Combined	Cure
87/M	Upper extremity	Sinus tract	Bone and SSTI	Traumatic amputation by a grain auger	21	<i>M. abscessus</i> complex	None	N/A	Yes	Surgical	Cure
30/F	Lower extremity	Abscess	Bone and SSTI	Thrown from lawnmower with resultant fibula fracture	38	<i>M. abscessus</i> subsp. <i>abscessus</i>	Cefoxitin, clarithromycin	6	Yes	Combined	Cure
51/F	Breast	Pain	SSTI	Breast augmentation	1275	<i>M. abscessus</i> subsp. <i>abscessus</i>	Amikacin, Linezolid, Tigecycline	4	Yes	Combined	Cure
39/F	Neck	Neck pain	SSTI	Cervical spine posterior fusion	58	<i>M. abscessus</i> subsp. <i>abscessus</i>	None	N/A	No	Surgical	Cure
51/F	Abdomen	abscess	SSTI	Recurrent abdominal surgeries after gastric bypass	35	<i>M. abscessus</i> subsp. <i>abscessus</i>	Amikacin, Imipenem, Tigecycline	1	Yes	Combined	Death
68/F	Jaw	Pain	Bone	Jaw osteonecrosis requiring multiple surgeries	86	<i>M. abscessus</i> subsp. <i>abscessus</i>	None	N/A	No	Surgical	Death
33/F	Abdomen	Nodular lesions	SSTI	Bowel injury during laparoscopic total hysterectomy	44	<i>M. abscessus</i> subsp. <i>abscessus</i>	Amikacin, Linezolid, Tigecycline	3	Yes	Combined	Cure
47/F	Lower extremity	Nodular lesions	SSTI	Unknown, immunocompromised	129	<i>M. abscessus</i> subsp. <i>massiliense</i>	Clarithromycin, omadacycline	14	Yes	Medical	Cure
59/F	Lower extremity	Abscess	SSTI	Unknown	51	<i>M. chelonae</i>	None	N/A	No	Surgical	Cure
66/M	Upper extremity	Nodular lesions	SSTI	Gardening	95	<i>M. chelonae</i>	Azithromycin, doxycycline	3	Yes	Medical	Cure
26/F	Abdomen	Nodular lesions	SSTI	Abdominoplasty	41	<i>M. fortuitum</i>	None	N/A	No	Surgical	Ongoing
24/F	Upper extremity	Abscess	SSTI	Contraceptive implant	28	<i>M. fortuitum</i>	None	N/A	No	Surgical	Cure
71/M	Upper extremity	Sinus tract	Bone and SSTI	Traumatic amputation from MVC with environmental contamination	106	<i>M. fortuitum</i> group	Ciprofloxacin, Tedizolid, Trimethoprim-Sulfamethoxazole	15+	Yes	Combined	Ongoing
40/M	Lower extremity	Sinus tract	Bone and SSTI	MVC with tibia fracture	90	<i>M. senegalense</i>	None	N/A	Yes	Surgical	Cure
69/F	Eyebrows	Cellulitis	SSTI, lymphadenitis	Cosmetic tattooing	107	<i>M. haemophilum</i>	Ciprofloxacin, Clarithromycin, Rifampin	5	Yes	Medical	Cure
71/F	Head	Leg weakness	SSTI, disseminated	Unknown, immunocompromised	45	<i>M. avium</i> complex	Azithromycin, Ethambutol, Rifabutin	6	Yes	Combined	Death
66/F	Upper extremity	Nodular lesions	SSTI	Cleaning garden bird bath, immunocompromised	96	<i>M. avium</i> complex	Azithromycin, Ethambutol, Rifampin	12	Yes	Medical	Cure

**Table 3**  
Skin, Soft Tissue, and Bone Isolates by Mycobacterial Species.

Mycobacterium isolates (total number)	All Patients with SSTI/Bone NTM Isolates	Patients Meeting Infection Criteria	Patients not Meeting Infection Criteria
<i>M. abscessus</i> complex	12 (41.4)	11 (91.7)	1 (8.3)
<i>M. avium</i> complex	5 (17.2)	2 (40)	3 (60)
<i>M. fortuitum</i>	5 (17.2)	3 (60)	2 (40)
<i>M. chelonae</i>	2 (6.9)	2 (100)	0 (0)
<i>M. goodii</i>	2 (6.9)	0 (0)	2 (100)
<i>M. senegalense</i>	1 (3.4)	1 (100)	0 (0)
<i>M. haemophilum</i>	1 (3.4)	1 (100)	0 (0)
<i>M. kansasii</i>	1 (3.4)	0 (0)	1 (100)

Data expressed as N (%) or Median (IQR).

one parenteral agent at the start of therapy, further increasing the challenging nature of these infections. [16] The majority (85 %) of infecting isolates in our study were RGM, with *M. abscessus* being the most common organism isolated, which is typical for SSTIs. Consistent with prior literature, our *M. abscessus* isolates were extremely drug resistant, with only 30 % demonstrating macrolide susceptibility. [14] Our antimicrobial susceptibility testing demonstrated relatively few treatment options based on *in vitro* testing, highlighting the need for new antimicrobials with activity against NTM. Although the correlation between *in vitro* drug susceptibility testing and successful NTM infection treatment is still being determined for most antimicrobials, in the absence of clear data, clinicians often use these results to guide prolonged and often toxic treatment courses [17].

One highlight of this study is the subset of patients for whom cure was achieved without antimicrobial therapy. Antimicrobial therapy for NTM SSTI and bone infections typically requires multiple medications for a prolonged period, often associated with toxicities. The number of patients in our study treated with surgical therapy alone was unusual. A decades-long population-based study in Minnesota identified 17 of 39 patients (44 %) treated with medical therapy alone versus 22 (56 %) treated with a combination of medical and surgical therapy, with no patients treated only with surgery. Several larger studies demonstrate rates of only 4 to 14 % of patients treated with surgery alone. [10–12] Notably, 6 of the 8 patients treated with surgery alone were cured at the end of our follow-up period, emphasizing the potential role of isolated surgical management.

This study has several limitations, including the small number of patients and the study’s retrospective nature. Although over 1400 mycobacterial isolates were identified during our study period, less than 3 % were from skin, soft tissue, or bone source. The small sample size limits our ability to evaluate for statistically significant differences in both microbiology of infections and in comorbidities often considered important in NTM infection. Furthermore, the retrospective nature of the study does not allow us to assess why particular treatment decisions

**Table 4**  
Antimicrobial susceptibility testing by nontuberculous mycobacterial species.

Antimicrobial	<i>M. abscessus</i> complex (N = 10)				<i>M. fortuitum</i> group (N = 6)				<i>M. avium</i> complex(N = 2)				<i>M. chelonae</i> (N = 2)			
	S	I	R	%S	S	I	R	%S	S	I	R	%S	S	I	R	%S
Amikacin	10	0	0	100	6	0	0	100	2	0	0	100	2	0	0	100
Cefoxitin	1	9	0	10	0	4	2	0					0	0	2	0
Ciprofloxacin	0	0	10	0	6	0	0	100					1	0	1	50
Clarithromycin	3	0	7	30	0	1	5	0	2	0	0	100	1	0	1	50
Doxycycline	0	0	10	0	2	0	3	40					1	0	1	50
Imipenem	0	9	1	0	5	1	0	83					0	1	1	0
Linezolid	6	3	1	60	6	0	0	100	0	0	2	0	1	1	0	50
Minocycline	0	1	8	0	0	0	3	0					1	0	1	50
Moxifloxacin	0	0	10	0	5	0	0	100	1	0	1	50	1	0	1	50
TMP/SMX	1	0	9	10	5	0	1	83					1	0	1	50
Tobramycin													2	0	0	100

were made. Clarity concerning this decision-making would help determine if a subset of patients can be successfully treated with surgery alone. The availability of histopathology in less than half of patients considered to have true infections further highlights the diagnostic difficulty of these infections. Moreover, as our facility cannot perform definitive species identification via gene sequencing, several of the isolates included were identified only to species level rather than subspecies level, such as *M. abscessus* complex isolates. [18] Given the significant differences in susceptibility profiles of the different *M. abscessus* subspecies, identification to species level would be helpful in these patients. However, the availability of clinical and microbiological data for these patients strengthens this study.

In contrast to NTM isolated from the respiratory tract, most isolates from skin, soft tissue, and bone sources were found to be indicative of a true infection. While management of NTM lung disease is well established, we lack similar guidelines directing diagnosis and treatment for NTM SSTI and bone infections. As surgery can be a part of management for refractory NTM lung disease, given the anatomic locations and etiology of NTM SSTI and bone infections, it is plausible that surgery may play a much more important role in treatment than currently recognized. [15] Additional studies to evaluate the role of surgical management, particularly how it may shorten the duration of antimicrobials, would be of particular interest.

Given the relative rarity of these infections, delay in diagnosis and treatment is common. As these infections are not reportable in most of the United States, there is limited population-based data to assess their incidence, and data to guide optimal diagnosis and treatment of NTM SSTI and bone infections remain limited. [15,19] Additionally, the first step in diagnosis often relies upon clinical suspicion of an NTM infection to obtain appropriate cultures, and many non-infectious disease providers are unaware of these infections. NTM SSTIs and bone infections are important, distinct clinical entities often requiring prolonged courses of antimicrobials with significant toxicity. To provide optimal patient outcomes, we must increase provider awareness of these infections and perform additional studies to delineate specific criteria for diagnosis and treatment.

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**6. Disclaimer**

The views expressed herein are those of the author(s) and do not necessarily reflect the official policy or position of the Defense Health Agency, Brooke Army Medical Center, the Department of Defense, nor any agencies under the U.S. Government.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- [1] Misch EA, Saddler C, Davis JM. Skin and soft tissue infections due to nontuberculous mycobacteria. *Curr Infect Dis Rep* 2018;20(4):6.
- [2] Pennington KM, Vu A, Challener D, Rivera CG, Shweta FNU, Zeuli JD, et al. Approach to the diagnosis and treatment of non-tuberculous mycobacterial disease. *J Clin Tuberc Other Mycobact Dis* 2021;24:100244.
- [3] Mirsaeidi M, Machado RF, Garcia JGN, Schraufnagel DE, Herrmann JL. Nontuberculous mycobacterial disease mortality in the United States, 1999–2010: a population-based comparative study. *PLoS One* 2014;9(3):e91879.
- [4] Adjemian J, Olivier KN, Seitz AE, Holland SM, Prevots DR. Prevalence of nontuberculous mycobacterial lung disease in U.S. Medicare beneficiaries. *Am J Respir Crit Care Med* 2012;185(8):881–6.
- [5] Cassidy PM, Hedberg K, Saulson A, McNelly E, Winthrop KL. Nontuberculous mycobacterial disease prevalence and risk factors: a changing epidemiology. *Clin Infect Dis* 2009;49(12):e124–9.
- [6] Franco-Paredes C, Marcos LA, Henaio-Martínez AF, Rodríguez-Morales AJ, Villamil-Gómez WE, Gotuzzo E, et al. Cutaneous mycobacterial infections. *Clin Microbiol Rev* 2018;32(1).
- [7] Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. *Am J Respir Crit Care Med* 2007;175(4):367–416.
- [8] Carretero O, Reyes C, San-Juan R, Chaves F, Lopez-Roa P. Mycobacterium senegalense infection after implant-based breast reconstruction. *Spain Emerg Infect Dis* 2020;26(3):611–3.
- [9] Diaz MAA, Huff TN, Libertin CR. Nontuberculous mycobacterial infections of the lower extremities: A 15-year experience. *J Clin Tuberc Other Mycobact Dis* 2019;15:100091.
- [10] Uslan DZ, Kowalski TJ, Wengenack NL, Virk A, Wilson JW. Skin and soft tissue infections due to rapidly growing mycobacteria: comparison of clinical features, treatment, and susceptibility. *Arch Dermatol* 2006;142(10):1287–92.
- [11] Wentworth AB, Drage LA, Wengenack NL, Wilson JW, Lohse CM. Increased incidence of cutaneous nontuberculous mycobacterial infection, 1980 to 2009: a population-based study. *Mayo Clin Proc* 2013;88(1):38–45.
- [12] Tokunaga DS, Siu AM, Lim SY. Nontuberculous mycobacterial skin and soft tissue infection in Hawai'i. *BMC Infect Dis* 2022;22(1):360.
- [13] Kartalija M, Ovrutsky AR, Bryan CL, Pott GB, Fantuzzi G, Thomas J, et al. Patients with nontuberculous mycobacterial lung disease exhibit unique body and immune phenotypes. *Am J Respir Crit Care Med* 2013;187(2):197–205.
- [14] Kim JH, Jung IY, Song JE, Kim EJ, Kim JH, Lee WJ, et al. Profiles of extrapulmonary nontuberculous mycobacteria infections and predictors for species: a multicenter retrospective study. *Pathogens* 2020;9(11):949.
- [15] Daley CL, Iaccarino JM, Lange C, Cambau E, Wallace RJ, Andrejak C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. *Eur Respir J* 2020;56(1):2000535.
- [16] Gonzalez-Santiago TM, Drage LA. Nontuberculous mycobacteria: skin and soft tissue infections. *Dermatol Clin* 2015;33(3):563–77.
- [17] Shen Y, Wang X, Jin J, Wu J, Zhang X, Chen J, et al. In Vitro Susceptibility of Mycobacterium abscessus and Mycobacterium fortuitum Isolates to 30 Antibiotics. *Biomed Res Int* 2018;2018:1–10.
- [18] Brown-Elliott BA, Woods GL, Kraft CS. Antimycobacterial susceptibility testing of nontuberculous mycobacteria. *J Clin Microbiol* 2019;57(10).
- [19] Winthrop KL, Henkle E, Walker A, Cassidy M, Hedberg K, Schafer S. On the reportability of nontuberculous mycobacterial disease to public health authorities. *Ann Am Thorac Soc* 2017;14(3):314–7.