Vital Surveillances

Antibiotic Susceptibility of *Nocardia* Clinical Isolates Collected from Chinese Patients — China, 2014–2024

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ABSTRACT

Introduction: *Nocardia* species are found worldwide in soil rich in organic matter and can cause nocardiosis in humans. Trimethoprim-sulfamethoxazole has long been the first-line treatment for *Nocardia* infections; however, resistance to this therapy has recently been reported.

Methods: Sixty-three clinical *Nocardia* isolates collected in China were tested against 32 antimicrobial agents using the broth microdilution method. Phylogenetic analysis of the 16S rRNA gene was performed to identify the species.

Results: Three sequences from samples collected in Hainan Province did not match any known *Nocardia* species, suggesting significant genetic diversity among *Nocardia* isolates. *Nocardia* strains generally exhibited high resistance to clarithromycin, clindamycin, and isoniazid. Clinical and reference strains of *N. farcinica* and *N. otitidiscaviarum* were susceptible to amikacin and linezolid. Amoxicillin-clavulanate and imipenem were effective against all clinical and reference strains of *N. farcinica*, whereas gentamicin was effective against all clinical and reference strains of *N. otitidiscaviarum*.

Conclusions: Linezolid and amikacin were the most consistently active drugs among the analyzed species. Variability of antimicrobial susceptibility was observed among clinical isolates of the same species and between clinical and reference isolates of the same species. Overall, this study highlights the need for better assessment of the burden of nocardiosis in China and for continuous monitoring of antimicrobial resistance among *Nocardia* isolates.

Nocardia species are found worldwide in soil rich in organic matter (*1*). As of April 2025, 252 *Nocardia* species have been identified, and approximately 50 of them are considered human pathogens (https://www.bacterio.net/) (*2*–*3*). Most *Nocardia* infections are acquired through inhalation or traumatic inoculation (*4*–*7*). Infections are often seen in immunocompromised hosts, such as patients with AIDS, autoimmune diseases, malignancies, diabetes mellitus, or organ transplants (*8*–*10*). Infection with Mycobacterium tuberculosis (TB) is associated with chronic lung disease, and the similarity in the diagnosis and clinical manifestations of nocardiosis and TB may lead to misdiagnosis (*11*). The treatment of choice for tuberculosis is ineffective against nocardiosis, underscoring the importance of accurate diagnosis for effective therapy. The antimicrobial susceptibility of *Nocardia* is highly variable and depends on the species. Several studies have raised concerns about increasing resistance among *Nocardia* isolates, particularly to trimethoprim-sulfamethoxazole (SXT). Similarly, breakthrough infections have been reported in immunocompromised individuals receiving SXT prophylaxis (*12*).

The present study is an extension of a previous investigation (*13*), focusing on 63 clinical *Nocardia* isolates collected from 11 provincial-level administrative divisions (PLADs) across 6 of the 7 administrative regions of China. Variability in antimicrobial susceptibility was observed among isolates of the same species. Overall, this study highlights the need for better assessment of the burden of nocardiosis in China and for continuous monitoring of antimicrobial resistance among *Nocardia* isolates.

METHODS

We collected 305 clinical samples, 63 of which were identified as *Nocardia* strains. These isolates were obtained from patients across 11 PLADs in China, representing 6 of the 7 administrative regions. Phylogenetic analysis of the 16S rRNA gene was conducted to determine the species. Antimicrobial susceptibility to 32 antibiotics was determined using the broth microdilution method in accordance with the Clinical and Laboratory Standards Institute (CLSI)

guidelines (*14*). The Alamar Blue assay was used as the visual endpoint indicator, as previously described (*13*). The minimum inhibitory concentration (MIC) was defined as the lowest drug concentration that inhibited visible growth of the tested isolates. Cluster analyses of samples and antibiotics were performed using SPSS Statistics (version 22.0; IBM, Armonk, New York, USA), and both antibiotic and sample clusters were analyzed through hierarchical cluster analysis.

RESULTS

The sample sources were diverse, including eye secretions, sputum, abscesses, blood, bronchoalveolar lavage fluid, cerebrospinal fluid, and lung or liver biopsies. The most represented species was *N. farcinica* (23; 36.5%), followed by *N. cyriacigeorgica* (17; 27.0%). Three species were marginally represented in the dataset: *N. brasiliensis* (6; 9.5%), *N. otitidiscaviarum* (5; 7.9%), and *N. beijingensis* (4; 6.3%). Four species were rarely represented: *N. asiatica*, *N. terpenica*, *N. veterana,* and *N. abscessus* (Supplementary Table S1, available at https://weekly.chinacdc.cn/). One sequence (159) showed 98.4% identity with *N. nova* based on BLASTn analysis, while two sequences (153 and 160) did not match any of the established *Nocardia* species (Supplementary Figure S1, available at https://weekly.chinacdc.cn/).

Antibiotic Resistance Patterns of the 63 Strains

MIC values were determined for 32 antibiotics from 13 drug classes, with β-lactam antibiotics (9 drugs) (Figure 1). The resulting heatmap was analyzed in two ways: based on MIC values themselves and based on breakpoint values determined for each antibiotic by CLSI. To identify trends between strains and antibiotics, cluster analysis was performed on both the strains and the drugs (Figure 1). As mentioned earlier, phylogenetic analysis of the 16S rRNA gene identified 10 groups — nine corresponding to known species and one containing the two undetermined sequences, 153 and 160. A cluster analysis was performed using 12 clusters, considering that strains 153 and 160 were genetically distinct. Overall, the cluster analysis did not correspond to species determination. For example, the 23 *N. farcinica* strains were distributed across six clusters, with cluster 1 containing 17 of these strains. The six remaining strains (170, 158, 178, 165, 176, and 335) showed significantly different MIC patterns. Strain 170 in cluster 4 and strains 158 and 178 in cluster 2 exhibited strong resistance to cefotaxime (CTX) (MIC 256 mg/L) compared with other *N. farcinica* strains. Strain 165 in cluster 5 showed an intermediate MIC value for isoniazid (INH) (8 mg/L). Strain 176 in cluster 3 showed strong resistance to gentamicin (GEN) (MIC 256 mg/L). Finally, strain 335 in cluster 6 showed strong resistance to cefmetazole (CMZ), ceftriaxone (CRO), cefotaxime (CTX), cefoxitin (FOX), ethambutol (ETH), streptomycin (STR), clofazimine (CLO), and kanamycin (KAN) (256 mg/L). A discrepancy between species determination and cluster analysis was observed for all species except *N. brasiliensis* and *N. asiatica*, which were found in clusters 1 and 7, respectively. *N. cyriacigeorgica* strains were found in clusters 1 and 4, *N. otitidiscaviarum* in clusters 11 and 12, and *N. beijingensis* in clusters 1 and 7, respectively. The 63 strains showed intermediate MIC values for clindamycin (CLI) (8–64 mg/L). All strains except one (165) showed high MIC values for INH (256 mg/L). Although the strains were initially divided into 12 clusters, these clusters could be grouped into two mega groups: A (clusters 1–5 and 7) and B (clusters 6 and 8–12). The main difference between these two mega groups involved CMZ, with group A showing a lower average MIC (27.1 mg/L) and group B showing a higher average MIC (243.2 mg/L). In group A, cluster 7 was characterized by high ciprofloxacin (CIP) and levofloxacin (LVX) (128–256 mg/L), whereas cluster 3 was characterized by high GEN (256 mg/L). In group B, cluster 6 was characterized by high GEN values (32–256 mg/L) compared with other strains in group B (average, 0.8 mg/L).

Cluster analysis was performed based on the drugs. The 32 drugs belonged to 13 drug classes. The most represented class was β-lactam antibiotics, comprising nine drugs that were distributed across three different clusters (1, 2 and 3). Five of these drugs were found in cluster 1. The drugs were further grouped into two mega groups, I and II, with three clusters (clusters 6–8) forming the mega group II. Overall, group I showed low MIC values, whereas group II was characterized by high MIC values and included INH, RIF, and VAN. The clusters differed in their overall MIC values, with cluster 1 showing the lowest and cluster 7 the highest.

The average MIC value was calculated for each drug across all 63 clinical samples. Three antibiotics (linezolid, amikacin, and meropenem) had mean MIC

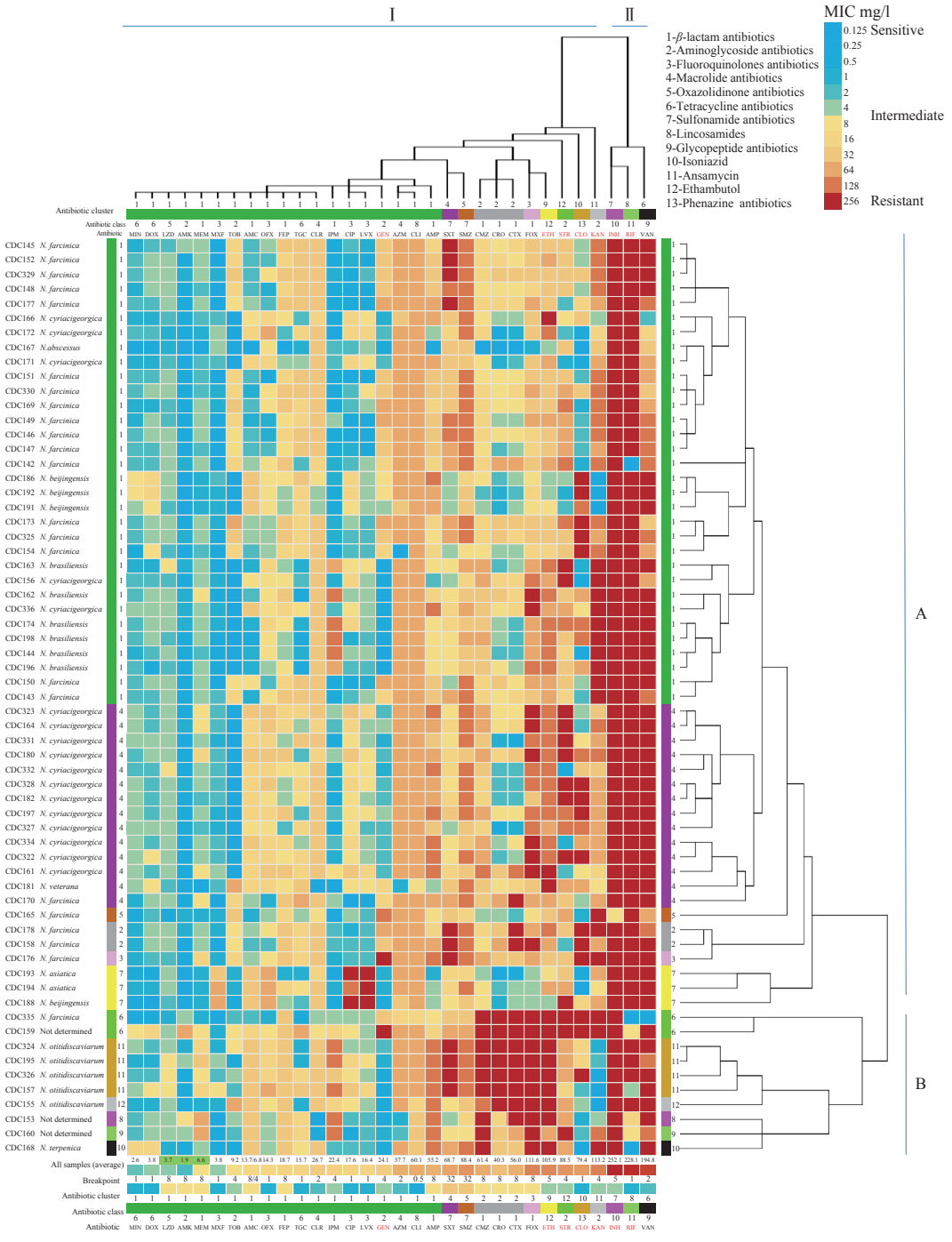

FIGURE 1. Heatmap showing MIC values of 63 *Nocardia* clinical isolates for 32 antimicrobial drugs.

Note: Drugs used to treat TB are shown in red font. Isolate species were determined by phylogenetic analysis of the 16S rRNA gene. MIC data were clustered by strains as well as drugs. Trees based on cluster analyses are shown on the right for the strains and at the top for the drugs. In both cases, 12 clusters were identified and are color-coded and numbered. Drug classes are indicated by a number. MIC values were also color-coded, from blue (MIC of 0.125 mg/L) for a susceptible strain to red (MIC of 256 mg/L) for a resistant strain. Clusters based on the strains were organized into two mega groups, labeled A and B. Similarly, clusters based on drugs were organized into two mega groups, labeled I and II. The average MIC value for each drug is shown at the bottom and is color-coded. Breakpoint values for each drug are also shown at the bottom. Average MIC values below the breakpoint are highlighted in green.

Abbreviation: MIC=minimum inhibitory concentration; TB=tuberculosis; AMK=amikacin; AMC=amoxicillin-clavulanate; AMP=ampicillin; AZM=azithromycin; FEP=cefepime; CMZ=cefmetazole; CTX=cefotaxime; FOX=cefoxitin; CRO=ceftriaxone; CIP=ciprofloxacin; CLR=clarithromycin; CLI=clindamycin; CLO=clofazimine; DOX=doxycycline; ETH=ethambutol; GEN=gentamicin; IPM=imipenem; INH=isoniazid; KAN=kanamycin; LVX=levofloxacin; LZD=linezolid; MEM=meropenem; MIN=minocycline; MXF=moxifloxacin; OFX=ofloxacin; RIF=rifampicin; STR=streptomycin; SMZ=sulfamethoxazole; TGC=tigecycline; TOB=tobramycin; SXT=trimethoprim-sulfamethoxazole; VAN=vancomycin.

values below their respective breakpoints, suggesting that these antibiotics were likely effective against all clinical isolates analyzed. However, variations were observed both between and within species. For example, *N. otidiscavarium* strains 155 and 324 had intermediate MIC values for tobramycin (TOB) (8–64 mg/L), whereas the other three *N. otidiscavarium* strains had MIC values below the TOB breakpoint value (4 mg/L). Three antibiotics — minocycline (MIN), doxycycline (DOX), and moxifloxacin (MXF) — had average MIC values (2.6, 3.8, and 3.8 mg/L, respectively) that were close to their breakpoint values (1 mg/L for all three) and might also be considered effective against most *Nocardia* species.

Antibiotic Resistance in Five Species

The previous analysis did not reveal any significant trend in antibiotic resistance across species. The next step was to assess whether any resistance pattern was consistent among all clinical strains of the same species. Although nine species were reported in this study, only five were analyzed because the remaining species were represented by only one or two clinical strains. Only the drugs for which MIC values exceeded the breakpoint value for each clinical isolate are listed in Table 1. Six resistance patterns were identified among the antibiotics and *Nocardia* species. Lincosamides (CLI) and INH were ineffective against all clinical isolates of the five *Nocardia* species. Six additional drug classes — ETH, ansamycin (rifampin, RIF), glycopeptides (vancomycin), tetracyclines (tigecycline), phenazine (clofazimine), and sulfonamides (sulfamethoxazole) — were ineffective against at least two species. Among macrolides, clarithromycin (CLR) was ineffective against all five species, whereas azithromycin (AZM) was ineffective against four of the five analyzed species. The effectiveness of *β-lactams* and fluoroquinolones varied by both drug and species. GEN was ineffective against *N. farcinica*, whereas KAN and STR were ineffective against two species. The last category concerned oxazolidinone (linezolid, LZD), which is not listed in Table 1, indicating that this drug might be effective against at least one clinical isolate from each of the five analyzed species. Consistent susceptibility to both amikacin (AMK) and LZD was observed across all five *Nocardia* species, while complete resistance was observed against CLR, CLI, and INH (Tables 2–3).

TABLE 1. List of antibiotics ineffective against all clinical isolates of the five *Nocardia* species.

Antibiotic class	Species†					Category
	N. farcinica (23)	*N. cyriacigeorgica* (17)	*N. brasiliensis* (6)	*N. otitidiscaviarum* (5)	*N. beijingensis* (4)	
Lincosamides (1)*	CLI§	CLI	CLI	CLI	CLI	1
Isoniazid (1)	INH	INH	INH	INH	INH	1
Ethambutol (1)	ETH	ETH	ETH	ETH		2
Ansamycin (1)		RIF	RIF	RIF	RIF	2
Glycopeptide (1)			VAN	VAN	VAN	2
Tetracyclines (3)		TGC			TGC	2
Sulfonamides (2)			SMZ	SMZ		2
Phenazine (1)				CLO	CLO	2
Macrolides (2)	CLR	CLR, AZM	CLR, AZM	CLR, AZM	CLR, AZM	3
β-lactams (9)		FOX	FOX, CMZ, IPM	AMP, AMC, FEP, CTX, FOX, CMZ, CRO, IPM	AMC	4
Fluoroquinolones (4)		CIP, LVX, OFX	LVX, OFX	CIP, LVX, OFX	CIP, LVX, OFX	4
Aminoglycosides (5)	GEN, KAN		KAN, STR	STR		5
Oxazolidinone (1)						6

Abbreviation: AMK=amikacin; AMC=amoxicillin-clavulanate; AMP=ampicillin; AZM=azithromycin; FEP=cefepime; CMZ=cefmetazole; CTX=cefotaxime; FOX=cefoxitin; CRO=ceftriaxone; CIP=ciprofloxacin; CLR=clarithromycin; CLI=clindamycin; CLO=clofazimine; DOX=doxycycline; ETH=ethambutol; GEN=gentamicin; IPM=imipenem; INH=isoniazid; KAN=kanamycin; LVX=levofloxacin; LZD=linezolid; MEM=meropenem; MIN=minocycline; MXF=moxifloxacin; OFX=ofloxacin; RIF=rifampicin; STR=streptomycin; SMZ=sulfamethoxazole; TGC=tigecycline; TOB=tobramycin; SXT=trimethoprim-sulfamethoxazole; VAN=vancomycin.

* Antibiotic classes were sorted based on the category column. The number of drugs in each class is indicated in parentheses.

† The number of clinical isolates for each species is indicated in parentheses.

§ Only drugs that were ineffective, i.e., with MIC values greater than breakpoint values for all clinical isolates of the analyzed species, are listed.

TABLE 2. Antibiotic categories based on the effectiveness of clinical and reference strains of the same *Nocardia* species.

Species*	Category	Antibiotic	
		Name	Class
N. farcinica, *N. otitidiscaviarum*	Antibiotics effective on all clinical and reference strains	AMK	Aminoglycoside
		LZD	Oxazolidinone
	Antibiotics effective on all reference strains	MXF	Fluoroquinolone
		SXT	Sulfonamide
N. farcinica	Antibiotics effective on all clinical and reference strains	AMC, IPM	β-lactam
	Antibiotics effective on all reference strains	MEM	β-lactam
N. otitidiscaviarum	Antibiotics effective on all clinical and reference strains	GEN	Aminoglycoside
	Antibiotics effective on all clinical strains	KAN	Aminoglycoside

* Only two *Nocardia* species were analyzed, as the remaining species were represented by fewer than four clinical or reference strains.

Overall, this analysis demonstrated that *Nocardia* species can exhibit variable responses to different antibiotics.

Comparison with *Nocardia* Standards

The present study identified different MIC patterns among strains of the same species as well as within the same antibiotic class. Comparison with the MIC patterns of *Nocardia* reference strains was necessary (Figure 2). The number of strains of each species with MIC values lower than or equal to the breakpoint value is shown for the 63 clinical strains (C) and the 26 reference strains (S). Some antibiotics had the same effect on all strains (clinical or/and reference) of the same species and are labeled as "100" in Figure 2. Only species with four or more strains (clinical or reference) were included in the comparison.

Overall, four categories of antibiotics were identified based on their effectiveness in both clinical and reference strains (Table 2). First, AMK and LZD were effective against all clinical and reference strains of *N. farcinica* and *N. otitidiscaviarum* (labeled with "100" in green in Figure 2). Second, amoxicillin-clavulanate (AMC), imipenem (IPM), and GEN were effective against all clinical and reference strains of one species. AMC and IPM were effective against all the clinical and reference strains of *N. farcinica,* whereas GEN was effective against all the clinical and reference strains of *N. otitidiscaviarum*. Third, MXF, SXT, and meropenem (MEM) were effective against all 10 *N. farcinica* reference strains, whereas lower effectiveness was observed among the 23 *N. farcinica* clinical strains. Finally, KAN was effective against all five *N. otitidiscaviarum* clinical strains, whereas one *N. otitidiscaviarum* reference strain was highly resistant (MIC value 256 mg/L; breakpoint 4 mg/L). None of the drug classes used in this study were consistently effective against all clinical strains of the analyzed species. Among the seven TB drugs, resistance to INH was observed in the clinical strains of all analyzed species. GEN and KAN were the only drugs used to treat TB that showed some effectiveness against all *Nocardia* strains. Other TB drugs, including STR, RIF, ETH, and CLO, were effective against only a few *Nocardia* clinical strains (Table 3).

DISCUSSION

The present study focused on the antibiotic susceptibility patterns of 63 clinical *Nocardia* strains collected in China. Recent studies identified *N. farcinica* and *N. otitidiscaviarum* as the most prevalent species, confirming the present findings (*4*,*13*,*15*). Although this study, which included 63 clinical isolates and nine known *Nocardia* species, extends a previous study that featured only 14 clinical isolates and three species, it is worth noting some limitations. Although clinical isolates from nine species were reported in the present study, only two species (*N. farcinica and N. cyriacigeorgica)* were represented by more than 10 strains. Another limitation concerned the number of reference strains for each species. Only three species (*N. farcinica, N. otitidiscaviarum*, and *N. veterana)* were represented by four or more standard strains. Geographic distribution was also a limitation, as one administrative region — Dongbei — was not represented in the present study. The reported strains were collected from 11 PLADs with relatively developed economies in China. Despite these limitations, the present study identified important trends that should be further confirmed by additional research.

The present study identified antibiotics based on their efficiency against *Nocardia* species, revealing that two drugs, LZD and AMK, were effective against all analyzed *N. farcinica, N. otitidiscaviarum* species.

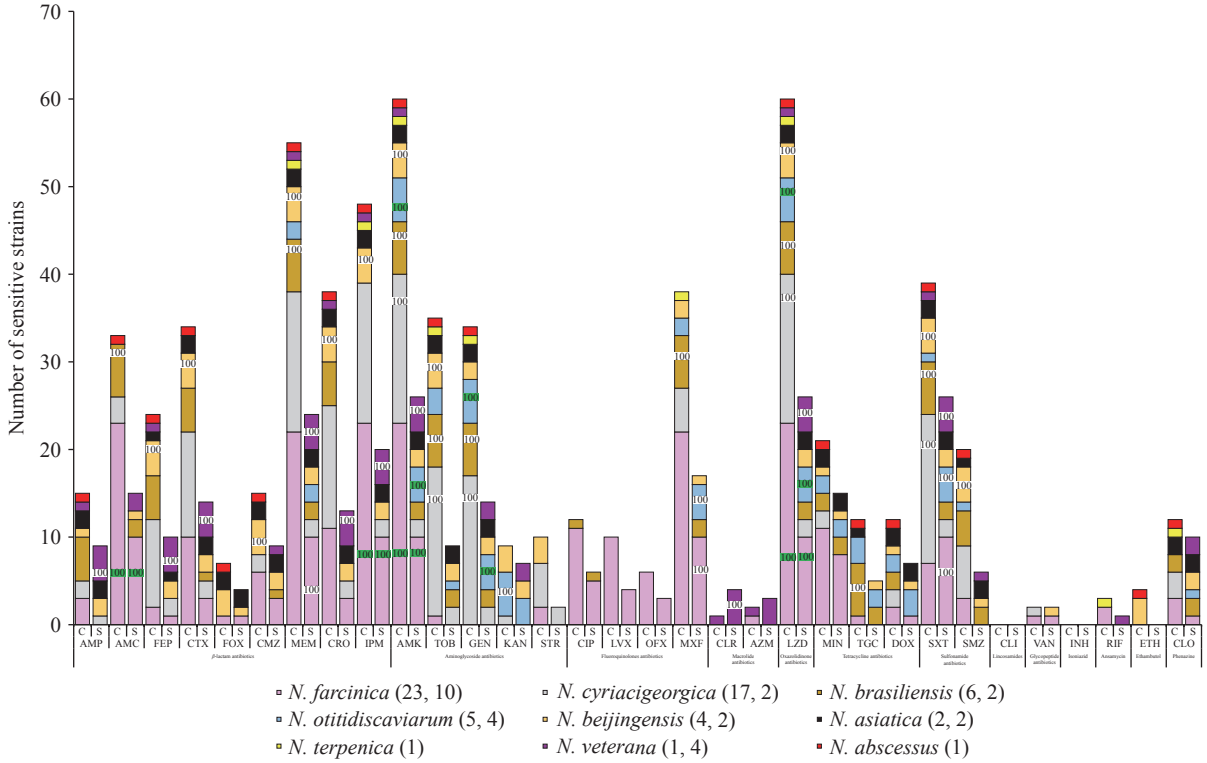

FIGURE 2. Number of susceptible strains for each antibiotic.

Note: The number of strains with MIC values lower than the breakpoint value for each antibiotic is shown. Clinical (C) and reference (S) strains were analyzed. Species are color-coded according to the legend at the bottom. The number of clinical and reference strains is indicated in parentheses. Species for which all clinical and/or reference strains were susceptible to an antibiotic are labeled with "100". Only species with four or more strains were included. Species for which all clinical and reference strains were susceptible to an antibiotic are shown with a green "100", and the results are summarized in Table 2.

Abbreviation: AMK=amikacin; AMC=amoxicillin-clavulanate; AMP=ampicillin; AZM=azithromycin; FEP=cefepime; CMZ=cefmetazole; CTX=cefotaxime; FOX=cefoxitin; CRO=ceftriaxone; CIP=ciprofloxacin; CLR=clarithromycin; CLI=clindamycin; CLO=clofazimine; DOX=doxycycline; ETH=ethambutol; GEN=gentamicin; IPM=imipenem; INH=isoniazid; KAN=kanamycin; LVX=levofloxacin; LZD=linezolid; MEM=meropenem; MIN=minocycline; MXF=moxifloxacin; OFX=ofloxacin; RIF=rifampicin; STR=streptomycin; SMZ=sulfamethoxazole; TGC=tigecycline; TOB=tobramycin; SXT=trimethoprim-sulfamethoxazole; VAN=vancomycin; MIC=minimum inhibitory concentration.

These antibiotics were also effective against all analyzed strains in studies conducted in Henan and Shandong provinces (*4*,*10*,*15*). Our recent systematic review of antimicrobial susceptibility data from *Nocardia* clinical isolates in China (as of 2024) revealed relatively low overall resistance rates to three antibiotics: LZD (0.30%, 1/336), AMK (3.87%, 13/336), and SXT (3.87%, 13/336) (in press, Disease Surveillance).

The present study revealed differences in antibiotic susceptibility among the same *Nocardia* species. Strains of the same species were not all sensitive to the same antibiotics. Moreover, antibiotics belonging to the same drug class did not exhibit equal effectiveness against *Nocardia* strains. The most consistent drug class was the aminoglycosides, which showed some degree of effectiveness, with variations observed among *Nocardia* strains. A previous study reported similar findings, with AMK being effective against six of seven tested species (*10*).

In summary, the present study revealed potential genetic diversity among *Nocardia* strains, at least based on the 16S rRNA gene, which resulted in incomplete species identification. Moreover, differences in antibiotic susceptibility were observed among strains of the same species. Finally, a comprehensive analysis of *Nocardia* strains in China would be beneficial for monitoring the potential emergence of antibiotic resistance.

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TABLE 3. Species-specific antimicrobial susceptibility of *Nocardia* strains.

Antibiotic class*	*N. farcinica* (23)†	*N. cyriacigeorgica* (17)	*N. brasiliensis* (6)	*N. otitidiscaviarum* (5)	*N. beijingensis* (4)
β-lactams (9)	AMP, FEP, CTX, FOX, CMZ, CRO, MEM¶	FOX§	FOX, CMZ, IPM§	AMP, AMC, FEP, CTX, FOX, CMZ, CRO, IPM§	AMC§
		AMP, AMC, FEP, CTX, CMZ, CRO, IPM, MEM¶	AMP, FEP, CTX, CRO¶	MEM¶	AMP, FOX¶
	AMC, IPM**		AMC, MEM**		FEP, CTX, CMZ, MEM, CRO, IPM**
Aminoglycosides (5)	GEN, KAN§		KAN, STR§	STR§	
	TOB, STR¶	KAN, STR¶		TOB¶	GEN, KAN, STR¶
	AMK**	AMK, TOB, GEN**	AMK, TOB, GEN**	AMK, GEN, KAN**	AMK, TOB**
Fluoroquinolones (4)	CIP, LVX, OFX, MXF¶	CIP, LVX, OFX§	LVX, OFX§	CIP, LVX, OFX§	CIP, LVX, OFX§
		MXF¶	CIP¶	MXF¶	MXF¶
			MXF**		
Macrolides (2)	CLR§	CLR, AZM§	CLR, AZM§	CLR, AZM§	CLR, AZM§
	AZM¶				
Oxazolidinone (1)	LZD**	LZD**	LZD**	LZD **	LZD**
Tetracyclines (3)		TGC§			TGC§
	MIN, TGC, DOX¶	MIN, DOX¶	MIN, DOX¶	MIN, TGC, DOX¶	MIN, DOX¶
			TGC**		
Sulfonamides (2)			SMZ§	SMZ§	
	SXT, SMZ¶	SMZ¶		SXT¶	
		SXT**	SXT**		SXT, SMZ**
Phenazine (1)				CLO§	CLO§
	CLO¶	CLO¶	CLO¶		
Lincosamides (1)	CLI§	CLI§	CLI§	CLI§	CLI§
Glycopeptide (1)			VAN§	VAN§	VAN§
	VAN¶	VAN¶			
Isoniazid (1)	INH§	INH§	INH§	INH§	INH§
Ansamycin (1)		RIF§	RIF§	RIF§	RIF§
	RIF¶				
Ethambutol (1)	ETH§	ETH§	ETH§	ETH§	
					ETH¶

Abbreviation: AMK=amikacin; AMC=amoxicillin-clavulanate; AMP=ampicillin; AZM=azithromycin; FEP=cefepime; CMZ=cefmetazole; CTX=cefotaxime; FOX=cefoxitin; CRO=ceftriaxone; CIP=ciprofloxacin; CLR=clarithromycin; CLI=clindamycin; CLO=clofazimine; DOX=doxycycline; ETH=ethambutol; GEN=gentamicin; IPM=imipenem; INH=isoniazid; KAN=kanamycin; LVX=levofloxacin; LZD=linezolid; MEM=meropenem; MIN=minocycline; MXF=moxifloxacin; OFX=ofloxacin; RIF=rifampicin; STR=streptomycin; SMZ=sulfamethoxazole; TGC=tigecycline; TOB=tobramycin; SXT=trimethoprim-sulfamethoxazole; VAN=vancomycin.

* The number of drugs in each class is indicated in parentheses.

† The number of clinical isolates for each species is indicated in parentheses.

§ Antimicrobial susceptibility of *Nocardia* species is resistant, MIC value greater than the breakpoint value for all clinical isolates of the analyzed species

¶ Antimicrobial susceptibility of *Nocardia* species is intermediate.

** Antimicrobial susceptibility of *Nocardia* species is susceptible; MIC value less than or equal to the breakpoint value for all clinical isolates of the analyzed species.

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SUPPLEMENTARY MATERIALS

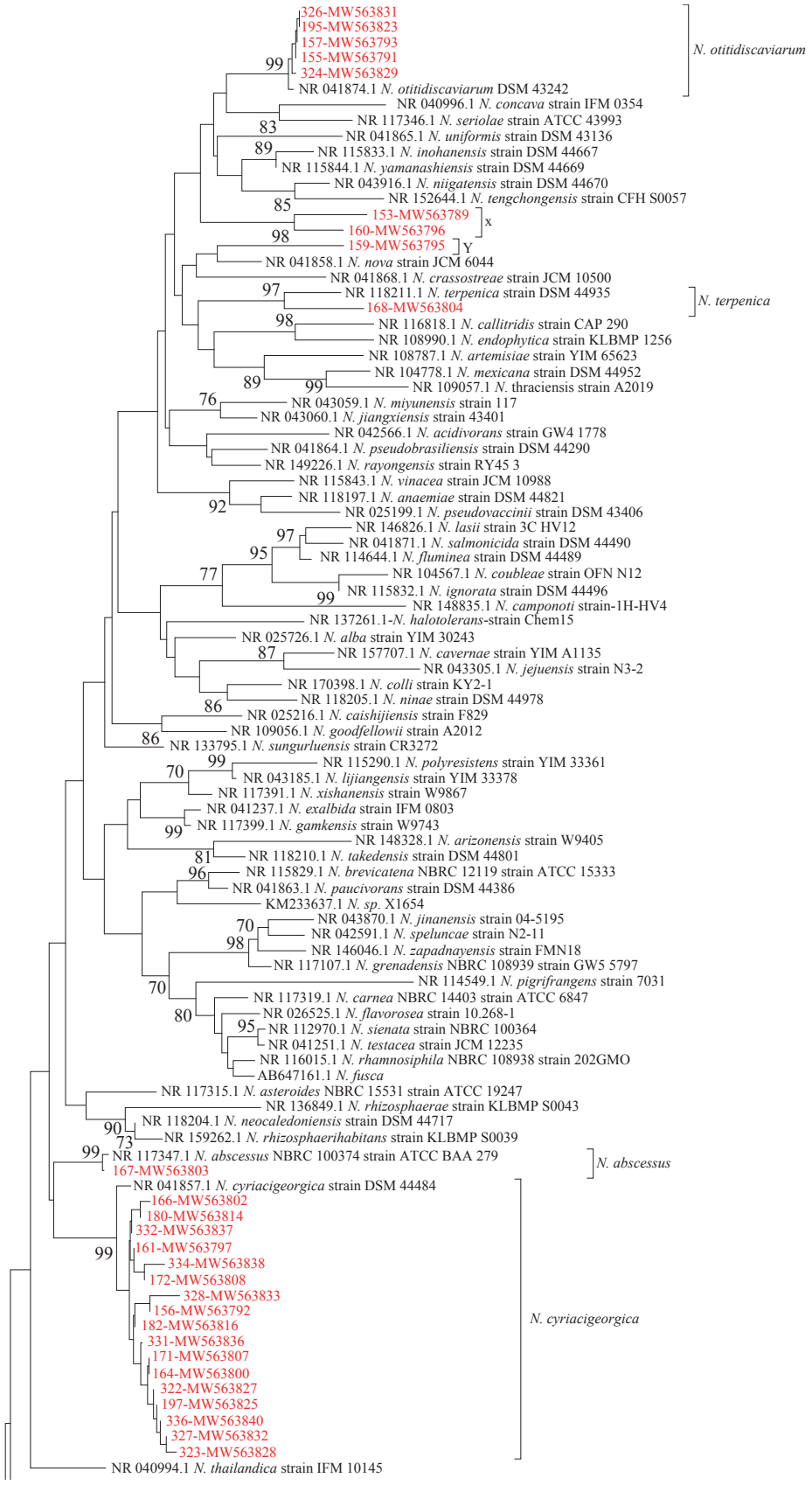
SUPPLEMENTARY TABLE S1. List of clinical *Nocardia* strains analyzed in this study.

Strain ID	GB-ID	Species	Cluster	Year	PLAD	Administrative region	Sex	Age	Sample source
CDC193	MW563821	*N. asiatica*	7	2015	Beijing	Huabei	–	–	Sputum
CDC194	MW563822	*N. asiatica*	7	2016	Guangxi	Huanan	–	–	Cerebrum
CDC186	MW563817	*N. beijingensis*	1	2015	Chongqing	Xinan	–	–	Sputum
CDC191	MW563819	*N. beijingensis*	1	2015	Chongqing	Xinan	–	–	Sputum
CDC192	MW563820	*N. beijingensis*	1	2015	Chongqing	Xinan	–	–	Sputum
CDC188	MW563818	*N. beijingensis*	7	2015	Unknown	–	–	–	Sputum
CDC162	MW563798	*N. brasiliensis*	1	2015	Beijing	Huabei	–	–	–
CDC196	MW563824	*N. brasiliensis*	1	2016	Zhejiang	Huadong	–	–	Hand abscess
CDC198	MW563826	*N. brasiliensis*	1	2016	Zhejiang	Huadong	–	–	Hand abscess
CDC144	MW563780	*N. brasiliensis*	1	2015	Sichuan	Xinan	–	–	–
CDC163	MW563799	*N. brasiliensis*	1	2015	Hunan	Huazhong	–	–	Abscess
CDC174	MW563810	*N. brasiliensis*	1	2015	Unknown	–	–	–	–
CDC156	MW563792	*N. cyriacigeorgica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC166	MW563802	*N. cyriacigeorgica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC171	MW563807	*N. cyriacigeorgica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC172	MW563808	*N. cyriacigeorgica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC336	MW563840	*N. cyriacigeorgica*	1	2016	Ningxia	Xibei	Female	53	Sputum
CDC161	MW563797	*N. cyriacigeorgica*	4	2015	Beijing	Huabei	–	–	–
CDC164	MW563800	*N. cyriacigeorgica*	4	2015	Beijing	Huabei	–	–	Sputum
CDC182	MW563816	*N. cyriacigeorgica*	4	2015	Inner Mongolia	Huabei	–	–	Sputum
CDC197	MW563825	*N. cyriacigeorgica*	4	2016	Zhejiang	Huadong	–	–	Lung
CDC322	MW563827	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Female	48	Purulent secretion
CDC323	MW563828	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Female	52	–
CDC327	MW563832	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Male	80	Sputum
CDC328	MW563833	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Male	48	Sputum
CDC331	MW563836	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Male	64	Sputum
CDC332	MW563837	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Male	40	Bronchoalveolar lavage fluid
CDC334	MW563838	*N. cyriacigeorgica*	4	2016	Ningxia	Xibei	Female	53	Sputum
CDC180	MW563814	*N. cyriacigeorgica*	4	2015	Unknown	–	–	–	–
CDC154	MW563790	*N. farcinica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC169	MW563805	*N. farcinica*	1	2015	Beijing	Huabei	–	–	–
CDC173	MW563809	*N. farcinica*	1	2015	Beijing	Huabei	–	–	Facial pustules
CDC177	MW563812	*N. farcinica*	1	2015	Beijing	Huabei	–	–	Sputum
CDC325	MW563830	*N. farcinica*	1	2016	Ningxia	Xibei	Female	53	Venous blood
CDC329	MW563834	*N. farcinica*	1	2016	Ningxia	Xibei	Female	71	Venous blood
CDC330	MW563835	*N. farcinica*	1	2016	Ningxia	Xibei	Male	51	Puncture fluid
CDC142	MW563778	*N. farcinica*	1	2015	Sichuan	Xinan	–	–	–
CDC143	MW563779	*N. farcinica*	1	2015	Sichuan	Xinan	–	–	–
CDC145	MW563781	*N. farcinica*	1	2015	Sichuan	Xinan	–	–	–
CDC146	MW563782	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–

Continued

Strain ID	GB-ID	Species	Cluster	Year	PLAD	Administrative region	Sex	Age	Sample source
CDC147	MW563783	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC148	MW563784	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC149	MW563785	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC150	MW563786	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC151	MW563787	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC152	MW563788	*N. farcinica*	1	2015	Guangdong	Huanan	–	–	–
CDC158	MW563794	*N. farcinica*	2	2015	Beijing	Huabei	–	–	–
CDC178	MW563813	*N. farcinica*	2	2015	Beijing	Huabei	–	–	Facial pustules
CDC176	MW563811	*N. farcinica*	3	2015	Guangdong	Huanan	–	–	–
CDC170	MW563806	*N. farcinica*	4	2015	Beijing	Huabei	–	–	Blood
CDC165	MW563801	*N. farcinica*	5	2015	Beijing	Huabei	–	–	Sputum
CDC335	MW563839	*N. farcinica*	6	2016	Ningxia	Xibei	Female	38	Cerebrospinal fluid
CDC157	MW563793	*N. otitidiscaviarum*	11	2015	Inner Mongolia	Huabei	–	–	Liver biopsy material
CDC324	MW563829	*N. otitidiscaviarum*	11	2016	Ningxia	Xibei	Male	33	Dialysate
CDC326	MW563831	*N. otitidiscaviarum*	11	2016	Ningxia	Xibei	Male	57	Sputum
CDC195	MW563823	*N. otitidiscaviarum*	11	2016	Guangxi	Huanan	–	–	Lung
CDC155	MW563791	*N. otitidiscaviarum*	12	2015	Hebei	Huabei	–	–	Sputum
CDC168	MW563804	*N. terpenica*	10	2015	Hunan	Huazhong	–	–	Sputum
CDC181	MW563815	*N. veterana*	4	2015	Inner Mongolia	Huabei	–	–	Alveolar lavage fluid
CDC167	MW563803	*N. abscessus*	1	2015	Beijing	Huabei	–	–	Sputum
CDC159	MW563795	N/D	6	2015	Hainan	Huanan	–	–	–
CDC153	MW563789	N/D	8	2015	Hainan	Huanan	–	–	Eye secretions
CDC160	MW563796	N/D	9	2015	Hainan	Huanan	–	–	–

Note: "-" means missing data.
Abbreviation: PLAD=provincial-level administrative division; GB-ID =GenBank ID.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NR 152644.1 N. tengchongensis strain CFH S0057
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160-MW563796
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Y
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NR 041868.1 N. crassostreae strain JCM 10500
97
NR 118211.1 N. terpenica strain DSM 44935
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NR 108990.1 N. endophytica strain KLBMP 1256
NR 108787.1 N. artemisiae strain YIM 65623
89
NR 104778.1 N. mexicana strain DSM 44952
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NR 109057.1 N. thraciensis strain A2019
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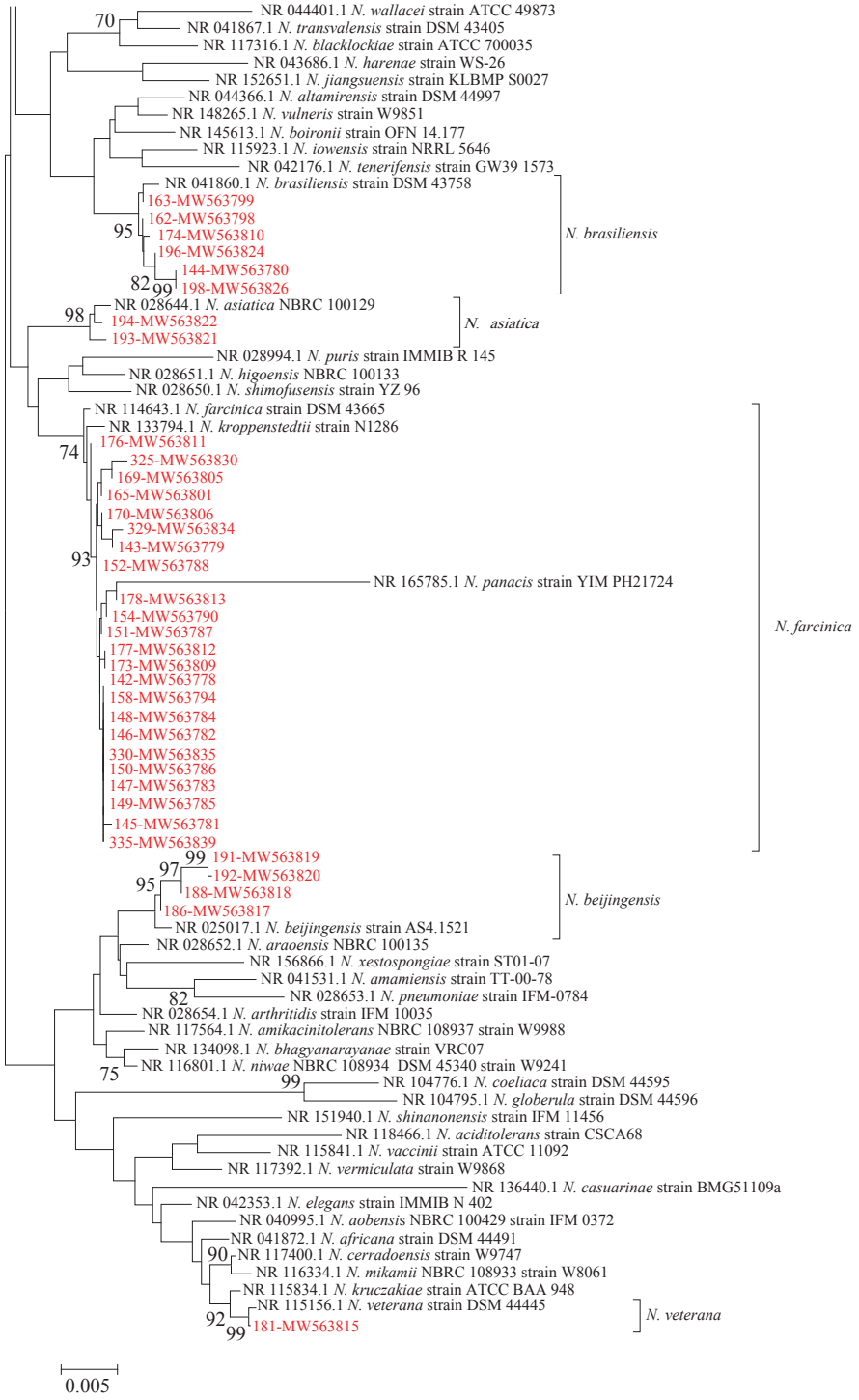

SUPPLEMENTARY FIGURE S1. NJ phylogenetic tree of 16S rRNA sequences from 63 clinical isolates in the context of *Nocardia* reference strains.

Note: *De novo* 16S rRNA sequences are shown in red and identified by both laboratory ID and GenBank ID. Clinical strains are listed in Supplementary Table S1. Reference strains were selected based on (3). Bootstrap values >70% are indicated. *De novo* sequences clustered with nine known species, indicated in brackets. Three strains did not match any known species. Strains 153 and 160 formed cluster X, while strain 159 was considered an outlier and is identified as Y. Abbreviation: NJ=Neighbor-joining.