

Treatment outcomes in *Mycobacterium abscessus* pulmonary disease: A systematic review

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ABSTRACT

Introduction: *Mycobacterium abscessus* complex (MABC) is an emerging global threat due to its intrinsic and acquired resistance to many antibiotics, making treatment particularly challenging. This systematic review aimed to evaluate current treatment regimens and clinical outcomes in patients with MABC pulmonary disease.

Methods: A comprehensive electronic search of PubMed, Embase and Cochrane databases was conducted for studies published between 1 January 2010 and 31 December 2024. A total of 28 studies met the inclusion criteria, comprising 24 retrospective chart reviews and 4 multicentre prospective studies.

Results: Sputum culture conversion (SCC) was reported in 25 studies, with rates ranging from 29% to 77%. Radiographic improvement was observed in 33% to 54% of patients, while clinical improvement varied widely, ranging from 14% to 91%. Notably, infections caused by *M. massiliense* were consistently associated with superior clinical, radiologic, and microbiologic outcomes compared to *M. abscessus*. Although surgical intervention was reported in selected cases, it was associated with higher SCC rates and remains a definitive treatment option in refractory disease. The overall risk of bias across studies was moderate to high, largely due to the predominance of retrospective study designs and heterogeneity in treatment protocols and outcome measures.

Conclusion: These findings underscore the suboptimal outcomes associated with current treatment strategies for MABC pulmonary disease. There is an urgent need for large-scale, multicentre prospective studies utilising standardised treatment outcome definitions and unified therapeutic regimens to improve patient care and clinical outcomes.

Keywords: antimicrobials, bronchiectasis, lung disease, *Mycobacterium abscessus*, non-tuberculous mycobacteria, respiratory medicine, treatment regimen

CLINICAL IMPACT

What is New

- This systematic review underscores the complexity of treating *M. abscessus* pulmonary disease, including drug resistance, frequent drug related adverse effects, variable treatment outcome definitions and poor treatment outcomes among patients with underlying chronic lung diseases.
- The findings highlight the potential disease burden in an ageing population with rising prevalence of chronic lung diseases.

Clinical Implications

- The review highlights the urgent need for the development of novel therapies, multicentre prospective studies using standardised treatment outcomes and unified therapeutic regimens to optimise patient care and clinical outcomes.

INTRODUCTION

Mycobacterium abscessus complex (MABC) is a group of rapidly growing, non-tuberculous mycobacteria (NTM) increasingly recognised as clinically significant pathogens worldwide.^{1,2} The complex comprises 3 subspecies: *Mycobacterium abscessus* subspecies *massiliense* (*M. massiliense*), *Mycobacterium abscessus* subspecies *bolletii* (*M. bolletii*), with *Mycobacterium abscessus* subspecies *abscessus* (*M. abscessus*) being the most frequently isolated.^{3,4} NTM are ubiquitous in the environment—particularly in soil and water—with municipal water systems serving as notable reservoirs.⁵ Pulmonary disease caused by MABC predominately affects immunocompromised individuals, such as

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patients receiving immunosuppressive therapy, and individuals with underlying structural lung diseases, notably bronchiectasis and cystic fibrosis.^{6,7} Despite the increasing incidence of MABC infections, diagnostic delays and misdiagnosis remain common due to overlapping clinical features with other chronic cough, weight loss, dyspnoea, fever and fatigue, which often mimic diseases like tuberculosis or non-MABC NTM infections. Importantly, MABC pulmonary disease is associated with recurrent pulmonary exacerbations, leading to airway remodelling and progressive lung damage.

Diagnosis of MABC pulmonary disease requires the integration of clinical, radiographic and microbiologic criteria as recommended by the American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA).⁶ Clinically, patients typically present with chronic respiratory symptoms. Radiographic imaging may reveal nodular or cavitary opacities, bronchiectasis, or tree-in-bud patterns. Microbiological confirmation is essential, necessitating either 2 positive cultures from separate expectorated sputum samples or 1 positive culture from bronchoalveolar lavage, bronchial wash or lung tissue biopsy showing histopathologic evidence of mycobacterial infection. Notably, other differential diagnoses—particularly pulmonary tuberculosis—must be rigorously excluded before establishing a definitive diagnosis.⁶ Management of MABC pulmonary disease remains challenging. The ATS/IDSA guidelines underscores the absence of a standardised, highly effective treatment regimen.⁶ Currently, therapy typically involves prolonged multidrug regimens, often centred around a macrolide in combination with intravenous agents such as amikacin, imipenem or tigecycline. However, these regimens are frequently associated with limited efficacy, poor tolerability and significant toxicity.

Treating MABC is difficult due to intrinsic and acquired antibiotic resistance.⁸ Key mechanisms include efflux pumps, drug-modifying enzymes, target gene mutations in *erm* (41) and *rrl*, and low membrane permeability.⁸ In refractory cases, surgical resection may be considered despite its risk.⁹ To standardise outcome reporting, the NTM-Network European Trials (NTM-NET) group proposed definitions such as sputum culture conversion (SCC), microbiological cure, clinical cure, treatment failure, relapse, reinfection and treatment discontinuation.¹⁰ In practice, outcomes are assessed through clinical symptoms, imaging and SCC—defined as sustained negative sputum cultures over time.⁶

Despite the increasing recognition of MABC as a major pulmonary pathogen, there is a lack of consolidated evidence assessing the comparative effectiveness of various antibiotic regimens in real-

world clinical settings. Furthermore, heterogeneity in study design, outcome measures and follow-up durations complicates the interpretation of existing data. Therefore, we conducted a systematic review of the literature to evaluate the treatment regimens used for MABC pulmonary disease and assess their impact on clinical, microbiologic and radiologic outcomes in accordance with internationally accepted criteria.

METHODS

This systematic literature review was conducted to identify and synthesise evidence on treatment regimens and clinical outcomes in patients with *M. abscessus* pulmonary disease. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and a PRISMA flow diagram is included in Fig. 1.

Search strategy

A comprehensive electronic search was conducted in 3 databases: PubMed, Embase and Cochrane Library, for studies published between 1 January 2010 and 31 December 2024. The search strategy employed a combination of Medical Subject Headings (MeSH) and free-text keywords related to *M. abscessus*, treatment regimens and pulmonary disease, using Boolean operators. The full search strategy is provided in Supplementary Table S1. All references were managed using EndNote X9 (Clarivate Analytics, Philadelphia, PA, US), and Covidence (Veritas Health Innovation, Melbourne, Australia) was used for duplicate removal, title/abstract screening and full-text review.

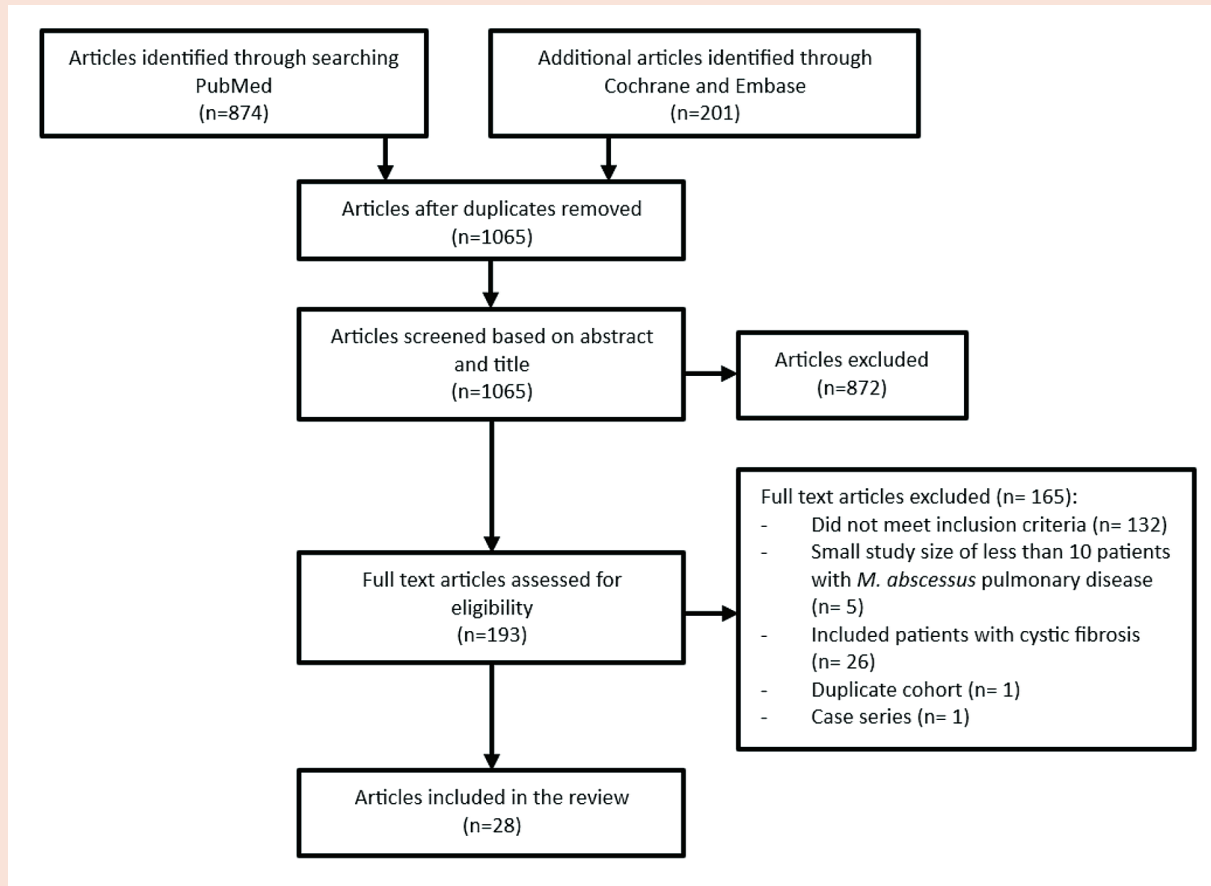
Inclusion and exclusion criteria

Studies were included if they met the following criteria: (1) published in English between 2010 to 2024; (2) reported on antimicrobial treatment regimens for *M. abscessus* pulmonary disease; and (3) reported treatment outcomes based on clinical, microbiologic or radiologic parameters. Studies were excluded if they were (1) conference abstract, editorials, letters to the editor, guidelines or narrative reviews; (2) case reports or small case series (fewer than 10 patients); (3) focused exclusively on cystic fibrosis populations; (4) not specifying treatment regimens and/or treatment outcomes; or (5) published in a non-English language.

Study selection

Title and abstract screening were conducted independently by 2 reviewers in a double-blind manner using Covidence. Full texts of potentially relevant studies were retrieved and assessed against inclusion criteria. Disagreements were resolved

Fig. 1. Flowchart of study selection.



through discussion and consensus. Reference lists of included studies were also manually searched; however, no additional eligible studies were identified.

Data extraction

Data extraction was conducted using a standardised data extraction template. One reviewer extracted data, which were independently verified by a second reviewer. Extracted variables included: (1) study design and setting, (2) sample size and population demographics, (3) treatment regimens (drug combinations, duration), (4) clinical outcomes (e.g. symptom improvement), (5) microbiological outcomes (e.g. sputum culture conversion), (6) radiologic outcomes (e.g. computed tomography or x-ray findings), (7) adverse events and complications and (8) follow-up duration.

Risk of bias assessment

The ROBINS-I tool (Risk of Bias in Non-randomised Studies – of Interventions) was used to assess the quality of included studies. The tool evaluates bias across 7 domains, including confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result.

RESULTS

A total of 1076 articles were identified in the initial search. Following screening and eligibility assessment, 28 studies were included in this review (Fig. 1).^{9,11-37} Table 1 summarises sample sizes, demography and underlying lung diseases of study population. Table 2 presents treatment regimens, adverse events and outcomes.

Study characteristics

Of the 28 included studies, 2 were prospective cohort studies^{14,15} and 26 were retrospective.^{9,11-13,16-37} Outcomes assessed included survival,²³ amikacin toxicity and pharmacokinetics,¹⁹ long-term disease progression²³ and treatment success.³⁴ Four studies were multicentre.^{25,27,28,37} Geographically, studies were conducted in 6 countries: South Korea,^{9,11-23,36,37} Japan,²⁴⁻²⁸ China,²⁹⁻³¹ Taiwan,^{32,33} Brazil³⁴ and the US.³⁵

Study participants

Across 28 studies, 4183 patients were diagnosed with MABC pulmonary disease based on the 2007 ATS/IDSA guidelines,⁶ of whom 2769 received treatment. The pooled prevalence of *M. abscessus* among treated patients was 72.4% (95% confidence interval

Table 1. Demography and underlying lung diseases of study population.

Author, year	Population (n)	No. of patients with underlying/previous lung disease	Mean age (SD) or median (range) in years	Female (%)
Huang 2010 (Taiwan)	Patients diagnosed with <i>M. abscessus</i> infection (n=22).	3 COPD, 7 previous PTB, 16 structural lung disease	NR	NR
Koh 2011 (South Korea)	Newly diagnosed with MABC lung disease with isolates that were typeable (n=145); <i>M. abscessus</i> (n=64) and <i>M. massiliense</i> (n=81).	11 COPD, 11 lung cancer, 77 previous PTB	57.6 (13.0) (<i>M. abscessus</i> patients) 56.0 (12.9) (<i>M. massiliense</i> patients)	74.5%
Lyu 2011 (South Korea)	Diagnosed with <i>M. abscessus</i> pulmonary disease and who were treated based on ATS guidelines without loss to follow-up or transfer to another hospital (n=41).	1 ILD, 25 previous PTB	53.2 (11.7)	75.6%
Harada 2012 (Japan)	diagnosed with <i>M. abscessus</i> lung disease excluding those with <i>M. boletii</i> (n=99), <i>M. abscessus</i> (n=72) and <i>M. massiliense</i> (n=27).	5 COPD, 6 interstitial pneumonia, 19 previous PTB, 19 MAC lung disease	68, no SD reported Range: 27–94	62.5%
Lyu 2014 (South Korea)	Patients who were diagnosed with MABC lung disease and received treatment without loss to follow up (n=48); <i>M. abscessus</i> (n=26) and <i>M. massiliense</i> (n=22).	21 previous PTB	57.7 (11.6)	72.9%
Tung 2014 (Taiwan)	All patients who had more than 1 positive culture of respiratory specimens for MABC (n=106).	29 bronchiectasis, 28 previous PTB, 2 previous MAC pulmonary diseases, 37 previous mycobacterium pulmonary diseases, 65 pre-existing pulmonary diseases	64.6 (14.05)	58.5%
Griffith 2015 (USA)	Patients who had isolation of <i>M. abscessus</i> during MAC lung disease therapy (n=21).	21 MAC pulmonary diseases	75.5 (8.5)	90%
Kang 2015 (South Korea)	Patients who had adjunctive pulmonary resection for NTM lung disease (n=70); MAC (n=45, 64%), <i>M. intracellular</i> / <i>M. avium</i> (n=24, 21%), MABC (n=23, 33%) and <i>M. abscessus</i> / <i>M. massiliense</i> (n=2, 3%).	6 recurrent NTM lung disease, 45 previous PTB	50, no SD reported	60%
Koh 2016 (South Korea)	Patients diagnosed with <i>M. abscessus</i> pulmonary disease who received antibiotic therapy for ≥12 months (n=67).	45 previous PTB, 7 previous <i>M. abscessus</i> pulmonary diseases, 2 previous MAC pulmonary diseases, 3 previous pulmonary diseases from other NTM	Median: 57 Range: 48–64	78%
Koh 2016 (South Korea)	<i>M. massiliense</i> lung disease who initiated antibiotic treatment of at least 12 months excluding patients with more than 1 month of macrolide containing antibiotic therapy or who underwent surgical resection within 3 months of drug therapy (n=71).	6 previous NTM, 39 previous PTB, 5 chronic pulmonary aspergillosis	60, no SD reported (4-week IV group) 57, no SD reported (2-week IV group)	4-week IV group- 89% 2-week IV group- 84%
Namkoong 2016 (Japan)	Patients with <i>M. abscessus</i> pulmonary disease who received the combination therapy and intravenous AMK therapy for more than 3 months (n=13).	5 MAC pulmonary disease, 2 pulmonary aspergillosis, 1 COPD, 1 sarcoidosis	63.6 (8.5)	84.6%
Park 2017 (South Korea)	Patients diagnosed with MAPD lung disease, without coinfection of other NTM bacteria, with a follow-up period of at least 6 months (n=110); <i>M. abscessus</i> (n= 56) and <i>M. massiliense</i> (n=54).	48 previous PTB, 18 COPD, 7 asthma	Median: 64 (<i>M. abscessus</i> patients) Median: 63 (<i>M. massiliense</i> patients)	64.5%

Table 1. Demography and underlying lung diseases of study population. (Cont'd)

Author, year	Population (n)	No. of patients with underlying/previous lung disease	Mean age (SD) or median (range) in years	Female (%)
Choi 2018 (South Korea)	Patients diagnosed with acquired macrolide-resistant <i>M. abscessus</i> pulmonary disease (n=13).	6 prior NTM pulmonary disease, 8 previous PTB, 1 COPD, 12 bronchiectasis, 1 chronic pulmonary aspergillosis	Median: 54 Range: 55–78	62%
Lee 2017 (South Korea)	Patients with <i>M. abscessus</i> lung disease who initiated antibiotic treatment (n=48).	36 previous PTB, 37 bronchiectasis, 3 COPD	Median: 57 Range: 52–66	70.8%
Yang 2017 (South Korea)	Patients with <i>M. abscessus</i> pulmonary disease who received clofazimine (n=42).	11 PTB, 36 bronchiectasis, 3 COPD, 5 chronic pulmonary aspergillosis	Median: 60 Range: 53–69	79%
Guo 2018 (China)	Patients aged >16 years being treated for <i>M. abscessus</i> pulmonary disease, received oral CLA-based combination treatment, have follow-up for >6 months, not being treated for active tuberculosis, no previous history of NTM disease, no co-infection with another NTM, negative HIV status (n=100).	45 previous PTB, 3 COPD	Median: 58 Range: 44–66 (CLA-resistant group) Median: 56 Range: 32–64 (CLA-sensitive group)	57%
Jhun 2018 (South Korea)	Patients who were started on AMK inhalation therapy for refractory MABC pulmonary disease, none had previously received AMK inhalation therapy (n=48); <i>M. abscessus</i> (n=35) and <i>M. massiliense</i> (n=12) and <i>M. bolletii</i> (n=1).	57 previous PTB, 17 chronic pulmonary aspergillosis, 9 COPD	Median: 60 Range: 53–69	69%
Kobayashi 2018 (Japan)	Patients with <i>M. abscessus</i> pulmonary disease according to ATS diagnostic criteria who had at least 1 year of follow-up (n=30).	5 previous PTB, 13 other NTM lung diseases, 1 bronchial asthma, 4 COPD, 2 lung cancer, 1 interstitial pneumonia, 1 aspergillosis	75, no SD reported	63.3%
Monteiro 2018 (Brazil)	Patients diagnosed with NTM pulmonary infection without concurrent isolation of <i>M. tuberculosis</i> (n=17).	6 isolated bronchiectasis, 5 associated bronchiectasis, 2 COPD and/or asthma and/or GERD	62.4 (13.7)	76.5%
Morimoto 2018 (Japan)	Patients with MABC (n=121); <i>M. abscessus</i> (n=68) and <i>M. massiliense</i> (n=53).	38 previous NTM disease, 27 previous PTB, 7 bronchial asthma, 3 COPD, 10 pneumonia, 7 aspergillosis	Median: 66 Range: 55–72	71.9%
Shin 2018 (South Korea)	NTM lung disease caused by mixed infection with MAC and MABC excluding those with prior antibiotics therapy for >1 month (n=71); MAC + <i>M. abscessus</i> (n=24) and MAC + <i>M. massiliense</i> (n=47).	23 previous PTB, 10 previous NTM, 2 COPD	Median: 60 Range: 49–68	79%
Yoshida 2018 (Japan)	Patients with non-CF bronchiectasis with isolates of <i>M. abscessus</i> who were not co-infected with other NTM species (n=24); <i>M. abscessus</i> (n=17) and <i>M. massiliense</i> (n=7).	NR	Median: 68 Range: 41–79 (unfavourable outcome patients) Median: 74 Range: 69–78 (favourable outcome patients)	58.3%
Chen 2019 (China)	Patients >16 years without co-infection with active tuberculosis or another NTM, HIV and with a follow-up period lasting >12 months (n=244): <i>M. abscessus</i> (n=185) and <i>M. massiliense</i> (n=59).	127 prior TB/NTM, 208 bronchiectasis, 16 COPD, 15 asthma	Median: 56.0 Range: 49–65.8	73%

Table 1. Demography and underlying lung diseases of study population. (Cont'd)

Author, year	Population (n)	No. of patients with underlying/previous lung disease	Mean age (SD) or median (range) in years	Female (%)
Jhun 2020 (South Korea)	Patients newly diagnosed with MAC or MABC pulmonary disease that was radiologically classifiable, with further subspecies identification. Patients with <i>M. bolletii</i> isolates or lacking death certificates, if applicable, were excluded (n=1445); includes pulmonary disease caused by MABC and MAC.	566 previous PTB, 147 COPD/ bronchial asthma, 31 chronic pulmonary aspergillosis, 45 pulmonary malignancy	Median ^a : 60 Range: 51–68 (*patients MAC+ MABC)	75.6%
Li 2019 (China)	Patients with <i>M. abscessus</i> lung disease who received antibiotics regimen (n=50).	NR	Median: 48 Range: 39.8–55.3 (conventional regimen) Median: 39.5 Range: 36–43.8 (intensified regimen)	88%
Moon 2019 (South Korea)	MAC or MABC pulmonary disease patients without fibrocavitary, cavitary nodular bronchiectasis or unclassifiable form, MABC pulmonary disease without further species identification and <i>M. bolletii</i> (n=1021) (includes NTM pulmonary disease caused by <i>M. avium</i> , <i>M. intracellulare</i> , <i>M. abscessus</i> or <i>M. massiliense</i>).	314 previous PTB, 178 COPD	59, no SD reported	68%
Park 2021 (South Korea)	Patients diagnosed with <i>M. abscessus</i> pulmonary disease treated with treated intravenous AMI and beta-lactams for ≥4 weeks (n=82).	73 bronchiectasis, 5 COPD,	58.7 (11.4)	65.9%

AMI: amikacin; ATS: American Thoracic Society; CLA: clarithromycin; cf: cystic fibrosis; COPD: chronic obstructive pulmonary disease; HIV: human immunodeficiency virus; ILD: interstitial lung disease; IV: intravenous; *M. abscessus*: *Mycobacterium abscessus* subspecies *abscessus*; *M. massiliense*: *Mycobacterium abscessus* subspecies *massiliense*; *M. bolletii*: *Mycobacterium abscessus* subspecies *bolletii*; MABC: *Mycobacterium abscessus* complex; MAC: *Mycobacterium avium* complex; MABC: *Mycobacterium abscessus* complex; NTM: non-tuberculosis *Mycobacterium*; NR: not reported; PTB: pulmonary tuberculosis; SD: standard deviation; TB: tuberculosis

[CI] 56.7–85.7) (Fig. 2). Subspecies identification was inconsistent; 7 studies did not specify the subspecies.^{12,21,23,29,32–34} Eighteen studies reported on 1047 patients with *M. abscessus*,^{9,11,13,14,16,18–20,22,24–28,30,31,35,37,38} and 11 studies documented 568 patients with *M. massiliense*.^{9,11,13,15,16,22,25–27,30,36} A history of pulmonary tuberculosis (PTB) was reported in 1452 patients (35.4%) across 22 studies, while NTM disease was noted in 124 patients (3%) from 11 studies. One study grouped prior PTB and NTM infections for analysis.³⁰ HIV status was reported in 13 studies, with only 1 study identifying 2 HIV-positive cases,³³ indicating low co-infection prevalence in this cohort.

Reported mortality

Mortality was reported in 13 of 27 studies (48.1%),^{9,15,17,18,22,24–26,32–36} with 328 deaths among 1334 treated patients, yielding an overall mortality rate of 24.6%. Three studies did not provide mortality data.^{15,24,35} A large population-based study found no significant difference in mortality between treated and untreated NTM pulmonary disease patients.²² Survival varied by subspecies: patients with *M. massiliense*

(n=174) had better outcomes than those with *M. abscessus* (n=129). Compared to *Mycobacterium avium* (*M. avium*), *M. abscessus* had a higher adjusted hazard ratio (aHR 2.19), while *M. massiliense* showed no increased risk (aHR 0.99), indicating poorer prognosis with *M. abscessus* infection.

Treatment regimens

Combined treatment regimes

Fourteen studies used a combination of a macrolide, amikacin and either cefoxitin or imipenem, with SCC rates ranging from 8% to 93%.^{11–20,22,29,31,37} Seven of these studies also included fluoroquinolones, reporting SCC rates between 40% and 100%.^{11,14,15,22,29,31,37}

Inhaled amikacin

Five studies evaluated inhaled non-liposomal amikacin as adjunct therapy.^{17,18,21,22,36} Jhun et al. reported an SCC rate of 13%, with clinical and radiological improvement in 44% and 33% of patients, respectively.³⁶ Adverse events, mainly ototoxicity, affected 38% (29 patients), leading to discontinuation in 27% (21

Table 2. Treatment regimens, adverse events and outcomes.

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment % treatment completion	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Huang 2010 (Taiwan)	CLA + other antimicrobials for 4–8 months (n=10) Tigecycline for 2 weeks + CLA for 8 months (n=1) A variety of combination of antibiotics including AMK, cefoxitin, fluoroquinolones, CLA (n=11) No dosage reported	Duration: 12 months Treatment completion: 100%	NR	NR	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=7, 31.8%) Clinical outcomes: Clinical cure: <i>M. abscessus</i> (n=5, 22.7%); improved: <i>M. abscessus</i> (n=3, 13.6%); Failure: <i>M. abscessus</i> (n=6, 27.2%); Indeterminate: <i>M. abscessus</i> (n=8, 36.3%). Radiological outcomes: NR
Koh 2011 (South Korea)	CLA-containing 3-drug oral regimen: CLA (1000 mg/d), CIP (1000 mg/d), DOX (200 mg/d), along with an initial 4-week course of AMK (15 mg/kg/d in 2 divided doses) and cefoxitin (200 mg/kg/d; maximum, 12 g/d in 3 divided doses) (n=67)	Mean (SD) duration: 23.1 (12.9) months (<i>M. abscessus</i>) 21.6 (7.7) (<i>M. massiliense</i>) Treatment completion: NR	NR	<i>M. abscessus</i> infection (n=4, 40%) <i>M. massiliense</i> infection (n=3, 9%)	Death: 3 deaths due to non-NTM related causes Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=6, 25%) and <i>M. massiliense</i> (n=29, 88%) Clinical outcomes: Improved: <i>M. abscessus</i> (75%) and <i>M. massiliense</i> (97%) Radiological outcomes: Improved: <i>M. abscessus</i> (42%) and <i>M. massiliense</i> (82%) Death: NR
Lyu 2011 (South Korea)	Macrolide (CLA (1000 mg/day)/ AZI (250 mg/ day) and AMK (15 mg/kg/day, maximum 1 g/day) (n=17) Macrolide and 2 IV agents (AMK and cefoxitin [10 g/day in 3 divided doses] or imipenem [500 mg, 3 times a day]) (n=24) Other antibiotics: DOX (n=2); CIP (n= 18; MOX (n=3) Surgery (n= 13): 7 from 2 IV drugs group and 3 from 1 IV drug group	Median (range) duration (overall): 511 (164–1249) days Median (range) duration (IV AMK): 230 (60–601) days Median (range) duration (IV cefoxitin or imipenem): 83 (25–288) days Treatment completion: 100%	43.9% (n=18) patients experienced adverse events: 17.1% (n=7) DILI 12.2% (n=5) GI symptoms 9.8% (n=4) Tinnitus/hearing difficulties 7.3% (n=3) Skin eruptions 7.3% (n=3) Fever 4.9% (n=2) Leukopenia 2.4% (n=1) Arthralgia 2.4% (n=1) Nephrotoxicity	N=4, 10%	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=33, 80.5%) Clinical outcomes: Improved: <i>M. abscessus</i> (n=33, 80.5%) Radiological outcomes: NR Death: NR

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment % treatment completion	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Harada 2012 (Japan)	Macrolide, rifampicin and ethambutol (n=8)	Mean (range) duration: 33 (3–178) months for <i>M. abscessus</i>	NR	<i>M. abscessus</i> infection (n=13, 65%)	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=13, 65%) and <i>M. massiliense</i> (n=7, 70%).
	Macrolide, carbapenem and aminoglycoside (n=6)	Mean (range) duration: 33 (1–122) months for <i>M. massiliense</i>		<i>M. massiliense</i> infection (n=3, 30%)	Clinical outcomes: NR
	Macrolide only (n=8)				Radiological outcomes: Improved: <i>M. abscessus</i> (n=17, 29%) and <i>M. massiliense</i> (n=12, 44%).
	Macrolide and fluoroquinolone (n=6).	Treatment completion: 100%			Death: NR
	Isoniazid, rifampicin and ethambutol (n=2)				
Lyu 2014 (South Korea)	Other regimens (n=12)				
	No dosage reported				
	Macrolide, AMK and cefoxitin (n=19)	Mean (SD) duration: 14.3 (9.4) months for <i>M. abscessus</i>	12.5% (n=6) patients mainly with GI problems attributed to clarithromycin	n=23, 47.9%	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=11, 42.3%) and <i>M. massiliense</i> (n=21, 95.5%).
	Macrolide, AMK and imipenem (n=12)	Mean (SD) duration: 16.3 (11.6) months for <i>M. massiliense</i>			Clinical outcomes: Improved: <i>M. abscessus</i> (n=13, 50%) and <i>M. massiliense</i> (n=16, 72.7%).
	Macrolide and AMK (n=11)	Treatment completion: 100%			Radiological outcomes: Improved: <i>M. abscessus</i> (n=9, 34.6%) and <i>M. massiliense</i> (n=16, 72.7%). Deteriorated: <i>M. abscessus</i> (n=8, 30.8%) and <i>M. massiliense</i> (0%).
Tung 2015 (Taiwan)	Macrolide and cefoxitin (n=4)				Death: NR
	Macrolide and imipenem (n=2)				
	Macrolide dosage: CLA (1000 mg/day) (n=42) and AZI (250 mg/day) (n=6)				
	Surgery (n=9) (8 with <i>M. abscessus</i> and 1 with <i>M. massiliense</i>)				
Tung 2015 (Taiwan)	CLA only (n=17)	Mean (SD) duration: 13.2 (13.19) months	NR	n=3, 17.6%	Microbiological outcomes: Persistent SCC after 1 year: <i>M. abscessus</i> (n=17, 65.4%)
	CLA and AZI (n=2)				Clinical outcomes: Clinical success: <i>M. abscessus</i> (n=15, 57.7%); Improved: <i>M. abscessus</i> (n=3, 11.5%); Failure: <i>M. abscessus</i> (n=3, 11.5%)
	CLA and MOX (n=9)	Treatment completion: 24.5%			Radiological outcomes: NR
	CLA and CIP (n=5)				Death: 15 deaths due to other causes
	IV AMK only (n=1)				
	IV AMK and meropenem (n=1)				
	IV AMK and imipenem/cilastatin (n=1)				
	Isoniazid, ethambutol, rifampicin and pyrazinamide (n=7)				
	No dosage reported				

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment (% treatment completion)	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Kang 2015 (South Korea)	Preoperative: All patients received macrolide (CLA or AZI) ± fluoroquinolone (CIP or MOX) with IV AMK and cefoxitin (or imipenem) for 4 weeks (6 patients had streptomycin injection) Perioperative: 19 patients received IV AMI, cefoxitin or imipenem Postoperative: Macrolide and/or oral fluoroquinolone for ≥12 months (n=23 combined medical and surgical treatment) No dosage reported	Median (range) duration of preoperative antibiotics: 8.3 (3.8–14.7) months Median (range) duration of perioperative antibiotics: 28 (25–33) days for MABC-PD Treatment completion: NR	8.3% (n=3) Skin rash or perioral tingling sensation due to streptomycin 21% (n=15) patients with postoperative complications	n=0	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=16, 69.6%) Clinical outcomes: NR Radiological outcomes: NR Death: <i>M. abscessus</i> : (n=1) due to complex pneumonia
Koh 2016 (South Korea)	Inpatient regimen: 4 weeks of macrolides (CLA or AZI), fluoroquinolones (CIP or MOX), DOX, IV AMK and IV cefoxitin. Followed by outpatient regimen: macrolide ± fluoroquinolone ± DOX for ≥12 months after SCC (n=67) DOX and fluoroquinolone were excluded from the treatment protocol beginning in February 2008 and March 2011, respectively Surgery (n=9) No dosage reported	Duration: >12 months Treatment completion: NR	NR	n=6, 17.6%	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=28, 41.8%) Clinical outcomes: NR Radiological outcomes: NR Death: NR
Koh 2016 (South Korea)	CLA (1000 mg/day), fluoroquinolone and 4 weeks IV AMK and cefoxitin. Followed by, CLA and fluoroquinolone for 24 months (n=28) CLA or AZI (250 mg/day) and 2 weeks of IV AMK and cefoxitin. (7 patients had a fluoroquinolone added to their regimen), followed by macrolides for 12 months or until their sputum cultures were negative (n=43) Surgery (n=5)	Mean duration (4-week of IV group): 23.9 months Mean duration (2-week IV group): 15.2 months Treatment completion: 100%	Adverse events such as neutropenia and DILI associated with cefoxitin occurred more frequently in the 4-week IV group (n=17, 61%) than in the 2-week IV group (n=3, 7%)	4-week IV group (n=2, 7%) 2-week IV group (n=3, 7%)	Microbiological outcomes: SCC (<i>M. massiliense</i>): 4-week IV group (n=28, 100%) and 2-week IV group (n=39, 91%) Clinical outcomes: Improved (<i>M. massiliense</i>): 4-week IV group (n=25, 89%) and 2-week IV group (n=43, 100%) Radiological outcomes: Improved (<i>M. massiliense</i>): 4-week IV group (n=22, 79%) and 2-week IV group (n=39, 91%) Death: 0

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment % treatment completion	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Namikoong 2016 (Japan)	A variety of combinations of IV AMK, CLA, sitafloxacin, faropenem, imipenem/ cilastatin and meropenem (n=13) Prior antibiotic treatment with CLA ± rifampicin ± ethambutol (n=10) No dosage reported	Median (range) duration: 4 (3–9) months Treatment completion: NR	NR	n=4, 30.8%	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=10, 77%); Persistent SCC after 1 year: <i>M. abscessus</i> (n=8, 62%) Clinical outcomes: Improved (<i>M. abscessus</i>): Cough (n=3, 23.1%); Sputum (n=4, 30.8%); Dyspnoea (n=2, 23%); Haemoptysis (n=3, 23.1%); Fever (n=1, 7.7%); Fatigue (n=1, 7.7%) Radiological outcomes: Improved: <i>M. abscessus</i> (n=7, 53.8%) Death: NR
Park 2017 (South Korea)	Macrolide and 3 rd IV agents such as AMK, cefoxitin, or imipenem for ≥3 weeks (n=29), followed by macrolide and IV AMK Surgery (n=5) No dosage reported	Median (range) duration: 61 (28–116) weeks (<i>M. abscessus</i>) Median (range) duration: 87 (64–120) weeks (<i>M. massiliense</i>) Treatment completion: NR	NR	<i>M. abscessus</i> infection (n=6, 24%)	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=5, 26.3%) and <i>M. massiliense</i> (n=14, 82.4%) Clinical outcomes: NR Radiological outcomes: NR Death: NR
Choi 2017 (South Korea)	All patients received a 4-week of IV AMK (15–20 mg/kg/day) and either cefoxitin (200 mg/kg/day; maximum, 12 g/day, in three divided doses) or imipenem (750 mg, 3 times per day), along with macrolide antibiotics (CLA 1000 mg/day or AZI 250 mg/day) (n=14)	Median (range) duration: 18.6 (14.7–24.1) months Treatment completion: 79%	NR	NR	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=13, 93%) Clinical outcomes: NR Radiological outcomes: NR Death: 2 deaths due to other causes
Choi 2018 (South Korea)	After detection of macrolide-resistance: Macrolide (CLA 1000 mg/day or AZI at 250 mg/day) (n=11) IV AMK, 15 mg/kg/day in 2 divided doses or 15 mg/kg/day with adjustment of a once-daily dose to target peak serum drug level of 55 to 65 g/mL (n=6) IV cefoxitin (200 mg/kg/day; maximum of 12 g/day in three divided doses) or imipenem (750 mg three times per day) (n=6)	Median (range) duration: 24 (16–43) months Treatment completion: 84.6%	NR	NR	Microbiological outcomes: SCC after surgery: <i>M. abscessus</i> (n=1, 8%) Clinical outcomes: Favourable outcome: <i>M. abscessus</i> (n=0) Radiological outcomes: NR Death: 2

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment (% treatment completion)	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
	Fluoroquinolone (CIP at 1000 mg/day or MOX at 400 mg/day) (n=1) CFZ, 100 mg/day (n=10) AMK inhalation, 250–500 mg/day (n=7) (n=13) Surgery (n=2)				
Yang 2017 (South Korea)	Initial treatment: CFZ (100 mg/day), macrolide (CLA 1000 mg/day or AZI 250 mg/day) and 4- week IV AMK (15 mg/kg/ day), IV cefoxitin (200 mg/kg/day, maximum 12 g/day) or imipenem (n=15) Salvage treatment: Macrolide, fluoroquinolones and IV combination antibiotics for 6 months (n=27) (13 patients re-hospitalised and had CFZ with 4 weeks of combination IV antibiotic treatment; CFZ was added to 14 patients on macrolide)	Median (range) duration: 48 (25.2–48) weeks Treatment completion: 57%	52% (n=12) GI symptoms 39% (n=9) Skin colour change 4% (n=1) Dizziness	NR	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=10, 24%) Clinical outcomes: Improved: <i>M. abscessus</i> (n=34, 81%) Radiological outcomes: Improved: <i>M. abscessus</i> (n=13, 31%) Death: NR
Guo 2018 (China)	4-week of IV AMK (15 mg/kg/d in 2 equally divided doses) and IV cefoxitin (200 mg/ kg/d with a maximum of 12 g/d in 3 equally divided doses) (n=100) Treatment completion: 100%	Median (range): 18 (9–30) months (CLA-resistant) Median (range): 15 (9–22) months (CLA-sensitive)	NR	n=12, 12%	Microbiological outcomes: Persistent SCC: <i>M. abscessus</i> (n=40, 40%) Clinical outcomes: NR Radiological outcomes: Improved: <i>M. abscessus</i> (n=47, 47%) Death: NR
Jhun 2018 (South Korea)	AMK 250 mg inhalation once daily be up- titrated to 500 mg once daily 2 to 4 weeks later (protocol was changed from 500 mg once daily to 500 mg 3 times weekly from September 2016) (n=48) Patients also received macrolide (100%) and CFZ (90%)	Median (IQR) duration: 12 (6.8–12) months Treatment completion: 96%	38% (n=29) patients had adverse effects: 19% (n=15) Ototoxicity 9% (n=7) Fatigue 5% (n=4) Tinnitus 3% (n=2) Cough 1% (n=1) Hoarseness	NR	Microbiological outcomes: 3 consecutive negative cultures: <i>M. abscessus</i> (n=6, 13%) Clinical outcomes: Improved: <i>M. abscessus</i> (n=21, 44%); Unchanged: <i>M. abscessus</i> (n=11, 23%); Deteriorated: <i>M. abscessus</i> (n=16, 33%) Radiological outcomes: Improved: <i>M. abscessus</i> (n=16, 33%); Unchanged: <i>M. abscessus</i> (n=11, 23%); Deteriorated: <i>M. abscessus</i> (n=21, 44%) Death: 10 deaths

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment % treatment completion)	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Kobayashi 2018 (Japan)	Macrolide, rifampicin and ethambutol (n=9) Macrolide, rifampicin, ethambutol and IV amikacin ± imipenem (n=14) No dosage reported	Duration: >12 months Treatment completion: 100%	NR	n=3, 13%	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=8, 34.8%) Clinical outcomes: NR Radiological outcomes: NR Death: NR
Monteiro 2018 (Brazil)	1st regimen: CLA (500mg q12hr), ethambutol (1200 mg q24hr) and rifampicin (600 mg q24hr) 2nd regimen: add IM AMK (500 mg, 3 times/ week) or IM streptomycin (1 g, 3 times/ week) to the 1st regimen. 3rd regimen: add IV imipenem (500 mg, q6hr) to the 2nd regimen (n=17)	Duration: NR Treatment completion: 82.4% (1st regimen)	NR	NR	Clinical outcomes: After 1st regimen: <i>M. abscessus</i> (n=3, 17.6%); After 2nd/3rd regimen: <i>M. abscessus</i> (n=10, 91.0%) Clinical outcomes: Improved: <i>M. abscessus</i> (n=3, 17.6%); Failure: <i>M. abscessus</i> (n=11, 64.8%) Radiological outcomes: NR Death: 1 death
Shin 2018 (South Korea)	Initial antibiotics (2–4 weeks) – IV AMK, ceftoxitin (or imipenem), and macrolide, ethambutol, rifampicin and/or fluoroquinolone ± CFZ MAC+M. <i>abscessus</i> (n=24) MAC+M. <i>massiliense</i> (n=47) No dosage reported	Median duration: 25.7 months (MAC+M. <i>abscessus</i>) Median duration: 18.5 months (MAC+M. <i>massiliense</i>) Treatment completion: 100%	NR	(MAC+M. <i>abscessus</i>): (n=0) (MAC+M. <i>massiliense</i>): (n=12, 57.1%)	Microbiological outcomes: SCC at 12 months: MAC+M. <i>abscessus</i> (n=3, 25) and MAC+M. <i>massiliense</i> (n=19, 61%) Clinical outcomes: (MAC+M. <i>abscessus</i>) — Improved: (n=11, 92%); Deteriorated (n=1, 8%); (MAC+M. <i>massiliense</i>) — Improved: (n=28, 90%); Deteriorated (n=1, 3%) Radiological outcomes: (MAC+M. <i>abscessus</i>) — Improved: (n=11, 92%); Deteriorated (n=1, 8%); (MAC+M. <i>massiliense</i>) — Improved: (n=28, 90%); Deteriorated (n=3, 10%) Death: NR
Yoshida 2018 (Japan)	A variety of antibiotics combinations: macrolides (CLA 800 mg/day or AZI 250 mg/ day), fluoroquinolone (sitafloxacin 100 mg/ day), and ≥2 IV antibiotics, such as AMK 400 mg/day and imipenem 1500 mg/day (n=21)	Median (range) duration (unfavourable group) (oral): 958 (219–1266) days Median duration (favourable group) (oral): 119 days Median (range) duration (unfavourable group) (oral + IV abx): 1623 (481–2975) days Median (range) duration (favourable group) (oral + IV abx): 32 (28–37) days Treatment completion: 100%	NR	19.1%	Microbiological outcomes: SCC (<i>M. abscessus</i>) – 5.9% (1/17); SCC (<i>M. massiliense</i>) – 28.6% (2/7) Clinical outcomes: NR Radiological outcomes: NR Death: 2 deaths

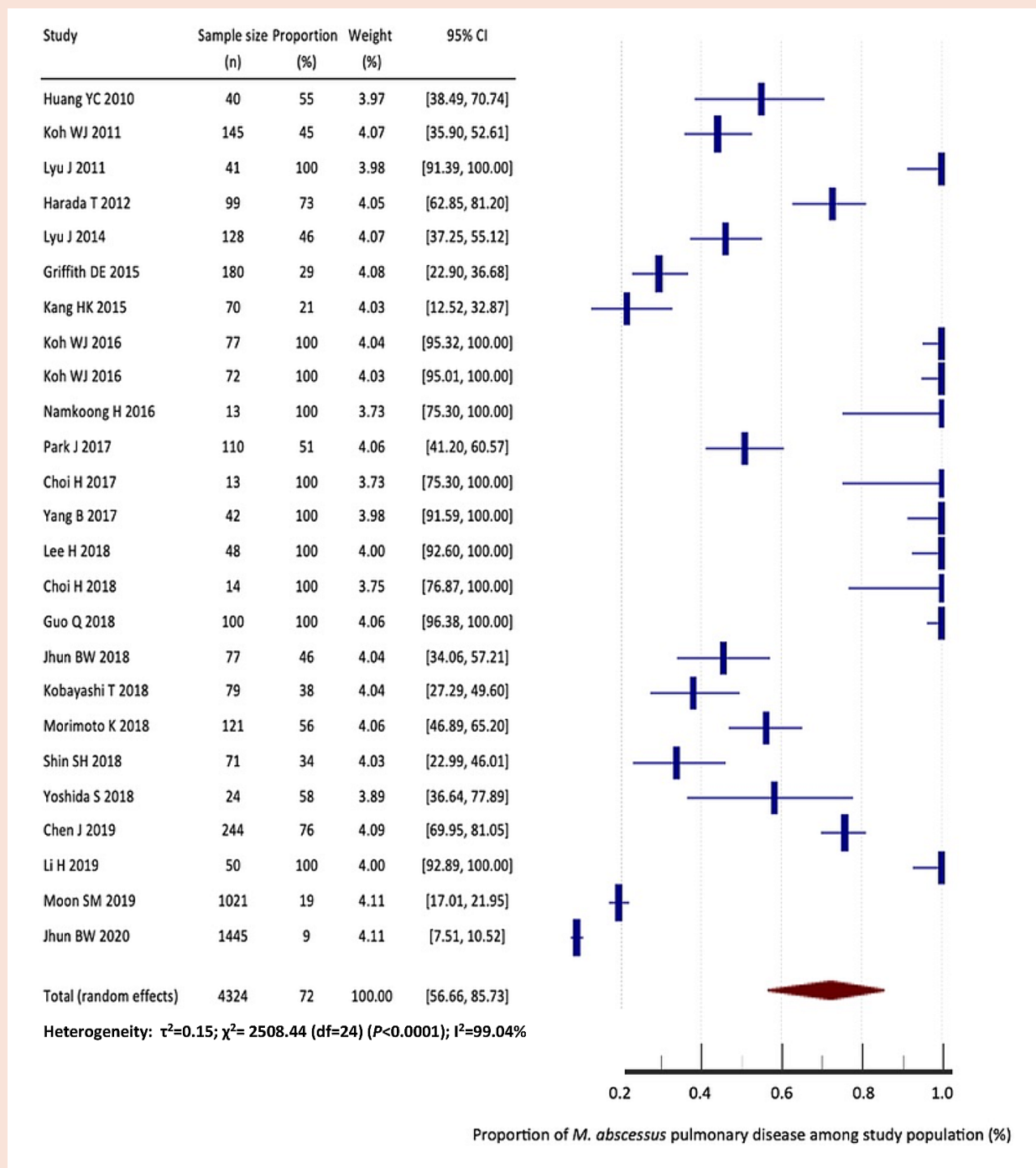
Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment (% treatment completion)	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Chen 2019 (China)	A variety of antibiotics combinations: CLA, AZI, AMK, tigecycline, linezolid, imipenem, meropenem, cefoxitin, CLP, MOX, DOX, minocycline, and levofloxacin (n=244) No dosage reported	Duration: NR Treatment completion: NR	78.7% (n=192) patients had adverse events Severe effects that resulted in treatment modification included: 48.4% (n=29) GI distress (mainly caused by tigecycline) 23.3% (n=14) ototoxicity (caused by AMK) 10% (n=6); myelosuppression (mainly caused by linezolid)	NR	Microbiological outcomes: SCC: <i>M. abscessus</i> (n=62, 33.5%) and <i>M. massiliense</i> (n=48, 81.4%), Clinical outcomes: NR Radiological outcomes: NR Death: NR
Jhun 2020 (South Korea)	Initial treatment (2 to 4 weeks): IV AMK, imipenem (or cefoxitin), oral macrolide and oral fluoroquinolone (or DOX) Followed by oral regimens. Some patients with refractory NTM PD received oral CFZ or inhaled AMK <i>M. abscessus</i> (n=129) <i>M. massiliense</i> (n=174) No dosage reported	Duration: NR. Treatment completion: NR	NR	NR	Microbiological outcomes: NR Clinical outcomes: NR Radiological outcomes: NR Death: <i>M. massiliense</i> mortality 5-year (7.3%), 10-year (18.1%), 15-year (23.5%); <i>M. abscessus</i> mortality 5-year (11.4%), 10-year (29.8%), 15-year (50.6%)

Table 2. Treatment regimens, adverse events and outcomes. (Cont'd)

References	Treatment regimen and dosages (n=number of patients on treatment)	Duration of treatment (% treatment completion)	Adverse events (n, %)	Relapse (n, %)	Treatment outcomes (n, %)
Li 2019 (China)	Convention regime (1 July 2010–31 July 2017): Macrolides (CLA [1000 mg/d] or AZI [250 mg/d], MOX 400 mg/d. Initial 12-week of IV cefoxitin (2 g, BD) and IV AMK (400 mg/d for weight ≤50 kg, 600 mg/d for weight >50 kg) Intensified regime (1 August 2017–1 February 2018). AZI (250 mg/d), MOX (400 mg/d), linezolid (600 mg/d for the first 3 months, followed by 300 mg/d for the following months); initial 4-week IV cefoxitin (12 g/d) and 12-week IV AMK (400 mg/d for weight ≤50 kg, 600 mg/d for weight >50 kg) Both the conventional and intensified regimens continued 12 months after the first sputum conversion (n=50).	Duration: NR Treatment completion: NR	14% (n=7) Leukopenia 12% (n=6) Hepatotoxicity 20 % (n=10) Nausea and vomiting 2% (n=1) Anaemia 4% (n=2) Arthralgia	8%	Microbiological outcomes: SCC at 1 month: <i>M. abscessus</i>: conventional Rx (n16, 47%) and Intensified Rx (n=12, 75%); SCC at 18 months: <i>M. abscessus</i>: Conventional Rx (n=9, 26.5%) and Intensified Rx (n=10, 62.5%) Clinical outcomes: Improved: at one month (n=28, 56%) and after 18 months (n=19, 38%) Radiological outcomes: NR Death: NR
Park 2021 (South Korea)	Initial antibiotics-IV AMK (median 8.9 weeks) and IV beta-lactam (median 5.3 weeks), and macrolide (100%), CFZ (28%), MOX (31.7%) and linezolid (4.9%) (n=82). No dosage reported	Median (IQR) duration: 15.4 (9.5–24.5) months Treatment completed: 100%	4.9 % (n=4) Skin abnormalities 7.3% (n=6) Fever 2.4% (n=2) GI abnormalities 25.6% (n=21) Haematologic abnormalities 9.8% (n=8) DILI 3.7% (n=3) nephrotoxicity 4.9% (n=4) ototoxicity 1.2% (n=1) peripheral neuropathy	NR	Microbiological outcomes: SCC: Abscesses (n=43, 52.4%); microbiological cure: <i>M. abscessus</i> (n=34, 41.5%) Clinical outcomes: NR Radiological outcomes: Improved: <i>M. abscessus</i> (n=35, 42.7%); Unchanged: <i>M. abscessus</i> (n=37.8 37.8%); Deteriorated: <i>M. abscessus</i> (n=16, 19.5%) Death: NR

abx: antibiotics; AML: amikacin; AZI: azithromycin; BD: twice a day; CLA: clarithromycin; CFZ: cefazolin; CIP: ciprofloxacin; COPD: chronic obstructive pulmonary disease; DILI: drug induced liver injury; DOX: doxycycline; GI: gastrointestinal; HIV: human immunodeficiency virus; IM: intramuscular; ILD: interstitial lung disease; IQR: interquartile range; IV: intravenous; *M. abscessus*: *Mycobacterium abscessus* subspecies *abscessus*; *M. bolletii*: *Mycobacterium abscessus* subspecies *bolletii*; *M. massiliense*: *Mycobacterium abscessus* subspecies *massiliense*; MABC: *Mycobacterium abscessus* complex; MAC: *Mycobacterium avium* complex; MABC: *Mycobacterium abscessus* complex; MOX: moxifloxacin; NR: not reported; NTM: non-tuberculosis *Mycobacterium*; PTB: pulmonary tuberculosis; TB: pulmonary tuberculosis; SCC: sputum culture conversion

Fig. 2. Prevalence of *M. abscessus* pulmonary disease among study population.

CI: confidence interval

patients). Reducing dosing frequency to 3 times per week decreased adverse effects.

Tigecycline and clofazimine

Tigecycline was used in 2 studies,^{30,32} both showing favourable outcomes, particularly for *M. abscessus*.³⁰ Clofazimine was included in 7 studies.^{17–22,37} Yang

et al. reported an SCC rate of 24%, including 15% in refractory *M. abscessus*. Gastrointestinal side effects occurred in 43% of patients, prompting dose adjustments or discontinuation, though no severe events were reported.¹⁹

Ten studies reported macrolide-contained regimens for all patients.^{11,13,14,17,20,21,24,27,32,37} For subgroup analysis

on the association between treatment duration and SCC rates for these regimens: median (range) SCC rates were 28.4 (25–31.8) for 1-year treatment, 42.1 (25–52.4) for 2-year treatment and 44.5 (24–65) for treatment exceeding 2 years. There was no statistically significant difference among the treatment durations, which may be attributed to small sample size (1-year versus [vs] 2-year treatment, $P=0.3$; 1-year vs exceeding 2-year treatment, $P=1$). Six studies used macrolide-intravenous (IV) amikacin contained regimens for all patients.^{11,13,14,17,21,37} There was no statistically significant difference in SCC rates between studies reported of all versus some patients that received the macrolide-IV amikacin regimens (median [range]: 42.1 [46.6–93] vs 33.3 [38.9–65] respectively, $P=0.6$).^{20,24,27,32} This may be attributed to small sample size.

Surgical treatment

Adjunctive pulmonary resection was reported in 9 studies.^{9,12-17,20,37} The criteria for surgery included inadequate response to medical therapy or recurrent NTM pulmonary disease with persistent sputum culture positive, cavitary lesions and or severe focal bronchiectasis with complications such as massive haemoptysis.^{9,12,13,15} In 5 studies, SCC rates post-surgery ranged from 42% to 100%.^{9,12,14,15,18} Choi et al. reported SCC in a patient with macrolide-resistant *M. abscessus* following surgery.¹⁸ Outcomes varied: Lyu et al. found no significant difference between surgical and medical therapy,¹² whereas Kang et al. reported an SCC rate of 81% with a 21% complication rate.⁹ Koh et al. noted higher SCC at 36 months in the surgery-plus-antibiotics group compared to antibiotics alone (54% vs 42%).¹⁴ Reported complications included pneumonia, bronchopleural fistula and wound dehiscence.¹³ In comparing SCC rate, patients who received both antibiotic therapy and surgical treatment had a higher SCC rate than those who received antibiotic therapy alone (median [range]: 76.9% [65–100%] vs 34.2% [5.9–93%], $P=0.007$).

Treatment-related adverse effects

Ten studies (35.7%) reported treatment-related side effects, which were experienced by 356 patients (12.8% of 2769).^{9,12,13,15,19,20,30,31,36,37} Among these, 147 patients required dose reduction or discontinuation of treatment due to adverse effects.

Amikacin-related adverse effects

Amikacin was administered via inhalation and intravenous (IV) routes.

Inhaled amikacin

Five studies evaluated inhaled non-liposomal amikacin.^{17,18,21,22,36} Jhun et al. reported detailed safety outcomes,³⁶ where all patients receiving 500 mg

once daily experienced adverse effects, leading to a reduced frequency (3 times weekly), which minimised further events. Overall, 29 patients (38%) experienced side effects, and 21 (27%) discontinued treatment. Common adverse events included ototoxicity (19.5%), fatigue (9.1%), tinnitus (5.2%) and cough (2.6%).

Intravenous amikacin

IV amikacin was included in 20 studies.^{11-22,24,26,28-31,33,37} No adverse effects were reported in 6 studies.^{13,15,19,20,28,31} Reported dosages ranged from 8 to 20.2 mg/kg/day.^{13,15} Two studies documented adverse events in 23 patients (8.1%), including ototoxicity, tinnitus and nephrotoxicity.^{12,30} Dosages varied: 6 studies used 15 mg/kg/day,^{11,12,17,18,20,29} while 2 used 400 mg/day.^{26,31} Therapeutic drug monitoring was noted in some studies: Namkoong et al. adjusted dosing based on trough levels,²⁸ Lee et al. used peak serum levels (Cmax) for dose optimisation.¹⁹

Cefoxitin-related adverse effects

Cefoxitin was used in 17 studies as part of combination therapy.^{9,11-22,29-31,37} Four studies reported adverse effects, primarily hepatotoxicity (11.2–14.3%) and leukopenia (9.9%).^{12,15,31,37} Symptoms typically resolved after switching to imipenem, highlighting the need for close monitoring and timely regimen adjustment.

Tigecycline-related adverse effects

Tigecycline was used in 2 studies,^{30,32} and was associated with gastrointestinal toxicity. Chen et al. reported nausea, vomiting, diarrhoea and abdominal pain as the most common effects.³⁰ Among 244 patients, 14 (5.7%) required dose reduction or discontinuation due to severity.

Clofazimine-related adverse effects

Clofazimine was included in 7 studies,^{17-22,37} with adverse effects reported in 2.^{19,20} In 1 cohort,²⁰ 55% experienced side effects, including gastrointestinal symptoms (26%) and skin discoloration (12%). These led to dose reduction in 12% and discontinuation in 43% of cases. While not life-threatening, these reactions impacted adherence and tolerability.

Treatment outcomes

Treatment outcomes were evaluated across 3 primary domains: clinical response, microbiological response (measured via SCC) and radiological improvement. Due to heterogeneity in outcome definitions and assessment methods, direct comparisons between studies were limited.

Clinical outcomes

Twelve studies assessed clinical outcomes based on symptoms such as cough, sputum production, dyspnoea and physician-assessed respiratory

status.^{11-13,20,21,26,28,32-34,36} However, interpretation was limited by the lack of standardised definitions for clinical improvement. Four studies used both symptom and radiological findings to evaluate response,^{21,26,32,33} with improvement rates ranging from 13.6% to 91% and a pooled estimate of 37.1 % (95% CI 29.3–45.2%) (Fig. 3).

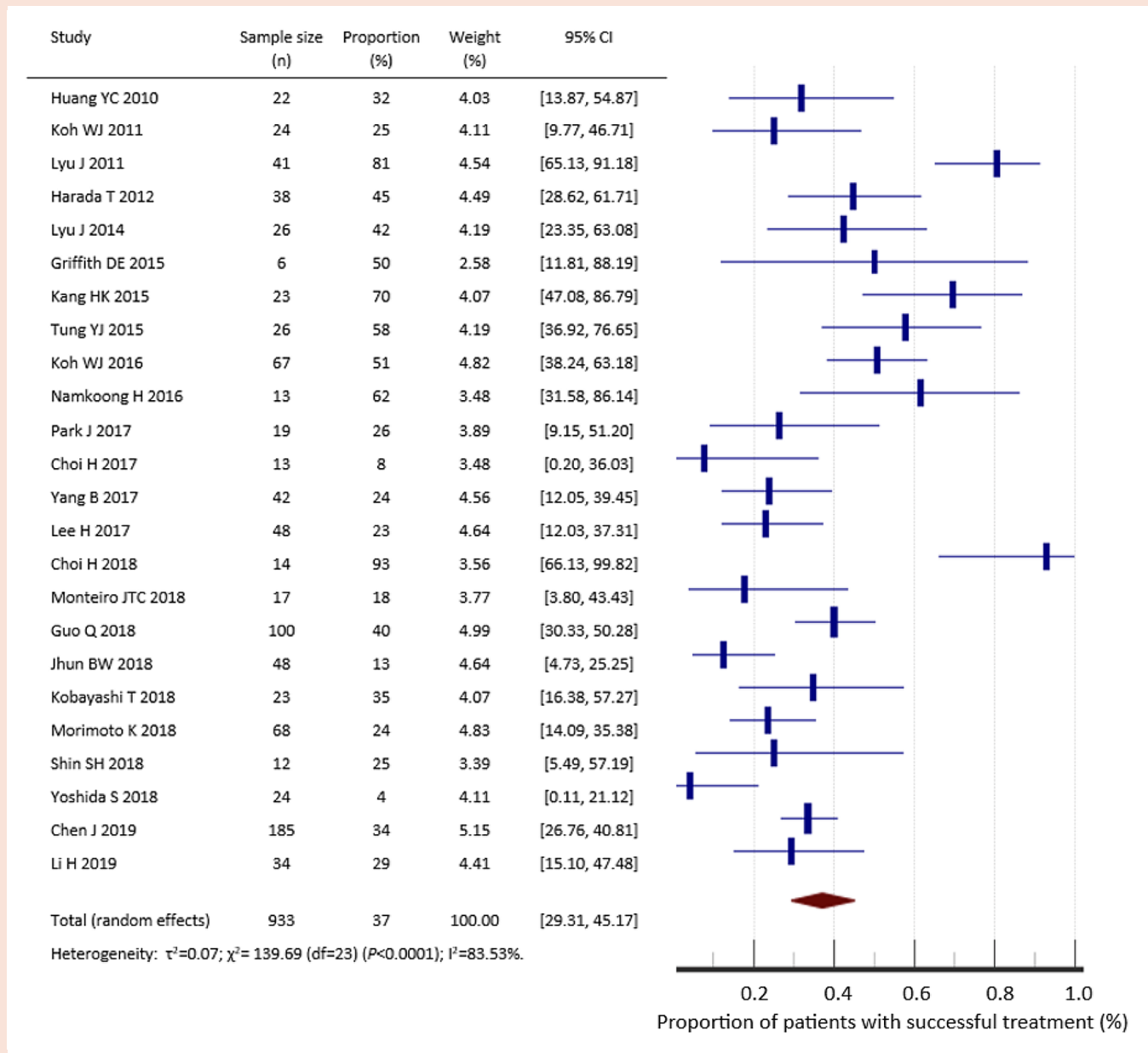
Six studies assessing symptoms alone reported improvement rates between 17.6% and 100%, reflecting heterogeneity in regimens, disease severity and study populations.^{13,15,20,28,34,36} Koh et al. found

higher response rates in *M. massiliense* (97%) than in *M. abscessus* (75%), emphasising the influence of subspecies.¹¹ Notably, 1 study reported spontaneous symptom improvement in 42.5% of untreated patients, suggesting possible host-related or self-limiting disease mechanisms.³³

Microbiological outcomes

SCC was reported in 25 studies,^{9,11-18,20,21,23-33,36,37} with 12-month SCC rates ranging from 29% to 77%. *M. massiliense* consistently showed higher SCC rates

Fig. 3. Successful treatment for *M. abscessus* pulmonary disease.



CI: confidence interval

(72.4–100%) compared to *M. abscessus* (31–81.3%). Park et al. reported SCC in 82.4% of *M. massiliense* cases versus 26.3% in *M. abscessus*.¹⁵ In an untreated cohort, Moon et al. observed spontaneous SCC in 34% (157/459),²³ although 26 later developed NTM disease from different species, highlighting the dynamic nature of NTM colonisation. A large study by Park et al. reported SCC and microbiological cure rates of 52.4% and 41.5%,³⁷ respectively, based on NTM-NET definitions.¹⁰ These findings emphasise the importance of standardised outcome measures in evaluating treatment efficacy.

Radiological outcomes

Nine studies assessed radiological response using high-resolution computed tomography (HRCT).^{11,13,15,20,27-29,36,37} Among 6 studies focusing on MABC,^{13,20,28,29,36,37} radiographic improvement ranged from 33–53.8%, with 23–37.8% showing no change and 19.5–33% demonstrating deterioration. Subspecies differences were evident. Koh et al. reported 91% radiologic improvement in *M. massiliense* cases after 2 weeks of IV antibiotics.¹⁵ Similarly, Koh et al. and Harada et al. found higher response rates in *M. massiliense* (82% and 48%) compared to *M. abscessus* (42% and 29%).^{11,29} In contrast, Tung et al. observed deterioration in 77% of patients, with only 13.9% showing improvement and 44.4% remaining stable.³²

Other factors associated with treatment outcomes

Three studies analysed demographic, clinical, and genetic factors potentially influencing treatment outcomes.^{22,23,29}

Genotypic associations

Guo et al. found that bacterial genotype significantly influenced outcomes, including SCC rates, radiological improvement and overall treatment success.²⁹ In their multivariate analysis, patients infected with clarithromycin-resistant genotypes were significantly less likely to experience favourable treatment outcomes compared to those with clarithromycin-sensitive genotypes (adjusted odds ratio: 0.185, 95% CI 0.059–0.579, $P=0.004$).

Host-related factors

Findings on the influence of age, sex, body mass index (BMI) and comorbidities on treatment outcomes were mixed. Guo et al. reported no significant association between these variables and treatment success.²⁹ Conversely, Jhun et al. identified several factors linked to increased mortality in NTM pulmonary disease, including age ≥ 65 years, male sex, low BMI (<18.5 kg/m²) and comorbidities such as chronic pulmonary aspergillosis, malignancy, chronic cardiac or hepatic disease.²² Moon et al. observed spontaneous SCC in 34% of untreated patients;²³ however,

some later developed NTM disease due to different species, highlighting the dynamic interaction between host immunity and pathogen behaviour.

DISCUSSION

Treatment of *M. abscessus* pulmonary disease remains highly challenging due to factors such as bacterial genotype, subspecies, antimicrobial resistance and patient-specific clinical variables. These elements contribute to heterogeneity in treatment outcomes and complicate cross-study comparisons. Clinical success depends on appropriate antibiotic selection, accurate subspecies/genotype identification, and host factors including comorbidities, immune status and underlying lung disease. Antibiotic regimens vary significantly across regions and institutions, influenced by drug availability and local protocols. The organism's intrinsic and acquired resistance limits consistent treatment responses. Interpretation of outcomes is further complicated by the absence of standardised definitions for clinical, microbiological and radiological responses, and differences in follow-up duration.

In this review, SCC rates for combination regimens—including a macrolide, amikacin and cefoxitin or imipenem—ranged from 8% to 93%. Some studies reported improved outcomes with the addition of fluoroquinolones. However, sustained SCC was more consistently linked to subspecies differences, with *M. massiliense* infections showing better microbiological response than *M. abscessus*. Tigecycline, clofazimine and inhaled amikacin were effective options for refractory cases.^{19,30,36}

Studies have underscored the importance of macrolide susceptibility as a key predictor of outcome. For instance, Choi et al. reported the poorest outcomes in patients with macrolide-resistant strains,¹⁷ while Park et al. emphasised that clarithromycin susceptibility significantly influenced treatment success.¹⁶ These findings reinforce the need for routine genotypic testing, including *erm*(41) and *rrl* mutations, to guide personalised antimicrobial therapy and improve prognostication.

Earlier studies and clinical guidelines have supported the use of inhaled amikacin in patients with refractory *M. abscessus* pulmonary disease,³⁸⁻⁴² although its application has been inconsistent across clinical settings. Jhun et al. reported low SCC rates but moderate clinical and radiological improvement with amikacin inhalation therapy.³⁸ However, frequent adverse events, particularly ototoxicity, necessitated a protocol adjustment from daily to thrice-weekly dosing, which reduced the incidence of toxicity. These findings suggest a potential role for inhaled amikacin as a supportive adjunct but emphasise the need for standardised protocols that balance efficacy and tolerability.

Emerging antimicrobials such as clofazimine and tigecycline have shown potent *in vitro* activity against *M. abscessus*,⁴ and their incorporation into multidrug regimens has yielded promising early clinical results.^{17,30} However, in most cases, their use was at the discretion of the treating physician and, therefore, direct causal conclusions regarding their individual efficacy could not be established. Future randomised controlled trials are warranted to determine the clinical utility of clofazimine and tigecycline as potential first-line agents, especially in patients infected with macrolide-resistant strains of *M. abscessus*. Surgical resection remains an important adjunctive therapy, particularly in cases of localised or drug-resistant disease. Several studies reported SCC rates exceeding 40% in patients undergoing surgical intervention. For instance, Kang et al. reported high SCC rates with a low incidence of postoperative complications, suggesting that surgical management should be considered in appropriately selected patients, especially those with multidrug-resistant or treatment-refractory disease.⁹

Treatment outcomes also vary significantly between MABC subspecies. Patients with *M. massiliense* infection consistently demonstrated better clinical, microbiological and radiological responses compared to those with *M. abscessus*.^{11,16,27} This is largely attributed to the dysfunctional *erm*(41) gene in *M. massiliense*, which results in macrolide susceptibility,²⁶ thereby improving the efficacy of macrolide-based regimens. Whole-genome sequencing (WGS) and genotypic analysis may therefore play a critical role in tailoring therapy, enabling more accurate predictions of antimicrobial response. Notably, Park et al. reported that clarithromycin susceptibility alone accounted for approximately 40% of the variation in treatment outcomes, highlighting the interplay of bacterial genetics and host-specific factors in determining treatment success.¹⁶

The interpretation of treatment outcomes remains challenging due to a lack of standardised definitions among the studies. Many studies relied on subjective criteria, such as symptom relief and radiological improvement, which are prone to bias and inter-observer variability. The NTM-NET group proposed outcome definitions such as SCC, microbiological cure, clinical cure, treatment failure, relapse, reinfection and treatment discontinuation, which are important for standardisation of treatment outcome reporting in future studies.¹⁰ While SCC is often used as a more objective outcome, recent studies have emphasised that patient-reported outcomes, quality of life and long-term survival may be more meaningful endpoints for evaluating therapy in MABC lung disease.⁴³ Furthermore, this review also revealed important methodological limitations in the existing literature. Of the 28 included studies, only 8 enrolled more than 100 participants;^{11,16,22,23,25,29,30,33} the remaining 20

studies were largely single-centre and retrospective, with limited sample sizes, thereby constraining the generalisability of findings. Additionally, most studies did not evaluate the pharmacokinetic or pharmacodynamic relationships of antibiotics, nor did they assess non-pharmacologic interventions, such as airway clearance techniques or nutritional status, which may also influence outcomes.

In addition to currently available treatment options, repurposing anti-tubercular drugs presents a promising strategy for developing new chemotherapeutic alternatives against *M. abscessus* complex (MABC) infections.⁴⁴ Several potential molecular targets have been identified, including RNA polymerase, aspartate decarboxylase PanD, enzymes involved in peptidoglycan synthesis, mycolic acid transport and the F-ATP synthase, a critical component of oxidative phosphorylation. Notably, rationally designed rifabutin analogs have demonstrated 50- to 100-fold increased potency against *M. abscessus* by targeting RNA polymerase.⁴⁵ Additionally, a first-in-class inhibitor of PanD has recently been identified, showing promising activity. A combination therapy involving the oral β -lactam tebipenem, which targets L,D-transpeptidases (LdtMab1 and LdtMab2) and D,D-transpeptidases (PonA1, PonA2 and PbpA), with the β -lactamase inhibitor avibactam, has shown low micromolar, bactericidal activity against *M. abscessus*, and may be co-administered with existing anti-MABC agents to enhance efficacy.⁴⁶

Further breakthroughs have emerged with validation of novel targets such as MmpL3, a transporter of mycolic acids across the plasma membrane,^{47,48} and InhA, the enoyl-ACP reductase involved in fatty acid synthesis.⁴⁹ While most current drugs target biomass-generating pathways, increasing attention has turned toward bioenergetic pathways, particularly the F-ATP synthase, which remains essential in both replicating and non-replicating bacterial states—the latter being highly drug-tolerant. Recent work has identified several F-ATP synthase inhibitors with promising *in vitro* and *in vivo* activity. These include repurposed compounds such as squaramide SQ31f,⁵⁰ the diarylquinoline bedaquiline,⁵¹ and newer analogues TBAJ-876 and TBAJ-5307.^{52,53} Novel inhibitors such as GaMF1 and Ep1MabF1 have also been developed, offering additional scaffolds for the discovery of curative regimens.^{54,55}

The persistently poor treatment outcomes in *M. abscessus* pulmonary disease emphasise the urgent need for stronger antimicrobials, improved drug delivery systems and resistance-reversing strategies. The intrinsic resistance mechanisms of *M. abscessus*, particularly its mycolic acid-rich, impermeable cell wall, continue to pose major barriers to drug efficacy.⁵⁶ Nonetheless, advances in whole-cell phenotypic screening and synergistic drug combination assays

have begun to yield new candidate molecules with potent anti-MABC activity.⁵⁶⁻⁵⁸ Improved delivery systems also hold potential. Novel pulmonary drug delivery technologies, including nanoparticle-based inhalation therapies and dry-powder formulations, may allow for higher local drug concentrations while minimising systemic toxicity.⁵⁹ Currently, treatment success relies on eradicating of *M. abscessus*, which often fails and does not reflect patients' functional status. Coping with daily activities may be more important to patients than the eradication of *M. abscessus*. Thus, functional status should be given importance equally as radiological and microbiological outcomes for indicating treatment response in NTM disease. It indicates the extent of clinical symptoms experienced in the daily activities of patients. This functional approach explains real life suffering rather than just pathological and radiological symptoms.⁶⁰

Finally, the development of relevant experimental models is critical to support the preclinical evaluation of new therapies. These models must accurately replicate host-pathogen interactions and reflect the complex immunopathology of *M. abscessus* infections.

CONCLUSION

This review highlights the complexity of treating *M. abscessus* pulmonary disease, largely due to intrinsic drug resistance, variable treatment responses, and frequent adverse effects. Outcomes are influenced not only by antibiotic regimens but also by bacterial subspecies, genotype and host-related factors. Surgical resection remains a valuable adjunct, particularly in localised or refractory cases, and is associated with higher sputum culture conversion (SCC) rates. Macrolide-IV amikacin contained regimens may potentially increase SCC rate and hence, is a preferred treatment option, particularly when *M. abscessus* is susceptible to these drugs. Optimising treatment will require integration of genotypic profiling, novel therapeutic agents and advanced drug delivery systems, supported by robust clinical and microbiological endpoints to enable more personalised and effective management strategies.

Supplementary material

Table S1. Search strategy with Boolean operators.

Ethics statement

Ethical approval was not required for this study as it used publicly available, anonymised data.

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. No generative

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