Citation number	Bibliographic citation	Study type	Ev lev	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding	General Comments
41	Bryant CE, Grogono DM, Rodriguez-Rincon D. Population-level genomics identifies the emergence and global spread of a human transmissible multidrug-resistant nontuberculous mycobacterium. Science 2016;354: 751-756	cohort study	2++	517	M. abscessus infected patients with cystic fibrosis	nil	whole genome sequence similarity between isolates form different patients and clnical outcome, antibiotic resistantce, and fullfilling ATS criteria	Variably between 2 - 10 years	clnical outcome, antibiotic resistantce, and fullfilling ATS criteria	Worse clinical outcomes and increases levels of antibioitic resistance. Evidence that most clinical isolates are from clusters of M. abscessus representing dominant circulating clones that have spread globally	Wellcome Trust, CF Trust and others	Evidence of human-based trasnmission of M. abscessus in individuals with CF
124	Steingart KR, Henry M, Ng V, et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. The Lancet. Infectious diseases 2006;**6**(9):570-81 doi: 10.1016/S1473-3099(06)70578-3[published Online First: Epub Date]|.	Not clear this study is relevant re NTM, although relevant for TB, as only relates to M tuberculosis and explicitly excludes NTM. **Further comments across relate to TB need to amend relevant text in main doc**	1-	> 52,000	Various, HIV, non HIV, low/high incidence TB countries	Nil	Flourescence v conventional sputum smear microscopy	Not appropriate	Not appropriate	Average 10% more sensitive than conventional microscopy (p<0.001). Specificity similar to convntional microscopy (0% p=0.21)	UNICEF/UNDP/World Abnk/specil Programme for Rearch an training in tropocal diseases and USAID.	Review of fluorescence v 'conventional' : (Ziehl-Neelsen or Kinyoun acid-fast stains), microscopy for TB diagnosis, explcitlly excludes NTM studies. 45 TB studies, overall fluoresence microsopy more (10%) senstive, with similar specificity.
125	Ulukanligil M, Aslan G, Tasci S. A comparative study on the different staining methods and number of specimens for the detection of acid fast bacilli. Memorias do Instituto Oswaldo Cruz 2000;**95**(6):855-8	Study of TB no mention of NTM. **Further comment relate to TB and may need to amend relevant text in main document.**	2+	295 patients	Turkey 1998-2000. No details on patient characteristics esp HIV.	Nil	Culture 6 weeks only on LJ slopes v flouorchrome v ZN. May under estimate numbers of culture positives.	Not appropriate	Compared microscopy modalities v culture with one, two or three specimens from a single patient	Fluorochrome at least 12% more sensitive than ZN in all groups.	Not stated. Members of Harran Univ Med School, Turkey.	No comment on blinding, how MTB confirmed, NTM culture or related results. It would seem likely that NTMs were excluded. Short period of culture on LJ - no liquid culture. Overall recovery likely to be less than optimal.
127	Murray SJ, Barrett A, Magee JG, et al. Optimisation of acid fast smears for the direct detection of mycobacteria in clinical samples. Journal of clinical pathology 2003;**56**(8):613-5	Comparison of processing methods carried out and compared after culture results were known. UK cohort. 78 culture positive specimens.	2++	78 culture postive sputa	UK cohort (Newcastle MRU)	none	Flourescence v Ziehl-Neelsen staining, after EACH step of processing.	Not appropriate	Culture v each microscopy method	Desciption is that AP was significantly better than ZN with all paretreatment regimens and difference between pretreamnt regimens were allso significant. P> 0.01 for all differences.	Public Health Laboratory Service, UK	Desciption is that AP was significantly better than ZN with all paretreatment regimens and difference between pretreamnt regimens were allso significant. P> 0.01 for all differences.
140	Hanna BA, Ebrahimzadeh A, Elliott LB, et al. Multicenter evaluation of the BACTEC MGIT 960 system for recovery of mycobacteria. Journal of clinical microbiology 1999;**37**(3):748-52	Mulitcentre comparison of mycobacteria culture systems including BACTEC MGIT 960. 132 MTB complex from a total of 362 mycobacterial isolates	2++	3330 specimens, 2210 respiratory, 1120 non respiratory from 2346 patients.	New York, Texas, Los Angeles, north Hollywood and Germany.	none	BACTEC MGIT 960 v BACTEC 460 TB, Lowenstien-Jensen and Middlebrook 7H11/selective plates.	Not appropriate	Each medium type with all others including solids.	See general comments	Manufacturer: Becton Dickinson	Liquid systems alone recovered more mycobacteria than solids alone. But greatest recovery was when both were used. 4% of isolates were only detected on solid media. No single system recovered all mycobacteria, the MGIT 960 detected more NTM than the BACTEC 460TB system. Contamination rates were greater with the former, which was the only fully automated continous monitoring system..
143	Brown-Elliott BA, Wallace RJ, Jr. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. Clinical microbiology reviews 2002;**15**(4):716-46	Review of rapidly growing mycobacteria only. No detail of how did searches to update. Well referenced 226 references. Dated 2000. One might consider referencing a more upto date overview or even the ATS 2007 document?	2-	Many case series under each type of RGM	Global selection of papers	none	Between species isolated and characteristics	Not appropriate	Not appropriate	See general comments	Not stated. From University of Texas Health Center.	Describes with references M. fortuitum, abscessus/chelone and others' taxonomy, clinical manifestations, diagnosis,treatment and laboratory aspects.
152	Fangous MS, Mougari F, Gouriou S, et al. Classification algorithm for subspecies identification within the Mycobacterium abscessus species, based on matrix-assisted laser desorption ionization-time of flight mass spectrometry. Journal of clinical microbiology 2014;**52**(9):3362-9 doi: 10.1128/JCM.00788-14[published Online First: Epub Date]|.	Series of French D355 M abscessus isolates ID methods compared MALDI-TOF v MLST	2++	49 strains validated against algorithim drawn up based on 43 isolates' peaks	40 epidemiologocally unrelated M. abscessus from French patients - CF, blood clutures,BAL, Id by Hain CM assay and 3 ref strains.	Nil Clinical.	None. 43 strains of M absc ID by HAIN, then MLST typed, had Maldi characterisation. Algorithm developed and applied blindly to panel of 49 reference strains with prior ID by erm (41) and hsp65 gene MLST.	Not applicable	Against prior ID by erm (41) and hsp65 gene MLST.	Not calculated. 46 (94%) of isolates correctly as *M. abscessus* subsp *abscessus, massiliense,* or *bolletii* .	Authors employed by Universities/Hostpitals. 'Advice' and 'go between' support by Bruker - Maldltoff manufacturer.	Excellent intra and intra laboratory reproducibility. Accuracy would likely improve with further isolates assessed/ added to the database. Further geographical and clinical spread of isolates would aid generalisability.
153	Rodriguez-Sanchez B, Ruiz-Serrano MJ, Marin M, et al. Evaluation of Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry for Identification of Nontuberculous Mycobacteria from Clinical Isolates. Journal of clinical microbiology 2015;**53**(8):2737-40 doi: 10.1128/JCM.01380-15[published Online First: Epub Date]	Spanish comparison of iisolates. 16S rRNA/hsp65 sequencing gold standard v MALD-TOF (Bruker) and Hain Genotype CM/AS	2++	125 NTM 2010-14	Possibly significant strains in Spain and 10 reference strains.	None	16S rRNA/hsp65 sequencing gold standard v MALD-TOF (Bruker) and Hain Genotype CM/AS	Not applicable	None	Comparison v gold standard ID. Agreements Mald, Hain and reference were 94.4% and 84.0%, respectively. Maldi agreed better than Hain in 17 (13.6% of results. P=0.002)	Miguel Servet Programme - Reseach Fund of Carols 3 Inst, Madrid and Eur Regiona Dvt Fund., Hospital and University Employees	Unlike othe rbacterial ID's score ≥ 1.7 or top 4 identifications can be consdiered a reliable NTM Id with maldi, without losing accuracy
197	Kitada SU, T.;Yoshimura, K.;Tateishi, Y.;Miki, K.;Miki, M.;Hashimoto, H.;Fujikawa, T.;Mori, M.;Matsuura, K.;Kuroyama, M.;Maekura, R. Long-term radiographic outcome of nodular bronchiectatic Mycobacterium avium complex pulmonary disease. International Journal of Tuberculosis & Lung Disease 2012;**16**(5):660-4	case control	2-	72	nodular bronchiectasis MAC	nil	progressive vs non progressive based on CXR outcome	≥5 years	CXR change	lower BMI cavitat0ry disease and macrolide resistance associated with progression		retrospective Xray based case series over 5 or 10 year follow up. Patients grouped into progressive or stable groups based on XR change and factors associated with these groups assessed in a univariate manner only. Only 16 pts in the deteriorated grp so hard to make any firm conclusions (eg only 3 macrolide resistant pts)
214	Jenkins PA et al. Clarithromycin vs ciprofloxacin as adjuncts to rifampicin and ethambutol in treating opportunistic mycobacterial lung diseases and an assessment of Mycobacterium vaccae immunotherapy. Thorax 2008	RCT	1-	167	Age 16 years or older, clinical / radiological evidence of active mycobacterial disease, sputum culture positive for M malmoense on at least two occasions a minimum of a week apart, not known to be HIV+ve.	Rifampicin, Ethambutol, Clarithromycin (+ / - M vaccae)	Rifampicin, Ethambutol, Ciprofloxacin (+ / - M vaccae)	2 years treatment + 3 years follow up	Primary outcomes 1) Death due to mycobacterial disease, 2) failure of treatment, 3) relapse	No significant differences in the primary outcome measures were found within species or overall between those receiving M. vaccae and those not. For the purposes of comparing the two antibiotic regimens, those that entered the immunotherapy trial were combined with those that did not. No difference between the REClari vs RECipro groups in death due to mycobacterial disease (4/86 vs 2/81 [no statistical significance given]). No apparent difference between the REClari vs RECipro groups in failure of treatment (1 vs 4) or relapse (3 vs 0), but no statistical analysis reported.	BTS	
213	Research Committee of the BTS. First randomised trial of treatments for pulmonary disease caused by M. avium intracellulare, M. malmoense, and M. xenopi in HIV negative patients: rifampicin, ethambutol and isoniazid versus rifampicin and ethambutol. Thorax 2001	RCT	1-	106	> 16 years, CXR compatible changes and / or clinical evidence of mycobacterial infection, sputum culture positive on 2 or more occasions for M. malmoense, not known to be HIV +ve	Rifampicin, ethambutol, isoniazid	Rifampicin, ethambutol	2 years treatment + 3 years follow up	Clinical, CXR, sputum cultures, death	No significant difference between RE and REH in all cause mortality (12/52 vs 15/54), deaths due to mycobacterial disease (1/52 vs 3/54), failure of treatment (3/52 vs 0/54), relapses (3/52 vs 5/54), or number completed Rx allocated alive cured at 5 years (20/52 vs 24/54). Also no difference in clinical progress, weight gain, radiological improvement.	BTS	
220	Kim SYL, S. T.;Jeong, B. H.;Jeon, K.;Kim, J. W.;Shin, S. J.;Koh, W. J. Clinical significance of mycobacterial genotyping in Mycobacterium avium lung disease in Korea. International Journal of Tuberculosis & Lung Disease 2012;16(10):1393-9 doi: http://dx.doi.org/10.5588/ijtld.12.0147[published Online First: Epub Date]|.	cohort	2+	102	m. avium	nil	VNTR m. avium genotype cluster (A, B, C)	47-63 months	progression	rate of Rx initiation 35% A, 20% B, 13% C. NS. Low BMI (0.04) and sputum smear (0.01) associated in multivariate	No differences in outcome (treatment) or presentation of patients with M. avium based on 3 VNTR clusters (A-C). In a multivariate analysis low BMI and sputum smear were related	

Citation number	Bibliographic citation	Study type	Ev lev	Number of patients	Patient characteristics	Intervention	Comparison	Length of follow up	Outcome measures	Effect size	Source of funding	General Comments
224	Kitada SM, Ryoji;Toyoshima, Naomi;Naka, Takashi;Fujiwara, Nagatoshi;Kobayashi, Masami;Yano, Ikuya;Ito, Masami;Kobayashi, Kazuo. Use of glycopeptidolipid core antigen for serodiagnosis of mycobacterium avium complex pulmonary disease in immunocompetent patients. Clinical & Diagnostic Laboratory Immunology 2005;**12**(1):44-51	Case control	2+/-	X section (106 MAC , 11colonised, 30 kansasii 77 tb, 126 healthy) case control 27 MAC		treatment	sputum converted vs non converted	minimum 1 year	sputum converted vs non converted	anti body reduced in the siccessfully treated grp (p<0.001) but not other grp	University and national grants	Study assessing the use of antibodies (and esp IgA) vs a common glycopeptidolipid core antigen for MAC. Study consisted of a cross sectional part assessing patients with MAC disease and cf healthy control, MAC colonisation (only 11 pts in this group and defined by a single cultue which may be contamination rather than colonisation!), MTB, M kansasii showing higher values in MAC disease although likely the ROC curve findings are related predominantly to controls rather than the colonised group which would be the most important grp to differentiate. Other part of the study was a case control study where 27 patients had measuments before and after at least 1 year of treatment with reduction in the sputum converted but not the non converted grp. Statistical comparison within groups rather than between them. Also small numbers so not sure adequately powered. Further studies needed with follow up of patients with different antibody levels however relevant study for the guidelines
227	Kobashi YM, Toshiharu;Oka, Mikio. A double-blind randomized study of aminoglycoside infusion with combined therapy for pulmonary Mycobacterium avium complex disease. Respiratory medicine 2007;**101**(1):130-8	RCT	1+	146 MAC	MAC	RECl +streptomycin or placbo (73 in each grp)		24 months after conversion	sputum conversion, clinical effect, relapse	conversion 71.2% w Strep vs 50.7% w placebo. No change in relapse, clinical efficacy or adverse effect no (except 3 vertigo pts)	not stated	Double blind RCT demostrating some microbiological advantage in the use of Strep for first 3/12
231	Fujita MK, Akira;Tao, Yoshiaki;Miyazaki, Masayuki;Ouchi, Hiroshi;Harada, Eiji;Ikegame, Satoshi;Matsumoto, Takemasa;Uchino, Junji;Watanabe, Kentaro;Nakanishi, Yoichi. The clinical efficacy and safety of a fluoroquinolone-containing regimen for pulmonary MAC disease. Journal of Infection & Chemotherapy 2012;**18**(2):146-51	RCT	1-	27	MAC pts no previous treatment matched	R,E + either Gatifloxacin or CAM	Between groups	1 year	sputum conversion, clinical effect, long term	64.3% vs 84.6% sputum conversion, non significant. 4 dropouts (3 GAT, 1 CAM)	not stated	General comments: Reasonable design randomised study. No blinding and no power calculation leaving very small numbers iin each group. No differences between the groups found but likely no adequately powered
232	Miwa, S.;Shirai, M.;Toyoshima, M.;Shirai, T.;Yasuda, K.;Yokomura, K.;Yamada, T.;Masuda, M.;Inui, N.;Chida, K.;Suda, T.;Hayakawa, H.Efficacy of clarithromycin and ethambutol for Mycobacterium avium complex pulmonary disease. A preliminary studyAnnals of the American Thoracic Society2014	RCT	1-	119 (59 Recl, 60 ecl)	ATS NTM Pulmonary disease – no previous treatment – included cavitary disease in some pts	Eth, CL	RECL	12 months	sputum conversion a -3 consecutive negs. Treatment success -ve for 12/12	ITT 24/59 and 33/60 converted in the PP 24/32 and 33/40 in the 3 drug and 2 drug regimens respectively with high dropout rates.		CL and etham not inferior to REcl with respect to sputum conversion at 12/12 endpoint. However this was an unblinded study with significant dropouts in both arms with the PP likely to not be powered. Additionally the Cl doses were below the standard doses.
234	Kobashi YM, Toshiharu. The microbiological and clinical effects of combined therapy according to guidelines on the treatment of pulmonary Mycobacterium avium complex disease in Japan - including a follow-up study. Respiration 2007;**74**(4):394-400	cohort	2-	71	MAC	RECIstrep	dose of CAM	12 months	sputum conversion, clinical effect	71% conversion in 600mg grp, 44% in 400mg grp	not stated	***Not a useful study, prospective description of outcome according to guidelines and mention that pts with 600mg CAM had better sputum conversion than those with 400mg, however dose seems to have been determined by weight. 57.7% sputum conversion at 6/12 but also contained pts with clari resistance.***
238	Jeong, B. H.;Jeon, K.;Park, H. Y.;Kim, S. Y.;Lee, K. S.;Huh, H. J.;Ki, C. S.;Lee, N. Y.;Shin, S. J.;Daley, C. L.;Koh, W. J.Intermittent antibiotic therapy for nodular bronchiectatic Mycobacterium avium complex lung diseaseAmerican Journal of Respiratory & Critical Care Medicine2015	Retrospective cohort study	2-	217	Treatment-naïve noncavitatory nodular bronchiectasis MAC lung disease. Macrolide resistance excluded.	Daily (n=99) or intermittent (3 times weekly, n=118) that included clarithromycin, orazithromycin, rifampicin, ethambutol	Daily versus intermittent (3 times weekly) treatment	Daily 24.3 months, intermittent 16.6 months		Modification of treatment regimen more common with daily versus intermittent 46 vs 21%, P < 0.001, ethambutol especially in daily. Symptom and radiographic improvement, and sputum conversion the same.	Grant from Korean Ministry for Health and Welfare A120647	
240	Kobashi YA, Masaaki;Mouri, Keiji;Obase, Yasushi;Kato, Shigeki;Oka, Mikio. Relationship between clinical efficacy for pulmonary MAC and drug-sensitivity test for isolated MAC in a recent 6-year period. Journal of Infection & Chemotherapy 2012;**18**(4):436-43	cohort	2-	60	age 60, 35 avium, 25 intracellulare. 24 cases treated with lower CAM doses 05-07, 36 cases treated with higher doses 08-10	standard MAC RX with different CAM doses given over different time periods	sputum conversion, clinical effect. 24 cases treated with lower CAM doses 05-07, 36 cases treated with higher doses 08-10	1 year	sputum conversion, clinical effect	avium (81%vs64% conversion p<.05). Intracelulare 87% vs 60% p<.05). Clinical not signif	not stated	Some improved sputum converson with higher dose of macrolide but no difference in clinical effect. But 2 different time periods, different doses (400mg and 600mg in first period, 800mg in 2nd period), retrospective, overall poor study
241	Hasegawa N, Nishimura T, Ohtani S, et al. Therapeutic effects of various initial combinations of chemotherapy including clarithromycin against Mycobacterium avium complex pulmonary disease. Chest 2009;**136**(6):1569-75	cohort	2+/-	34	MAC pts no previous treatment	3 different regimens CAM 400 or 800, R/E 2/12 induction or not	sputum conversion	18 months	sputum conversion	91.7 cpnversion at 18/12 in group B (higher CAM dose) compared to 55.6 group A (lower CAM dose)	not stated	Some improved sputum converson with higher dose of macrolide. But 3 different time periods, retrospective, small group sizes
276	Varadi RGM, T. K. Pulmonary Mycobacterium xenopi infection in non-HIV-infected patients: a systematic review. International Journal of Tuberculosis & Lung Disease 2009;**13**(10):1210-8	Systematic review	1-	1255	Generally middle aged men with a history of obstructive lung disease or prior TB, presenting with upper lobe cavitation.	34 distinct drug regimens in 188 subjects	Variable	Variable	Variable	Could not demonstrate any advantage of specific drugs in treatment of pulmonary M. xenopi infection. However, regimens containing fluoroquinolones were associated with a significantly greater proportion of relapse free success; and a significantly lower proportion of short-term and sustained successes were seen after treatment with regimens including isoniazid or aminoglycosides. Unclear if this reflects that more severe patients being more likely to receive an injectable agent.	Not declared	
291	MACGAM Study Group.Adjuvant interferon gamma in patients with pulmonary atypical Mycobacteriosis: A randomized, double-blind, placebo-controlled study.BMC Infectious Diseases 2008, 8:17	RCT	1-	Eighteen patients were included in the IFN group and 14 received placebo. BUT 13 iFN and 8 placebo completed trial	Groups were homogeneous at entry; average age was 60 years, 75% men, 84% white (more white in IFN arm); More smokers in non-IFN arm. More advanced disease in non-IFN arm. MAC infection prevailed (94%). ATS criteria applied.	adjuvant IFN-G	IFN-G vs no IFN-G	18 months	The main efficacy outcome was an overall response that integrated clinical, bacteriological and radiological results, at the end of treatment (month 6) and after 12 additional months of follow-up (month 18). This composite variable was considered as complete if all symptoms disappeared, sputum acid-fast-bacilli smear and culture were negative, and X-ray pulmonary lesions improved.	83% 'responders' in IFN-G arm vs 35.7% in no IFN-G arm	The authors received free drug (IFN gamma) from Heber Biotec, Havana, Cuba. The Ministry of Public Health of Cuba took care of hospital facilities and medical attention of the patients, including diagnostic procedures and the rest of the medicaments.	Small study, best regarded as experimental. Composite end-point debatable. High drop-out 9 13 and 8 patients completed trial.
328	BM Knoll, S Kappagoda, RR Gill, et al.Non-tuberculous mycobacterial infection among lung transplant recipients: a 15 year cohort study. Transplant Infectious Diseases 2012;14:452-460.	cohort study	2+	53 cases from a cohort of 237 lung transplant recipients	cases developing NTM infection after lung transplantation	antibiotic therapy	survival and morbidity	median 25 months	N/A	N/A	Not Attributed	General Comments: Single centre cohort study. 22.4% of post transplant patients isolated NTM. Commonest organism was MAC in 69.8% then M.Abscessus in 9.4% and M.Gordonae in 7.5%. 6 of the 53 fulfilled criteria for NTM disease whereas others had evidence of colonisation only. 1 of these 6 died and 3 had persistent disease, one was cured and 1 developed colonisation but no further disease. 5 patients had pre-tx colonisation with MAC (4) and Scrofulaceum(1), 3 of these 5 did not grow NTM post transplant.

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330	W Chalermskulrat, N Sood, IP Neuringer et al. Non-tuberculous mycobacteriua in end stage cystic fibrosis: implications for lung transplantation. Thorax 2006;61:507-513.	cohort study	2+	177 patients with CF waiting for lung tranpslant, 144 of which were transplanted	effect of NTM infections in pre and post transplant patients with cystic fibrosis	antibiotic therapy	survival and morbidity	up to 7 years	N/A	N/A	CF Foundation NIH	General Comments: large single centre experienceover a 13 year period.19.7% of CF patients had NTM positive cultures pre-transplant. MAC and M.Abs were commonest with 45% and 41% of isolates. Those with NTM pre-transplant had an odds ratio of 5.03 of growing NTM post transplant. 25% of those with post-tx NTM developed invasive disease this was mainly limited to M.Abs. Overall survival in NTM group after transplant was similar to non NTM group. None of the patients who developed NTM de novo post transplant developed invasive disease. 7 cases reported of outcomes for patients pre-colonised with M.Abs, in 5/7 organism was grown post transplant. 2/7 developed wound infections which were successfully treated with antibiotics.
335	Lobo LJ, Chang LC, Esther CR et al. Lung transplant outcomes in cystic fibrosis patients with pre-operative Mycobacterium abscessus respiratory infections. Clinical Transplantation 2013; 27(4): 523-9.	cohort study	2+	13 patients with M.Abs prior to transplant	Adult CF patients	NA	survival and morbidity		N/A	N/A	Not Attributed	General Comments: 13 patients with CF who were infected with M.Abscessus prior to lung transplantation. Only 3 individuals in the cohort developed post-operative complications due to M.Abscessus and all responded to prolonged antibiotic therapy. The overall survival in this group of 13 was 50% at 5 years and was not statistically different to a contemporaneous cohort of lung transplant recipients without M.Abscessus infection.

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