

| Citation number | Bibliographic citation                                                                                                                                                                                                                                                                                                                                     | Study type                                                                                                                                                                                                                | Ev lev | Number of patients                                                          | Patient characteristics                                                                                                            | Intervention  | Comparison                                                                                                                                                                                                    | Length of follow up           | Outcome measures                                                                                | Effect size                                                                                                                                                                                                      |
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| 39              | Bryant CE, Grogono DM, Rodriguez-Rincon D. Population-level genomics identifies the emergence and global spread of a human transmissible multidrug-resistant nontuberculous mycobacterium. <i>Science</i> 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 clinical outcome, antibiotic resistance, and fulfilling ATS criteria                                                            | Variably between 2 - 10 years | clinical outcome, antibiotic resistance, and fulfilling ATS criteria                            | Worse clinical outcomes and increases levels of antibiotic resistance. Evidence that most clinical isolates are from clusters of M. abscessus representing dominant circulating clones that have spread globally |
| 123             | Steingart KR, Henry M, Ng V, et al. Fluorescence versus conventional sputum smear microscopy for tuberculosis: a systematic review. <i>The Lancet. Infectious diseases</i> 2006;6 (9):570-81 doi: 10.1016/S1473-3099(06)70578-3[published Online First: Epub Date].                                                                                        | Not clear this study is relevant to NTM, although relevant for TB, as only relates to M tuberculosis and explicitly excludes NTM.                                                                                         | 1-     | > 52,000                                                                    | Various, HIV, non HIV, low/high incidence TB countries                                                                             | Nil           | Fluorescence v conventional sputum smear microscopy                                                                                                                                                           | Not appropriate               | Not appropriate                                                                                 | Average 10% more sensitive than conventional microscopy (p<0.001). Specificity similar to conventional microscopy (0% p=0.21)                                                                                    |
| 124             | 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. <i>Memorias do Instituto Oswaldo Cruz</i> 2000;95(6):855-8                                                                                                                                          | Study of TB no mention of NTM.                                                                                                                                                                                            | 2+     | 295 patients                                                                | Turkey 1998-2000. No details on patient characteristics esp HIV.                                                                   | Nil           | Culture 6 weeks only on LJ slopes v fluorochrome 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.                                                                                                                                                  |
| 126             | Murray SJ, Barrett A, Magee JG, et al. Optimisation of acid fast smears for the direct detection of mycobacteria in clinical samples. <i>Journal of clinical pathology</i> 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 positive sputa                                                   | UK cohort (Newcastle MRU)                                                                                                          | none          | Fluorescence v Ziehl-Neelsen staining, after EACH step of processing.                                                                                                                                         | Not appropriate               | Culture v each microscopy method                                                                | Description is that AP was significantly better than ZN with all pretreatment regimens and difference between pretreatment regimens were also significant. P> 0.01 for all differences.                          |
| 139             | Hanna BA, Ebrahimzadeh A, Elliott LB, et al. Multicenter evaluation of the BACTEC MGIT 960 system for recovery of mycobacteria. <i>Journal of clinical microbiology</i> 1999;37(3):748-52                                                                                                                                                                  | Multicenter 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, Lowenstein-Jensen and Middlebrook 7H11/selective plates.                                                                                                                     | Not appropriate               | Each medium type with all others including solids.                                              | See general comments                                                                                                                                                                                             |
| 142             | Brown-Elliott BA, Wallace RJ, Jr. Clinical and taxonomic status of pathogenic nonpigmented or late-pigmenting rapidly growing mycobacteria. <i>Clinical microbiology reviews</i> 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                                                                                                                                                                                             |
| 151             | 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. <i>Journal of clinical microbiology</i> 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 algorithm drawn up based on 43 isolates' peaks | 40 epidemiologically unrelated M. abscessus from French patients - CF, blood cluteres, BAL, id by Hain CM assay and 3 ref strains. | Nil Clinical. | None. 43 strains of M abscessus 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 ballettii.                                                                                                       |
| 152             | 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. <i>Journal of clinical microbiology</i> 2015;53(8):2737-40 doi: 10.1128/JCM.01380-15[published Online First: Epub Date]         | Spanish comparison of isolates. 16S rRNA/hsp65 sequencing gold standard v MALDI-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 MALDI-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. Mald agreed better than Hain in 17 (13.6% of results. P=0.002)                                            |
| 196             | Kitada SU, T.Yoshimura, K.;Tateishi, Y.;Miki, K.;Miki, M.;Hashimoto, H.;Fujikawa, T.;Mori, M.;Matsuuura, K.;Kuroyama, M.;Maekura, R. Long-term radiographic outcome of nodular bronchiectatic Mycobacterium avium complex pulmonary disease. <i>International Journal of Tuberculosis &amp; Lung Disease</i> 2012;16(5):660-4                              | case control                                                                                                                                                                                                              | 2-     | 72                                                                          | nodular bronchiectasis MAC                                                                                                         | nil           | progressive vs non progressive based on CXR outcome                                                                                                                                                           | 25 years                      | CXR change                                                                                      | lower BMI cavitatdry disease and macrolide resistance associated with progression                                                                                                                                |

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| 213             | 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. |
| 214             | 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.                                                                                                                                                                                                                                    |
| 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 224             | Kitada SM, Ryoji-Toyoshima, Naomi,Naka, Takachi,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 kansasi 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 successfully treated grp (p<0.001) but not other grp                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 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                                                                                                                                                                                                           | RECI +streptomycin or placebo (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)                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 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)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 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 study Annals of the American Thoracic Society 2014                          | 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.                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| 238             | Jeong, B. H., Jeon, K., Park, H. Y., Kim, S. Y., Lee, K. S., Huh, H. J., Ji, C. S., Lee, N. Y., Shin, S. J., Daley, C. L., Koh, W. J. Intermittent antibiotic therapy for nodular bronchiectatic Mycobacterium avium complex lung disease American Journal of Respiratory & Critical Care Medicine 2015                               | Retrospective cohort study | 2-     | 217                                                                               | Treatment-naive noncavitary 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.                                                                                                                                                                                                                                                                                                                                                                                             |

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|-----------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|--------|--------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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). Intracellulare 87% vs 60% p<.05). Clinical not signif                                                                                                                                                                                                                                                                                                                                                                                                            |
| 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)                                                                                                                                                                                                                                                                                                                                                                                                     |
| 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. |
| 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                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 330             | W Chalermkulrat, N Sood, IP Neuringer et al. Non-tuberculous mycobacteria in end stage cystic fibrosis: implications for lung transplantation. Thorax 2006;61:507-513.                                                                                         | cohort study      | 2+     | 177 patients with CF waiting for lung transplant, 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |