Nichttuberkulöse Mycobacteriosen

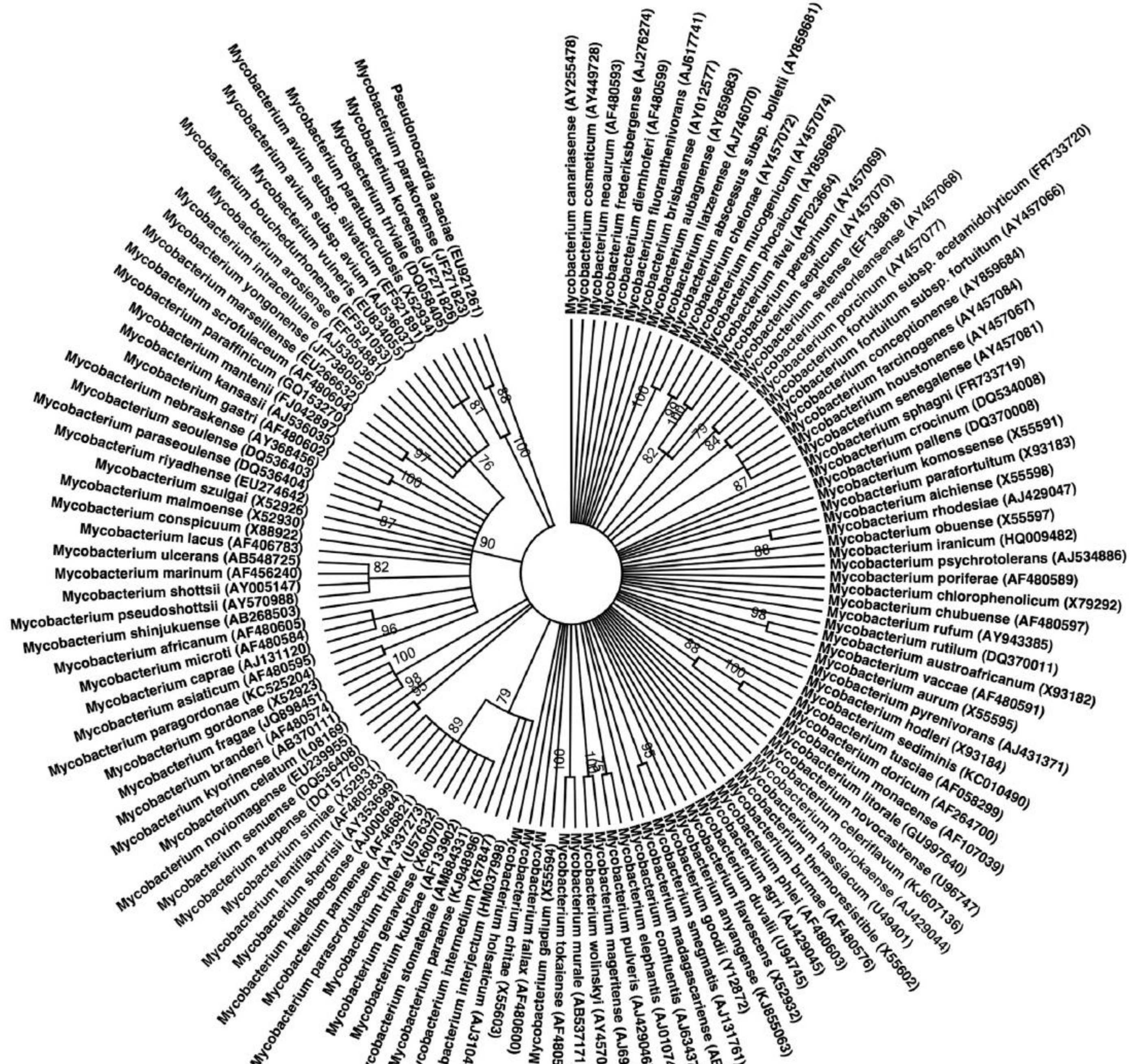
Andreas Schmid

KU MEDICAL CENTER
The University of Kansas


gitsdrschi


R U OK?™


Are you ok?



Mycobacterium canariasense (AY255478)
Mycobacterium cosmeticum (AY449728)
Mycobacterium neoaurum (AF480593)
Mycobacterium frederiksbergense (AJ276274)
Mycobacterium diernhoferi (AF480599)
Mycobacterium fluoranthenivorans (AJ617741)
Mycobacterium brisbanense (AY012577)
Mycobacterium aubagnense (AY859683)
Mycobacterium llatzerense (AJ746070)
Mycobacterium abscessus subsp. bolletii (AY859681)
Mycobacterium chelonae (AY457072)
Mycobacterium mucogenicum (AY457074)
Mycobacterium phocaicum (AY859682)
Mycobacterium alvei (AF023664)
Mycobacterium peregrinum (AY457069)
Mycobacterium septicum (AY457070)
Mycobacterium setense (EF138818)
Mycobacterium neworleansense (AY457068)
Mycobacterium porcinum (AY457077)
Mycobacterium fortuitum subsp. acetamidolyticum (FR733720)
Mycobacterium fortuitum subsp. fortuitum (AY457066)
Mycobacterium conceptionense (AY859684)
Mycobacterium farcinogenes (AY457084)
Mycobacterium houstonense (AY457067)
Mycobacterium senegalense (AY457081)
Mycobacterium sphagni (FR733719)
Mycobacterium crocinum (DQ534008)
Mycobacterium pallens (DQ370008)
Mycobacterium komossense (X55591)
Mycobacterium parafortuitum (X93183)
Mycobacterium aichiense (X55598)
Mycobacterium rhodesiae (AJ429047)
Mycobacterium obuense (X55597)
Mycobacterium iranicum (HQ009482)
Mycobacterium psychrotolerans (AJ534886)
Mycobacterium poriferae (AF480589)
Mycobacterium chlorophenolicum (X79292)
Mycobacterium chubuense (AF480597)
Mycobacterium rufum (AY943385)
Mycobacterium rutilum (DQ370011)
Mycobacterium austroafricanum (X93182)
Mycobacterium vaccae (AF480591)
Mycobacterium aurum (X55595)
Mycobacterium pyrenivorans (AJ431371)
Mycobacterium hodleri (X93184)
Mycobacterium sediminis (KC010490)
Mycobacterium tusciae (AF058299)
Mycobacterium doricum (AF264700)
Mycobacterium monacense (AF107039)
Mycobacterium litorale (GU997640)
Mycobacterium novocastrense (U96747)
Mycobacterium celeriflavum (KJ607136)
Mycobacterium moriokaense (AJ429044)
Mycobacterium hassiacum (U49401)
Mycobacterium thermoresistible (X55602)
Mycobacterium brumae (AF480576)
Mycobacterium phlei (AF480603)
Mycobacterium agri (AJ429045)
Mycobacterium duvalii (U94745)
Mycobacterium flavescens (X52932)
Mycobacterium anyangense (KJ855063)
Mycobacterium goodii (Y12872)
Mycobacterium smegmatis (AJ131761)
Mycobacterium madagascariense (AB537170)
Mycobacterium confluentis (AJ634379)
Mycobacterium elephantis (AJ010747)
Mycobacterium pulveris (AJ429046)
Mycobacterium mageritense (AJ699399)
Mycobacterium wolinskyi (AY457083)
Mycobacterium murale (AB537171)
Mycobacterium tokaiense (AF480590)
Mycobacterium gadium (X55594)
Mycobacterium fallax (AF480600)
Mycobacterium chitae (X55603)
Mycobacterium holsaticum (HM037998)
Mycobacterium interjectum (AJ310467)
Mycobacterium intermedium (X67847)
Mycobacterium paraense (KJ948996)
Mycobacterium stomatepiae (AM884331)
Mycobacterium kubicae (AF133902)
Mycobacterium genavense (X60070)
Mycobacterium triplex (U57632)
Mycobacterium parascrofulaceum (AY337273)
Mycobacterium parmense (AF466821)
Mycobacterium heidelbergense (AJ000684)
Mycobacterium sherrisii (AY353699)
Mycobacterium lentiflavum (AF480583)
Mycobacterium simiae (X52931)
Mycobacterium arupense (DQ157760)
Mycobacterium senuense (DQ536408)
Mycobacterium noviomagense (EU239955)
Mycobacterium celatum (L08169)
Mycobacterium kyorinense (AB370111)
Mycobacterium branderi (AF480574)
Mycobacterium fragae (JQ898451)
Mycobacterium gordonae (X52923)
Mycobacterium paragordonae (KC525204)
Mycobacterium asiaticum (AF480595)
Mycobacterium caprae (AJ131120)
Mycobacterium microti (AF480584)
Mycobacterium africanum (AF480605)
Mycobacterium shinjukuense (AB268503)
Mycobacterium pseudoshottsii (AY570988)
Mycobacterium shottsii (AY005147)
Mycobacterium marinum (AF456240)
Mycobacterium ulcerans (AB548725)
Mycobacterium lacus (AF406783)
Mycobacterium conspicuum (X88922)
Mycobacterium malmoense (X52930)
Mycobacterium szulgai (X52926)
Mycobacterium riyadhense (EU274642)
Mycobacterium paraseoulense (DQ536404)
Mycobacterium seoulense (DQ536403)
Mycobacterium nebraskense (AY368456)
Mycobacterium gastri (AF480602)
Mycobacterium kansasii (AJ536035)
Mycobacterium mantenii (FJ042897)
Mycobacterium paraffinicum (GQ153270)
Mycobacterium scrofulaceum (AF480604)
Mycobacterium marseillense (EU266632)
Mycobacterium yongonense (JF738056)
Mycobacterium intracellulare (AJ536036)
Mycobacterium arosiense (EF054881)
Mycobacterium bouchedurhonense (EF591053)
Mycobacterium vulneris (EU834055)
Mycobacterium avium subsp. avium (AJ536037)
Mycobacterium avium subsp. silvaticum (EF521891)
Mycobacterium paratuberculosis (X52934)
Mycobacterium triviale (DQ058405)
Mycobacterium koreense (JF271826)
Mycobacterium parakoreense (JF271823)
Pseudonocardia acaciae (EU921261)

NTM: Non-Tuberculous Mycobacteria

Who is NTM

- All species of mycobacteria (about 200)

EXCEPT

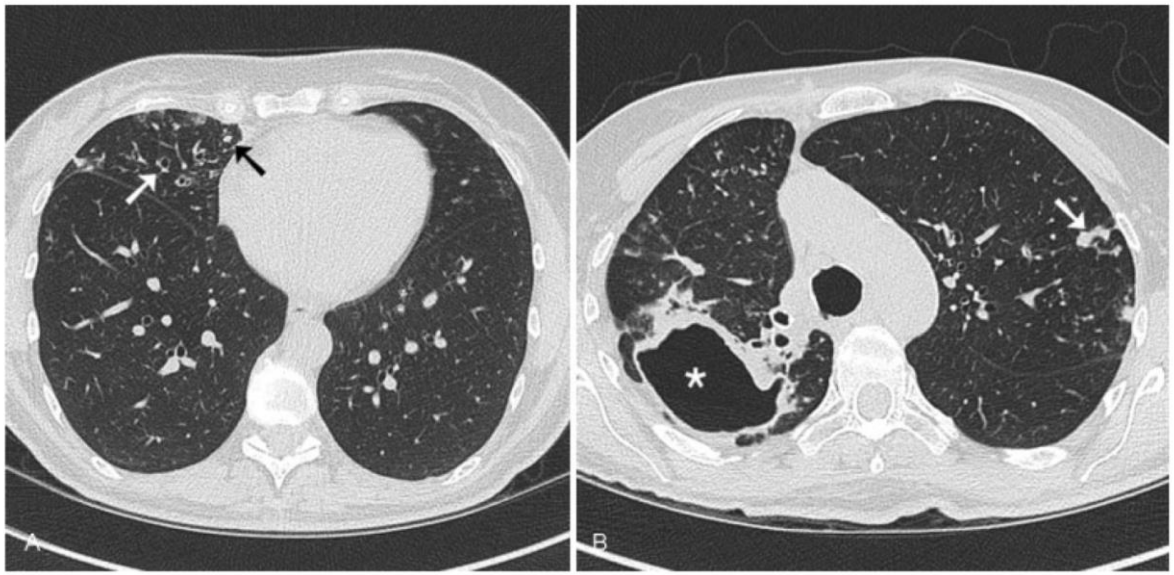
- Mycobacteria that cause tuberculosis
  - M. tuberculosis, M. bovis and M. africanum in human
- Mycobacteria that cause leprosy
  - M. leprae

Typical clinical presentations

- Chronic pulmonary disease
- Lymphadenitis
- Cutaneous disease
- Disseminated disease

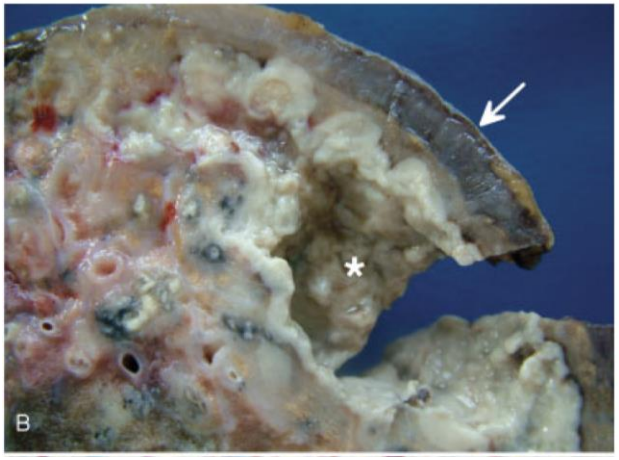
Types of pulmonary NTM

nodular bronchiectatic

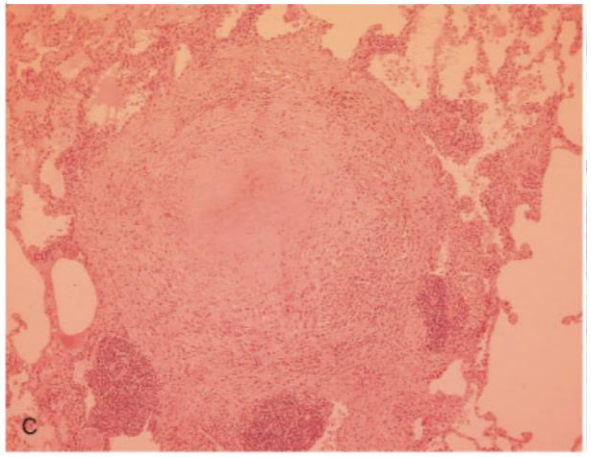


Fibro-cavitary

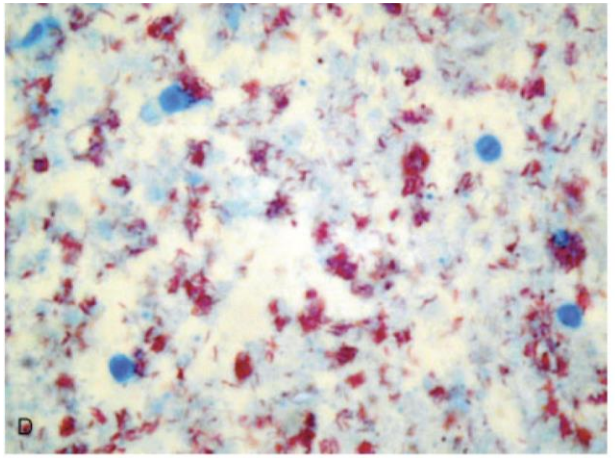
Seminars in Respiratory and Critical Care Medicine Vol. 39 No. 3/2018



Macroscopic pathology RUL



Necrotizing granuloma



Ziehl Neelsen stain

ATS criteria for pulmonary NTM DISEASE

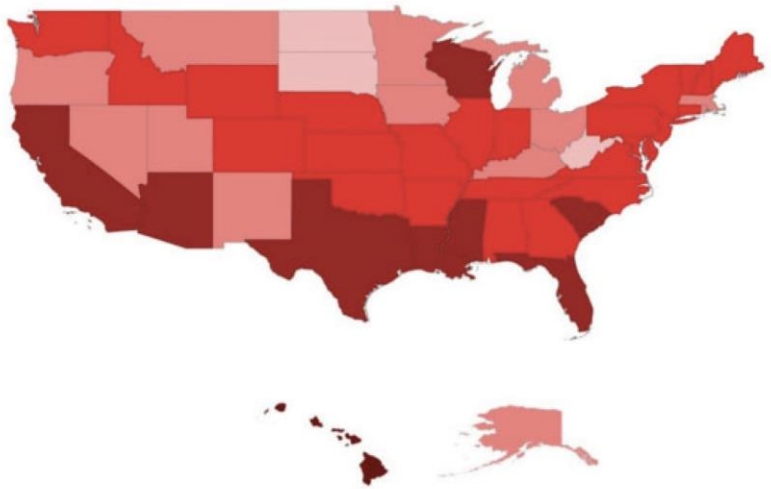
Microbiological	Positive culture from ≥ 2 sputum samples **or** Positive culture form bronchoalveolar lavage or wash **or** Lung biopsy with compatible histology *and* positive culture from biopsy or sputum sample
Radiological	Nodular or cavitary opacities on chest radiograph **or** Multifocal bronchiectasis and multiple small nodules on HRCT chest
Clinical	Compatible symptoms **and** Exclusion of alternative diagnoses

Abbreviations: HRCT, high-resolution computed tomography; NTM, nontuberculous mycobacterial.

Semin Respir Crit Care Med 2018;39:343–350.

Epidemiology for pulmonary NTM in USA

- Annual prevalence in USA 1.4 to 13.9 per 100’000
  - Up to 44% in Hawaii
- Depends on region, sex and ethnicity
  - Increased for women
  - Increased for Asian
  - Increased Southern United States USA and Hawaii
- Reported to increase 3 to 8% per year

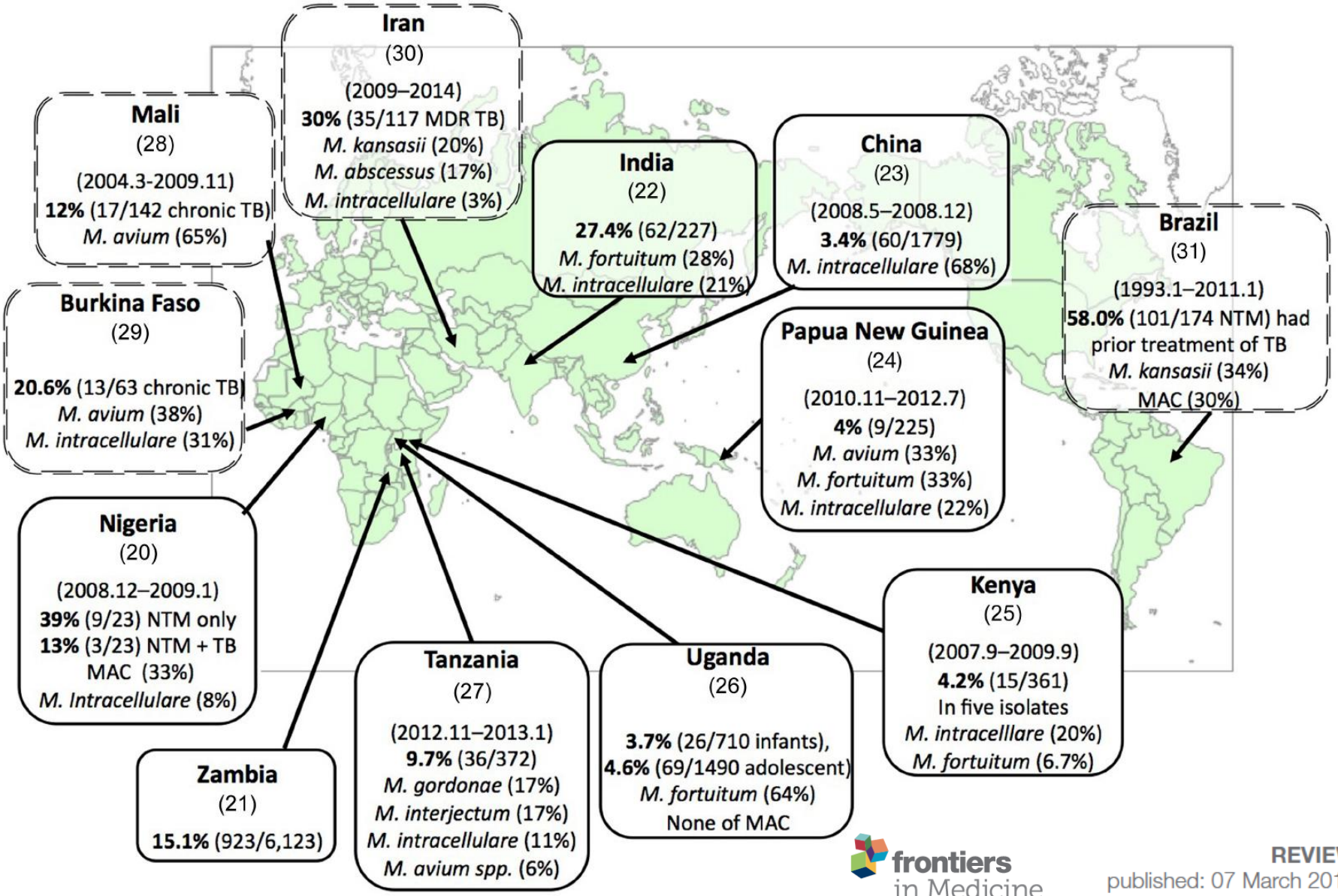


NTM cases/100’000
in patient older then 65

- 0-26
- 27-77
- 78-131
- 132-192
- 193-396

Semin Respir Crit Care Med 2018;39:325–335.

NTM around the world



frontiers in Medicine
REVIEW
published: 07 March 2017
doi: 10.3389/fmed.2017.00027

Reason for increased prevalence NTM

- Decreased rates of mycobacteria infection with possible decreased population immunity
- Increased exposure through more decreased temperatures in home water heaters
- Increased exposure to shower aerosols
- Increased long – term antibiotic use in inflammatory lung disease (bronchiectasis, CF) creating favorable niche for NTM (changes in microbiome)
- More use of medications that might impair host immunity (macrolides) Possibly by blocking autophagic killing of NTM in macrophages
- Questionable person to person transmission

Haworth CS, *et al*. *Thorax* 2017;**72**:ii1–ii64.

Predispositions for NTM infections

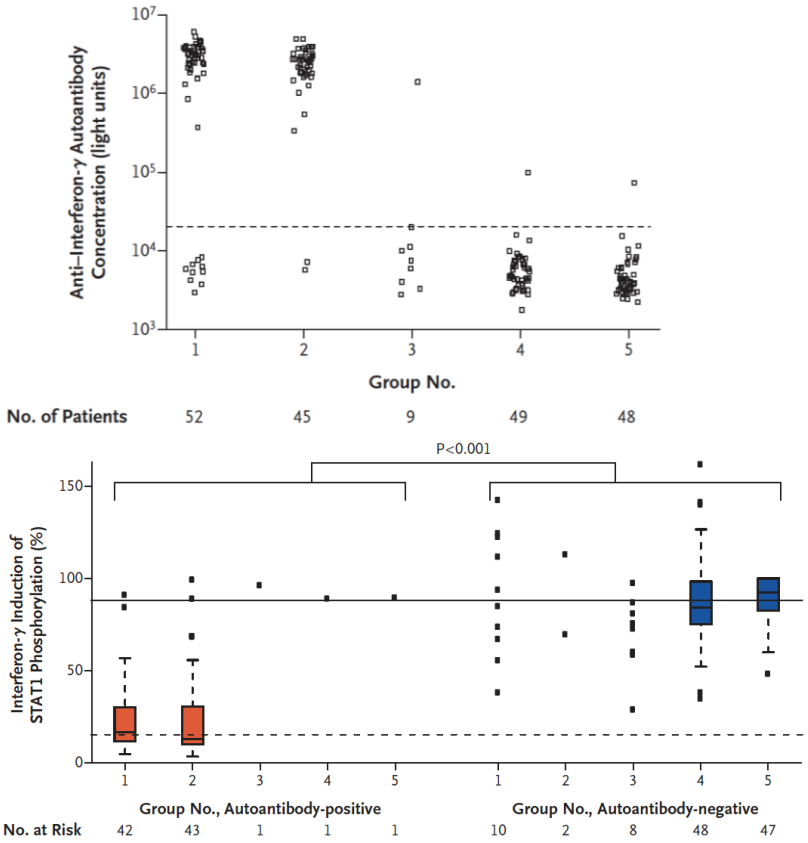
- Chronic lung disease with decreased mucociliary clearance
  - (COPD, asthma, bronchiectasis, A1ATD, CF, PCD, ABPA)
- Gastroesophageal Reflux disease
- Low BMI
- Immunodeficiency
- Immunosuppression
  - steroids
  - TNFa inhibition
  - s/p organ transplant
  - Chemotherapy for cancer
  - HIV/AIDS
- Inhaled antibiotics (change of bacterial microbiome)
- Proton Pump Inhibitors (decreased acidity in stomach)

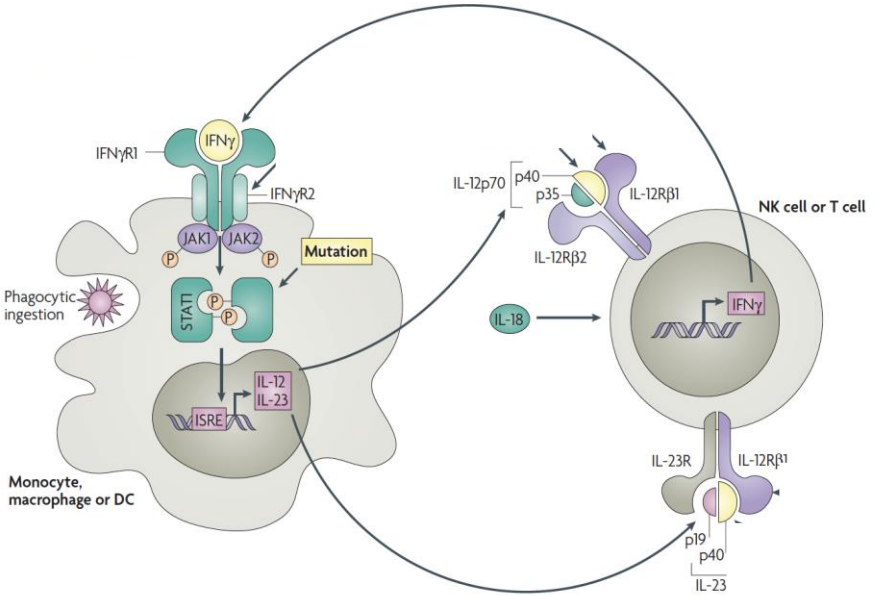
Haworth CS, *et al*. *Thorax* 2017;**72**:ii1–ii64.

IFNγ autoantibodies

203 patient in 5 groups

1: disseminated NTM infection
2: other opportunistic infection ± NTM
3: disseminated tuberculosis
4: pulmonary tuberculosis
5: healthy controls

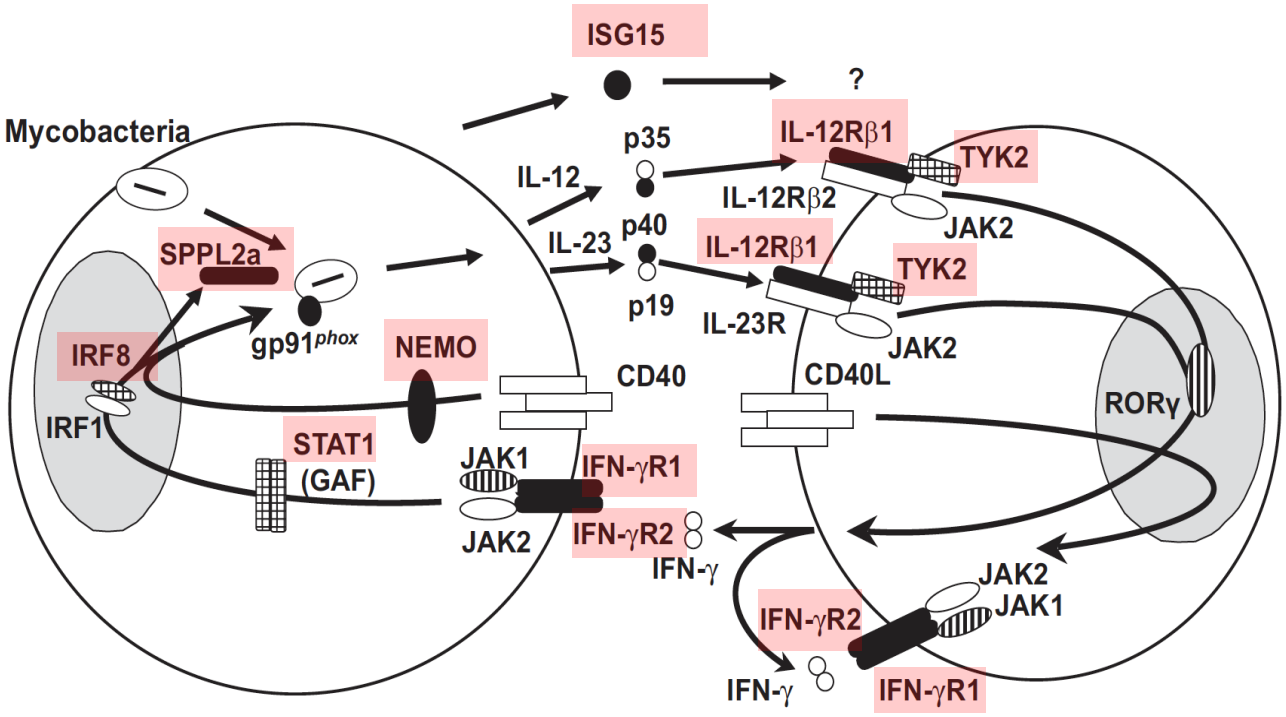


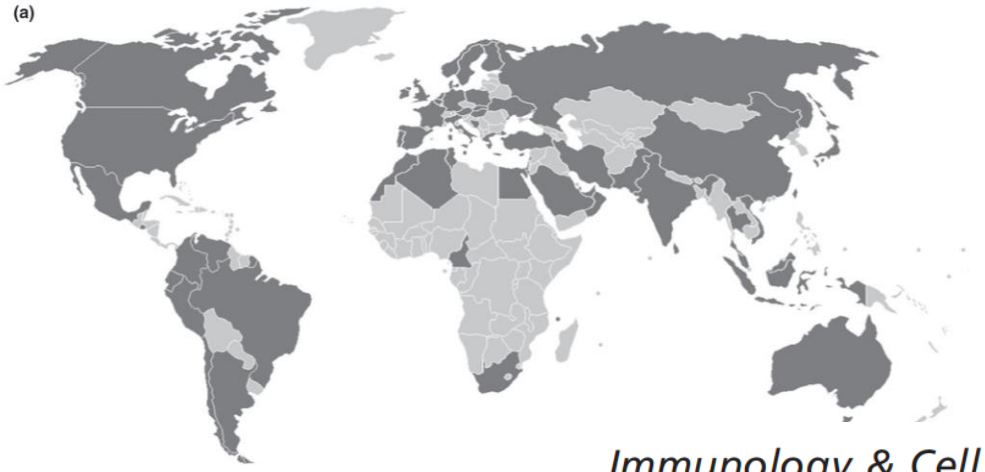


Nature reviews Immunology 2007:7;851-61

N ENGL J MED 367;8 NEJM.ORG AUGUST 23, 2012

Mendelian susceptibility to mycobacteria





Immunology & Cell Biology 2018; 1–8

Salmeterol and Fluticasone Propionate and Survival in Chronic Obstructive Pulmonary Disease

NEJM 2007;356(8).

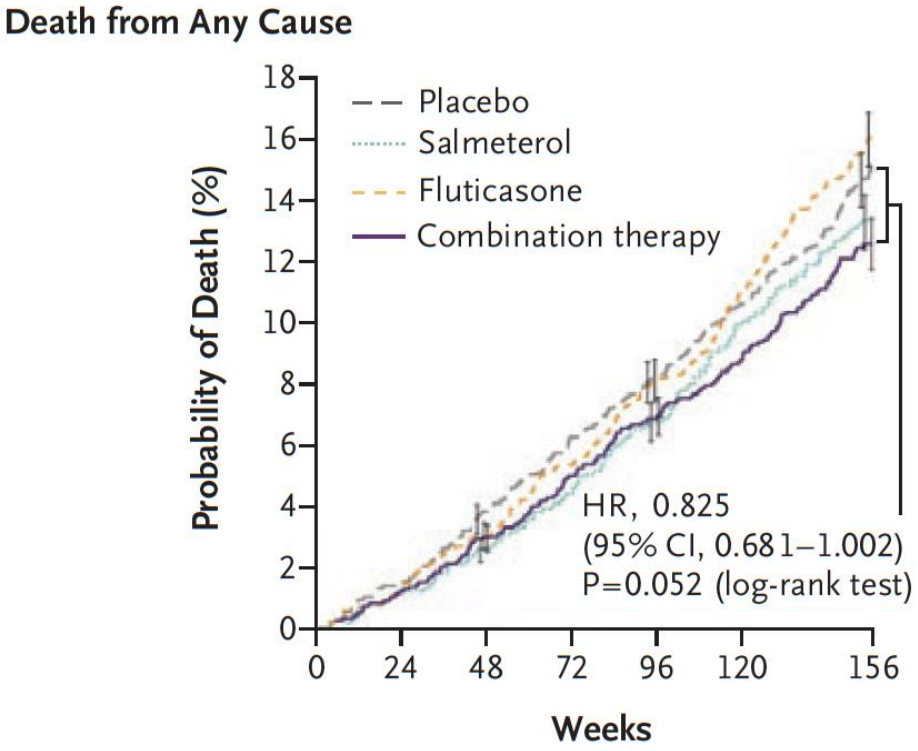
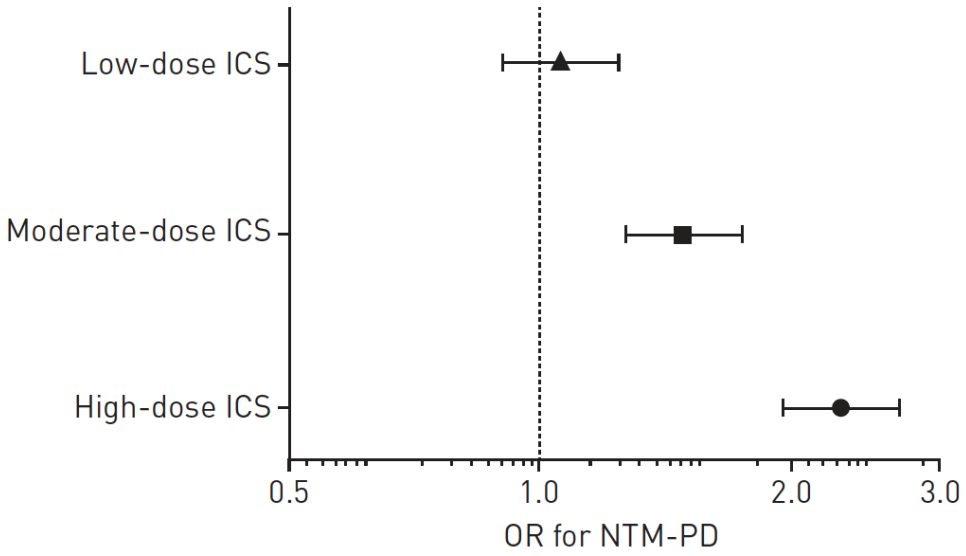


Table 4. Adverse Events among 6184 Patients in the Safety Population and 658 Patients in the Substudy of Bone Mineral Density.

Adverse Event	Placebo Group (N=1544)	Salmeterol Group (N=1542)	Fluticasone Group (N=1552)	Combination-Therapy Group (N=1546)
Of specific interest during treatment — % of patients*				
Pneumonia	12.3	13.3	18.3†	19.6‡

The risk of mycobacterial infections associated with inhaled corticosteroid use

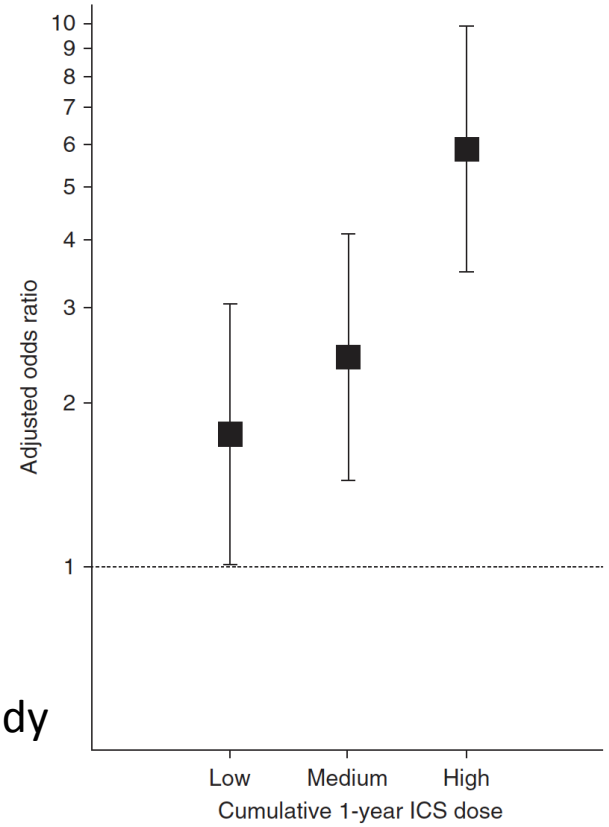
Eur Respir J 2017; 50: 1700037



Association between Inhaled Corticosteroid Use and Pulmonary Nontuberculous Mycobacterial Infection

Vincent X. Liu[1,2], Kevin L. Winthrop[3], Yun Lu[1], Husham Sharifi[4], Hekmat U. Nasiri[2], and Stephen J. Ruoss[4]

AnnalsATS Volume 15 Number 10 | October 2018



case-control study

National Jewish Health®
Science Transforming Life®

LABORATORY TEST RESULTS

1400 Jackson Street
Denver, Colorado 80206
www.njlabs.org
ClinRefLabs@njhealth.org

House samples

ENVIRONMENTAL WATER SAMPLE
YELLOW BATHROOM SHOWER
08/07/2019

Mycobacterium massiliense identified by gel analysis for erm(41) gene product and sequence analysis for hsp65 gene.
09/14/2016 (TECH 702)

ENVIRONMENTAL SAMPLE
KITCHEN
08.07.2016

MYCOBACTERIUM CHIMAERA IDENTIFIED BY RPOB GENE SEQUENCING.
09/07/2016 TECH 439

MYCOBACTERIUM PHOCAICUM IDENTIFIED BY RPOB GENE SEQUENCING.
09/08/2016 TECH 439

ENVIRONMENTAL SAMPLE
YELLOW BATHROOM SINK
08.07.2016

MYCOBACTERIUM GORDONAE IDENTIFIED BY RPOB GENE SEQUENCING.
09/07/2016 TECH 439

Mycobacterium massiliense identified by gel analysis for erm(41) gene product and sequence analysis for hsp65 gene.
09/14/2016 (TECH 702)

ENVIRONMENTAL SAMPLE
BLUE BATHROOM SINK, FLORIDA ROOM
08.07.2016

MYCOBACTERIUM, MOST CLOSLEY RELATED TO MYCOBACTERIUM PHOCAICUM IDENTIFIED BY RPOB GENE SEQUENCING.
09/07/2016 TECH 439

MYCOBACTERIUM GORDONAE IDENTIFIED BY RPOB GENE SEQUENCING.
09/29/2016 TECH 277

ENVIRONMENTAL SAMPLE
GUEST ROOM BATH

MYCOBACTERIUM GORDONAE IDENTIFIED BY RPOB GENE SEQUENCING.
09/07/2016 TECH 439

MYCOBACTERIUM MUCOGENICUM IDENTIFIED BY RPOB GENE SEQUENCING.
09/13/2016 TECH 777

ENVIRONMENTAL SAMPLE
INITIAL SUBMISSION OF COMBINED HOUSE WATER
800 ML SUBMITTED
07/05/2016

MYCOBACTERIUM CHIMAERA IDENTIFIED BY RPOB GENE SEQUENCING.
08/11/2016 TECH 439

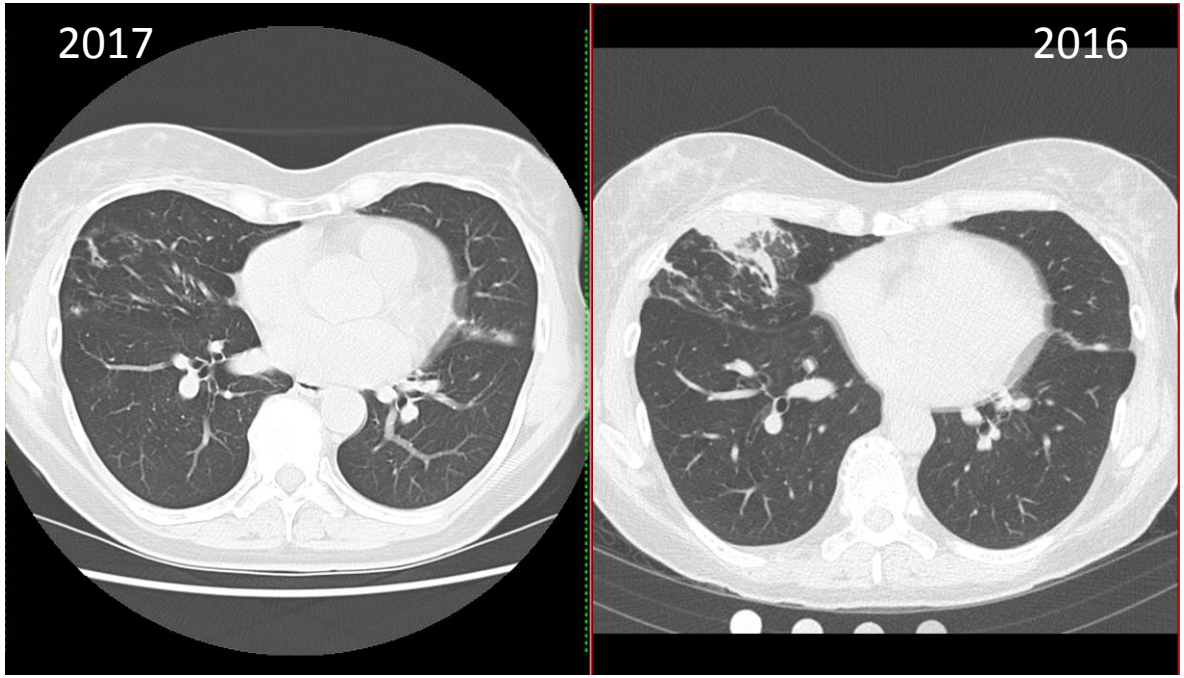
Patient samples

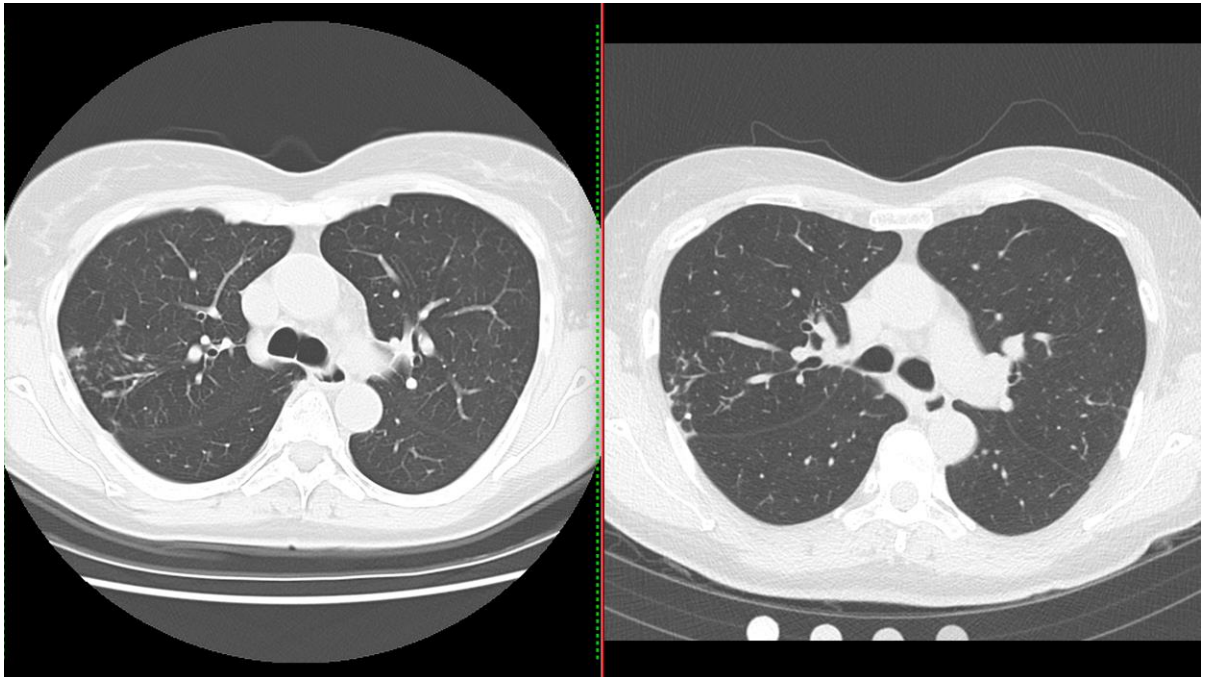
SPUTUM
06.23.2016

MYCOBACTERIUM CHIMAERA IDENTIFIED BY RPOB GENE SEQUENCING.
03/09/2016

SPUTUM
08.24.2016

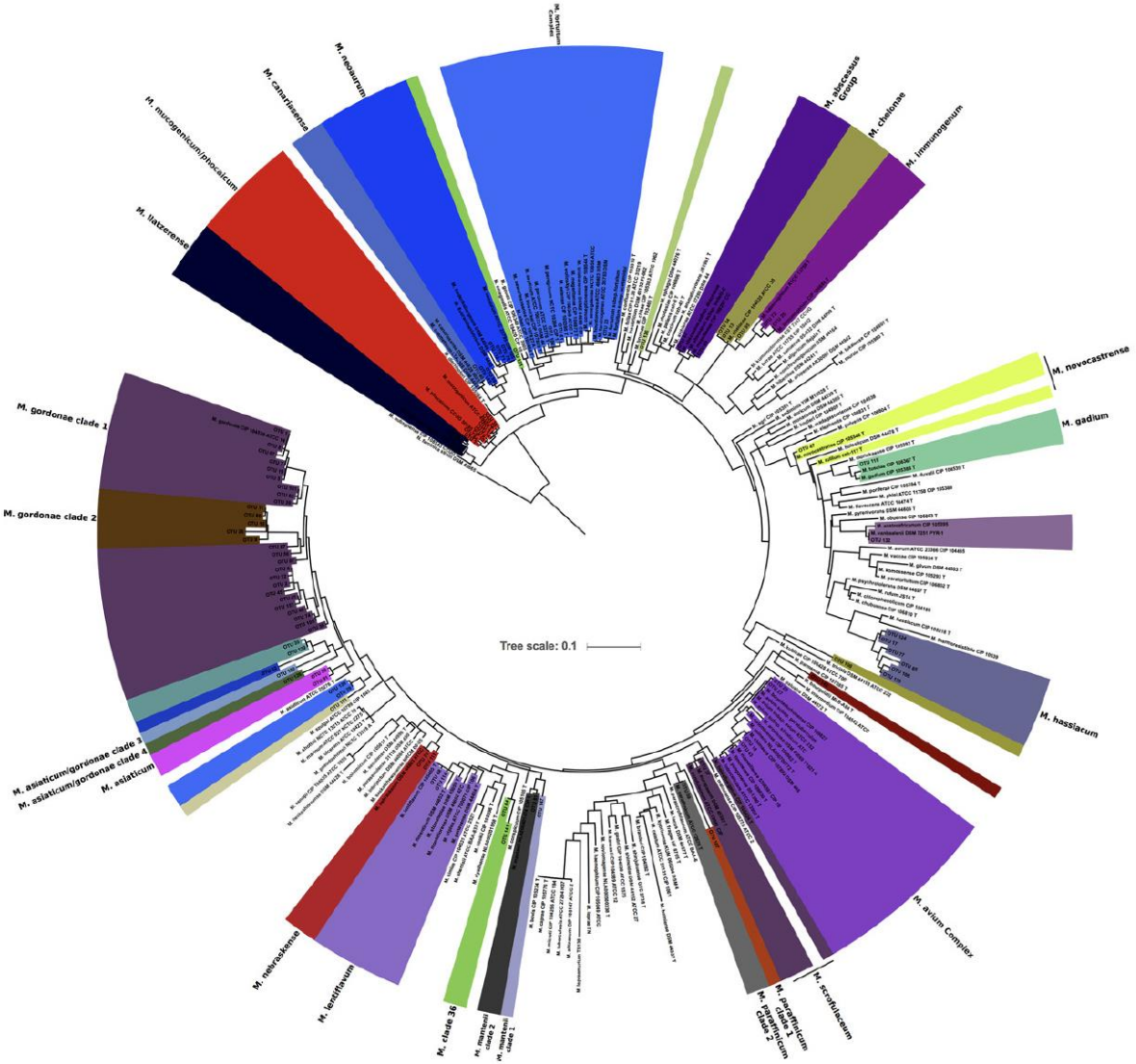
MYCOBACTERIUM AVIUM IDENTIFIED BY RPOB GENE SEQUENCING.
09/14/2016 TECH 439

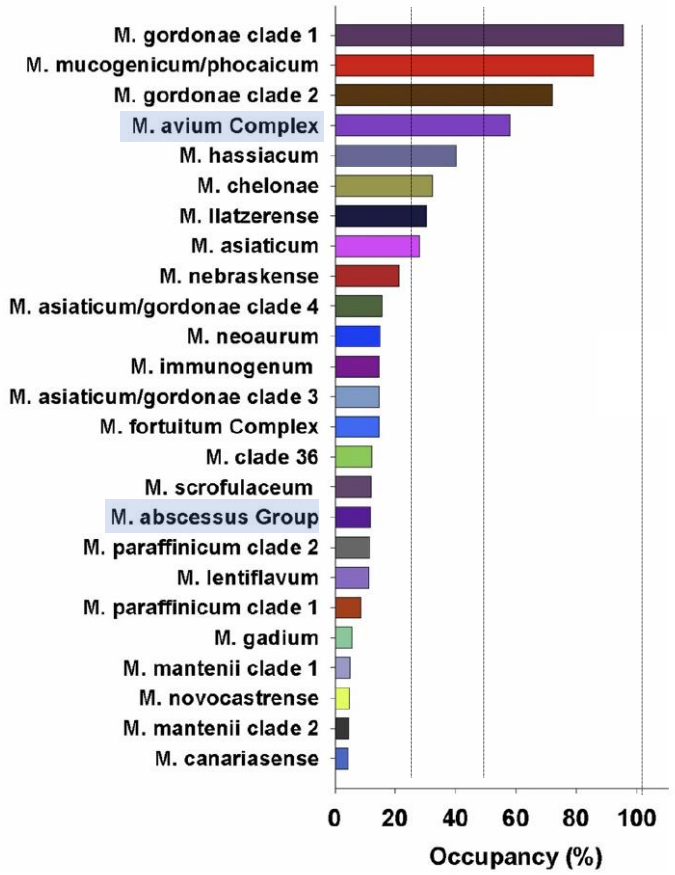

2017
2016



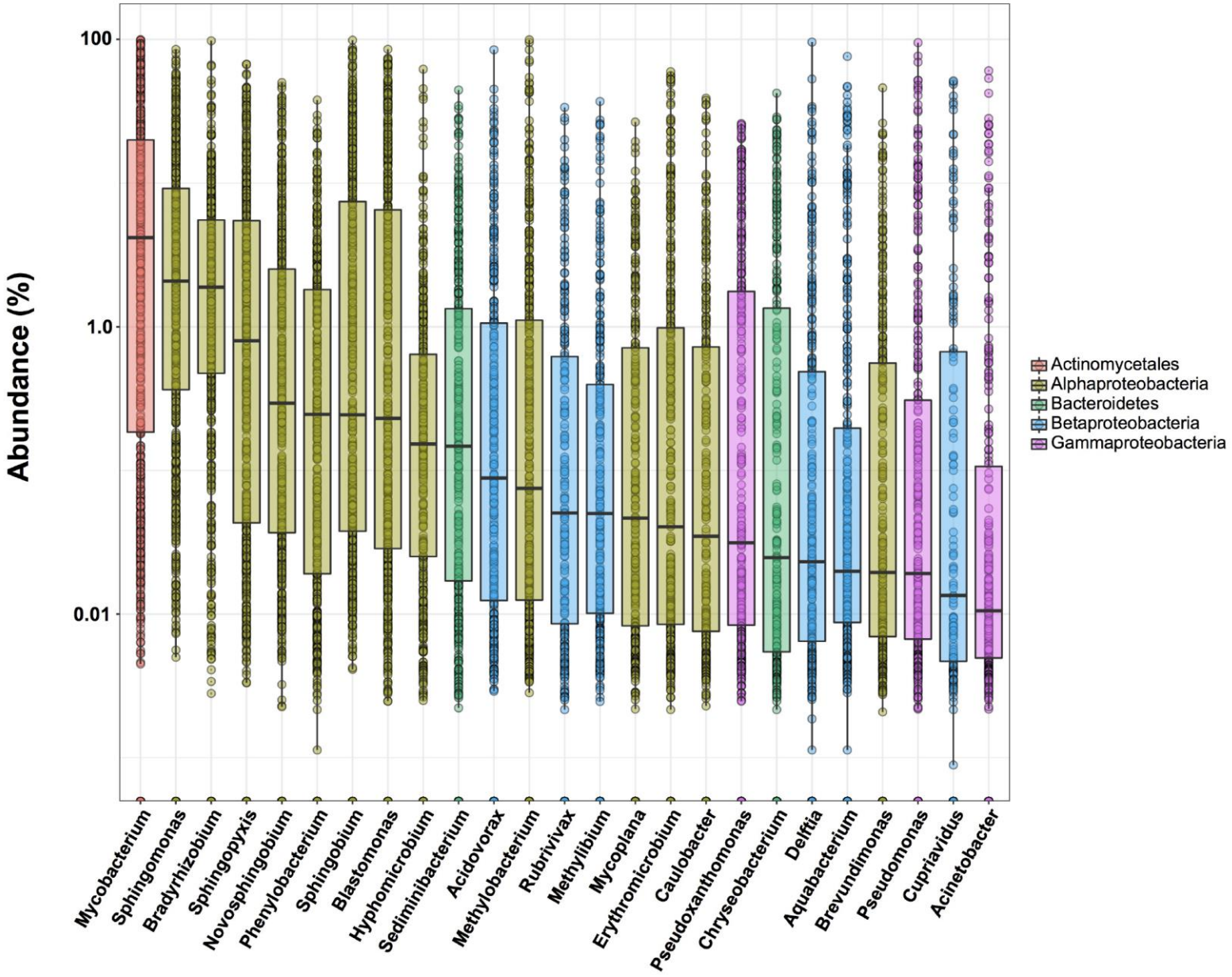
656 showerheads in the USA and Europe

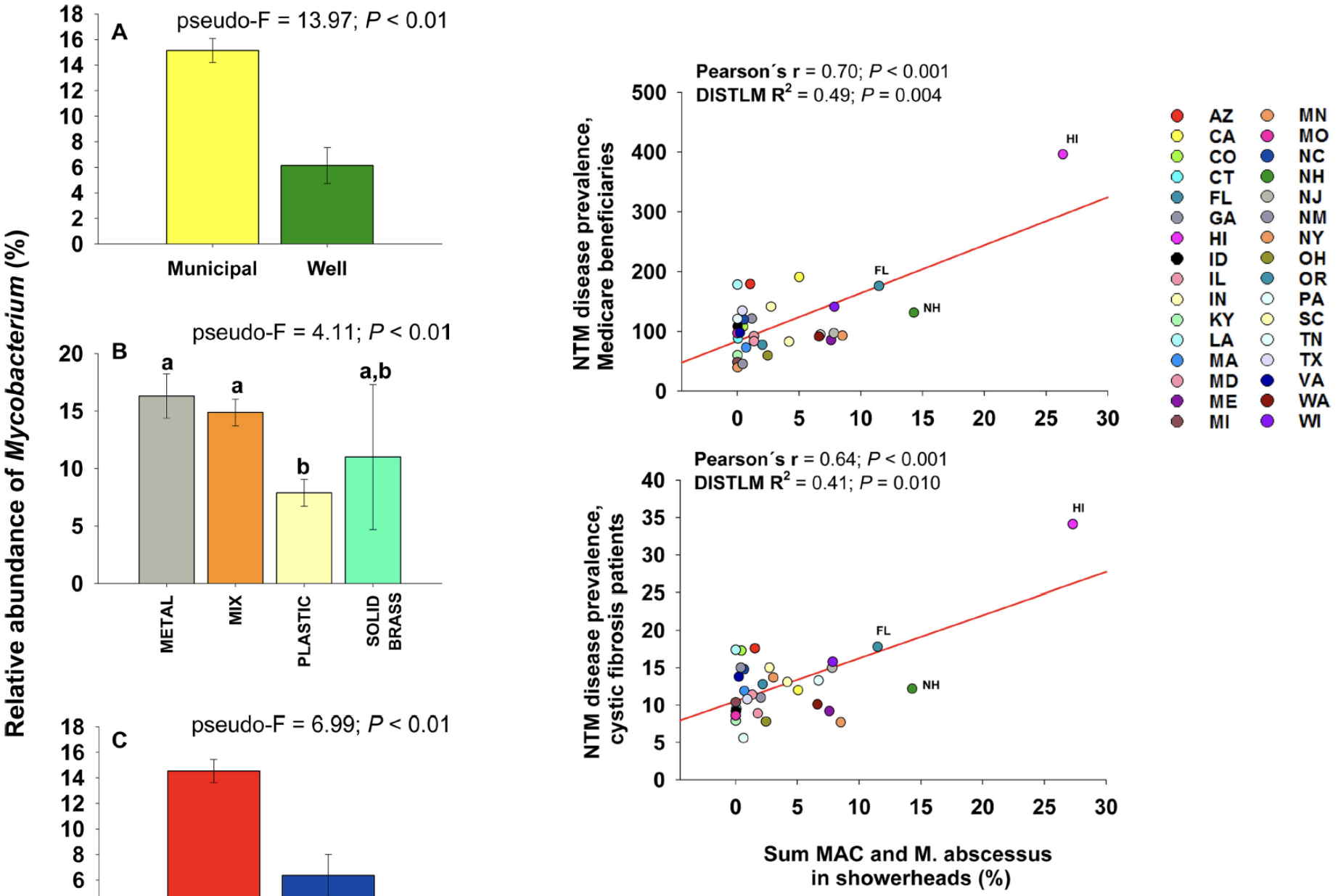
mBio® mbio.asm.org September/October 2018 Volume 9 Issue 5 e01614-18



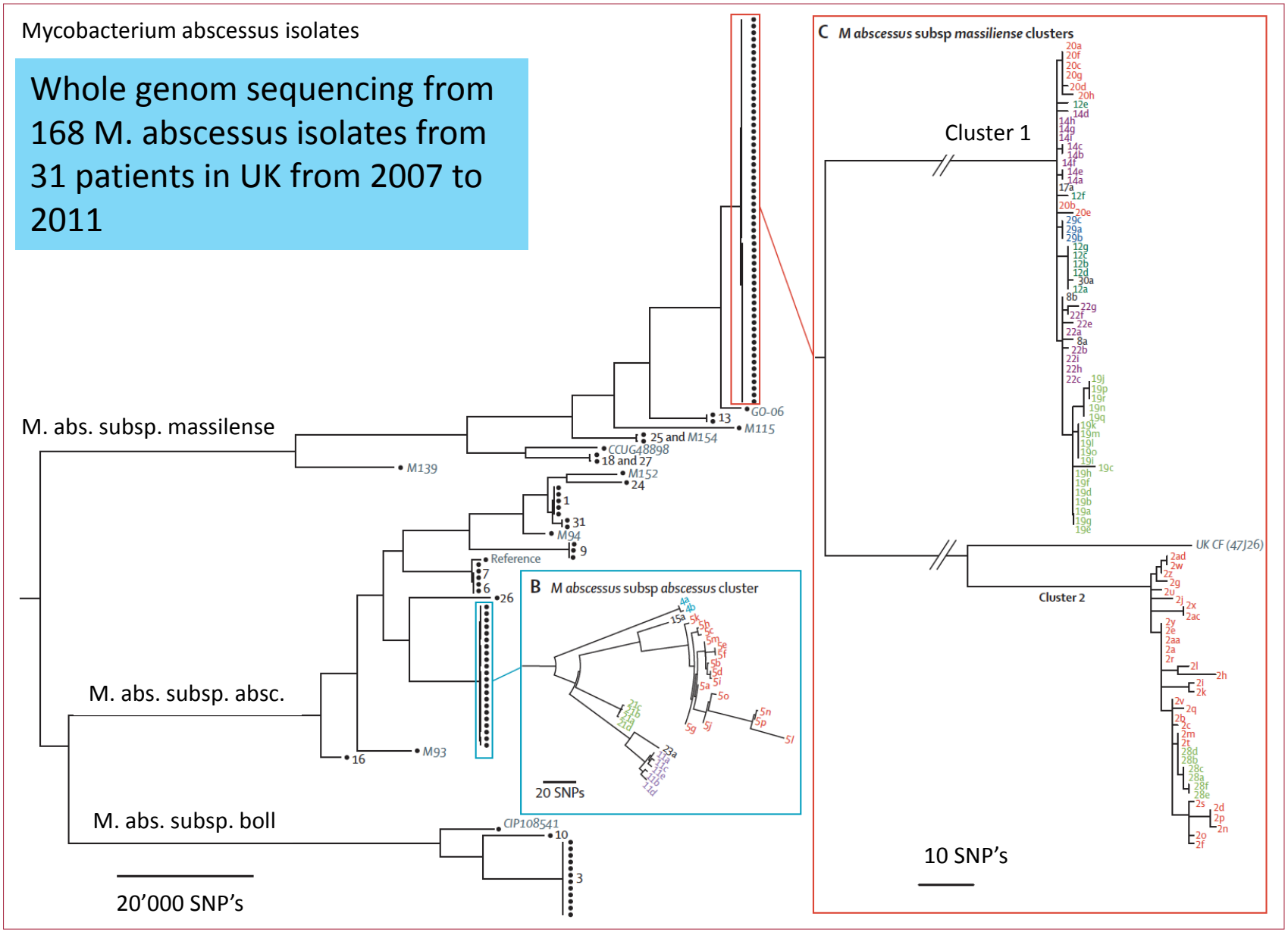


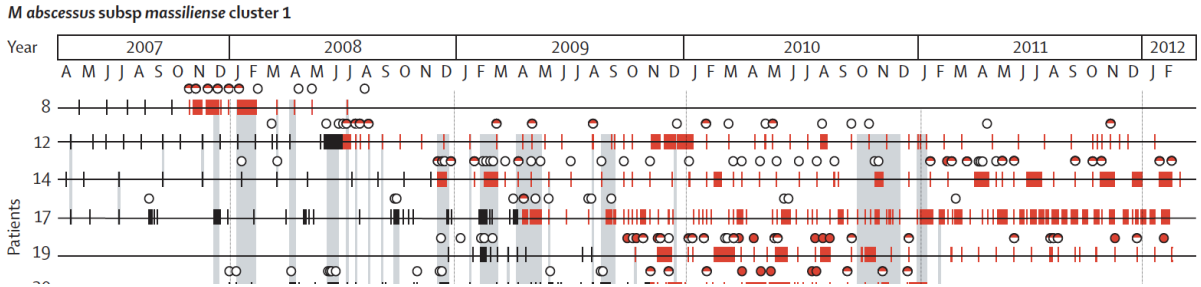
656 showerheads in the USA and Europe



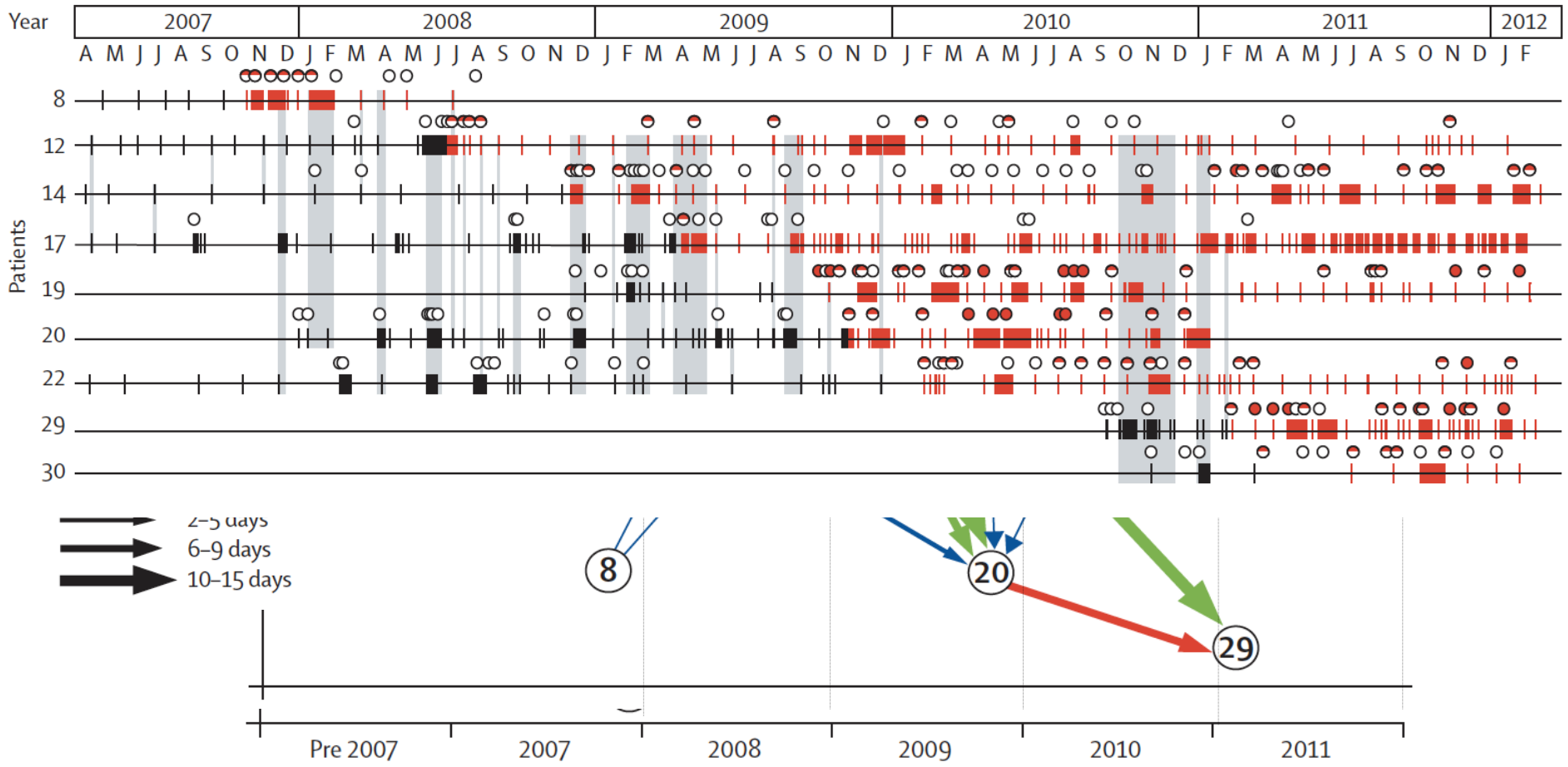

A
pseudo-F = 13.97; P < 0.01
Municipal
Well
B
pseudo-F = 4.11; P < 0.01
a
a
b
a,b
METAL
MIX
PLASTIC
SOLID BRASS
C
pseudo-F = 6.99; P < 0.01
US
EUROPE
Relative abundance of Mycobacterium (%)
Pearson´s r = 0.70; P < 0.001
DISTLM R2 = 0.49; P = 0.004
NTM disease prevalence, Medicare beneficiaries
HI
FL
NH
Pearson´s r = 0.64; P < 0.001
DISTLM R2 = 0.41; P = 0.010
NTM disease prevalence, cystic fibrosis patients
Sum MAC and M. abscessus in showerheads (%)
AZ CA CO CT FL GA HI ID IL IN KY LA MA MD ME MI
MN MO NC NH NJ NM NY OH OR PA SC TN TX VA WA WI

NTM transmission in CF patients

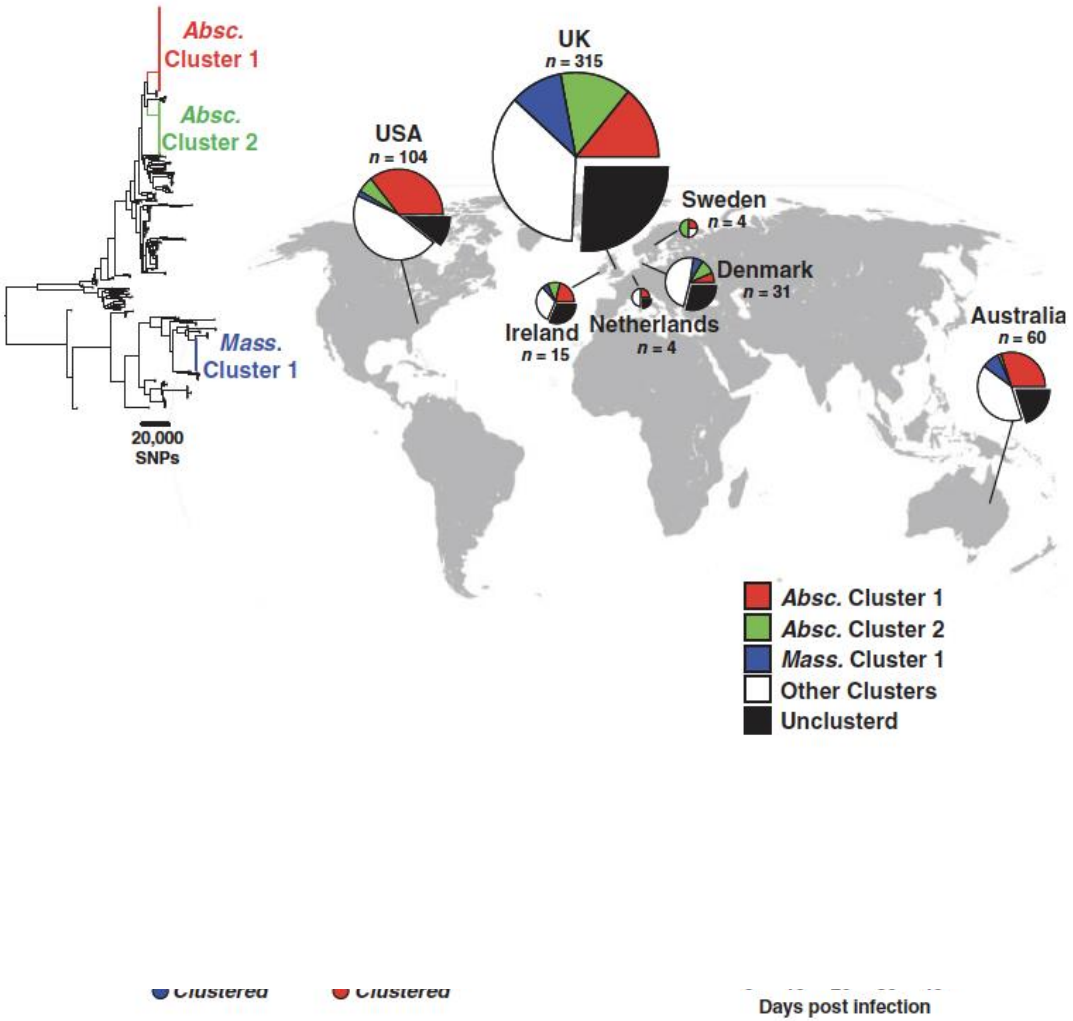


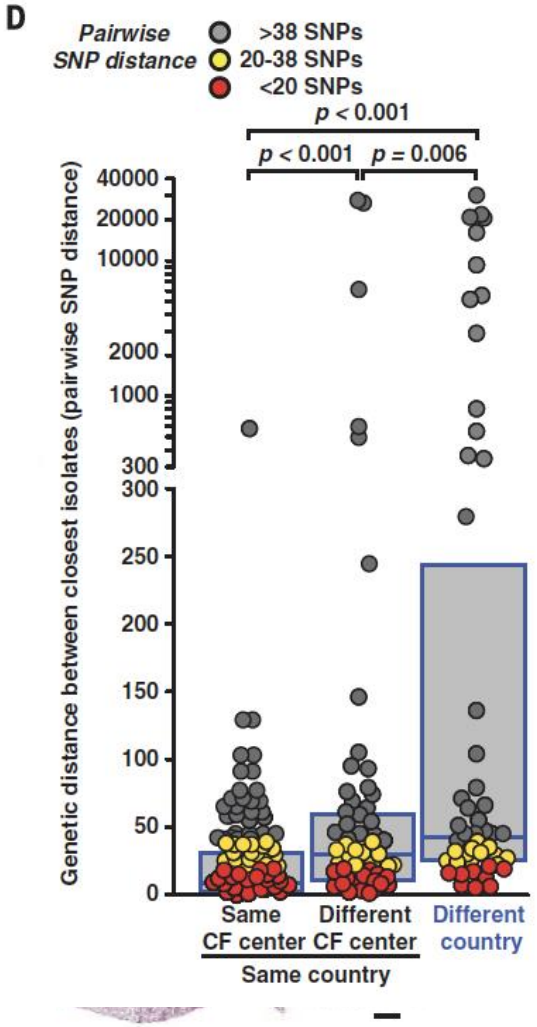


M abscessus subsp massiliense cluster 1



NTM transmission in CF patients





Risk of Bacterial Transmission in Bronchiectasis Outpatient Clinics

Philip Mitchelmore [1,2] · Catherine Wilson [1] · David Hettle [1]

Current Pulmonology Reports (2018) 7:72–78

Table 1 Summary of studies suggesting evidence of cross-infection with *P. aeruginosa* in bronchiectasis

Authors	Sample sizes	Outpatient setting	Genotyping techniques	Likelihood of cross-infection
De Soyza A et al. *Eur Respir J. 2014* [53••]	40 patients 56 isolates	Single-centre CF managed on different site	- ArrayTube genotyping - Variable number tandem repeat (VNTR) analysis - Pulsed-field gel electrophoresis	"Only one probable case of cross-infection"
Hilliam Y et al. *Eur Respir J. 2017* [49••]	91 patients 189 isolates	Multi-centre (16 "non-CF bronchiectasis" centres)	- Whole genome sequencing	Closely related isolates found between patients "implying the possible occurrence of cross-infection"
Mitchelmore PJ et al. *Thorax. 2017* [54••]	46 patients 459 isolates	Single-centre CF managed on same site	- Random amplification of polymorphic DNA - Multi-locus sequence typing - Whole genome sequencing	A shared strain identified between three patients had little genetic difference. Believed to be "indicative of cross-infection"

M. Avium complex (MAC) taxonometry

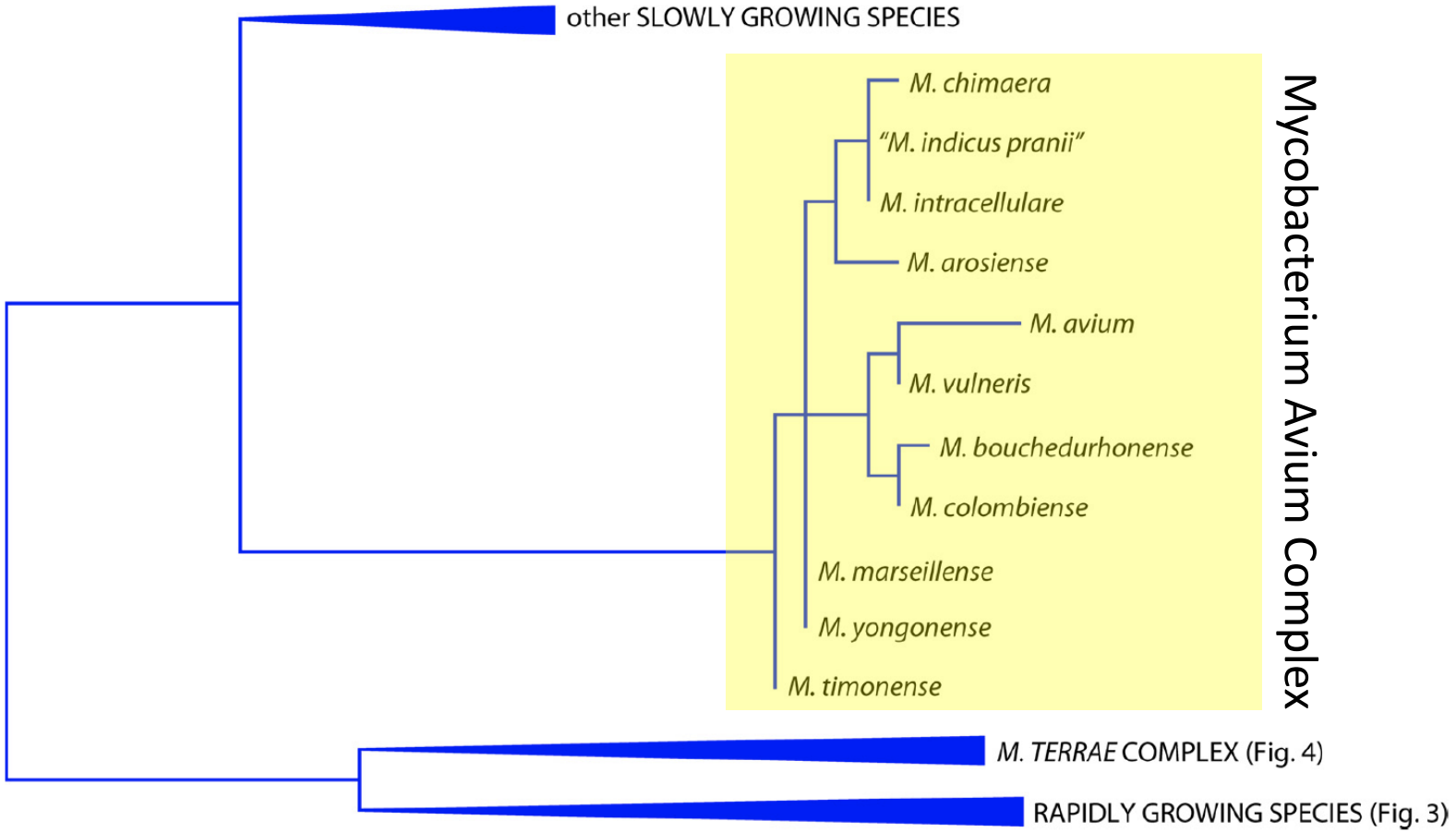


FIG 5 Phylogenetic tree, based on the 16S rRNA gene, for the species belonging to the *M. avium* complex.

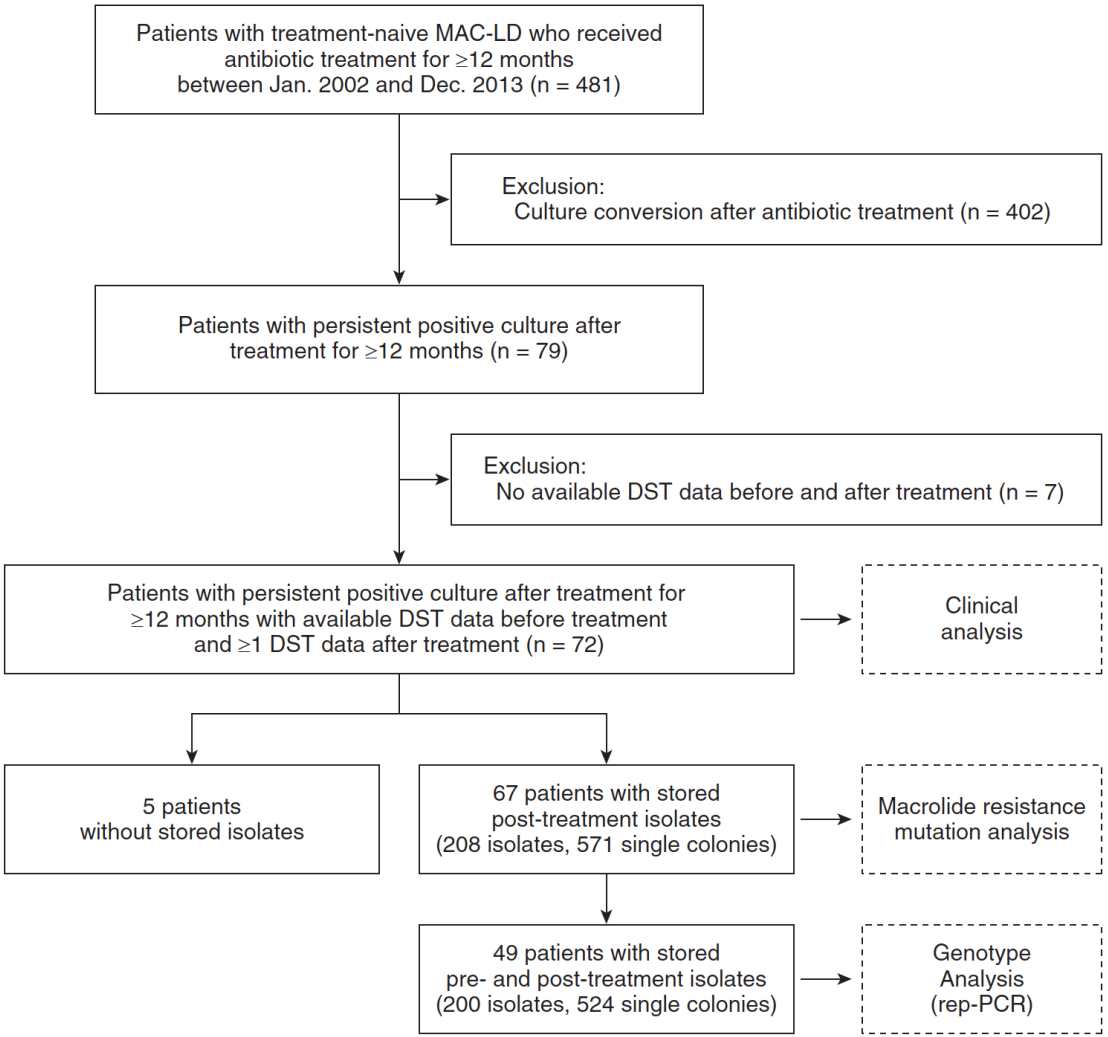
Antibiotic therapy of MAC

Recommended antibiotics
Non-cavitary nodular bronchiectatic form: Clarithromycin 1000 mg or azithromycin 500 mg TIW plus Ethambutol 25 mg/kg TIW plus Rifampicin 600 mg TIW
Fibrocavitary form or cavitary nodular bronchiectatic form: Clarithromycin 1000 mg or azithromycin 250 mg daily plus Ethambutol 15 mg/kg daily plus Rifampicin 450–600 mg daily and/or streptomycin 10–15 mg/kg IM TIW or amikacin 10–15 mg/kg IV TIW

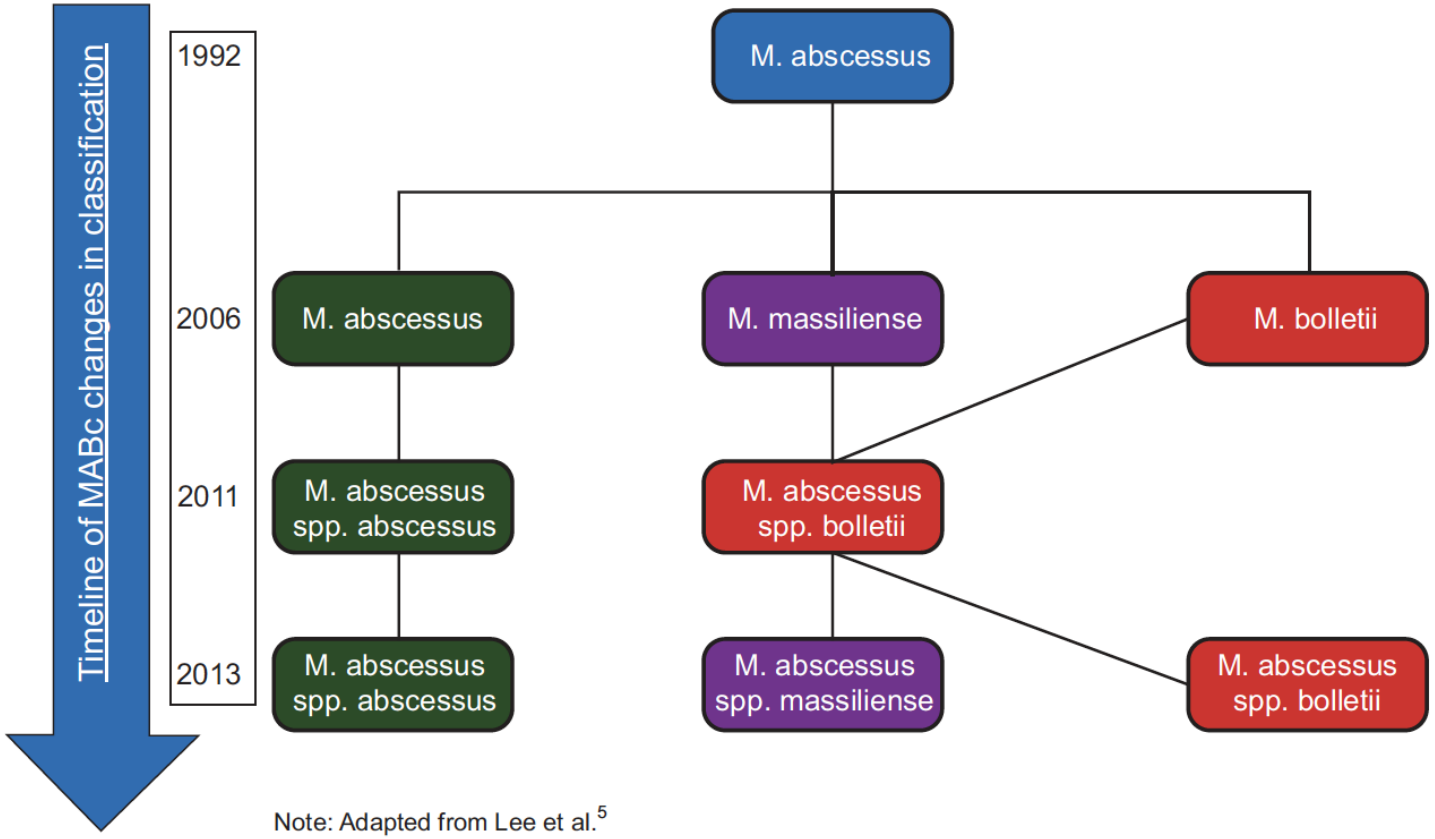
Alternative antibiotics
Clofazimine Moxifloxacin Linezolid Inhaled amikacin

International Journal of Infectious Diseases 45 (2016) 123–134

Reinfection vs relaps of MAC



	P Value
Etiology	0.171
M. avium	
M. intracellu	
Type	0.493
Nodular bro	
Fibrocavitar	
Development	0.269



Note: Adapted from Lee et al.[5]

Antibiotic therapy of M. abscessus

Recommended antibiotics
Amikacin 10–15 mg/kg IV daily plus Cefoxitin up to 12 g IV or imipenem 1000–2000 mg IV daily plus Clarithromycin 1000 mg or azithromycin 250 mg daily

Alternative antibiotics
Clofazimine Linezolid Bedaquiline Tigecycline Inhaled amikacin Streptomycin

International Journal of Infectious Diseases 45 (2016) 123–134

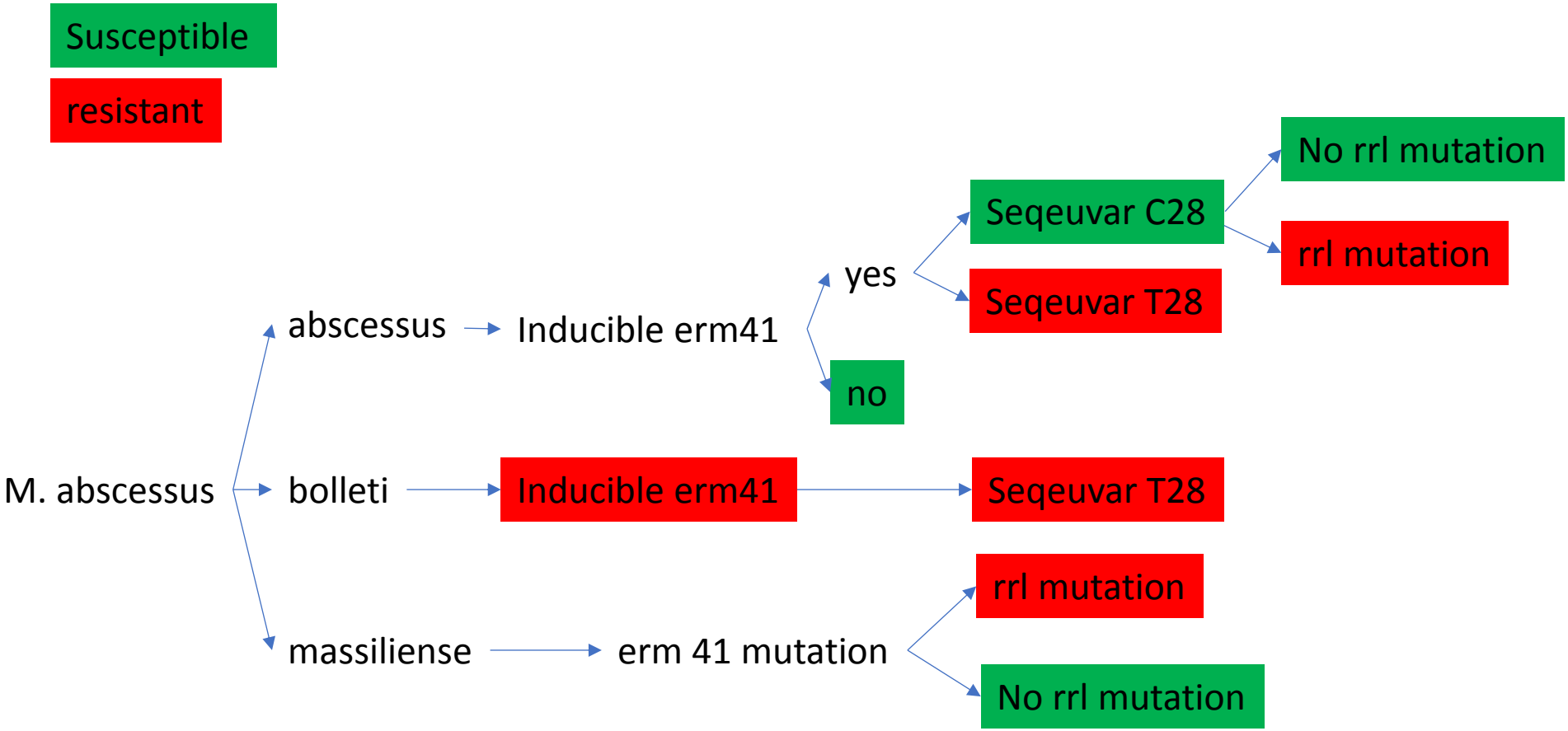
In vitro clarithromycin susceptibility against Mycobacterium abscessus complex

Identification†	Incubation time days	Susceptible *n* (%)	Intermediate *n* (%)	Resistant *n* (%)	Not culturable *n* (%)	MIC range mg/l
M. abscessus subsp. *abscessus* (*n* = 74)	3	57 (77.0)	9 (12.1)	7 (9.5)	1 (1.4)	0.06–64<
	14	12 (16.2)	3 (4.1)	58 (78.4)	1 (1.4)	0.12–64<
M. abscessus subsp. *bolletii* (*n* = 2)	3			2 (100)		64<
	14			2 (100)		64<
M. abscessus subsp. *massiliense* (*n* = 69)	3	67 (97.1)		2 (2.9)		0.03–64<
	14	67 (97.1)		2 (2.9)		0.03–64<

* Breakpoint values are referenced from Clinical and Laboratory Standards Institute recommendations (8 mg/l).[16]
† Subspecies were determined by sequencing *rpo*B and *hsp*65.
MIC = minimum inhibitory concentration.

INT J TUBERC LUNG DIS 22(4):413–418

Inducible macrolide resistance in M. abs



Rx response M. abscessus vs M. massiliense

Am J Respir Crit Care Med Vol 183. pp 405–410, 2011

TABLE 3. TREATMENT RESPONSES FOR PATIENTS WITH *MYCOBACTERIUM ABSCESSUS* AND *MYCOBACTERIUM MASSILIENSE* LUNG DISEASE

	M. abscessus (*n* = 24)	*M. massiliense* (*n* = 33)	*P* Value
Symptomatic response			0.040
Improved	18 (75%)	32 (97%)	
Unchanged	4 (17%)	1 (3%)	
Worsened	2 (8%)	—	
Radiographic response on HRCT			0.003
Improved	10 (42%)	27 (82%)	
Unchanged	7 (29%)	5 (15%)	
Worsened	7 (29%)	1 (3%)	
Microbiologic response			<0.001
Initial sputum conversion and maintenance of conversion	6 (25%)	29 (88%)	
Initial sputum conversion, with sputum relapse	4 (17%)	3 (9%)	
Failure to sputum conversion	14 (58%)	1 (3%)	

Definition of abbreviation: HRCT = high-resolution computed tomography.

Recommendations for susceptibility testing

Recommendations

- Drug susceptibility testing and reporting should follow the CLSI guidelines. (Grade D)
- For MAC, clarithromycin and amikacin susceptibility testing should be performed on an isolate taken prior to initiation of treatment and on subsequent isolates if the patient fails to respond to treatment or recultures MAC after culture conversion (Grade C).
- Macrolide-resistant MAC isolates should be tested against a wider panel of antibiotics to guide, but not dictate, treatment regimens. (Grade D).
- For *M. kansasii*, rifampicin susceptibility testing should be performed on an isolate prior to initiation of treatment and on subsequent isolates if the patient fails to respond to treatment or recultures *M. kansasii* after culture conversion. (Grade D)
- Rifampicin-resistant *M. kansasii* isolates should be tested against a wider panel of antibiotics to guide, but not dictate, treatment regimens. (Grade D)
- Susceptibility testing for *M. abscessus* should include at least clarithromycin, cefoxitin and amikacin (and preferably also tigecycline, imipenem, minocycline, doxycycline, moxifloxacin, linezolid, co-trimoxazole and clofazimine if a validated method is available) to guide, but not dictate, treatment regimens. (Grade D)

Haworth CS, *et al*. *Thorax* 2017;**72**:ii1–ii64.

Surgical therapy for NTM infections

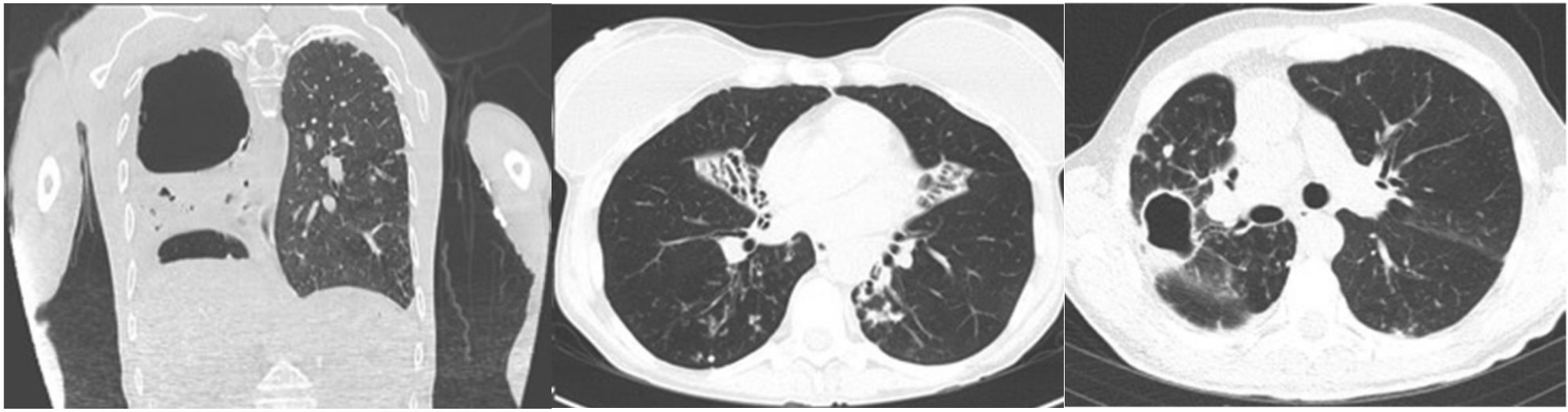


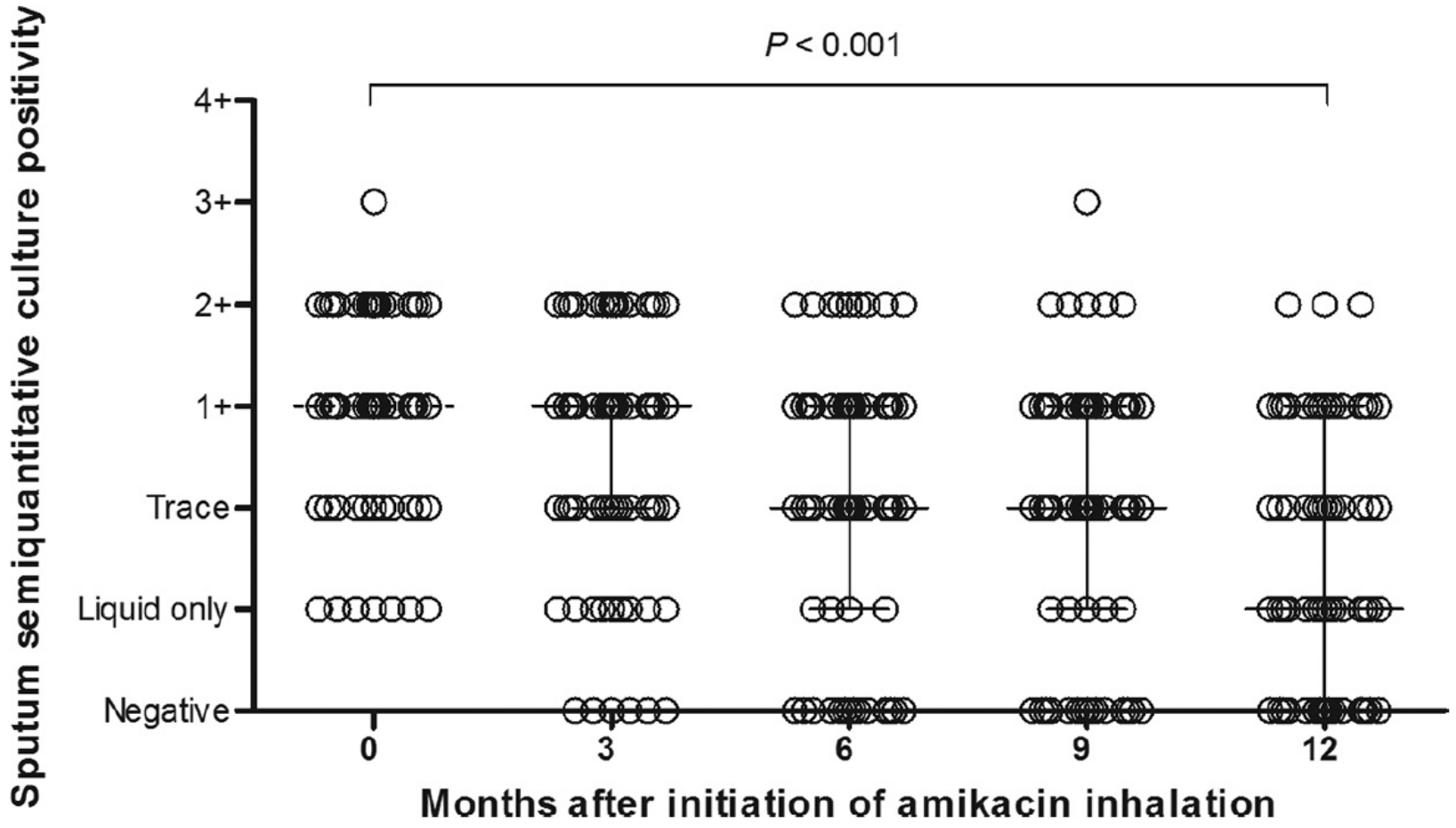
Table 1
Selected series of anatomic resection for pulmonary nontuberculous mycobacterial infection

Author, Year	N	Mortality (%)	Morbidity (%)	BPF (%)	Sputum Conversion (%)
Corpe,[9] 1981	131	6.9	NR	5.3	93
Nelson et al,[12] 1998	28	7.1	32	3.6	88
Watanabe et al,[14] 2006	22	0	NR	NR	95
Koh et al,[11] 2008	23	4.3	35	8.7	100
Mitchell et al,[7] 2008	265	2.6	18.5	4.2	NR
Yu et al,[3] 2011	172	0	7	0	84
Shiraishi et al,[13] 2013	65	0	12	0	100
Kang et al,[10] 2015	70	1.4	21	6.8	81
Asakura et al,[8] 2017	125	3	22	6	91

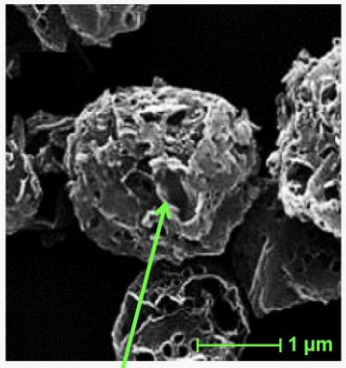
Abbreviations: BPF, bronchopleural fistula; NR, not reported.

Thorac Surg Clin 29 (2019) 77–83

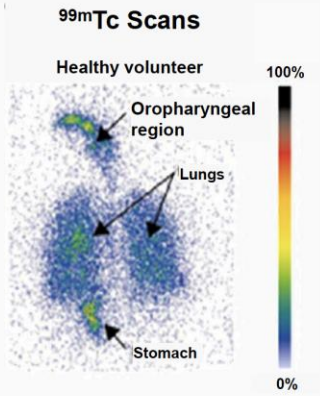
Inhaled regular amikacin for NTM



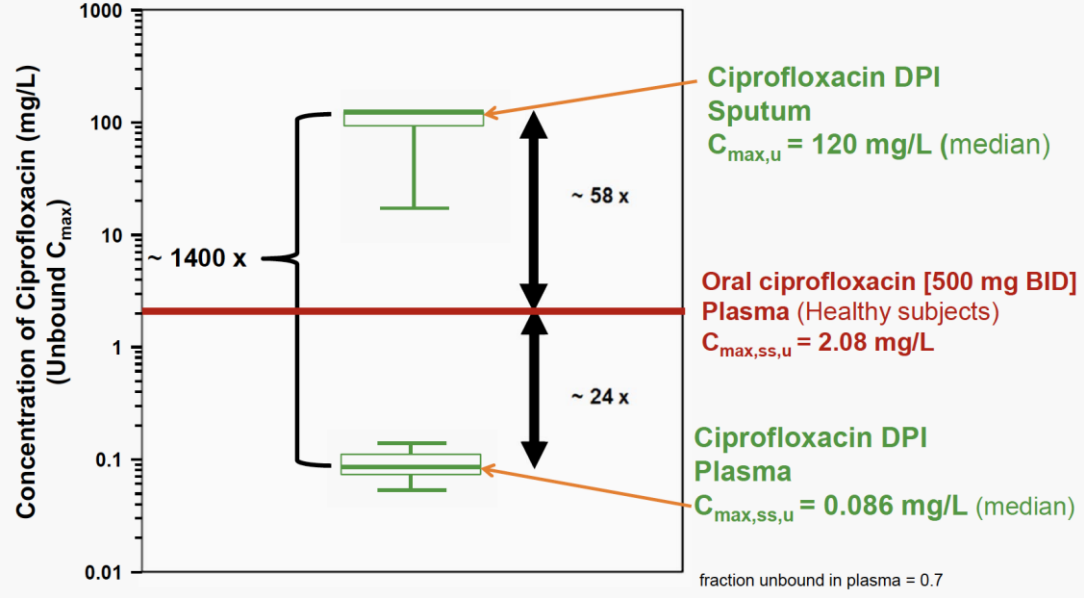
Liposomal preparation for inhaled abx



^{99m}Tc Scans



- PulmoSphere™: small size and dispersion characteristics produce deep penetration into lung
- Achieves high ciprofloxacin concentrations in lung (site of infection) and low systemic levels
- >50% of the dose is deposited in the lung



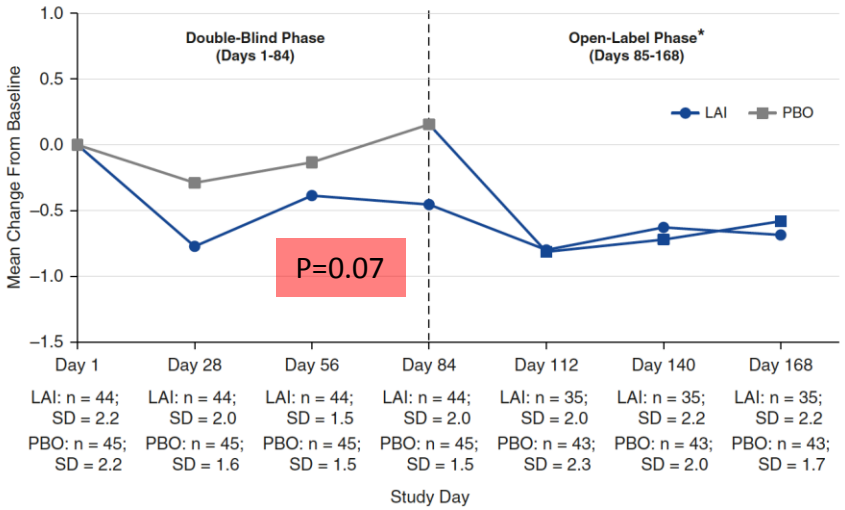
Ciprofloxacin DPI
For reduction of exacerbations in non-cystic fibrosis bronchiectasis (NCFB) adult patients (≥18 years of age) with respiratory bacterial pathogens

FDA Antimicrobial Drugs Advisory Committee
November 16, 2017

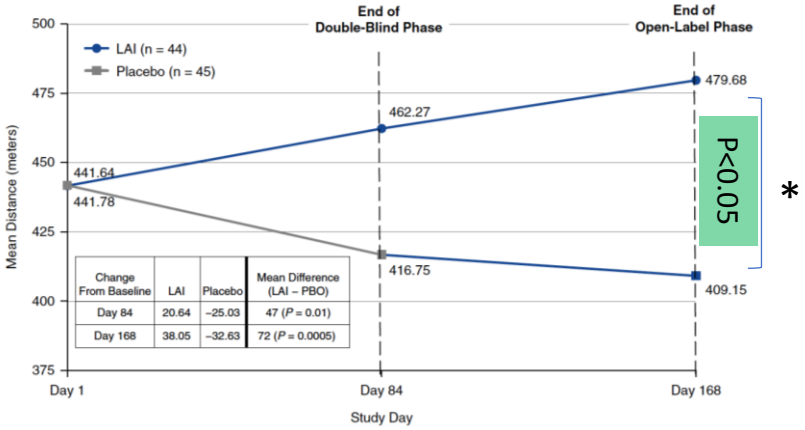
Inhaled liposomal amikacin for NTM

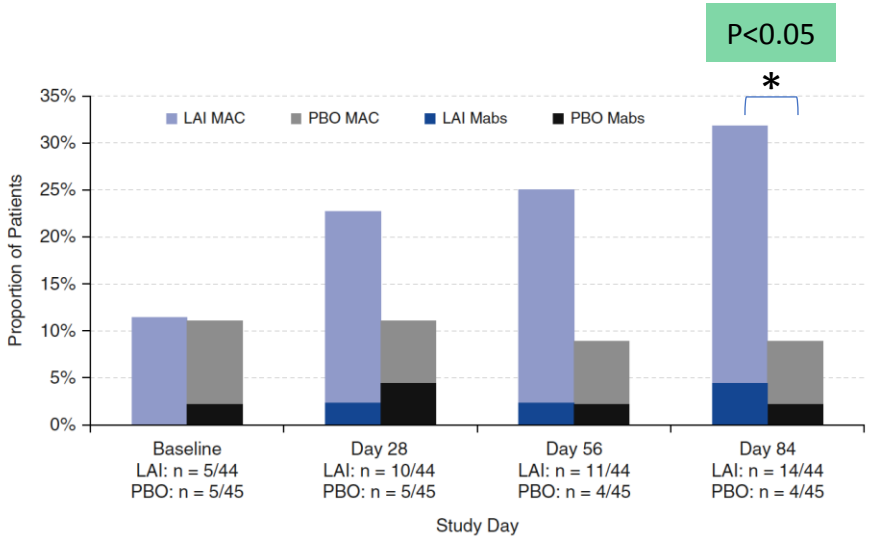
Inclusion criteria

Patients with MAC or M. absc.
Refractory disease with persistent
Positive sputum after 6 months Rx as per guidelines
Cystic Fibrosis patients included



6 min walk





American Journal of Respiratory and Critical Care Medicine Volume 195 Number 6 | March 15 2017

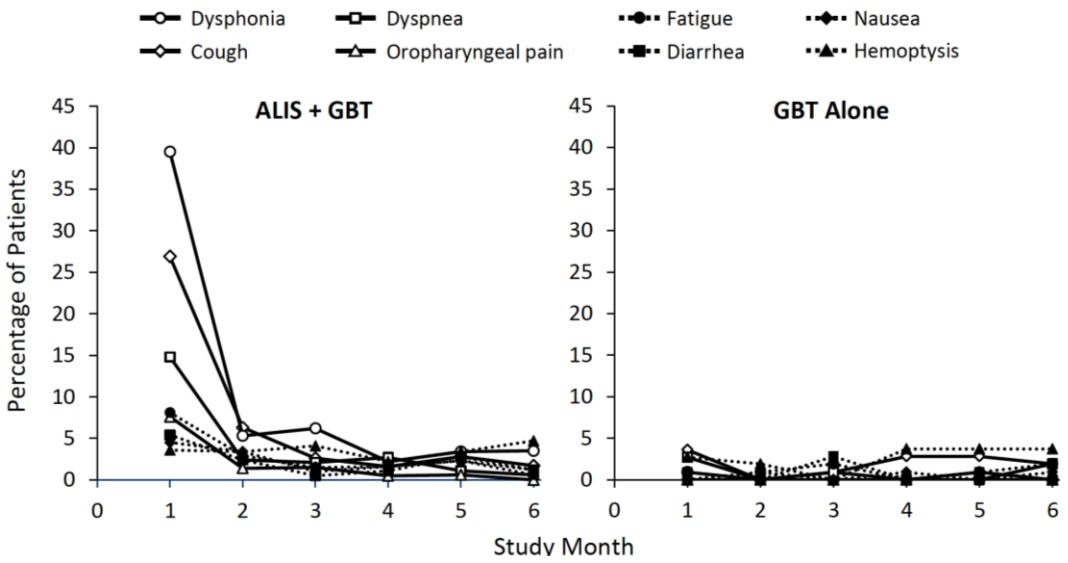
Inhaled liposomal amikacin for MAC

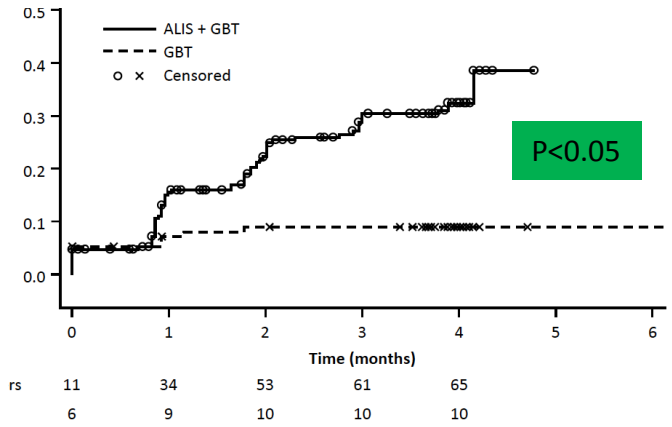
Inclusion criteria

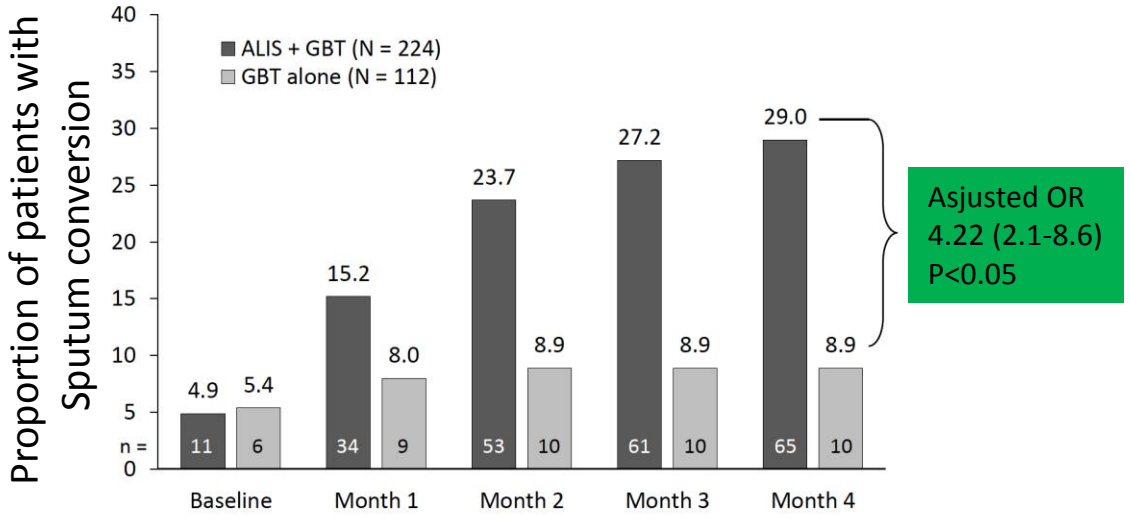
Patients with MAC only

Refractory disease with persistent Positive sputum after 6 months Rx as per guidelines

Cystic Fibrosis patients excluded



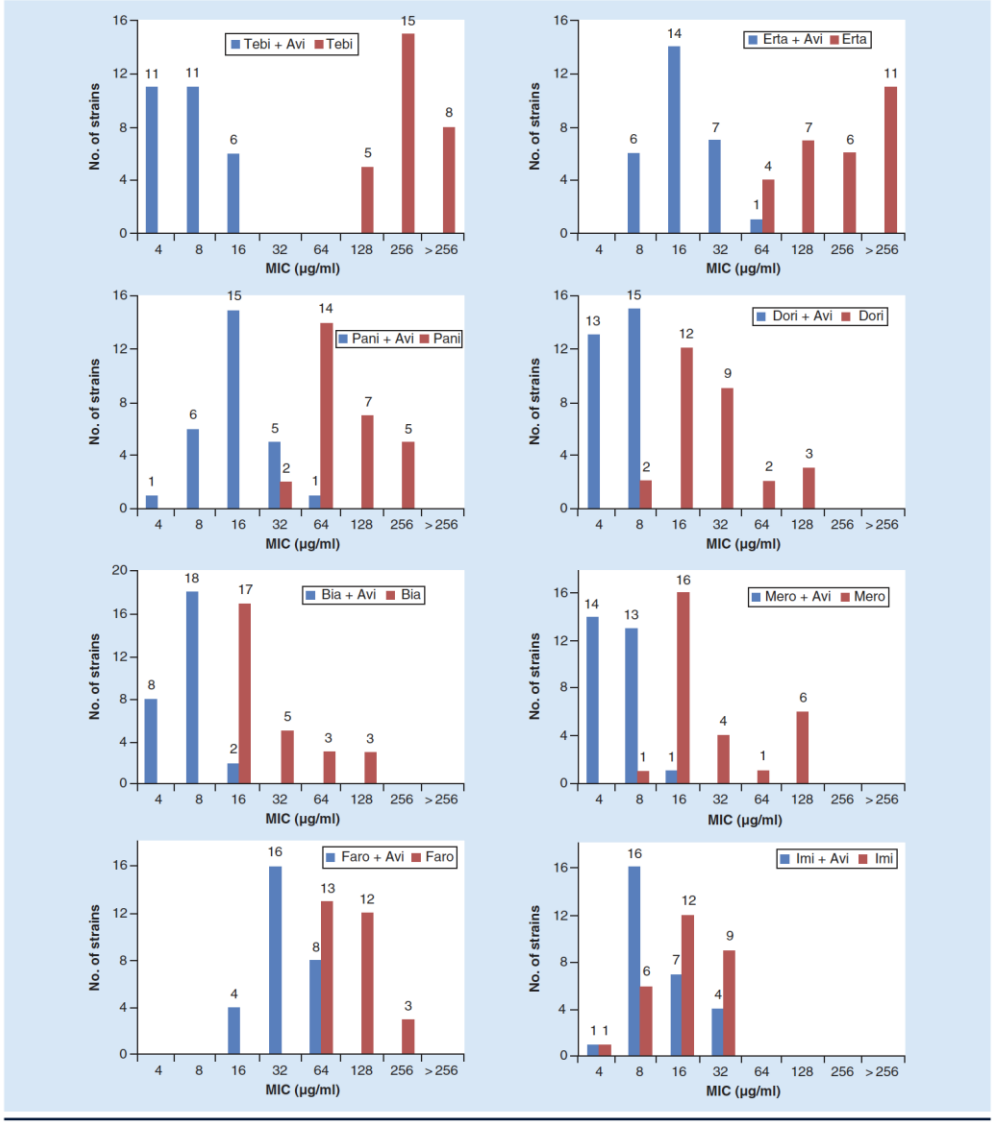




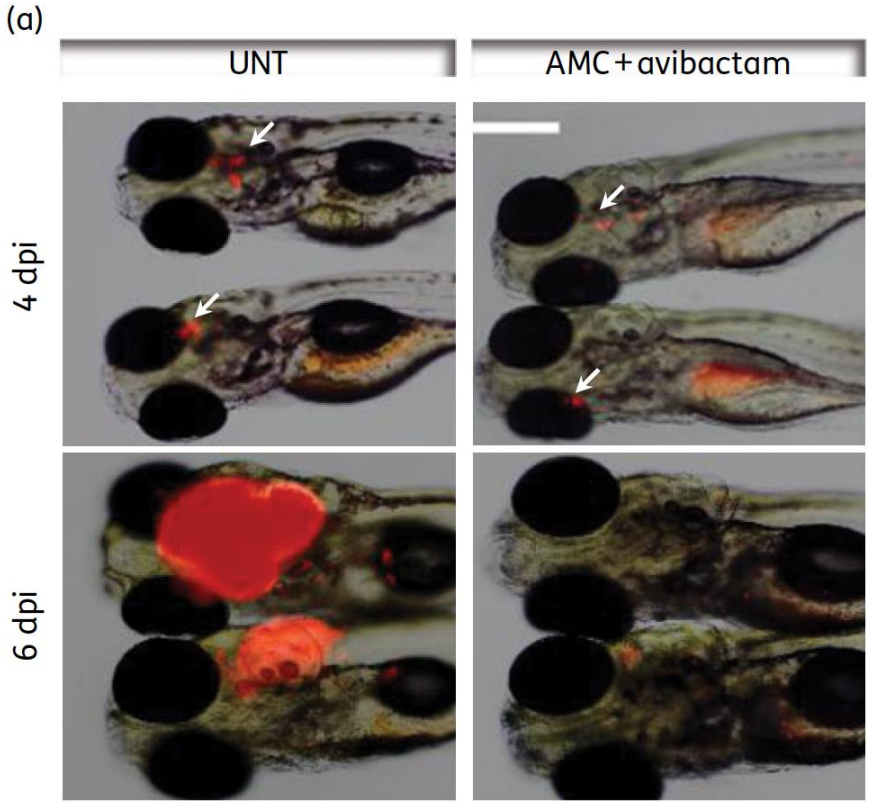
American Journal of Respiratory and Critical Care Medicine Volume 195 Number 6 | March 15 2017

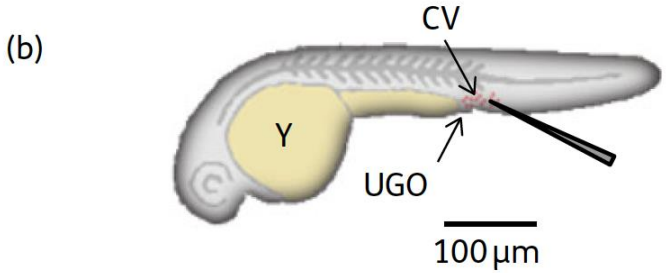
ß-lactamase inhibitors and M. abscessus

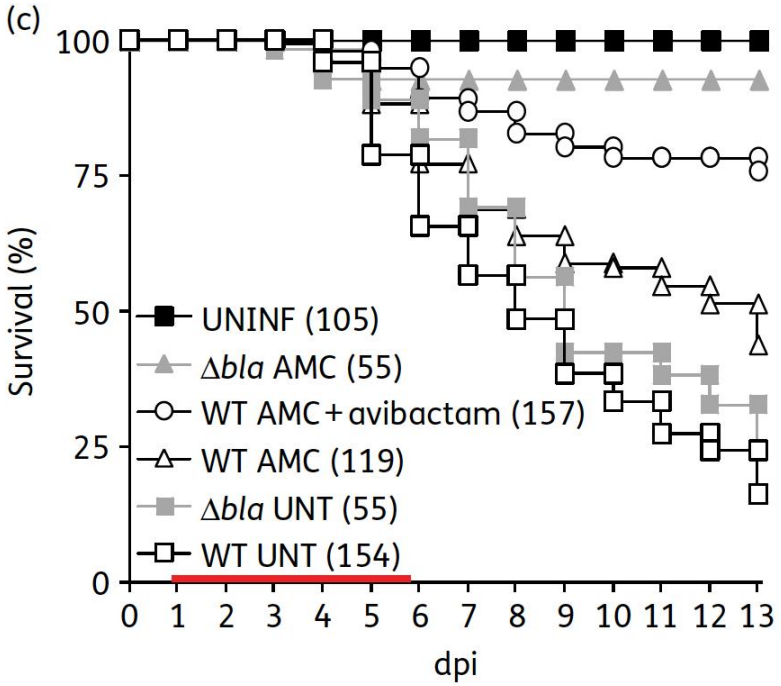
Drug	7H9 broth	7H9 + avibactam
Ertapenem	64–128	4–8
Meropenem	8–16	2–4
Imipenem	4–8	2–4
Doripenem	8–16	2–4
Biapenem	8–16	2–4
Faropenem	32–64	8–16
Tebipenem	128–256	4–8
Panipenem	64–128	8–16
Sulbactam	>64	ND
Tazobactam	>64	ND
Avibactam	>256	ND

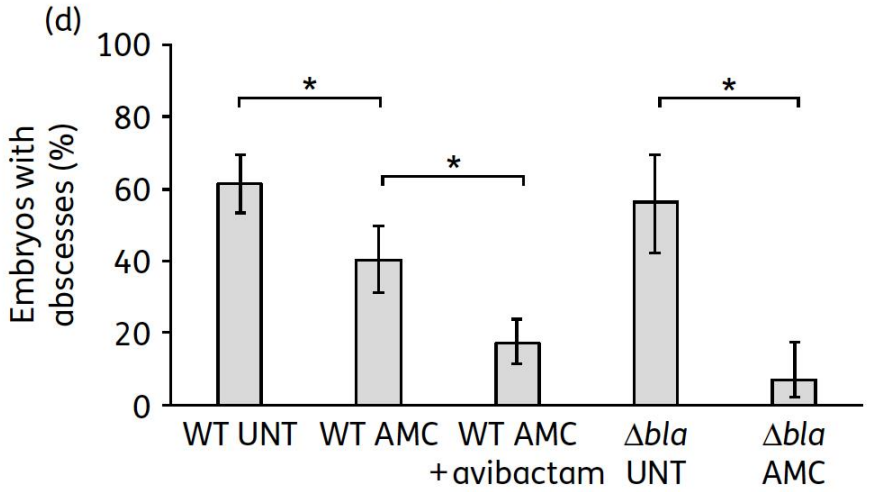


ß-lactamase inhibitors and M. abscessus







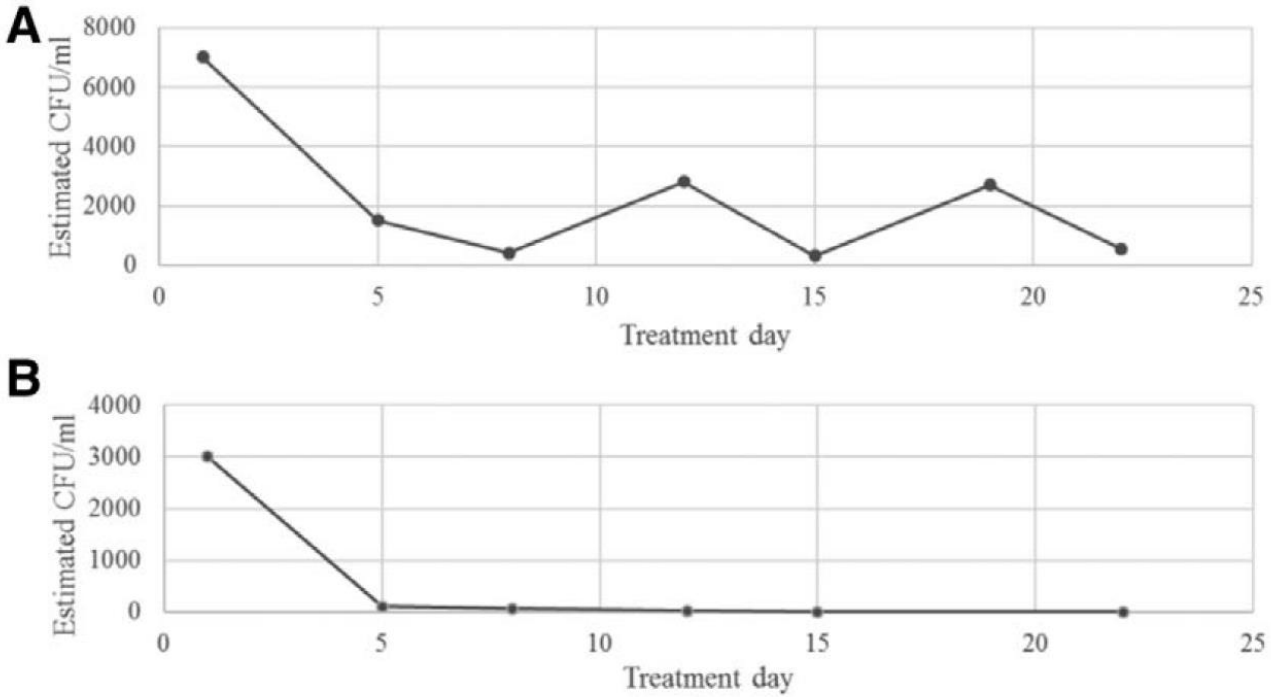


J Antimicrob Chemother 2015; **70**: 1051–1058

Nitric oxide inhalation and M. abs in CFR

Treatment Protocol

The device for the treatment was supplied by AIT Ltd. It provides 800 ppm (0.08%) NO with 99.99% nitrogen purity balanced with N_2, delivered by inhalation mask at 160 ppm NO (with a blend of air and O_2 at a minimum concentration of 21% O_2). A minimal time interval of 3.5 hours between treatments was required.



CHEST

Preliminary Results of Bedaquiline as Salvage Therapy for Patients With Nontuberculous Mycobacterial Lung Disease

CHEST 2015; 148(2):499-506

TABLE 1] Semiquantitative Monthly Sputum Cultures of 10 Patients on a Bedaquiline-Containing Regimen

Patient No.	Baseline (at the Start of Therapy)	1 mo	2 mo	3 mo	4 mo	5 mo	6 mo
1 Mab	4+	3+	1+	2+	3+	1+	2+
2 Mab	1+	3+	1+	35 colonies	37 colonies	16 colonies	3+
3 Mab	4+	28 colonies	Negative	8 colonies	Negative	Negative	32 colonies
4 Mab	4+	4+	4+	4+	4+	4+	4+
5 MAC	4+	3+	4+	4+	4+	4+	4+
6 MAC	4+	4+	Negative	Negative	2+	4+	3+
7 MAC	4+	4+	30 colonies	Negative	Negative	...[a]	...[a]
8 MAC	4+	1+	Negative	3+	4+	4+	4+
9 MAC	4+	2+	3+	1 colony	4 colonies	1+	4 colonies
10 MAC	30 colonies	8 colonies	Negative	1+	Negative	9 colonies	Negative

Solid media with countable colonies = 0-49 colonies; 1+ solid media growth = 50-99 colonies; 2+ solid media growth = 100-199 colonies; 3+ solid media growth = 200-299 colonies; 4+ solid media growth = ≥ 300 colonies. Negative indicates no bacterial growth. Mab = *Mycobacterium abscessus*; MAC = *Mycobacterium avium* complex. Negative = no bacterial growth.

[a] Unable to produce sputum.

Drug blood level

INFECTIOUS DISEASE PHARMACOKINETICS LABORATORY
1600 SW Archer Rd., P4-30
Gainesville, FL 32610
Phone: 352-273-6710
Fax: 352-273-6804
E-mail: peloquinlab@cop.ufl.edu
Website: http://idpl.pharmacy.ufl.edu

UFHealth
UNIVERSITY OF FLORIDA HEALTH

Today's date: 9/1/2017
Sample tracking number: AZI08311701

Azithromycin (AZI) Concentration (in mcg / mL): Trace

If the time of the dose and blood draw were not accurately recorded, accurate interpretation of the concentration is not possible.

Oral doses of Azithromycin 250-500 mg produce peak serum concentrations of 0.20-0.70 mcg/ml approximately 2.0-3.0 hours post dose. Weekly doses of 1200 mg produce proportionately larger concentrations. Some accumulation may occur over the first week of treatment, so for patients on long-term treatment for mycobacterial infections, concentrations may be obtained 7 days or more into treatment.

ETHAMBUTOL (EMB) Concentration (in mcg / mL): 1.41

If the time of the dose and blood draw were not accurately recorded, accurate interpretation of the concentration is not possible.

The normal range for ETHAMBUTOL (EMB) serum or plasma concentrations is 2-6 mcg/ml approximately 2 to 3 hours after an oral dose of 15-25 mg per kg. Higher, twice weekly doses (50 mg/kg) appear to produce proportionally higher ethambutol concentrations (4-12 mcg/ml). Samples later than 3 hours after the dose may display concentrations below the normal range. Two to three plus six to seven hour post dose samples help to distinguish between malabsorption versus delayed absorption.

RIFAMPIN (RIF) Concentration (in mcg / mL): 15.54

If the time of the dose and blood draw were not accurately recorded, accurate interpretation of the concentration is not possible.

The normal range for RIFAMPIN (RIF) serum or plasma concentrations is 8-24 mcg/ml approximately 2 hours after an oral dose. Samples later than 2 hours after the dose may display concentrations below the normal range. Two plus six hour post dose samples help to distinguish between malabsorption versus delayed absorption.