Online Supplemental File 2: Tables and Figure

Online Supplemental File 2 for 'Global prevalence of nontuberculous mycobacteria in adults with non-cystic fibrosis bronchiectasis 2006-2021: a systematic review and meta-analysis'.

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Table S1: Search strings

Database and date	Yield	Duplicates	Search String used
Medline Jan 31, 2022	414	0	"Bronchiectasis" [Mesh]) AND ("Nontuberculous Mycobacteria" OR "non tuberculous mycobacter" [Mesh]) AND ("Atypical Mycobacter" [Mesh] OR ("Mycobacter abscessus" [Mesh]) OR "Mycobacter avium complex" [Mesh] OR "Mycobacter chelonae" [Mesh] OR "Mycobacter fortuitum" [Mesh] OR "Mycobacter kansasii" [Mesh] OR "Mycobacter marinum" [Mesh] OR "Mycobacter scrofulaceum" [Mesh] OR "Mycobacter smegmatis" [Mesh] OR "Mycobacter ulcerans" [Mesh] OR "Mycobacter xenopi" [Mesh])
Embase Jan 31, 2022	678	32	"Bronchiectasis" [Mesh]) AND ("Nontuberculous Mycobacteria" OR "non tuberculous mycobacter" [Mesh]) AND ("Atypical Mycobacter" [Mesh] OR ("Mycobacter abscessus" [Mesh]) OR "Mycobacter avium complex" [Mesh] OR "Mycobacter chelonae" [Mesh] OR "Mycobacter fortuitum" [Mesh] OR "Mycobacter kansasii" [Mesh] OR "Mycobacter marinum" [Mesh] OR "Mycobacter scrofulaceum" [Mesh] OR "Mycobacter smegmatis" [Mesh] OR "Mycobacter ulcerans" [Mesh] OR "Mycobacter xenopi" [Mesh])
Cochrane Library Jan 31, 2022	19	9	Bronchiectasis AND Nontuberculous Mycobacteria" OR "non tuberculous mycobacter
Web of Science Jan 31, 2022	504	70	"nontuberculous mycobacter" OR TOPIC: "non tuberculous mycobacter") OR TOPIC: "Atypical Mycobacter") OR TOPIC: (("Mycobacter abscessus" or "Mycobacter avium complex" OR "Mycobacter chelonae" OR "Mycobacter fortuitum" OR "Mycobacter* kansasii OR "Mycobacter marinum" OR "Mycobacter scrofulaceum" OR "Mycobacter smegmatis" OR "Mycobacter ulcerans" OR "Mycobacter xenopi")) OR TOPIC: "ntm"
Total	1615	111	
Other sources Jan 31, 2022	514		'Nontuberculous Mycobacteria' OR 'non-cystic fibrosis bronchiectasis'; publication date from 2006 to 2021, including citations
111 duplicates were removed to give a total of 2014 studies			

Table S2: Characteristics of studies included in the initial analysis of selected studies

Author; year	Country	Data Source	Time of sampling	Mean age (Y)	Sample size	Patients with NTM	Study design	Method of detection	NTM [%]
1. McShane, et al. 2012 [1]	USA	University Referral Center	2009-2011	≥18	106	9	RS	Sputum culture	8.5
2. Xu, et al. 2014 [2]	China	Pulmonary Hospital	2009-2012	47.4	3857	431	RS	Sputum culture	11.2
3. Guan, et al. 2015 [3]	China	Outpatient Respiratory Clinics	2012-2013	44.6	144	5	PS	Sputum culture	3.5
4. Kadowaki, et al. 2015 [4]	Japan	Medical Center	2008-2012	73	147	26	RS	Sputum culture	17.7
5. Máiz, et al. 2016 [5]	**Spain**	**Teaching hospitals**	**2012-2015**	**55.7**	**218**	**18**	**PS**	**Sputum culture**	**8.3**
6. Izhakian, et al. [6] 2016	Israel	Rabin Medical Center	2006-2014	64	339	29	RS	Bronchoalveolar lavage cultures	8.6
7. Faverio, et al. 2016 [7]	Italy	San Gerardo Hospital	2006-2014	65	162	32	PS	Bronchoalveolar /sputum culture	19.8
8. Buscot, et al. 2016 [8]	France	University Hospital	2002-2012	61.0	196	7	RS	Sputum/ bronchoalveolar lavage culture	3.6
9. Dimakou, et al. 2016 [9]	Greece	Hospital of Chest Diseases	2009-2014	60.5	205	2	PS	Sputum culture	0.9
10.* Park, et al. 2016 [10]	**Korea**	**University Hospital >5 years**	**2003-2013**	**59.6**	**155**	**69**	**RS**	**Sputum/BAL culture**	**44.5**
11.* Aksamit, et al. 2017 [11]	**USA**	**Bronchiectasis Research Registry**	**2008-2014**	**66**	**1,314**	**653**	**RS**	**Sputum culture**	**49.7**
12.* Hsieh, et al. 2018 [12]	**China**	**Bronchiectasis Medical Center**	**2005-2014**	**65.3**	**96**	**35**	**RS**	**Sputum culture**	**36.5**
13. Sin, et al. 2019 [13]	Korea	National University Hospital	2005-2016	59.6	6957	1740	RS	Sputum culture	25
14.* Amorim, et al. 2019 [14]	**Portugal**	**Bronchiectasis Referral Center**	**2011-2017**	**54.7**	**186**	**27**	**PS**	**Sputum culture**	**14.5**
15.* Visser, et al. 2019 [15]	**Australia**	**Australian Bronchiectasis Registry**	**2016-2018**	**71**	**169**	**40**	**PS**	**Sputum culture**	**23.6**
16. Pieters, et al. 2019 [16]	Netherland	University Medical Center	2012-2016	60	120	6	RS	Sputum culture	5.0
17.* Dhar, et al. 2019 [17]	**India**	**bronchiectasis registry**	**2015-2017**	**56**	**1299**	**8**	**PS**	**Sputum culture**	**0.6**

Continued next page

Author; year	Country	Data Source	Time of sampling	Mean age (Y)	Sample size	Patients with NTM	Study design	Method of detection	NTM [%]
18. Huang, et al. 2020 [18]	China	Medical Record Database	2002-2016	65.5	8385	304	RS	Sputum culture	3.6
19. Darwish, et al. 2020 [19]	Egypt;	University Hospital	2017-2018	55.2	40	3	PS	Sputum PCR	7.5
20.* Kwak, et al. 2020 [20]	**Korea**	**Hospital**	**2011-2019**	**62**	**221**	**35**	**PS**	**Sputum culture**	**15.8**
21. Sharif, et al. 2020 [21]	Pakistan	Hospital	2017-2019	NA	196	2	PS	Sputum culture	1.0
22.* Choate, et al. 2021 [22]	**USA**	**Bronchiectasis & NTM Research Registry**	**2008-2018**	**63.7**	**1831**	**885**	**RS**	**Sputum culture**	**48.3**
23.* Metersky, et al. 2021 [23]	**USA**	**Bronchiectasis & NTM Research Registry**	**NA-2020**	**61.1**	**410**	**47**	**PS**	**Sputum culture**	**11.5**
24.Yin, et al. 2021 [24]	China	Hospital	2018-2020	62	202	47	RS	Sputum/BAL culture	23.3

Abbreviations: NA: Not Available; NTM: Nontuberculous Mycobacteria; MBC: mycobacteria culture; AFB: acid fast bacillus smear; BAL: bronchoalveolar lavage; RS: Retrospective Study; PS: prospective Study; UK: United Kingdom; US: United States. PCR: Polymerase Chain Reaction.

Note: Bold type with an asterisk * indicate the studies with source/selection bias. Please refer to the supplementary Table S3.

Table S3: Ratings of the quality of the evidence and Risk of Bias assessment

Study	Study Design	Domain	Source of bias	Support for Judgement	Review Author's Judgement	Risk of Bias
1. McShane, et al. 2012; US [1]	Retrospective cohort study	Attrition bias	Patient follow-up	Of all 114 patients. Two declined consent, and six patients did not follow up with the evaluation.	Eight patients were not available for the complete analysis.	Low
2. Xu, et al. 2014; Shanghai, China [2]	Retrospective cohort study	Detection bias	Detection bias	Diagnosis criterium was at least one positive culture result of NTM.	Only one positive culture result of NTM may be due to false positive or wrong operation.	Low
3. Guan, et al. 2015; Guangzhou, China [3]	Prospective randomized control cohort study	Selection bias	Patient population	Consecutively recruited from outpatient respiratory clinics.	Mild and severe symptom patients were excluded	Medium
4. Kadowaki, et al. 2015; Japan [4]	Retrospective cohort study	Selection bias	Patient selection	1. Could not perform a full screening for immunodeficiency. 2. Could not eliminate the possibility of cystic fibrosis	1. Patients with immunodeficiency were more vulnerable to NTM infection. 2. CF patients might not be completely excluded.	Low
5.* Máiz, et al. 2016; Spain [5]	**Prospective cohort study**	**Source bias**	**Population selection**	**An observational study of historical cohorts from 4 Spanish teaching hospitals with multidisciplinary and standardized non-CF bronchiectasis outpatient clinics.**	**1. Patients were outpatients, causing severe patients excluded.** **2. No unified standard for patient selection.**	**High**
6. Izhakian，et al. 2016; Israel [6]	Retrospective cohort study	Performance bias; Selection bias	Population selection	1.The study precluded patients not under medical care 2.The study is not generalizable to patients treated by other hospital staff members.	1. Patients were in hospital with severe symptoms, causing outpatients excluded. 2. Patients at the same location but from other hospital were not included.	Medium
7. Faverio, et al. 2016; Italy [7]	Prospective cohort study	Selection bias	Population selection	Data were from outpatient clinic and only patients in a stable state were recruited.	Severe patients were excluded for data analysis.	Medium
8. Buscot, et al. 2016; France [8]	Retrospective cohort study	Attrition bias	Follow-up	Functional follow-up was available in 30% of patients with a median duration of 2.7 years.	Only 30% of patients could be followed up, cause attrition bias.	Low
9. Dimakou, et al. 2016; Greece [9]	Prospective cohort study	Detection bias	Detection methods	CF screening, sweat test, saccharin test, and electron microscopy and etc. were employed for patients with different symptoms.	A standard detection method is better for diagnosis and study.	Low

Study	Design	Bias Domain	Source of bias	Support for Judgement	Review Author's Judgement	Risk of Bias
10.* Park et al. 2016; Korean [10]	**Retrospective cohort study**	**Source bias**	**Patient selection**	**The author only included the Non-CF bronchiectasis patients with followed- up for a minimum of 5 years with CT.**	**The patients were not selected randomly, but have been sick for more than 5 years, causing an overestimate of the prevalence of NTM.**	**High**
11.* Aksamit, *et al.* 2017; US [11]	**Retrospective cohort study**	**Source bias**	**Data source**	**Data was from Bronchiectasis Research Registry (BRR).**	**The cohort of patients enrolled from tertiary referral institutions with interest in NTM lung disease, the demographic information described is potentially biased, including overrepresentation of patients with NTM.**	**High**
12.* Hsieh, et al. 2018; Taiwan, China [12]	**Retrospective cohort study**	**Source bias; Selection bias**	**Data source and sample size**	**1. All 96 patients were from Linkou Medical Center. Patients with previous pulmonary tuberculosis and those who had received anti-NTM therapy were excluded. 2. Small sample population (<100).**	**Cases from medical center have source bias; Exclusion of some patients causes selection bias.**	**High**
13. Sin, et al. 2019; South Korea [13]	Retrospective controlled cohort study	Detection bias	False positive	They diagnosed by the isolation of NTM from a respiratory specimen at least once.	Isolation of NTM only once may increase the prevalence due to false positive, causing higher infection rates.	Medium
14.* Amorim, et al. 2019; Portugal [14]	**Prospective cohort study**	**Source bias; performance bias**	**Patient selection and sample size**	**1. The data was from a bronchiectasis referral center. 2. The sample size is lower than 200.**	**Cases from a bronchiectasis referral center have source bias; lower sample size increased the prevalence of NTM.**	**High**
15.* Visser, et al. 2019; Australia [15]	**Prospective cohort study**	**Selection bias; Attrition bias**	**Patient selection Incomplete and missing data**	**1. Potentially selects patients with prominent symptoms, more severe disease, and/or a higher prevalence of NTM. 2. predominantly represents non-indigenous patients 3. Patients with missing variable data were removed.**	**1. Severe patients with prominent symptoms may cause a higher prevalence of NTM. 2. Non-indigenous patients did not represent the whole population 3. Data completeness limits the number of participants.**	**High**
16. Pieters et al. 2019; Netherland [16]	Retrospective cohort study	Performance bias	Incomplete data	The majority of patients were seen every 3 months at the outpatient clinic.	Not all the patients were seen every 3 months at the outpatient clinic.	Low

Study	Design	Bias Domain	Source of bias	Support for Judgement	Review Author's Judgement	Risk of Bias
17.* Dhar, et al. 2019; India [17]	**Prospective cohort study**	**Source Bias**	**Patient selection**	**All the patients were from Indian bronchiectasis registry centers.**	**Patients from registry centers would inevitably cause an overestimation of the prevalence of NTM infections.**	**High**
18. Huang, et al. 2020; Taiwan, China [18]	Retrospective cohort study	Source bias; Detection bias	Patient Selection	1. Inability to completely confirm the bronchiectasis diagnosis. 2. A portion of bronchiectasis diagnoses based on clinical symptoms and chest radiographs, not a reliable diagnostic tool. 3. underestimated the prevalence of immunodeficiency in our cohort.	Some patients might not be bronchiectasis; immunodeficiency may cause high prevalence due to vulnerability.	Medium
19. Darwish, et al. 2020; Egypt [19]	Prospective cohort study	Detection bias Performance bias	NTM were detected by PCR Too small sample size	1. The sputum samples were assessed by PCR, and positive cases did another PCR after 2 months. 2. Sample size 40 < 200	PCR may cause false positive. The only study (of all 13 studies) NTM was not diagnosed by MBC; Small sample size increased prevalence	Medium
20.* Kwak, et al. 2020; South Korea [20]	**Prospective cohort study**	**Source Bias**	**Patient selection**	**Only the patients without NTM infection were included, and then studied their NTM infection afterwards.**	**The patients are not random cases.**	**High**
21. Sharif, et al. 2020; Pakistan [21]	Prospective cohort study	Source bias	Patient selection	This observational cohort study was conducted in the inpatient department only.	Inpatients were usually with severe symptoms, and that may cause overestimation.	Low
22.* Choate, et al. 2021; US [22]	**Retrospective cohort study**	**Source Bias**	**Patient selection**	**All the patients were from the bronchiectasis and NTM Research Registry (BRR).**	**Patients from registry centers would cause an overestimation of the prevalence of NTM infections.**	**High**
23.* Metersky et al. 2021; US [23]	**Prospective cohort study**	**Source Bias**	**Patient selection**	**All the patients were from the bronchiectasis and NTM Research Registry (BRR).**	**Patients from registry centers would cause an overestimation of the prevalence of NTM infections.**	**High**
24. Yin, et al. 2021; China [24]	Retrospective cohort study	Performance bias	Patient information collection	Much patient information was self-reported and recorded.	The self-reported information might be inaccurate and hidden.	low

Note: Bold type with an asterisk * indicate the studies with source/selection bias.

Table S4: Statistics and calculation of NTM subspecies

Subspecies of NTM	Number of Studies	All NTM Isolated Patient*	Patients with NTM subspecies	% of NTM Subspecies **	McShane	Kadowaki	Máiz	Izhakian	Faverio	Kwak	Darwish	Buscot	Dimakou	Metersky	Yin	% of NTM Isolated patients
MAC	11	255	193	**75.687**	7	28	9	14	24	29	2	7	2	40	31	
M. simiae	3	56	10	**17.857**	1		1	8								
M. gordonae	3	59	7	**11.864**	1		2		4							
M. xenopi	1	9	1	**11.111**	1											
M. fortuitum	4	103	7	**6.796**	1		2	2						2		
M. abscessus	6	208	21	**10.096**			3	3	1	3				1	10	
M. chelonae	6	182	11	**6.044**	1		1	2	2					2	3	
M. lentiflavum	1	18	1	**5.556**			1									
M. kansasii	3	88	5	**4.88**	1				1						3	
M. terrae	1	47	1	**2.128**										1		
M. shimoidei	1	32	1	**3.125**					1							
Undetermined	3	82	6	**7.317**						4	1			1		
Sum (person)	**7**	**1139**			**9**	**26**	**18**	**29**	**32**	**35**	**3**	**7**	**2**	**47**	**47**	
sum (time)					**13**	**28**	**19**	**29**	**33**	**36**	**3**	**7**	**2**	**47**	**47**	
Bronchiectasis Patients					**106**	**147**	**218**	**339**	**162**	**221**	**40**	**196**	**205**	**410**	**202**	**50.712**

Note: Of all 14 included studies, only 9 provided detection methods of NTM subspecies. *The number of all NTM is the sum of all the patients in the studies with the subspecies. **The percentage (%) of NTM infected patients is the sum of all patients with NTM infection divided by the sum of all bronchiectasis patients in all the 9 studies.

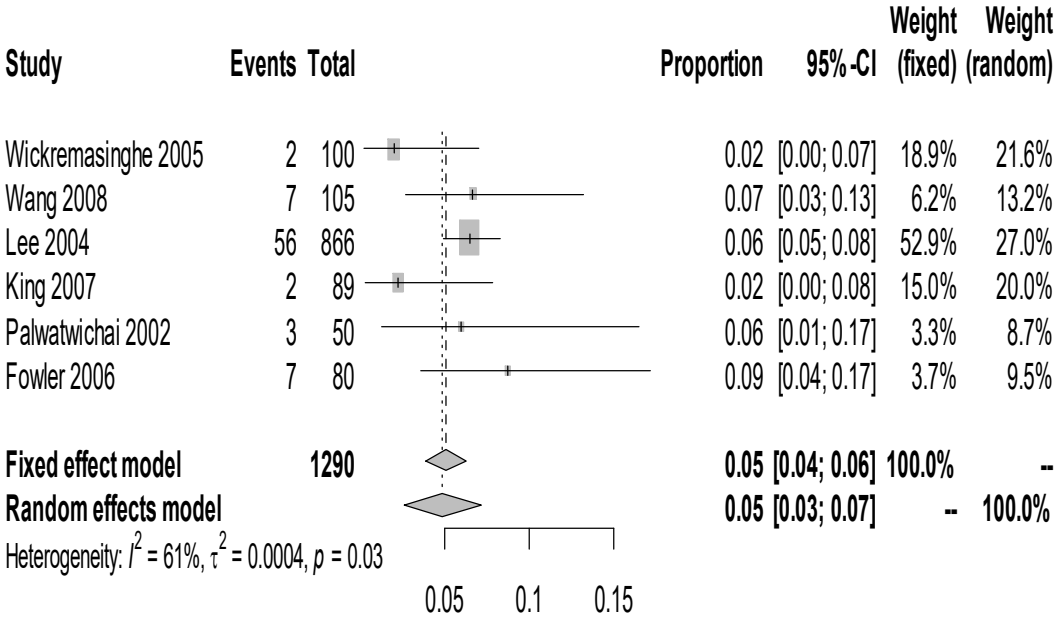

Figure S1: Re-calculating the prevalence of NTM in adults with non-cystic fibrosis bronchiectasis from 1990 to 2006 in Chu's paper "Prevalence of nontuberculous mycobacteria in patients with bronchiectasis: A meta-analysis" published in 2014 [25].

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