Online supplementary data

Study Title:

Comorbidities and the risk of mortality in patients with bronchiectasis: an international cohort study

Material contained in this document:

- Process to define bronchiectasis aetiologies
- Data collection procedure at each site
- Standardised definitions of comorbidities
- Guide to interpretation of Spearman's rho correlation coefficient
- Table S1: Comorbidities prevalence for the full cohort and prevalence comparison between survivors and non-survivors
- Figure S1: Solid tumour prevalence chart
- Table S2: Derivation of the bronchiectasis comorbidity index (BCI)

Process to define bronchiectasis aetiologies

Patients in each site underwent the same comprehensive diagnostic work-up as suggested by the 2010 British Thoracic Society (BTS) guidelines including: full blood count, serum electrophoresis, serum immunoglobulin (Ig) G, IgA, IgM, total IgE, specific IgE and precipitins for A. fumigatus, and pulmonary function testing with reversibility testing and diffusion capacity test.(1) If there was a clinical suspicion of primary ciliary dyskinesia, such as recurrent sinusitis and/or chronic otitis media, patients were referred for further testing with nasal mucociliary clearance measured by the saccharin test and/or nasal nitric oxide at specialist primary ciliary dyskinesia centres. $Alpha_1$-antitripsin deficiency (A1AT) was evaluated in the presence of emphysema affecting lower lobes on high-resolution computed tomography (HRCT) scan and/or significant family history. Autoimmunity testing including anti-nucleolar antibodies, extractable nuclear antigens, anti-neutrophil cytoplasmic antibodies, rheumatoid factor and anti–citrullinated protein antibody were requested if a rheumatological disease was clinically suspected. Sweat test and cystic fibrosis (CF) transmembrane conductance regulator genetic testing were requested if there were signs and symptoms suggestive for CF as suggested by BTS guidelines.(1)

An evaluation of CT images and testing results was performed, including immunoglobulins, skin prick testing or serum IgE resting to *A. fumigatus* and *Aspergillus* precipitins, and serum electrophoresis, in order to differentiate patients into categories of congenital abnormalities, post-obstructive bronchiectasis, primary or secondary immunodeficiency, A1AT or allergic bronchopulmonary aspergillosis (ABPA). If all of the above tests were negative, a history of prior severe respiratory infections was investigated, including previous infection with tuberculosis (TB) or non-tuberculous mycobacteria (NTM). If no history of previous respiratory infections was present, an association between bronchiectasis and other diseases, such as COPD, asthma, inflammatory bowel disease (IBD), overt aspiration on barium studies

or connective tissue disease (CTD) was investigated. If tests were negative and no association with other diseases was found, a diagnosis of idiopathic bronchiectasis (IB) was made.

A serum IgE of >1000 IU/ml, positive *Aspergillus* precipitins and skin prick, blood eosinophilia of >0.4 and compatible radiology was required to fulfil the diagnosis of ABPA.(2) Post-infective bronchiectasis (PIB) was diagnosed in patients reporting a history of symptom onset within 5 years of a severe respiratory tract infection, such as pneumonia, whooping cough or complicated measles infection. Where a patient reported a history of severe respiratory infections, but with a five-year symptom free period, the post-infective diagnosis was not attributed. Post-TB bronchiectasis was diagnosed in patients with clearly documented prior TB and compatible radiology. COPD-associated bronchiectasis was classified in the presence of significant smoking history and airflow obstruction according to GOLD criteria.(3) Bronchiectasis associated with asthma was diagnosed in patients without post-infective bronchiectasis and with normal or negative results of blood investigations, according to GINA guidelines.(4) Bronchiectasis associated with IBD was diagnosed if patients had ulcerative colitis or Crohn's disease and no other suggested aetiology for bronchiectasis. In the presence of a diagnosis of both bronchiectasis and CTD, including rheumatoid arthritis (RA), Sjögren's syndrome, systemic sclerosis, psoriatic arthritis, ankylosing spondylosis or mixed CTD, a diagnosis of CTD-associated bronchiectasis was made. Yellow nail syndrome was diagnosed when examination showed yellow discoloration of dystrophic nails together with bronchiectasis and sinusitis, whether or not patients had other features of the syndrome. Young's syndrome was diagnosed when there was a history of bronchiectasis, sinusitis and azoospermia in males and negative CF testing.(5) A diagnosis of IB was made by exclusion of any known cause.

Data collection

Demographics, comorbidities, disease severity, bronchiectasis aetiology, symptoms, sputum evaluation, baseline radiological, functional and laboratory findings, quality of life, and long-term treatments and outcomes - including exacerbations, hospitalisations and mortality - over a five-year follow-up period were recorded in each site. Radiological severity was assessed using the modified Reiff score incorporating number of lobes and degree of dilatation as previously described.(6) Bronchiectasis severity was evaluated according to the BSI.(6) Quality of life was assessed using the St. George's Respiratory Questionnaire (SQRQ).(7) Microbiological examinations were performed on sputum, bronchial aspiration or bronchoalveolar lavage during stable state. Identification of microorganisms and susceptibility testing were performed according to standard methods. Chronic infection was defined by the presence of pathogenic bacteria in sputum culture on two or more occasions at least three months apart over a one-year period.(8) The predominant pathogen was the organism grown most frequently over the study period. Patients who were unable to provide sputum samples due to absence of a productive cough were classified as not having chronic infection for the purposes of analysis.

Study outcomes

Exacerbations: An exacerbation of bronchiectasis was defined as a clinical diagnosis of exacerbation for which antibiotics were prescribed in the presence of at least one (and usually more than one) of the following symptoms: increasing cough, increasing sputum volume, worsening sputum purulence, worsening dyspnea, increased fatigue/malaise, fever, and hemoptysis.(1)

Hospitalization for severe exacerbations: Severe exacerbations were defined according to the BTS guidelines, and unscheduled hospitalizations or emergency department visits for severe

bronchiectasis exacerbations or complications were recorded from patient histories and verified using administrative databases that record admissions.(1, 6)

Mortality: All-cause mortality up to 5 years of follow up was evaluated.

Details of each individual cohort are displayed below:

Dundee, United Kingdom

This cohort consisted of 286 consecutive bronchiectasis patients attending a specialist bronchiectasis clinic in Tayside, Scotland, UK. Patients in this cohort were included in 2011 with follow-up data to September 2015. Patients were assessed according to a standardised protocol based on the British Thoracic Society (BTS) guidelines including standardised testing for aetiology. Clinic data were recorded at baseline and subsequent clinic review. All bacteriology was performed on early morning sputum samples. Patients were routinely asked to provide sputum samples at least twice a year at clinic reviews. Data on exacerbations were obtained from patient histories and verified against electronic general practice prescribing data to ensure all exacerbations treated with antibiotics were captured. Hospital admissions and mortality data were obtained from patient follow-up and verified by electronic medical records containing all hospital admissions and deaths regionally. Follow-up status was verified in 100% of participants. Outcomes available in this database were 5-year mortality, subsequent hospital admissions and exacerbations, and quality of life data.

Galway, Ireland

This database included 280 consecutive patients attending respiratory clinics at Galway University Hospitals and Merlin Park University Hospitals in Galway, Ireland. Patients in this cohort were included in 2009-2011 with follow-up data to September 2015. All patients undergoing diagnostic investigation for bronchiectasis were assessed according to BTS

guidelines including standardised testing for aetiology. In this centre, all patients referred for investigation routinely undergo bronchoscopic evaluation and lavage as part of their work-up. Clinic data were recorded at baseline and subsequent review. Patients were asked to provide 6-monthly samples of sputum where possible for microbiological surveillance. Data on exacerbations, hospitalisations and mortality were obtained from patient histories and full review of medical and electronic records. Data on exacerbations and hospitalisations was verified against prescribing practices and admission records. Data pertaining to mortality and causes of death were verified against the Health Service Executive Civil Register. Follow-up status was verified in 100% of participants. Outcomes available in this database were 5-year mortality, subsequent hospital admissions and exacerbations.

Leuven, Belgium

The bronchiectasis cohort from the University of Leuven, Belgium, contains data on 190 patients seen at the department with a radiological and clinical diagnosis of bronchiectasis from June 2006 to October 2012. All patients had a high resolution CT scan confirming the presence of bronchiectasis. Patients underwent testing for aetiological causes in accordance with British Thoracic Society guidelines. Clinical data were collected at baseline and survival data determined for a mean of 49 months. The definitions of colonisation and the assessments of radiological severity were in accordance with those used in the other derivation cohorts. Outcomes available in this cohort were 5-year mortality, subsequent hospital admissions and exacerbation frequency.

Monza, Italy

This cohort included 230 consecutive patients with bronchiectasis (defined by clinical history and high-resolution computed tomography scan) attending respiratory clinics at the San Gerardo Hospital in Monza, Italy. Patients in this cohort were included in 2011 and 2012 with

follow up data to September 2015. As with other cohorts, patients with cystic fibrosis or traction bronchiectasis secondary to pulmonary fibrosis were excluded. Patients were assessed according to a standardised protocol based on BTS guidelines including standardised testing for aetiology. Data on exacerbations, hospital admissions and mortality were obtained from patient histories and follow-up. Follow-up status was verified in 100% of participants. Outcomes available in this cohort were 5-year mortality, subsequent hospital admissions and exacerbation frequency.

Comorbidity assessment

Comorbidity assessment was performed according to standardized definitions with review of objective assessment and confirmatory tests to verify diagnosis where possible. Below are a few examples of how comorbidity was determined in the most prevalent or significant comorbidities among this patient population.

GERD: Based on a presumptive diagnosis of GERD in the setting of typical symptoms of heartburn and regurgitation or by improvement in symptoms after trial of therapy as per American College of Gastroenterology recommendations. Patients were considered to have GERD where a diagnosis of GERD was recorded in the notes by a primary or secondary care physician, or in a patient taking a prescribed anti-reflux medication.

Hypertension: Based on previous guidelines of clinic blood pressure readings of >140/90mmHg on three separate occasions taking the lowest of at least two readings at each visit. Note: since 2011 guidelines, ambulatory and/or home blood pressure measurements are included in the diagnosis of arterial hypertension according to the British Hypertension and European Society of Cardiology guidelines. Patients were considered to have hypertension

where a diagnosis of hypertension was recorded in the notes by a primary or secondary care physician, or in a patient taking a prescribed anti-hypertensive medication.

High cholesterol: Based on an objective fasting total cholesterol level of >5 mmol/L for healthy adults and/or >4 mmol/L in high risk patients and/or a ratio of total cholesterol to HDL above 4.The 2014 guidelines allow measurement of cholesterol in non-fasting samples. Patients were considered to have high cholesterol where a diagnosis of high cholesterol was recorded in the notes by a primary or secondary care physician AND objective evidence of cholesterol levels could be assessed, or in a patient taking a prescribed cholesterol medication for primary or secondary prevention.

COPD: Based on the presence of a significant smoking history of >10 pack years and objective confirmation of airflow obstruction according to GOLD criteria. Patients were considered to have COPD where a diagnosis of COPD was recorded in the notes in patients with a significant smoking history AND objective evidence of airflow obstruction in primary or secondary care. In patients prescribed inhaled medications without objective evidence of airflow limitation, a diagnosis of COPD was not recorded.

Osteoporosis: Based on a bone mineral density that is 2.5 SD or more below that of a "young normal" adult (T-score at or below -2.5) on DEXA scanning and/or clinical diagnosis in at-risk individuals who have sustained a low-trauma fracture according to World Health Organization guidelines. Patients were considered to have osteoporosis where a diagnosis of osteoporosis was recorded in the notes by a primary or secondary care physician AND objective evidence on DEXA scanning or in patients taking bisphosphonate treatment.

CTD: Based on assessment by an expert rheumatologist according to American College of Rheumatology guidelines incorporating history, physical examination, laboratory and radiographic findings according to individual disease.

Myocardial infarction (MI): Based on a rise and/or fall of cardiac biomarker values plus at least one of: symptoms of ischemia, new or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB), development of pathological Q waves in the ECG, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality and/or identification of an intracoronary thrombus by angiography or autopsy according to the universal definition in the European Cardiac Society (ESC) guidelines. Patients were considered to have had an MIwhere a diagnosis was recorded in the notes AND objective evidence in the form of blood tests, ECG or imaging studies was available.

Chronic heart failure: Based on the presence of symptoms and signs of heart failure with measurement of ejection fraction on echocardiography to determine if reduced or preserved and to determine the presence of structural heart disease or diastolic dysfunction in the presence of a preserved ejection fraction according to the European Society of Cardiology guidelines. Patients were considered to have heart failure where a diagnosis of heart failure was recorded in the notes or patients were prescribed heart failure medications AND objective evidence on echocardiography was available.

Depression: Based on the presence of at least four out of ten depressive symptoms, present for at least 2 weeks for most of every day according to ICD-10 criteria. Patients were considered to have depression where a diagnosis of depression was recorded in the notes by primary or secondary care physicians or in patients prescribed anti-depressant medications.

Solid tumor/metastatic malignancy: Based on assessment by an expert physician and/or oncologist with appropriate objective staging imaging and histopathological investigations.

Peripheral vascular disease: Based on the presence of symptoms and signs of peripheral vascular disease, objective measurement of ankle brachial pressure indices in primary care setting or confirmatory imaging investigations such as Doppler ultrasound, angiography or

digital subtraction arteriography according to European Society of Cardiology guidelines. Patients were considered to have peripheral vascular disease where a diagnosis of peripheral vascular disease was recorded in the notes AND objective evidence was available.

Atrial fibrillation: Based on an irregular heart rate with ECG confirmation. Patients were considered to have atrial fibrillation where a diagnosis of atrial fibrillation was recorded in the notes by a primary or secondary care physician AND objective ECG evidence was available.

Chronic kidney disease (CKD): Based on objective reduced eGFR values for staging of chronic kidney disease as per national and international guidelines.

Diabetes mellitus: Based on plasma glucose criteria, with fasting glucose >7.0 mmol/L, random or 2-h glucose post-oral glucose tolerance test > 11.1 mmol/L, or HbA1C ≥6.5% according to the American Diabetes Association guidelines. Patients were considered to have diabetes mellitus where a diagnosis of diabetes mellitus was recorded in the notes by a primary or secondary care physician AND objective blood glucose levels were available.

Cerebrovascular accident (CVA)/Transient ischemic attack (TIA): Based on the presence of symptoms and signs with confirmatory imaging findings on CT brain, MRI brain, Doppler USS neck or other investigations according to the American Heart Association/ American Stroke Association guidelines. Patients were considered to have a CVA/TIA where a diagnosis was recorded in the notes, patients were prescribed anticoagulant medications AND objective evidence on imaging was available.

RA: Based on assessment by an expert rheumatologist according to American College of Rheumatology guidelines incorporating history, physical examination, laboratory and radiographic findings with four of seven of the diagnostic criteria present, one of which must have been present for a minimum of 6 weeks.

Pulmonary hypertension: Based on an increase in mean pulmonary arterial pressure ≥25 mmHg at rest as assessed by echocardiography or right heart catheterisation where performed. Patients were considered to have pulmonary hypertension where a diagnosis was recorded in the notes AND objective evidence on imaging was available.

Thromboembolic disease: Based on objective confirmation of deep vein thrombosis on Doppler ultrasound or pulmonary embolism on CT pulmonary angiography (CTPA). Patients were considered to have thromboembolic disease where a diagnosis was recorded in the notes, patients were prescribed anticoagulant medications AND objective evidence on imaging was available.

Overt aspiration: Based on objective confirmation of aspiration on barium swallow studies. Patients were considered to have overt aspiration where a diagnosis was recorded in the notes AND objective evidence on imaging was available.

Leukemia: Based on assessment by an expert oncologist according to World Health Organization guidelines incorporating history, physical examination, full blood count and film, imaging, bone marrow biopsy and cytogenetic abnormality conformation.

Lymphoma: Based on assessment by an expert oncologist according to World Health Organization guidelines incorporating history, physical examination, full blood count and film, imaging and histopathological confirmation.

Iron deficiency anemia: Based on objective low iron stores and a hemoglobin level two standard deviations below normal as per national and international guidelines.

Cognitive impairment: Based on a clinical diagnosis by a primary or secondary care physician whereby acquired cognitive deficits in more than one area of cognition interfere with normal activities of daily living and represent a decline from a previously higher level of functioning. Patients were considered to have cognitive impairment where a diagnosis was recorded in the

notes, deficits on structured memory tests were noted, and/or patients were prescribed medications to treat dementia.

Guide to interpretation of Spearman's rho correlation coefficient

Interpretation of Spearman's rho correlation coefficient: Spearman's correlation coefficient is a statistical measure of the strength of the relationship between paired data. The closer the value is to 1, the stronger the relationship. Correlation is an effect size; the strength of the correlation can therefore be described using the following guide for the absolute value Spearman's rho: ≤0.19 - very weak; 0.2-0.4 weak; 0.40-0.59 moderate; 0.60-0.79 strong; ≥ 0.80 very strong.

Table S1: Comorbidities prevalence for the full cohort and prevalence comparison between survivors and non-survivors.

	Comorbidity prevalence	Total cohort (n=986) %	Survivors (n=864) %	Non-survivors (n=122) %	P value
1	*GORD	34.3	32.4	47.6	**0.001**
2	HTN	27.5	26.5	34.4	0.080
3	High cholesterol	20.1	19.6	23.8	0.281
4	*COPD	17.1	14.2	37.7	**<0.001**
5	Osteoporosis	15.9	15.2	20.5	0.147
6	Rhinosinusitis	13.1	13.5	9.8	0.315
7	Asthma	12.4	12.5	11.5	0.883
8	*CTD	12	10.9	19.7	**0.010**
9	*MI	11.7	10.3	21.3	**0.001**
10	*CHF	10	8.7	19.7	**<0.001**
11	Depression	9.3	9.1	10.7	0.496
12	*Solid tumour	9.1	8.7	12.3	**0.028**
	*Lung cancer	1.4	0.9	4.9	**0.004**
	*Oesophageal cancer	0.8	0.5	3.3	**0.010**
13	*PVD	8.9	6.8	23.8	**<0.001**
14	*PUD	8.9	6.8	23.8	**<0.001**
15	*Atrial fibrillation	8.7	7.6	16.4	**0.003**
16	Anxiety	8.4	8.2	9.8	0.372
17	*CKD	8.2	6.8	18.1	**<0.001**
18	*Diabetes Mellitus	7.1	6.0	14.8	**0.002**
19	Immunodeficiency	6.8	6.7	7.4	0.704
20	*CVA	6.1	5.2	12.3	**0.007**
21	ABPA	5.8	6.1	3.3	0.298
22	*RA	5.7	4.9	11.5	**0.007**
23	Osteoarthritis	5.6	5.6	9	0.151
24	Thyroid disorder	5.6	5.9	4.9	0.836
25	*Pulmonary hypertension	4.4	3.5	10.7	**0.001**
26	TB	4.1	3.8	6.6	0.151
27	Childhood infection	4	3.9	4.1	0.808
28	Valvulopathy	3.5	3.1	6.6	0.066
29	*Thromboembolic disease	3.4	2.9	6.6	**0.028**
30	Liver disease	3.4	3.5	3.3	1.000
31	Sarcoidosis	2.5	2.7	0.8	0.346
32	IBD	2.4	2.4	2.5	1.000
33	Morbid obesity	2.3	2.1	4.1	0.191
34	Overt aspiration	1.9	1.8	2.5	0.721
35	*Psoriasis	0.7	0.5	2.5	**0.045**
36	*Metastatic malignancy	1.8	0.9	8.2	**<0.001**
37	Spinal problems	1.8	1.5	4.1	0.061
38	OSA	1.6	1.6	1.6	1.000
39	Pulmonary nodules	1.5	1.6	0.8	0.710

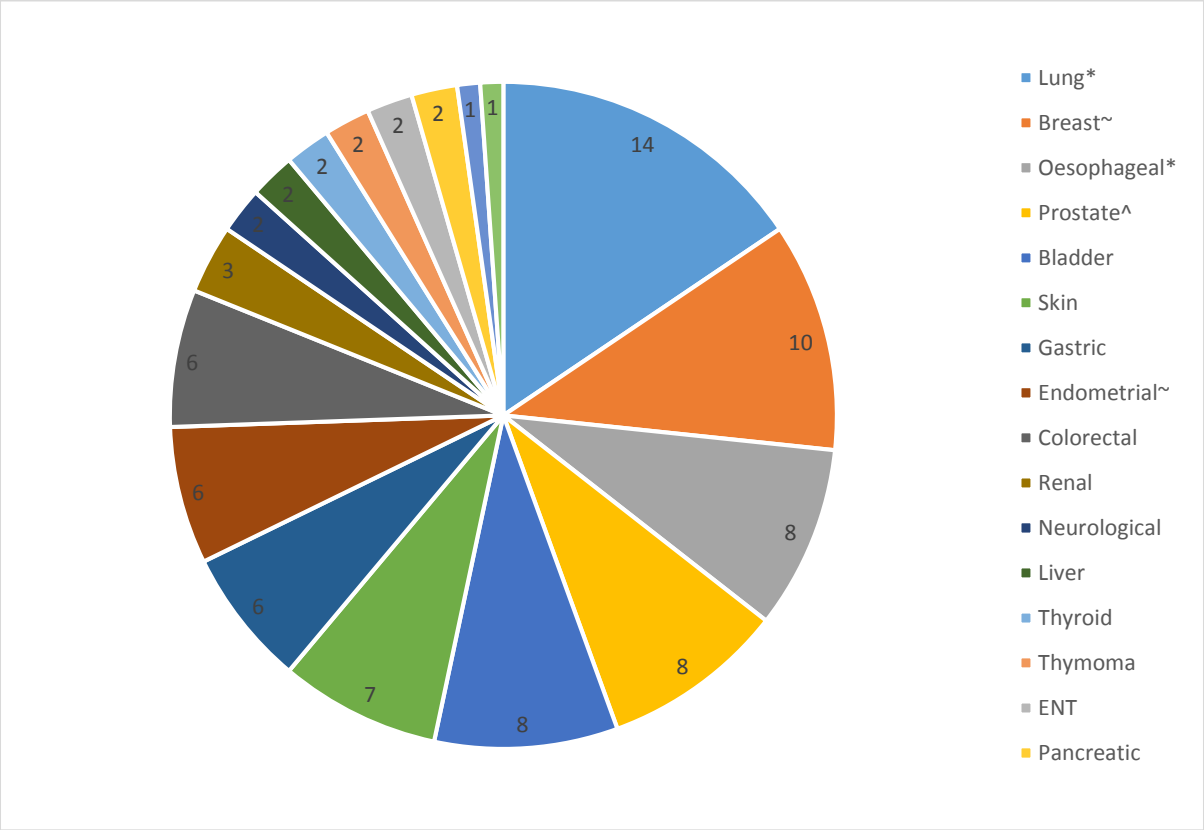
40	*TIA	1.5	1	4.9	**0.006**
41	*Leukaemia	1.4	1.1	3.3	**0.021**
42	BPH	1.4	1.0	2.5	0.177
43	PCD	1.3	1.5	0	0.388
44	*Iron deficiency anaemia	1.3	0.9	4.1	**0.015**
45	Gout	1.3	1.2	2.5	0.211
46	Cataracts	1.3	1.3	1.6	0.669
47	*Cognitive impairment	1.1	0.8	2.6	**0.010**
48	*Lymphoma	1.1	0.4	2.6	**0.006**
49	Vasculitis	1.1	1	1.7	0.635
50	PMR	1.1	1.2	0.8	1.000
51	Recurrent cystitis	1.1	0.9	2.5	0.145
52	A1AT deficiency	1	1.2	0	0.621
53	Diverticular disease	1	0.8	2.5	0.116
54	Gallstones	0.9	1	0	0.611
55	Congenital disorders	0.8	0.8	0.8	1.000
56	Other psychological disorder	0.6	0.7	0	1.000
57	Epilepsy	0.6	0.5	1.6	0.163
58	Postural hypotension	0.6	0.5	1.6	0.163
59	*Multiple myeloma	0.6	0.3	2.5	**0.028**
60	Coeliac disease	0.5	0.3	1.7	0.118
61	Pernicious anaemia	0.5	0.3	1.6	0.118
62	Parkinson’s disease	0.5	0.4	0.9	0.484
63	Pneumothorax	0.4	0.2	1.6	0.077
64	Hemochromatosis	0.4	0.5	0	1.000
65	Fibromyalgia	0.4	0.2	1.6	0.077
66	Primary renal disease	0.4	0.2	1.6	0.077
67	Migraine	0.4	0.3	0.8	0.411
68	Other neurological disorders	0.4	0.2	1.6	0.077
69	Glaucoma	0.4	0.3	0.8	0.411
70	Haemangioma	0.4	0.5	0	1.000
71	AIDS	0.2	0	0.2	1.000
72	Cardiomyopathy	0.2	0.1	0.8	0.232
73	*AAA	0.2	0	1.6	**0.015**
74	Ovarian problems	0.2	0.2	0	1.000
75	Syphilis	0.2	0.2	0	1.000
76	Asbestosis	0.1	0.1	0	1.000
77	Spinal muscular atrophy	0.1	0.1	0	1.000
78	Myasthenia gravis	0.1	0.1	0	1.000
79	Pancreatitis	0.1	0.1	0	1.000
80	Tracheomalacia	0.1	0.1	0	1.000
81	Swyer James McLeod	0.1	0.1	0	1.000

Definition of abbreviations: GORD: gastro-oesophageal reflux disease; HTN: hypertension; COPD: chronic obstructive pulmonary disease; CTD; connective tissue disease; MI:

myocardial infarction; CHF: congestive heart failure; PVD: peripheral vascular disease; PUD: peptic ulcer disease; CKD: chronic kidney disease; CVA: cerebrovascular attack; ABPA: allergic bronchopulmonary aspergillosis; RA: rheumatoid arthritis; TB: tuberculosis; IBD: inflammatory bowel disease; OSA: obstructive sleep apnoea; TIA: transient ischaemic attack; BPH: benign prostatic hyperplasia; PCD: primary ciliary dyskinesia; PMR: polymyalgia rheumatica; A1AT: Alpha$_{-1}$ anti-trypsin deficiency; AIDS: acquired immunodeficiency syndrome; AAA: abdominal aortic aneurysm.

Figure S1: Solid tumour prevalence chart

Solid tumours were identified in 90 (9.1%) of total cohort. This pie chart provides a breakdown of the prevalence of tumor type among these patients.



Definition of abbreviations: ENT = Ears, nose and throat cancers.

*Represents statistically significant difference between survivors and non-survivors. ~Represents female-specific malignancies. ^Represents male-specific malignancies.

Lung and oesophageal cancer, conferred a significant increased risk of death with prevalence rates of 5% vs. 1% and 3.5% vs. 0.5% in non-survivors *versus* survivors (p=0.004 and p=0.01), respectively.

Table S2: Derivation of the Bronchiectasis Comorbidity Index (BCI) and Point Allocation

Comorbidity	Hazard Ratio	95% CI	P value	Points
Metastatic malignancy	5.21	2.83-9.58	<0.0001	**10**
Iron deficiency anaemia	2.52	1.15-5.55	0.02	**6**
Liver disease	2.21	0.91-5.37	0.08	**5**
Haematological malignancy*	1.87	0.79-4.45	0.16	**4**
Diabetes mellitus	1.77	1.13-2.79	0.01	**3**
Solid tumour	1.60	1.00-2.57	0.048	**3**
Pulmonary hypertension	1.56	0.87-2.80	0.14	**3**
Peptic ulcer disease	1.49	0.85-2.59	0.16	**2**
Peripheral vascular disease	1.44	0.97-2.15	0.07	**2**
Gastro-oesophageal reflux disease	1.31	0.96-1.79	0.09	**2**
Ischaemic heart disease	1.31	0.91-1.87	0.14	**2**

*Although haematological malignancy can be a cause of bronchiectasis, we retained this in the model where haematological malignancy was not considered by the clinician as the underlying aetiology after testing.

References

1. Pasteur MC, Bilton D, Hill AT. British Thoracic Society guideline for non-CF bronchiectasis. *Thorax* 2010; 65 Suppl 1: i1-58.
2. Schwartz HJ, Greenberger PA. The prevalence of allergic bronchopulmonary aspergillosis in patients with asthma, determined by serologic and radiologic criteria in patients at risk. *The Journal of laboratory and clinical medicine* 1991; 117: 138-142.
3. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA, Sin DD, Rodriguez-Roisin R. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *American journal of respiratory and critical care medicine* 2013; 187: 347-365.
4. Reddel HK, Bateman ED, Becker A, Boulet LP, Cruz AA, Drazen JM, Haahtela T, Hurd SS, Inoue H, de Jongste JC, Lemanske RF, Jr., Levy ML, O'Byrne PM, Paggiaro P, Pedersen SE, Pizzichini E, Soto-Quiroz M, Szefler SJ, Wong GW, FitzGerald JM. A summary of the new GINA strategy: a roadmap to asthma control. *The European respiratory journal* 2015; 46: 622-639.
5. Handelsman DJ, Conway AJ, Boylan LM, Turtle JR. Young's syndrome. Obstructive azoospermia and chronic sinopulmonary infections. *The New England journal of medicine* 1984; 310: 3-9.
6. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, Poppelwell L, Salih W, Pesci A, Dupont LJ, Fardon TC, De Soyza A, Hill AT. The bronchiectasis severity index. An international derivation and validation study. *American journal of respiratory and critical care medicine* 2014; 189: 576-585.
7. Wilson CB, Jones PW, O'Leary CJ, Cole PJ, Wilson R. Validation of the St. George's Respiratory Questionnaire in bronchiectasis. *American journal of respiratory and critical care medicine* 1997; 156: 536-541.
8. Pasteur MC, Helliwell SM, Houghton SJ, Webb SC, Foweraker JE, Coulden RA, Flower CD, Bilton D, Keogan MT. An investigation into causative factors in patients with bronchiectasis. *American journal of respiratory and critical care medicine* 2000; 162: 1277-1284.