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Epidemiology and economic burden of bronchiectasis requiring hospitalisation in Singapore

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Epidemiology and Economic Burden of Bronchiectasis Requiring Hospitalization in Singapore

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ABSTRACT:

Background and objective: Little is known about the epidemiology and cost of bronchiectasis in Asia. This study describes the disease burden of bronchiectasis in Singapore.

Methods: A nationwide administrative dataset was used to identify hospitalizations with bronchiectasis as a diagnosis. Population statistics and medical encounter data were used to estimate the incidence, mortality, prevalence and direct medical costs associated with hospitalization-requiring bronchiectasis.

Results: There were 420 incident hospitalized bronchiectasis patients in 2017, giving an incidence rate of 10.6/100,000. Age-standardized incidence declined on average by 2.7% per year between 2007 and 2017. Incidence rates increased strongly with age in both men and women. Tuberculosis was a secondary diagnosis in 37.5% of incident hospitalizations in 2007, but has declined sharply since then. Patient survival was considerably lower in both men (5-year Relative Survival Ratios (RSR) of 0.63 (95% CI, 0.59 to 0.66)) and women ((5-year RSR of 0.75 (95% CI, 0.72 to 0.78)). The point prevalence of bronchiectasis was 147.1/100,000 in 2017, and increased sharply with age, with more than 1% of people aged 75 years and older having bronchiectasis. Total first-year costs among incident bronchiectasis patients in 2016 varied widely, with an average of $7,331 (standard deviation of $8,863). About 10% of the patients admitted in 2016 had total first-year costs of more than $14,380.

Conclusion: Bronchiectasis is common and imposes a substantial burden on health care costs and survival rates of patients in Singapore.

INTRODUCTION

Non-cystic fibrosis bronchiectasis is characterized by permanent dilatation of the airways leading to persistent cough, sputum production, dyspnoea, and recurrent exacerbations.[1] Epidemiologic studies from the United States of America (USA) and Europe have highlighted the high prevalence and rate of hospitalization of bronchiectasis, particularly among older people and women.[2-5] Few studies have been conducted in Asia. A national health survey in Korea reported that bronchiectasis was diagnosed in 0.8% of adults 40 years and above.[6] Studies in Asia suggest post-tuberculosis is the commonest aetiology of bronchiectasis.[7-8]

In the USA, patients with bronchiectasis were associated with 2.0 additional hospital days per patient, 6.1 additional outpatient encounters and 27.2 additional days of antibiotic therapy in 2001. The health care cost per patient with bronchiectasis was US$5,681 higher than patient without.[9] In Germany, the health care cost for patients with bronchiectasis was a third higher than in matched controls, and antibiotic expenditures were nearly 5 times higher.[10]

Singapore is an Asian city-state that has experienced rapid economic development in the past 60 years, accompanied by both epidemiologic and demographic transitions, resulting in an ageing population, low birth rate and relatively long life expectancies.[11] The major causes of disease burden are chronic non-communicable conditions such as cancers, cardiovascular diseases, and mental and neurological disorders.[12] The epidemiology of bronchiectasis in Singapore is unknown. In this paper, we report the incidence, mortality and prevalence of bronchiectasis requiring hospitalization in Singapore, as well as associated healthcare utilization and costs.

METHODS

Singapore has a mixed healthcare provision system with both private sector and public sector providers.[13] Overall, the public sector market share is approximately 80% for hospital-based care, and 20% in primary care.[13] Health care in the public sector is heavily subsidized by the government. Subsidies are mean-tested in all healthcare settings, primarily using patient's per capita household income or individual monthly income, to ensure resources are better targeted at those who need them. Inpatient treatment at public acute hospitals receives ward subsidies of up to 80%.[14] At specialist outpatient clinics (SOCs) based in public hospitals and polyclinics providing subsidized primary care, subsidies are up to 70% for SOC services and 75% for medications. In primary care dominated by private players, the Community Health Assist Scheme (CHAS) enables Singaporeans from lower- to middle-income families to receive subsidies for medical and/or dental care at accredited private general practitioner (GP) and dental clinics.[15]

Study Design

A Ministry of Health (MOH)-hosted administrative database was used. This database contains de-identified individual-level hospitalization records (containing demographic information, dates of admission and costs of hospitalization, both before and after government subsidies, and mortality information, and primary and secondary discharge diagnoses coded using ICD-9-CM for the years 1999-2011 and ICD-10-AM [Australian Modification] for year 2012 and after) from all public and private acute hospitals for the years 1999-2017. MOH conducts annual checks on the hospitalisation database to ensure its completeness. The database also contains records of visits at Emergency Department (ED), public SOCs and polyclinics as well as government-subsidised visits at private GP clinics.

For these encounters, the diagnosis as well as the amount charged before and after government subsidies are available, except for SOC visits. To estimate public sector outpatient costs, we used a set of norm costs derived for the purposes of government subvention. All encounters were linked using anonymised patient identity numbers to give patient-level data. We considered the amount charged before subsidies as “costs”, and the amount post-subsidy as ‘bills”.

The period of analysis for this study is 2007-2017. Bronchiectasis was defined using ICD-9-CM 011.50-011.56 (tuberculous bronchiectasis), 494 (bronchiectasis) and 748.61 (congenital bronchiectasis), and ICD-10-AM J47 (bronchiectasis) and Q33.4 (congenital bronchiectasis). Incident hospitalized bronchiectasis for any year was defined as patients with a first admission for bronchiectasis as the primary diagnosis (i.e. without a prior admission for bronchiectasis as a primary cause). The prevalence of ever-hospitalized bronchiectasis was estimated as of 30th June 2017 by identifying all patients with a recorded inpatient hospitalization of bronchiectasis as either the primary or secondary discharge diagnosis between 1st January 1999 and 30th June 2017, and removing those who died on or before 30th June 2017. We excluded patients who are not residents (Singapore citizen or Permanent Resident) of Singapore.

Analysis

Singapore’s mid-year resident populations estimates from the Department of Statistics for 2007-2017[16] were used, and age-standardization was performed by the direct method using the 2017 population as the reference population.

Relative Survival Ratios (RSRs)[17] were derived using the Ederer II method[18] and from official life tables for Singapore stratified by sex, age and calendar year[19]. Survival was calculated from the date of first admission with bronchiectasis as a primary diagnosis to the date of death, or 31st December 2017, whichever came first. Poisson regression was used to model excess mortality associated with incident hospitalized bronchiectasis comparing two calendar periods of 'first admission' 2012-2016 vs. 2007 - 2011, adjusted for sex, age groups at incident hospitalization and restricting the analysis to the first five years of follow-up.

Total inpatient and outpatient costs and patient bills were summed for a cost-of-illness analysis. All costs were adjusted to Singapore dollars (2017) using the general consumer price index in Singapore,[20] and converted to US dollars at an exchange rate of US$1 = S$1.38.[21] A societal perspective was adopted for this analysis.

All p-value and confidence intervals (CI) were set at a two-tailed statistical significance level of 0.05. Data analyses was performed using Stata version 14.0.[22]

Ethics Approval

The study was approved by the Domain Specific Review Board in National Healthcare Group (reference number: 2018/00724).

RESULTS

Incidence of hospitalized bronchiectasis

There were 420 incident hospitalized bronchiectasis patients in 2017, with an average annual growth rate of 1.6% per year between 2007 and 2017 (Table 1). 54.0% of patients in 2017 were women, up from 45.3% in 2007, with a mean age of 70 years during the study period (2007- 2017).

Age-standardized incidence has declined from 13.9/100,000 persons in 2007 to 10.6 /100,000 persons in 2017 (an average decline of 2.7% per year). This decline was steeper among men (15.6/100,000 in 2007 to 9.9/100,000 in 2017, an average decline of 4.4% per year) than women (12.4/100,000 in 2007 to 11.2/100,000 in 2017, an average decline of 1.0% per year), and the age-standardized incidence rate of bronchiectasis in women was slightly higher than men in 2017. The incidence rate of bronchiectasis increased sharply with age for both men and women (Figure 1).

Coexisting diagnoses

Most patients with incident hospitalization-requiring bronchiectasis were admitted to public acute hospitals (average proportion of 95.9%). Of those admitted in 2017, the majority (86.4%) had at least one co-morbidity. The most common co-morbidity was hypertension (25.3%), followed by diabetes mellitus (23.1%) and hyperlipidaemia (19.3%). Chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD) and asthma as a co-morbidity were relatively less common, and were diagnosed in 8.3% and 3.6% of those admitted in 2017 respectively.

The prevalence of mycobacterium tuberculosis (MTB) infection as a co-morbidity amongst the study population has declined during the period (37.5% in 2007 and 8.0% in 2017) (Supplementary Table S1).

Relative survival and excess mortality

Of the 3,934 incident hospitalized bronchiectasis patients from 2007 to 2017, 1,628 (41.4%) had died by 31st Dec 2017. Relative survival of incident hospitalized bronchiectasis patients was lower than the expected survival of the Singapore population for both genders and all age-groups, except for females aged 18 years and below (Supplementary Figure S1). One-, 5- and 10-year RSRs were 0.91 (95% CI, 0.89 to 0.92), 0.75 (95% CI, 0.72 to 0.78) and 0.59 (95% CI, 0.54 to 0.65) for women, and 0.83 (95% CI, 0.81 to 0.85), 0.63 (95% CI, 0.59 to 0.66) and 0.48 (95%CI, 0.43 to 0.53) for men, respectively, suggesting that female patients had better survival than male patients (Figure 2).

Excess mortality was seen especially in elderly males, and decreased with increasing number of years after a diagnosis of bronchiectasis. No difference in survival of patients first admitted in the recent period 2012-2016 compared to those admitted 2007-2011 was seen (Excess Mortality Rate Ratio, 0.95; 95% CI, 0.82 to 1.10) (Table 2).

Prevalence of ever-hospitalized bronchiectasis

3,501 ever-hospitalized patients with bronchiectasis were alive as of 30th June 2017, giving a point prevalence of 88.3/100,000. There were more women (52.1%) than men with a mean age of 71.2 years (Table 3). When patients with bronchiectasis as a secondary diagnosis for any hospitalization were included, the number of prevalent cases and point prevalence as of 30th June 2017 were 5,835 and 147.1/100,000 respectively, with more men

(51.5%) than women. The prevalence of patients with bronchiectasis as a hospital discharge diagnosis (whether primary or secondary) increases sharply with age, and was as high as 1,738.6/100,000 and 1,222.3 /100,000 among men and women 75 years and older (Supplementary Figure S2).

Hospitalization episodes for bronchiectasis

In 2017, there were a total of 1,105 hospitalization episodes with bronchiectasis as a primary diagnosis from 813 unique patients, with an average length of stay (ALOS) of 6.4 days per episode. ALOS is 1.7 days higher than hospitalized patients without bronchiectasis. Bronchiectasis hospitalisations accounted for 0.2% of total acute hospitalisations and 0.3% of total acute inpatient bed-days in 2017. These proportions were relatively stable throughout the study period (Supplementary Table 2).

Total inpatient costs and bills of bronchiectasis

Inpatient cost among patients with a discharge diagnosis of bronchiectasis were $5.3 million in 2017, an average increase of 7.0% per year, from $2.7 million in 2007 (Supplementary Table S2). There has been an average annual increase of 5.0% for inpatient cost per patient ($4,032 in 2007 vs. $6,563 in 2017) and an increase of 6.6% for bill per patient ($1,388 in 2007 vs. $2,634 in 2017).

Healthcare utilization and total costs in the first year of follow-up

The total cost (both in- and out-patient) during the first year after an incident admission for bronchiectasis was $2.96 million in 2016 (n=404). The majority of the cost was for inpatient care (81.2%), followed by SOC (11.8%), ED (3.3%), and primary care attendances (3.7%) (Table 4). The median number of visits at ED, SOCs and primary care were 1, 4 and 1

respectively. However, patients at the 90th percentile have 3 ED visits, 13 SOC visits, and 16 primary care visits. Likewise, total first-year cost varied widely: the average was $7,331 among incident bronchiectasis patients in 2016, but with a standard deviation of $8,863, and about 10% had costs of more than $14,380. A unit increase in the number of co-morbidity was significantly associated with a 7.6% increase in first-year total cost (95% CI, 3.0% to 12.2%; p-value = 0.001) after adjustment for gender and age at admission (results not shown).

Total costs in 2017

Among prevalent and newly incident patients with bronchiectasis, the total direct medical costs were $9.55 million, amounting to 0.2% of all costs collected in the database in 2017. The majority of this cost was due to hospitalization, representing 55.8% of direct medical costs, while primary care was 11.3%. The mean cost per patient was $2,476 with a standard deviation of $6,311. Median cost was $1,014 and about 10% had costs greater than $5,414. Costs per patient were similarly greater in patients with higher number of comorbidities (Supplementary Table S3).

DISCUSSION

The age-standardized incident hospitalization for patients with bronchiectasis declined in Singapore during the 10-year period from 2007 to 2017. The potential explanations are the advancement in treatment and imaging could have reduced the need for hospitalization.[23,24] In Singapore, dedicated bronchiectasis clinics have been set up in most hospitals and doctors have better understanding on the management of bronchiectasis. Furthermore, there have been easy accessibility on investigations such as computed tomography (CT) thorax, allowing early diagnosis of the disease. Home intravenous antibiotics services have

also been available in most of the hospitals. Secondly, improvement of outpatient services such as using a multidisciplinary approach in management could also have contributed to the reduction.[25] Lastly, improved accessibility to information such as international guidelines for diagnosis and treatment may have led to more appropriate and timely treatment for patients.

The average annual rate of age-standardized hospitalization in Singapore was 30.4/100,000 population between 2007 and 2017. This is higher than published data from other countries, which range from 1.8 to 25.7/100,000.[26,27] A study conducted in Hong Kong reported a hospitalization rate of 21.9/100,000.[27] In this study, the rate of hospitalization with bronchiectasis increased with age and were higher in older women. Our study also demonstrates that incidence rates of hospitalization-requiring bronchiectasis in women are starting to exceed those in men.

Survival for patients with bronchiectasis requiring hospitalization is considerably lower than that expected for the general Singapore population. Recent studies have shown that frequency of exacerbations, and in particularly three or more exacerbations per year, was associated with an increased risk of mortality among bronchiectasis patients.[28,29] However, this could not be tested in our study as data on exacerbations are not available. Using bronchiectasis hospitalizations as a crude proxy for exacerbations, 5% of incident hospitalizations in 2016 had at least 3 bronchiectasis hospitalizations during the first year of admission, and the proportion hovered between 4% and 8% in the years 2007 till 2016.

The prevalence of ever-hospitalized bronchiectasis patients was estimated at 147.1/100,000 in 2017 in Singapore, with a prevalence of 1.4% in the population aged 75 years and above. International studies have reported much higher prevalence, especially in studies that were

able to identify patients in primary care. For example, a study in Spain reported prevalence rates in Catalonia of 362/100,000 in a primary care database.[30] A UK study on the primary care database reported a prevalence of 379/100,000 in women and 281/100,000 in men in 2012.[31] However, there is substantial variation in prevalence estimates. A German population-based study conducted in 2005-2011 suggested a prevalence of only 67/100,000,[5] while a US study estimated a prevalence in the USA of 139/100,000.[4] The prevalence estimates obtained in our study are best viewed as "floor estimates", as we were unable to include patients with mild bronchiectasis who did not require hospitalization during the 10-year period of study.

Of interest is the decline of TB as a secondary diagnosis among incident hospitalized bronchiectasis patients, which we see throughout the period of 2007-217. Bronchiectasis is a well-known sequela of tuberculosis. The incidence of TB was very high in Singapore in the 1960s but declined to a nadir of 35/100,000 in 2007, and there has since been a plateau in the incidence.[32] Patients with incident TB were more likely to be male and older.[33] This long-term secular decline in TB may partly explain the reduction in TB as a secondary diagnosis over the 10-year period, and may also explain the sharper decline in incidence of bronchiectasis in men compared to women over the same period.

Our study estimated that the annual direct medical cost associated with bronchiectasis was US$9.6 million in 2017. The mean total annual cost for patients with COPD has been estimated at US$9.9 million between 2005-2009.[34] Methodologic differences between studies prevent direct comparisons of these costs.

The average annual cost was US$7,331 per patient, with a substantial variation in cost in 2017. 10% of patients admitted in 2016 had first-year costs above US$14,380, a significant amount in Singapore where the median monthly household income from work is about US$6,508 in 2016.[35] Our study shows that comorbidities was an important driver of costs in bronchiectasis.

Recent research has highlighted the significant cost burden of bronchiectasis. Weycker and co-workers reported an incremental cost of US$5,681 in bronchiectasis patients compared to matched controls (1999-2001) and 56% of the incremental cost was attributed to inpatient admissions.[9] Another study in the USA reported an increase of US$2,319 for bronchiectasis patients compared to controls.[36] A recent German study using statutory health insurance data reported that total direct expenditure per bronchiectasis patient was EUR18,634, and 31% higher than matched controls. Of note, hospitalization costs and antibiotics expenditures were substantially higher in bronchiectasis patients.[10]

A key advantage of our study is the use of a comprehensive nationwide dataset giving unbiased estimates for incidence, prevalence, survival and costs. Some limitations were that patients with bronchiectasis who were not hospitalized were not included. We relied on administrative data to identify patients with bronchiectasis, and errors in coding could cause misclassification. Not all expenditures were included - we used norm costs to estimate public sector specialist outpatient costs, and we did not have costs associated with most private sector primary and specialist outpatient care encounters, nor nursing home and other long-term care and palliative care costs, medication and medical device costs that were not linked to a hospital admission.

In summary, we find that bronchiectasis is common and imposes a substantial burden on health care costs and survival of patients in Singapore.

(2774 words)

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Figure 1. (A) Age-standardized incidence of hospitalized bronchiectasis patients in Singapore by sex, 2007-2017; (B) Incidence of hospitalized bronchiectasis patients in Singapore by sex and age group, 2017

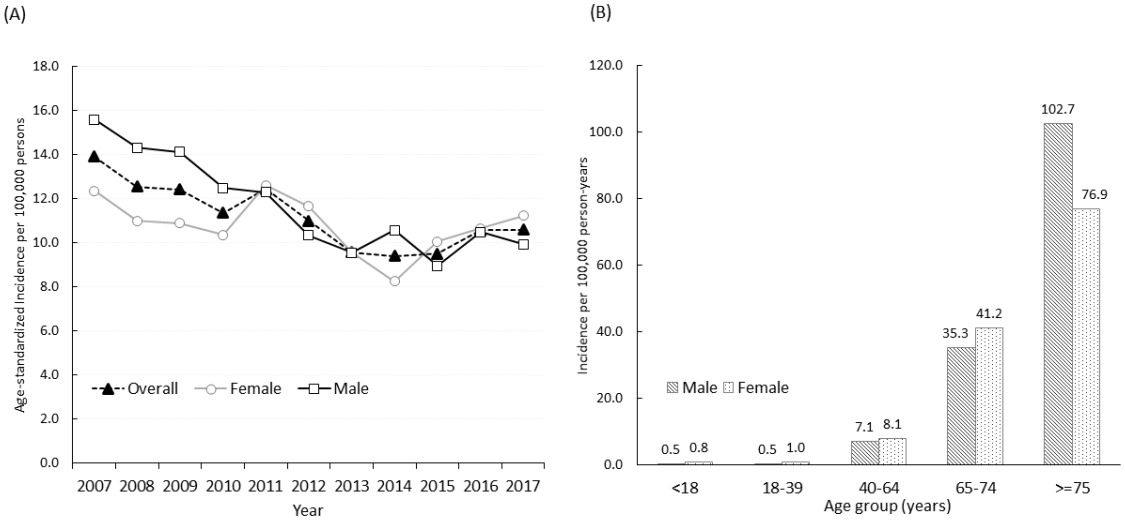
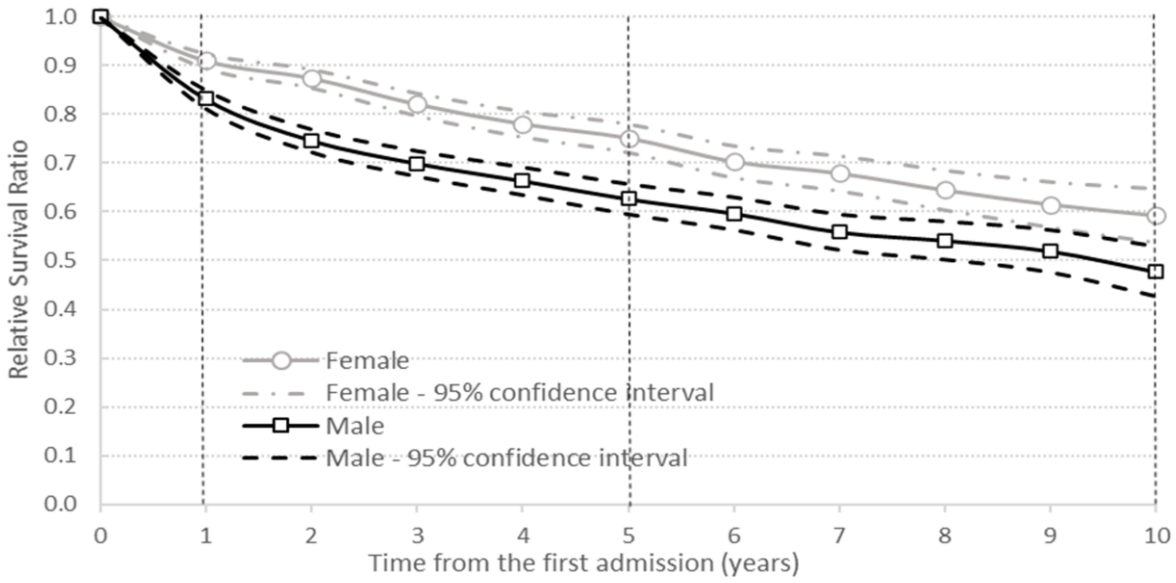


Figure 2. Cumulative relative survival among incident hospitalized bronchiectasis patients in Singapore by sex and time from the first admission



TABLES

Table 1: Incidence and profile of incident hospitalized bronchiectasis (as primary diagnosis), 2007-2017

	Year	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	CAGR (2017 vs. 2007)
Total	N	360	339	352	330	382	353	319	328	347	404	420	1.6%
	Age-standardized Incidence*	13.9	12.5	12.4	11.4	12.4	11.0	9.6	9.4	9.5	10.6	10.6	-2.7%
Sex, (%)	Female	45.3	45.7	45.2	47.0	52.5	54.1	50.8	44.8	53.9	51.5	54.0	
	Male	54.7	54.3	54.8	53.0	47.8	45.9	49.2	54.9	46.1	48.5	46.0	
Age, years	Mean (SD)	69.7 (14.9)	69.5 (15.4)	70.1 (13.9)	70.1 (14.9)	68.8 (15.2)	68.8 (16.3)	69.1 (16.7)	69.9 (15.8)	70.7 (14.3)	69.6 (14.7)	69.9 (14.4)	
Age group, (%)	<18 years	0.6	1.2	0.6	1.2	1.0	1.4	2.2	2.1	0.9	0.7	1.2	
	18-39 years	4.2	2.4	0.9	2.4	1.6	3.1	2.2	1.5	2.0	3.0	2.1	
	40-64 years	25.3	28.3	32.1	25.8	33.5	31.4	29.2	27.1	25.1	28.7	26.9	
	64-74 years	29.2	25.7	25.0	24.5	23.6	21.5	23.8	27.4	28.2	27.2	29.5	
	≥75 years	40.8	42.5	41.5	46.1	40.1	42.5	42.6	41.8	43.8	40.3	40.2	
Ethnic group, (%)	Chinese	68.3	75.8	76.7	78.2	75.3	75.4	73.0	74.1	77.8	74.5	74.0	
	Malays	18.9	15.9	14.2	10.3	13.1	13.0	15.7	14.0	12.4	13.1	15.2	
	Indians	6.7	5.0	6.3	7.6	7.9	5.1	7.2	6.1	6.1	5.9	6.2	
	Others	6.1	3.2	2.8	3.9	3.9	6.5	4.1	5.5	3.7	6.4	4.5	

CAGR: Compound Annual Growth Rate

* per 100,000 person-years

Table 2: Excess Mortality Rate Ratios

Characteristics	Excess Mortality Rate Ratio	95% Confidence Interval	P-value
Time since first admission, years			
1	1.00 (reference)		
2	0.53	0.43 to 0.64	< .0001
3	0.46	0.36 to 0.58	< .0001
4	0.37	0.27 to 0.49	< .0001
5	0.34	0.24 to 0.48	< .0001
Sex			
Female	1.00 (reference)		
Male	1.90	1.63 to 2.22	< .0001
Age of first admission, years			
<18 years	1.00 (reference)		
18-39 years	1.44	0.38 to 5.39	0.589
40-64 years	2.99	0.95 to 9.43	0.006
65-74 years	4.52	1.44 to 14.25	0.010
≥75 years	6.35	2.02 to 19.96	0.002
Year of first admission			
2007-2011	1.00 (reference)		
2012-2016	0.95	0.82 to 1.10	0.499

Table 3: Prevalence and characteristics of surviving patients ever-hospitalized with bronchiectasis (as primary diagnosis vs. all diagnoses of discharge), as of 30th June 2017

	Bronchiectasis as			
	Primary diagnosis		Any diagnoses	
	Number or %	Prevalence^	Number or (%)	Prevalence^
Total	3,501	88.3	5,835	147.1
Sex				
Female	52.1	90.2	48.5	140.0
Male	47.9	86.3	51.5	154.5
Age group				
<18 years	0.9	4.4	1.1	8.4
18-39 years	2.5	7.2	2.7	12.8
40-64 years	26.2	61.4	24.7	96.8
64-74 years	24.9	269.0	24.1	434.1
≥75 years	45.6	825.4	47.5	1,433.0
Ethnic group				
Chinese	63.6	75.5	60.9	120.6
Malays	12.7	83.5	13.5	148.3
Indians	6.1	59.9	6.8	109.8
Others	17.6	481.2	18.8	858.5
Age, years				
Mean (SD)	71.2 (15.7)		71.8 (16.2)	

^ per 100,000 persons

Table 4: Total first-year cost (U.S. dollars) and healthcare utilization incurred by incident hospitalized bronchiectasis patients admitted in 2016

	Total	%	Mean	Standard Deviation	Median	90th Percentile	95th Percentile
	First-year Costs (U.S. $)						
Number of bronchiectasis patients (n = 404)							
Hospitalizations *(inclusive of the first admission)*	$2,404,345	81.2%	$5,951	$8,799	$3,017	$12,853	$23,716
ED visits	$96,785	3.3%	$240	$399	$118	$664	$1,058
Specialist outpatient visits	$350,660	11.8%	$868	$922	$589	$1,913	$2,502
Primary care visits (polyclinics)	$70,140	2.4%	$174	$277	$41	$536	$531
Primary care visits (community health assistance scheme)	$39,723	1.3%	$98	$210	$0	$321	$531
Total	$2,961,654	100.0%	$7,331	$8,863	$4,479	$14,381	$25,024
	First-year Utilization						
Hospitalizations *(inclusive of the first admission)*							
Number	533	-	1.3	0.8	1	2	3
Total length of stay (days)	3,083	-	7.6	11.8	4	15	24
ED visits	515	-	1.3	2.0	1	3	5
Specialist outpatient visits	2,383	-	5.9	6.3	4	13	17
Primary care visits (polyclinics)	1,608	-	4.0	12.4	1	8	12
Primary care visits (community health assistance scheme)	978	-	2.4	5.1	0	8	12

SUPPLEMENTARY MATERIAL

Epidemiology and Economic Burden of Bronchiectasis Requiring Hospitalization in Singapore

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Figure S1: Five-year relative survival among incident hospitalized bronchiectasis patients in Singapore by age group and sex

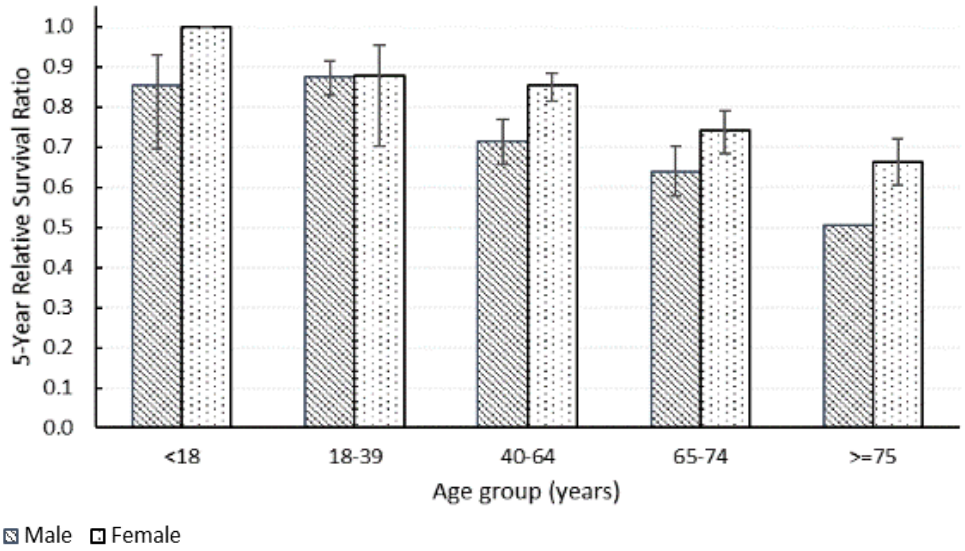

Figure S2: Prevalence of surviving patients ever-hospitalized for bronchiectasis by sex and age group, as of 30th June 2017: (A) as Primary Diagnosis, (B) as All

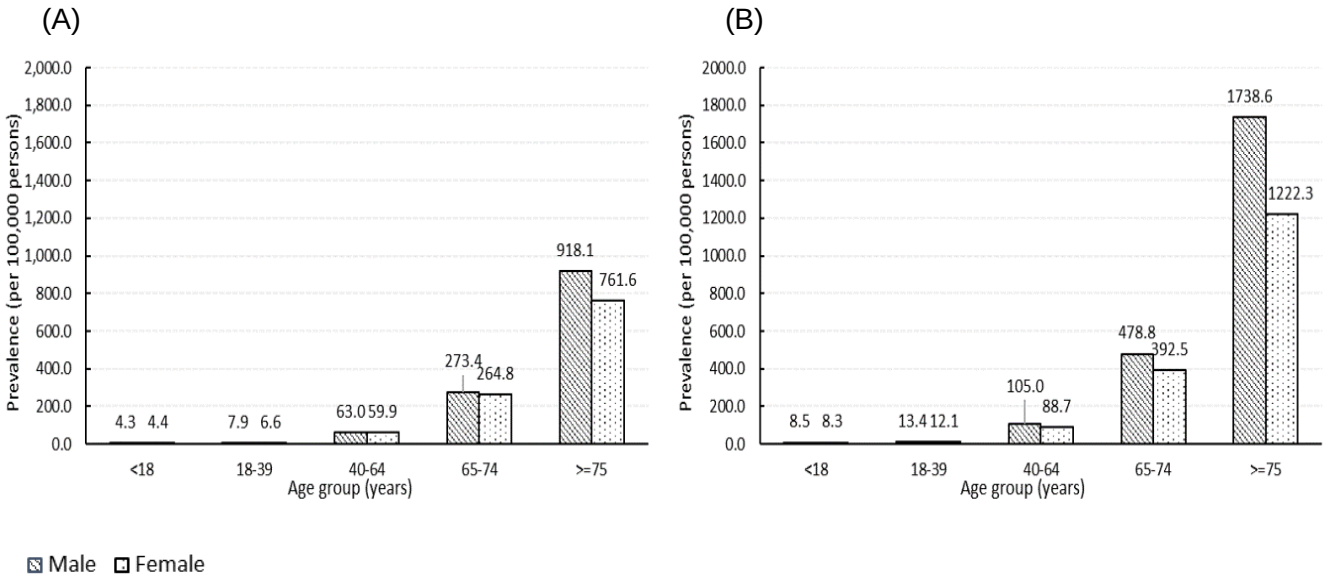

Table S1: Selected comorbidities among incident hospitalized bronchiectasis patients at public acute hospitals, 2007-2017

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Number with secondary diagnoses, N	307	295	323	286	332	303	273	286	303	344	363
Disease Category (%)											
Hypertension	25.7%	28.8%	30.3%	28.7%	31.3%	27.7%	28.9%	32.2%	26.1%	24.1%	25.3%
Diabetes mellitus	20.8%	18.6%	22.3%	18.9%	24.1%	15.2%	21.6%	29.0%	20.1%	20.9%	23.1%
Hyperlipidemia	16.0%	18.0%	20.4%	18.2%	23.8%	11.2%	18.3%	19.2%	15.5%	16.3%	19.3%
Chronic renal disease	3.6%	6.1%	4.6%	6.6%	4.8%	6.6%	6.6%	9.8%	9.6%	7.8%	8.5%
Chronic obstructive pulmonary disease	7.8%	8.1%	9.6%	9.8%	6.0%	5.3%	7.3%	8.4%	8.3%	4.9%	8.3%
Tuberculosis	37.5%	32.9%	28.2%	24.5%	22.6%	12.5%	11.0%	11.9%	10.9%	9.9%	8.0%
Ischaemic heart disease	8.8%	6.1%	7.4%	6.3%	3.0%	6.3%	5.1%	7.7%	3.6%	3.5%	7.4%
Asthma	4.6%	2.0%	2.5%	3.8%	3.3%	2.6%	3.3%	1.7%	3.0%	2.3%	3.6%
Alzheimer's & other dementias	2.3%	3.1%	3.4%	2.4%	3.3%	2.0%	1.5%	1.0%	1.7%	2.3%	3.0%
Rheumatoid arthritis	0.3%	0.7%	0.6%	1.0%	1.2%	0.3%	1.5%	0.0%	0.0%	0.6%	1.7%
Connective tissue disease	0.0%	0.0%	0.6%	0.0%	0.9%	0.3%	0.4%	0.0%	0.3%	0.6%	1.1%
Stroke	4.2%	3.7%	1.5%	3.1%	1.8%	0.3%	1.1%	0.7%	0.7%	0.3%	0.8%
Anxiety & Depression	0.3%	0.3%	0.6%	0.7%	0.3%	0.3%	1.5%	0.7%	2.0%	0.3%	0.6%
Schizophrenia	0.0%	0.0%	0.0%	0.3%	0.9%	0.3%	0.0%	0.0%	0.0%	0.3%	0.3%
Inflammatory bowel disease	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Bipolar disorder	0.0%	0.0%	0.3%	0.0%	0.0%	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%

Table S2: Annual utilization and cost (U.S. dollars) of inpatient services due to bronchiectasis as the primary diagnosis, 2007-2017

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	CAGR (2017 vs. 2007)
Number of bronchiectasis patients	672	659	644	649	729	684	670	643	700	761	813	1.9%
Bronchiectasis hospitalization episodes	973	931	895	894	1,012	981	955	915	947	1,070	1,105	1.3%
Patient day	4,947	5,387	5,462	5,174	5,868	6,436	6,507	5,836	6,113	6,764	7,040	3.6%
Average length of stay (days)	5.1	5.8	6.1	5.8	5.8	6.6	6.8	6.4	6.5	6.3	6.4	2.3%
Cost (in thousands)	$2,710	$2,832	$3,406	$2,992	$3,496	$4,047	$4,204	$3,925	$4,245	$4,612	$5,336	7.0%
Cost per patient	$4,032	$4,297	$5,288	$4,611	$4,796	$5,916	$6,274	$6,104	$6,065	$6,061	$6,563	5.0%
Cost per patient day	$548	$526	$624	$578	$596	$629	$646	$673	$694	$682	$758	3.3%
Bill (in thousands)	$933	$1,079	$1,374	$1,101	$1,419	$1,598	$1,574	$1,521	$1,638	$1,833	$2,142	8.7%
Bill per patient	$1,388	$1,637	$2,133	$1,696	$1,947	$2,336	$2,349	$2,366	$2,341	$2,408	$2,634	6.6%
Bill per patient day	$189	$200	$251	$213	$242	$248	$242	$261	$268	$271	$304	4.9%
Non-bronchiectasis hospitalization episodes (in thousands)	382.8	380.9	385.6	396.2	414.2	432.6	443.6	458.4	473.8	514.0	535.7	3.4%
Patient day (in thousands)	1,835	1,852	1,842	1,931	2,081	2,199	2,262	2,323	2,411	2,445	2,517	3.2%
Average length of stay (days)	4.8	4.9	4.8	4.9	5.0	5.1	5.1	5.1	5.1	4.8	4.7	-0.2%
% hospitalization episodes due to bronchiectasis	0.3	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	
% patient days due to bronchiectasis	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	

Table S3: Results of multiple linear regression analysis: Association of patient's characteristics with log-transformed total cost in 2017

Characteristics	Regression Coefficient	Standard Error	t-statistics	P-value	95% Confidence Interval for Regression Coefficient	
Sex						
Female (Reference)						
Male	0.0261	0.0439	0.60	0.551	-0.060	0.112
Age Group in 2017						
<18 years (Reference)						
18-39 years	-0.0147	0.2875	-0.05	0.959	-0.578	0.549
40-64 years	0.0082	0.2453	0.03	0.973	-0.473	0.489
65-74 years	0.1965	0.2452	0.80	0.423	-0.284	0.677
≥75 years	0.1499	0.2443	0.61	0.539	-0.329	0.629
Number of comorbidities§	0.1141	0.0127	8.98	<0.0001	0.089	0.139
Intercept	7.1154	0.2424	29.36	<0.0001	6.640	7.591

§ Comorbid conditions considered in the Charlson Comorbidity Index (CCI). The index takes into account 19 comorbid conditions, including cardiovascular disease, diabetes mellitus, liver disease, and pulmonary disease. Reference: Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373-383.