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ORIGINAL RESEARCH

Healthcare Costs and Trends of Multimorbidity in COPD Patients: A Population-Based Study in Singapore

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Purpose: Chronic obstructive pulmonary disease (COPD) and its comorbidities impose substantial economic burdens on healthcare systems, but evidence remains scarce in Asian countries where patients exhibit distinct clinical and inflammatory phenotypes, as well as policy and health system differences. This study aimed to estimate direct medical costs of COPD multimorbidity, comparing to non-COPD patients in Singapore, and identify high-cost users.

Patients and Methods: Using Singapore's health administrative data (2012–2019), we created a propensity score-matched COPD and non-COPD cohort and applied generalised linear models to estimate all-cause, index disease- and comorbidity-attributable costs. All costs were measured in patient-years (PYs) in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69). Patient characteristics and comorbidity prevalence were compared across patients incurring top 10%, 11%–50%, and bottom 50% of average annualised costs.

Results: The study included 18,866 patients from each group (83% males, 17% females). Average annual direct medical costs were significantly higher among COPD patients ($5,290.9/PY; 95% confidence interval [CI]: 5,242.9–5,350.1) than non-COPD patients ($1,110.4/PY; 95% CI: 1,085.9–1,135.9). 33.8% of total costs were COPD-attributable, with major contributions from other respiratory (15.0%), circulatory (14.9%), metabolic (7.8%), and digestive (4.7%) diseases. From 2012 to 2019, hospitalisation costs declined (-$59.0/year), while primary care (polyclinic) costs increased sharply (+$148.8/year). Indian patients comprised 67% of the top 10th cost percentile and experienced frequent hospitalisations (≥2/year).

Conclusion: In Singapore's multi-ethnic Asian context, COPD patients incurred substantial multimorbidity costs, particularly from respiratory, circulatory, and metabolic diseases, underscoring distinct Asian multimorbidity patterns and highlighting the need for integrated, multimorbidity-focused care models. Disproportionately high costs among Indian patients and low female prevalence warrant further investigation.

Keywords: COPD, multimorbidity, comorbidities, economic burden, direct costs, health administrative data

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Introduction

Chronic obstructive pulmonary disease (COPD), the fourth leading cause of death globally, affected 380 million people and caused 3.5 million deaths in 2021.[1] COPD ranks among the top causes of hospital admissions worldwide, with Organisation for Economic Co-operation and Development (OECD) countries reporting average rates of 112.3 per 100,000 population in 2020.[2] Furthermore, the annual economic burden was estimated at US$56.0 billion in Europe[3] and US$31.3 billion[4] in the US, with a projected 20-year total of US$3.5 trillion in China (2020–2039),[5] underscoring its substantial burden.

Comorbidities are increasingly recognised due to ageing and shifting demographic profiles.[6] COPD patients have substantially elevated comorbidity risks due to shared inflammatory pathways and risk factors (eg, smoking and sedentary lifestyles[7]), leading to increased hospitalisations and mortality.[8] Cardiovascular diseases (CVDs) represent some of the most potent comorbidities, with COPD patients showing a two- to five-fold increased risk worldwide.[9] In the European EpiChron cohort, other multimorbidity patterns emerged: neuropsychiatric disorders, cardio-metabolic, and cancer.[10] Evidence from Canadian health administrative data also showed that circulatory, respiratory, and digestive conditions accounted for twice the healthcare costs of COPD itself.[11]

Importantly, Asian COPD populations exhibit distinct clinical phenotypes that may influence multimorbidity patterns and healthcare use. These include lower body mass index (BMI), a higher prevalence of non-smoking-related COPD, and greater exposure to environmental and biomass pollutants.[12,13] Such phenotypic differences have been associated with unique multimorbidity clusters in Asian populations, including low comorbidity: low risk, low comorbidity: high risk, diabetic, ex-tuberculosis (TB), and CVD, with the latter two associated with high clinical risk.[14] Additional comorbidities such as anxiety, pneumonia, and osteoporosis also contribute to the burden, often related to COPD itself[15,16] or its treatment, particularly repeated corticosteroid use.[17] Despite this growing complexity, there is a notable lack of studies examining the cost of COPD multimorbidity in Asia, where robust longitudinal data remain limited. While comprehensive cost estimates are available for OECD countries,[11,18] contemporary data on disease-specific cost components in multi-ethnic Asian populations, such as Singapore, are lacking. In Singapore, COPD ranks among the top 10 causes of mortality,[19] yet the most recent economic burden study was conducted over a decade ago,[20] reporting per-patient costs rising from $8,427 to $11,018 (2005–2009), driven by hospitalisations (73%), without examining comorbidity-attributable costs.[20]

Aligned with Singapore's "Healthier SG" initiative,[21] which emphasises preventive care, population health management, and value-based disease management, the Ministry of Health (MOH)'s Trusted Research and Real World-Data Utilisation (TRUST) platform, launched in 2022, offers an unprecedented opportunity to comprehensively estimate the economic burden and COPD multimorbidity trends in a multi-ethnic Asian context. This large-scale real-world study is the first in Asia to quantify COPD multimorbidity cost patterns, which was based on a representative and generalisable multi-ethnic Asian population, included a comprehensive breakdown of cost components by disease categories, and adopted a longitudinal perspective (2012–2019) to decode the cost impacts of both time trends and disease natural history. These findings provide evidence to support targeted, value-based care strategies in Singapore and may also inform policy and practice in other Asian health systems undergoing comparable primary care and health system reforms, such as Hong Kong and Japan, which share mixed public–private financing structures and ongoing primary care and chronic disease care reforms.

Using Singapore's health administrative data from MOH TRUST[22] (2012–2019), this study aimed to estimate the direct medical costs of multimorbidity and its trends in COPD patients in Singapore, compared to non-COPD patients, and to characterise high-cost patients.

Methods

Data Source

We analysed de-identified, patient-level health administrative data comprising sociodemographic and claim records of 4.1 million Singapore residents.[22] Established for administrative and billing purposes across public healthcare institutions, the TRUST database reflected subsidised charges in public healthcare, providing accurate estimates of out-of-

pocket costs. Episode-level records were merged across hospitalisations (1998–2020), emergency department (ED) (2006–2020), specialist care (2006–2020), and primary care visits (2012–2020). Data covered >90% of public and private hospitals, with primary care limited to the government-run public-sector polyclinics, offering subsidised outpatient services, including chronic disease management and screenings. Outpatient claims included dispensed medication costs but not confirmation of use.

Study Design and Sample

We conducted a retrospective propensity score-matched (PSM) cohort study comparing newly diagnosed COPD patients with matched non-COPD cohort from 2012 to 2019 (Figure A1). COPD cases were identified using a validated case definition[23] requiring ≥1 hospitalisation or ED visit, or ≥2 primary care visits with a primary COPD diagnosis (International Classification of Diseases [ICD]-9: 491.xx, 492.xx, 496.xx; ICD-10: J43.xx, J44.xx) within a rolling 12-month period.[23] This validated definition has demonstrated high sensitivity (0.850) and specificity (0.784) in Western COPD populations,[24,25] providing a pragmatic and reliable approach for identifying COPD cases in real-world administrative data.[23] Of note, this study was the first to adopt the algorithm across Asian health administrative databases, where spirometry function test and inhalers are commonly underutilised.[26] Table A1 details the ICD-9 and ICD-10 diagnosis codes for the other major comorbidity categories, with "multimorbidity" referring broadly to the presence of any combination of these comorbidities. The index date was the first COPD-related encounter. Patients aged ≥40 on index date were included to prevent potential misdiagnosis, while those with asthma (ICD-9: 493.x except 493.2; ICD10: J45.x, J46.x) within 2 years pre- and post-index were excluded to reduce misclassification. Data from 2020 were excluded to avoid COVID-19-related disruptions, ensuring a stable baseline for assessing healthcare utilisation (HCU) trends.

The non-COPD cohort had no COPD-related HCU, possibly capturing undiagnosed cases. Index dates were their first recorded healthcare encounter, with patients in both cohorts having ≥1 year of baseline washout and follow-up until death, loss to follow-up, or December 31, 2019. PSM was performed using multivariable logistic regression on age, sex, race, housing, residency, and index year to control for key demographic and temporal confounders that may influence HCU and disease progression. All COPD patients were matched 1:1 to non-COPD patients by nearest-neighbour matching (caliper=0.01) without replacement.

Outcomes

Costs were adjusted to 2023 Singapore dollars (SGD$1=US$0.76=£0.60=€0.69) using consumer price index (CPI)-based inflation rates.[27] Direct medical costs were summed from hospitalisation, ED, specialist, and primary care (including medications). Hospitalisation and primary care costs were directly extracted from episode-level billing records. Specialist care was identified from hospitalisation records by corresponding codes or inferred from same-day discharges. ED visits were partially captured within hospitalisation dataset by same-day discharge and absence of one-day procedures or specialist care; remaining visits were captured in the ED dataset. Healthcare records with missing diagnosis or cost data were excluded.

All-cause medical costs were broken down into COPD-attributable or comorbidity-attributable costs, respectively derived by attributing healthcare encounters to a primary COPD diagnosis or major comorbidity categories. Costs were stratified by cohort and categorised into 11 major disease categories: COPD, circulatory diseases, other respiratory conditions, digestive disorders, infectious diseases, neuropsychiatric disorders, metabolic diseases, neoplasms, genitourinary disorders, musculoskeletal diseases, and other comorbidities (Table A1). To assess cardiopulmonary risk, we examined costs associated with major adverse cardiovascular events (MACE),[28] including acute myocardial infarction (AMI), acute coronary syndrome/ischemic heart disease (ACS/IHD), stroke, and heart failure (Table A1).

Statistical Analyses

Analyses were conducted using R version 4.1.1. Baseline balance was assessed using standardised mean differences (SMD≤0.10). Missing sociodemographic data (<10%) were imputed via a non-parametric random forest. Annualised non-zero costs were truncated at the 97.5th percentile to minimise outlier impacts.

Per person-year (PY) costs were estimated using generalised linear models (GLM) [normal distribution, identity link], consistent with best practices for large sample sizes.[29] The large sample size ensures robust estimation of model parameters, with extremely high-cost outliers truncated to avoid undue influence on model estimates.[29] Additionally, the identity link allows direct interpretation of absolute cost differences, which is particularly relevant for policy and economic decision-making. In a sensitivity analysis, we re-estimated annualised multimorbidity costs among COPD patients using alternative distributional assumptions (Normal versus Tweedie distributions) to assess the robustness of cost estimates. Dependent variables included total, COPD-, and comorbidity-attributable costs by cost components (hospitalisation, ED, primary care, specialist care). Explanatory variables included age-sex subgroups (Males/Females aged 40–64, aged 65 or above), ethnicity (Chinese, Malay, Indian, others), residency (resident, non-resident), and socioeconomic status (SES) using the modified Singapore Housing Index (SHI)[30] (Low: 1–3 room Housing Development Board [HDB] flats, Middle: 4–5 room HDB flats, High: executive/studio apartments, private housing, or commercial units). Other covariates included calendar year, follow-up year since index diagnosis, and index year.

Multinomial regression of average annualised total costs classified patients into cost groups (top 10%, 11–50%, bottom 50%) to examine HCU variations while ensuring sufficient sample size for comparisons. Differences across cost groups were tested using Analysis of Variance (ANOVA) and Chi-Square tests (with Bonferroni correction). Covariate-adjusted effects and 95% credible intervals were estimated with 50 bootstrap iterations to balance computational efficiency and precision.

Results

Table 1 compares baseline characteristics and HCU between 18,866 matched COPD and non-COPD patients (Figure A2). The mean age of COPD patients was 68.7 years, 17.0% were female, and 80.4% Chinese. Matching was adequate

Table 1 Baseline Characteristics of Matched Patient Sample

Characteristics	COPD Patients (n=18,866)	Non-COPD Patients (n=18,866)	SMD
Age, mean (SD)	68.7 (11.2)	68.7 (12.1)	0.003
Age group, n (%)			
40-64	6,271 (33.2)	6,679 (35.4)	0.046
65 or above	12,595 (66.8)	12,187 (64.6)	
Sex, n (%)			
Male	15,656 (83.0)	16,007 (84.8)	0.051
Female	3,210 (17.0)	2,859 (15.2)	
Ethnicity, n (%)			
Chinese	15,159 (80.4)	15,640 (82.9)	0.072
Malay	1,993 (10.2)	1,734 (9.2)	
Indian	1,013 (5.4)	918 (4.9)	
Others	761 (4.0)	574 (3.0)	
SES, n (%)			
Lower	7,596 (40.3)	7,461 (39.5)	0.025
Middle	9,392 (49.8)	9,617 (51.0)	
Upper	1,878 (10.0)	1,788 (9.5)	

(*Continued*)

Table 1 (Continued).

Characteristics	COPD Patients (n=18,866)	Non-COPD Patients (n=18,866)	SMD
Residency status, n (%)			
Resident	18,011 (95.5)	18,440 (97.7)	0.126
Non-resident	855 (4.5)	426 (2.3)	
Comorbidities, n (%)			
Diseases of the circulatory system	5,073 (26.9)	4,561 (24.2)	0.062
Other respiratory diseases	5,737 (30.4)	2,601 (13.8)	0.409
Diseases of the digestive system	3,663 (19.4)	3,277 (17.4)	0.053
Metabolic diseases	4,188 (22.2)	1,927 (10.2)	0.330
Infectious diseases	2,209 (11.7)	546 (2.9)	0.344
Diseases of the genitourinary system	2,955 (15.7)	1,927 (10.2)	0.163
Diseases of the nervous system and psychiatric disorders	1,192 (6.3)	531 (2.8)	0.168
Diseases of the musculoskeletal system	3,356 (17.8)	1,358 (7.2)	0.324
Neoplasms	760 (4.0)	522 (2.8)	0.070
Other comorbidities	6,070 (32.2)	8,512 (45.1)	0.268
Per PY HCU, mean (SD)			
Hospitalisation	2.1 (6.4)	0.5 (0.5)	0.368
ED visit	2.9 (9.2)	0.5 (0.6)	0.367
Primary care visit	13.7 (34.4)	0.1 (0.9)	0.556
Specialist care visit	0.5 (1.7)	0.0 (0.2)	0.344
Per PY hospital bed-days, mean (SD)			
Bed-days	12.8 (40.9)	3.1 (7.5)	0.333

Abbreviations: ED, emergency department; HCU, healthcare utilisation; PY, person-year; SD, standard deviation; SES, socio-economic status; SMD, standardised mean difference.

(SMDs<0.10), except for residency status (SMD=0.126). COPD patients had higher baseline prevalence of other respiratory, infectious, metabolic, and musculoskeletal diseases. They also had more hospitalisations (2.2 vs 1.1), ED (2.5 vs 1.1), primary care (13.6 vs 4.6), specialist care visits (1.4 vs 1.1), and longer hospital bed-days (14.9 vs 8.3 days), but a lower annual median mortality rate (7.8% vs 14.0%) (Table A2).

Figure 1 shows trends in all-cause healthcare costs and annual mortality rates from 2012 to 2019. While total costs were stable among non-COPD patients (8-year average: $1,110.4/PY, 95% CI: 1,085.9–1,135.9), COPD patients incurred nearly 5-times higher and greatly increased costs (8-year average: $5,290.9/PY, 95% CI: 5,242.9–5,350.1). Hospitalisations accounted for the largest share at 70.1% ($3,703.0/PY), followed by primary care (including medications) at 20.4% ($1,077.5/PY), ED at 7.7% ($406.6/PY), and specialist care costs at 1.9% ($99.8/PY). Over the 8 years, total costs for COPD patients increased by $745.4/PY (+15.3%), driven mainly by rising primary care costs (+$1,190.4/PY; +287.1%), while hospitalisation costs, the largest cost driver, declined gradually (−11.9%). Minor fluctuations in ED and specialist care costs were observed ($14–41/PY). Total costs for non-COPD patients remained relatively stable over

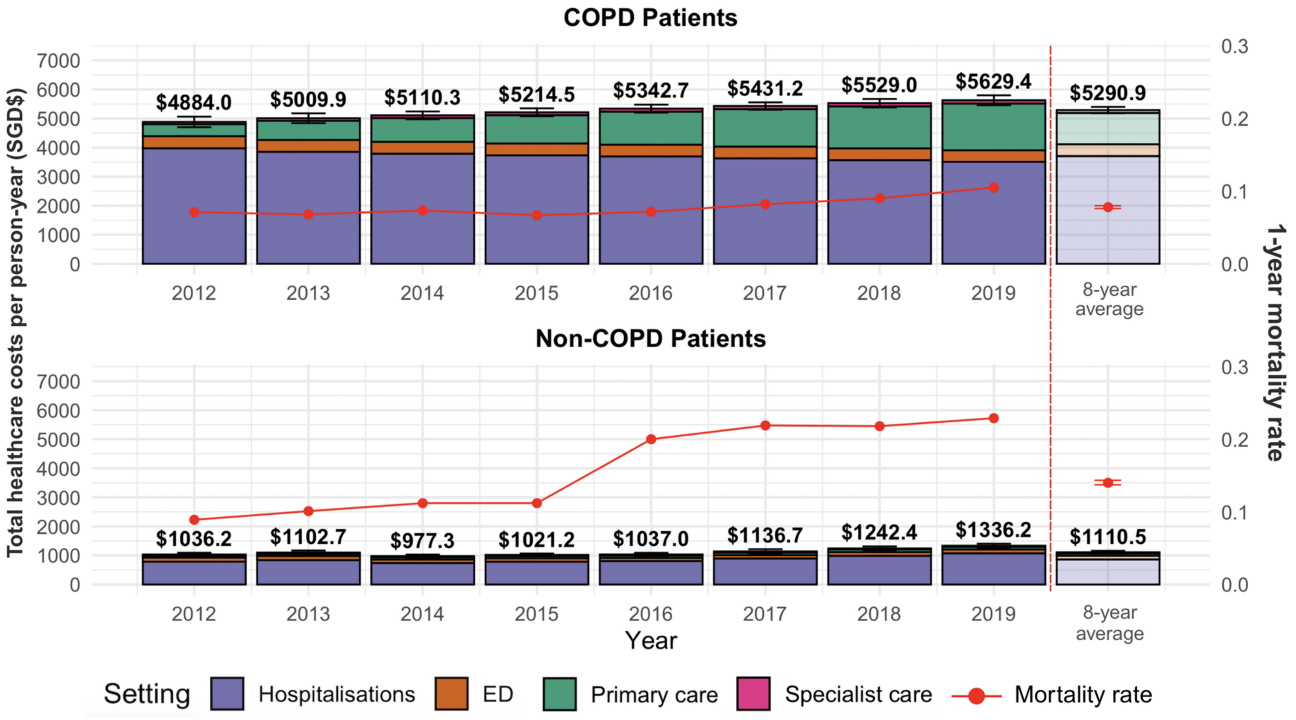

Figure 1 Time trends of total healthcare costs and 1-year mortality rates for COPD and non-COPD cohorts by setting from 2012 to 2019. The translucent column represents the 8-year average costs in each cohort. The error bars indicate the 95% confidence intervals of the total cost estimates and 1-year median mortality rates. All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).
Abbreviations: COPD, chronic obstructive pulmonary disease; ED, emergency department; SGD, Singapore dollar.

8 years (Table A3). Annual mortality rose from 2012 to 2019 in both cohorts: COPD (2012: 7.1% to 2019: 11.1%) and non-COPD patients (2012: 8.9% to 2019: 22.9%).

Figure 2A shows per PY condition-attributable costs for COPD and non-COPD cohorts. In COPD patients, top contributors were COPD itself ($1,785.7/PY) [33.8%], other respiratory ($793.7/PY) [15.0%], circulatory ($788.1/PY) [14.9%], metabolic ($412.7/PY) [7.8%], digestive ($250.8/PY) [4.7%], neoplasms ($197.4/PY) [3.7%] and genitourinary diseases ($189.6/PY) [3.6%], all of which were 2–6 times higher than in non-COPD patients ($45.8–248.6/PY) (Table A4). Hospitalisations comprised 22–95% of costs across all comorbidity categories. In the sensitivity analysis which assumed Tweedie distribution, cost estimates were highly consistent (Table A5).

Figure 2B shows the per PY MACE-attributable costs for COPD and non-COPD cohorts. Compared to non-COPD group, COPD patients incurred substantially higher MACE costs, particularly for heart failure ($140.9/PY vs $32.8/PY), followed by stroke ($114.5/PY vs $48.3/PY), ACS/IHD ($110.1/PY vs $48.1/PY) and AMI ($107.3/PY vs $46.4/PY). For both cohorts, hospitalisations accounted for 73–97% of costs across MACE categories.

Table 2 shows annualised multimorbidity costs by age-sex subgroups. Total costs were lowest in females 40–64 ($4,287.9/PY), with other respiratory diseases being the largest contributor ($794.7/PY), followed by males 40–64 ($4,958.6/PY), where circulatory diseases were the top cost driver ($755.4/PY). Among older adults, total costs were slightly lower in females ≥65 ($5,339.7/PY), primarily driven by other respiratory conditions ($874.8/PY), and highest in males ≥65 ($5,658.8/PY), with other respiratory diseases again accounting for the largest share ($901.2/PY).

Table 3 summarises COPD patient characteristics and HCU by average annualised total costs (Top 10%, 11%–50%, Bottom 50%). Age, sex, and ethnicity were significantly associated with costs ($p<0.001$), whereas SES and residency were not. Top 10% spenders (n=229, $10,247.9/PY; 80.9% hospitalisation) were older (mean age: 67.7 years), and mainly Indians (67.2%), while bottom 50% (n=7,056, $4,724.7/PY; 69.5% hospitalisation) were younger (mean age: 65.8

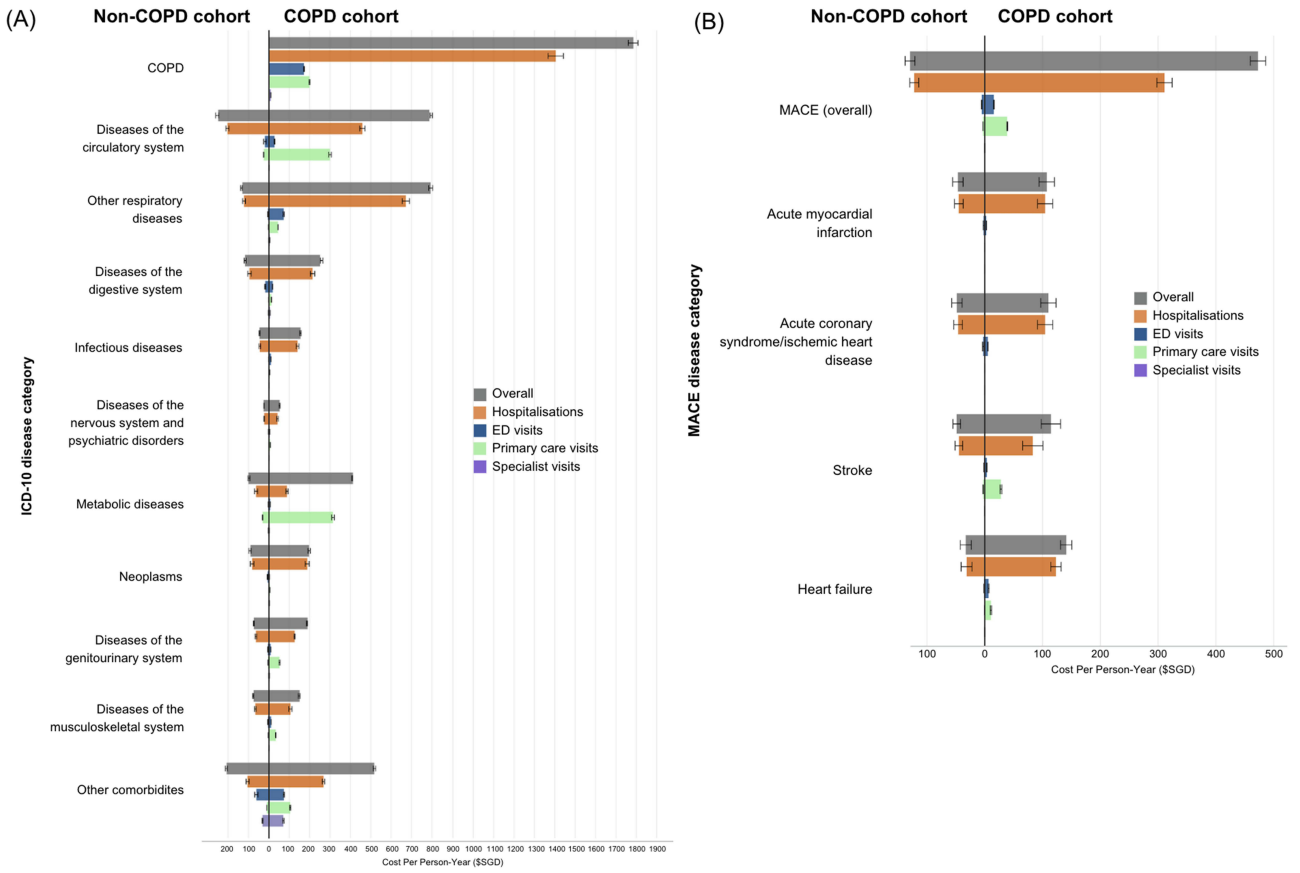

Figure 2 Annualised total cost of multimorbidity in COPD patients versus non-COPD patients. Annualised healthcare costs by (**A**) major disease categories and (**B**) major adverse cardiovascular events. The error bars indicate the 95% confidence intervals of the cost estimates. All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).
Abbreviations: COPD, Chronic obstructive pulmonary disease; ED, emergency department; ICD, International Classification of Diseases; MACE, major adverse cardiovascular events; SGD, Singapore dollar.

years), and mostly Chinese (97.2%). Top 10% spenders had highest comorbidity prevalence, particularly infectious diseases (30.2% vs 16.6%), neoplasms (15.7% vs 8.7%), neuropsychiatric disorders (15.3% vs 9.8%), diabetes (25.8% vs 18.5%), and respiratory diseases like pneumonia (45.0% vs 18.9%) and asthma (11.8% vs 3.4%), compared to the bottom 50%.

Table 2 Estimated Annualised Total Costs of Multimorbidity by Age-Sex Subgroup for COPD Patients

Disease Category	Females Aged 40–64	Males Aged 40–64	Females Aged 65 or Above	Males Aged 65 or Above	p-value
Cost (SGD$), mean (95% CI)					
Total	4287.9 (4156.9–4497.9)	4958.6 (4831.8–4986.2)	5339.7 (5199.2–5461.7)	5658.8 (5613.3–5798.6)	<0.001
COPD	1213.3 (1137.2–1241.3)	1771.7 (1716.4–1816.4)	1747.5 (1710.2–1791.9)	1859.2 (1835.3–1892.0)	<0.001
Diseases of the circulatory system	475.5 (403.5–556.8)	755.4 (768.0–789.1)	787.4 (787.6–845.3)	844.7 (820.4–836.9)	<0.001
Other respiratory diseases	794.7 (735.6–848.8)	645.9 (622.8–668.6)	874.8 (820.0–914.7)	901.2 (887.9–911.7)	<0.001
Diseases of the digestive system	207.6 (198.4–247.5)	222.6 (221.0–246.0)	301.4 (279.7–343.7)	265.5 (253.5–280.9)	<0.001
Infectious diseases	143.6 (118.0–161.6)	148.2 (141.2–155.4)	146.2 (141.7–153.0)	165.6 (159.6–167.1)	0.26
Diseases of the nervous system and psychiatric disorders	47.4 (37.2–52.1)	51.6 (49.8–53.1)	50.0 (47.8–58.5)	55.5 (48.1–60.0)	0.93

(*Continued*)

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Table 2 (Continued).

Disease Category	Females Aged 40–64	Males Aged 40–64	Females Aged 65 or Above	Males Aged 65 or Above	p-value
Metabolic diseases	388.1 (360.6–440.9)	400.9 (392.1–402.0)	382.2 (359.2–392.5)	433.5 (426.1–436.1)	0.55
Neoplasms	146.4 (101.5–174.3)	193.3 (189.7–209.7)	139.1 (114.3–134.2)	221.5 (206.6–244.7)	<0.001
Diseases of the genitourinary system	194.4 (137.8–212.9)	133.5 (130.0–139.4)	224.7 (219.1–244.8)	228.9 (217.2–226.6)	<0.001
Diseases of the musculoskeletal system	199.5 (123.3–222.6)	156.1 (151.1–163.0)	194.9 (167.3–207.6)	130.6 (125.4–135.7)	<0.001
Other comorbidities	485.0 (446.5–506.8)	483.5 (467.2–504.7)	494.9 (485.7–529.2)	555.0 (546.6–559.7)	0.15

Note: All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).
Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; SGD, Singapore dollars.

Table 3 Characteristics of COPD Patients Stratified by Percentile of Average Annualised Total Costs

Parameter	Top 10% (n=229)	Top 11–50% (n=4,649)	Bottom 50% (N=7,056)	Bonferroni Pairwise Comparison (Adjusted p-values)		
				Top 10% vs Top 11–50%	Top 10% vs Bottom 50%	Top 11–50% vs Bottom 50%
Patient demographics						
Age, mean (SD)	67.7 (10.4)	67.4 (10.7)	65.8 (10.9)	<0.001	<0.001	<0.001
Sex, n (%)						
Male	221 (96.5)	3,875 (83.4)	5,942 (84.2)	<0.001	<0.001	0.68
Female	8 (3.5)	774 (16.6)	1,114 (15.8)	<0.001	<0.001	0.68
Ethnicity, n (%)						
Chinese	62 (27.1)	2,650 (57.0)	6,857 (97.2)	<0.001	<0.001	<0.001
Malay	13 (5.7)	1,135 (24.4)	134 (1.9)	<0.001	<0.001	<0.001
Indian	154 (67.2)	476 (10.2)	36 (0.5)	<0.001	<0.001	<0.001
Others	0 (0.0)	388 (8.3)	29 (0.4)	<0.001	1.00	<0.001
SES, n (%)						
Lower	130 (56.8)	1,837 (39.5)	2,919 (41.4)	<0.001	<0.001	0.14
Middle	75 (32.8)	2,358 (50.7)	3,397 (48.1)	<0.001	<0.001	0.02
Upper	24 (10.5)	454 (9.8)	740 (10.5)	1.00	1.00	0.65
Residency status, n (%)						
Resident	229 (100.0)	4,629 (99.6)	6,841 (97.0)	1.00	0.039	<0.001
Non-resident	0 (0.0)	20 (0.4)	215 (3.0)	1.00	0.039	<0.001
Healthcare utilisation (HCU)						
Annual total costs (SGD$), mean (95% CI)	10,247.9 (613.5–28,427.6)	7,620.6 (100.8–26,878.0)	4,724.7 (72.0–22,167.6)	<0.001	<0.001	<0.001
Hospitalisation						
Annual episodes, mean (95% CI)	1.6 (0.0–4.2)	1.3 (0.0–5.2)	0.7 (0.0–3.8)	<0.001	<0.001	<0.001
Annual costs (SGD$), mean (95% CI)	8,287.0 (0.0–26,371.8)	6,061.6 (0.0–24,159.4)	3,286.0 (0.0–20,436.5)	<0.001	<0.001	<0.001

(*Continued*)

Table 3 (Continued).

Parameter	Top 10% (n=229)	Top 11–50% (n=4,649)	Bottom 50% (N=7,056)	Bonferroni Pairwise Comparison (Adjusted p-values)		
				Top 10% vs Top 11–50%	Top 10% vs Bottom 50%	Top 11–50% vs Bottom 50%
ED visits						
Annual episodes, mean (95% CI)	1.6 (0.0–6.5)	1.5 (0.0–6.7)	1.2 (0.0–5.0)	1.00	0.014	<0.001
Annual costs (SGD$), mean (95% CI)	550.0 (0.0–2,782.3)	539.0 (0.0–2,553.3)	410.4 (0.0–1,999.7)	1.00	0.0093	<0.001
Primary care visits						
Annual episodes, mean (95% CI)	5.3 (0–29.4)	4.2 (0–24.8)	4.9 (0–24.5)	0.11	1.00	<0.001
Annual costs (SGD$), mean (95% CI)	1,293.9 (0.0–8,058.7)	937.9 (0.0–6,849.4)	944.5 (0.0–5,762.1)	0.016	0.017	1.00
Specialist care visits						
Annual episodes, mean (95% CI)	0.0 (0.1)	0.0 (0.1)	0.0 (0.0)	1.00	1.00	1.00
Annual costs (SGD$), mean (95% CI)	117.1 (0.0–1374.0)	82.1 (0.0–926.4)	83.8 (0.0–863.0)	0.28	0.32	1.00
Prevalence of comorbidities						
Diseases of the circulatory system, n (%)	142 (62.0)	2,637 (56.7)	3,839 (54.4)	0.39	0.083	0.043
Other respiratory diseases, n (%)	140 (61.1)	2,750 (59.2)	3,966 (56.2)	1.00	0.47	0.0052
Diseases of the digestive system, n (%)	77 (33.6)	1,576 (33.9)	2,076 (29.4)	1.00	0.58	<0.001
Metabolic diseases, n (%)	90 (39.3)	1,716 (36.9)	2,907 (41.2)	1.00	1.00	<0.001
Infectious diseases, n (%)	63 (30.2)	1,068 (23.0)	1,170 (16.6)	0.39	<0.001	<0.001
Diseases of the genitourinary system, n (%)	69 (30.1)	1,318 (28.4)	1,815 (25.7)	1.00	0.46	0.0054
Diseases of the nervous system and psychiatric disorders, n (%)	35 (15.3)	454 (9.8)	693 (9.8)	0.028	0.028	1.00
Diseases of the musculoskeletal system, n (%)	73 (31.9)	1,352 (29.1)	2,024 (28.7)	1.00	0.99	1.00
Neoplasms, n (%)	36 (15.7)	515 (11.1)	616 (8.7)	0.12	0.0012	<0.001
Diabetes, n (%)	59 (25.8)	893 (19.2)	1,308 (18.5)	0.055	0.023	1.00
Lung cancer, n (%)	10 (4.4)	170 (3.7)	195 (2.8)	1.00	0.64	0.023
Tuberculosis, n (%)	8 (3.5)	95 (2.0)	135 (1.9)	0.63	0.44	1.00
Pneumonia, n (%)	103 (45.0)	1,704 (36.7)	1,331 (18.9)	0.040	<0.001	<0.001
Asthma, n (%)	27 (11.8)	417 (9.0)	243 (3.4)	0.55	<0.001	<0.001
Bronchiectasis, n (%)	16 (7.0)	216 (4.6)	200 (2.8)	0.43	0.0017	<0.001
Interstitial lung disease, n (%)	1 (0.4)	18 (0.4)	40 (0.6)	1.00	1.00	0.67
Nontuberculous mycobacteria, n (%)	0 (0.0)	37 (0.8)	20 (0.3)	1.00	1.00	<0.001
Other comorbidities, n (%)	171 (74.7)	3,294 (70.9)	4,706 (66.7)	0.73	0.042	<0.001

Note: All costs were measured in 2023 Singaporean dollars (SGD$1=US$0.76=£0.60=€0.69).

Abbreviations: ED, emergency department; CI, confidence interval; COPD, chronic obstructive pulmonary disease; SGD, Singapore dollars; SD, standard deviation; SES, socioeconomic status.

Discussion

To our knowledge, this study was the first to estimate the economic burden and trends of COPD multimorbidity in a representative, multi-ethnic Asian population using longitudinal administrative data. By leveraging comprehensive records from 4.1 million Singapore residents (2012–2019), our study provides robust, granular multimorbidity-related cost estimates compared to prior Asian studies that relied on modelling,[31] surveys,[32] or cross-sectional data,[33,34] which

are limited by recall bias and parameter uncertainty. The substantially higher all-cause medical costs observed among COPD patients relative to non-COPD patients underscore the significant system-level burden of COPD and the need for earlier detection and proactive chronic disease management. Overall, the rising mortality trends in both cohorts likely reflect population ageing and the cumulative burden of multimorbidity, with age-related vulnerability and competing health risks contributing to accelerated health decline and an increased likelihood of sudden acute, life-threatening episodes.[8]

In Singapore, COPD-related costs rose by 2.2% annually (2012–2019) and are projected to reach ~SGD$6,500/PY by 2025. In terms of cost distribution, hospitalisations accounted for the bulk of costs ($3,707.0/PY; 70.1%), similar to OECD countries like Italy (US$5,798/PY, 70.7%)[3] and Sweden (US$5,611/PY, 72.3%).[3] From a health system perspective, our findings suggest that the observed profile of COPD care in Singapore—characterised by an older, predominantly male population, relatively low prevalence, and persistently high hospitalisation costs—likely reflected late diagnosis and advanced disease at presentation, partially explaining the greater overall reliance on inpatient care over community-based alternatives like hospital-at-home services. In parallel, rapidly rising outpatient costs appear to reflect the introduction of newer and more advanced pharmacological therapies, such as long-acting bronchodilators (LABA/LAMA) and triple therapy (eg, Trelegy Ellipta, ~US$602/month (~SGD$767) pre-subsidy),[35] and the gradual strengthening of outpatient management, although specialist care utilisation remained low (SGD$99.8/PY), indicating further scope to shift care from inpatient to ambulatory settings. On the other hand, hospitalisation costs remained relatively stable, declining by only 11.8% over 8 years. While these therapies aim to reduce exacerbations and hospitalisations, their effectiveness may be limited in Singapore's predominantly older, often late-diagnosed COPD population, which may help explain the persistently high inpatient costs despite rising outpatient expenditures. Notably, between 2012 and 2018, Singapore also underwent several incremental changes in health financing and subsidy schemes aimed at improving affordability and access to care, including the progressive enhancement of MediShield Life,[36] expansion of outpatient and chronic disease subsidies under schemes such as the Community Health Assist Scheme (CHAS), first introduced in 2012,[37] and a greater emphasis on primary care–based chronic disease management, which likely contributed to increased outpatient utilisation and cost-sharing protection over time, while hospital care remained a major cost driver for patients with advanced, multimorbid conditions such as COPD. Aligning COPD management more closely with the Healthier SG initiative,[21] toward value-based care, could support earlier diagnosis, more appropriate use of inhaled therapies with reduced reliance on oral corticosteroids (OCS), and strengthened outpatient and community-based care to reduce preventable hospitalisation costs. Beyond this, enhanced integrated care pathways with multidisciplinary teams, shared care plans, and coordinated discharge planning are needed, particularly to address Asian-specific multimorbidity patterns involving respiratory, cardiovascular, post-TB, and metabolic conditions. Additionally, leveraging digital health solutions, such as remote monitoring, clinical decision support, and environmental risk alerts, may further enable early identification of high-risk and high-cost COPD subgroups.[38,39] Collectively, these system-level shifts call for more sustainable payment reforms, including bundled or episode-based payments for multimorbidity care, risk-stratified capitation or shared-savings models for high-risk patients, and broader financing mechanisms to support digital monitoring and targeted interventions, thereby facilitating a transition from reactive, hospital-centred care toward preventive and predictive value-based care to improve outcomes and optimise resource use in this complex, multimorbid COPD population.

Previous Asian studies on the economic burden of COPD offered valuable insights but limited comparability due to differences in study design, populations, and data sources. Existing studies—such as hospital-based analyses from Singapore,[20] and cross-sectional surveys from China[34] and Thailand[33]—lack detailed comorbidity-specific cost breakdowns or exclude comorbidity costs altogether. Therefore, comparisons were best made with countries using similar longitudinal population-level data, like Canada. Specifically, our COPD-specific cost (~SGD$1,786/PY) aligned with Canadian claims (~CAD$1,500/PY) in an overlapping time period.[11] While the top comorbidity cost drivers of Singaporean and Canadian COPD patients were broadly consistent in circulatory (SGD$788.1/PY vs CAD$696/PY [1 SGD=1.01 CAD, 2023]), other respiratory (SGD$793.7/PY vs CAD$312/PY), and digestive diseases (SGD$250.8/PY vs CAD$274/PY),[11] our findings showed a substantial and markedly elevated contribution from metabolic diseases—approximately four times higher than Canadian estimates (SGD$412.7/PY vs <CAD$100/PY).[11] This pattern likely reflects an Asian-specific diabetic-COPD phenotype, previously reported by Tiew PY et al in 2020,[14] and this phenotype was associated with elevated clinical risk.

Consistently, our study found that 26% of Singaporean COPD patients in the top 10th percentile of multimorbidity costs had diabetes. Metabolic costs were largely driven by primary care utilisation and subsequent medication dispensations, reflecting Singapore's high and rising diabetes prevalence (0.24% increase annually)[40,41] and contributing factors such as racial-genetic predisposition (eg, insulin resistance, beta-cell dysfunction, and visceral adiposity), diet and lifestyle changes, and ageing.[42] In our study, other respiratory conditions were the largest cost driver, likely due to high pneumonia (45.0%) and asthma (11.8%) prevalence among high-cost patients. This pattern may represent another distinct Asian COPD phenotype (8.0% of COPD patients), also described by Tiew PY (2020),[14] characterised by a history of post-TB lung disease, which was historically highly prevalent in Singapore and the region until the 1970s.[43] Post-TB lung damage substantially increases the risk of COPD,[44] secondary non-TB lung infections,[45] bronchiectasis,[46] and other organ damage.[47] Meanwhile, OCS, commonly prescribed for COPD management in Singapore,[48] may further contribute to adverse outcomes, as both pneumonia and diabetes are well-known OCS-related complications.[49,50] Although infectious disease-related costs were less dominant overall, they remain clinically relevant in Asia due to historical TB exposure and the heightened infection-related COPD exacerbations.[14] Elevated neoplasm costs ($197.4/PY) may also stem from increased lung cancer incidence, particularly epidermal growth factor receptor (EGFR)-mutant adenocarcinomas common in Asians.[51] These distinct multimorbidity patterns, particularly respiratory and metabolic conditions, highlight limitations of Western-centric COPD-CVD care models and underscore the need for Asian-specific strategies. On the other hand, the link between CVD and COPD is well established; thus, it was unsurprising that circulatory costs ranked second, consistent with COPD-CVD associations observed across Western and Asian populations.[9,11] More importantly, neuropsychiatric costs were likely underestimated due to stigma leading to underdiagnosis,[52] and reliance on private counselling, underscoring the need for integrated mental health support for holistic COPD care.

A notable study finding was the underrepresentation of female COPD patients, likely reflecting underdiagnosis and distinct Asian phenotypes. Similar trends are observed in Japan (males: 16.4%; females: 5.0%)[53] and South Korea (males: 25.8%; females: 9.6),[54] where diagnosis often hinges on smoking history,[55] potentially overlooking non–smoking-related COPD more common in women. Despite lower smoking rates, females often experience worse symptoms and higher mortality,[56] warranting targeted research. Additionally, Indian individuals comprised 67% of the top 10% cost group but were underrepresented in the mid- and low-cost groups. This disparity may reflect a combination of social and metabolic factors, including delayed care-seeking behaviors,[57] higher Type 2 diabetes prevalence,[58] and other cardiometabolic conditions[59] that drive COPD exacerbations and costs. Combined with lower physical activity levels[60] and higher smoking prevalence among Indian males compared with Chinese individuals,[61] these factors contribute to increased cumulative respiratory risk and exacerbate the burden of COPD.[62,63] In addition, limited health literacy among Indians[64] (eg, low awareness of COPD symptoms), alongside socioeconomic constraints, may delay healthcare seeking,[65] with patients often presenting only at advanced stages of the disease. These combined factors highlight the importance of culturally tailored interventions and proactive management strategies for high-cost patients within Singapore's multi-ethnic population. Future research could examine COPD underdiagnosis in females, care-seeking patterns in Indians, and how ethnicity interacts with socioeconomic factors to influence healthcare costs. Notably, limited spirometry use and low clinical awareness in primary care[66] likely contribute to under- or misdiagnosis in Singapore, resulting in late-stage presentation and higher HCU. Enhancing spirometry access and provider awareness could potentially reverse this trend.

Our study has several limitations. First, our comparator group comprised patients without COPD-related visits, rather than true non-COPD individuals. Second, neuropsychiatric costs were likely underestimated due to underdiagnosis, stigma, and missing private counselling data. Third, cardiovascular deaths were excluded from MACE due to missing ICD codes in the death registry. Fourth, the lack of smoking data limited analysis of its role in multimorbidity and overall costs. Fifth, missing healthcare records from private primary care and community hospitals likely led to an underestimation of primary care costs, as prescriptions from private general practitioners are often filled externally and not routinely captured. Sixth, although asthma–COPD overlap syndrome (ACOS) diagnoses are still used in some Asian settings, we excluded these patients (6.1%) due to concerns of misclassification with asthma and the diagnostic uncertainty surrounding ACOS. Sensitivity analyses indicated that their exclusion did not greatly influence the study findings. Data were also unavailable beyond 2020, preventing assessment of more recent trends. Furthermore, the absence of spirometry and Global Initiative for Chronic Obstructive Lung Disease (GOLD) grade data limited assessment

of COPD severity and its impact on HCU and costs. Also, potential ex-TB phenotypes could not be ascertained due to unavailable or unreliable historical TB records in administrative data. In addition, the COPD case definition may underestimate prevalence in Singapore, as COPD is often diagnosed late due to low awareness and limited spirometry use, particularly among non-smokers. Nonetheless, while the case definition warrants further validation, it appropriately captured individuals with substantial HCU, providing a reasonable reflection of real-world costs and HCU borne by the public health system, including those related to later diagnosis. Lastly, despite adjustment for observed covariates, residual confounding due to unavailable behavioral factors, such as smoking status and BMI, cannot be ruled out.

Conclusion

To conclude, this population-based study of 18,866 COPD patients in Singapore (2012–2019) highlighted substantial and rising healthcare costs, largely driven by hospitalisation (70%). The observed cost burden from respiratory, cardiovascular, and metabolic conditions likely reflects Asian-specific COPD phenotypes and highlights the complexity of managing multimorbid patients. The increasing primary care costs alongside persistently high inpatient expenditures underscore the need for integrated, better-coordinated, multidisciplinary care. Notably, the underrepresentation of females and the disproportionately high costs among Indian patients identify priority groups for targeted diagnosis and interventions. Overall, while acknowledging limitations such as missing spirometry and private-sector data, these findings support the adoption of value-based care approaches in Singapore, including structured longitudinal follow-up, integrated multimorbidity care management, and early identification of patients at risk of high utilisation and costs, alongside the development of more sustainable, flexible, and comprehensive payment models. The insights generated may also inform policy and clinical practice in other Asian health systems facing comparable COPD care burdens and undergoing similar primary care and health system reforms.

Abbreviations

CAD, Canadian dollar; CI, Confidence interval; ED, Emergency department; GP, General practitioner; HCU, Healthcare utilisation; ICD, International Classification of Diseases; OECD, Organisation for Economic and Co-operation and Development; OR, Odds ratio; PSM, Propensity score matching; PY, Patient-year; SES, Socioeconomic status; SD, Standard deviation; SGD, Singapore dollar; SMD, Standardised mean difference; USD, US dollar.

Data Sharing Statement

The datasets used in this study are analysed in a secure environment and are not available for external request.

Ethics Approval and Informed Consent

This study was performed in accordance with the Declaration of Helsinki. This study was approved by the National University of Singapore Institutional Review Board (NUS-IRB-2021-967). Participant consent was not required as the research involved only anonymised health administrative data.

Consent for Publication

Not applicable as the research involved only anonymised health administrative data.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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This paper has been uploaded to [ResearchGate] as a preprint: [https://www.researchgate.net/publication/398275571_High_Multimorbidity_Costs_and_Trends_of_COPD_Patients_in_a_Multiethnic_Asian_Population_Evidence_from_Singapore_Health_Administrative_Data]

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