Pragmatic and Observational Research Dovepress

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Patient Characteristics, Management, and Outcomes of Adult Asthma in a Singapore Population: Data from the SDG-CARE Asthma Registry

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Purpose: Patients with asthma in Singapore often have complex patient journeys, with diagnosis and management across various primary and speciality care settings. Real-world population health data is needed to identify care gaps and inform policies.

Patients and Methods: This retrospective, longitudinal cohort study assessed real-world data from adults (aged ≥18 years) with asthma in the SingHealth Chronic Obstructive Pulmonary Disease and Asthma Data Mart, an integrated database of electronic medical records of patients who attended primary and/or speciality care clinics in the SingHealth Regional Health System 01/01/2015–12/31/2020. Patients were indexed by first asthma diagnosis and categorized into cohorts of index year. Patient characteristics, asthma management and outcomes were described during baseline (1-year pre-index) and follow-up periods (1-year post-index).

Results: Overall, 21,215 patients were included across 4 cohorts: 2016, N=12,947; 2017, N=3419; 2018, N=2816; 2019, N=2033. Most common baseline asthma medication changed from inhaled corticosteroids (ICS) alone in the 2016 cohort (32.8% [n=4252]) to ICS/long-acting β_2-agonist in the 2019 cohort (33.3% [n=677]). Asthma symptom control (mean [SD] Asthma Control Test scores) improved from 2016 to 2019 during baseline (18.38 [4.93] vs 19.87 [4.56]; $p<0.001$) and follow-up (18.34 [4.23] vs 21.07 [3.51]; $p<0.001$). Mean (standard deviation [SD]) number of exacerbations per patient during follow-up decreased from 2016 to 2019 (1.91 [3.11] vs 0.89 [2.07]; $p<0.001$). Mean (SD) number of emergency department visits per patient during follow-up decreased from 0.21 (0.75) in 2016 to 0.17–0.18 (0.60–0.65; $p<0.001$) between 2017 and 2019.

Conclusion: Health status at first asthma diagnosis improved for each succeeding cohort from 2016 to 2019, along with improvements in patient management and outcomes. This reflects greater awareness of the condition and improved use of medication and referrals in recent years, suggesting policy changes and their implementation, including promotion of disease awareness and adoption of guideline recommendations, may improve asthma outcomes in Singapore.

Plain Language Summary: In Singapore, up to 4 in 100 people are living with asthma. People with asthma can experience frequent symptoms and attacks that affect day-to-day activities, create emotional stress and reduce quality of life. Asthma has a financial impact on patients and the economy, as it can lead to missed work and reduced productivity. In Singapore, managing asthma can be complex, with patients often seeing both primary care physicians and specialists from diagnosis to treatment. This study assessed trends in the care that patients with asthma in Singapore received and their outcomes over a 4-year period. Patients' medical records from primary

Received: 9 May 2024
Accepted: 15 November 2024
Published: 7 December 2024

and specialist care were collected for 1 year before and after their asthma diagnosis to determine whether treatment changed over time, whether symptoms improved and whether use of healthcare services changed.

Between 2016 and 2019, patients with asthma had fewer, less severe asthma attacks, and fewer emergency department visits over time. The treatment types also changed; in 2019 versus 2016, more patients received combination inhalers of corticosteroids with a long-acting beta 2 (β_2) agonist, or other add-on treatments, which improve patients' asthma, including symptoms. This indicates that there was an increasing trend for physicians following new guidelines for recommended asthma care and these changes in practice ensured combination inhalers were made available to patients by the government, leading to improvement in asthma outcomes.

This study shows that asthma management in Singapore improved over the 4-year period, potentially through healthcare professionals taking on board improved treatment guideline recommendations and policy changes.

Keywords: asthma, asthma control, exacerbations, real world, Singapore, health outcomes

Introduction

Asthma affects approximately 262 million people worldwide, corresponding to a global prevalence of 3.4%.[1] In Singapore, the prevalence of asthma is estimated to be 2.6–3.9% in the overall population,[1–3] with higher prevalence (6.3%) reported among those with Chinese ethnicity.[4] Patients with asthma in Singapore experience substantial disease burden, including frequent symptoms, high levels of rescue medication use, absenteeism from work/school, and exacerbations.[5] In particular, patients with severe asthma report high healthcare resource utilization (HCRU) and oral corticosteroid (OCS) use, and poor health-related quality of life.[2,6] The economic burden of asthma in Singapore is considerable, with total annual costs for adults estimated at 1.25 billion United States dollars (US$) in 2020, with 79% of costs due to lost productivity.[7] Asthma control status is also associated with individual economic burden; among employed patients, annual direct and indirect costs range from $5,230 for patients with well-controlled asthma to $25,630 for uncontrolled asthma.[7]

The patient journey for individuals with asthma in Singapore is complex; patients can choose their healthcare provider, with options including publicly-funded primary care polyclinics, private primary care clinics, and publicly- and/or privately-funded hospitals and speciality care clinics.[8] As such, diagnosis and disease management often occur across different care settings, resulting in limited real-world information regarding patients' healthcare data. Consequently, the SingHealth-Duke-GSK Chronic Obstructive Pulmonary Disease (COPD) and Asthma Real-World Evidence (SDG-CARE) collaboration was formed in 2017, with the aim of improving use and accessibility of real-world healthcare data in Singapore.[9] The collaboration led to development of the SingHealth COPD and Asthma Data Mart (SCDM), an integrated database comprising real-world data for patients with asthma and/or COPD attending primary and/or speciality care clinics in the SingHealth Regional Health System, the largest public healthcare system in Singapore.[9] As of 2019, the SCDM included 36,047 unique patients with asthma and COPD across SingHealth's public primary and specialist care clinics.[9] Given asthma prevalence of 2.6–3.9%[1–3] in a population of ~5.7 million in 2019,[10] the SCDM captures approximately 20% of people living with asthma in Singapore. The SCDM records patients' demographic, clinical, laboratory and radiology data, which are updated every 24 hours, ensuring near real-time, clinically relevant data.[9]

Given the burden of asthma in Singapore, there is a need to identify and address gaps in asthma management. Analyzing longitudinal trends in patient characteristics and outcomes from clinical visits may help inform and improve the delivery of asthma care. As such, the objective of this study was to describe the patient characteristics of an adult asthma population, along with places of care and healthcare outcomes over a 4-year period (2016–2019), using real-world primary and speciality care data collected in the SCDM.

Methods

Study Design and Data Source

This retrospective cohort study included real-world data from adults with asthma in the SCDM from January 01, 2015 to December 31, 2020 (Supplementary Figure 1). The SCDM contained electronic medical records (EMRs) of patients who

attended a SingHealth Polyclinic (SHP; primary care) and/or Singapore General Hospital respiratory medicine specialist outpatient clinic (SGH-SOC; specialty care). Patients who attended an SHP could be referred to SGH-SOCs or other speciality care clinics, while patients who attended SGH-SOCs could be referred from primary care clinics other than SHPs. Some patients included in the SCDM attended both SHPs and SGH-SOCs. Further information about the SCDM has been reported elsewhere.[9]

The first recorded diagnosis of asthma during the identification period (January 01, 2016 to December 31, 2019) was defined as the index event; incident patients were confirmed by the absence of an asthma diagnosis or prescription for asthma in the year prior to the date of the index event (baseline period). Asthma management was assessed at baseline (ie the index date or closest to index date) and in the 1-year follow-up period after index.

Study Population

Eligible patients were aged ≥18 years at index with a diagnosis of asthma (301485011), asthma-COPD overlap (ACO; 3046475015) or severe asthma (1208972017) by Systematized Nomenclature of Medicine codes[11] recorded in the SCDM during the study period and had ≥1 year of follow-up data. Patients were excluded if they had ≤1 asthma-related visit, to ensure that patients included were routinely monitored in primary or speciality care settings.

Study Outcomes

Patients were categorized into 4 cohorts based on index year, from 2016 to 2019. Full details of study variables are provided in Supplementary Table 1. Briefly, patients' demographic and clinical characteristics (including age, sex, race, Global Initiative for Asthma [GINA] Treatment Step, smoking status, and body mass index), and asthma medication use were assessed at the index date or the closest date after index with available data. Definitions for GINA Steps were derived from the 2015 GINA report,[12] and are summarized in Supplementary Table 2. Comorbidity data were collected during the study period and identified by the presence of International Statistical Classification of Diseases and Related Health Problems – 10th revision codes.[13]

Blood eosinophil (EOS) count and asthma symptom control status (Asthma Control Test [ACT]) data were collected during the baseline and follow-up periods. In addition, data for asthma-related HCRU (outpatient and emergency department [ED] visits), documentation of vaccinations (influenza, pneumococcal PCV13, pneumococcal PPSV23), asthma counselling and written asthma action plans (WAAPs), and asthma exacerbations were assessed during the follow-up period. Definitions for asthma exacerbations are presented in Supplementary Table 3. To mitigate any bias in quantifying the number of exacerbations partly based on OCS burst prescriptions, we discounted one OCS prescription per patient to account for prescriptions for standby use, and only OCS prescriptions lasting 5–7 days were considered as burst treatment for an asthma exacerbation.

Statistical Analyses

Statistical analyses were descriptive, and patients were included in cohorts by index year. Continuous variables were reported using mean and standard deviation (SD); statistical significance was assessed using one-way analysis of variance (ANOVA). Categorical variables were reported using relative frequencies and percentages; statistical significance was assessed using Chi-square tests. Statistical significance was set at $p<0.05$ for all analyses. All statistical analyses were performed with STATA statistical software (StataCorp. 2017. Stata Statistical Software: Release 17.0. College Station, TX: StataCorp LLC).

Results

Study Population

Overall, 36,405 patients were identified in the SCDM with a total of 192,832 unique asthma-related visits (Supplementary Figure 2). After applying exclusion criteria, the final study population included 21,215 adults with asthma. Baseline demographic and clinical characteristics are presented in Table 1. The proportion of patients aged ≥54 years was highest in the 2016 cohort (57.7% [n=7468]); this decreased to 37.6% (n=1286) in the 2017 cohort, followed

Table 1 Baseline Demographic and Clinical Characteristics

	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)	*p* value
Age (year), n (%)					
≥18–<34	2381 (18.4)	1119 (32.7)	836 (29.7)	559 (27.5)	<0.001
≥34–<54	3098 (23.9)	1014 (29.7)	847 (30.1)	606 (29.8)	
≥54–<80	6548 (50.6)	1175 (34.4)	1012 (35.9)	781 (38.4)	
≥80	920 (7.1)	111 (3.3)	121 (4.3)	87 (4.3)	
Male, n (%)	5531 (42.7)	1626 (47.6)	1326 (47.1)	947 (46.6)	<0.001
Race, n (%)					
Chinese	7039 (54.4)	1645 (48.1)	1389 (49.3)	1095 (53.9)	<0.001
Malay	3042 (23.5)	947 (27.7)	760 (27.0)	525 (25.8)	
Indian	1865 (14.4)	507 (14.8)	401 (14.2)	232 (11.4)	
Other	1001 (7.7)	320 (9.4)	266 (9.5)	181 (8.9)	
GINA Step, n (%)					
1	4875 (37.7)	1603 (46.9)	1277 (45.4)	752 (37.0)	<0.001
2	3035 (23.4)	764 (22.4)	578 (20.5)	463 (22.8)	
3	2700 (20.9)	564 (16.5)	513 (18.2)	425 (20.9)	
4	2330 (18.0)	488 (14.3)	448 (15.9)	391 (19.2)	
5	7 (0.1)	0 (0.0)	0 (0.0)	2 (0.1)	
BMI (kg/m^2), n (%)	n=10,245	n=2507	n=2303	n=1802	
Underweight (<18.5)	436 (4.3)	136 (5.4)	110 (4.8)	105 (5.8)	0.004
Normal (≥18.5–<22.9)	2361 (23.1)	554 (22.1)	586 (25.5)	412 (22.9)	
Overweight (≥23–<27.5)	3431 (33.5)	837 (33.4)	747 (32.4)	627 (34.8)	
Obese (≥27.5)	4017 (39.2)	980 (39.1)	860 (37.3)	658 (36.5)	
Smoking status, n (%)	n=10,388	n=2739	n=2523	n=1742	
Never smoked	9540 (91.8)	2390 (87.3)	2161 (85.7)	1330 (76.4)	<0.001
Ex-smoker	175 (1.7)	59 (2.2)	59 (2.4)	55 (3.2)	
Current smoker	673 (6.5)	290 (10.6)	303 (12.0)	357 (20.5)	

Notes: Patients were categorized into 4 cohorts based on their index year, from 2016 to 2019.
Abbreviations: BMI, body mass index; GINA, Global Initiative for Asthma.

by a gradual increase to 42.7% (n=868) in the 2019 cohort (p<0.001). Similarly, the proportion of patients at GINA Step 3 or above decreased from 38.9% (n=5037) in the 2016 cohort to 30.8% (n=1052) in the 2017 cohort, before increasing to 40.2% (n=818) in the 2019 cohort (p<0.001), whereas the proportion of current smokers increased from 2016 (6.5% [n=673]) to 2019 (20.5% [n=357]) (p<0.001) (Table 1).

There was a decreasing trend for comorbid pneumonia from 7.9% (n=1023) in 2016 to 4.8% (n=98) in 2019 (p<0.001) during the baseline period, while comorbid hypertension and heart failure decreased from 52.3% (n=6772) and 3.0% (n=390) in 2016 to 29.0% (n=991) and 1.8% (n=62) in 2017, respectively, before remaining relatively stable from 2017 to 2019 (p<0.001 for all) (Supplementary Table 4). Mean (SD) blood EOS counts were similar across index years during the baseline period (0.30–0.31 [0.29–0.47] × 10^9 cells/L; p<0.999) (Supplementary Table 5).

Asthma Medication Use

The most common asthma medication during the baseline period changed with increasing index year; inhaled corticosteroid (ICS) monotherapy was the most frequently prescribed medication in the 2016 cohort (32.8% [n=4252]) but was less frequently prescribed in the 2019 cohort (26.1% [n=531]), whereas the proportion of patients prescribed ICS/long-acting β_2-agonist (LABA) therapy increased from 25.1% (n=3252) in the 2016 cohort to 33.3% (n=677) in 2019 (p<0.001) (Figure 1; Supplementary Table 6). Among patients receiving ICS monotherapy, the proportion receiving low-dose ICS increased between the 2016 and 2019 cohorts (71.6% vs 85.2%), while the proportion using medium-dose

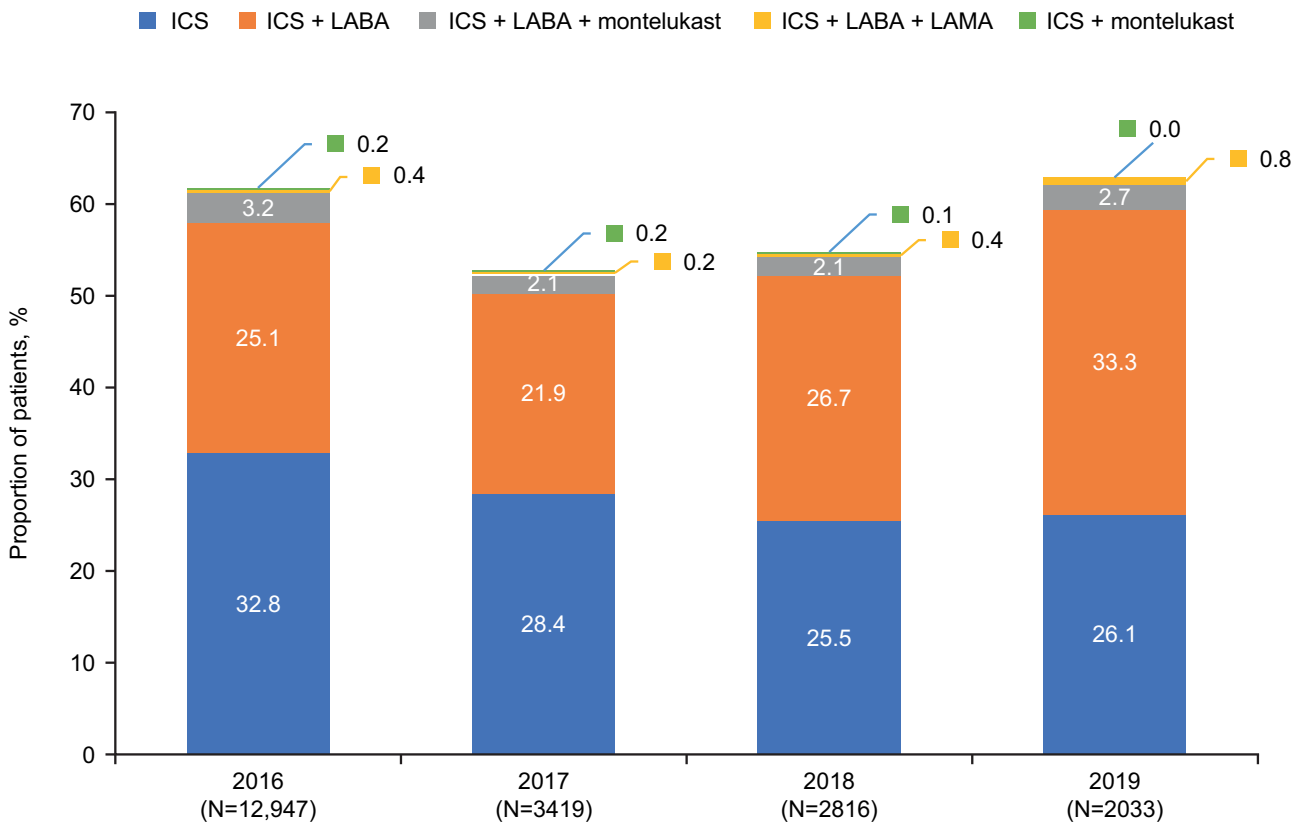


Figure 1 Inhaled medication use during the baseline period. Differences across index years per medication type were tested for significance using Chi-square tests: ICS + LABA, $p<0.001$; ICS + LABA + montelukast, $p<0.001$; ICS + LABA + LAMA, $p<0.011$; ICS + montelukast, $p<0.236$. Differences in ICS monotherapy use across index years were not assessed.
Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist.

(24.2% vs 13.3%) or high-dose ICS decreased (3.3% vs 0.6%) ($p<0.001$ for all) (Supplementary Table 6). Similar trends for high- and low-dose ICS were also reported for ICS/LABA (Supplementary Table 6).

The proportion of patients prescribed OCS (maintenance or burst) showed a significant decreasing trend from 27.3% (n=3533) in the 2016 cohort to 15.5% (n=316) in the 2019 cohort ($p<0.001$); similar results were seen for those receiving systemic corticosteroid (SCS) bursts defined as those comprising more than two 5- to 7-day SCS courses (2016: 1.3% [n=174]; 2019: 1.0% [n=21]; $p<0.001$) (Table 2). The mean SCS dose and proportion of patients prescribed rescue therapy remained broadly similar across cohorts.

Table 2 OCS and SCS and Rescue Therapy Use During the Baseline Period

	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)	*p* value
OCS prescription (prednisolone), n (%)	3533 (27.3)	747 (21.9)	626 (22.3)	316 (15.5)	<0.001
SCS bursts*, n (%)	174 (1.3)	43 (1.3)	59 (2.1)	21 (1.0)	<0.001
SCS dose (mg, prednisolone), mean (SD)	32.17 (9.15)	32.39 (9.74)	32.67 (10.24)	32.85 (10.17)	0.432
Rescue therapy prescription†, n (%)	2156 (16.7)	575 (16.8)	465 (16.5)	333 (16.4)	0.976

Notes: *SCS burst prescriptions were defined as those comprising ≥2 5- to 7-day SCS courses; †salbutamol (SABA, 10 puffs) or ipratropium bromide (LAMA, 4 puffs) recorded in EMRs from SHPs.
Abbreviations: EMR, electronic medical record; LAMA, long-acting muscarinic antagonist; OCS, oral corticosteroid; SABA, short-acting β_2-agonist; SCS, systemic corticosteroid; SD, standard deviation; SHP, SingHealth Polyclinic.

Exacerbations

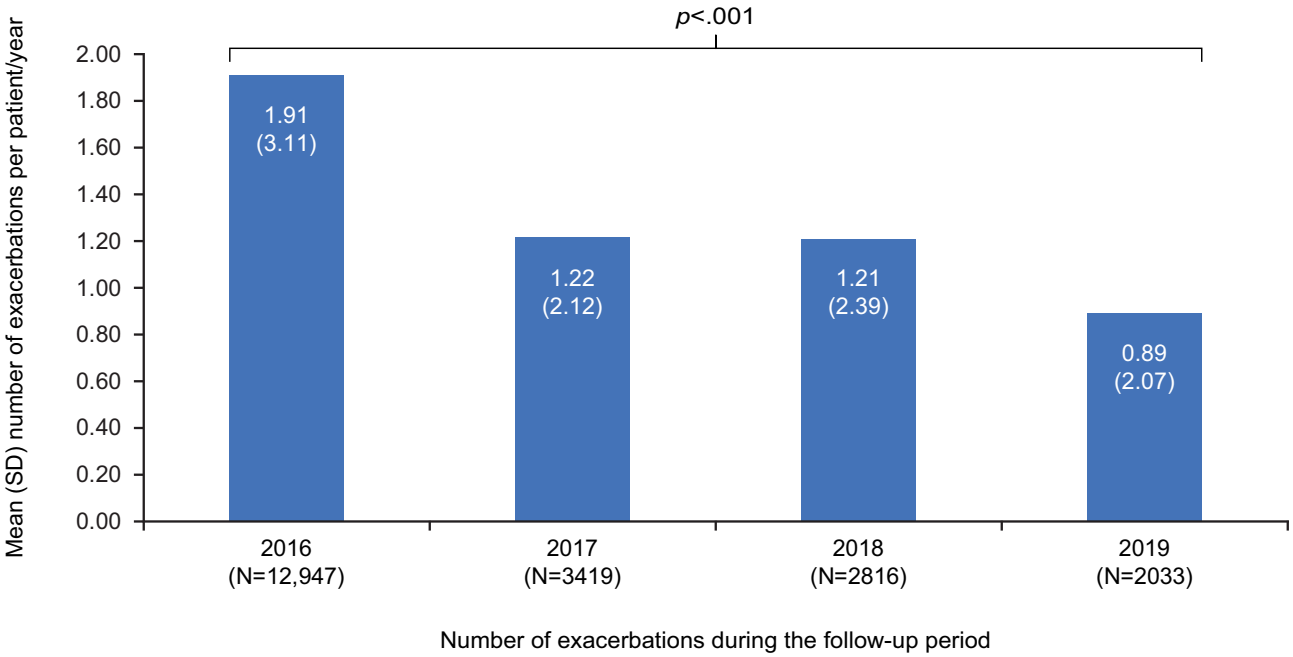
The mean (SD) number of exacerbations per patient during follow-up showed a significantly decreasing trend from 2016 to 2019, with 1.91 (3.11) exacerbations in the 2016 cohort compared with 0.89 (2.07) in the 2019 cohort ($p<0.001$) (Figure 2). The proportion of patients with ≥2 exacerbations during follow-up also decreased between 2016 and 2019 (48.6% [n=6295] vs 19.5% [n=396]), while the proportion of patients with no exacerbations increased between these cohorts (2016: 46.3% [n=5994]; 2019: 73.3% [n=1490]) (Figure 2).

HCRU

HCRU during the follow-up period from 2016 to 2019 is presented in Figure 3. The mean (SD) number of primary care (SHP) outpatient visits per patient decreased from 1.89 (1.66) in 2016 to 1.19 (1.37) in the 2017 cohort, before increasing to 1.63 (1.87) in the 2019 cohort ($p<0.001$). The number of speciality care (SOC) outpatient visits showed an increasing trend from 2016 (0.28 [0.85]) to 2019 (0.55 [1.2]; $p=0.0015$). The mean (SD) number of ED visits was highest in the 2016 cohort (0.21 [0.75]), before decreasing and remaining relatively stable from 2017 to 2019 (0.17–0.18 [0.60–0.65]; $p<0.001$). The proportion of patients with no ED visits increased between the 2016 and 2019 cohorts (70.5% [n=9124] vs 86.5% [n=1758]), whereas the proportion with ≥1 visit decreased from 2016 to 2019 (29.5% [n=3823] vs 13.5% [n=275]) (Figure 3).

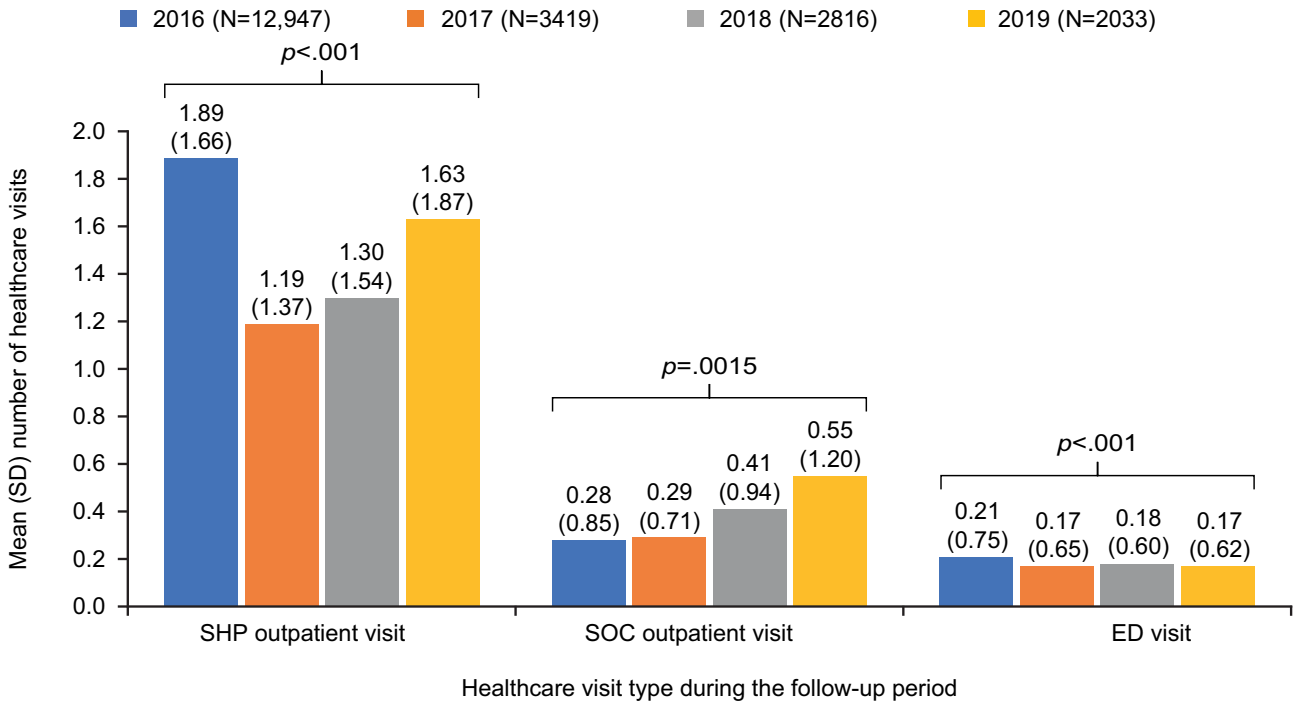
Asthma Symptom Control

Asthma symptom control generally improved with increasing index year (Figure 4). During the baseline period, the mean (SD) ACT score increased from 18.38 (4.93) in the 2016 cohort to 19.87 (4.56) in the 2019 cohort ($p<0.001$); mean (SD)



Exacerbations per year, n (%)	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)
0	5994 (46.3)	1883 (55.1)	1724 (61.2)	1490 (73.3)
1	403 (3.1)	122 (3.6)	100 (3.6)	86 (4.3)
2	255 (2.0)	99 (2.9)	93 (3.3)	61 (3.0)
>2	6295 (48.6)	1315 (38.5)	899 (31.9)	396 (19.5)

Figure 2 Exacerbations during the follow-up period.
Abbreviation: SD, standard deviation.



ED visits per year, n (%)	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)
0	9124 (70.5)	2706 (79.2)	2286 (81.2)	1758 (86.5)
1	1617 (12.5)	357 (10.4)	285 (10.1)	173 (8.5)
2	785 (6.1)	134 (3.9)	104 (3.7)	50 (2.5)
>2	1421 (11.0)	222 (6.5)	141 (5.0)	52 (2.6)

Figure 3 HCRU during the follow-up period.
Abbreviations: ED, emergency department; HCRU, healthcare resource utilization; SD, standard deviation; SHP, SingHealth Polyclinic; SOC, specialist outpatient clinic.

ACT scores also increased between the 2016 and 2019 cohorts during follow-up (18.34 [4.23] vs 21.07 [3.51]) ($p<0.001$) (Figure 4). Asthma symptom control levels also generally improved after index, with mean (SD) ACT scores increasing from baseline to the follow-up period in all cohorts except for 2016, which remained stable (Figure 4). In addition, the proportion of patients with not well-controlled asthma (ACT score <20) decreased between baseline and follow-up in all cohorts except for the 2016 cohort, which increased from 51.6% (n=112) to 53.3% (n=171) (Figure 4).

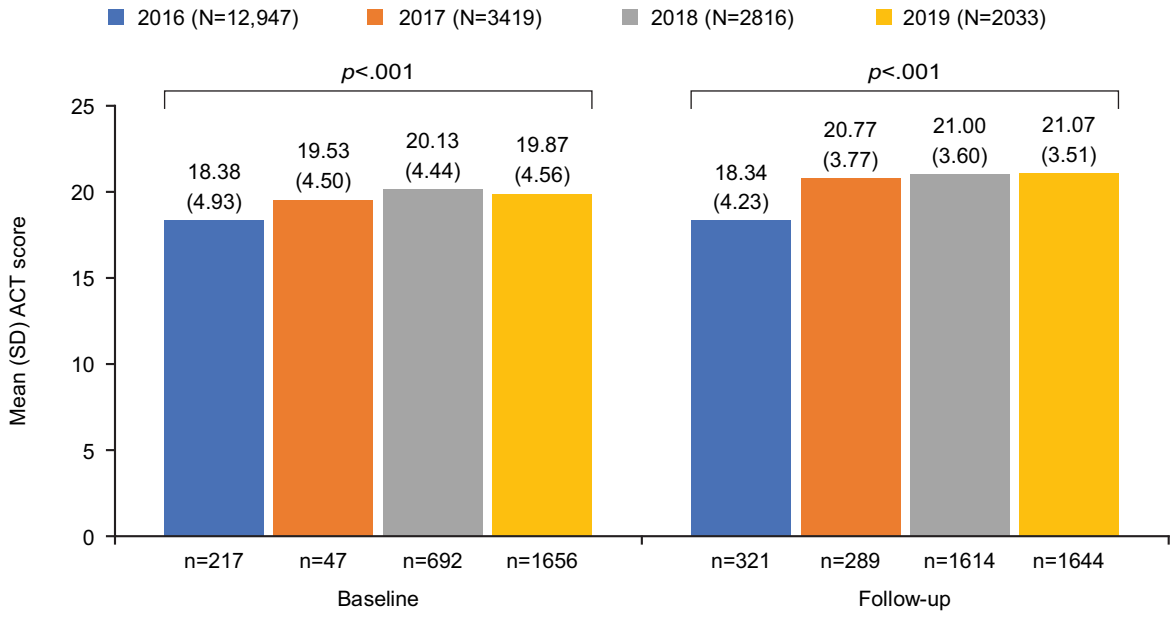
Vaccinations and Asthma Counselling

Vaccination rates during the follow-up period decreased between the 2016 and 2019 cohorts, with a greater proportion of patients in 2016 receiving an influenza (43.2% [n=5598] vs 33.4% [n=679]), pneumococcal PCV13 (16.5% [n=2139] vs 9.8% [n=199]; $p<0.001$), or pneumococcal PPSV23 vaccination (13.7% [n=1775] vs 7.6% [n=154]; $p<0.001$) versus in 2019 (Supplementary Table 7).

Documentation of asthma counselling at least once in EMRs increased significantly from 16.5% (n=2131) in 2016 to 33.6% (n=682) in 2019 ($p<0.001$) (Table 3). Similarly, there was a significant increase in the proportion of patients with ≥1 documentation of a WAAP from 66.5% (n=8612) in 2016 to 90.8% (n=1846) in 2019 ($p<0.001$) (Table 3).

Discussion

This retrospective study is the first in Singapore to describe real-world characteristics of patients with asthma across a 4-year period (2016–2019), using both primary and speciality care data collected from EMRs. The proportion of patients aged ≥54 years during the baseline period decreased from 2016 to 2017, before gradually increasing in the 2018



ACT score <20, n (%)	2016 (N=12,947)	2017 (N=3419)	2018 (N=2816)	2019 (N=2033)	*p* value
Baseline	n=217 112 (51.6)	n=47 16 (34.0)	n=692 233 (33.8)	n=1656 596 (36.2)	<.001
Follow-up	n=321 171 (53.3)	n=289 85 (29.4)	n=1614 430 (26.6)	n=1644 433 (26.3)	<.001

Figure 4 Asthma symptom control during the baseline and follow-up periods.
Abbreviations: ACT, Asthma Control Test; SD, standard deviation.

and 2019 cohorts. Health outcomes generally improved from 2016 to 2019, with reductions in exacerbations and ED visits, and improvements in asthma symptom control in the 2019 cohort compared with the 2016 cohort.

Previous data from patients with severe, life-threatening asthma presenting at four public hospitals in Singapore from 2011 to 2015 show that 17% of patients had no regular asthma follow-up, and almost a third had no prior ICS controller medication,[14,15] suggesting suboptimal asthma care before 2016. In this study, we observed a greater proportion of patients at GINA Steps 3, 4, and 5 in the 2019 cohort versus the 2016 cohort. Moreover, between 2016 and 2019, the proportion of patients receiving asthma counselling more than doubled and the proportion receiving a WAAP increased from 67% to more than 90%. In addition, the most frequently prescribed asthma medication changed from ICS monotherapy in 2016 to ICS/LABA dual therapy in 2019. Collectively, these findings likely reflect improved patient management in recent years, where therapy is stepped-up appropriately for patients with uncontrolled asthma, potentially leading to the reduction in exacerbations and ED visits, and improvements in asthma symptom control reported between 2016 and 2019. The apparent improved care in recent cohorts may be due to wider adoption of asthma management

Table 3 Asthma Counselling and WAAP During the Follow-Up Period

	2016 (N=12,947)	**2017 (N=3419)**	**2018 (N=2816)**	**2019 (N=2033)**	***p* value**
≥1 documentation of asthma counselling in EMRs, n (%)	2131 (16.5)	567 (16.6)	733 (26.0)	682 (33.6)	<0.001
≥1 documentation of a WAAP, n (%)	8612 (66.5)	2007 (58.7)	2118 (75.2)	1846 (90.8)	<0.001

Abbreviations: EMR, electronic medical record; WAAP, written asthma action plan.

guidelines and greater awareness among clinicians of the importance of achieving asthma control earlier in the treatment course.

Between the 2016 and 2019 index dates, an increasing trend in the frequency of SOC visits was observed. In contrast, the average number of primary care SHP visits was highest in the 2016 cohort and dropped considerably in the 2017 cohort. This reduction may have been influenced by the considerably larger patient population in the 2016 cohort versus 2017, 2018, or 2019 cohorts. Similar to the trend observed with SOC visits, from 2017 to 2019 the frequency of SHP visits also gradually increased, suggesting in later index years, patients were more often visiting their physicians in any care setting. As a result, patients likely received closer monitoring and more appropriate treatments, potentially leading to the improved outcomes observed at later index years in this study.

These improved outcomes possibly reflect the impact of local initiatives in Singapore, such as the "Towards Zero Asthma Deaths" campaign, which aimed to improve awareness of the importance of adhering to asthma management guidelines.[16] In addition, several ICS/LABA combinations were included on the Singapore Ministry of Health's (MOH) list of subsidized drugs during this period.[17] Improved access and affordability of ICS/LABA may account for the shift in prescription patterns from 2016 to 2019, affording patients the opportunity to receive more appropriate treatments. The findings from this study may be useful in providing further evidence to physicians in Singapore, particularly those in primary care, that adhering to asthma management guidelines can lead to improved patient outcomes.

The data reported here indicate there are still aspects of clinical practice and asthma management in Singapore that warrant improvement. Although the proportion of patients prescribed OCS or receiving SCS bursts decreased from the 2016 cohort to the 2019 cohort, the mean dose of SCS and proportion of patients prescribed rescue therapy remained relatively stable between cohorts. This suggests that despite greater focus on GINA-recommended treatment step-up with increasing year, there is an issue of high OCS/SCS and rescue therapy prescribing. These findings are notable given that short-acting β_2-agonist reliever use has been associated with reduced asthma control and increased risk of exacerbations,[18–20] while OCS/SCS use has been shown to result in greater asthma burden and increased risk of adverse effects.[21–25] These observations may also be a consequence of limited access and affordability of asthma biologics (GINA Step 5) in Singapore due to lack of government reimbursement.[6,26] Improving affordability and access to biologics in patients with severe asthma will likely reduce OCS burden and further reduce HCRU as shown in clinical trials[27,28] and real-world large registry data.[6,26]

In the present study, ACT scores showed an increasing trend across index years, suggestive of improved disease management over time. However, approximately 1 in 4 patients in the 2019 cohort continued to have asthma that was not well controlled during the follow-up period. Notably, although ICS/LABA was the most prescribed asthma medication in the 2019 cohort, more than a quarter of patients still received ICS monotherapy. This suggests that an unmet need remains for optimized treatment for patients in this study population. In line with 2023 GINA recommendations, the Singapore MOH Agency for Care Effectiveness guidelines for asthma recommend a step-wise treatment approach, whereby ICS is the mainstay of asthma management, and treatment decisions are based on long-term assessment of patients' symptoms, risk of exacerbations and hospital admissions.[29] For patients with uncontrolled asthma despite low-dose ICS, the addition of a LABA at Step 3 is recommended, while for those with uncontrolled asthma despite medium-dose ICS/LABA, addition of a LAMA is recommended at Step 4.[29] Raising awareness among clinicians about treatment optimization may help to promote best practice and improve patient outcomes, and further research could be done to assess the impact that these more recent guidelines are having on asthma management and patient outcomes, and to understand the barriers to patients and clinicians carrying out the guideline recommendations.

The inclusion of patients with ACO in this study was intended to provide a comprehensive view of real-world asthma management in Singapore, recognizing the frequent coexistence of asthma and COPD in clinical practice. While the classification of ACO is not universally standardized and may introduce some variability into the study's findings, including these patients was considered crucial to accurately capture the complexities of managing asthma in patients with overlapping characteristics of COPD. This approach enhances the study's applicability to real-world settings, where such comorbid conditions are often encountered.

This real-world, longitudinal study addresses knowledge gaps regarding characteristics, change in care patterns, and impact on health outcomes among patients with asthma in Singapore over a 4-year period, and provides valuable insight

from a population health perspective. The study draws from a comprehensive dataset including primary and speciality care data, which have previously been scarcely reported in the literature, as well as patient-level EMR data, which have not previously been reported for South-East Asia. However, the study has several limitations that should be noted. There were considerably more patients in the 2016 cohort versus the other cohorts due to the inclusion of pre-existing and newly diagnosed asthma cases in 2016, which may potentially have impacted the trends observed across cohorts. The intent of the study was to assess broader trends in asthma management and outcomes at the population level, reflecting changes in clinical practice and policy implementations over the years, rather than to compare identical cohorts across different years. As a result, the comparison of different cohorts by year may involve patient populations with inherent differences due to variations in demographic factors, disease severity, or treatment approaches over time, which introduces a limitation in interpreting the observed trends. The lag time or incomplete data capture of asthma symptom control may be due to a lack of integration of ACT results into the main SCDM platform following practice changes during the observation period. Compounded by a multiplicity of possible ACT reporting systems, the asthma symptom control trends observed in this study may not be representative of the entire cohort. Moreover, medication data are based on prescriptions rather than consumption and may instead have been prescribed as standby medication, rather than for immediate use. A further limitation is that the dataset only included patients treated in SHP or SGH outpatient clinics. Therefore, data for patients who visited other public or private clinics[30] were not captured. Additionally, patients in primary care may experience severe exacerbations or be referred to clinics not included in the SCDM; these events were not captured, therefore, the asthma severity of these patients may be underestimated. Furthermore, the study's design was not intended to track individual patients over extended periods due to the database structure, which limited follow-up to 1 year post index diagnosis. While this reflects the pragmatic nature of the analysis, it restricts the ability to capture long-term changes in asthma management and outcomes. Finally, the SCDM database primarily focuses on clinical data related to asthma management, without detailed socioeconomic information. Future studies will need to incorporate socioeconomic data to provide a more comprehensive analysis of asthma management and outcomes.

Conclusions

This is the first study in Singapore to describe the real-world characteristics and outcomes of an incident asthma population over a 4-year period in patients managed in both primary and tertiary care settings. These results show overall improvements in outcomes for patients with asthma with increasing index year from 2016 to 2019, including reduced exacerbations and ED visits, improved asthma symptom control, and more asthma counselling. This provides evidence that policy changes and implementation such as improving disease awareness and adoption of guideline recommendations is successful in improving quality of care and outcomes at a population level for people with asthma in Singapore.

Abbreviations

ACO, asthma-COPD overlap; ACT, Asthma Control Test; COPD, chronic obstructive pulmonary disease; ED, emergency department; EMR, electronic medical record; EOS, eosinophil; GINA, Global Initiative for Asthma; HCRU, healthcare resource utilization; ICS, inhaled corticosteroid; LABA, long-acting β_2-agonist; MOH, Ministry of Health; OCS, oral corticosteroid; SCDM, SingHealth COPD and Asthma Data Mart; SCS, systemic corticosteroid; SD, standard deviation; SDG-CARE, SingHealth-Duke-GSK COPD and Asthma Real-World Evidence; SGH-SOC, Singapore General Hospital respiratory medicine specialist outpatient clinic; SHP, SingHealth Polyclinic; US$, United States dollar; WAAP, written asthma action plan.

Data Sharing Statement

Data from the SingHealth COPD and Asthma Data Mart (SCDM) may be available on reasonable request with de-identified patient data, subject to data owners, PIs, HODs and other stakeholders' approval, from the corresponding author.

Ethics Approval and Informed Consent

This study complied with all applicable laws regarding subject privacy. No direct patient contact or primary collection of individual human participant data occurred. Study results are in tabular form and presented as aggregate analyses that omit patient identification, therefore, informed consent, ethics committee or International Review Board approval were not required; waiver of appropriate consent can be found under the Human Biomedical Research Act (HBRA) Fifth Schedule, Part 2, Section 3 (individually identifiable health information or human biological material obtained or compiled before, on and/or after 1 Nov 2017).

Acknowledgments

Editorial support, in the form of preparation of the first draft based on input from all authors, and collation and incorporation of author feedback to develop subsequent drafts, was provided by Ben Usher, PhD, of Fishawack Indicia Ltd, UK, part of Avalere Health, and was funded by GSK.

The authors would like to thank Mr See Wei Qiang (HSRC) for his help with project management and the Singapore General Hospital Airway coordinators (Ms Karen Tan, Ms Yvonne Tiang, Ms Noor Syifa Binte Shamsuddin, Ms Sherine Lim Shu Gim and Ms Cheong Ai Wei) for their help with clinical service and data entry.

Author Contributions

All authors made a significant contribution to the work reported; MSK, SSWL, NCT and CML contributed to the conception and design of the study and data interpretation. MEHO contributed to the data analysis and interpretation. XX and DBM contributed to the conception and design of the study and data interpretation. JTW contributed to the acquisition of data and data analysis. PR and RM contributed to data interpretation. All authors 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.

Funding

This study and the SGD-CARE colllaboration were funded by GSK (GSK study 218080).

Disclosure

MSK reports grant support from AstraZeneca and honoraria for lectures and advisory board meetings paid to Singapore General Hospital from GSK, AstraZeneca, Novartis, Sanofi and Boehringer Ingelheim, and Roche outside of the submitted work. XX is an employee of GSK and has financial equities in GSK. PR was an employee of GSK at the time of the study. RM is an employee of GSK. SSWL, JTW, MEHO, DBM, NCT and CML declare no competing interests for this work.

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