

## Association of quality-of-care indicators with asthma outcomes: A retrospective observational study for asthma care in Singapore

Sean Shao Wei Lam<sup>1-5</sup> PhD, Jingwei Chen<sup>\*1</sup> BEng, Jun Tian Wu<sup>1-4</sup> MPH, Chun Fan Lee<sup>1</sup> PhD, Narayanan Ragavendran<sup>1-4</sup> MBA, Marcus Eng Hock Ong<sup>1-4</sup> MBBS, Ngiam Chuan Tan<sup>1,6</sup> FCFPS, Chian Min Loo<sup>1,7</sup> MBBS, David Bruce Matchar<sup>\*\*1,8</sup> MD, Mariko Siyue Koh<sup>1,7</sup> MBBS

### ABSTRACT

**Introduction:** Asthma guidelines have advocated for the use of quality-of-care indicators (QCI) in asthma management. To improve asthma care, it is important to identify effective QCIs that are actionable. This study aimed to evaluate the effect of the presence of 3 QCIs: asthma education, Asthma Control Test (ACT) and spirometry testing on the time to severe exacerbation (TTSE).

**Method:** Data collected from the SingHealth COPD and Asthma Data Mart (SCDM), including asthma patients managed in 9 SingHealth polyclinics and Singapore General Hospital from January 2015 to December 2020, were analysed. Patients receiving Global Initiative for Asthma (GINA) Steps 3–5 treatment, with at least 1 QCI recorded, and at least 1 severe exacerbation within 1 year before the first QCI record, were included. Data were analysed using multivariate Cox regression and quasi-Poisson regression models.

**Results:** A total of 3849 patients in the registry fulfilled the criteria. Patients with records of asthma education or ACT assessment have a lower adjusted hazard ratio (HR) for TTSE (adjusted HR=0.88,  $P=0.023$ ; adjusted HR=0.83,  $P<0.001$ ). Adjusted HR associated with spirometry is higher (adjusted HR=1.22,  $P=0.026$ ). No QCI was significantly associated with emergency department (ED)/inpatient visits. Only asthma education and ACT showed a decrease in the number of exacerbations for multivariate analysis (asthma education estimate: -0.181,  $P<0.001$ ; ACT estimate: -0.169,  $P<0.001$ ). No QCI was significant for the number of exacerbations associated with ED/inpatient visits.

**Conclusion:** Our study suggests that the performance of asthma education and ACT was associated with increased TTSE and decreased number of exacerbations, underscoring the importance of ensuring quality care in clinical practice.

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**Keywords:** asthma, quality-of-care indicators, asthma exacerbations, real-world evidence, asthma education, Asthma Control Test, spirometry

### CLINICAL IMPACT

#### What is New

- This large real-world study highlights that the performance of asthma education and Asthma Control Test (ACT) is associated with improved outcomes.
- Findings underscore the importance of ensuring quality care in clinical practice augmented by important quality-of-care indicators.

#### Clinical Implications

- The study supports the need to ensure asthma education and ACT in the management of asthma patients in Singapore.
- This evidence can potentially guide efforts to improve the outcomes of asthma patients and population health.

### INTRODUCTION

Asthma, a chronic inflammatory disorder of the airways,<sup>1</sup> is a common respiratory condition, with an estimated 262 million people affected worldwide.<sup>2</sup> In Singapore, 5% of residents aged 18–69 years are affected.<sup>3</sup> Despite the high standard of healthcare in

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<sup>1</sup> Duke-NUS Medical School, National University of Singapore, Singapore

<sup>2</sup> Health Services and Systems Research, Duke-NUS Medical School, Singapore

<sup>3</sup> Health Services Research Centre, Singapore Health Services, Singapore

<sup>4</sup> Health Services Research Institute, SingHealth Duke-NUS Academic Medical Centre, Singapore

<sup>5</sup> Lee Kong Chian School of Business, Singapore Management University, Singapore

<sup>6</sup> SingHealth Polyclinics, SingHealth, Singapore

<sup>7</sup> Department of Respiratory and Critical Care Medicine, Singapore General Hospital, Singapore

<sup>8</sup> Department of Internal Medicine (General Internal Medicine), Duke University Medical School, Durham, North Carolina, US

Correspondence: Prof Sean Shao Wei Lam, Health Services Research Centre, Singapore Health Services, 20 College Road, The Academia, Ngee Ann Kongsi Discovery Tower Level 6, Singapore 169856.

Email: gmslasws@nus.edu.sg

\* Joint first author

\*\* Joint last author

Singapore, asthma control is a concern, as evidenced by high mortality rates, admissions, healthcare utilisation, uncontrolled symptoms relative to global averages,<sup>4</sup> and high annual estimated economic burden of SGD 2.09 billion.<sup>5</sup>

According to the Global Initiative for Asthma (GINA) 2022 recommendations, asthma is diagnosed clinically based on symptoms, such as wheezing, shortness of breath, chest tightness or cough, with confirmatory lung function testing like as spirometry.<sup>1</sup> Asthma control is then assessed in terms of symptom control using various tools.<sup>6</sup> Based on the risk factors, baseline symptom severity and frequency, the GINA guidelines recommend patients to be placed on treatment plans across the 5 GINA steps. GINA recommends inhaled corticosteroids (ICS) for all treatment steps.<sup>1,7</sup> It recommends 2 treatment pathways; track 1 in GINA 2022 recommends the use of formoterol, a long-acting beta agonist (LABA) with ICS, as a preferred reliever to reduce the risks of exacerbations, while track 2 recommends a short-acting beta agonist (SABA) as an alternative reliever, taken with ICS. Singapore's Ministry of Health (MOH) Agency for Care Effectiveness (ACE) guidelines also emphasise the use of ICS from Steps 1 to 5.

Barriers to the diagnosis and treatment of asthma, such as lack of knowledge of asthma or the medications, and improper inhaler technique are common.<sup>8</sup> To improve asthma care, it is important to identify effective quality-of-care indicators (QCI) that are actionable. A number of guidelines have recommended some of these QCIs,<sup>1,7,9-11</sup> including assessments used in randomised controlled trials (RCTs) and real-world studies (see Supplementary Materials, Appendix Table S1). These indicators include processes performed by healthcare professionals to either diagnose or assess disease control, such as lung function testing (e.g. spirometry, peak expiratory flow rate [PEFR], fractional exhaled nitric oxide), symptom control (e.g. Asthma Control Test [ACT]), vaccination and allergen testing and management, and patient engagement activities that empower patients to manage their asthma (e.g. asthma education, counselling, or the use of Written Action Asthma Plan [WAAP]).<sup>12</sup>

The frequency of the performance of QCIs and their impact on patient outcomes in the Singapore healthcare setting have not been evaluated before. This research aims to determine if the following QCIs are associated with the time to severe exacerbation (TTSE) among patients with prior severe exacerbations: (1) asthma symptom control with ACT; (2) lung function testing for diagnosis and assessment (spirometry); (3) asthma education (asthma counselling and explanation of WAAP).

## METHOD

### Study design

This is a retrospective observational study leveraging on the SingHealth COPD and Asthma Data Mart (SCDM) developed under the SingHealth-Duke-NUS-GSK COPD and Asthma Real-World Evidence (SDG-CARE) study.<sup>13</sup> The cohort comprises 21,215 eligible patients identified from the SDG-CARE registry over the study time frame of January 2015 to December 2020.<sup>13</sup> The study sites are: the acute care hospital, Singapore General Hospital (SGH), and the primary care clinics, SingHealth polyclinics, within the Singapore Health Services (SingHealth) public healthcare system. SingHealth is the largest of 3 public health systems in Singapore and is an Academic Medical Centre with Duke-NUS Medical School as the medical school partner.<sup>13</sup> Singapore is a city state with approximately 5.6 million population in 2020.<sup>14</sup> The SingHealth healthcare system comprises 3 comprehensive acute care hospitals, 1 paediatric and maternity hospital, and 9 primary care clinics. From March 2020 to March 2021, the SingHealth cluster saw over 200,000 inpatients and approximately 2.5 million outpatient clinic attendances in both the acute and primary care settings. There were over 400,000 emergency department (ED) attendances.<sup>14</sup>

Patients are included if they have asthma-related visits to either the primary care (PC) or specialist care (SC)/acute care setting, or both (PC&SC), identified by an asthma diagnosis recorded in the SCDM. We included high-risk patients with prior asthma exacerbations, with asthma severity classification of moderate to high, as asthma severity is a strong independent risk factor for future exacerbations.<sup>15</sup> This was achieved by taking a subset of the SCDM patient cohort with the following inclusion criteria: (1) patients on GINA Steps 3–5 treatment; (2) at least 1 QCI recorded; (3) at least 1 severe exacerbation within 1 year before the first QCI record; (4) at least 1 month of follow-up after the QCI. GINA steps were determined by the medications prescribed in accordance with the GINA 2015 (LABA, long-acting muscarinic antagonist, ICS dosage, montelukast, biologics, systemic steroids; see Appendix Table S2) at the indexed date.<sup>7</sup> These inclusion criteria ensure that patients included in the study were routinely monitored in the PC or acute care setting in the study site.

QCIs were chosen based on the review of international and local asthma guidelines, review of literature (see Appendix Table S1) and availability in the SDG-CARE dataset. The final QCIs that were chosen for evaluation are: (1) asthma symptom control with ACT; (2) lung function test

for the diagnosis of asthma and assessment of risk (spirometry); (3) asthma education (including asthma counselling and explanation of WAAP). Patients are adjudged to have had more than 1 type of QCI (e.g. ACT and spirometry), provided that the dates of the subsequent QCIs are recorded within 1 month after the first QCI date detected. The index date is defined as the date of the patient's first recorded QCI from 1 January 2016 to 31 October 2020. We allowed for 1 year of baseline observations over 2015 and 1 month of follow-up QCI observations in November 2020, followed by another month of follow-up observation for the outcomes (e.g. exacerbations) in December 2020. The follow-up period of 1-month after each index date allowed us to consider any other QCIs done within that month until the end of the study period, or death. Fig. 1 shows the study timeline. The primary outcome measure is TTSE, and the secondary outcome measure is TTSE associated with ED or inpatient visits. We also conducted a secondary analysis looking at the yearly counts of severe exacerbations and the yearly counts of severe exacerbations associated with ED or inpatient visits after the indexed QCI.

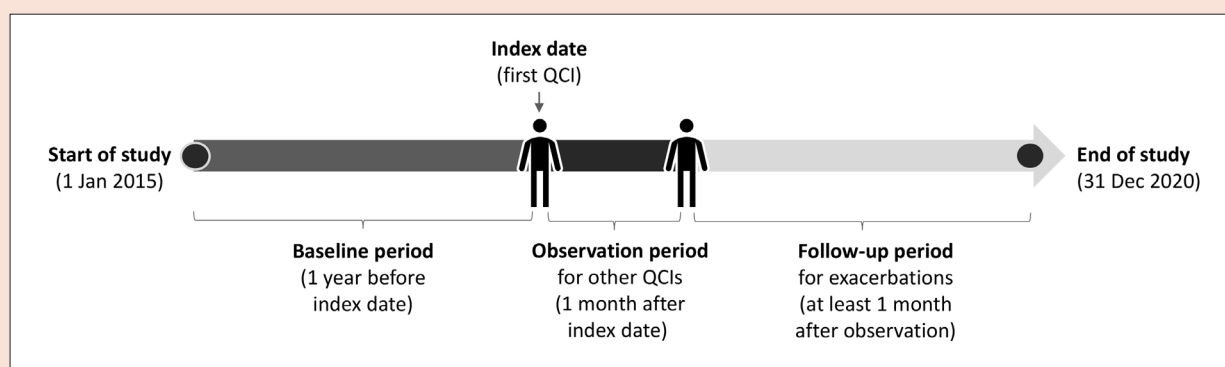
Patient outcomes are measured in terms of severe exacerbations, which are defined as patient records with any of the following: (1) rescue therapy received at primary care;<sup>13</sup> (2) ED or inpatient encounter for acute asthma exacerbation (case type description of Accident & Emergency or inpatient) with ICD-10-AM<sup>16</sup> diagnosis code of J459; (3) oral corticosteroid (OCS) prescription for acute asthma exacerbation, and/or; (4) prescription of short-acting muscarinic antagonist. For the OCS prescription, the first prescription or prescriptions marked as "standby" are excluded from the exacerbation count.

Baseline characteristics, comorbidities and past medical history were analysed as covariates.

Relevant comorbidities considered are allergic rhinitis, atopic dermatitis, allergic conjunctivitis, gastroesophageal reflux disease, obstructive sleep apnoea, anxiety disorder, depressive disorder, hypertension, heart failure, pulmonary tuberculosis, pneumonia, and chronic obstructive pulmonary disorder.<sup>13</sup> The comorbidities were identified with ICD-10-AM<sup>16</sup> diagnosis codes within the entire study timeline. Categorical variables were summarised as counts and percentages while continuous variables were described in mean and standard deviation. The comorbidities were evaluated as an index score, adapted from Comorbidity Components of Asthma Assessment<sup>17</sup>—ranging from 0 to 3. Each comorbidity was given equal weight of 1 point; patients with more than 3 comorbidities were assigned an index of 3. Differences between groups were tested using one-way analysis of variance (ANOVA) and chi-squared analysis, for continuous and categorical variables, respectively.

The primary outcome is the first severe exacerbation event that occurred after the indexed QCI, and the secondary outcome is the first severe exacerbation with ED or in-hospital visit. TTSE was measured as the number of days from the first QCI performed. In the primary analysis, univariate and multivariate Cox regression analyses were performed to evaluate TTSE. Patient baseline characteristics, annual average counts of previous exacerbations and comorbidities were included in the analysis. Secondary analysis involved quasi-Poisson regression to evaluate the effects on the average counts of severe exacerbations and exacerbations associated with ED or inpatient analysis. Right censoring was assumed if no exacerbations were detected within the follow-up period due to the loss of follow-up (including death). Statistical significance was set at  $P < 0.05$  with 95% confidence interval (CI) for hazard ratio

Fig. 1. Study design and timeline.



QCI: quality-of-care indicator

(HR) calculated, with the covariates for the multivariate analysis determined via a family-wise error rate (FWER) of  $P < 0.05$ . A Holm-Bonferroni correction was applied to control the FWER due to multiple comparisons.<sup>18</sup> All analyses were performed using R statistical software version 4.2.2 (R Core Team, Vienna, Austria).

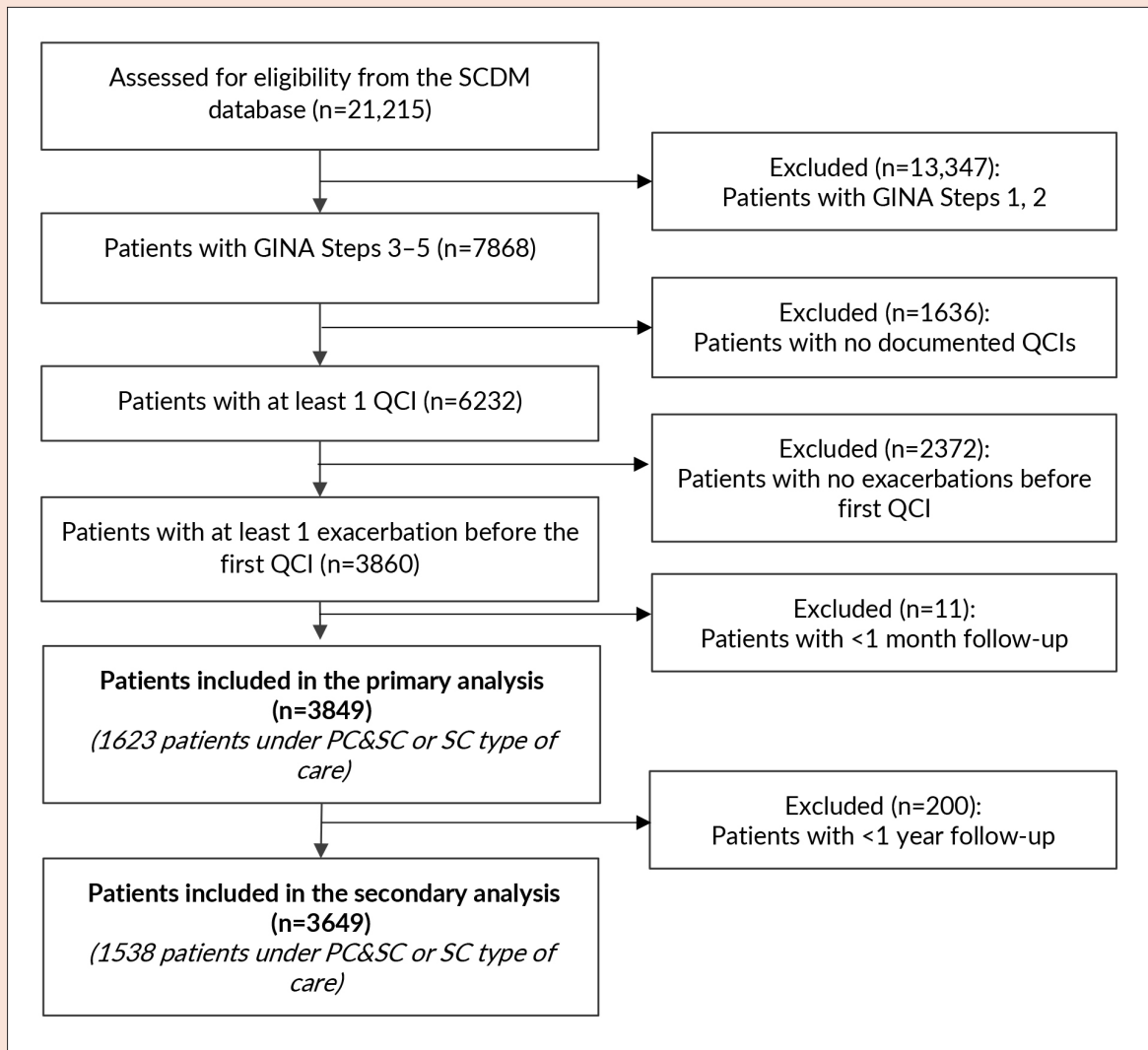
**RESULTS**

Out of 21,215 patients found in the SCDM, 62.9% were in GINA Steps 1 and 2. For patients in the higher GINA steps (3–5), 1636 (7.7%) do not have a documented QCI within the observation period. For those patients with QCI detected, 2372 (11.2%) do not have any exacerbations in the baseline observation period. Based on the inclusion and exclusion criteria, we have 3849 eligible patients for

the primary analysis and 3649 eligible patients for the secondary analysis (Fig. 2).

Baseline characteristics and comorbidities/past medical history are shown in Table 1. Out of the cohort with QCI, approximately 43% of the cohort are males, 74% received asthma education/counselling, 80% having ACT records and 39% having spirometry records. Demographic characteristics are shown below in Table 1A, which reflect the ethnic composition of Singapore.<sup>19</sup> A total of 1623 (42%) patients have encounters in the acute care hospital, which includes ED, inpatient and specialist outpatient visits. There are 2980 patients with at least 1 of the comorbidities considered in the cohort (Table 1B). Demographic information and clinical characteristics for the cohort are relatively complete (Table 1).

Fig. 2. Study flow chart.



GINA: Global Initiative for Asthma; PC: primary care; QCI: quality-of-care indicator; SC: specialist care/acute care; SCDM: SingHealth COPD and Asthma Data Mart

Table 1. Baseline characteristics according to the presence of type of quality-of-care indicator (QCI).

(A) Characteristics of patients with QCI										
Characteristics of patients with QCI	Entire population (n=3849)	Patients receiving asthma education (n=2865)	Patients not receiving asthma education (n=984)	P value	Patients with ACT record (n=3088)	Patients without ACT record (n=761)	P value	Patients with spirometry record (n=368)	Patients without spirometry record (n=3481)	P value
Mean age (SD), years	56.25 (16.35)	55.59 (16.42)	58.19 (16)	<0.001	50.65 (16.22)	55.91 (16.88)	<0.001	56.18 (18.66)	56.16 (16.42)	0.98
Median age (IQR), years	58.37 (45.90–67.74)	57.64 (45.40–67.13)	60.40 (48.55–69.32)	<0.001	58.50 (46.31–67.73)	57.53 (44.86–67.81)	<0.001	59.37 (46.17–68.94)	58.24 (45.84–67.64)	0.98
Male sex, no. (%)	1651 (42.89)	1264 (44.12)	387 (39.33)	0.01	1326 (42.94)	325 (42.7)	0.94	144 (39.13)	1507 (43.29)	0.14
Mean BMI (SD), kg/m <sup>2</sup>	25.27 (9.0)	24.9 (9.4)	26.35 (7.64)	<0.001	25.7 (8.6)	23.52 (10.31)	<0.001	25.96 (5.93)	25.2 (9.27)	0.12
Median BMI (IQR), kg/m <sup>2</sup>	25.80 (22.10–29.90)	25.70 (21.90–29.90)	25.80 (22.50–30.20)	<0.001	25.90 (22.30–30.10)	24.80 (20.80–29.30)	<0.001	25.40 (22.20–28.90)	25.80 (22.10–30.00)	0.12
Mean prior exacerbations (SD), per year	2.26 (1.76)	2.09 (1.56)	2.74 (2.16)	<0.001	2.16 (1.63)	2.63 (2.15)	<0.001	3.04 (2.53)	2.17 (1.63)	<0.001
Median prior exacerbations (IQR), per year	1.85 (1.00–3.00)	1.71 (1.00–2.74)	2.31 (1.07–3.47)	<0.001	1.79 (1.00–2.86)	2.14 (1.00–3.43)	<0.001	2.40 (1.00–4.00)	1.80 (1.00–2.87)	<0.001
Race, no. (%)										
Chinese	2061 (53.55)	1502 (52.43)	559 (56.81)		1665 (53.92)	396 (52.04)		234 (63.59)	1827 (52.48)	
Malay	921 (23.93)	723 (25.24)	198 (20.12)	0.009	727 (23.54)	194 (25.49)		50 (13.59)	871 (25.02)	<0.001
Indian	544 (14.13)	396 (13.82)	148 (15.04)		444 (14.38)	100 (13.14)		46 (12.5)	498 (14.31)	
Others	323 (8.39)	244 (8.52)	79 (8.03)		252 (8.16)	71 (9.33)		38 (10.33)	285 (8.19)	
GINA Step, no. (%)										
3	2047 (53.18)	1623 (56.65)	424 (43.09)		1704 (55.18)	343 (45.07)		95 (25.82)	1952 (56.08)	
4	1800 (46.77)	1242 (43.35)	558 (56.71)	<0.001	1383 (44.79)	417 (54.8)	<0.001	272 (73.91)	1528 (43.9)	<0.001
5	2 (0.05)	0	2 (0.20)		1 (0.03)	1 (0.13)		1 (0.27)	1 (0.03)	
Smoking status, no. (%)										
Never-smoker	3447 (89.56)	2578	869		2780	667		306	3141	
Ex-smoker	82 (2.13)	40 (1.4)	42 (4.27)	<0.001	54 (1.75)	28 (3.68)	0.005	34 (9.24)	48 (1.38)	<0.001
Current smoker	320 (8.31)	247 (8.62)	73 (7.42)		254 (8.23)	66 (8.67)		28 (7.61)	292 (8.39)	

Table 1. Baseline characteristics according to the presence of type of quality-of-care indicator (QCI). (Cont'd)

<b>(A) Characteristics of patients with QCI</b>										
Characteristics	Entire population (n=3849)	Patients receiving asthma education (n=2865)	Patients not receiving asthma education (n=984)	P value	Patients with ACT record (n=3088)	Patients without ACT record (n=761)	P value	Patients with spirometry record (n=368)	Patients without spirometry record (n=3481)	P value
Type of care care, no. (%)										
PC	2226 (57.83)	1887 (65.87)	339 (34.45)		1862 (60.3)	364 (47.83)		1 (2.72)	2225 (63.92)	
PC&SC	1326 (34.45)	924 (33.25)	402 (40.85)	<0.001	1022 (33.1)	304 (39.95)	<0.001	185 (50.27)	1141 (32.78)	<0.001
SC	297 (7.72)	54 (24.7)	243 (24.7)		204 (6.61)	93 (12.22)		182 (49.46)	115 (3.3)	
ACT: Asthma Control Test; BMI: body mass index; GINA: Global Initiative for Asthma; IQR: interquartile range; PC: primary care; SC: specialist care/acute care; SD: standard deviation										
<b>(B) Comorbidities according to the presence of type of QCI</b>										
Comorbidities/past medical history, no. (%)	Entire population (n=3849)	Patients receiving asthma education (n=2865)	Patients not receiving asthma education (n=984)	P value	Patients with ACT (n=3088)	Patients without ACT (n=761)	P value	Patients with spirometry record (n=368)	Patients without spirometry record (n=3481)	P value
Allergic rhinitis	1344 (34.92)	1037 (36.2)	307 (31.2)	0.0051	1085 (35.14)	259 (34.03)	0.6	92 (25)	1252 (35.97)	<0.001
Atopic dermatitis	2 (0.05)	0 (0)	2 (0.2)	NA	1 (0.032)	1 (0.13)	NA	2 (0.54)	0 (0)	NA
Allergic conjunctivitis	34 (9.41)	282 (9.84)	80 (8.13)	0.13	286 (9.26)	76 (9.99)	0.59	25 (6.79)	337 (9.68)	0.087
GERD	306 (7.95)	197 (6.88)	109 (11.08)	<0.001	224 (7.25)	82 (10.78)	0.0017	56 (15.22)	250 (7.18)	<0.001
OSA	74 (1.92)	41 (1.43)	33 (3.35)	<0.001	55 (1.78)	19 (2.5)	0.25	22 (5.98)	52 (1.49)	<0.001
Anxiety disorder	27 (0.7)	17 (0.59)	10 (1.02)	0.25	21 (0.68)	6 (0.79)	0.94	8 (2.17)	19 (0.55)	NA
Depressive disorder	47 (1.22)	33 (1.15)	14 (1.42)	0.62	39 (1.26)	8 (1.05)	0.77	5 (1.36)	42 (1.21)	NA
Hypertension	1966 (51.08)	1470 (51.31)	496 (50.41)	0.65	1626 (52.66)	340 (44.68)	<0.001	129 (35.05)	1837 (52.77)	<0.001
Heart failure	115 (2.99)	72 (2.51)	43 (4.37)	0.0045	89 (2.88)	26 (3.42)	0.51	17 (4.62)	98 (2.82)	0.076
Pulmonary TB	1 (0.03)	1 (0.03)	0	NA	1 (0.03)	0	NA	0	1 (0.03)	NA
History of Pneumonia	392 (10.18)	245 (8.55)	147 (14.94)	<0.001	286 (9.26)	106 (13.93)	<0.001	73 (19.84)	319 (9.16)	<0.001
COPD	211 (5.48)	150 (5.24)	61 (6.2)	0.29	133 (4.31)	78 (10.25)	<0.001	38 (10.33)	173 (4.97)	<0.001
ACT: Asthma Control Test; COPD: chronic obstructive pulmonary disease; GERD: gastroesophageal reflux disease; NA: No applicable value; OSA: obstructive sleep apnoea; TB: tuberculosis										

For the primary analysis, patients with the QCI of asthma education or ACT assessment have a lower HR of TTSE for the univariate analysis of both severe exacerbations and exacerbations associated with ED or inpatient visits (Table 2). In the multivariate analysis, asthma education and ACT remain significant after considering the confounding effects for severe exacerbations (adjusted HR=0.88, P=0.023 and adjusted HR=0.83, P<0.001). The HR of spirometry performed is higher for both severe exacerbations (HR=1.33, P<0.001) and exacerbations associated with ED or inpatient visits (HR=1.85, P<0.001). The effects of spirometry performed for the patients remain significant in the multivariate analysis for severe exacerbations only (adjusted HR=1.22, P=0.026). After applying Holm-Bonferroni correction for the multivariate analysis, all 3 QCIs remained significant (at a FWER of 0.05) for the primary analysis of any severe exacerbations.

For the secondary analysis (Table 3), only asthma education and ACT show decrease in the number of exacerbations for multivariate analysis (asthma education estimate: -0.181, P<0.001; ACT estimate: -0.169, P<0.001). The effects of all 3 QCIs performed for the patients are insignificant in the multivariate analysis for the number of exacerbations associated with ED or inpatient visits.

### DISCUSSION

This study sought to determine whether the presence of certain QCIs has effects on TTSE and number of future exacerbations. The performance of asthma education and ACT assessment was found to be associated with reduced HR for TTSE and fewer future exacerbations. Multivariate analysis adjusted for confounders showed statistically significant reduced HR for TTSE for patients who were given either asthma education or ACT.

Table 2. Primary analysis (multivariable) for the risks of severe exacerbations.

<b>(A) Risk of any severe exacerbation</b>					
<b>Variable</b>	<b>HR</b>	<b>P value</b>	<b>Adjusted HR</b>	<b>95% CI</b>	<b>P value</b>
Quality-of-care indicators					
Asthma education	0.82	<0.001	0.88	0.793–0.983	0.023
ACT	0.77	<0.001	0.83	0.743–0.917	<0.001
Spirometry	1.33	<0.001	1.22	1.024–1.443	0.026
Confounders					
Number of previous exacerbations per year	1.14	<0.001	1.15	1.127–1.168	<0.001
Sex: female (reference male)	0.94	0.165	0.99	0.907–1.075	0.771
Current smoker	1.11	0.156	1.19	1.029–1.385	0.020
Age	1.00	<0.001	1.00	1.002–1.007	<0.001
Cumulative comorbidity index (reference <3)	1.43	<0.001	1.31	1.156–1.493	<0.001
BMI	1.01	<0.001	1.01	1.008–1.018	<0.001
Type of care (reference PC)					
PC&SC	1.12	0.011	0.93	0.848–1.025	0.148
SC	0.91	0.254	0.58	0.476–0.696	<0.001
GINA Step 4/5 (reference Step 3)	1.12	0.008	1.04	0.952–1.126	0.415
Race (reference Chinese)					
Indian	1.00	0.990	1.01	0.888–1.137	0.937
Malay	1.04	0.492	1.05	0.950–1.168	0.326
Others	0.90	0.186	0.87	0.741–1.016	0.079

ACT: Asthma Control Test; BMI: body mass index; CI: confidence interval; GINA: Global Initiative for Asthma; HR: hazard ratio; PC: primary care; SC: specialist care/acute care

## (B) Risk of severe exacerbation associated with ED or inpatient visit

Variable	HR	P value	Adjusted HR	95% CI	P value
Quality-of-care indicators					
Asthma education	0.55	<0.001	0.77	0.520–1.152	0.206
ACT	0.66	0.009	0.91	0.636–1.303	0.607
Spirometry	1.85	<0.001	1.43	0.912–2.241	0.120
Confounders					
Number of previous exacerbations per year	1.16	<0.001	1.12	1.060–1.185	<0.001
Sex: female (reference male)	1.10	0.530	1.02	0.743–1.407	0.891
Current smoker	2.09	<0.001	2.25	1.427–3.539	<0.001
Age	1.01	0.274	1.01	0.997–1.018	0.157
Cumulative comorbidity index (reference <3)	2.63	<0.001	2.42	1.747–3.356	<0.001
BMI	1.02	0.106	1.01	0.986–1.030	0.476
Type of care: SC (reference PC&SC)	1.34	0.098	0.93	0.631–1.366	0.706
GINA Step 4/5 (reference Step 3)	2.48	<0.001	1.85	1.289–2.661	<0.001
Race (reference Chinese)					
Indian	2.08	<0.001	2.00	1.385–2.898	<0.001
Malay	1.05	0.819	1.09	0.701–1.706	0.693
Others	1.19	0.564	1.07	0.590–1.926	0.832

ACT: Asthma Control Test; BMI: body mass index; CI: confidence interval; GINA: Global Initiative for Asthma; HR: hazard ratio; PC: primary care; SC: specialist care/acute care

To our understanding, this is the first study in Singapore to use real-world data to analyse the association between the provision of QCI and its effect on patient outcomes. Our results reinforce the findings from previous studies that showed the benefit of asthma education on patient outcomes. A review of 26 RCTs on WAAP found that WAAP based on patients' lung function test results reduced hospital admissions and ED visits, while improving lung function.<sup>20</sup> These studies differed from ours as they explored the interaction of lung function test results and WAAP, while similarly investigating the effect of WAAP (as part of asthma education) on severe exacerbations. A review of 36 RCTs on self-management with asthma education found that it reduced hospitalisations, emergency room visits, unscheduled medical visits, days off work or school, and nocturnal asthma.<sup>21</sup> These studies differed from our study in their definition of asthma education, which included self-monitoring by PEFR. A similar cohort study on the effect of an asthma education programme showed a decrease in ED visits and inpatient admissions, with improved asthma control reflected by higher ACT

scores,<sup>22</sup> albeit with a smaller population size of 234. Another systematic review leveraging on the evaluated multiple QCIs with expert panellists ranked asthma education from Certified Asthma Educators as the highest in terms of reliability, validity, availability and feasibility.<sup>23</sup> Spirometry testing for monitoring was ranked second, while WAAP ranked eighth. In our study, WAAP was considered as part of asthma education, which is associated with reduced HR for TTSE and fewer future exacerbations.

The ACT is a 5-question, multiple-choice questionnaire, used as a numerical asthma symptom control tool. Scores range from 5 to 25, with higher scores indicating a better control of asthma. It can be performed concurrently during the asthma education session by the asthma educator and is offered in multiple languages. Previous studies on ACT assessment have mostly investigated the validity of the questions in the assessment,<sup>24,25</sup> and the correlation of its scores to asthma control.<sup>26</sup> No other study has investigated the performance of ACT in improving patient outcomes. A previous study that investigated the ACT-guided treatment of



Table 3. Secondary analysis (multivariable) (quasi-Poisson regression).

<b>(A) Yearly count of severe exacerbations</b>			
<b>Variable</b>	<b>Coefficient</b>	<b>95% CI</b>	<b>P value</b>
Quality-of-care indicators			
Asthma education	-0.181	-0.267 to -0.095	<0.001
ACT	-0.169	-0.255 to -0.083	<0.001
Spirometry	-0.073	-0.221 to 0.073	0.331
<b>Confounders</b>			
Number of previous exacerbations per year	0.027	0.021 to 0.032	<0.001
Sex: female (reference male)	0.005	-0.064 to 0.074	0.878
Current smoker	0.050	-0.080 to 0.177	0.441
Age	0.007	0.005 to 0.009	<0.001
Cumulative comorbidity index (reference <3)	0.258	0.159 to 0.354	<0.001
BMI	0.010	0.006 to 0.014	<0.001
Type of care (reference PC)			
PC&SC	-0.040	-0.116 to 0.036	0.307
SC	-0.352	-0.519 to -0.190	<0.001
GINA Step 4/5 (reference Step 3)	0.066	-0.003 to 0.135	0.059
Race (reference Chinese)			
Indian	-0.007	-0.109 to 0.092	0.886
Malay	0.040	-0.046 to 0.125	0.354
Others	-0.062	-0.195 to 0.067	0.353

ACT: Asthma Control Test; BMI: body mass index; CI: confidence interval; GINA: Global Initiative for Asthma; PC: primary care; SC: specialist care/acute care

asthma concluded that patients under ACT-guided treatment had better lung function test results and ACT scores as compared to usual care. It differed from our study in that both groups of patients had ACT performed, instead, the physician was blinded from the ACT scores of the usual care group. The previous study did not find any difference in exacerbation rate between the treatment groups.<sup>27</sup> For our study, approximately 74.4% of the patients received asthma education (asthma counselling and WAAP) and approximately 80.2% had ACT recorded. Our analysis showed that the HR for TTSE and number of future exacerbations for patients receiving asthma education or ACT was significantly lower than for patients not receiving these QCI. Asthma education consists of explaining the disease, medications, inhaler technique (use of spacer if required), discussing individualised WAAP—including warning signs for

worsening asthma and subsequent actions (e.g. increasing medication dosage, OCS and visiting the ED). Medication adherence and regular follow-up are encouraged, with the emphasis on inculcating self-management skills.<sup>11</sup> Given the study evidence, there should be continued efforts to offer these QCIs to asthma patients.

Implementing QCIs would entail the hiring and training of certified asthma educators. Time is required to train staff, and the additional time spent in clinics may lead to longer wait times for patients and increase the burden of care by service providers. An alternative to in-person ACT assessment would be teleconsultations, preferably before clinical consultation. ACT or other asthma symptom control tools (e.g. Asthma Control Questionnaire, GINA risk assessment) can be assessed online.<sup>6</sup> For asthma education, studies have shown that encouraging self-education

## (b) Yearly count of severe exacerbations associated with ED or inpatient visits

Variable	Coefficient	95% CI	P value
<b>Quality-of-care indicators</b>			
Asthma education	-0.431	-0.889 to 0.031	0.066
ACT	-0.123	-0.556 to 0.319	0.580
Spirometry	-0.081	-0.621 to 0.445	0.765
<b>Confounders</b>			
Number of previous exacerbations per year	0.026	-0.003 to 0.046	0.035
Gender: female (reference male)	-0.126	-0.512 to 0.252	0.517
Current smoker	0.854	0.324 to 1.342	<0.001
Age	-0.000	-0.012 to 0.012	0.961
Cumulative comorbidity index (reference <3)	1.056	0.670 to 1.435	<0.001
BMI	-0.011	-0.035 to 0.015	0.398
Type of care: SC (reference PC&SC)	0.336	-0.132 to 0.791	0.153
GINA Step 4/5 (reference Step 3)	0.728	0.305 to 1.181	0.001
<b>Race (reference Chinese)</b>			
Indian	0.454	-0.026 to 0.909	0.056
Malay	0.074	-0.475 to 0.585	0.783
Others	0.578	-0.055 to 1.141	0.056

ACT: Asthma Control Test; BMI: body mass index; CI: confidence interval; GINA: Global Initiative for Asthma; PC: primary care; PC&SC: primary and specialist/acute care; SC: specialist/acute care

improves patient outcomes<sup>21</sup> with the WAAP accessible online.<sup>11</sup> These measures would reduce manpower burden, while potentially improving patient outcomes in terms of decreasing future exacerbations. Other implementation barriers towards effective implementation of QCI include language and cultural issues.<sup>28</sup> Language barriers would hinder the effectiveness of asthma education, and translation services incur higher costs.<sup>29</sup> The multiracial and cultural make-up of Singapore also has bearing on the beliefs and perceptions of asthma treatment (e.g. use of Traditional Chinese Medication, steroid phobia). Hence, more time and resources may be required to convince such groups of the effectiveness of evidence-based asthma treatment.<sup>30</sup>

Some significant factors associated with decreased TTSE and increased future exacerbations are age, BMI and smoking. These are risk factors for asthma exacerbations that have been reported in previous studies.<sup>31,32</sup> In terms of type of care, patients attending SC had better outcomes in terms of increased HR of TTSE and decreased future exacerbations, however, studies have shown mixed

results in terms of risk of future exacerbations of patients under SC.<sup>33,34</sup> One possible reason is the increased asthma severity of patients referred to SC, which was adjusted for in our study. The quality of asthma care in the PC setting in Singapore has been improving, with a study demonstrating increased proportions of patients with higher asthma attendance, improved asthma control and updated individualised WAAP, with reduced proportion of usage of rescue therapy and referral to ED.<sup>35</sup> Such improvements in asthma care are encouraging, as improved control for milder asthma severities would slow the progression of such patients to higher GINA steps, potentially reducing the healthcare burden on SC in Singapore. It is also worthy to note that the results point to the significance of association for these interventions. A potential future area of research will be to understand the causal effects of these interventions.

We acknowledge some limitations of the study. We have used medications as a retrospective indicator of asthma severity based on GINA guidelines (see Appendix Table S2).<sup>1</sup> This is then used to define the eligibility criteria. Furthermore,

prescription of medication does not equate to adherence. This has been mitigated in an earlier study which described the development of the SCDM where a sample of patients extracted from the SCDM was manually compared with data displayed on the electronic medical records which is used for routine clinical care. Nonetheless, even with the integrity of prescription data, asthma treatment should also be guided by personalised asthma review with the appropriate adjustments where needed.<sup>36</sup> Consequently, the selection and dosing of medications from retrospective prescribed medication records may not offer a precise definition of the severity of the disease. The use of medications as a proxy classifier for asthma severity could be improved by statistical or machine learning-based methods which can consider multiple factors in defining asthma severity from retrospective data.<sup>37</sup>

Our analysis only considers the first severe exacerbation after the first QCI; this excludes the analysis of subsequent QCIs and exacerbations throughout the treatment course. Ideally, we could analyse both QCIs and exacerbations as time-varying covariates.<sup>38</sup> Furthermore, only 501 out of 3849 patients in the study cohort had documentation of spirometry. Spirometry was carried out mostly in SC; only 3 out of 9 primary care clinics provided it. Hence, the patients with spirometry performed are likely to have more severe or uncontrolled asthma. The delivery of asthma education was also not standardised, with sparse information about the content of the counselling. There was also a lack of data on the referral of smokers to a smoking cessation programme. Given the scope of this study, we did not include patients without any QCI. This allowed TTSE to be defined from the indexed QCI. Consequently, the study cohort may limit the generalisability of the results without considering patients with no QCIs. The refinement of this analysis is an area of future research.

Another limitation in our study is that the cost effectiveness of QCIs was not considered. A recent study found that asthma education is a cost-effective measure in improving patient knowledge and quality of life, leading to daily household savings of around US\$36.<sup>39</sup> No cost effectiveness analyses were found pertaining to ACT assessment. A simulated analysis done for spirometry testing showed that through the correct identification of potentially missed diagnoses, there was a significant gain of quality-adjusted life years over 20 years.<sup>40</sup> The economic evaluation of QCIs is an area of future research, especially with the MOH's initiatives

to implement value-driven care and outcomes in Singapore. This could further inform clinical guidelines and policy decision-making.

## CONCLUSION

Our study suggests that the performance of asthma education and ACT was associated with increased TTSE. This emphasises the importance of ensuring quality care through these QCIs in our clinical practice. Our findings have the potential to inform clinical guidelines and policy decision-making.

## Competing interest

MSK reports grant support from Astra-Zeneca, outside the submitted work. The SCDM used in this study is funded by the GlaxoSmithKline plc (study number PRJ3057). Apart from these, all authors declare that they have no other competing interest.

## Ethics approval

Ethics board approval was obtained as part of the SDG-CARE collaboration, prior to developing the SCDM. Informed consent has been waived by SingHealth Centralised Institutional Review Board (Ref No. 2017/2950), as this study is based on deidentified patient data.

## Availability of data and materials

Data from the SingHealth COPD and Asthma Data Mart (SCDM) may be made available on reasonable request. The process for external parties to obtain the data are outlined in Reference 13.

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