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Assessment of asthma severity according to treatment steps in Japanese pediatric patients: a descriptive cross-sectional study using an administrative claims database

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ABSTRACT

Objectives: Japan has one of the highest asthma prevalence rates in Asia; however, there is a lack of epidemiological studies on asthma among children in Japan. This study aimed to describe the severity of asthma and the prescription patterns for its treatment among pediatric patients, by using a large-scale claims database.

Methods: The analysis datasets were extracted from the JMDC database for the period of April 1, 2009 to March 30, 2015; included records were restricted to patients between 2 and 15 years of age. The Japanese Pediatric Guidelines for the treatment and management of asthma (JPGL) steps were used as a proxy for asthma treatment and severity. We also described the characteristics of asthma in children by stratifying the prevalence and incidence cohorts by index years.

Results: In the prevalence cohort (56% male), from 2010 to 2014, approximately 80–90% of the children received step 1 or 2 treatment, with the remainder receiving step 3 or 4 treatment, as defined by the JPGL. The majority (approximately 90%) of patients visited clinics for asthma treatment, while a minority visited hospitals.

Conclusions: Our study showed the severity of asthma among Japanese pediatric patients, as well as their demographic characteristics, using a large-scale claims database. The majority of pediatric asthma patients received treatment for mild-to-moderate asthma, while less than 10% received treatment for severe asthma.

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Introduction

Asthma is the most prevalent chronic disease worldwide (1). The World Health Organization estimates that approximately 235 million individuals have asthma, and Japan has one of the highest asthma prevalence rates in Asia (2,3). The absolute asthma prevalence reported differs depending on the survey. Nevertheless, a general increase in asthma prevalence among school children in Japan was observed from 1980 to 2000, followed by a plateau between 2005 and 2008. A decrease was subsequently observed in 2015 (4,5). Asthma imposes a major burden on healthcare resources in Japan and other developed countries. One systematic review reported that the economic costs associated with asthma are one of the highest

among chronic diseases due to the high level of healthcare utilization associated with it (6).

Previous studies have identified a group of pediatric asthma patients who have suboptimal disease control, despite the use of high-dose inhaled corticosteroids and maximal add-on therapies (7). While severe asthma is estimated to account for only 4.5% of asthma cases among children, it represents the major source of asthma-related costs (8). Therefore, it is important to investigate the prevalence, incidence, and severity of asthma among children, and its associated healthcare utilization.

Epidemiological studies on children with asthma in Japan are limited. Nishima et al. (4) conducted a nationwide questionnaire survey for the prevalence of pediatric asthma in Japan, and Ebisawa et al. (9)

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reported the prevalence of pediatric allergy, including food allergy. Hamada et al. (10) used a claims database to examine the use of asthma medication among children in Japan. However, to the best of our knowledge, no prior studies have used claims databases to systematically examine the burden of asthma in the Japanese pediatric population. Therefore, the purpose of our study was to examine the severity of asthma according to treatment steps among pediatric patients, using a large-scale claims database in Japan. We describe the demographic and clinical characteristics of Japanese pediatric asthma patients, based on the Japanese Pediatric Guidelines for the treatment and management of asthma (JPGL) (11).

Methods

Study design and participants

This was a descriptive cross-sectional study using an administrative claims database in Japan. Participant information was obtained from a commercial claims database maintained by the JMDC Co., Ltd (Tokyo, Japan) (12). The database consists of insurance eligibility data and medical and pharmacy claims from approximately 5.6 million beneficiaries (corporate employees and their dependent family members), as of 2018 (13); it represents 4.7% of the total Japanese population. The analysis datasets were extracted from the JMDC database between April 1, 2009 and March 30, 2015 and included patients aged 2–15 years old. Asthma patients were defined as follows: children aged 2–15 years on the index date (April 1st) of each year, with a diagnosis of asthma at least twice during the study period (with at least 30 days between the two recorded diagnoses), according to the 10th Revision of the International Classification of Diseases (ICD-10: J45.x–J46.x). Children were categorized into subgroups of 2–5 and 6–15 years based on the JPGL (11). Patients who had an asthma diagnosis in the given year and a recorded asthma diagnosis in the previous year were included in the prevalence cohort (14,15). Patients who had an asthma diagnosis in the given year, but had no recorded asthma diagnosis in the previous year, were included in the incidence cohort for that year. [Supplementary Figure 1](#) shows how each of the yearly cohorts was identified.

Asthma severity according to the JPGL

The treatment step, as defined by the JPGL, was used as a proxy for asthma severity. As an algorithm to identify the treatment step, patients were considered

to have entered a step from the date of prescription of the relevant medication. Meeting any of the inclusion and exclusion criteria items in each row ([Supplementary Tables 1 and 2](#)) classified patients into the relevant treatment step. If a patient received more than two treatment steps in 1 year, the treatment step for that year was defined as the most severe step.

Characteristics of children with asthma

We described the characteristics of children with asthma in the prevalence and incidence cohorts, stratified by index years. These included sex, age at index date, institution type (clinic, university hospital, public hospital, and other hospital), department (allergology, general internal medicine, pediatrics, respiratory, and others), comorbidities (anaphylaxis, anxiety or depression, atopic dermatitis, cardiac diseases, food allergy, gastroesophageal reflux disease, rhinitis/rhinosinusitis, sleep apnea), and prior asthma medication used in the pre-index period (short-acting beta-agonist [SABA], inhaled corticosteroid [ICS], LABA, ICS/LABA, leukotriene receptor antagonist [LTRA], and theophylline).

Statistical analysis

Treatment steps, based on the JPGL, and characteristics of children with asthma were summarized using descriptive statistics (number and percentage). All statistical analyses were performed using STATA version 13.0 (StataCorp LP, College Station, TX).

Ethical considerations

This study protocol was approved by the ethics committee of the Kyoto University Graduate School and the Faculty of Medicine (R1035). The need to obtain patient consent was waived due to the use of anonymized data.

Results

[Tables 1 and 2](#) show the demographics and clinical characteristics of pediatric asthma patients in the prevalence and incidence cohorts, respectively. In the prevalence cohort ([Table 1](#)), we included 31,004 children in 2010, 50,392 children in 2011, 52,989 children in 2012, 59,923 children in 2013, and 99,923 children in 2014. Over half (56%) were male. Most patients visited a clinic (89%) for asthma treatment. A minority visited a public or other hospital (10%) or a university

Table 1. Demographics and clinical characteristics of pediatric asthma patients at index date in the prevalence cohort.

Characteristics	Year: 2010 N (%)	Year: 2011 N (%)	Year: 2012 N (%)	Year: 2013 N (%)	Year: 2014 N (%)
n	31,004	50,392	52,989	59,923	99,923
Sex					
Male	17,522 (56.5)	28,319 (56.2)	29,705 (56.1)	33,590 (56.1)	56,058 (56.1)
Female	13,482 (43.5)	22,073 (43.8)	23,284 (43.9)	26,333 (43.9)	43,865 (43.9)
Age (years) at index					
Mean (SD)	6.77 (3.31)	6.82 (3.33)	7.02 (3.43)	7.05 (3.46)	6.97 (3.46)
Age categories					
2 ≤ age < 6	15,135 (48.8)	24,094 (47.8)	24,452 (46.1)	27,577 (46.0)	47,149 (47.2)
6 ≤ age < 12	13,129 (42.4)	21,647 (43.0)	22,858 (43.1)	25,596 (42.7)	41,727 (41.8)
12 ≤ age < 16	2740 (8.8)	4651 (9.2)	5679 (10.7)	6750 (11.3)	11,047 (11.1)
Institution type					
Clinic	27,537 (88.8)	45,132 (89.6)	47,381 (89.4)	53,452 (89.2)	89,521 (89.6)
University hospital	347 (1.1)	454 (0.9)	504 (1.0)	516 (0.9)	904 (0.9)
Public hospital	1179 (3.8)	1796 (3.6)	1951 (3.7)	2333 (3.9)	3688 (3.7)
Other hospital	1941 (6.3)	3010 (6.0)	3153 (6.0)	3622 (6.0)	5810 (5.8)
Department					
Allergology	0 (0.0)	2 (0.0)	0 (0.0)	0	1 (0.0)
General internal medicine	12,353 (39.5)	19,042 (37.8)	19,610 (37.0)	21,766 (36.3)	34,066 (34.1)
Pediatrics	11,378 (36.7)	18,029 (35.8)	19,219 (36.3)	22,009 (36.7)	37,921 (38.0)
Respiratory	175 (0.6)	264 (0.5)	275 (0.5)	298 (0.5)	666 (0.7)
Others	7098 (22.9)	13,055 (25.9)	13,885 (26.2)	15,850 (26.5)	27,269 (27.3)
Comorbidities					
Anaphylaxis	69 (0.2)	144 (0.3)	213 (0.4)	355 (0.6)	797 (0.8)
Anxiety or depression	115 (0.4)	183 (0.4)	259 (0.5)	336 (0.6)	551 (0.6)
Atopic dermatitis	7348 (23.7)	12,342 (24.5)	13,270 (25.0)	14,575 (24.3)	24,211 (24.2)
Cardiac diseases	409 (1.3)	694 (1.4)	823 (1.6)	972 (1.6)	1713 (1.7)
Food allergy	1343 (4.3)	2355 (4.7)	2725 (5.1)	3436 (5.7)	6754 (6.8)
Gastroesophageal reflux disease	72 (0.2)	133 (0.3)	167 (0.3)	195 (0.3)	391 (0.4)
Rhinitis/rhinosinusitis	1509 (4.9)	2358 (4.7)	2610 (4.9)	2875 (4.8)	4777 (4.8)
Sleep apnea	125 (0.4)	244 (0.5)	297 (0.6)	327 (0.6)	561 (0.6)
Prior asthma medication in pre-index period					
SABA	12,184 (32.3)	19,007 (29.9)	20,496 (28.6)	20,133 (28.1)	28,617 (26.6)
ICS	5009 (13.3)	7655 (12.1)	8529 (11.9)	8407 (11.7)	11,850 (11.0)
LABA	12,669 (33.6)	20,031 (31.5)	21,312 (29.8)	20,225 (28.2)	28,754 (26.7)
ICS/LABA (fixed dose combination)	1863 (4.9)	3332 (5.3)	4433 (6.2)	4554 (6.4)	6872 (6.4)
LTRA	27,191 (72.1)	46,499 (73.2)	53,779 (75.1)	54,074 (75.5)	82,691 (76.8)
Theophylline	4404 (11.7)	5446 (8.6)	5021 (7.0)	3969 (5.5)	5084 (4.7)

SABA, short-acting beta-agonists; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; LTRA, leukotriene receptor antagonist; DSCG, disodium cromoglycate.

hospital (1%). Approximately 34%–39% visited a general internal medicine department, and a similar proportion (36%) visited a pediatric department. Less than 1% visited a respiratory department, and the remaining children visited other departments. A quarter (25%) of the children had comorbid atopic dermatitis. Approximately 4%–6% and 5% of children had food allergy and rhinitis (or rhinosinusitis), respectively.

In the incidence cohort (Table 2), we included 15,221 children in 2010, 22,737 children in 2011, 22,527 children in 2012, 23,304 children in 2013, and 42,214 children in 2014. Compared with the prevalence cohort, there were almost equal numbers of boys and girls (males: 51%–52% in each year's incidence cohort). The percentage of clinic visits was somewhat higher (approximately 92%) than that in the prevalence cohort. The percentage of general internal medicine visits in the incidence cohort in 2010 and 2011 was slightly higher (40% and 41%, respectively) than that of the prevalence cohort, but was similar in 2013 (38.5%) to that of the

prevalence cohort. Furthermore, comorbidities, including atopic dermatitis (15%–16%), food allergy (2%–3%), and rhinitis or rhinosinusitis (3%), in the incidence cohort were less frequent than those in the prevalence cohort.

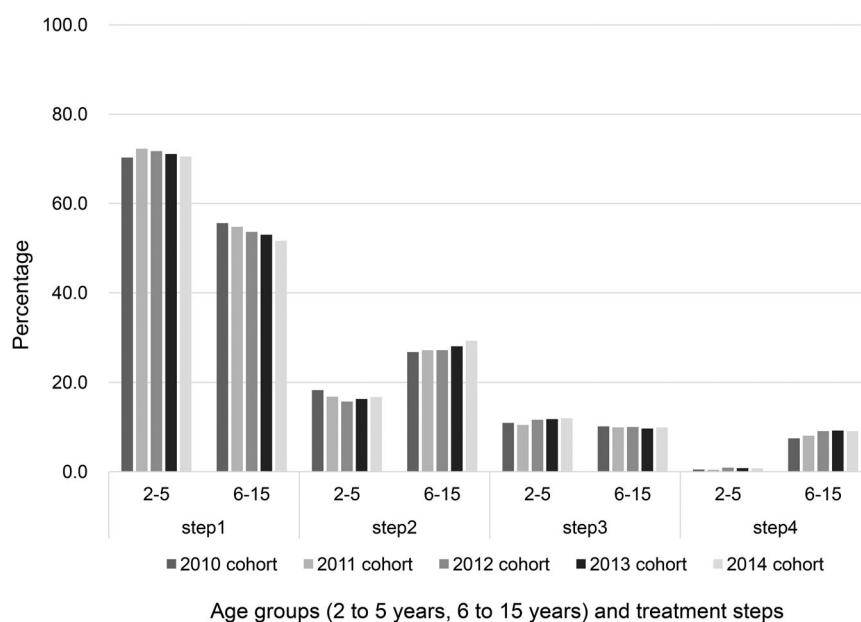
Figure 1 shows the yearly asthma severity in the prevalence cohort. In terms of treatment steps among those aged 2–5 years in the prevalence cohort, 70% received step 1 treatment, while less than 20% received step 2 treatment. Step 3 and 4 treatments were received by 10% and less than 1% of children, respectively. Among those aged 6–15 years, approximately 50% received step 1 treatment, and less than 30% received step 2 treatment. Step 3 and 4 treatments were received by approximately 10% and less than 10% of children, respectively.

Among children aged 2–5 years in the incidence cohort (Figure 2), more than 85% received step 1 treatment, and approximately 7% received step 2 treatment. Step 3 and 4 treatments were received by approximately 6% and less than 1% of the children, respectively. Among children aged 6–15 years, three-

Table 2. Demographics and clinical characteristics of pediatric asthma patients at index date in the incidence cohort.

Characteristics	Year: 2010 N (%)	Year: 2011 N (%)	Year: 2012 N (%)	Year: 2013 N (%)	Year: 2014 N (%)
n	15,221	22,737	22,527	23,304	42,214
Sex					
Male	7990 (52.5)	11,678 (51.4)	11,571 (51.4)	12,057 (51.7)	21,708 (51.4)
Female	7231 (47.5)	11,059 (48.6)	10,956 (48.6)	11,247 (48.3)	20,506 (48.6)
Age (years) at index					
Mean	7.58 (3.81)	7.89 (3.86)	7.95 (3.89)	7.81 (3.90)	8.05 (3.93)
Age categories					
$2 \leq \text{age} < 6$	6489 (42.6)	8875 (39.0)	8748 (38.8)	9500 (40.8)	16,024 (38.0)
$6 \leq \text{age} < 12$	6278 (41.3)	9722 (42.8)	9455 (42.0)	9515 (40.8)	17,733 (42.0)
$12 \leq \text{age} < 16$	2454 (16.1)	4140 (18.2)	4324 (19.2)	4289 (18.4)	8457 (20.0)
Institution type					
Clinic	13,931 (91.5)	20,794 (91.5)	20,616 (91.5)	21,454 (92.1)	39,154 (92.8)
University hospital	88 (0.56)	108 (0.5)	108 (0.5)	92 (0.4)	151 (0.4)
Public hospital	384 (2.5)	590 (2.6)	563 (2.5)	553 (2.4)	904 (2.1)
Other hospital	818 (5.4)	1245 (5.5)	1240 (5.5)	1205 (5.2)	2005 (4.8)
Department					
Allergology	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)
General internal medicine	6298 (41.4)	9338 (41.1)	9063 (40.2)	8964 (38.5)	15,527 (36.8)
Pediatrics	4720 (31.0)	6801 (29.9)	6945 (30.8)	7374 (31.6)	12,830 (30.4)
Respiratory	50 (0.3)	90 (0.4)	88 (0.4)	94 (0.4)	183 (0.4)
Others	4153 (27.3)	6508 (28.6)	6431 (28.6)	6872 (29.5)	13,673 (32.4)
Comorbidities					
Anaphylaxis	14 (0.1)	17 (0.1)	37 (0.2)	39 (0.2)	85 (0.2)
Anxiety or depression	43 (0.3)	68 (0.3)	60 (0.3)	65 (0.3)	147 (0.4)
Atopic dermatitis	2270 (14.9)	3639 (16.0)	3506 (15.6)	3548 (15.2)	6330 (15.0)
Cardiac diseases	147 (1.0)	181 (0.8)	242 (1.1)	272 (1.2)	492 (1.2)
Food allergy	307 (2.0)	449 (2.0)	528 (2.3)	696 (3.0)	1317 (3.1)
Gastroesophageal reflux disease (GERD)	9 (0.1)	28 (0.1)	27 (0.1)	44 (0.2)	85 (0.2)
Rhinitis/rhinosinusitis	537 (3.5)	750 (3.3)	722 (3.2)	717 (3.1)	1231 (2.9)
Sleep apnea	26 (0.2)	54 (0.2)	44 (0.2)	55 (0.2)	95 (0.2)
Prior asthma medication in pre-index period					
SABA	444 (2.9)	698 (3.1)	633 (2.8)	611 (2.6)	1017 (2.4)
ICS	13 (0.09)	22 (0.10)	9 (0.04)	7 (0.03)	9 (0.02)
LABA	603 (4.0)	883 (3.9)	847 (3.8)	744 (3.2)	1018 (2.4)
ICS/LABA (fixed dose combination)	2 (0.01)	15 (0.07)	3 (0.01)	1 (0.00)	1 (0.00)
LTRA	689 (4.5)	1207 (5.3)	1317 (5.9)	2106 (9.0)	3874 (9.2)
Theophylline	47 (0.3)	62 (0.3)	40 (0.2)	25 (0.1)	50 (0.1)

SABA, short-acting beta-agonists; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; LTRA, leukotriene receptor antagonist; DSCG, disodium cromoglycate.

**Figure 1.** Yearly asthma severity in the prevalence cohort.

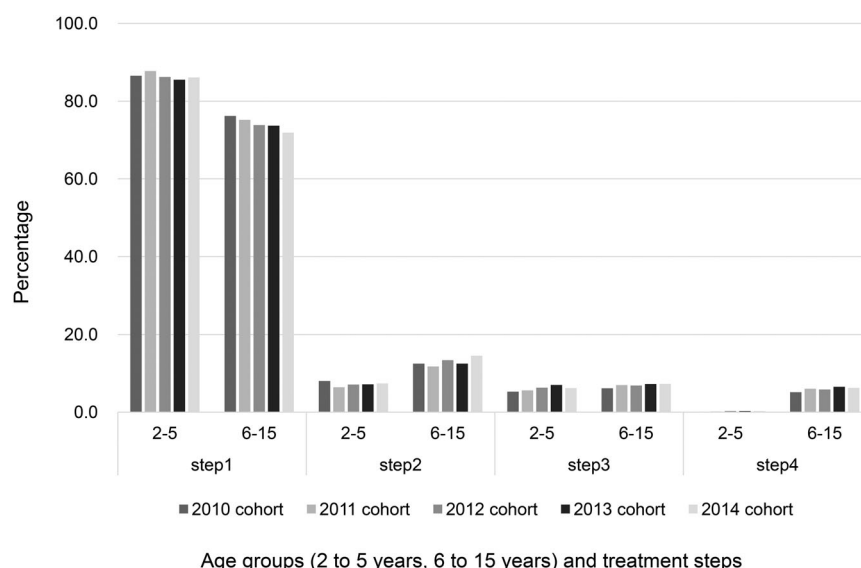


Figure 2. Yearly asthma severity in the incidence cohort.

quarters (75%) received step 1 treatment, and just over a tenth (12%) received step 2 treatment. Step 3 and 4 treatments were received by 7% and 6% of children, respectively.

Discussion

Our study described the severity of asthma among Japanese pediatric patients and their clinical characteristics, based on annual prevalence and incidence cohorts from 2010 to 2014. The results provide a unique insight into the current status of pediatric asthma patients in Japan.

Approximately 80%–90% of children with asthma received step 1 or 2 treatments, as defined by the JPGL. Furthermore, there was a trend for younger patients to have received lower treatment steps. Newly diagnosed patients started treatment at a lower step than patients who had already been diagnosed. In contrast, a minority of children aged 2–5 years (10%) or 6–15 years (20%) received step 3 or 4 treatments in the prevalence cohort. Although data regarding the cost of severe asthma in children are limited, previous reports among adult populations have shown that asthma-related costs are associated with asthma severity (16). These costs include treatment costs, intangible quality-of-life costs, and the economic burden of asthma on society (17,18).

Boys were more affected by asthma. This trend was in accordance with previous studies, which have consistently reported a higher prevalence of wheezing and asthma among boys (19,20). Nearly half of the children in our study were aged 2–5 years, and more than 40% were 6–11 years old. Although the percentage of

those aged 12–15 years was relatively lower than the younger age groups, these children required treatment for more severe asthma. Many children experience severe asthma as they reach school age (21), and this is often characterized by poor symptom control, despite high-dose ICS treatment (22). Thus, further studies investigating the control status of severe asthma in children are required.

Asthma is characterized by various phenotypes, which are related to the age of onset, comorbidities, and severity (23). Among children with asthma aged 0–17 years, based on the National Health Interview Survey in the United States, approximately 25% had skin allergy and 10% had food allergy (24). Our study agreed with these results; 25% of children had atopic dermatitis. However, fewer of our participants had food allergies (4%–6%). It has also been reported that these comorbidities are more commonly found among younger age groups (25), and that food allergy is associated with an increased risk of asthma (26). Our study did not consider whether age may be associated with the incidence of comorbidities, and therefore, further studies related to age and asthma comorbidity may also be needed.

A strength of this study was its use of a large-scale claims database, which has less information bias than self-administered questionnaire surveys. To the best of our knowledge, no previous study has analyzed the prevalence, incidence, and severity of asthma in pediatric patients in Japan using a large-scale claims database. Furthermore, we described the demographic and clinical characteristics of Japanese pediatric patients with asthma based on JPNG steps and drug-use patterns, which represent the current treatment status of pediatric asthma in Japan.

There were several study limitations. First, our study used a claims database and specified the use of treatment steps, which were only based on drug prescription records. Claims data do not document patient symptoms; therefore, our categorization of asthma treatment steps may contain misclassifications. This may also apply to asthma patients in whom accurate diagnosis may not have been possible; for example, cases of mild asthma that cannot be strictly separated from wheezing (27). Furthermore, we only considered treatment steps as a proxy for asthma severity. However, overestimated or underestimated severity may occur for it. For a better assessment of asthma severity, symptoms, lung function, and patients' asthma history, such as hospitalization and asthma attacks, should also be included (28). Second, we defined treatment steps for each participant as the most severe treatment step in a given year to avoid duplicate counting. Nevertheless, asthma treatment steps often move from one step to another, in accordance with the severity of the patient's condition. Some asthma treatments start with higher steps, followed by lower ones when the asthma attack is controlled. Similarly, some asthma treatments start with lower steps, but then step up when the asthma attack is not well controlled. Thus, our results may be biased toward more severe treatment in asthma patients. Third, to standardize patient evaluation, we only used the previous year to identify incident cases, because the follow-up period of each child in the claims database was different. This method may have caused misclassification related to patient history and errors in identification of incident cases. Fourth, our study did not consider the environmental or socioeconomic status of the patients, due to the limited scope of the information documented in the database (29,30). These factors have been reported to affect the risk of developing asthma, and therefore, analysis based on stratification by these factors could be more informative for the treatment of pediatric asthma. Finally, our study only showed the treatment steps during the target periods, and we could not confirm whether each patient's asthma was well controlled. Ascertaining whether asthma is well controlled or not is important for asthma studies, and information regarding the need for acute care or oral steroids could help to show this. Therefore, the control status and factors associated with exacerbation should be considered in future studies.

Conclusion

Our study showed the severity of asthma among pediatric patients using a large-scale claims database.

Furthermore, we described the demographic and clinical characteristics of Japanese pediatric asthma patients, based on JPNG treatment, and their drug-use patterns. Our results demonstrate the current status of pediatric asthma treatment in Japan and could provide a basis for comparison with other countries.

Declaration of interest

Hajime Yoshisue and Masanari Kozawa are company employees of Novartis Pharma K.K. Koji Kawakami received research funds from Sumitomo Dainippon Pharma Co., Ltd., Stella Pharma Corporation, CMIC Co., Ltd., Suntory Beverage & Food Ltd., Novartis Pharma K.K., and Bayer Yakunin Ltd.; consulting fees or speaker honoraria from Kyowa Hakko Kirin Co., Ltd., Kaken Pharmaceutical Co., Ltd., Astellas Pharma Inc., Mitsubishi Tanabe Pharma Co., AbbVie Inc., Santen Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Takeda Pharmaceutical Co., Ltd., Boehringer Ingelheim Japan, Inc., JMDC Inc., and Agree, Inc.; and is a stockholder of Real World Data Co., Ltd. Shiro Tanaka has received lecture fees from Bayer Yakuhin Ltd., Amgen Astellas BioPharma K.K., and Research Institute of Healthcare Data Science; a consultation fee from Boehringer Ingelheim Japan, Inc.; an outsourcing fee from the Public Health Research Foundation; and grants from the Japan Agency for Medical Research and Development, the Japanese Ministry of Health Labor and Welfare, and the Japanese Ministry of Education, Science, and Technology. He engaged in a research project by the Japan Agency for Medical Research and Development. Yuichi Adachi has received honoraria from GSK, MSD, and Kyorin Pharmaceutical Co., Ltd. The other author has no conflicts of interest to declare.

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Supplementary Table 1 Inclusion and exclusion criteria to identify treatment steps of JPGL for children 2–5 years old

Step 1	Inclusion	1. SABA prescription 2. LTRA prescription < 28 days of continuous use 3. DSCG prescription < 28 days of continuous use 4. LTRA and DSCG prescription < 28 days of continuous use
	Exclusion	1. ICS 2. ICS/LABA 3. LTRA prescription ≥ 28 days of continuous use 4. DSCG prescription ≥ 28 days of continuous use 5. OCS prescription ≥ 28 days of continuous use
Step 2	Inclusion	1. Low-dose ICS 2. LTRA prescription ≥ 28 days of continuous use 3. DSCG prescription ≥ 28 days of continuous use
	Exclusion	1. Medium/High-dose ICS 2. ICS/LABA 3. OCS prescription ≥ 28 days of continuous use
Step 3	Inclusion	1. Medium-dose ICS 2. Low-dose ICS/LABA
	Exclusion	1. High-dose ICS 2. Medium/More than medium-dose ICS/LABA 3. OCS prescription ≥ 28 days of continuous use
Step 4	Inclusion	1. High-dose ICS 2. Medium/More than medium-dose ICS/LABA 3. OCS prescription ≥ 28 days of continuous use
	Exclusion	1. OCS prescription ≥ 28 days of continuous use without concomitant ICS or ICS/LABA
~~Exploratory: LABA- monotherapy~~	~~Inclusion~~	~~1. LABA~~
	~~Exclusion~~	~~1. ICS~~ ~~2. ICS/LABA~~ ~~3. LTRA~~ ~~4. DSCG~~

SABA: Short-acting beta-agonists; LTRA: Leukotriene receptor antagonist; DSCG: Disodium cromoglycate; ICS: Inhaled corticosteroids; OCS: Oral systemic corticosteroids; LABA: Long-acting beta-agonists; JPGL: Japanese guideline.

Supplementary Table 2 Inclusion and exclusion criteria to identify treatment steps of JPGL for children 6–15 years old

Step 1	Inclusion	1. SABA prescription 2. LTRA prescription < 28 days of continuous use 3. DSCG prescription < 28 days of continuous use 4. LTRA and DSCG prescription < 28 days of continuous use
	Exclusion	1. ICS 2. ICS/LABA 3. LTRA prescription ≥ 28 days of continuous use 4. DSCG prescription ≥ 28 days of continuous use 5. OCS prescription ≥ 28 days of continuous use 6. Omalizumab
Step 2	Inclusion	1. Low-dose ICS 2. LTRA prescription ≥ 28 days of continuous use 3. DSCG prescription ≥ 28 days of continuous use
	Exclusion	1. Medium/High-dose ICS 2. ICS/LABA 3. OCS prescription ≥ 28 days of continuous use 4. Omalizumab
Step 3	Inclusion	1. Medium-dose ICS 2. Low-dose ICS/LABA
	Exclusion	1. High-dose ICS 2. Medium/ More than medium-dose ICS/LABA 3. OCS prescription ≥ 28 days of continuous use 4. Omalizumab
Step 4	Inclusion	1. High-dose ICS 2. Medium/More than medium-dose ICS/LABA 3. OCS prescription ≥ 28 days of continuous use 4. Omalizumab
	Exclusion	1. OCS prescription ≥ 28 days of continuous use without concomitant ICS or ICS/LABA
Exploratory :- LABA- monotherapy	Inclusion	~~1. LABA~~
	Exclusion	~~1. ICS~~ ~~2. ICS/LABA~~ ~~3. LTRA~~

		4. ~~DSCG~~
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SABA: Short-acting beta-agonists; LTRA: Leukotriene receptor antagonist; DSCG: Disodium cromoglycate; ICS: Inhaled corticosteroids; OCS: Oral systemic corticosteroids; LABA: Long-acting beta-agonists; JPGL: Japanese guideline.

