

ORIGINAL ARTICLE

EPIDEMIOLOGY AND GENETICS

Healthcare use and prescription patterns associated with adult asthma in Korea: analysis of the NHI claims database

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asthma; health care; insurance claim review; prescriptions; prevalence.

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Abstract

Background: National Health Insurance (NHI) claim records could provide valuable data for epidemiological studies of asthma in Korea. The aim of this study is to estimate the prevalence of adult asthma and to investigate asthma-related healthcare use and prescription patterns in Korea over 5 years.

Methods: National Health Insurance claim records from January 1, 2006 to December 31, 2010 were analyzed in a retrospective, population-based study. Outcome measures included asthma prevalence, healthcare use, and prescription patterns over time, by type of hospital, and by medical specialty. Additionally, we assessed differences in healthcare use between newly diagnosed and previously diagnosed patients in 2009.

Results: Over 5 years, the prevalence of asthma among Korean adults increased from 4944 to 5707 cases per 100 000 population (from 3760 to 4445 in men and from 6108 to 6951 in women). Asthma-related outpatient visits decreased from 4.82 ± 8.02 to 3.44 ± 5.50 . Approximately 3% of all patients were hospitalized and 2.4% received asthma-related emergency treatment each year. Pulmonary function tests were performed in 10–11% of patients an average of 1.3 times per year. Newly diagnosed patients experienced fewer asthma-related hospitalizations (1.78% vs 4.35%) and emergency department visits (0.80% vs 2.11%) than the previously diagnosed group. Prescriptions of inhaled corticosteroids-based inhalers were maintained with about 20% of average of all types of hospitals.

Conclusions: The prevalence of asthma in Korea has increased over a recent 5-year period, and asthma is still suboptimally controlled. Public health strategies are needed to improve the management of asthma in adults.

Large-scale longitudinal studies are the best available tools for improving our understanding of asthma as a public health issue. While several large cohort studies have been conducted, the high proportion of patients lost to follow-up has been an important limitation. Another drawback has been the inclusion of only those patients who received treatment at specialist hospitals. By contrast, health insurance (HI) claims records combine the advantages of long follow-up with the absence of selection bias. Claims data can be analyzed to measure the prevalence of diseases, patterns of

healthcare use, clinical outcomes, accessibility of health services, duration of treatment, cost of care, and adherence to good practice guidelines (1–9). The findings can then be used to modify the guidelines and to improve the management of diseases.

In Korea, the National Health Insurance (NHI) system includes the HI system financed by mandatory contributions and medical aid (MA), a social assistance scheme for the very poor, which is financed by general taxation. Approximately 96.7% of all residents in the country are covered by HI, and

the rest of the population, who do not earn an income above the poverty level and cannot afford to contribute to HI system, are covered by MA (the data from the census 2009 in Korea) (10). The NHI claims database includes information about diagnostics, treatments, health service providers, and associated costs (11) that could be used to study the impact of asthma on public health. However, access to the NHI data of all Korean patients is restricted, and only a few studies have been carried out to date (4, 7, 12).

The aim of our study was to estimate the prevalence of adult asthma in Korea and to investigate the patterns of asthma-related healthcare use and drug prescription in a recent 5-year period, by analyzing the NHI claims records of all adult asthma patients in Korea.

Methods

Study design and subjects

Using claims data in the complete NHI database, we conducted a retrospective, population-based study to investigate trends associated with asthma healthcare use between January 1, 2006 and December 31, 2010. We included all patients who met the following criteria throughout the entire study period: (i) aged 18 years or older; (ii) diagnosed with asthma according to the 10th Revision of the International Classification of Diseases (ICD-10, and J45.x–J46.x for the principal and additional diagnoses), and (iii) prescribed at least one asthma-related medication (inhaled, oral, or injected) or asthma-related test. Asthma-related medications included inhaled corticosteroids

Table 1 Demographic data and asthma-related healthcare use in Korea

	2006		2007		2008		2009		2010	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Total N. of population included in the NHI database (Age ≥18)	38 288 695		38 849 158		39 349 430		39 889 189		40 435 086	
Male	18 974 476		19 258 584		19 518 883		19 795 167		20 075 632	
Female	19 314 219		19 590 571		19 830 547		20 094 022		20 359 454	
Total subjects	1 892 953	100	1 956 491	100	2 037 322	100	2 160 255	100	2 307 581	100
Gender										
Male	713 146	37.7	744 034	38.0	779 733	38.3	824 460	38.2	892 309	38.7
Female	1 179 807	62.3	1 212 457	62.0	1 257 589	61.7	1335 795	61.8	1 415 272	61.3
Age (Mean ± SD)	51.69 ± 18.70		51.82 ± 20.30		52.86 ± 30.33		51.95 ± 19.94		51.81 ± 19.52	
Insurance type										
Health insurance	1 755 826	92.8	1 817 128	92.9	1 892 781	92.9	2 014 674	93.3	2 162 462	93.7
Medical aid	137 127	7.2	139 363	7.1	144 541	7.1	145 581	6.7	145 119	6.3
Outpatient visits										
No	35 585	1.9	40 373	2.1	46 058	2.3	47 632	2.2	51 558	2.2
Yes	1 857 368	98.1	1 916 118	97.9	1 991 264	97.7	2 112 623	97.8	2 256 023	97.8
Mean ± SD†	4.82 ± 8.02		4.17 ± 6.71		3.62 ± 5.90		3.55 ± 5.73		3.44 ± 5.50	
Hospitalizations										
No	1 838 326	97.1	1 896 721	96.9	1 971 858	96.8	2 094 510	97.0	2 237 816	97.0
Yes	54 627	2.9	59 770	3.1	65 464	3.2	65 745	3.0	69 765	3.0
Mean ± SD†	1.6 ± 1.38		1.62 ± 1.44		1.57 ± 1.3		1.57 ± 1.34		1.57 ± 1.32	
Hospitalization days (Mean ± SD)†										
Per person per year	21.36 ± 31.04		21.71 ± 32.76		20.42 ± 27.75		19.66 ± 26.95		19.26 ± 25.90	
Per each admission	13.34 ± 20.75		13.38 ± 21.92		13.03 ± 18.45		12.54 ± 17.98		12.30 ± 17.13	
ICU hospitalizations										
No	1 884 200	99.54	1 947 100	99.52	2 027 305	99.51	2 150 661	99.56	2 297 479	99.56
Yes	8 753	0.46	9 391	0.48	10 017	0.49	9 594	0.44	10 102	0.44
Mean ± SD†	1.00 ± 0.0		1.00 ± 0.0		1.00 ± 0.0		1.00 ± 0.0		1.00 ± 0.0	
Emergency department visits*										
No	1 850 196	97.7	1 825 258	97.6	1 988 450	97.6	2 109 073	97.6	2 253 988	97.7
Yes	42 757	2.3	45 068	2.4	48 872	2.4	51 182	2.4	53 593	2.3
Mean ± SD†	1.43 ± 1.12		1.48 ± 0.95		1.51 ± 0.81		1.43 ± 1.41		1.47 ± 1.06	
Pulmonary function tests										
No	1 685 933	89.1	1 737 171	88.8	1 815 571	89.1	1 926 474	89.2	2 077 226	90.0
Yes	207 020	10.9	219 320	11.2	221 751	10.9	233 781	10.8	230 355	10.0
Mean ± SD†	1.28 ± 0.99		1.28 ± 0.99		1.28 ± 0.99		1.27 ± 0.91		1.27 ± 0.89	

*The number of patients who have been treated in an emergency department due to asthma exacerbation without admission at least once.

†The mean values of subjects who experienced at least one event.

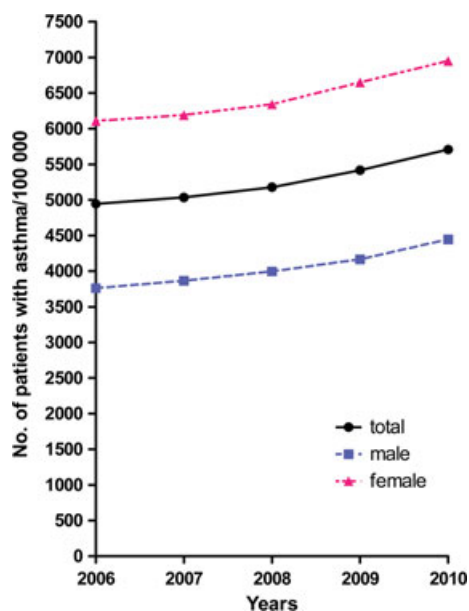


Figure 1 Prevalence of asthma in Korea.

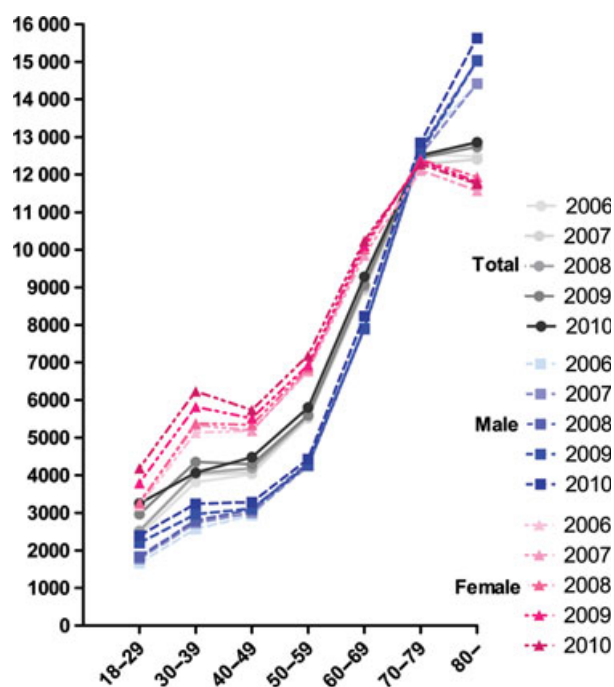


Figure 2 Prevalence of asthma in Korea by age.

(ICS), long-acting β 2-agonists (LABA), ICS and LABA combined in a single inhaler (ICS/LABA), oral leukotriene antagonists (LTRA), short-acting β 2-agonists (SABA), xanthine derivatives, and systemic corticosteroids. Asthma-related tests included spirometry, with or without bronchodilator response, and the bronchial provocation test.

Data sources and ethical considerations

The NHI claims data were provided by the Korean Health Insurance Review and Assessment Service (HIRA), an independent body established to review the claims data and assess the quality of health care in Korea. As NHI cover is mandatory, the HIRA-run database contains information concerning all submitted claims and prescriptions for entire beneficiaries of HI and MA. This study was approved by the Ethics Committee of the National Evidence-Based Healthcare Collaborating Agency (NECA).

Outcome measures and statistical analysis

See Data S1 (Supporting Information).

Results

Asthma prevalence

In 2006, the number of asthma patients on record was 1 892 953, and it increased steadily to 2 307 581 in 2010 (Table 1). An increase in prevalence throughout the study was noted in both men and women. In 2006, 4944 patients per 100 000 adults (3760 men and 6108 women) had asthma, compared to 5707 patients (4445 men and 6951 women) in 2010 (Fig. 1; Table S1). The patients' mean age was 51 years, and asthma prevalence increased remarkably with age. The highest prevalence was in the age group ≥ 70 (12 280–12 860 per 100 000 adults), while the lowest was in individuals between the ages of 18 and 29 years (2401–3250 per 100 000). Asthma affected 1.3–2 times more women than men under the age of 70, but there was little difference between the sexes in the 70–79 age group. By contrast, men over 80 were 1.2–1.3 times more likely to have asthma than women of the same age. The age-specific differences in asthma prevalence between men and women remained consistent throughout the study (Fig. 2; Table S1).

There was a notable difference in the prevalence of asthma depending on the type of insurance. Asthma was around twice as frequent among patients covered by the MA scheme than among patients covered by standard HI. However, regardless of the type of insurance, the prevalence of asthma increased over time (HI: 4749–5529 per 100 000; MA: 10 429–11 187 per 100 000; Table S1).

Asthma-related healthcare use

Table 1 summarizes the trends in asthma-related healthcare use during the study period. The number of outpatient visits per person per year decreased from 4.82 ± 8.02 in 2006 to 3.44 ± 5.50 in 2010. Each year, approximately 3% of all asthma patients were hospitalized, and about 0.4% were admitted to an ICU at least once due to exacerbation of the asthma. While the number of hospitalizations per person per year remained stable in the range 1.57–1.62, the number of hospitalization days per person decreased from 21.36 in 2006 to 19.26 in 2010. At the same time, the number of

Table 2 Asthma-related outpatient visits by type of hospital and medical specialty

	2006	2007	2008	2009	2010
Number of subjects	1 857 368	1 916 118	1 991 264	2 112 623	2 256 023
Total visits by type of hospital (%)					
Primary hospital	7 529 854 (85.15%)	6 562 038 (82.06%)	5 713 420 (79.27%)	5 912 539 (78.86%)	6 137 654 (79.09%)
Secondary hospital	444 600 (4.97%)	443 634 (5.55%)	471 052 (6.54%)	500 832 (6.68%)	510 059 (6.57%)
Tertiary hospital	974 077 (10.89%)	991 218 (12.40%)	1 023 293 (14.20%)	1 084 033 (14.46%)	1 112 919 (14.34%)
Total visits by medical specialty (%)					
IM	6 720 397 (75.10%)	6 131 869 (76.68%)	5 628 995 (78.10%)	5 840 468 (77.90%)	6 012 523 (77.47%)
ENT	590 195 (6.60%)	551 597 (6.90%)	548 229 (7.61%)	595 414 (7.94%)	666 128 (8.58%)
FM	393 184 (4.39%)	331 785 (4.15%)	265 220 (3.68%)	281 333 (3.75%)	299 959 (3.87%)
PED	104 021 (1.16%)	87 749 (1.10%)	76 450 (1.06%)	79 093 (1.05%)	80 531 (1.04%)
GP	63 072 (0.70%)	59 383 (0.74%)	56 415 (0.78%)	55 509 (0.74%)	47 597 (0.61%)
OS	530 360 (5.93%)	373 557 (4.67%)	247 239 (3.43%)	252 623 (3.37%)	255 881 (3.30%)

IM, internal medicine; ENT, ear, nose, and throat medicine; FM, family medicine; PED, pediatrics; GP, general practice; OS, orthopedics.

hospitalization days per admission decreased from 13.34 in 2006 to 12.30 in 2010. Between 2.3% and 2.4% of patients received treatment in an emergency department each year due to asthma exacerbation. Pulmonary function tests, including spirometry with or without bronchodilator response, and bronchial provocation tests were performed in 10–11% of patients, on average approximately 1.3 times per year.

We analyzed the frequency of asthma-related outpatient visits according to the type of medical facility and the physicians' specialties. Throughout the study, the frequency of visits to primary hospitals was markedly higher (79.09–85.15%) than to secondary (4.97–6.57%) and tertiary hospitals (10.89–14.34%). Over the 5-year period, outpatient visits to primary hospitals showed a tendency to decrease, while visits to secondary and tertiary hospitals increased. Asthma-related visits to physicians specializing in internal medicine (IM) were the most frequent, followed by visits to ear, nose, and throat (ENT) specialists and family medicine (FM) doctors. About 1% of all outpatient visits were to pediatricians (PED), despite the fact that all the patients were ≥ 18 years old (Table 2).

Additionally, all variables of asthma-related healthcare use were analyzed by type of insurance. The subjects who were covered by MA were about 10 years older, and they were three times more likely to be admitted or visit an emergency department, while less likely to have outpatient visits than subjects who covered by HI. However, as there exists such a small proportion of MA beneficiaries among asthma subjects (HI, about 93%; MA, about 7% in Table 1), the overall trend of outcomes was not influenced by analyses according to the type of insurance (Tables S2 and S3).

Differences in healthcare use between newly diagnosed and previously diagnosed asthma patients

Of 2 160 255 asthma patients in 2009, about 51% were newly diagnosed, the remainder previously diagnosed. The gender ratio was similar in the two groups (38% men and 62% women), but there were differences in age distribution. The

mean age was higher among the patients with an existing diagnosis (56.10 ± 17.86 vs 47.9 ± 21.0 years), and new diagnoses were more frequent in patients under 50, while previous diagnoses were more common among patients aged ≥ 60 . There were about twice as many recipients of MA among the previously diagnosed patients as there were among the newly diagnosed.

In terms of asthma-related healthcare use, the proportion of patients who visited the emergency department or were hospitalized due to asthma exacerbation at least once during 2009 was higher in the previously diagnosed group (4.35% vs 1.78% were hospitalized; 2.42% vs 1.22% received emergency treatment). Additionally, newly diagnosed patients underwent fewer pulmonary function tests and more skin prick tests (Table 3).

Patterns of asthma medication prescriptions

Figure 3 shows the prescription patterns associated with each class of asthma medication and type of hospital over the study period. Prescriptions of ICS-based inhalers, including ICS monotherapy and ICS/LABA combination inhalers, increased slightly over time. Almost half of all asthma patients in tertiary hospitals were prescribed an ICS-based inhaler at least once, and the highest annual increment in the number of ICS prescriptions was observed in tertiary hospitals. The overall proportion of patients who were prescribed ICS-based inhalers was only around 20%, as most visits took place at primary care centers (79.09–85.15%; Fig. 3A; Table S4). About 15% of the patients in secondary and tertiary hospitals were prescribed ICS monotherapy, compared with only about 9% in primary hospitals. Importantly, more subjects were prescribed ICS/LABA combination inhalers than ICS alone in secondary and tertiary hospitals (>23% and 40%, respectively), but there was little difference in primary hospitals (10%; data not shown).

Prescriptions of LTRA gradually increased in all types of hospitals between 2006 and 2010. The proportion of patients prescribed LTRAs was the highest at tertiary centers (18.7–29.4%) and approximately 10% overall (Fig. 3B; Table S4).

Table 3 Comparison of asthma-related healthcare use by newly diagnosed and previously diagnosed patients in 2009

	Newly diagnosed group		Previously diagnosed group	
	<i>n</i>	%	<i>n</i>	%
Number of subjects	1 098 418	100	1 061 837	100
Gender				
Male	422 422	38.46	402 038	37.86
Female	675 996	61.54	659 799	62.14
Age				
Mean $\pm$ SD	47.93 $\pm$ 21.0		56.10 $\pm$ 17.86	
18–29	174 852	15.92	77 699	7.32
30–39	229 476	20.89	141 520	13.33
40–49	212 876	19.38	165 471	15.58
50–59	185 526	16.89	182 017	17.14
60–69	154 230	14.04	214 998	20.25
70–79	105 956	9.65	203 366	19.15
80+	35 318	3.22	76 739	7.23
Insurance type				
Health insurance	1 045 523	95.18	969 151	91.27
Medical aid	52 895	4.82	92 686	8.73
Hospitalizations				
No	1 078 900	98.22	1 015 610	95.65
Yes	19 518	1.78	46 227	4.35
Mean $\pm$ SD	1.28 $\pm$ 0.78		1.69 $\pm$ 1.50	
ICU Hospitalizations				
No	1 098 168	99.98	1 061 194	99.94
Yes	250	0.02	643	0.06
Mean $\pm$ SD	1.08 $\pm$ 0.34		1.10 $\pm$ 0.33	
Emergency department visits				
No	1 085 051	98.78	1 036 200	97.58
Yes	13 367	1.22	25 635	2.42
Mean $\pm$ SD	1.39 $\pm$ 1.44		1.41 $\pm$ 1.20	
Spirometry				
No	993 275	90.43	933 199	87.89
Yes	105 143	9.57	128 638	12.11
Mean $\pm$ SD	1.09 $\pm$ 0.41		1.41 $\pm$ 1.16	
Bronchial provocation test				
No	1 071 028	97.51	1 020 407	96.10
Yes	27 390	2.49	41 430	3.90
Mean $\pm$ SD	1.05 $\pm$ 0.26		1.15 $\pm$ 0.47	
Skin prick test				
No	1 084 322	98.72	1 052 283	99.10
Yes	14 096	1.28	9554	0.90
Mean $\pm$ SD	1.00 $\pm$ 0.06		1.01 $\pm$ 0.08	

By contrast, the percentage of patients prescribed xanthine derivatives declined by more than 15% across all hospitals during the same period, although the prescription rate remained quite high (Fig. 3C; Table S4).

Short-acting β 2-agonists were prescribed at least once to 31–37% of the patients in secondary or tertiary hospitals and to 20% of the patients in primary hospitals, but the number of prescriptions declined slightly over time (Fig. 3D; Table S4). The number of oral LABA prescriptions varied slightly depending on the type of hospital and also declined over time (Fig. 3E; Table S4). Overall, only about 0.1% of all patients

were prescribed inhaled LABAs, and this proportion declined to 0.01% after 2009 (data not shown).

Regardless of the type of hospital, half of all patients received at least one prescription for systemic corticosteroids. The proportion of patients prescribed systemic corticosteroids remained stable at secondary and tertiary hospitals (about 55% and 40%, respectively), while it declined by almost 7% at primary hospitals over the course of the study (Fig. 3F; Table S4). The number of prescribed days of systemic corticosteroids per person per year fell from 14.03 ± 37.04 in 2006 to 12.50 ± 34.27 days in 2010. The number of days prescribed was the highest in tertiary hospitals (34–40 days per person per year) followed by secondary (22–29 days) and primary hospitals (10–12 days; Fig. 3G). Prescription patterns of asthma medications by type of hospital according to the insurance type were shown in Table S5. Prescription patterns were also analyzed according to physicians' specialties, which were presented in the supplement.

Discussion

Using HI claims data, we assessed the prevalence of adult asthma and investigated the patterns of asthma-related healthcare use and prescription in Korea in 2006–2010. While HI databases have been used in a number of epidemiological studies of asthma in several countries (1, 2, 5–7), most of them have limitations associated with incomplete population coverage or fragmentation of the insurance systems. The NHI system in Korea is unique in that it covers almost the entire population of the country. We found that the prevalence of asthma among adults increased between 2006 and 2010 and was higher among women, the elderly, and patients covered by MA. For the purpose of our study, we chose a definition of asthma that included a range of severities, to give us a broader understanding of the condition and its management in Korea.

A codiagnosis of asthma and chronic obstructive pulmonary disease (COPD) could possibly be a contributing factor to asthma prevalence in the elderly. An analysis of our data showed that 4.86% of asthma patients aged 20–39, 11.34% of those aged 40–64, and 24.25% of those aged ≥ 65 had been codiagnosed with COPD (ICD-10 code J41–44). However, it is difficult to differentiate COPD from asthma in older patients, who are more likely to have impaired reversibility of airway obstruction or fixed obstruction than younger asthma sufferers (13–16).

Several studies have identified differences in asthma prevalence between men and women (17, 18). The average number of asthma-related outpatient visits and length of hospital stay declined consistently throughout the study period. This may be associated with continued improvements in the management of asthma thanks to a growing number of international and domestic good practice guidelines. On the other hand, it should be noted that while the number of outpatient visits declined at primary hospitals, there was a slight increase in secondary and tertiary hospitals. This could be a reflection of cuts and savings imposed on the health sector due to financial constraints, which may be a big problem in future. In

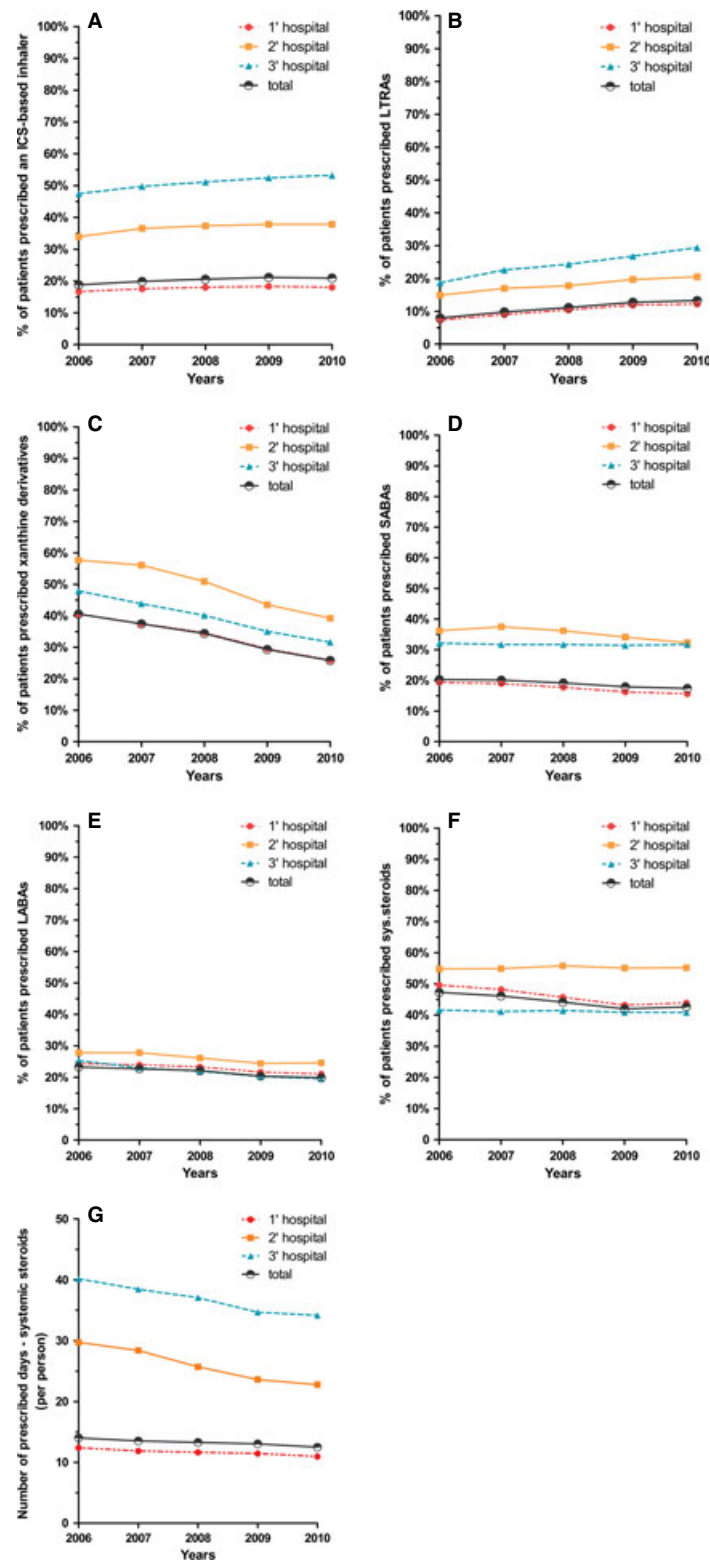


Figure 3 Patterns of asthma prescriptions according to type of hospital. Graphs show the proportion of patients prescribed each class of medication among those who received asthma-related treatment at a medical center on at least one occasion. (A) Inhaled corticosteroid (ICS)-based inhaler. (B) Oral leukotriene antagonists (LTRAs). (C) Xanthine derivatives. (D) Short-acting β agonists (SABA). (E) Long-acting β agonists (LABA, oral). (F) Systemic corticosteroids. (G) Prescribed days of systemic corticosteroids (per person).

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the Asthma Insights and Reality in Asia-Pacific (AIRIAP) study in 2000, only 1.3% of asthma patients in Korea reported using ICS, which was the lowest among all countries in the region. Throughout the period of our study, around 50% of asthma patients in tertiary hospitals were prescribed ICS-based inhalers. However, due to much lower prescription rates in primary and secondary hospitals, the overall ICS prescription rate reached only 20% of all asthma patients. An important barrier to effective asthma management with ICS is inadequate technique among inhaler users (19).

The prescription rate of systemic corticosteroids was quite high in our study, particularly in primary and secondary hospitals. However, in tertiary hospitals, the duration of therapy per patient per year was longer than in other types of hospital, suggesting that cases of more severe asthma were treated there. The high prescription rates in primary and secondary hospitals may suggest that they are being overused in situations where an ICS-based inhaler would be the preferred treatment. It is generally thought that, in the limited time allocated to each patient, it is difficult to educate the patients and to monitor their adherence to the treatment.

A gradual increase in the number of prescriptions for oral LTRAs was observed in all types of hospitals and across all medical specialties. The traditional preference for oral treatment in patients who show less compliance with inhalers may have contributed to this trend in Korea.

Long-acting β 2-agonists monotherapy has been contraindicated in asthma due to reports of serious adverse events, and recommendation has been made to combine LABAs with ICS in a single inhaler (20, 21). Our results confirm that the number of prescribed LABA inhalers has decreased dramatically, in compliance with these guidelines. However, our study shows that oral LABAs continue being used by a number of patients.

One limitation of this study is that only those who received medical treatment were enrolled. It is possible that some asthma sufferers with less severe symptoms or limited access to a medical center did not seek medical advice, leading to an underestimation of asthma prevalence in Korea. By contrast, asthma prevalence could be overestimated in those groups who seek medical advice frequently, such as the elderly or recipients of MA, due to comorbidities or financial incentives. Another limitation is that there were not enough clinical data to assess the severity of asthma phenotypes. Therefore, we could not examine the relationship between severity of disease, healthcare use, and prescription patterns.

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Lastly, it is possible that a proportion of the newly diagnosed patients may, in fact, have been diagnosed some time prior to the study period and not been to regular follow-up visits.

In summary, the prevalence of asthma among adults in Korea has increased over a recent 5-year period. However, the proportion of subjects with a prescription for ICS-based controller medication was low compared with that of systemic steroids, showing that more effort is needed to improve asthma control. An integrated strategy among healthcare providers and support from the government are required in order to overcome the burden to public health associated with asthma management.

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Conflict of interest

There are no potential conflicts of interest related to this article or the research described.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Methods.

Table S1. Prevalence of asthma according to age and sex (per 100 000 population).

Table S2. Demographic data and asthma-related healthcare use according to the insurance type.

Table S3. Asthma-related outpatient visits by type of hospital and medical specialty according to the insurance type.

Table S4. Prescription patterns of asthma medications by type of hospital.

Table S5. Prescription patterns of asthma medications by type of hospital according to the insurance type.

Table S6. Patterns of asthma prescriptions by medical specialty.

Table S7. Patterns of asthma prescriptions by medical specialty according to the insurance type.

Figure S1. Patterns of asthma prescriptions by medical specialty.

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Supplement

Table S1 Criteria for inclusion and exclusion

Inclusion criteria:

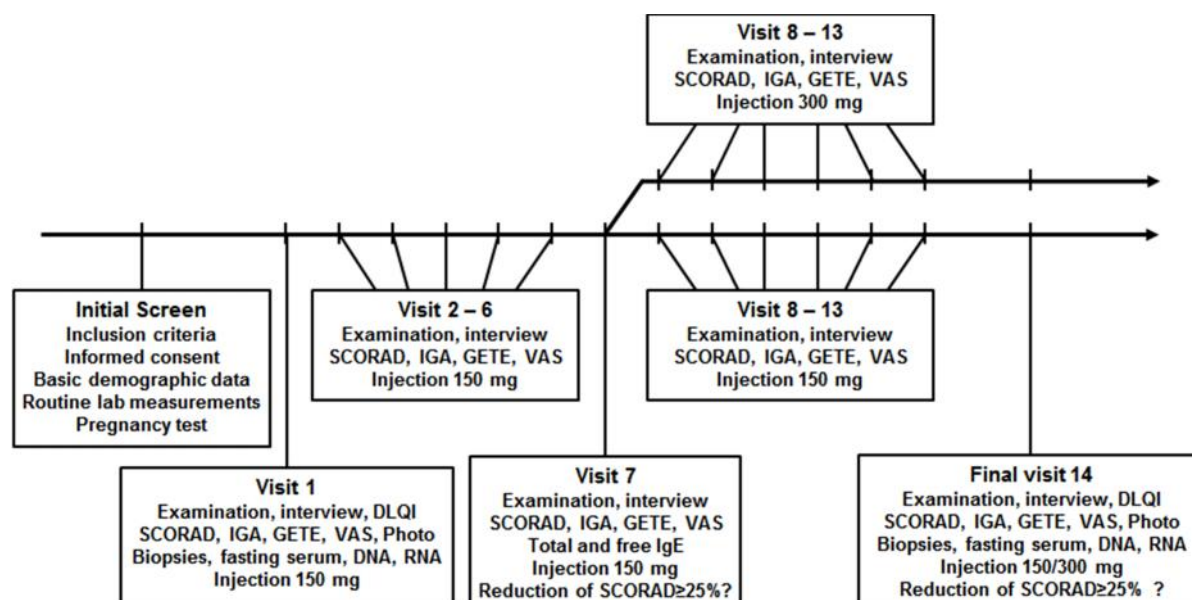
- Age $\geq$ 18-70 years of age, body weight $\geq$ 20 kg and $\leq$ 150 kg
- Dermatological diagnosis of AD, SCORAD $\geq$ 20
- A positive RAST (ϵ CAP1) result for at least one aeroallergen specific IgE and total IgE $\geq$ 100kU/l at screening (or within the previous 12 months)
- Eligible to receive systemic therapy for AD in accordance to local guidelines
- Signed informed consent from patient

Exclusion criteria:

- Evidence of skin disease other than AD (e.g. psoriasis) at the inclusion time
- Treatment with systemic AD medications or any investigational drug within a 30-day washout period
- Concomitant treatment with substances interfering with the immune system.
- Permanent severe diseases, especially those affecting the immune system, except asthma
- Pregnancy or breast feeding
- History of food or drug related severe anaphylactoid or anaphylactic reaction(s)
- History or presence of epilepsy, significant neurological disorders, cerebrovascular attacks or ischemia
- History or presence of myocardial infarction or cardiac arrhythmia which requires drug therapy
- Elevated serum IgE levels for reasons other than allergy and/or urticaria (e.g.: parasite infections, hyperimmunoglobulin E syndrome, Wiskott-Aldrich-Syndrome or clinical allergic bronchopulmonary aspergillosis).
- Evidence of severe renal dysfunction or significant hepatic disease
- Evidence for active infection that in the opinion of the investigator would compromise the patient's ability to tolerate therapy.
- History of malignancy of any organ system, treated or untreated, whether or not there is evidence of local recurrence or metastases, with the exception of localized basal cell carcinoma of the skin
- Clinically significant laboratory abnormalities (not associated with AD) at Visit 1
- Known hypersensitivity to any ingredients, including excipients (sucrose, histidine, polysorbate 20) of the study medication or drugs related to Omalizumab® (e.g.: monoclonal antibodies, polyclonal gammaglobulin)
- Patients who are considered potentially unreliable or where it is envisaged the patient may not consistently attend scheduled study visits
- Patients with serious psychiatric and/or psychological disturbances.
- Patients with a history of drug or alcohol abuse.
- Patients who are unable to complete a patient diary or complete questionnaires on paper
- Patients with any other condition or prior/current treatment, which in the opinion of the investigator renders the patient ineligible for the study schedule.

Table S2 Study population

	cases	responder	non-responder
Mean age (SD)	46 (16.36)	43.25 (17.33)	47.83 (16.18)
Sex (male/female)	9 / 11	3 / 5	6 / 6
FLG mutation carriers, n/N	5 / 20	0 / 8	5 / 12
Asthma, n/N	10 / 20	3 / 8	7 / 12
Mean body weight [kg] (SD)	73.15 (13.35)	76.94 (13.18)	70.63 (13.42)
Mean SCORAD score at inclusion (SD)	45.81 (15.13)	45.60 (14.88)	45.96 (16.03)
Mean OSCORAD score at inclusion (SD)	39.54 (12.33)	38.03 (11.28)	40.51 (13.40)
Geom. mean serum IgE at inclusion [IU/ml] (SD)	935.51 (4.89)	983.67 (3.99)	883.36 (6.73)
Geom. mean serum TARC at inclusion [pg/ml] (SD)	938.23 (2.29)	963.15 (2.45)	910.53 (2.26)
Mean SCORAD score at Visit 14 (SD)	40.52 (23.01)	23.13 (14.72)	53.16 (19.58)
Geom. mean serum IgE at Visit 14 [IU/ml] (SD)	88.20 (2.90)	89.25 (2.70)	87.03 (3.40)
Geom. mean serum TARC at Visit 14 [pg/ml] (SD)	687.18 (1.79)	637.90 (1.88)	748.17 (1.74)

**Figure S1 Study design**

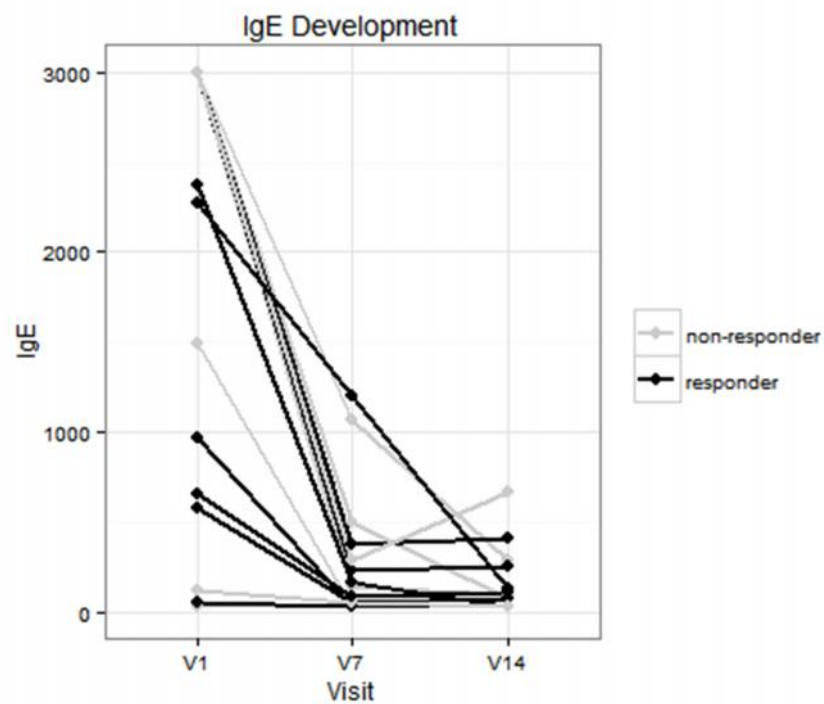


Figure S2 Development of IgE between Visit 1 and Visit 14

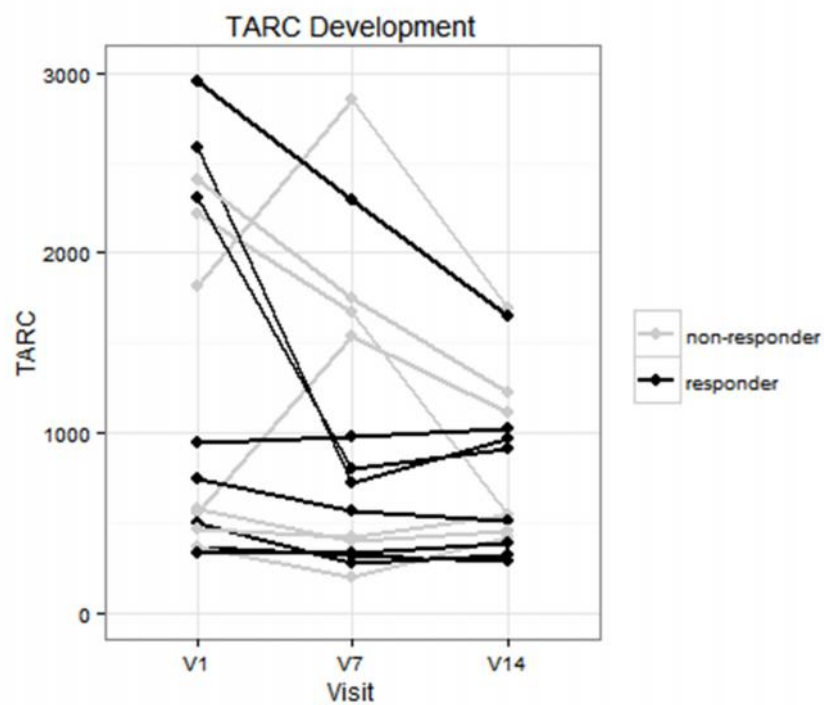


Figure S3 Development of TARC between Visit 1 and Visit 14