

Long-Term Inhaled Corticosteroid Adherence in Asthma Patients with Short-Term Adherence



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What is already known about this topic? Although adherence to inhaled corticosteroids (ICS) is known to be poor in asthma, it is unclear to which extent patients regularly using ICS during consecutive months remain adherent to therapy in the longer-term.

What does this article add to our knowledge? Identifying asthma patients' regular use of ICS during several months does not predict long-term adherence, which suggests quickly waning use in asthma. In our population, markers of asthma severity or lower control, younger age (children and teenagers), and factors contributing to the continuity of care improved drug coverage.

How does this study impact current management guidelines? To allow valid assessment, adherence to asthma therapy should be studied for prolonged periods, because episodes of regular use do not last.

BACKGROUND: Although the use of inhaled corticosteroids (ICS) in asthma is known to be overall erratic, the long-term use of ICS by patients selected during an episode of regular use is poorly documented.

OBJECTIVE: In a cohort of patients with asthma regularly acquiring ICS therapy over several months, we verified whether these patients remained treated in the following 12 months. The correlates of regular ICS use over this period were investigated.

METHODS: A historical cohort of patients with asthma was identified from the *Echantillon généraliste de bénéficiaires* national French health care reimbursement data (2007-2012). Patients (6-40 years) were selected during a regular ICS use

episode, with 3 or more ICS refills within 120 days. Continuous multiple-interval measures of medication availability (CMA) were computed for the 12 months after the third dispensation, and the factors associated with a CMA value of 80% or more (adherent patients) were identified.

RESULTS: Among 5096 patients (42.1% children/teenagers, 48.8% females), only 24.0% had a CMA value of 80% or more (mean CMA = 54.4%) over the 12 months following the ICS selection period. Achieving a CMA value of 80% or more was primarily associated with being a child/teenager ($P = .002$), having more severe or less controlled asthma ($P = .007$), more previous dispensing of short-acting beta agonists ($P < .0001$), and receiving devices with 200 unit doses ($P < .0001$). Adherent patients had more frequent general practitioner visits ($P < .0001$), more distinct prescribers of respiratory therapy ($P = .0002$), and more frequent switches of ICS ($P < .0001$).

CONCLUSIONS: Most patients with asthma selected during an episode of regular ICS use did not maintain therapy over the following months. Adherence should be repeatedly monitored, and the reasons for discontinuation should be investigated, at prescriber and patient levels. © 2016 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2016;4:890-9)

Key words: Asthma; Inhaled corticosteroids; Treatment episodes; Adherence; Claims data

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This study was supported by GlaxoSmithKline France.

Conflicts of interest: G. Devouassoux is a board member for GlaxoSmithKline, AstraZeneca, Novartis Pharma, Boehringer Ingelheim, Chiesi, TEVA, and ALK-Abello and has received 1 or more grants from or has 1 or more grants pending with GlaxoSmithKline, Novartis, and Chiesi. A. Didier has received 1 or more fees for participation (advisory board) from Novartis, AstraZeneca, Mundipharma, Boehringer Ingelheim, and Chiesi and has an additional relationship with Novartis. E. Van Ganse has received 1 or more grants from or has 1 or more grants pending with ALK-Abello, Bayer, Bristol-Myers Squibb, GlaxoSmithKline, and Merck Sharp and Dohme and has received 1 or more fees for participation from ALK-Abello, Bayer, Bristol-Myers Squibb, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, IMS, and LASER. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication May 30, 2016; revised July 19, 2016; accepted for publication July 20, 2016.

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2213-2198

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<http://dx.doi.org/10.1016/j.jaip.2016.07.008>

The regular use of controllers, more particularly inhaled corticosteroids (ICS), is recommended in the management of persistent asthma, even in the absence of symptoms.¹ Irregular use of ICS is however a common issue in persistent asthma.^{2,3} Irregularity has detrimental effects on quality of life and health outcomes, and, at societal level, it brings additional costs because of avoidable medical resource utilization.⁴⁻⁶

Abbreviations used

CMA- continuous multiple-interval measures of medication availability
EGB- Echantillon généraliste de bénéficiaires (permanent sample of beneficiaries, a 1/97th random sample of the French claims database)
FDC- fixed dose combinations
GPs- general practitioners
ICS- inhaled corticosteroids
LTD- long-term disease
SABA- short-acting beta agonist
SNIIR-AM- Système National d'Information Inter-Régimes de l'Assurance Maladie

Although interruptions of chronic therapy can happen at any time, the first weeks following initiation are critical for regular long-term use.^{7,8} A successful initiation requires acceptance of the drug and behavioral changes.⁷ Caregivers should provide at this early stage explanations about the condition and the effects of treatment. The quality of these explanations is pivotal for appropriate use,⁹ because they may impact concerns and perceptions about the drug.¹⁰ Furthermore, tolerability issues, which may impact drug use, generally occur during this early phase.

Patients with asthma getting regular refills in the first months following ICS initiation should have overcome this critical step and the first barriers of adequate use. Nonetheless, maybe from the assumption that regularity is maintained, their longer-term exposure to ICS is poorly documented. More generally, it is unclear whether patients with asthma identified during an episode of regular ICS use remain properly treated over subsequent months, or whether a group of irregularly treated patients eventually appears. In addition, it is of major interest to investigate whether patients with long-term adherence differ from others as to specific personal characteristics or factors related to disease management, namely, ICS treatment or characteristics of follow-up.

Claims data are efficient tools in pharmacoepidemiology because they enable investigation of extensive reimbursed medical resource utilization in large populations of beneficiaries over prolonged periods. Proxies of implementation, such as continuous multiple-interval measures of medication availability (CMA), have been developed to approach drug coverage during specific time windows from dispensation data.¹¹

Using national French claims data, we determined long-term drug coverage by ICS in a cohort of patients with asthma regularly treated by ICS therapy at selection, to verify whether such patients would maintain prolonged use of ICS therapy in the subsequent months. Correlates of an appropriate ICS coverage (CMA \geq 80%) were then identified, according to patient characteristics and factors related to asthma management.

METHODS

Data source

The study was conducted in the permanent sample of beneficiaries (*Echantillon généraliste de bénéficiaires* [EGB]). The EGB database is a 1/97th representative random sample of the Système national d'information inter-régimes de l'Assurance maladie (SNIIR-AM),^{12,13} a French nationwide population-based record of individual and anonymized data on all reimbursements for health care utilization, including therapy and outpatient medical and nursing care. No direct information on the medical indication is linked with

each reimbursement, but the SNIIR-AM includes information on long-term disease (LTD) status coded in *International Classification of Diseases, Tenth Revision*. LTD status allows patients to receive treatment for severe and costly conditions without out-of-pocket payment. SNIIR-AM also contains information on free-access-to-care status, which enables patients of lower socioeconomic status to receive free medical care. Information from the SNIIR-AM database and medical information from the French hospital discharge database (Programme de Médicalisation des Systèmes d'Information) about all patients admitted to hospital in France, including discharge diagnoses coded in *International Classification of Diseases, Tenth Revision* codes, medical procedures, and French diagnosis related groups, are cross-referenced. This observational study was conducted on anonymized data, and the National Informatics and Liberty Committee has delivered an overall authorization to use EGB data for research purposes. This study was performed after approval by the French Institute for Health Data (Institut des Données de Santé, approval no. 86, July 2, 2014).

Study design and study population

ICS-treated patients were identified on the basis of recorded episodes of dispensed ICS therapy.

Inclusion criteria. Treatment episodes were defined from the first occurrence of a cluster of 3 or more refills of the same ICS product consecutively dispensed between January 1, 2007, and December 31, 2012. The 3 consecutive ICS refills could be dispensed at 2 or 3 different dates, but the interval between the first refill and the third refill had to be less than 120 days. Patients were to be aged 6 to 40 years at the date of the first ICS dispensation (cohort entry; Figure 1). Older patients were excluded because of the possible diagnosis of chronic obstructive pulmonary disease. ICS products were those available in France at the time of the study (beclometasone, fluticasone, budesonide, fluticasone/salmeterol, budesonide/formoterol, and beclometasone/formoterol fixed-dose combinations) and the different studied ICS are listed in this article's Online Repository at www.jaci-inpractice.org, based on product, device, strength, and unit doses per device.

Exclusion criteria. Exclusion criteria consisted of any active LTD status for respiratory diseases other than asthma. The patients who received uncommon types of ICS (<10,000 dispensed devices in 2012 in France) were excluded, as were nebulized corticosteroids.

Computation of CMA. Our definition of CMA was the percentage of days covered by dispensed ICS during a defined time window¹¹ (Figure 2). CMA was computed during the 12-month study period following the third dispensation (index date) of the first recorded treatment episode meeting inclusion criteria (Figure 1). The study period corresponded to the 12 months following the index date. Drug coverage provided by the ICS dispensation immediately preceding the index date was counted according to the size of its overlap over the study period. Conversely, drug supply extending beyond the end of the study period was excluded (CMA capped at 100%).

Prescribed daily doses assessed from external data. Given the absence of prescribed daily doses in the EGB, the computation of the number of days supplied by each ICS pack required external data (primary care electronic health records: longitudinal patient data database). General practitioners (GPs) in the longitudinal patient data database are representative of the French

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