Original Article

Inhaled Corticosteroid Adherence Patterns in a Longitudinal Asthma Cohort

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What is already known about this topic? Inhaled corticosteroid (ICS) adherence in asthma is often low, and detrimental to health. Persistence with and implementation of treatment are distinct adherence components with different causes and consequences. Electronic records–based adherence calculations rarely consider this distinction.

What does this article add to our knowledge? During long-term ICS-based asthma treatment, nonpersistence periods alternated with periods of regular, albeit variable, ICS use (implementation). When accounting for (non-)persistence, implementation rates were relatively high, suggesting that nonpersistence contributes substantially to suboptimal ICS adherence.

How does this study impact current management guidelines? In clinical practice, assessing both (non-)persistence and implementation provides a more nuanced diagnosis of ICS adherence. These 2 adherence components should be separately investigated in relation to possible health consequences and tailored interventions.

BACKGROUND: Electronic prescribing records can enable exploration of medication adherence, but analysis decisions may influence estimates and require alignment to new consensus-based definitions.

OBJECTIVE: To compare different computations of inhaled corticosteroid (ICS) implementation in a primary care asthma population initiating ICS therapy when assessed within episodes of persistent use, and examine longitudinal variation in implementation.

METHODS: A historical cohort study was conducted on UK's Optimum Patient Care Research Database. Eligible patients had physician-diagnosed asthma, initiated ICS therapy, and had 3 or

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Abbreviations used
ICS- Inhaled corticosteroid
CMA- Continuous medication availability
OPCRD- Optimum Patient Care Research Database
ID- Index prescription date

more years of continuous registration. ICS treatment episodes were constructed on the basis of 3 definitions, permitting 30-, 90-, and 182-day gaps between prescriptions. Implementation was estimated using 2 continuous medication availability (CMA I and II) definitions to explore effects of carryover of previous prescriptions in 4 observation windows: 6, 8, 12, and 24 months. Impact of methodology was assessed by descriptive statistics, linear mixed models, and measures of agreement.

RESULTS: A total of 13,922 eligible patients (mean age, 39.9 years; 48.7% men) were identified. For CMA I, permitting a 90-day gap, mean ICS implementation for the 2-year period was 89.3% (±16.0%; range, 14.4%-100%). Sensitivity analyses with 30- and 182-day gaps resulted in increased (97.0% ± 7.2%) and decreased (81.1% ± 21.6%) estimates. CMA II produced estimates with varying concordance (0.69-0.87). Substantial variance was found between and within patients (intraclass coefficient, 0.30-0.36).

CONCLUSIONS: Different analysis choices resulted in substantial variation in implementation estimates, highlighting the need for transparent and clinically relevant methododology. Distinguishing between (non)persistence and implementation is important in clinical practice, and may require different interventions in routine consultations. **(J Allergy Clin Immunol Pract 2017;5:448-56)**

Key words: *Adherence; Asthma; CMA; Inhaled corticosteroids; OPCRD; Pharmacoepidemiology; Cohort study*

Medication adherence in people with chronic illnesses is generally low. In asthma, adherence to inhaled corticosteroids (ICSs), used as long-term controller medication, is often estimated to be below 50%.[1] Low adherence rates have been associated with increased mortality and morbidity, and escalating treatment costs.[2-4] Outside the strict control of randomized controlled trials, patients may decide, in agreement with their health care provider or independently, to adopt a symptom-driven approach to self-titrate therapy, for example, reducing daily ICS dose during periods with milder symptoms and increasing their daily ICS dose during periods with less controlled asthma.[5,6] Thus, ICS adherence requires careful consideration in routine asthma care.

To date, many studies have focused on identifying factors influencing medication adherence to develop adherence-enhancing interventions.[7,8] However, there is still a need to improve methods of assessing adherence given the substantial heterogeneity in terminology and measurements.[9,10] In a recent consensus-based taxonomy, Vrijens et al[10] described medication adherence as a process of taking medication as prescribed, with 3 components: initiation, implementation, and discontinuation (or nonpersistence). Initiation is the event of taking the first dose of a medication. Discontinuation is the event of omitting a next planned dose followed by no medication intake for a substantial time period (nonpersistence). Between initiation and discontinuation is a period of medication persistence, wherein implementation represents the extent to which the drug was used as prescribed during a specific period of active treatment. Long-term treatment may include several treatment episodes, which can be individually characterized by these components.[11] Adherence patterns in ongoing long-term treatment need to distinguish between 2 main adherence components: persistence (a time-to-event variable) and implementation (a statistic comparing actual medication use to prescribed use). Clinically relevant methods to implement this taxonomy in different conditions based on various data sources are yet to be developed and tested.[10]

Electronic medical records (EMRs)[12] represent a relatively accessible data source that includes information on many patients with minimal interference in the care process. EMRs can provide more ecologically valid assessments of medication adherence in long-term care compared with randomized controlled trials, which require high adherence to the trial medication to test its efficacy and therefore may not reflect accurately the reality of daily clinical practice.[12] However, arriving at a clinically meaningful adherence assessment is a complex process. Although it is known that the choice of algorithms may influence estimates,[13,14] evidence is scarce regarding the impact on adherence assessments of distinguishing implementation from persistence, and of different analytical choices on appropriate observation window lengths and data handling methods. Also, the extent to which adherence varies between and within persons in long-term care has received little attention. For an optimal use of administrative data sets in assessing long-term ICS adherence in routine care, understanding the impact of these analytical decisions on estimates, and their clinical implications, is essential.

This study aimed to compare different EMR-based methods to compute ICS adherence in asthma, and focused on 2 questions: (1) what is the impact of distinguishing implementation from persistence on adherence assessment, considering several analytical choices? and (2) does EMR-based implementation vary within and between patients in long-term care? Answering these questions may lead to improved diagnosis of (non-)adherence from routine data available in primary care, and subsequently more effective adherence support.

METHODS

Study design and setting

We conducted a historical cohort study using EMRs from primary care practices in the United Kingdom within the Optimum Patient Care Research Database (OPCRD),[15] a quality-controlled respiratory-enriched database. At the time of data extraction, OPCRD contained anonymized data for approximately 350,000 patients with asthma collected from more than 350 practices across the United Kingdom that subscribed for respiratory review service. The database includes information on diagnosis codes, clinical evaluation, and prescriptions (eg, date, drug name, amount, and dosage prescribed). Prescribing records are a good approximation for dispensing records in the United Kingdom.[16,17] The OPRCD has been approved by Trent Multicentre Research Ethics Committee for clinical research use. Use of the database for this study was approved by the OPCRD Annonymised Data Ethics and Transparency Committee (approval 2.9) and the protocol was registered with the