

Quantifying beta-agonist utilization: Occasions or puffs?



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Clinical Implications

- The 2009 American Thoracic Society/European Respiratory Society report on end-point standardization raised the issue of reporting rescue inhaler use as “occasions” or puffs used. We addressed this using digital sensors and recommend reporting puffs until the definition of an “occasion” is standardized and validated.

TO THE EDITOR:

The Global Initiative for Asthma and the National Asthma Education and Prevention Program (NAEPP) both recommend assessing the frequency and number of inhalations of short-acting beta-agonists (SABAs) in asthma as important measures of asthma control and severity.^{1,2} Some ambiguity exists, though, as to whether to quantify SABA use as the number of puffs used or the number of “occasions” of use, and which measure best reflects the level of asthma control.

In an effort to standardize outcome measures, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) Task Force assessed the literature for the utility of these 2 measures of rescue medication use.³ They acknowledged that clinical trials reported SABA use as inhalations per day and proposed that practicing physicians should report SABA occasions, because patients may use 1 or 2 inhalations for rescue treatment. Furthermore, the dosage and administration statement in the package insert for albuterol recommends 2 inhalations every 4 to 6 hours for the treatment of bronchospasm and for some patients 1 inhalation every 4 hours may be sufficient.⁴

The duration of an “occasion” is not specified in the ATS/ERS Task Force report or defined in the literature. Use of multiple inhalations of SABA within 10 to 15 minutes of the index dose is probably for treatment of a single occasion of bronchospasm. Use of SABA 2 to 4 hours after the index dose may suggest a second occasion. A standard, defined cutoff point for when one “occasion” becomes a second occasion is needed. Does a second occasion occur at 15, 30, 60, 90, 120, or 240 minutes after the index dose?

If occasions were to be adopted as the standard in clinical practice, further refinement would be required, including whether an occasion is the response to a single trigger or the duration of medication use. This would help resolve ambiguity in the guidelines’ determination of control. GINA¹ and the NAEPP² both specify that partly or not well-controlled asthma may be defined by SABA use on greater than 2 times/wk or 2 d/wk, respectively, over the previous 2 to 4 weeks. However, neither report specifies how multiple occasions of SABA on the

same day alters the determination of control. For asthma severity, in contrast, the NAEPP states that asthma severity increases from intermittent to persistent asthma if there are 2 or more occasions of use in a day over the previous 2 to 4 weeks.

Previously, assessment of patterns of SABA have relied on patient-completed paper or electronic diaries requiring patient recall, and rarely specified time of use and number of puffs.⁵ In this study, we leveraged electronic medication monitors (EMMs) with sensors fitted on SABA inhalers (Propeller Health, Madison, Wis) to report on the temporal patterns of SABA use.

Patients actively enrolled in the Propeller Health system between March 2015 and February 2017 were included in this analysis. Patients had a diagnosis of asthma and were treated with a SABA alone or in combination with a controller. A Bluetooth-enabled EMM was attached to their SABA that recorded the time and date of each inhalation. Eligible patients were required to accept Propeller Health’s Terms of Use.⁶ The first use of SABA on a given date was the index event of interest. We then report the number of puffs of SABA taken 2, 10, 30, 60, 120, and 240 minutes after the index inhalation. A patient could have only 1 index event per day.

There were 3,373 patients with a self-reported diagnosis of asthma (mean age, 31.0 years) who recorded index use of SABA (ie, events) on 56,487 days. A total of 141,586 puffs of SABA were recorded. Within 2 minutes of the index puff, 30% of events consisted of a single puff, 53% had 2 puffs, and 17% had 3 or more puffs of SABA. During the 4-hour window, the total number of puffs used (141,586 puffs) was 21% higher than the 117,450 puffs (83%) used within the first 2 minutes. In addition, the distribution of puffs was relatively constant for each of the 6 time periods studied. The most noticeable change is that 5% of events with 1 puff in the first 2 minutes had additional puffs over the next 2 to 4 hours, with minimal increases in the use of multiple puffs (see [Figure 1](#)). During the 4-hour postindex event, the percentage of events with additional rescue medication use for the 6 times periods studied ranged from 2.4% to 14.6% (see [Figure 2](#)).

Although the recommended dosing of SABA is 1 to 2 puffs over 4 to 6 hours, some patients use more than 2 puffs within 2 minutes, appropriately because of real and perceived intensity of the bronchospasm, need for device priming, or unnecessarily because of improper inhalation technique or incorrect assessment of the degree of airflow obstruction.

The duration of an “occasion of use” for a SABA may be determined by (1) the pharmacokinetics and pharmacodynamics of the bronchodilator, (2) the duration of the event caused by the trigger, and/or (3) the effectiveness of the treatment in addressing the variable airflow limitation. These 3 parameters each have inherent limitations. The albuterol package insert sections on clinical studies suggest 4 to 6 hours as the duration of an occasion based on clinical trials using 4-times daily SABA and measuring change in serial FEV₁ and not for the treatment of acute symptoms.⁴ Events differ in duration by triggers that produce symptoms of varying intensity and duration and therefore the magnitude and duration of response to treatment is highly variable, further limiting the definition of an occasion.

Approximately 80% of rescue inhaler use occurred within the first 2 minutes from the index puff, with the remainder of

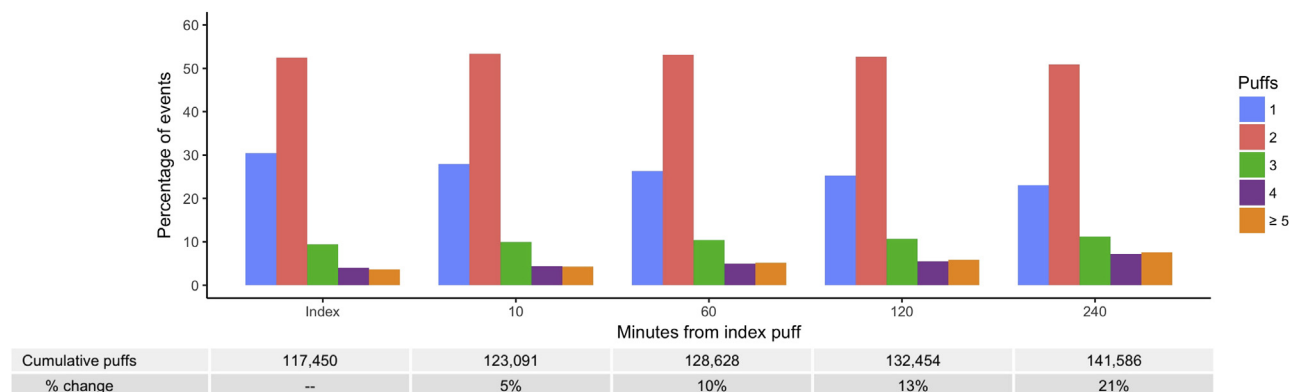


FIGURE 1. The percentage of rescue events (n = 56,487) with 1 to 5 or more puffs within 2 to 240 minutes from the index puff.

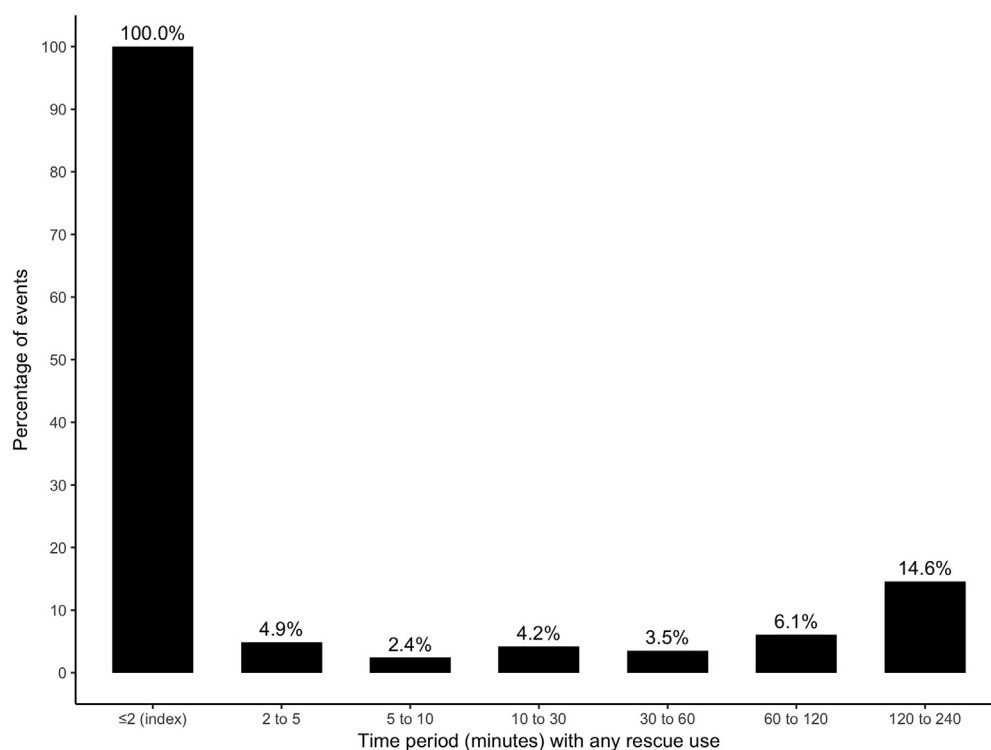


FIGURE 2. The percentage of rescue events (n = 56,487) per time period from the index puff.

inhalations taken over the next 4 hours. Although criterion 1 may suggest that an occasion be defined as 4 to 6 hours, the highly variable nature of asthma supports the use of puffs compared with occasions. Standardization of criteria will allow for comparable assessment of clinical response in practice and research and recognizes the need for a personalized approach.

Previous measures of asthma control and asthma risk have used either the number of canisters of albuterol dispensed⁷ or the controller to total asthma medication ratio.⁸ Such analyses are generally conducted using pharmacy claims. The present data objectively recorded actual daily medication use, providing a more sensitive assessment of SABA use. In comparison, occasions of use are dependent on patient report and recall and may mask important variability of use.

The use of EMMs provides a passively collected record of when rescue medication was used. This is potentially a more consistent and accurate assessment of SABA use compared with self-reporting. The validity of using EMMs is limited by patients keeping sensors attached to their medications or using multiple devices that are not consistently monitored. EMMs differ from current practice where patients' response to provider queries about occasions of use is dependent on patient report and recall. What remains to be demonstrated is whether decreased precision based on self-report masks important information on medication use. Accurate assessment of puffs of SABA may be used to inform clinical decision making to determine changes to treatment. Whether objective data collected from EMMs will result in better clinical outcomes still needs to be established. Guidelines and

decision making will evolve as data collected digitally is integrated with expert opinion.

Data from clinical trials reveal a directional consistency for SABA use when compared with symptom scores and asthma control. We suggest that SABA should be presented as puffs per day or puffs per week on the basis of experience in the research literature and EMM data presented in this report.

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