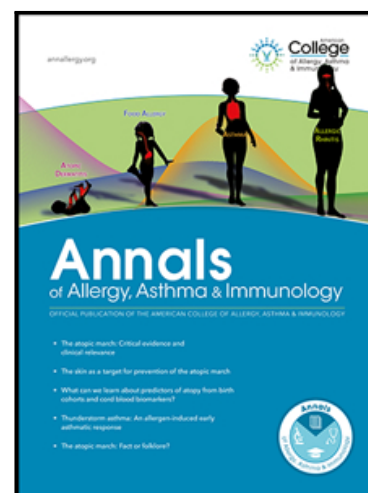


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Dose counting and use of short-acting beta-agonist inhalers in emergency department patients with asthma exacerbation

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Author contributions: S.K.L. and K.H. take the responsibility for the paper as a whole. S.K.L., T.G., B.E.C, C.A.C., and K.H. conceived the study. C.A.C., and K.H obtained the research funding. D.J.P, C.A.C., and K.H. collected the data. S.S., C.A.C., and K.H. supervised the conduct of the study. K.H. provided statistical advice. S.K.L. and T.G. analyzed the data. S.K.L. drafted the manuscript, and all authors contributed substantially to its revision.

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Keywords: asthma exacerbation, emergency department, medication non-adherence, short-acting beta-agonist inhaler, metered-dose inhaler, dose counting, integrated dose counter, inhaler techniques

Abbreviations:

ED, emergency department

SABA, short-acting beta-agonist

MDI, metered-dose inhaler

MARC, Multicenter Airway Research Collaboration

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Tables: one Table and two Supplement Tables

Medication non-adherence in asthma is a well-recognized problem.¹ Non-adherence includes asthma patients using run-out (empty) inhalers and incorrect inhaler techniques.² These lead to suboptimal disease control and asthma-related emergency department (ED) visits that are potentially preventable.² Indeed, studies have shown that patients with asthma commonly overestimate the remaining doses of their short-acting beta-agonist (SABA) in metered-dose inhalers (MDIs).^{3,4} Overestimating the remaining doses of SABA can cause patients to use inhalers beyond the labeled number of actuations, when the drug delivered per actuation can range from 20% to 80% of the therapeutic dose.³ To determine whether SABA inhalers are depleted, patients often use inaccurate methods such as shaking, spraying, and floating the canister.³ In an attempt to improve the correct use of MDIs, the US Food and Drug Administration recommended the integration of dose-counting devices into MDIs in 2003.⁵ However, little is known about how current ED patients with asthma identify the remaining doses of their SABA inhalers and their inhalation techniques.

This is a multicenter observational cohort study to investigate the methods used by ED adult patients with asthma exacerbation to identify the remaining doses of their SABA inhalers and the correctness of their inhalation techniques. The study was conducted at three EDs in Boston (Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, and Massachusetts General Hospital) from 2015 through 2017 as part of the Multicenter Airway Research Collaboration (MARC). MARC is part of the Emergency Medicine Network research consortium (www.emnet-usa.org). We included adults aged 18-54 years with a history of asthma

and a current prescription for SABA inhaler who presented to the ED with asthma exacerbation. In the present analysis, we excluded patients who reported no use of SABA inhalers within four weeks prior to their index ED visit. The investigators performed a structured ED interview that asked how patients identify the remaining doses of the SABA inhalers and objectively evaluated their inhalation technique, using methods of previous studies.^{3,6} The Institutional Review Board at each hospital approved this study. Informed consent was obtained from all participants.

Among the 203 ED patients with asthma exacerbation eligible for the current analysis, the median age was 32 years, 67% were female, 40% were non-Hispanic white, and 52% had public insurance (**Supplemental Table 1**). While 86% of the patients had a primary care physician, 55% reported that the ED was their preferred source of asthma care. Two-thirds of patients did not have a written action plan. Overall, 92% of the ED patients were using a SABA inhaler with an integrated dose counter (**Table 1**). However, only 34% of patients were advised to keep track of the number of doses and 26% were unable to correctly identify the number of doses. With regard to their primary method to identify the remaining doses, 32% reported spray testing, and 24% reported the use of dose counter. Approximately half of the patients had experienced needing SABA and finding their SABA inhaler empty. Among these, 60% sought medical care including 7% who called for ambulance. Objective assessment of patients' MDI use showed that correct techniques were lowest for expiration before firing (79%) and breath holding after firing the SABA inhaler (63%) (**Supplemental Table 2**).

Similar to our findings, in a telephone survey of 500 households in 2003 (the pre-dose counter era), Sander *et al.* demonstrated that only 36% of MDI users reported ever having been

told to keep track of the MDI doses used, and that 82% used “spray testing” to assess their inhaler.³ Additionally, a systematic review on patients’ inhaler use showed that incorrect techniques (e.g., postinhalation breath-hold) are frequent, without improvement over the past 40 years.⁷ While the proportion of accurate use in the present study was higher compared to the literature,⁷ the difference might be attributable to the differences in study population and settings. Our study corroborates these earlier reports and extends them by demonstrating, for the first time, how ED patients with asthma exacerbation identify the remaining doses of their SABA inhalers. The mechanism(s) underlying our observation – persistently suboptimal use of asthma inhalers in the dose-counter era – is likely multifactorial. Potential contributing factors are insufficient education on dose counting and underutilization of written action plans⁸ (two-thirds of these ED patients), which could both be symptoms of the larger problems such as provider-related factors (e.g., inadequate time, staff, and infrastructure for self-management education) and social determinants of health (e.g., limited access to healthcare). Additionally, individual health behaviors may be associated with this type of medication non-adherence. For example, our data demonstrated that 55% of the patients reported ED as the preferred source of asthma care. These findings should facilitate further investigations into the identification of mechanisms underlying the inappropriate inhaler use (e.g., dose counting) and the development of effective interventions on this population at high risk.

We acknowledge several potential study limitations. First, our data did not include outpatient management information including asthma self-management education, which might be associated with medication non-adherence. Second, we did not address psychosocial issues and barriers to healthcare access. Third, as the present study was designed with a structured ED

interview by investigators asking how patients identify the remaining doses of the SABA inhalers, there is a potential for recall bias. Fourth, our study did not investigate the correctness of techniques in inhaled corticosteroid (ICS) use. Yet, it is plausible that there is an association between SABA and ICS inhalers with regard to the inhaler technique. Lastly, our data were collected in urban teaching hospital EDs, which might not be generalizable to other clinical settings. Nevertheless, our results are directly relevant to the ED populations with asthma exacerbation that account for 1.6 million ED visits each year in the US.⁹

Based on the multicenter data of 203 ED patients with asthma exacerbation in 2015-2017, we observed that only 24% used the dose counter to identify remaining doses of their SABA inhaler and inhalation technique was suboptimal. These findings might be attributable to modifiable factors, such as underutilization of written action plans, lack of education in appropriate inhaler use, and individual health behaviors of patients preferring ED as their source of asthma care. These observations reflect the failure of current measures to manage these patients, and signal ongoing gaps in asthma care. Our findings should encourage clinicians and researchers to develop educational interventions to optimize patient's self-asthma management and inhaler use (e.g. advising patients to keep track of doses), which will improve disease control and reduce acute healthcare utilizations in patients with asthma.

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Table 1. Methods used by emergency department patients with asthma exacerbation to identify remaining of their short-acting beta-agonist inhalers and acts taken when discovering the empty inhaler (n=203)

	n (%)
Having inhaler with an integrated dose counter	187 (92)
Ever received instructions on how to use a quick relief inhaler	174 (86)
Ever been shown how to find the number of doses	129 (64)
Ever been advised to keep track of the number of doses	69 (34)
Unable to identify the number of doses remaining	52 (26)
Methods to identify the number of doses*	
Spray testing	65 (32)
Dose counter	49 (24)
Shake testing	16 (8)
Track record of inhaler use	1 (<1)
Float testing	1 (<1)
Ever found inhaler empty when needed	107 (53)
Acts taken when patients discovered the “quick relief” inhaler was empty	
Presented to emergency department	23 (23)
Called physician's office	20 (20)
Use home / handy nebulizer	12 (12)
Went to urgent care or doctor's office	10 (10)

Called ambulance	7 (7)
Use family or friend's inhaler	7 (7)
Use back-up inhaler	5 (5)
Call family member or friend	3 (3)
Call pharmacy	3 (3)
Other†	9 (9)

167 * Among 107 patients who answered, "yes" to the following question: "Have you ever needed the "quick
 168 relief" inhaler and found that it was empty?" some patients selected ≥ 2 methods to identify remaining
 169 dose. Therefore, the sum of the numbers is not equal to 107.

170 † Other include "drink a lot of water", "go to bathroom", and "wait it out".

171

Supplemental Table 1. Characteristics of emergency department patients with asthma exacerbation (n=203)

	n (%)
Age (year), median (IQR)	32 (25-44)
Female sex	137 (67)
Pregnant*	4 (3)
Race/ethnicity	
Non-Hispanic white	82 (40)
Non-Hispanic black	58 (29)
Hispanic	53 (26)
Other	10 (5)
Primary health insurance	
Public	105 (52)
Private	92 (45)
No insurance	6 (3)
Educational level	
8 th grade or less	5 (2)
Some high school education	16 (8)
High school graduates and above	54 (27)
Some college	63 (31)
College graduate	52 (26)
Any post-graduate work	13 (6)
Current smoker	40 (20)
Chronic asthma factors	
Asthma Control Test, median (IQR)	13 (10-18)
Hospitalized for asthma in the past year	62 (31)
ED visit for asthma in the past year	111 (55)
Ever intubated for asthma	36 (18)
Current use of oral corticosteroids	64 (32)
Current use of ICS	99 (49)
Current use of leukotriene modifiers	42 (21)
Having a primary care physician	175 (86)
Having an asthma specialist†	117 (58)
ED as preferred source of asthma care	111 (55)
ED as preferred source of prescription for asthma medications	22 (11)
Having a written action plan	67 (33)

Abbreviations: IQR, interquartile range; ED, emergency department; ICS, inhaled corticosteroids

Data are expressed as number (percentage) unless otherwise indicated.

*There were 4 pregnant women among 137 women overall.

† Defined as pulmonologists, allergists, or other providers in asthma clinics.

Supplemental Table 2. Patient techniques of short-acting beta-agonist inhaler use

MDI checklist of proper inhalation technique, performed correctly (%)	<i>n=186</i>
1. Remove mouthpiece cap	183 (98)
2. Shake inhaler (suspensions only)	175 (94)
3. Breathe out before firing	147 (79)
4. Inhaler upright during firing	185 (99)
5. One inhalation for actuation	176 (95)
6. Place mouthpiece between lips and over tongue	181 (97)
7. Actuation in the first half of inhalation	180 (97)
8. Fire while breathing in deeply and slowly and continue until total lung capacity	174 (94)
9. Inhalation by mouth	183 (98)
10. Hold breath for ten seconds	118 (63)
DPI step-by-step checklist of proper inhalation technique, performed correctly (%)	<i>n=5</i>
1. Loading medication dose: open mouthpiece cap	5 (100)
2. Breathe out before inhalation	5 (100)
3. Inhaler upright during firing	4 (80)
4. Place mouthpiece between lips and over tongue	5 (100)
5. Breathe in deeply and slowly and continue until total lung capacity	5 (100)
6. Inhalation by mouth	5 (100)
7. Hold breath for ten seconds	5 (100)
8. Close mouthpiece cap after completing dosing	5 (100)

Abbreviations: ED, emergency department; MDI, metered-dose inhalers; DPI, dry powder inhalers

Data are expressed as number (percentage).