

# Comparing Ran-Out Status of Inhaled Short-Acting Beta-Agonists in Emergency Department Patients with Acute Asthma: 1996-1998 versus 2015-2017



Tadahiro Goto, MD, MPH<sup>a</sup>, Carlos A. Camargo, Jr, MD, DrPH<sup>a</sup>, Catalina Gimenez-Zapiola, BA<sup>a</sup>, Daniel J. Pallin, MD, MPH<sup>b</sup>, Nathan I. Shapiro, MD, MPH<sup>c</sup>, Thomas J. Ferro, MD<sup>d</sup>, Carolyn Rainville, BA<sup>d</sup>, Stanislav Stoyanov, MD, MBA<sup>d</sup>, and Kohei Hasegawa, MD, MPH<sup>a</sup> Boston, Mass; and Frazer, Pa

**What is already known about this topic?** Medication nonadherence in asthma, such as running out of inhaled medications, is a well-recognized problem. However, no study has investigated the temporal changes in the ran-out status of short-acting beta-agonist (SABA) inhalers among the emergency department (ED) patients with acute asthma and their health behaviors.

**What does this article add to our knowledge?** Between 1996 and 2017, the proportion of ED patients with asthma who ran out of SABA inhalers significantly increased (18% in 1996-1998 vs 26% in 2015-2017).

**How does this study impact current management guidelines?** To achieve optimal use of asthma medications by patients, our findings facilitate multifaceted approaches including a written action plan and establishing partnership.

**BACKGROUND:** Medication nonadherence, including running out of inhaled asthma medications, is an important problem.

**OBJECTIVE:** The objective of this study was to examine the changes in the proportion of adults with acute asthma who ran out of their short-acting beta-agonist (SABA) inhalers before presenting to the emergency department (ED) between 1996-1998 and 2015-2017.

**METHODS:** We analyzed data from prospective multicenter observational cohort studies of ED adult patients (aged 18-54 years) with acute asthma. Within the same 3 EDs, we performed a structured interview during 2 time periods: 1996-1998 and 2015-2017. We fitted multivariable models to compare ran-out status between the 2 periods, adjusting for the baseline patient demographics, socioeconomic status, chronic asthma factors, and health care utilization factors. We further adjusted for the presence of a written action plan—an intervenable factor.

**RESULTS:** The analytic cohort comprised 353 patients (150 from the 1996-1998 studies and 203 from the 2015-2017 study).

Over the approximately 20-year period, the proportion of patients who ran out of SABA inhalers increased (18% in 1996-1998 vs 26% in 2015-2017). In the multivariable model, compared with patients in 1996-1998, those in 2015-2017 had a significantly higher risk of running out of their SABA inhalers (adjusted odds ratio [OR] 2.01; 95% confidence interval [CI] 1.06-3.81;  $P = .03$ ). With further adjustment for the presence of a written action plan, this difference attenuated (adjusted OR 1.66; 95% CI 0.75-3.68;  $P = .21$ ).

**CONCLUSIONS:** Between 1996 and 2017, the proportion of ED patients with asthma who ran out of SABA inhalers significantly increased. The increase was explained, at least partially, by a lack of a written action plan. © 2018 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;6:1999-2005)

**Key words:** Asthma; Asthma exacerbation; Inhaled short-acting beta-agonists; Emergency department; Medication nonadherence

<sup>a</sup>Department of Emergency Medicine, Massachusetts General Hospital, Boston, Mass

<sup>b</sup>Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Mass

<sup>c</sup>Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, Mass

<sup>d</sup>Teva Pharmaceuticals Industries, Frazer, Pa

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Corresponding author: Tadahiro Goto, MD, MPH, Department of Emergency Medicine, Massachusetts General Hospital, 125 Nashua Street, Suite 920, Boston, MA 02114-1101. E-mail: tag695@mail.harvard.edu.

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**Abbreviations used**

CI- Confidence interval

ED- Emergency department

ICS- Inhaled corticosteroids

LABA- Long-acting beta-agonist

MARC- Multicenter Airway Research Collaboration

OR- Odds ratio

SABA- Short-acting beta-agonist

Asthma affected 25 million US residents in 2015.<sup>1</sup> Each year, asthma exacerbations account for approximately 1.6 million emergency department (ED) visits.<sup>1</sup> Medication nonadherence in asthma is a well-recognized problem, with adherence rates ranging from 30% to 70%.<sup>2-7</sup> One important form of nonadherence is running out of inhaled medications, such as short-acting beta-agonist (SABA) inhalers.<sup>8</sup>

Studies have demonstrated that patients with asthma often overestimate the remaining amount of asthma medication in their metered dose inhalers.<sup>9</sup> Up to 40% of patients believed that they were taking their asthma medications when they activated an empty or nearly empty inhaler.<sup>10,11</sup> In addition, with continued use of the inhaler beyond the recommended number of doses, active medication delivery per actuation becomes inconsistent and unpredictable.<sup>12</sup> A potential consequence of running out of inhaled medications is suboptimal disease control and ED visits for acute asthma.<sup>9,13</sup> To achieve the optimal use of asthma medications by patients, the national guidelines have underscored the importance of providing asthma education and a written asthma action plan.<sup>14</sup> Nevertheless, no study has investigated the changes in the ran-out status of SABA inhalers in ED patients with acute asthma and their health behavior over the past decades.

To address the knowledge gap, we analyzed the data from 3 similar prospective studies—2 prior studies conducted during 1996-1998 and a new study conducted during 2015-2017—to examine potential changes in the proportion of ED patients with acute asthma who ran out of their SABA inhalers before presenting to the ED.

## METHODS

### Study design and settings

The current analysis combined data from 3 multicenter prospective cohort studies of adult ED patients with acute asthma that were performed in 1996-1998 and 2015-2017, as part of the Multicenter Airway Research Collaboration (MARC). MARC is part of the Emergency Medicine Network,<sup>15</sup> a research collaboration with 245 participating EDs.

In the earlier multicenter prospective observational studies (the MARC-1 and MARC-2 studies), investigators enrolled patients who presented to the ED with acute asthma during 1996-1998. These MARC-1 and MARC-2 studies consisted of structured ED interviews to measure the patients' characteristics and medical record reviews to assess aspects of their ED presentation, asthma management, and disposition. The details of design, setting, and methods for data collection used in the studies have been reported previously.<sup>8</sup>

More recently, and using a similar protocol, we completed the MARC-39 study, a multicenter prospective cohort study that sought to characterize adult ED patients with acute asthma who ran out of their SABA inhalers before presenting to the ED during October

2015 to April 2017. To examine the temporal changes in the running-out status of SABA inhalers in ED patients with acute asthma, we recruited 3 urban EDs in Boston that also had participated in the earlier MARC studies in 1996-1998. The participating EDs were Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, and Massachusetts General Hospital (all in Boston). In both studies (MARC-1/-2 and MARC-39), all patients were managed at the discretion of the treating physician. The institutional review board at each of the participating hospitals approved the studies. Informed consent was obtained from all study participants.

### Study population

We included adults aged 18 to 54 years with a history of asthma and a current prescription for SABA inhaler who presented to the ED with acute asthma. We excluded patients 55 years or older because of potential difficulty in distinguishing between asthma and chronic obstructive pulmonary disease. This inclusion criterion is consistent across the MARC-1, -2, and -39 studies.<sup>8,16</sup> In MARC-1/-2, there were 2670 patients with acute asthma from 64 EDs in North America. Of these, we identified 264 patients who presented to the ED in any of 3 MARC-39 sites in Boston. Among the 264 patients, we excluded 89 patients without information on SABA ran-out status and 25 patients who reported no use of SABA inhalers in the 4 weeks before their index ED visit. The remaining 150 patients in the MARC-1/-2 were eligible for the analysis. In the MARC-39 study, of 215 patients enrolled, we excluded 12 patients who reported no use of SABA inhalers in the 4 weeks before their index ED visit. The remaining 203 patients in MARC-39 were eligible for the current analysis.

### Data collection

In MARC-39, the structured ED interview measured patient demographics, socioeconomic status, Asthma Control Test,<sup>17</sup> chronic asthma history and medications, and health care utilization factors.<sup>18</sup> By using a standardized form,<sup>8,19</sup> medical record review abstracted the data on the index ED visits, including the vital signs, peak expiratory flow, ED course, and ED disposition. All reviewers completed an in-person training session and 2 practice charts (using a detailed manual of procedures), which were then evaluated against a "criterion standard" for these same charts; the criterion was established by a board-certified allergist/immunologist and a board-certified emergency physician. If a reviewer's accuracy was <80% per chart, the reviewer was retrained. To measure post-ED course, site investigators performed follow-up interviews by telephone 2 weeks after the ED visit. These measurements were consistent across the studies (ie, 1996-1998 and 2015-2017 studies).

The primary outcome measure was the ran-out status of SABA inhaler for asthma during the 7-day period before the index ED visit.<sup>8</sup>

### Statistical analysis

First, we used summary statistics to present the patient characteristics, ED course, and post-ED course, and examined their differences between the study periods (1996-1998 and 2015-2017) by using  $\chi^2$ , Fisher's exact, and Mann-Whitney *U* tests, as appropriate. Next, to determine the changes in the proportion of patients with acute asthma who ran out of their SABA inhaler before presenting to the ED between the 2 study periods, we constructed an unadjusted logistic regression model (model 1) and a multivariable logistic regression model adjusting for the patient demographics (age, sex, and race/ethnicity), marker for socioeconomic status (health insurance), chronic asthma factors (ED visits for asthma in

**TABLE I.** Patient characteristics according to the study period

| Characteristics                                                  | 1996-1998<br>n = 150 | 2015-2017<br>n = 203 | P value |
|------------------------------------------------------------------|----------------------|----------------------|---------|
| Patient characteristics                                          |                      |                      |         |
| Demographics                                                     |                      |                      |         |
| Age (y), median (IQR)                                            | 33 (26-42)           | 32 (25-44)           | .32     |
| Female sex                                                       | 105 (70)             | 137 (67)             | .62     |
| Pregnant                                                         | 4 (4)                | 4 (3)                | .70     |
| Race/ethnicity                                                   |                      |                      | .13     |
| Non-Hispanic white                                               | 73 (49)              | 82 (40)              |         |
| Non-Hispanic black                                               | 43 (29)              | 58 (29)              |         |
| Hispanics                                                        | 31 (21)              | 53 (26)              |         |
| Others                                                           | 2 (1)                | 10 (5)               |         |
| Health insurance                                                 |                      |                      | <.001   |
| Private                                                          | 80 (54)              | 92 (45)              |         |
| Public                                                           | 44 (30)              | 105 (52)             |         |
| No insurance                                                     | 25 (17)              | 6 (3)                |         |
| Educational level                                                |                      |                      | .08     |
| Eighth grade or less                                             | 10 (6)               | 5 (2)                |         |
| Some high school education                                       | 58 (39)              | 70 (34)              |         |
| High school graduate                                             | 82 (55)              | 128 (63)             |         |
| Current smoker                                                   | 47 (31)              | 40 (20)              | .02     |
| Chronic asthma factors                                           |                      |                      |         |
| Asthma Control Test, median (IQR)                                | —                    | 13 (10-18)           | —       |
| Hospitalized for asthma in the past year                         | 51 (34)              | 62 (31)              | .49     |
| ED visit for asthma in the past year                             | 90 (64)              | 111 (55)             | .09     |
| Ever intubated for asthma                                        | 26 (17)              | 36 (18)              | .92     |
| Current use of oral corticosteroids                              | 40 (27)              | 64 (32)              | .32     |
| Current use of ICS                                               | 92 (61)              | 99 (49)              | .02     |
| Current use of ICS/long-acting beta-agonist inhalers             | 12 (8)               | 78 (41)              | <.001   |
| Current use of leukotriene modifiers                             | 0 (0)                | 42 (20)              | <.001   |
| Having primary care physician                                    | 127 (85)             | 175 (86)             | .68     |
| Having asthma specialist                                         | —                    | 117 (58)             | —       |
| ED as a preferred source for asthma care                         | 87 (58)              | 111 (55)             | .59     |
| ED as a preferred source of prescriptions for asthma medications | 25 (17)              | 22 (10)              | .11     |
| Having written action plans                                      | 45 (52)              | 67 (32)              | .003    |

Data were expressed as n (%) unless otherwise indicated.

ED, Emergency department; ICS, inhaled corticosteroid; IQR, interquartile range.

the preceding year, use of inhaled corticosteroids [ICS] and ICS/long-acting beta-agonist [LABA] combined therapy), and health care utilization factors (ED as a preferred source of asthma care, ED as a preferred source of prescriptions for asthma medications) (model 2).<sup>8</sup> Furthermore, to investigate the potential contribution of having a written action plan—an intervenable factor—we fitted another multivariable model adjusting for the covariates above and written action plan status (model 3). In the sensitivity analysis, we also fit another multivariable model adjusting for the covariates above and patient comorbidity. For all regression models, random-effects models were used to account for potential patient clustering within the hospitals. We also compared selected variables that are potentially related to the outcome (ie, ED as a preferred source for asthma care, ED as a preferred source of prescriptions for asthma medications, and having written action plans), among patients who ran out of their SABA inhalers.<sup>8</sup> All analyses were conducted using STATA version 14.1 software (StataCorp, College Station, Tex). A 2-sided  $P < .05$  was considered statistically significant.

## RESULTS

The analytic cohorts comprised 353 adult patients: 150 patients from 1996-1998 and 203 patients from 2015-2017. In both study periods, there were no significant differences in patient demographics between the analytic and nonanalytic cohorts (all  $P > .05$ ; Table E1 in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). Between the analytic cohorts, there were no significant differences in age, sex, race/ethnicity, and educational level (all  $P \geq .05$ ; Table I). However, patients in the recent cohort were more likely to have public insurance and were less likely to be current smokers (both  $P < .05$ ). With regard to the chronic asthma factors, ED patients in more recent years were more likely to use ICS/LABA combined therapy and leukotriene modifiers (both  $P < .001$ ). Although most patients had a primary care physician in both time periods (85% in 1996-1998 vs 86% in 2015-2017;  $P = .68$ ), the majority continued to report the ED as their preferred source for asthma care (58% vs 55%;  $P = .68$ ). Despite the persistently high

**TABLE II.** Unadjusted and adjusted changes in the proportion of patients with acute asthma who ran out of their short-acting beta-agonist inhaler before the emergency department visit between 1996-1998 and 2015-2017

|                                                                  | Unadjusted model (model 1)*<br>OR (95% CI) | P value | Adjusted model (model 2)*<br>Adjusted OR (95% CI) | P value | Adjusted model (model 3)*<br>Adjusted OR (95% CI) | P value |
|------------------------------------------------------------------|--------------------------------------------|---------|---------------------------------------------------|---------|---------------------------------------------------|---------|
| 2015-2017 (vs 1996-1998)                                         | 1.61 (0.96-2.71)                           | .07     | 2.01 (1.06-3.81)                                  | .03     | 1.66 (0.75-3.68)                                  | .21     |
| Covariates                                                       |                                            |         |                                                   |         |                                                   |         |
| Age ≥45 y (vs age <45 y)                                         | —                                          |         | 0.62 (0.30-1.27)                                  | .19     | 0.64 (0.30-1.38)                                  | .26     |
| Female (vs male)                                                 | —                                          |         | 1.02 (0.57-1.83)                                  | .94     | 1.01 (0.54-1.89)                                  | .98     |
| Race/ethnicity                                                   |                                            |         |                                                   |         |                                                   |         |
| Non-Hispanic white                                               | —                                          |         | 1 (reference)                                     | —       | 1 (reference)                                     | —       |
| Non-Hispanic black                                               | —                                          |         | 1.33 (0.67-2.62)                                  | .42     | 1.38 (0.67-2.87)                                  | .38     |
| Others                                                           | —                                          |         | 1.82 (0.95-3.49)                                  | .07     | 1.87 (0.92-3.80)                                  | .09     |
| Public insurance (vs nonpublic)                                  | —                                          |         | 1.01 (0.58-1.78)                                  | .96     | 1.12 (0.61-2.04)                                  | .72     |
| ED visit for asthma in the past year                             | —                                          |         | 1.23 (0.65-2.34)                                  | .53     | 1.00 (0.49-2.03)                                  | .99     |
| Current use of ICS                                               | —                                          |         | 0.81 (0.44-1.49)                                  | .50     | 0.81 (0.41-1.57)                                  | .53     |
| Current use of ICS/LABA                                          | —                                          |         | 0.80 (0.40-1.63)                                  | .55     | 0.86 (0.42-1.78)                                  | .69     |
| ED as a preferred source for asthma care                         | —                                          |         | 0.91 (0.48-1.71)                                  | .76     | 1.01 (0.51-2.03)                                  | .97     |
| ED as a preferred source of prescriptions for asthma medications | —                                          |         | 2.48 (1.17-5.24)                                  | .02     | 2.51 (1.10-5.72)                                  | .03     |
| Having written action plans                                      | —                                          |         | —                                                 |         | 0.88 (0.46-1.66)                                  | .68     |

CI, Confidence interval; ED, emergency department; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; OR, odds ratio.

\*Random-effects models accounting for patient clustering within the hospitals.

chronic asthma burden (eg, 64% and 55%, respectively, had an ED visit for asthma in the preceding year), the proportion of patients who had not received a written action plan increased significantly over the study period (48% vs 68%;  $P = .003$ ).

Table E2 (available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)) demonstrates the ED presentations and course as well as post-ED course according to the study period. There were no clinically important differences in the vital signs or peak expiratory flow measurement between the 2 time periods. Compared with the patients in the 1996-1998 period, those in the 2015-2017 period had modestly lower respiratory rate and higher oxygen saturation at the presentation while they were more likely to have concomitant medical disorders. In addition, those in the 2015-2017 period were more likely to receive inhaled anticholinergics and intravenous magnesium in the ED (both  $P < .001$ ). Although the statistical power is limited, there were no significant differences in the proportion of relapse or ED revisit (both  $P > .05$ ).

Over the approximately 20-year period, the proportion of patients with acute asthma who ran out of their SABA inhaler before the ED visit remained high (18% in 1996-1998 vs 26% in 2015-2017; unadjusted odds ratio [OR] 1.61; 95% confidence interval [CI] 0.96-2.71;  $P = .07$ ; Table II). After adjusting for the 9 baseline patient characteristics (Model 2), the patients in more recent years had a significantly higher risk of running out of their SABA inhalers (adjusted OR 2.01; 95% CI 1.06-3.81;  $P = .03$ ). With further adjustment for written action plan status, this association attenuated (model 3 adjusted OR 1.66; 95% CI 0.75-3.68;  $P = .21$ ), suggesting that some of the difference in the ran out status is explained by a lack of a written action plan. In the multivariable model adjusting for the covariates including patient comorbidity, the results did not materially change (Table E3, available in this article's Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). In these models, the use of ED as a

preferred source of prescriptions for asthma medications was associated with a significantly higher risk of ran-out status. In contrast to the ran-out status of SABA inhalers, that of ICS did not change significantly between the study periods (5% in 1996-1998 vs 6% in 2015-2017;  $P = .37$ ).

Figure 1 shows selected factors that may be related to medication adherence, according to the study period. Among patients who did not run out of SABA inhalers, the proportion of patients who preferred the ED as the source of asthma care decreased over the study period (59% in 1996-1998 vs 51% in 2015-2017) in contrast to an apparent increase among the patients who ran out of SABA inhalers (56% in 1996-1998 vs 66% in 2015-2017). In addition, the proportion of ED use as the prescription for asthma medications decreased both in patients who did not run out of SABA inhalers (14% in 1996-1998 vs 8% in 2015-2017) and in those who did (30% in 1996-1998 vs 19% in 2015-2017). Among the patients who ran out of SABA inhalers, 70% of the 2015-2017 patients reported not having a written action plan before their index ED visit.

## DISCUSSION

In this multicenter analysis based on 3 prospective observational studies of 353 adult patients with acute asthma, we observed that, within the same EDs over approximately 20 years, the proportion of patients who ran out of SABA inhalers before their ED visit increased from 18% to 26%. This between-period difference was significant after adjusting for the baseline patient-level characteristics and patient clustering within the hospitals (model 2). Among the patients who ran out of their SABA inhalers, the proportion of patients who preferred the ED as the source of asthma care and prescription remained high. In addition, 70% of these patients reported that they had not received a written asthma action plan before their index ED visit in

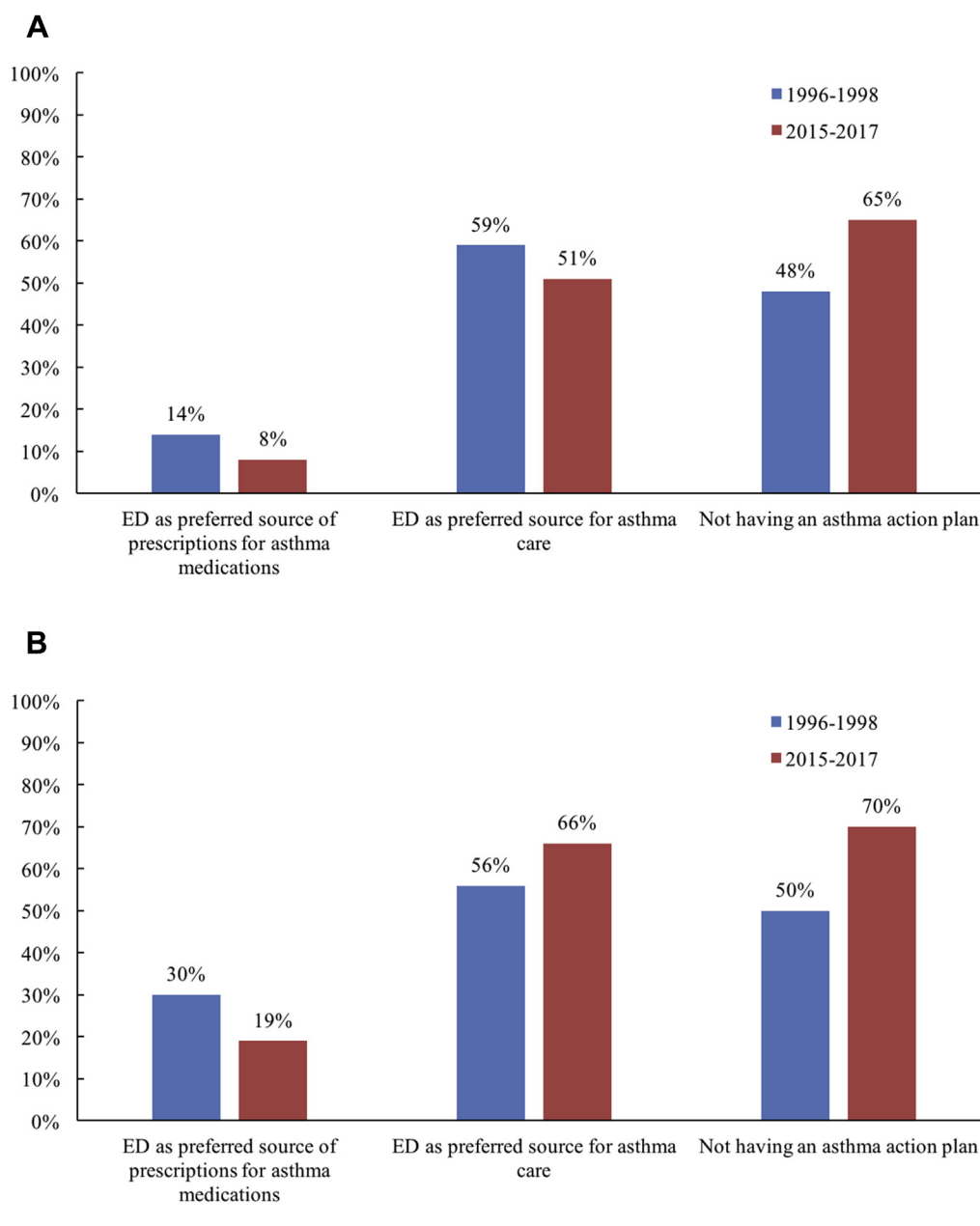


**FIGURE 1. A,** Factors potentially related to medication adherence among patients who did not run out of their short-acting beta-agonist inhalers, according to study period. **B,** Factors potentially related to medication adherence among patients who ran out of their short-acting beta-agonist inhalers, according to study period. Between the 1996-1998 and 2015-2017 study periods, among patients who did not run out of their short-acting beta-agonist (SABA) inhalers before the ED visit, the proportion of patients who preferred the ED as the preferred source of care remained high (59% vs 51%;  $P = .19$ ). In addition, the proportion of patients who reported not having written action plans significantly increased (48% vs 65%;  $P = .02$ ) between the 2 study periods. Among patients who ran out of their SABA inhalers before the ED visit, the proportion of patients who preferred the ED as the source of care and prescription for asthma medications remained high (56% vs 66% in asthma care,  $P = .47$ ; and 30% vs 19% in prescription for asthma medications,  $P = .28$ ). In addition, the proportion of patients who reported not having written action plans nonsignificantly increased (50% vs 70%;  $P = .11$ ) between the 2 study periods. ED, Emergency department.

2015-2017. Further adjustment for written action plan status—an intervenable factor—attenuated the between-period difference (model 3), indicating that some of the difference in the ran-out status is explained by a lack of a written action plan. To the best

of our knowledge, this is the first study that has investigated the change in the ran-out status of SABA inhalers over the 2 decades.

We are struck by the persistently high proportion of patients who ran out of their SABA inhaler in the ED population during

the 2 study periods. The importance of asthma medication adherence has been widely recognized, particularly among patients with poor disease control.<sup>14</sup> Thus, an improvement of asthma medication adherence has been of great interest to a variety of stakeholders. Indeed, the US government has identified improving asthma care and reducing ED visits as national objectives in the “*Healthy People 2020*” via “increasing the proportion of persons with current asthma with prescribed inhalers who receive instruction on their use.”<sup>20</sup> There are several potential explanations for the observed lack of improvement (and the increase) in the inhaler ran-out status in the ED population. First, the importance of the instruction for the appropriate use of SABA inhalers has not been fully realized.<sup>9,21</sup> For example, a survey of 342 adult patients with asthma reported that only 36% have been advised to keep track the dose and that 82% used “spray testing” to assess their inhaler contents.<sup>9</sup> Second, the lack of written action plans may also have contributed to the observed high ran-out status in this population.<sup>22</sup> Third, we found that ED as the preferred source of prescriptions for asthma medications was associated with a higher risk of ran-out status in the multivariable model. However, the observed decrease in its proportion does not fully explain the main inference (ie, the increase in the ran-out status). Lastly, the increased cost due to the limited availability of branded albuterol inhalers in the recent market might have led to lack of refills and purchase of the medication, thereby contributing to the observed increase in the ran-out status.

Our data also show that the proportion of patients who reported to have no written action plans increased over the 2 time periods and that lack of a written action plan explained, at least partially, the risk of SABA inhaler ran-out status. Our finding is consistent with prior studies reporting that asthma education and written action plans are underused.<sup>23–25</sup> Indeed, a recent multicenter study of US patients hospitalized for asthma demonstrated that approximately 40% of patients did not receive a written action plan at hospital discharge.<sup>24</sup> Furthermore, our data also indicate that individual health behavior may be related to this type of medication nonadherence. We found that, among the patients who ran out of their SABA inhaler, approximately 60% used the ED as the preferred source of asthma care and 20% preferred the ED as the source of asthma medication prescriptions. Any of combination of these potential mechanisms may explain our primary finding—the persistently high SABA inhaler ran-out status in ED patients with acute asthma.

To achieve the optimal use of asthma medications by patients, health care providers can implement several strategies.<sup>26</sup> First, care coordination and self-management education in the ED have been reported as the key domains for the improvement of adherence. For example, implementation of the asthma care pathway in the ED care increased patient recollection of teaching done in the ED and referral rates to primary care physician.<sup>27,28</sup> Yet, there is conflicting evidence that when patients relate that they “have” a primary care physician, it does not necessarily mean that they are managed in primary care setting.<sup>29,30</sup> As a component of self-management education in the ED, providers should give patients a written action plan according to the national guidelines.<sup>14</sup> Studies have indicated the provision of an individualized written action plan—including the appropriate use of medications and guidance for changing the dose or adding medications, and information for acute health care resource—improves asthma health outcomes.<sup>23,31</sup> In addition, establishing

partnership is also an important step to change the personal health behavior—physicians should discuss the goals of asthma therapy including the optimal use of SABA inhalers with the patient.<sup>32,33</sup> Furthermore, there have been many recommendations to improve inhalers—For example, an integration of simple dose-counting mechanism although it has been only available since the last decade. Emerging evidence indicates that the advanced technology may improve the medication adherence in patient with asthma. For example, a clustered randomized controlled trial of 143 adult patients with moderate-to-severe asthma reported that electronic inhaler reminders improved the medication adherence to the use of prescribed asthma controllers compared with a behavioral intervention or usual care.<sup>34</sup> Another randomized controlled trial of 408 adult patients with asthma also demonstrated that simple and brief online patient reminders improved their Asthma Control Test score.<sup>35</sup> These innovative tools (eg, “smart inhalers,” which use Bluetooth technology to detect inhaler use, remind patients when to take their medication and gather data to help guide care) should offer a novel avenue for optimizing the medication adherence in patients with asthma.

### Potential Limitations

Several potential limitations should be noted. First, although our data were collected within the same EDs in these 2 periods, the enrolled patients were not identical across the studies. Nevertheless, despite the persistently high chronic asthma burden among the patients in recent years, our data demonstrated no decrease in the medication ran-out status, indicating an important gap in asthma care. Second, selection bias may exist through missing information on ran-out status and patient enrollment processes. However, there were no significant differences in the patient demographics between the analytic and nonanalytic cohorts in both study periods, minimizing this concern. Third, our data did not include the information on outpatient management or cost data that might be related to the medication ran-out status, such as asthma self-management education. In addition, our data also did not include psychosocial problems and barriers to health care access in this population. Fourth, this study relied on patients’ self-report on the SABA ran-out status; therefore, error in data measurement is possible. However, we measured this outcome by using a standardized structured interview in both the time periods. Lastly, because our observations were based on the EDs of urban, teaching hospitals in Boston, these results may not be generalizable to other clinical settings, such as community hospitals. However, urban populations have disproportionately high morbidity of asthma,<sup>36</sup> and it is precisely this population for which targeted preventive measures are most urgently needed.

### CONCLUSIONS

Between 1996 and 2017, the proportion of ED patients with acute asthma who ran out of SABA inhalers significantly increased. The increase was explained, at least partially, by a lack of a written action plan. These findings present important gaps in the current asthma management. Our data should encourage researchers, policymakers, and industry to develop more effective, multifaceted approaches to improve patients’ medication adherence, which will, in turn, lead to better asthma care and mitigate the asthma-related health care utilization.

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## ONLINE REPOSITORY

TABLE E1. Patient demographics in analytic and nonanalytic cohorts, according to the study periods

|                            | Analytic cohort | Nonanalytic cohort |         |
|----------------------------|-----------------|--------------------|---------|
|                            | n = 150         | n = 114            | P value |
| <b>1996-1998</b>           |                 |                    |         |
| Age (y), median (IQR)      | 33 (26-42)      | 33 (25-40)         | .84     |
| Female sex                 | 105 (70)        | 78 (68)            | .78     |
| Race/ethnicity             |                 |                    | .33     |
| Non-Hispanic white         | 73 (49)         | 46 (51)            |         |
| Non-Hispanic black         | 43 (29)         | 24 (26)            |         |
| Hispanics                  | 31 (21)         | 18 (19)            |         |
| Others                     | 2 (1)           | 4 (4)              |         |
| Health insurance           |                 |                    | .77     |
| Private                    | 80 (54)         | 56 (49)            |         |
| Public                     | 44 (30)         | 34 (30)            |         |
| No insurance               | 25 (17)         | 24 (21)            |         |
| Educational level          |                 |                    | .88     |
| Eighth grade or less       | 10 (6)          | 1 (4)              |         |
| Some high school education | 58 (39)         | 10 (40)            |         |
| High school graduate       | 82 (55)         | 14 (56)            |         |
| Current smoker             | 47 (31)         | 22 (41)            | .21     |
| <b>2015-2017</b>           |                 |                    |         |
|                            | n = 203         | n = 12             | P value |
| Age (y), median (IQR)      | 32 (25-44)      | 31 (27-37)         | .74     |
| Female sex                 | 137 (67)        | 10 (83)            | .25     |
| Race/ethnicity             |                 |                    | .41     |
| Non-Hispanic white         | 82 (40)         | 4 (33)             |         |
| Non-Hispanic black         | 58 (29)         | 6 (50)             |         |
| Hispanics                  | 53 (26)         | 2 (17)             |         |
| Others                     | 10 (5)          | 0                  |         |
| Health insurance           |                 |                    | .32     |
| Private                    | 92 (45)         | 8 (67)             |         |
| Public                     | 105 (52)        | 4 (33)             |         |
| No insurance               | 6 (3)           | 0 (0)              |         |
| Educational level          |                 |                    | .35     |
| Eighth grade or less       | 5 (2)           | 0                  |         |
| Some high school education | 70 (34)         | 2 (17)             |         |
| High school graduate       | 128 (63)        | 10 (83)            |         |
| Current smoker             | 40 (20)         | 4 (33)             | .27     |

Data were expressed as n (%) unless otherwise indicated.

IQR, Interquartile range.

**TABLE E2.** Emergency department (ED) course and post-ED course, according to the study period

|                                                         | 1996-1998<br>n = 150 | 2015-2017<br>n = 203 | P value |
|---------------------------------------------------------|----------------------|----------------------|---------|
| ED presentations                                        |                      |                      |         |
| Initial respiratory rate (breaths/min), median (IQR)    | 24 (20-28)           | 20 (18-24)           | <.001   |
| Initial oxygen saturation (%), median (IQR)             | 96 (94-98)           | 97 (95-99)           | .006    |
| Peak expiratory flow (L/min), median (IQR)*             | 220 (160-280)        | 248 (170-305)        | .26     |
| Concomitant medical disorder†                           | 16 (11)              | 46 (21)              | .01     |
| ED management                                           |                      |                      |         |
| Inhaled anticholinergics                                | 9 (6)                | 112 (55)             | <.001   |
| Systemic corticosteroids                                | 91 (63)              | 143 (70)             | .07     |
| Intravenous magnesium                                   | 2 (1)                | 38 (19)              | <.001   |
| Noninvasive positive pressure ventilation               | 0 (0)                | 3 (1)                | .27     |
| ED disposition                                          |                      |                      |         |
| Sent home                                               | 88 (59)              | 116 (57)             | .83     |
| Hospitalization (hospital ward and/or observation unit) | 60 (41)              | 82 (40)§             | .94     |
| ICU admission                                           | N/A                  | 4 (2)                | —       |
| Other (eg, left against medical advice)                 | 2 (1)                | 1 (1)                | .58     |
| VRelapse within 2 wk from the ED discharge‡             |                      |                      |         |
| ED revisit                                              | 18 (12)              | 10 (6)¶              | .10     |
| Hospital readmission                                    | N/A                  | 5 (3)¶               | —       |

ICU, Intensive care unit; IQR, interquartile range.

\*Analyzed for 134 patients in the MARC-1 study (1996-1998) and 80 patients in the MARC-39 study (2015-2017) with initial peak expiratory flow data available.

†Including pneumonia, pneumothorax, congestive heart failure, arrhythmia, otitis, sinusitis, and others.

‡Worsening asthma exacerbation that led to urgent medical treatment, including clinic visit, ED visit, and hospitalization within 2 wk from the index ED discharge.

§A total of 57 (28%) patients were admitted to the observation unit.

¶Analyzed for 162 patients with a response to the follow-up question.

**TABLE E3.** Adjusted changes in the proportion of patients with acute asthma who ran out of their short-acting beta-agonist inhaler before the emergency department visit between 1996-1998 and 2015-2017

|                                                                | Adjusted OR (95% CI)* | P value |
|----------------------------------------------------------------|-----------------------|---------|
| 2015-2017 (vs 1996-1998)                                       | 1.74 (0.78-3.90)      | .18     |
| Covariates                                                     |                       |         |
| Age $\geq 45$ y (vs age $< 45$ y)                              | 0.69 (0.32-1.50)      | .35     |
| Female (vs male)                                               | 1.00 (0.53-1.89)      | .99     |
| Race/ethnicity                                                 |                       |         |
| Non-Hispanic white                                             | 1 (reference)         | —       |
| Non-Hispanic black                                             | 1.36 (0.65-2.84)      | .41     |
| Others                                                         | 1.84 (0.90-3.76)      | .09     |
| Public insurance (vs nonpublic)                                | 1.09 (0.59-2.00)      | .78     |
| ED visit for asthma in the past year                           | 1.05 (0.51-2.16)      | .89     |
| Current use of ICS                                             | 0.78 (0.40-1.53)      | .47     |
| Current use of ICS/LABA                                        | 0.90 (0.43-1.86)      | .78     |
| ED as preferred source for asthma care                         | 0.98 (0.49-1.96)      | .95     |
| ED as preferred source of prescriptions for asthma medications | 2.54 (1.11-5.80)      | .03     |
| Having written action plans                                    | 0.86 (0.45-1.63)      | .64     |
| Having any comorbidity                                         | 0.61 (0.25-1.47)      | .27     |

CI, Confidence interval; ED, emergency department; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; OR, odds ratio.

\*Random-effects model accounting for patient clustering within the hospitals.