

Corticosteroid Use after Hospital Discharge among High-risk Adults with Asthma

Jerry A. Krishnan, Kristin A. Riekert, Jonathan V. McCoy, Dana Y. Stewart, Spencer Schmidt, Arjun Chanmugam, Peter Hill, and Cynthia S. Rand

Departments of Medicine and Emergency Medicine, Johns Hopkins University, Baltimore, Maryland; Department of Emergency Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; and Department of Pediatrics, Wright State University, Dayton, Ohio

Despite the efficacy of corticosteroid therapy, patients hospitalized for asthma exacerbations are at high risk for re-exacerbation and death after discharge. The objective of this prospective cohort study was to evaluate adherence to inhaled corticosteroids (ICS) and oral corticosteroids (OCS) after discharge in adults hospitalized for asthma exacerbations. ICS and OCS were equipped with electronic medication monitors and were provided at discharge. Adherence (use/prescribed use \times 100%) was measured by self-report and canister weight (ICS), pill count (OCS), and electronic medication monitors (both ICS and OCS) 2 weeks after discharge. Poor adherence was defined as adherence of less than 50%. The Asthma Control Questionnaire was used to assess symptom control. Sixty patients were enrolled (age 42.2 years, 98.3% African American, 65.0% female, 46.7% with history of near-fatal asthma). Electronically measured adherence to both corticosteroids dropped to approximately 50% within 7 days of discharge. Poor adherence to both corticosteroids predicted significantly worse symptom control ($p = 0.04$). Self-report, canister weight, and pill count all had low sensitivity (29.2%, 65.0%, and 7.7%, respectively) for detecting poor adherence. We conclude that adherence to ICS and OCS deteriorates within days of hospital discharge but may not be recognized in a substantial proportion of patients.

Keywords: adherence; asthma; exacerbation; severe asthma; hospitalization

Asthma affects 15 to 20 million people in the United States and is characterized by chronic airway inflammation and episodic respiratory symptoms (1). Although there are effective medical therapies, severe asthma exacerbations are common and result in approximately 465,000 hospitalizations and nearly 5,000 deaths per year (2). Hospitalizations represent the single largest portion of the estimated annual \$12.7 billion in asthma-related expenditures (3) and serve as a marker of disease severity, which strongly predicts risks of re-exacerbation, readmission, near-fatal asthma (NFA), and death in the subsequent 12 months (4–7). These poor outcomes are particularly common among African-American and inner-city patients, where, for example, both hospitalizations and deaths related to asthma exacerbations are two to three times more likely than in other patient populations (1, 8–10).

Several cross-sectional and retrospective studies suggest that overreliance on symptom relief and underuse of medications effective for long-term asthma control are common in patients who present with severe exacerbations resulting in hospitalizations and/or deaths (11–13). Although corticosteroids are widely used for the treatment of patients hospitalized for severe asthma exacerbations, there are no published studies that have prospectively examined patterns and time trends in patients' use of corticosteroids after hospital discharge. Such data are critical to further our understanding about the determinants of poor outcomes in this high-risk population. The primary objective of this study was to evaluate adherence to inhaled and oral corticosteroid therapy after discharge home in an inner-city adult population hospitalized for asthma exacerbations, a population at high risk for near-fatal and fatal re-exacerbations. Preliminary results of this study have been previously reported in the form of an abstract (14).

METHODS

This was a 2-week prospective cohort study conducted from April 2001 through October 2002. Adults (≥ 18 years) admitted with a physician diagnosis of asthma exacerbation to an innercity academic medical center were screened for eligibility. Patients who had another chronic respiratory disorder or contraindication to inhaled corticosteroids (ICS) and/or oral corticosteroids (OCS), patients discharged to locations other than home, patients whose physician declined consent, investigators' patients, and previous participants of this study were excluded. Asthma medications prescribed after hospital discharge were standardized and provided for free as follows: prednisone (20 mg/tablet, two tablets each morning for 7 days), fluticasone via metered-dose inhaler (MDI) (220 μ g/puff, two puffs twice every day), albuterol MDI (two puffs every 4 hours as needed), and a spacer. Patients received training to optimize the MDI technique as well as written and verbal instructions about their asthma medication regimen. Teaching was repeated until participants could successfully demonstrate mastery of their medication regimen and appropriate MDI and spacer technique. Based on a review of medical records and patient responses to an interviewer-administered survey, patients were classified as (1) previous NFA only (mechanical ventilation during a previous but not current exacerbation), (2) current NFA (mechanical ventilation during current exacerbation), or (3) no NFA (no history of mechanical ventilation).

At a 2-week follow-up visit, participants returned study medications and completed a survey about corticosteroid use and asthma symptoms during the past 7 days. To minimize interviewer bias, medication data were collected after the follow-up survey. Three measures were used to assess adherence to corticosteroid therapy (percentage of prescribed dose = use/prescribed use \times 100%): (1) Self-reported use of ICS: Participants were shown a fluticasone MDI canister and asked the following question: "How many puffs of did you use on each of the past 7 days, starting with today?" We recorded the number of puffs that they reported using each day and added the total number of puffs over the 7-day period. (2) Medication measurement (ICS and OCS): Differences in canister weights and pill counts between hospital discharge and follow-up were used to calculate a mean ICS and OCS use after discharge, respectively. (3) Electronic monitoring (ICS and OCS): Validated electronic medication monitors were employed to measure each day the use of ICS (Doser CT; Meditrac, Inc., Hudson, MA) (15,

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Correspondence and requests for reprints should be addressed to Jerry A. Krishnan, M.D., Johns Hopkins Asthma & Allergy Center, 5501 Hopkins Bayview Circle, Room 4B.74, Baltimore, MD 21224. E-mail: jkrishnan@jhmi.edu

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16) and OCS (MEMS TrackCap; AARDEX Ltd., Union City, CA) (17–19). Participants were informed that medication use was assessed but were not told about the precise monitoring abilities of the devices (i.e., ability to record number of uses each day). In the analyses, electronically measured use was truncated at 100% adherence each day to prevent excess use on some days (e.g., test puffs or deliberate emptying of canister) from masking underuse on other days.

Poor adherence to ICS was defined *a priori* as mean electronically measured ICS use less than 50% from hospital discharge to the follow-up visit. Poor adherence to OCS was defined as electronically measured use of OCS less than 50% during the first 7 days after hospital discharge. Asthma symptom control was assessed using the symptom items from the Asthma Control Questionnaire (20). Possible symptom scores range from 0 (well controlled) to 6 (extremely poorly controlled), reflecting the level of symptom control during the past 7 days.

Descriptive statistics employed means (SD or SE, as indicated), medians, and proportions. Student's *t* tests, chi-square tests, and Pearson's correlation coefficient were employed in bivariate analyses. Backward stepwise multivariable logistic regression models were used to identify the most influential predictors of poor adherence to ICS and poor adherence to OCS. A two-tailed *p* value of less than 0.05 defined statistical significance. Computations were performed using STATA, version 7.0 (21). Additional details regarding the methods are available in an online supplement.

RESULTS

Of 185 admissions for asthma exacerbations, 101 met exclusion criteria: history of another chronic lung disease (*n* = 35), discharged to a location other than home (*n* = 7), physician-declined consent (*n* = 7), clinic patient of an investigator (*n* = 6), contraindication to corticosteroids (*n* = 5), and 41 admissions among previous study participants (representing 25 unique patients). Of 84 eligible patients, 16 (19.0%) declined consent, and 8 (9.5%) could not be contacted before hospital discharge. Sixty of 84 eligible patients (71.4%) were enrolled; their mean age was 42.2 years. Most were women, African American, unemployed, and unmarried (Table 1). There was substantial evidence of previous asthma morbidity among participants, with approximately half reporting at least one other hospitalization and 80.0% with at least one other emergency department (ED) visit for an asthma exacerbation in the previous 12 months. Nearly half (46.7%) the participants had either a previous or current episode of NFA.

Fifty-two participants (86.7%) returned for their 2-week fol-

low-up visit. ICS adherence data were available in 49 of 60 (81.7%) participants, and OCS adherence data were available in 48 of 60 (80.0%) participants. Adherence to both ICS and OCS were available in 46 of 60 (76.7%) participants. Younger participants (34.5 vs. 44.6 years, *p* = 0.002) and men (61.9% vs. 84.6%, *p* = 0.05) were less likely to have complete (both ICS and OCS) adherence data. Other baseline patient characteristics were similar whether or not study medications were returned at follow-up.

Use of ICS

Comparison between measures of ICS use. Electronic monitoring data indicated that the overall use of ICS after hospital discharge was significantly lower than measurements by canister weights (55.9% ± 4.4% vs. 77.4% ± 6.2%, *p* < 0.0001; mean ± SE). Electronic data indicated that only one participant used ICS everyday as prescribed after hospital discharge, with 20 (40.8%) participants demonstrating poor adherence to ICS after discharge home. The sensitivity of canister weight for identifying patients with poor adherence to ICS was 65.0% (13 of 20 participants).

In the 7 days before the follow-up visit, self-reported corticosteroid use was higher than was measured by electronic monitors (85.8% ± 5.0% vs. 51.1% ± 5.0%, *p* < 0.0001). In this period, 24 (49.0%) patients had poor adherence based on electronic medication data. The sensitivity of self-report for identifying electronically measured poor adherence was 29.2% (7 of 24 participants).

Patterns and predictors of ICS use. The mean electronically measured use of ICS fell an average 2.7% per day (*p* < 0.0001; Figure 1) to 48.1% at 2 weeks. In a multivariable backward stepwise logistic regression model, there was a trend suggesting poor ICS adherence was more likely among participants with previous NFA (odds ratio vs. no NFA or current NFA, 3.49;

TABLE 1. PATIENT CHARACTERISTICS*

	Participants (<i>n</i> = 60)
Sociodemographics	
Age, mean yr (SD)	42.2 (10.8)
Female	39 (65.0)
Race	
African American	59 (98.3)
White	1 (1.7)
Employed full-time or part-time	18 (30.0)
Married	7 (11.7)
Asthma-related healthcare use	
Hospitalization past 12 mo [†]	32 (53.3)
Median (interquartile range)	1 (0 to 2)
ED visit past 12 mo [†]	48 (80.0)
Median (interquartile range)	3 (1 to 7)
NFA	
Previous NFA only	20 (33.3)
Current NFA	8 (13.3)

Definition of abbreviations: ED = emergency department; NFA = near-fatal asthma.

* Number (%) unless otherwise noted.

[†] Excludes current hospitalization/emergency department visit.

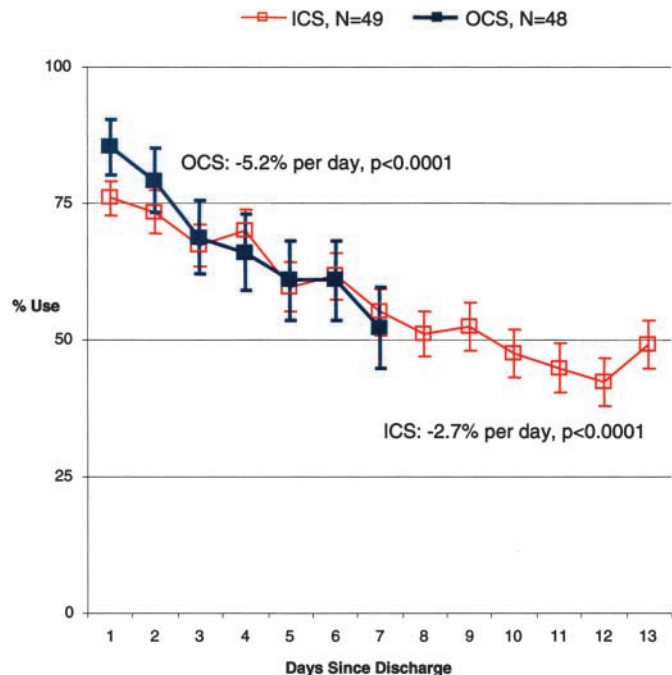


Figure 1. Corticosteroid use after hospital discharge home. Electronically measured use (percentage prescribed dose; error bars represent SE) of inhaled corticosteroids (ICS) and oral corticosteroids (OCS) after hospital discharge. Use was measured using electronic medication monitors.

95% confidence interval, 0.93–13.14; $p = 0.06$). Patients with a current NFA were less likely than patients with no NFA to demonstrate poor adherence to ICS after discharge home, although the difference between groups was not significant (odds ratio, 0.22; 95% confidence interval, 0.02–2.05, $p = 0.18$). None of the other baseline patient characteristics was associated with poor adherence after discharge.

Use of OCS

Comparison between measures of OCS use. Electronic data indicated a significantly lower use of OCS than measurements based on pill counts ($66.1\% \pm 4.4\%$ vs. $102.0\% \pm 3.3\%$, $p < 0.0001$, mean \pm SE). Twelve (25.0%) participants used OCS every day as prescribed and 2 (4.2%) did not use OCS on any of the 7 days after discharge. Thirteen (27.1%) participants had poor adherence to OCS, but pill counts only identified one (7.7% sensitivity) participant.

Patterns and predictors of OCS adherence. Electronic data indicated that use of OCS therapy decreased with time to a mean of 52.2% at 1 week after discharge (-5.2% per day, $p < 0.0001$; Figure 1). None of the baseline patient characteristics was identified as predictors of poor adherence to OCS in a multivariable model.

Among 46 participants who returned electronic medication data for both ICS and OCS, the mean use of OCS was significantly higher than use of ICS ($68.6\% \pm 4.2\%$ vs. $56.5\% \pm 4.6\%$, $p = 0.03$, mean \pm SE). Interestingly, there was no apparent relationship between the level of use of OCS and ICS after discharge (Figure 2). Also, the rate of discontinuation of corticosteroids was faster for OCS than for ICS (-5.5% vs. -2.6% per day, $p = 0.04$) during the first 7 days after hospital discharge.

Use of Corticosteroids and Asthma Control

Symptom control and electronically measured medication use data were available in 48 of 49 with ICS use data, 46 of 48 patients with OCS use data, and 45 of 46 patients with both OCS and ICS use data. Asthma symptom control was significantly worse in participants with electronically measured poor adherence to ICS or both ICS and OCS but not to OCS alone

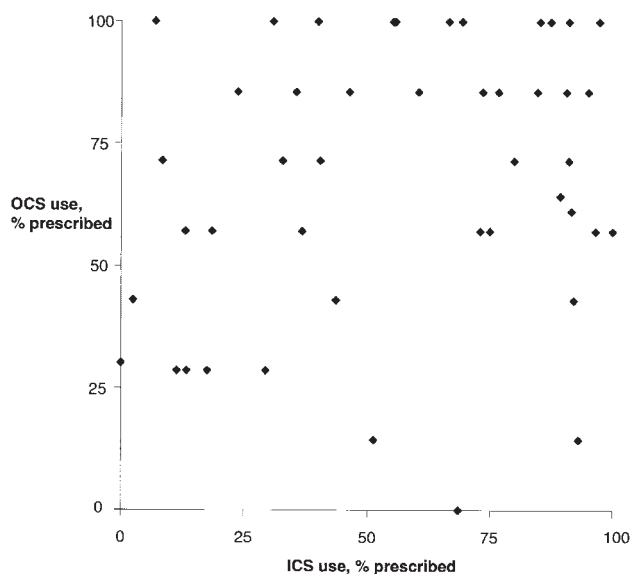


Figure 2. Use of inhaled versus oral corticosteroids, $n = 46$. Use of OCS (percentage of prescribed dose; measured by electronic medication monitors) was not related to use of ICS (Pearson's $r = 0.23$, $p = 0.12$).

(Figure 3A–3C). There was substantial overlap, however, between the level of asthma symptom control in patients with or without poor adherence to corticosteroids.

DISCUSSION

In this high-risk inner-city adult population with asthma, the use of ICS and OCS fell rapidly to approximately 50% of prescribed dose within 7 days after hospital discharge. Although nonadherence

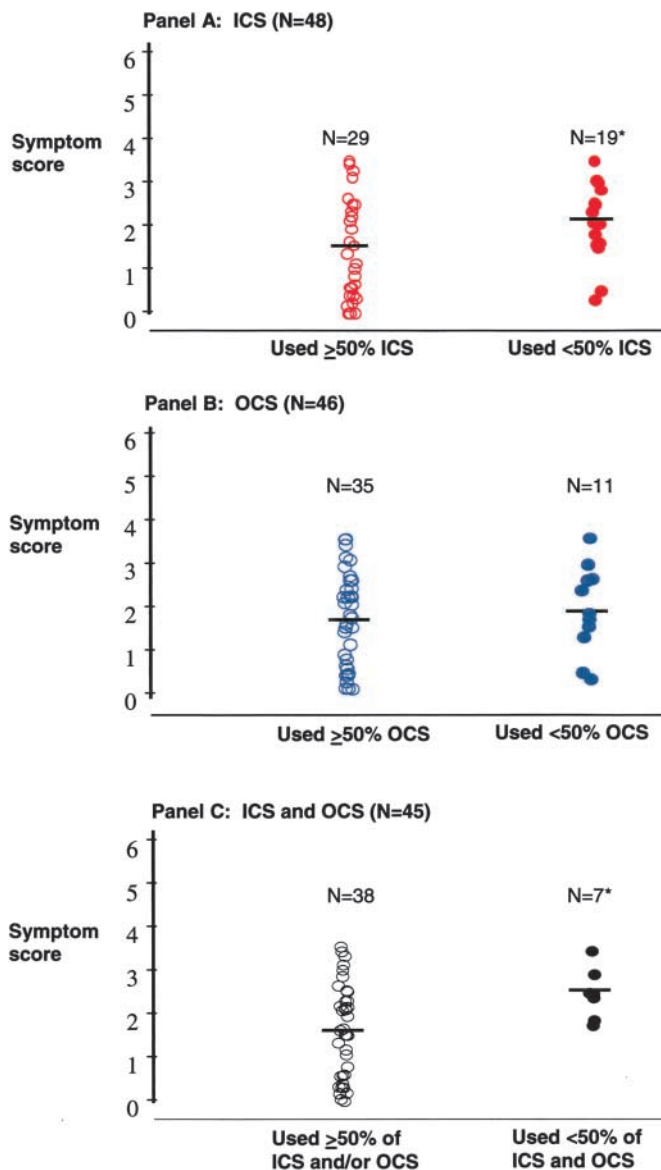


Figure 3. Asthma symptom control according to use of corticosteroids. Symptom control during the past 7 days (recorded at the 2-week follow-up visit) is shown according to level of electronically measured corticosteroid use after hospital discharge ($\geq 50\%$ of prescribed dose vs. $< 50\%$ of prescribed dose). (A) ICS (1.5 ± 0.2 vs. 2.1 ± 0.2 ; mean \pm SE symptom score). One participant with ICS adherence data had missing symptom control data. (B) OCS (1.7 ± 0.2 vs. 1.9 ± 0.3). Two participants with OCS adherence data had missing symptom control data. (C) ICS and OCS (1.6 ± 0.2 vs. 2.5 ± 0.2). One participant with adherence data had missing symptom control data. Higher symptom control scores indicate worse asthma symptom control (0 [well controlled] to 6 [extremely poorly controlled]). * $p < 0.05$.

to both ICS and OCS was common, participants were significantly less likely to use ICS. Moreover, poor adherence to ICS (as well as poor adherence to both ICS and OCS) was a significant predictor of worse asthma symptom control 2 weeks after discharge home.

Previous retrospective or cross-sectional studies have reported underuse of appropriate medications in patients hospitalized or dying from asthma (7, 11, 22, 23). This investigation is the first, however, to evaluate prospectively and objectively the use of medications after a severe asthma exacerbation. We focused on corticosteroids because they are recommended for treatment of severe asthma exacerbations (24). Our results provide strong evidence that even under optimized conditions (i.e., free medications and intensive inpatient education), discontinuation of both ICS and OCS is common within 7 days of discharge home. The decline in ICS adherence (2.7% per day) in our hospital-based participants is approximately nine times the rate reported in a previous study of adults with asthma recruited from outpatient clinics (approximately 2% per week) (25).

Electronic medication monitors have been previously used to assess adherence to leukotriene modifiers (26) but not other oral asthma medications. This investigation is the first to employ electronic monitoring to examine OCS use, providing a unique opportunity to compare directly rates of ICS and OCS use in the same patient. We found that use of OCS was modestly higher than ICS (absolute difference, 12%; 95% confidence interval, 1.1%–23.1%). The rate of discontinuation of OCS, however, was approximately twice as fast as for ICS, with the use of both corticosteroids reaching approximately 50% within 7 days of discharge. Moreover, patients who used OCS regularly (e.g., 75–100% of prescribed dose) did not necessarily use ICS regularly. These findings suggest that patients hospitalized for asthma may preferentially use OCS over ICS after discharge home, although the relative difference in use between the two corticosteroids is modest, short-lived, and varies substantially between individual patients.

Although benefits of OCS for acute asthma exacerbations are well established (27), we did not find that poor adherence to the 1-week course of OCS was, by itself, associated with worse asthma control 2 weeks after hospital discharge. However, poor adherence to ICS (or to both ICS and OCS) was significantly associated with worse asthma symptom control. A clinical trial of patients with asthma exacerbations found significant benefits when a 3-week course of ICS was taken along with 1-week course of OCS (28), suggesting that continued ICS use among our participants may have at least temporarily offset the risk of re-exacerbation from nonadherence to OCS. We found substantial overlap in the level of asthma symptom control in patients with and without poor adherence to corticosteroid therapy, potentially reflecting differences in underlying disease severity and exposure to environmental triggers (29–31) after hospital discharge. Further research is necessary, however, to clarify the interrelationships between the use of corticosteroids, underlying disease severity, environmental exposures, and the resolution of severe asthma exacerbations.

This study has some potential limitations. Electronic data were less often available in men and younger participants. Because adherence may be lower in patients with missing medication data (32) and participants were informed that corticosteroid use was being measured, overall levels of corticosteroid use may be even lower than our analyses indicate. If so, poor adherence is likely to play even a larger role in contributing to the excess morbidity and mortality in this population. Participation was limited to innercity adults hospitalized for an asthma exacerbation, and thus, results may not be generalizable to other populations with asthma. However, we consider this focus a major

strength of this investigation because there have been no studies that have prospectively measured use of corticosteroids in this high-risk asthma population. Also, this study only addressed short-term corticosteroid use after hospital discharge in a modest number of patients. Additional studies in larger populations are needed to evaluate longer term patterns of ICS use, examine other aspects of asthma self-management after hospital discharge (e.g., avoidance of environmental triggers), and assess the clinical consequences of nonadherence.

Results of this study have several implications. Study conditions provided multiple educational and tangible supports to promote optimal adherence to corticosteroids (e.g., free medications, intensive education about appropriate medication use, and MDI technique). We suspect that hospitalized patients without such supports (approximately half of whom may fail to even fill prescriptions) (33) are likely to have an even lower rate adherence to corticosteroid therapy after discharge. Further research is urgently needed in this high-risk population about interventions to improve adherence to corticosteroids after hospital discharge and other important aspects of asthma self-management (e.g., avoidance of environmental triggers and decisions about when to seek medication attention). Participants with worse asthma control were also the ones who, in general, were less likely to have used corticosteroids after discharge. This observation suggests the need to evaluate additional strategies (e.g., home nurse visits) to improve outcomes in this high-risk asthma population. Also, self-report, canister weights, and pill counts all had low sensitivity in detecting poor adherence to ICS and OCS. This finding, together with the high prevalence of poor adherence to ICS (41%) and OCS (27%) among study participants, highlights the importance of rigorously measuring adherence to therapy in clinical practice and in research studies of patients phenotypically labeled as having “severe” or “refractory” asthma (34). In fact, our results, taken together with findings from studies in other chronic health conditions (e.g., diabetes, coronary artery disease, human immunodeficiency virus infection), provide strong evidence that nonadherence to therapy should be routinely considered in the evaluation and management of patients with an incomplete response to effective medical therapy (35–37).

In summary, despite multiple supports, adherence to corticosteroid therapy (ICS and OCS) dropped to approximately 50% within 1 week of hospital discharge after a severe asthma exacerbation. The low sensitivity of self-report, canister weights, and pill counts for identifying poor adherence suggests that patient discontinuation of corticosteroids may not be recognized in a substantial proportion of these high-risk patients.

Conflict of Interest Statement: J.A.K. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; K.A.R. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; J.V.M. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; D.Y.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; S.S. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; A.C. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; P.H. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript; C.S.R. does not have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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