A multifaceted stewardship intervention helps curb steroid overprescribing in hospitalized patients with acute exacerbations of COPD

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Purpose. Corticosteroid overprescribing is well documented in real-world practice. There is currently no evidence to guide best practices for steroid stewardship. The aim of this study was to assess the effects of a 3-part stewardship intervention strategy on inpatient steroid prescribing in patients with acute exacerbations of COPD (AECOPD).

Summary. Investigators implemented a 3-part stewardship initiative consisting of (1) an anonymous survey for providers on steroid prescribing in a simplified case of AECOPD, (2) face-to-face education and review of survey results, and (3) prospective audit and feedback from a clinical pharmacist. This was a quasi-experimental before-and-after study evaluating hospitalized adults diagnosed with AECOPD in two 12-month study periods before (April 2019-March 2020) and after (May 2020-April 2021) implementation. The primary outcome was mean inpatient steroid dosing. Secondary outcomes were duration of therapy, length of stay (LOS), 30-day readmissions, 30-day mortality, and incidence of hyperglycemia. Per power analysis, there were 27 patients per cohort. The interventions resulted in a significant reduction in prednisone equivalents during hospitalization: 118 mg vs 53 mg ($P = 0.0003$). This decrease was similar in ICU (160 mg vs 61 mg, $P = 0.008$) and non-ICU (102 mg vs 49 mg, $P = 0.004$) locations. There was no significant difference in duration of therapy (8 days vs 7 days, $P = 0.44$), length of stay (3.3 days vs 3.9 days, $P = 0.21$), 30-day mortality (4% vs 7%, $P = 0.55$), 30-day readmissions (15% vs 7%, $P = 0.39$), or rate of hyperglycemia (48% vs 44%, $P = 0.78$).

Conclusion. A multifaceted stewardship intervention significantly reduced steroid dosing in hospitalized AECOPD patients. This reduction was not associated with known deleterious effects.

Keywords: hospitalization; inappropriate prescribing; intensive care units; prednisone; pulmonary disease, chronic obstructive; surveys and questionnaires

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Chronic obstructive pulmonary disease (COPD) affects nearly 16 million people in the United States (US) and was the fourth leading cause of death nationwide in 2019.[1] The veteran population is particularly affected, with acute exacerbations of COPD (AECOPD) being one of the most common discharge diagnoses at VA hospitals across the country.[2] Additionally, veterans with COPD have higher overall healthcare utilization in terms of outpatient, inpatient, and pharmacy metrics than those without COPD.[2]

A 2019 Global Initiative for Chronic Obstructive Lung Disease (GOLD) report provides expert consensus guidance on the management of COPD, including acute exacerbations.[3] Systemic steroids are recommended (based on level A evidence) during AECOPD to improve lung function, improve oxygenation, and shorten recovery time. The recommended dose

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is the equivalent of prednisone 40 mg given for a duration of 5 to 7 days. This recommendation is largely due to results of the Reduction in the Use of Corticosteroids in Exacerbation of COPD (REDUCE) trial.[4] This randomized, multicenter, noninferiority trial compared 5- and 14-day regimens of prednisone 40 mg daily in a controlled, double-blind fashion. Longer-duration steroid therapy did not improve the primary outcome of time to next exacerbation: 29 days (interquartile range [IQR], 16-85 days) versus 43.5 days (IQR, 13-118 days) in the short-course group. Additionally, rates of re-exacerbation (defined as use of systemic steroids or other intensified treatment) were not significantly different between groups: 37.2% versus 38.4% (absolute difference, –1.2%; 95% CI, –12.2% to –9.8%). Despite the availability of these recommendations, research indicates that medication therapy discordance with guideline recommendations is common,[5,6] with many providers continuing to use high-dose steroid regimens used in respiratory failure, which were compared with placebo in clinical trials.[7,8]

A 2014 meta-analysis of 12 randomized controlled trials evaluating steroid use in AECOPD demonstrated no significant difference in success rates in avoiding mechanical ventilation, noninvasive ventilation, or tracheal intubations compared to standard therapy or placebo. While steroids significantly improved treatment success overall in non–intensive care unit (ICU) patients (odds ratio [OR], 1.72; 95% CI, 1.15-2.57, $P = 0.01$), this success was not seen in critically ill patients (OR, 1.34; 95% CI, 0.61-2.95, $P = 0.46$). The analysis also found an increased odds of adverse effects, defined as hyperglycemia, psychiatric disorders, infections, hypertensive episodes, and gastrointestinal bleeds, with steroid use (OR, 2.36; 95% CI, 1.67-3.33; $P < 0.0001$). The investigators went on to state that the equipoise surrounding steroid use in AECOPD is in question.[9]

KEY POINTS

- Practices around steroid prescribing for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) may stem from long-held beliefs among prescribers that often lead to steroid overprescribing, and dedicated engagement and education may be needed to promote practice change.
- A multifaceted intervention involving (1) engaging providers with an anonymous survey, (2) face-to-face focused education, and (3) prospective audit and feedback moving forward can be utilized with success to decrease steroid doses prescribed for AECOPD.
- This structured intervention strategy led to a 50% reduction in mean daily prednisone equivalents in both the ICU and non-ICU settings at 1 healthcare facility.

Two large pharmacoepidemiologic studies compared the use of higher steroid doses and lower doses in AECOPD. Lindenauer et al[10] reviewed the records of 79,985 patients admitted to 414 US hospitals for AECOPD. After propensity matching, patients treated with lower, oral doses of steroids (20-80 mg in prednisone equivalents) had a significantly lower odds of treatment failure (OR, 0.84; 95% CI, 0.75-0.95), defined as initiation of mechanical ventilation (by hospital day 2), inpatient mortality, or 30-day readmission, than those who received high-dose intravenous (IV) steroids (120-180 mg in prednisone equivalents). Kiser et al[11] reviewed the records of 17,239 patients admitted to an ICU with AECOPD in 473 hospitals. Patients treated with higher steroid doses (methylprednisolone doses of >240 mg/d) on hospital day 1 or 2 demonstrated no benefit and worse outcomes than those treated with lower steroid doses (methylprednisolone doses of ≤240 mg/d). After propensity matching, use of lower steroid doses was associated with shorter ICU and hospital length of stay (LOS), shorter time on a ventilator, fewer fungal infections, less need for insulin therapy, lower hospital costs, and a lower odds of mortality (OR, 0.76; 95% CI, 0.65-0.89; $P < 0.01$).

The CHEST foundation recently advocated for steroid stewardship to protect patients from overexposure to steroids, with a focus on patients with asthma.[12] Given the known adverse effects of steroids, such as hypertension, hyperglycemia, immunosuppression, sleep disruption and psychosis, coupled with worse outcomes listed above, facilities should work to curb steroid overprescribing in AECOPD.

Medication stewardship programs can be employed when there is low-quality evidence to support a particular intervention coupled with the potential for patient harm. There are limited data to guide best practices for implementing steroid stewardship programs.[13] Therefore, data from other modalities, such as guidance for antimicrobial, opioid, and proton pump inhibitor stewardship, may need to first be extrapolated.[14-16] Research indicates that stewardship programs should not rely on education alone but should be multifaceted, with a focus on a specific disease state to better define goals and monitoring. Additionally, programs should adjust to the needs of and barriers present in individual facilities and have support from the facility leadership. Education should be active (rather than passive), with ongoing reminders provided for sustainability.[13,14,17]

A baseline needs assessment for the study facility was established with a retrospective quality assessment review, which identified very low guideline adherence in treatment of AECOPD in the ICU.[18] Steroid dosing was determined to be the biggest driver of nonadherence, with only 1.7% of

patients with AECOPD admitted to the ICU on guideline-recommended dosing (the mean daily dose was 114 mg in prednisone equivalents). Researchers subsequently developed a multifaceted steroid stewardship intervention for quality improvement (QI). The objective of the study described here was to evaluate the effects of this intervention on steroid dosing in hospitalized patients with AECOPD.

Study methodology

The study facility is a small, 52-bed primary Veterans Affairs (VA) hospital. The licensed bed total includes 7 ICU beds and 28 medical/surgical general ward beds. The emergency department (ED) consists of 14 prescribing clinicians (both physicians and mid-level providers). There are 5 hospitalists (not including nocturnists and residents) and only 1 pulmonologist, who is board certified in critical care and pulmonary medicine. All providers have ICU admitting privileges, while the pulmonologist is involved on a consult-only basis. Both the pharmacy and the laboratory are staffed 24 hours a day. There is 1 inpatient clinical pharmacy specialist, who covers the ICU and general wards Monday through Friday from 7:30 AM to 4:00 PM.

The first intervention was the development of a voluntary and anonymous survey to establish baseline prescribing practices and potential areas of focus for education (data previously reported[19]). The survey consisted of a simplified case of AECOPD, to which providers responded as to how they would treat the patient in regards to steroid therapy. Following the facility survey, a meeting was scheduled with the facility's pulmonologist to ensure buy-in and that there were no objections to a steroid stewardship project.

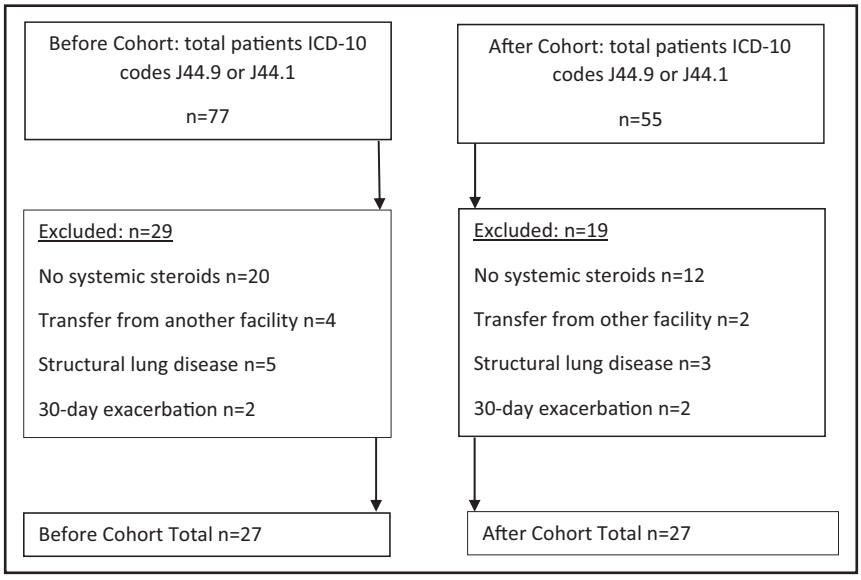
Next, an educational component was conducted. Three separate face-to-face meetings were scheduled with the ED providers, the inpatient providers, and the medical residents. In an effort to facilitate a more dynamic discussion, providers were sent the meeting materials (current consensus guideline recommendations, evidence behind recommendations, results of the baseline needs assessment, and the results of the survey) at least 24 hours in advance to review. The meetings consisted of a dynamic discussion of the education materials during which providers were asked about barriers to guideline adherence. They were also empowered to select an ongoing intervention for reminders for sustainability.

Based on feedback from the educational meetings, the third intervention consisted of prospective audit with feedback by the rounding clinical pharmacy specialist. Providers were notified both verbally and in writing when steroid dosing for AECOPD exceeded guideline recommendations, with a request to lower the steroid dose. These interventions were manually documented for reporting.

The facility survey and education meetings were performed in March 2020. A 6-week "washout" period prior to data collection was allowed in the postintervention cohort. This was a retrospective before-and-after study evaluating steroid dosing for AECOPD in two 12-month time periods: April 2019 through March 2020 (before), and May 2020 through April 2021 (after). A preliminary power analysis revealed that 27 patients from each group would be needed to detect a 50% reduction in mean daily steroid dose with 80% power at a 2-sided α of 0.05.

To identify patients for inclusion, a computerized report of either primary or secondary discharge diagnosis International Classification of Diseases, 10th Revision (ICD-10) codes for COPD (code J44.9) and AECOPD (code J44.1) was generated. The records of patients selected via random number generator were then reviewed until 27 patients in each group who met both inclusion and exclusion criteria were identified (Figure 1). Adult patients were eligible for inclusion if they had received systemic steroids (IV or oral) and were hospitalized for 24 hours or more. Exclusion criteria included baseline steroid use of ≥20 mg in prednisone equivalents daily, structural lung disease (bronchiectasis, lung cancer, abscess, or pulmonary fibrosis), development of acute respiratory distress syndrome (ARDS), active infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), use of steroids for any indication other than AECOPD, and documented AECOPD within 30 days prior to admission.

Figure 1. Flowchart of application of inclusion and exclusion criteria. ICD-10 indicates International Classification of Diseases, 10th Revision.



The primary endpoint was mean daily steroid dose during hospitalization (calculated as total dose divided by days of inpatient steroid therapy). Barcoded medication administration reports were used to verify doses received. All steroid options were converted to prednisone equivalents for reporting. One-time doses given in the ED prior to admission were excluded from analysis, as this location does not utilize the barcoded drug administration system. Outpatient steroid doses after discharge were not included in mean daily doses, but days of prescribed therapy were included in the total duration of therapy. Secondary endpoints included total duration of therapy, inpatient LOS, both inpatient and 30-day mortality, 30-day readmissions, and incidence of hyperglycemia (defined as any serum glucose concentration of ≥180 mg/dL).

Baseline characteristics were collected to compare groups. Severity of exacerbation was compared with documented PaO_2/FIO_2 (ratio of arterial partial pressure of oxygen to fraction of inspired oxygen) upon admission, presence of acidemia (defined as arterial pH of ≤7.33), need for mechanical or noninvasive ventilation, and the Acute Physiology and Chronic Health Evaluation (APACHE) II scores.[20] Additionally, preexisting comorbidities were compared using the Charlson Comorbidity Index.[21] GOLD classification of chronic disease severity was determined using documented FEV_1 (forced expiratory volume in 1 second) when available.

Normally distributed variables are represented as means with standard deviation (SD), while non-normally distributed variables are reported as medians with IQR. Continuous outcomes were analyzed with Student's *t* test or Mann-Whitney *U* test where appropriate. Nominal outcomes were analyzed with a chi-square or Fisher's exact test where appropriate. All comparisons were analyzed in R software, version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria). These methods were granted nonresearch status by the facility's institutional review board, which waived the requirement for informed consent.

Results

Per preliminary power analysis, 27 patients were enrolled in each cohort (Figure 1). The most common reason for exclusion was not having received systemic steroids. The lower number of AECOPD admissions seen in the after cohort was felt to be due to restricted admissions resulting from the coronavirus disease 2019 pandemic. Baseline characteristics in the before and after groups were similar, with the groups being well matched for exacerbation severity and comorbid conditions (Table 1). The 2 groups were similar with regard to baseline COPD disease severity in terms of medications, GOLD classification, and baseline supplemental oxygen dependency. The rates of ICU admission and the use of noninvasive ventilation were similar. No patients in either cohort required mechanical ventilation.

The intervention resulted in a significant reduction in mean daily prednisone equivalents while hospitalized: 118 mg before versus 53 mg after (P = 0.0003). The mean dose reduction was similar in both ICU (160 mg vs 61 mg, P = 0.008) and non-ICU (102 mg vs 49 mg, P = 0.004) locations (Table 2). Total duration of therapy was not statistically different in the before and after group (a median of 8 days vs 7 days, P = 0.44), and hospital LOS was similar between groups (3.3 days vs 3.9 days, P = 0.21).

There were four 30-day readmissions in the before cohort: 2 were for respiratory symptoms related to COPD (the patients were prescribed further systemic steroids), 1 was for hypoxic respiratory failure due to inhalation injury (the patient was prescribed further steroids), and 1 was for pneumonia (for which steroids were not prescribed). There were two 30-day readmissions in the after cohort: 1 was due to infectious complications of osteomyelitis (steroids were not prescribed), and the other was for recurrent pneumonia (systemic steroids were prescribed). There were no inpatient deaths in either group. There was 1 instance of 30-day mortality in the before group versus 2 in the after group; all these patients died while receiving hospice care.

The incidence of hyperglycemia was similar between groups. There were 24 documented interventions by the clinical pharmacist to lower steroid doses during the 12-month follow-up period; the acceptance rate was not recorded.

Discussion

While there were several steps in the overreaching project (Figure 2), there were 3 primary interventions: (1) the case survey, (2) education of providers, with peer comparison, and (3) ongoing assessment with feedback by a clinical pharmacist. To the authors' knowledge, this is the first study describing a multifaceted intervention aimed at curbing steroid dosing in AECOPD. An education-only method has been described, with some success reported, but questions remain about sustainability.[22] The decrease in mean daily steroid dosing was due to a combination of converting IV steroid therapy to oral therapy after prospective intervention and lower initial starting doses.

The needs assessment was a valuable component in that it helped secure support for the steroid stewardship project from the facility leadership. The project was supported by the pharmacy and therapeutics committee as well as the medical executive committee. It was pointed out that there are several areas of quality indicators potentially affected by this QI project, such as ICU mortality, ICU LOS, ICU hyperglycemia, and 30-day readmissions.

The anonymous survey was an integral part of the intervention for multiple reasons. First, it helped establish baseline prescribing habits and identify barriers or areas of focus for the implementers. Second, it engaged providers in the learning process. Finally, by going over the survey results in the education component, providers could see how their answers compared with those of others within the facility (reported dosing was in the

Table 1. Baseline Characteristics of Pre- and Postimplementation Cohorts

Variable	Before Group (*n* = 27)	After Group (*n* = 27)	*P* Value
Age, mean (SD), y	71 (7.0)	70 (8.3)	0.44
Male, No. (%)	27 (100)	26 (97)	
GOLD classification, No. (%)			
Class I	2 (7)	0 (0)	
Class II	8 (30)	8 (30)	>0.99
Class III	8 (30)	8 (30)	>0.99
Class IV	4 (15)	5 (18)	0.75
FEV_1 not recorded	5 (18)	6 (22)	0.74
Smoking status, No. (%)			
Active	10 (27)	10 (27)	>0.99
Former	17 (63)	17 (63)	>0.99
Home medications for COPD, No. (%)			
Long acting beta-agonist inhaler	15 (56)	19 (70)	0.26
Long acting anticholinergic inhaler	13 (48)	14 (52)	0.79
Corticosteroid inhaler	15 (56)	19 (70)	0.26
Systemic steroids (<20 mg daily)	2 (7)	0	
PDE4 inhibitor	2 (7)	0	
Pao_2/Fio_2, median (IQR)	217 (194, 257)	254 (190, 283)	0.52
Arterial pH≤7.33, No. (%)	3 (11)	4 (15)	0.69
ICU admission, No. (%)	8 (30)	9 (33)	0.77
Noninvasive ventilation, No. (%)	2 (7)	5 (18)	0.22
Mechanical ventilation, No. (%)	0 (0)	0 (0)	
Charlson Comorbidity Index, median (IQR)	5 (4, 6)	7 (4, 8)	0.20
APACHE II score, median (IQR)	14 (13, 16)	10 (5, 17)	0.20
Oxygen dependence, No. (%)	17 (63)	18 (67)	0.78
Diabetes mellitus, No. (%)	10 (37)	14 (52)	0.27
Congestive heart failure, No. (%)	2 (7)	5 (18)	0.22
Coronary artery disease, No. (%)	7 (26)	10 (37)	0.38
Hypertension, No. (%)	23 (85)	19 (70)	0.19
Peptic ulcer disease, No. (%)	2 (7)	3 (11)	0.64

Abbreviations: APACHE, Acute Physiology and Chronic Health Evaluation II; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICU, intensive care unit; IQR, interquartile range; Pao_2/Fio_2, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen; PDE4, phosphodiesterase 4; SD, standard deviation.

range of 40 to 625 mg/d in prednisone equivalents). This may have served as a peer-comparison or "social pressure" intervention, which has been shown to be effective in antibiotic stewardship.[23]

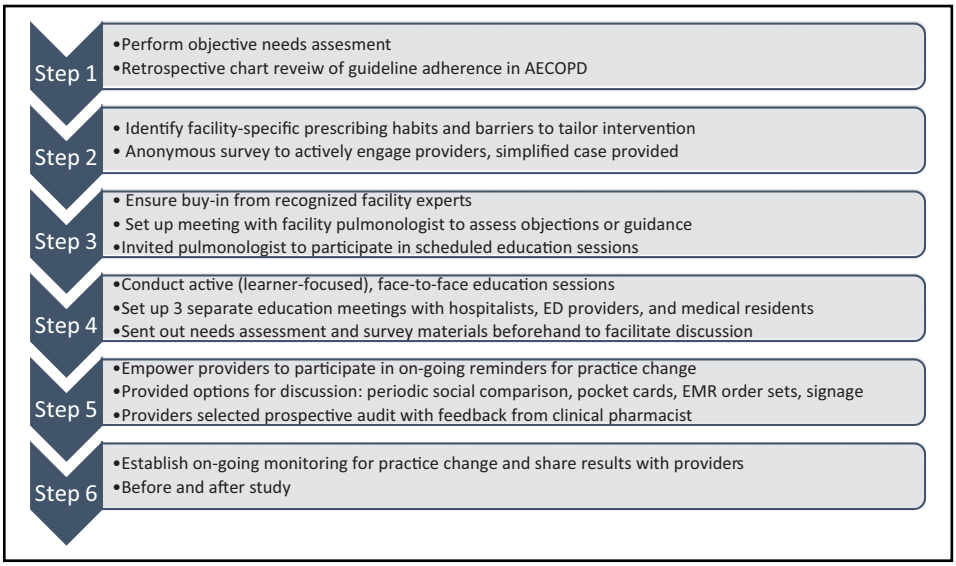
The face-to-face meetings were also helpful in assessing barriers to practice change. As expected, there was a mixed level of alacrity among providers regarding guideline adherence. A common theme was that there was little incentive for change coupled with the fear of theoretical repercussions. For example, one provider suggested that if a patient went into respiratory failure while on steroid doses lower than what is perceived to be the "local standard of care," the case might go to peer review. One provider questioned the validity of consensus guidelines as compared to years of clinical experience (eg, "guidelines change all the time"). The residents indicated that prescribing behavior was reinforced when they watched older dosing methods used by their attendings resulting in successful outcomes. The

Table 2. Clinical Outcomes

Outcome	Before Group (*n* = 27)	After Group (*n* = 27)	*P* Value
Daily prednisone equivalents, mean (SD), mg	118 (88)	53 (26)	0.0003
ICU prednisone equivalents, mean (SD), mg	160 (92)	61 (39)	0.008
Non-ICU prednisone equivalents, mean (SD), mg	102 (93)	49 (22)	0.004
Total duration of steroid therapy, median (IQR), d	8 (6, 12.5)	7 (5, 8)	0.44
Hospital LOS, mean (SD), d	3.3 (1.4)	3.9 (2.1)	0.21
Inpatient mortality, No. (%)	0 (0)	0 (0)	
30-day mortality, No. (%)	1 (4)	2 (7)	0.55
30-day readmission, No. (%)	4 (15)	2 (7)	0.39
Hyperglycemia, No. (%)	13 (48)	12 (44)	0.78

Abbreviations: ICU, intensive care unit; LOS, length of stay; SD, standard deviation.

Figure 2. Multifaceted approach to the facility steroid stewardship project. AECOPD indicates acute exacerbations of chronic obstructive pulmonary disease; ED, emergency department; EMR, electronic medical record.



group dynamic discussion proved to be beneficial, as other providers offered rebuttals to these reported barriers. Of note, several cases of higher-than-recommended steroid dosing remained, thereby affecting the mean daily dosages reported.

Other facilities should be prepared for similar barriers in changing long-standing practices, which research indicates involves not difficulty in learning new material, but rather a hesitancy to let go of current understanding and beliefs. This can be addressed through a process known as "un-learning," "de-implementation," "de-adoption," or "de-diffusion."[24] Providers may feel uncomfortable when practice change disturbs the status quo, and establishing a new practice equilibrium may be a struggle. It is recommended that stewardship implementers should focus on practices that are based on limited evidence and pose potential harm.[25] Based on this guidance, steroid stewardship in AECOPD seems, anecdotally, an optimal framework. At the study facility, the more resistant providers were encouraged to incorporate incremental reductions in starting dose (eg, 25%-50% reductions).

Finally, it was important to allow providers to select their own intervention for ongoing promotion of adherence, as this empowerment has been shown to facilitate buy-in.[17] To facilitate discussion, researchers offered multiple methods of reminders, such as order sets or quick orders in the computerized medical record, the use of signage or pocket cards, and peer-comparison methods. Ultimately, the inpatient providers elected prospective audit and intervention from the inpatient clinical pharmacist.

Strengths of this study include the power analysis with randomized selection, utilization of both a washout period and a 12-month observation period to account for the Hawthorne effect, utilization of barcode reporting for dosing accuracy, and clinically relevant subject matter that is likely to affect many healthcare facilities. There are several limitations to consider when interpreting these results. The quasi-experimental study design did not account for possible confounding variables; however, there were no significant changes in providers or patient population between cohorts. The study was not powered to detect clinically meaningful changes in outcomes (eg, insulin usage, re-exacerbation rates, and infectious complications), as the small facility size limited enrollment capacity; given the limited data, some may consider this intervention a priori. A post hoc analysis to evaluate the magnitude of hyperglycemia and insulin requirements at the study facility is planned. The lack of use of mechanical ventilation in both cohorts may infer these findings are not applicable to these patients. The magnitude of change seen in dosing brings external validity into question, as the preintervention doses at the facility were quite high. Nonetheless, even more modest reductions (eg, 25%-30% reductions) may prove to be beneficial. Additionally, outpatient compliance was not addressed in either cohort. Finally, patients could have presented to outside facilities after the index admission, making the analysis of 30-day follow-up endpoints less inclusive.

Conclusion

A multifaceted intervention consisting of provider engagement with a case survey, education with peer comparison, and prospective audit and feedback significantly reduced steroid doses prescribed in hospitalized patients with AECOPD. The reduction in dosing was not associated with known deleterious effects.

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Disclosures

The authors have declared no potential conflicts of interest.

Additional information

Dr. Cole was responsible for the inception, study design, some data collection, and the majority of manuscript development. Dr. Smith was responsible for data collection and assisted in authoring the manuscript. Both authors provided final approval of the current version and agree to be accountable for all aspects of this work. The views expressed are those of the authors and do not necessarily reflect the position of the US Department of Veterans Affairs or the US government.

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