






Original Research

Impact of targeted educational interventions on appropriateness of stress ulcer prophylaxis in critically ill adults

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Abstract

Background: Acid suppression therapy (AST) is routinely used in critically ill patients to prevent stress-related mucosal bleeding (SRMB).

Objective: Our objective was to determine the impact of a structured educational intervention on AST used for prevention of SRMB on appropriateness of AST.

Methods: A single-center, retrospective, cohort study of appropriate use of AST in critically ill patients admitted to the medical intensive care unit (ICU) at an academic medical center between January to June of 2014 (no intervention) and January to June of 2015 (intervention) was conducted. The percentage of patients prescribed inappropriate AST, inappropriate AST at ICU transfer and hospital discharge, doses of inappropriate AST, and adverse effects associated with AST use were compared between periods using chi-square tests.

Results: Patients in the intervention group (n=118) were 5 years older than patients in the no intervention group (n=101). AST was inappropriately initiated more frequently in the no intervention group (23% vs. 11%, p=0.012). Continuation of inappropriate AST at ICU transfer and hospital discharge was similar between groups (60% vs. 53%, p=0.277 and 18% vs. 14%, p=0.368, respectively).

Conclusion: Patients had appropriate AST initiated and inappropriate AST withheld more frequently when formal education was provided. This low-cost intervention strategy can be implemented easily at institutions where pharmacists interact with physicians on rounding services and should be evaluated in institutions where interactions between pharmacists and physicians occur more frequently in non-rounding situations.

Keywords

Anti-Ulcer Agents; Inappropriate Prescribing; Intensive Care Units; Pharmacists; Academic Medical Centers; Retrospective Studies; United States

INTRODUCTION

Stress ulcer prophylaxis (SUP) is routinely used in critically ill patients to prevent stress-related mucosal bleeding (SRMB) because of hypo-perfusion to mucosal cells and impaired mucosal repair mechanisms.¹ Estimates of the incidence of gastrointestinal bleeding (GIB) range from 0.1% to 31%, but most studies conclude that less than 6% of critically ill patients will develop GIB during their hospitalization.²⁻⁵ Over the last few decades the incidence of SRMB has decreased, likely because of advancements in supportive care practices provided to critically ill patients, such as improvements in recognizing, preventing, and treating sepsis, shock, and nutrition deficiencies.⁶⁻⁸

Acid suppression therapies (AST) are consistently effective in preventing SRMB in the majority of patients; however, these therapies are not benign. Multiple large trials and meta-analyses have found an increased risk of both community and nosocomial pneumonia in patients on AST.⁸⁻¹⁰ Patients on AST have also been found to have more cases of *Clostridium difficile* infection (CDI).^{11,12} These risks highlight the importance of reserving AST for patients with an appreciable risk of SRMB. Major risks factors for SRMB include mechanical ventilation for greater than 48 hours and severe coagulopathy.¹³ The most commonly used agents for SUP are proton pump inhibitors (PPI) and histamine2-receptor antagonists (H2RA).¹⁴

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Up to 70% of patients receiving AST do not have an appropriate indication.¹⁵⁻¹⁸ The Society of Hospital Medicine has prioritized decreasing the inappropriate use of AST by including it as one of five opportunities to improve health care as part of the American Board of Internal Medicine's Choosing Wisely Campaign.¹⁹ The economic burden of both the direct cost of the medications as well as the indirect costs arising from adverse effects is significant. A recent evaluation of appropriateness of AST at a hospital in Belgium determined that avoiding inappropriate initiation of AST during the hospital stay for non-critically ill patients could lead to a saving of 3,805 EUR (4,224 USD) during hospitalization plus an additional 17,441 EUR (19,360 USD) per month after hospital discharge.²⁰ If these data were extrapolated to other hospitals across the world, the cost of inappropriate AST would be considerable. When choosing AST in patients who possess an appropriate indication, either a PPI or a H2RA are viable options. Recently, however, H2RAs have been shown to be more cost-effective than PPIs in critically ill patients due to reduced rates of pneumonia and CDI and comparable or reduced rates of SRMB.²¹⁻²³

Unfortunately, many patients are also being discharged inappropriately on AST, leading to unnecessary costs to the patient and health care system and risks to the patient despite minimal or no therapeutic benefit.^{20,24-31} Hospitals should consider emphasizing appropriate identification of patients who may benefit from AST, use of the most cost-effective therapies, and efforts to reduce the incidence of patients being discharged on AST when not indicated and the associated risks. In the intensive care unit (ICU) in particular, pharmacists often are members of the primary care team; however, the impact of pharmacists providing consistent education to other health care providers on the appropriateness of AST is unknown. This study was performed to determine the impact of a structured educational intervention on AST used for prevention of SRMB on appropriateness of AST.

METHODS

Study Design

This was a single-center, retrospective, cohort study of appropriate use of AST in critically ill patients admitted to the medical ICU at an academic medical center between January to June of 2014 (no intervention period) and January to June of 2015 (intervention period). The University of Arkansas for Medical Sciences institutional review board approved this study (#203820). All patients admitted to the medical ICU for the first time during that hospitalization, who were at least 18 years of age, and who had an order for AST were considered for inclusion. Patients were excluded if they possessed a current diagnosis of GIB, were on AST prior to admission to the ICU (either from home or from another health care setting), or had a history of Zollinger-Ellison syndrome. During this study period, the ICU team made the decisions to initiate or discontinuation AST, pharmacists did not have prescriptive authority, and AST was not available to order directly from an ICU admission order set.

Beginning in January 2015, a clinical pharmacist provided medical residents and pulmonary/critical care fellows with an educational intervention lasting approximately 5 minutes on guideline-recommended AST for SUP, supplied a pocket card on SUP initiation and choice of agent that had been developed by a multidisciplinary team, and answered questions related to AST for SUP. A clinical pharmacist rounded with the medical ICU treatment team during both study periods; however, no formal intervention of this nature was performed in the no intervention period. Appropriate SUP for a critically ill patient was defined as meeting the requirements listed in the Online Appendix. Patients who did not meet these criteria were considered to have received inappropriate SUP. Appropriateness was assessed at the time of AST initiation and at the time of transfer from the ICU. Patients continuing therapy when transferred to a non-ICU setting and after discharge were considered to be appropriately prescribed AST if any of the following criteria were met: (1) documentation of a new diagnosis during their hospital stay requiring treatment, such as gastroesophageal reflux disease or peptic ulcer disease; (2) receiving AST prior to admission to the ICU; (3) documentation of need to continue mechanical ventilation at a skilled nursing facility; (4) or a coagulopathy with specific recommendation by a physician for continued AST. Because a multitude of factors and patient characteristics could impact the duration of SUP, only the initial AST agent ordered for a patient was considered when evaluating appropriateness of AST.

Statistical Analysis

The primary outcome was the percentage of patients prescribed inappropriate SUP in a medical ICU before and after targeted educational interventions combined with multidisciplinary endorsement and distribution of a SUP pocket card. Secondary outcomes were inappropriate AST at ICU transfer and hospital discharge, number of inappropriate AST doses provided, adverse effects associated with AST (pneumonia and CDI, as defined by first mention in the medical record after at least one dose of an AST agent), and ineffectiveness of AST (SRMB, as defined by first mention in the medical record after at least one dose of an AST agent). For continuous variables, two-sample Wilcoxon rank-sum (Mann-Whitney) tests were used. Nominal variables were compared using chi-square or Fisher exact tests, as appropriate. A significance level of 0.05 was used for all statistical analyses. In order to detect a significant difference in the primary outcome with 95% confidence, 80% power, and an expected 10% of patients in the intervention group and 25% of patients in the no intervention group receiving inappropriate AST, 97 patients were needed in each group. All analyses were conducted using SAS version 9.3 (Cary, NC).

RESULTS

A total of 574 patients were evaluated, of which 101 of the 291 evaluated patients in the no intervention group and 118 of the 283 evaluated patients in the intervention group met the inclusion criteria. Patients in the intervention group were 5 years older at baseline. Hospital and ICU length of stay as well as choice of agent for AST were similar between groups. Mechanical ventilation was the

	No Intervention (n=101)	Intervention (n=118)	P-value
Age (years) mean (SD)	51.07 (4.52)	56.24 (18.35)	0.034
Length of stay (days) mean (SD)			
ICU	4.52 (4.92)	4.85 (4.8)	0.625
Hospital	14.42 (13.52)	11.85 (10.92)	0.122
Indication for SUP, n (%)			
Mechanical ventilation	52 (51%)	61 (52%)	0.975
Severe coagulopathy	5 (5%)	10 (8%)	0.423
2+ minor indications	28 (28%)	50 (42%)	0.024
None	25 (25%)	18 (15%)	0.078
Initial AST, n (%)			
H2RA	64 (63%)	68 (58%)	0.387
PPI	36 (36%)	45 (38%)	0.703
None	1 (1%)	5 (4%)	0.221

AST: acid suppression therapy; H2RA: histamine-2 receptor antagonist; ICU: intensive care unit; PPI: proton pump inhibitor; SUP: stress ulcer prophylaxis

most common indication for SUP in both groups. The intervention group had more patients on AST due to the presence of two or more minor indications (Table 1).

AST was inappropriately initiated more frequently in the no intervention group (23% vs. 11%, $p=0.012$). Continuation of inappropriate AST at ICU transfer and hospital discharge was similar between groups (60% vs. 53%, $p=0.277$ and 18% vs. 14%, $p=0.368$, respectively). No significant differences were found in the number of inappropriate AST doses between the no intervention and intervention groups (4.426 doses vs. 3.015 doses, $p=0.128$). Adverse events occurred infrequently in both groups (Table 2).

DISCUSSION

Inappropriate AST use is common across all patient settings in health care.¹⁵⁻¹⁸ AST was prescribed inappropriately in ICU and non-ICU hospital settings in this study. During the time period when house staff received formal education on appropriate prescribing of SUP, inappropriate AST was initiated less frequently in the ICU. However, rates of inappropriately continued AST when patients transferred to a non-ICU setting within the hospital and at hospital discharge did not change during the intervention period.

Discussions with medical residents during patient care rounds prior to the formal intervention period allowed us to identify two main factors leading to a lack of adherence to appropriate AST prescribing. First, many of the medical residents appeared to be unfamiliar with the nuances of the SUP guidelines and new literature outlining indications and choice of SUP agent. Second, consistent education on AST use may not have been provided in all settings where medical residents rounded in our institution, likely owing to the initiative for proper use of AST not being coordinated

by any single health care profession prior to this initiative. This formal intervention sought to resolve both of these factors; however, gaps in the educational process and transition of care points were identified as deterrents to sustained appropriate use of AST throughout each patient's hospitalization and upon hospital discharge.

Inappropriate AST continuation at ICU transfer and hospital discharge was not reduced in the intervention group. Other studies demonstrated similar findings, also suggesting the continued need to discover and implement solutions to discharge patients without inappropriately prescribed AST.²⁴⁻²⁷ Several studies did find a decreased rate of inappropriate AST at hospital discharge in their post-intervention groups.²⁸⁻³⁰ Buckley and colleagues observed a significant decrease in patients inappropriately discharged on AST from the ICU (29.9% to 3.6%, $p<0.001$) and non-ICU (36.2% to 5.4%, $p<0.001$) settings. At this institution, pharmacists were allowed to discontinue any AST that lacked an appropriate indication pursuant to a protocol.²⁸ Another effective strategy was to use a pharmacist-directed medication reconciliation program at discharge from the hospital.²⁹ Currently, pharmacists do not provide this service at our institution. Implementing this value-added service could reduce rates of inappropriate AST discharge prescriptions. However, initiation of inappropriate AST at the time of transfer from the ICU to a non-ICU setting would require a separate intervention. Reviewing the ICU transfer summary for medications without an appropriate indication is one method that could prove beneficial.³²

If education were provided to medical residents from sources other than the formal educational interventions, these likely occurred regardless of study period. Pharmacists are not present in the ICU overnight or on the

	No Intervention (n=101)	Intervention (n=118)	P-value
AST inappropriately initiated, n (%)	24 (23%)	15 (11%)	0.012
AST inappropriately continued at ICU transfer, n (%)	61 (60%)	63 (53%)	0.297
AST inappropriately continued at hospital discharge, n (%)	18 (18%)	16 (14%)	0.368
Doses of inappropriate AST, n*	4.4	3.1	0.128
Adverse effect due to AST, n (%)			
SRMB, n (%)	1 (1%)	0	0.458
Pneumonia, n (%)	5 (5%)	6 (5%)	>0.99
<i>Clostridium difficile</i> , n (%)	0	0	>0.99

AST: acid suppression therapy; ICU: intensive care unit; SRMB: stress-related mucosal bleeding.
*mean

weekends, which are two times where a reduced presence of house staff in the hospital may affect prescribing practices.^{33,34} Additionally, a complete past medical history can be difficult to obtain for patients in an ICU setting, which may affect the rate of home medications for AST that are undocumented in a patient's chart, regardless of whether the patient had a previous diagnosis warranting AST or the study period.

For programs considering a similar educational intervention, the resources utilized in preparation and maintenance of the program were manageable and similar to other low-cost, pharmacist-provided educational intervention programs.^{35,36} Educational materials were developed using extensive literature search and evaluation, which has been conducted already. The most accurate and relevant information was then used to make pocket-size, laminated cards that were easily distributable. Education on the materials was provided individually and in small group sessions with residents during the first few days of their ICU service, which is achievable if the pharmacist has a close relationship with physicians through a consult or rounding service. Due to scheduling constraints, some residents that worked night shifts during their first week in the ICU did not receive the education; this might have impacted the prescribing habits in the intervention arm. The total time spent preparing and providing education to the residents totaled approximately six hours over the six-month formal intervention period.

We plan to implement future changes within the hospital to further improve the appropriate use of AST. Implementation of the initiative hospital-wide could potentially decrease the number of patients inappropriately prescribed AST in non-ICU settings and at hospital discharge significantly. Additionally, by providing education at new resident orientation on appropriate AST indications in the hospital and the risks of unnecessary AST use, more patients throughout the hospital could be affected. Integrating the information on appropriate AST prescribing into the computerized physician order entry system could increase the likelihood that patients without a need for AST do not inappropriately receive therapy. Finally, we feel that pharmacist involvement in discharge medication reconciliation and facilitating a successful transition of care from the inpatient to the outpatient setting could significantly decrease the number of patients inappropriately continued on AST at discharge and improve follow-up for these patients if AST is inappropriately continued.

Our study had important limitations. The study took place in one medical ICU at a single academic medical center, which may provide results that do not perfectly extrapolate to other institutions. Additionally, because of the retrospective nature of the study, there may have been other reasons for the results in the post-intervention group that were unrelated to the intervention that were unable to be observed or controlled for in the analysis. Possibly inaccurate or incomplete medication reconciliation at the time of ICU admission may have obscured the patients who already were on AST prior to admission and falsely elevated the incidence of inappropriate AST during the ICU stay. We also had no way to determine if patients developed an adverse effect, such as pneumonia or CDI soon after hospital discharge and likely underestimated the true incidence of these adverse events. At our institution, the medical residents who provided care for patients not admitted to the ICU had not received the educational interventions, which may have affected the rate of inappropriately utilized and continued AST after patients were transferred from the ICU. Our institution also has non-resident services, which would not have been affected by the intervention. Implementing education more broadly in our hospital could potentially reduce the incidence further. Despite these limitations, this study suggests positive effects of a pharmacist-led educational intervention on several aspects of appropriate AST use.

CONCLUSIONS

In a pre-post study of patients in a medical ICU before and after a formal educational intervention on appropriate use of AST was implemented, patients had appropriate AST initiated more frequently in the formal educational intervention period. This low-cost intervention strategy can be implemented easily at institutions where pharmacists interact with physicians on rounding services and should be evaluated in institutions where interactions between pharmacists and physicians occur more frequently in non-rounding situations.

CONFLICT OF INTEREST

There are no real or perceived conflicts of interest for any of the authors.

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References

1. Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, Winton TL, Rutledge F, Todd TJ, Roy P. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. *N Engl J Med*. 1994;330(6):377-381. doi: [10.1056/NEJM199402103300601](https://doi.org/10.1056/NEJM199402103300601)
2. Zandstra DF, Stoutenbeek CP. The virtual absence of stress ulceration related bleeding in ICU patients receiving prolonged mechanical ventilation without any prophylaxis. *Intensive Care Med*. 1994;20(5):335-340.
3. Cook D, Guyatt G, Marshall J, Leasa D, Fuller H, Hall R, Peters S, Rutledge F, Griffith L, McLellan A, Wood G, Kirby A. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. *N Engl J Med*. 1998;338(12):791-797. doi: [10.1056/NEJM199803193381203](https://doi.org/10.1056/NEJM199803193381203)
4. Levy MJ, Seelig CB, Robinson NJ, Ranney JE. Comparison of omeprazole and ranitidine for stress ulcer prophylaxis. *Dig Dis Sci*. 1997;42(6):1255-1259.

5. Kantorova I, Svoboda P, Scheer P, Doubek J, Rehorkova D, Bosakova H, Ochmann J. Stress ulcer prophylaxis in critically ill patients: a randomized controlled trial. *Hepatogastroenterology*. 2004;51(57):757-761.
6. Marik PE, Vasu T, Hirani A, Pachinburavan M. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. *Crit Care Med*. 2010;38(11):2222-2228. doi: [10.1097/CCM.0b013e3181f17adf](https://doi.org/10.1097/CCM.0b013e3181f17adf)
7. MacLaren R, Reynolds PM, Allen RR. Histamine-2 receptor antagonists vs proton pump inhibitors on gastrointestinal tract hemorrhage and infectious complications in the intensive care unit. *JAMA Intern Med*. 2014;174(4):564-574. doi: [10.1001/jamainternmed.2013.14673](https://doi.org/10.1001/jamainternmed.2013.14673)
8. Alhazzani W, Alenezi F, Jaeschke RZ, Moayyedi P, Cook DJ. Proton pump inhibitors versus histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. *Crit Care Med*. 2013;41(3):693-705. doi: [10.1097/CCM.0b013e3182758734](https://doi.org/10.1097/CCM.0b013e3182758734)
9. Eom CS, Jeon CY, Lim JW, Cho EG, Park SM, Lee KS. Use of acid suppressive drugs and risk of pneumonia: a systematic review and meta-analysis. *CMAJ*. 2011;183(3):310-319. doi: [10.1503/cmaj.092129](https://doi.org/10.1503/cmaj.092129)
10. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid suppressive medication use and the risk for hospital-acquired pneumonia. *JAMA*. 2009;301(20):2120-2128. doi: [10.1001/jama.2009.722](https://doi.org/10.1001/jama.2009.722)
11. Howell MD, Novack V, Grgurich P, Soulliard D, Novack L, Pencina M, Talmor D. Iatrogenic gastric acid suppression and the risk of nosocomial *Clostridium difficile* infection. *Arch Intern Med*. 2010;170(9):784-790. doi: [10.1001/archinternmed.2010.89](https://doi.org/10.1001/archinternmed.2010.89)
12. Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of *Clostridium difficile* infection with acid suppressing drugs and antibiotics: meta-analysis. *Am J Gastroenterol*. 2012;107(7):1011-1019. doi: [10.1038/ajg.2012.108](https://doi.org/10.1038/ajg.2012.108)
13. American Society of Health-System Pharmacists. ASHP therapeutic guidelines on stress ulcer prophylaxis. *Am J Health Syst Pharm*. 1999;56(4):347-379.
14. Barletta JF, Kanji S, MacLaren R, Lat I, Erstad BL; American-Canadian consortium for Intensive care Drug utilization (ACID) Investigators. Pharmacoepidemiology of stress ulcer prophylaxis in the United States and Canada. *J Crit Care*. 2014;29(6):955-960. doi: [10.1016/j.jcrc.2014.06.025](https://doi.org/10.1016/j.jcrc.2014.06.025)
15. Wohlt PD, Hansen LA, Fish JT. Inappropriate continuation of stress ulcer prophylactic therapy after discharge. *Ann Pharmacother*. 2007;41(10):1611-1616. doi: [10.1345/aph.1K227](https://doi.org/10.1345/aph.1K227)
16. Scagliarini R, Magnani E, Pratico A, Bocchini R, Sambo P, Pazzi P. Inadequate use of acid-suppressive therapy in hospitalized patients and its implications for general practice. *Dig Dis Sci*. 2005;50(12): 2307-2311. doi: [10.1007/s10620-005-3052-4](https://doi.org/10.1007/s10620-005-3052-4)
17. Heidelbaugh JJ, Inadomi JM. Magnitude and economic impact of inappropriate use of stress ulcer prophylaxis in non-ICU hospitalized patients. *Am J Gastroenterol*. 2006;101(10):2200-2205. doi: [10.1111/j.1572-0241.2006.00839.x](https://doi.org/10.1111/j.1572-0241.2006.00839.x)
18. Grube RR, May DB. Stress ulcer prophylaxis in hospitalized patients not in intensive care units. *Am J Health Syst Pharm*. 2007;64(13):1396-1400. doi: [10.2146/ajhp060393](https://doi.org/10.2146/ajhp060393)
19. Bulger J, Nickel W, Messler J, Goldstein J, O'Callaghan J, Auron M, Gulati M. Choosing wisely in adult hospital medicine: five opportunities for improved healthcare value. *J Hosp Med*. 2013;8(9):486-492. doi: [10.1002/jhm.2063](https://doi.org/10.1002/jhm.2063)
20. De Rijdt T, Spriet I, Willems L, Blanckaert M, Hiele M, Wilmer A, Simoens S. Appropriateness of acid suppression therapy. *Ann Pharmacother*. 2017;51(2):125-134. doi: [10.1177/1060028016670414](https://doi.org/10.1177/1060028016670414)
21. MacLaren R, Campbell J. Cost-effectiveness of histamine receptor-2 antagonist versus proton pump inhibitor for stress ulcer prophylaxis in critically ill patients. *Crit Care Med*. 2014;42(4):809-815. doi: [10.1097/CCM.0000000000000032](https://doi.org/10.1097/CCM.0000000000000032)
22. Hammond DA, Kathe N, Shah A, Martin BC. Cost-effectiveness of histamine(2) receptor antagonists versus proton pump inhibitors for stress ulcer prophylaxis in critically ill patients. *Pharmacotherapy*. 2017;37(1):43-53. doi: [10.1002/phar.1859](https://doi.org/10.1002/phar.1859)
23. Barkun AN, Adam V, Martel M, Bardou M. Cost-effectiveness analysis: stress ulcer bleeding prophylaxis with proton pump inhibitors, H2 receptor antagonists. *Value Health*. 2013;16(1):14-22. doi: [10.1016/j.jval.2012.08.2213](https://doi.org/10.1016/j.jval.2012.08.2213)
24. Tasaka CL, Burg C, VanOsdol SJ, Bekeart L, Anglemyer A, Tsurounis C, Rennke S. An interprofessional approach to reducing the overutilization of stress ulcer prophylaxis in adult medical and surgical intensive care units. *Ann Pharmacother*. 2014;48(4):462-469. doi: [10.1177/1060028013517088](https://doi.org/10.1177/1060028013517088)
25. Herzig SJ, Guess JR, Feinbloom DB, Adra M, Afonso KA, Howell MD, Marcantonio ER. Improving appropriateness of acid-suppressive medication use via computerized clinical decision support. *J Hosp Med*. 2015;10(1):41-45. doi: [10.1002/jhm.2260](https://doi.org/10.1002/jhm.2260)
26. Meena N, Costner M, Joshi M. Stress ulcer prophylaxis use in the intensive care unit before and after house staff education. *J Ark Med Soc*. 2015;112(3):38-40.
27. Agee C, Coulter L, Hudson J. Effects of pharmacy resident led education on resident physician prescribing habits associated with stress ulcer prophylaxis in non-intensive care unit patients. *Am J Health Syst Pharm*. 2015;72(11 Suppl 1):S48-S52. doi: [10.2146/sp150013](https://doi.org/10.2146/sp150013)
28. Buckley MS, Park AS, Anderson CS, Barletta JF, Bikin DS, Gerkin RD, O'Malley CW, Wicks LM, Garcia-Orr R, Kane-Gill SL. Impact of a clinical pharmacist stress ulcer prophylaxis management program on inappropriate use in hospitalized patients. *Am J Med*. 2015;128(8):905-913. doi: [10.1016/j.amimed.2015.02.014](https://doi.org/10.1016/j.amimed.2015.02.014)
29. Hatch JB, Schulz L, Fish JT. Stress ulcer prophylaxis: reducing non-indicated prescribing after hospital discharge. *Ann Pharmacother*. 2010;44(10):1565-1571. doi: [10.1345/aph.1P167](https://doi.org/10.1345/aph.1P167)
30. Liberman JD, Whelan CT. Brief report: reducing inappropriate usage of stress ulcer prophylaxis among internal medicine residents. A practice-based educational intervention. *J Gen Intern Med*. 2006;21(5):498-500. doi: [10.1111/j.1525-1497.2006.00435.x](https://doi.org/10.1111/j.1525-1497.2006.00435.x)
31. Mousavi M1, Dashti-Khavidaki S, Khalili H, Farshchi A, Gatmiri M. Impact of clinical pharmacy services on stress ulcer prophylaxis prescribing and related cost in patients with renal insufficiency. *Int J Pharm Pract*. 2013;21(4):263-269. doi: [10.1111/ijpp.12005](https://doi.org/10.1111/ijpp.12005)

32. Anthes AM, Harinstein LM, Smithburger PL, Seybert AL, Kane-Gill SL. Improving adverse drug event detection in critically ill patients through screening intensive care unit transfer summaries. *Pharmacoepidemiol Drug Saf.* 2013;22(5):510-516. doi: [10.1002/pds.3422](https://doi.org/10.1002/pds.3422)
33. Tully MP, Ashcroft DM, Dornan T, Lewis PJ, Taylor D, Wass V. The causes of and factors associated with prescribing errors in hospital inpatients: a systematic review. *Drug Saf.* 2009;32(10):819-836. doi: [10.2165/11316560-000000000-00000](https://doi.org/10.2165/11316560-000000000-00000)
34. Hendey GW, Barth BE, Soliz T. Overnight and postcall errors in medication orders. *Acad Emerg Med.* 2005;12(7):629-634. doi: [10.1197/j.aem.2005.02.009](https://doi.org/10.1197/j.aem.2005.02.009)
35. Hammond DA, Hughes CA, Painter JT, Pennick RE, Chatterjee K, Boye B, Meena N. Impact of targeted educational interventions on clostridium difficile infection treatment in critically ill adults. *Hosp Pharm.* 2016;51(11):901-906. doi: [10.1310/hpj5111-901](https://doi.org/10.1310/hpj5111-901)
36. Hope NH, Ray SM, Franks AS, Heidel E. Impact of an educational intervention on steroid prescribing and dosing effect on patient outcomes in COPD exacerbations. *Pharm Pract (Granada).* 2010;8(3):162-166. doi: [10.4321/s1886-36552010000300002](https://doi.org/10.4321/s1886-36552010000300002)