

Impact of clinical decision support therapeutic interchanges on hospital discharge medication omissions and duplications

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Purpose. Automatic therapeutic substitution (ATS) protocols are formulary tools that allow for provider-selected interchange from a nonformulary preadmission medication to a formulary equivalent. Previous studies have demonstrated that the application of clinical decision support (CDS) tools to ATS can decrease ATS errors at admission, but there are limited data describing the impact of CDS on discharge errors. The objective of this study was to describe the impact of CDS-supported interchanges on discharge prescription duplications or omissions.

Methods. This was a single-center, retrospective cohort study conducted at an academic medical center. Patients admitted between June 2017 and August 2019 were included if they were 18 years or older at admission, underwent an ATS protocol-approved interchange for 1 of the 9 included medication classes, and had a completed discharge medication reconciliation. The primary outcome was difference in incidence of therapeutic duplication or omission at discharge between the periods before and after CDS implementation.

Results. A total of 737 preimplementation encounters and 733 postimplementation encounters were included. CDS did not significantly decrease the incidence of discharge duplications or omissions (12.1% vs 11.2%; 95% confidence interval [CI], -2.3% to 4.2%) nor the incidence of admission duplication or inappropriate reconciliation (21.4% vs 20.7%; 95% CI, -3.4% to 4.8%) when comparing the pre- and postimplementation periods. Inappropriate reconciliation was the primary cause of discharge medication errors for both groups.

Conclusion. CDS implementation was not associated with a decrease in discharge omissions, duplications, or inappropriate reconciliation. Findings highlight the need for thoughtful medication reconciliation at the point of discharge.

Keywords: formulary stewardship, medication reconciliation, medication-use policy, pharmacy technology, therapeutic interchange

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Medication formularies are maintained by many hospitals and health systems in an effort to guide prescribing toward safe and efficacious therapies.¹ With continued growth in the number of Food and Drug Administration-approved therapies, coupled with rising healthcare costs, appropriate formulary management has become a priority for healthcare entities as a mechanism to contain medication costs and improve

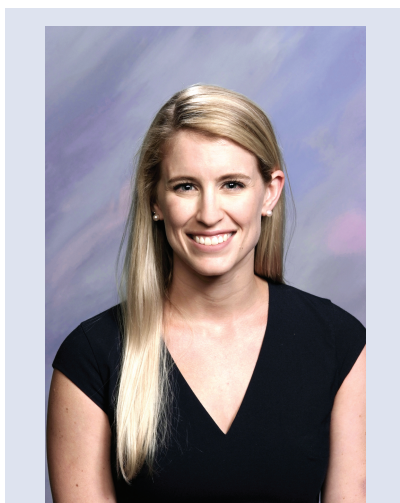
safety.² Therapeutic interchange (TI), defined as the dispensing of a medication that is deemed therapeutically equivalent to the agent originally prescribed by an authorized provider, has been identified as one such formulary management strategy.^{1,2} Automatic therapeutic substitution (ATS) protocols allow for pharmacist- or provider-driven TI conversion from a nonformulary preadmission medication to a pharmacy and

therapeutics committee (P&T)-approved formulary equivalent upon hospital admission. These protocols are common practice at many healthcare institutions as they serve to simplify pharmacy workflow and improve patient safety while contributing to cost-saving efforts.¹

Although ATS protocols are valuable tools for formulary management, there is concern that this practice may lead to errors during transitions of care. Previous studies published on this topic have estimated that between 21% and 32% of patients experience ATS-related medication errors upon hospital admission.^{3,4} Similarly, up to 22% of discharge medication lists include at least 1 error that is the direct result of an inpatient TI.^{3,5-7}

In light of these data, healthcare administrators have looked to technology to facilitate appropriate use of TIs to decrease medication errors during transitions of care. Clinical decision support (CDS) tools are electronic systems designed to aid in patient assessment and clinical decision-making.⁸ CDS can be applied in a number of ways to reduce the likelihood of medication errors and improve prescribing practices; alerts can be basic, such as alerting providers to a drug-drug interaction, or more advanced, guiding therapeutic dosing based on patient-specific factors.⁹ With respect to TIs, CDS can be a useful tool to manage appropriate prescribing during care transitions, and a number of publications have provided support for leveraging CDS tools to improve the accuracy of ATS. These studies have demonstrated that implementation of CDS technology can result in an absolute decrease in ATS-related admission errors of 12.6% to 14.4%.^{4,10}

While there are data to support the utility of CDS in guiding TI at patient admission, the impact of CDS on discharge errors following application of an ATS protocol has not been fully addressed. Further, there is concern that discharge errors pursuant to a TI may lead to consequences in the outpatient setting where monitoring and provider follow-up are less frequent. Lending credence to these concerns, a 2020



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study evaluating the relationship between TI protocols and discharge medication changes found that TI increased the incidence of discharge medication errors by 70% when compared to medications that were not converted during admission.⁶

A study by Kang et al¹⁰ is one of the only published studies evaluating CDS impact on discharge medication reconciliation. Before CDS implementation, the authors reported that 65% of all TI-eligible discharge medications were associated with at least 1 discrepancy, with the most common error being continuation of an interchange medication (60% of errors) upon discharge.

Following CDS implementation, however, the frequency of inappropriate discharge orders decreased to 16%; again, continuation of formulary interchange medication upon discharge was the most common error. This study was the first to support CDS use in discharge prescribing after TI, but the results lacked generalizability owing to the study design. Additionally, discharge medication accuracy was a secondary endpoint, and the study was not powered to detect a significant difference in pre- and postimplementation outcomes. Further, the investigators looked at only 3 medication classes, which is not representative of the multitude of potential therapeutic conversions that are allowable in most ATS protocols.

Despite limitations in the available literature, this line of research has important clinical and operational implications, and a more thorough investigation of this clinical topic is warranted. The objective of the current study was to describe the impact of CDS-supported ATS interchanges on discharge prescription duplications and omissions as compared to manual ATS without CDS technology.

Methods

Study design. The study was a single-center, retrospective cohort study conducted at an academic medical center with over 900 licensed inpatient beds. The study cohort included adult patients who were subject to a predefined ATS upon admission following the implementation of CDS technology; the control group included patients who were subject to an ATS change before implementation of the CDS tool.

Our institution uses a P&T committee-approved TI protocol for patients admitted with an order for a nonformulary medication. This protocol supports P&T-approved pharmacist prescribing practices, allowing pharmacists to make therapeutic substitutions for nonformulary medications. Starting in July 2017, the P&T committee began to integrate provider alerts into the electronic health record (EHR; Epic Systems, Verona, WI). The CDS tool

alerts providers to the appropriate TI, that is, P&T-approved agent, strength, dose, and frequency, when an order is placed for a nonformulary medication. CDS was not employed to guide discharge reconciliation; however, a function of the EHR at our institution groups medications together by class at the time of discharge, effectively alerting providers and pharmacists of potential duplications and omissions. This grouping mechanism was active during both the pre- and postimplementation periods.

Before study initiation, the institutional review board approved this study with a waiver of consent.

Data collection. Patients admitted between June 1, 2017, and August 31, 2019, were included if they were 18 years of age or older at the time of hospitalization, were subject to an ATS protocol-approved TI, and had a completed medication reconciliation as part of their discharge paperwork. Patients who had a nonformulary medication on their home medication list and at least 1 documented inpatient administration of a formulary medication for which there was a predefined ATS protocol were selected for review.

Investigators included 9 tier 2 and tier 3 medication classes, as defined by the American Hospital Formulary Service (AHFS),¹¹ that had P&T-approved interchanges both before and after CDS implementation in the study. These classes included angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), second-generation antihistamines, selective and nonselective beta-blockers, carbonic anhydrase inhibitors, calcium channel blockers, intranasal corticosteroids, and ophthalmic prostaglandins. It is important to note that, at our institution, CDS implementation occurred at different times for each included medication class; the approach was adopted to decrease workload on informatics and operational pharmacists. To ensure that relevant encounters were identified for classes with an active CDS alert, the authors designated specific data collection periods for each medication

class. These periods encompassed the 6 months immediately before and after the implementation date and were different for each medication class.

In the case of combination medications, each was assigned to only 1 medication class for the purposes of data collection and analysis; assignments were made based on how the combination medication is defined in the P&T-approved protocol. For example, the approved TI for olmesartan/amlodipine at our institution is listed under “angiotensin II receptor blocker (ARB) interchanges” per our policy; therefore, any TI encounters with this combination were included as part of the ARB medication class for the purposes of this study.

Patients who met inclusion criteria were identified via the Carolina Data Warehouse for Health, a database that maintains administrative and clinical data for the health system. Data points included admission characteristics (eg, length of stay and admitting and discharging service), ATS interchange characteristics (eg, medication class, nonformulary home medication, and interchange medication), and discharge disposition.

Interchanges were evaluated for inappropriate vs appropriate TI reconciliation at both admission and discharge. An admission TI was considered appropriate if the nonformulary outpatient medication was changed to a P&T-approved therapeutic equivalent during inpatient stay. For discharge, medication lists were reviewed for omissions, duplications, and inappropriate reconciliation of the ATS medication. Therapeutic duplication was defined as continuation of more than 1 agent from the same AHFS class at discharge. Omission was defined as discontinuation of both the preadmission nonformulary medication and the inpatient formulary equivalent medication. Inappropriate reconciliation was defined as the continuation of a formulary medication at discharge. Of note, if inappropriate reconciliation also resulted in a therapeutic duplication, the encounter was classified as having both types of error. When a discharge error

of any type was identified, pharmacist documentation was reviewed within the EHR to determine whether there was documented rationale for discharge errors as defined by the study protocol. If a rationale was provided, this was noted during data collection.

Outcomes. The primary outcome was incidence of therapeutic duplication or omission on the discharge medication list. The main secondary outcome was incidence of therapeutic duplication, omission, or inappropriate reconciliation at the time of discharge. Additional secondary outcomes included the incidence of each error type (ie, omission, duplication, and inappropriate reconciliation), the incidence of omissions and duplications by medication class and by discharge disposition, and the overall rate of compliance with the P&T-approved protocol for admission TIs.

Statistical analysis. A power analysis was completed before study initiation. We calculated that 1,442 TIs were required to achieve 80% power to detect a 4% absolute decrease in discharge prescription duplication or omission following implementation of a provider-facing CDS tool, assuming a baseline error rate of 10%.⁵

Descriptive statistics were used to report baseline characteristics and to determine the incidence of the primary and secondary outcomes. Nominal variables were analyzed using a χ^2 test or Fisher's exact test, as appropriate. Continuous data were assessed for normality using a Shapiro-Wilk test. Normally distributed data were analyzed using Student's *t* tests and are presented as mean (SD); nonnormally distributed data were analyzed using the Mann-Whitney *U* test and are presented as median (interquartile range). All analyses utilized a 2-tailed test for statistical significance with a predefined α threshold of ≤ 0.05 , which was not adjusted for multiple comparisons. Statistical analyses were performed using SPSS Statistics 26.0 (IBM Corporation, Armonk, NY).

Results

ATS encounters. A total of 1,499 ATS interchanges were reviewed for

Table 1. Characteristics of Included Automatic Therapeutic Interchanges

Characteristic ^a	Preimplementation Interchanges (n = 737)	Postimplementation Interchanges (n = 733)
Length of stay, mean (range), days	5.5 (0-107)	5.4 (0-113)
Medication class		
ACE inhibitor	196 (26.6)	187 (25.5)
ARB	83 (11.3)	94 (12.8)
Antihistamine (second generation)	43 (5.8)	44 (6)
Selective BB	102 (13.8)	93 (12.7)
Nonselective BB	63 (8.5)	58 (7.9)
CAI	19 (2.6)	20 (2.7)
CCB	75 (10.2)	105 (14.3)
Intranasal corticosteroid	74 (10)	55 (7.5)
Ophthalmic prostaglandin	82 (11.1)	77 (10.5)
Admitting service type		
Medical	468 (63.5)	499 (68.1)
Surgical	259 (35.1)	220 (30)
Other	10 (1.36)	14 (1.9)
Discharge service type		
Medical	461 (62.6)	489 (66.7)
Surgical	259 (35.1)	229 (31.2)
Other	17 (2.3)	15 (2.1)
Discharge disposition		
Home with self-care	468 (63.5)	473 (64.5)
Home health	156 (21.2)	158 (21.6)
Skilled nursing facility	85 (11.5)	69 (9.4)
Outside hospital or care facility	24 (3.3)	35 (3.3)

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BB, beta-blocker; CAI, carbonic anhydrase inhibitor; CCB, calcium channel blocker.

^aData are presented as No. (%) unless indicated otherwise.

inclusion. Of these, 29 (1.9%) were excluded because the discharge medication list associated with the index encounter was either incomplete or absent. Ultimately, 737 pre-CDS encounters and 733 post-CDS encounters were included in the final analysis (Table 1).

Primary outcome. CDS implementation did not significantly decrease the incidence of discharge medication duplications or omissions when comparing the pre- and

postimplementation periods (12.1% vs 11.2%; difference, -0.9%; 95% confidence interval [CI], -2.3% to 4.2%). Observed discharge medication omissions vs duplications were similar between the groups (Table 2).

Secondary outcomes. Incidence of the main secondary outcome—discharge medication omission, duplication, or inappropriate reconciliation—was comparable between the pre- and postimplementation periods

with an incidence of 21.4% vs 20.7% (difference, -0.7%; 95% CI, -3.4% to 4.8%). Inappropriate reconciliation was the primary cause of discharge medication errors in both the pre-CDS and post-CDS groups (12.1% vs 12.6%), followed by therapeutic omissions (8.3% vs 8.2%) and duplications (3.8% vs 3.0%).

CDS implementation did not decrease the incidence of discharge medication errors within any of the individual drug classes. Admission formulary compliance and adherence to P&T-approved ATS interchanges increased from 63.6% to 73.0% (difference, 9.4%; 95% CI, -14.2 to 4.8) following CDS implementation. Additional secondary outcomes are presented in Table 3.

Discussion

TI programs and associated P&T-approved ATS protocols are commonly used across many health systems.¹² While there are many advantages to this practice, TI protocols are also associated with medication errors that originate at transitions of care.^{3,5,6} Results from this study suggest that CDS integration does not significantly decrease discharge medication errors following TI.

The current study was designed to expand upon data from a previous publication by Kang et al.¹⁰ In that study, investigators implemented a provider-facing alert to facilitate admission and discharge medication reconciliation. The authors of the study evaluated 3 medication classes (ACE inhibitors, ARBs, and statins) to determine whether CDS implementation decreased the number of discharge errors, which the protocol defined as any change in a patient's home medication regimen. Results from this study showed that CDS implementation decreased the absolute incidence of discharge medication errors from 64.5% to 16.3% of all TI encounters ($P < 0.05$). In contrast to these data, we were unable to realize a significant difference between the groups before and after CDS implementation at our hospital site. In comparing results from the previous publication with our own findings, it is important to note that, in the reference study by Kang et al,¹⁰

Table 2. Discharge Medication Errors for Automatic Therapeutic Substitution Interchanges

Outcome ^a	Preimplementation Interchanges (n = 737)	Postimplementation Interchanges (n = 733)	Difference, % (95% CI)
Discharge omission or duplication ^b	89 (12.1)	82 (11.2)	-0.9 (-2.3 to 4.2)
Discharge omission, duplication, or inappropriate reconciliation ^{c,d}	158 (21.4)	152 (20.7)	-0.7 (-3.4 to 4.8)
Omission	61 (8.3)	60 (8.2)	-0.2 (-2.9 to 2.6)
Duplication	28 (3.8)	22 (3.0)	-0.8 (-2.7 to 1.1)
Inappropriate reconciliation	89 (12.1)	92 (12.6)	-0.5 (-3.0 to 3.7)

Abbreviation: CI, confidence interval.

^aData are presented as No. (%) unless indicated otherwise.

^bPrimary outcome.

^cInappropriate reconciliation was defined as continuation of formulary medication at discharge.

^dIf an interchange was associated with both duplication and inappropriate reconciliation, it was counted as both; the sum of the error types may therefore exceed 100%.

Table 3. Secondary Outcomes

Outcome ^a	Preimplementation Interchanges (n = 737)	Postimplementation Interchanges (n = 733)	P Value
Appropriate interchange at admission	468 (63.6)	535 (72.9)	<0.001
Discharge errors ^b by class			
ACE inhibitor	196 (26.6)	187 (25.5)	0.73
Antihistamine	43 (5.8)	44 (6)	0.35
ARB	83 (11.3)	94 (12.8)	0.98
CAI	19 (2.6)	20 (2.7)	0.77
CCB	75 (10.2)	105 (14.3)	0.29
ICS	74 (10.1)	55 (7.5)	0.08
Nonselective BB	62 (8.4)	58 (7.9)	0.68
PGE	102 (13.9)	93 (12.7)	0.44
Selective BB	82 (11.1)	77 (10.5)	0.08
Discharge errors ^b by discharge location			
Hospice	4 (0.5)	9 (1.2)	0.17
Home	623 (84.6)	631 (86.1)	0.69
Rehab	96 (13.1)	84 (11.4)	0.33
Other hospital	13 (1.7)	9 (1.2)	0.39
Discharge errors with pharmacist documentation ^c	15 (9.5)	27 (17.8)	0.06

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BB, beta-blocker; CAI, carbonic anhydrase inhibitor; CCB, calcium channel blocker; ICS, intranasal corticosteroid; PGE, ophthalmic prostaglandin.

^aData are presented as No. (%) unless indicated otherwise.

^bError was defined as omission, duplication, or inappropriate reconciliation.

^cPercentage was calculated based on total errors for the pre- and postimplementation periods; the total number of errors for these periods was 158 and 152, respectively.

ATS protocols were a new initiative at the study site. The increased awareness around ATS protocols during the study

period likely contributed to the significant decrease in errors. In contrast, ATS protocols at our institution were well

established before CDS implementation; it is unknown whether our findings would have been more impressive if we

had studied the impact of ATS interchanges earlier in their adoption.

Another explanation for why our study did not realize a significant difference lies in the knowledge that the baseline discharge error rate at our hospital was lower than the error rates described in previous studies. Most studies relating to this topic estimate an 8% to 22% baseline TI-related error rate at the time of discharge.^{3-5,7} In our study, the error rate before CDS implementation was roughly 12%, which is on the lower end of the range. Furthermore, the observed 1.4% decrease in discharge medication discrepancies in our study was much smaller than the expected delta we used to calculate sample size. As such, our study was likely underpowered to detect such a small difference in proportions, and the true impact of our intervention is still ill defined. These considerations highlight systematic differences between studies that may explain discrepancies between our findings and published literature.

Discharge errors in our study were driven largely by inappropriate reconciliation (ie, continuation of a formulary medication at discharge); these errors accounted for more than 50% of errors in both the pre- and postimplementation periods. Findings from this study were similar to those of previous publications, which also report inappropriate discharge reconciliation as a top reason for discharge medication errors. One study by Glaholt et al⁷ found that, of 47 patients discharged on inappropriate therapy, 32% were inappropriately discharged on a formulary agent rather than their home medication. A similar study found that 8% of patients discharged from an academic medical center were inappropriately prescribed a formulary agent at discharge following ATS interchange and that this was the most common discrepancy type only behind omissions (10% of patients).⁶ There is no clear explanation for why this type of error is so common, but it may be a function of familiarity; inpatient providers, anecdotally, are more comfortable dosing and prescribing medications that they

see on a daily basis and may gravitate toward formulary agents when planning discharge. In contrast to inappropriate reconciliation, therapeutic duplication was the least common type of error in our study (3.8% vs 3.0% in the pre- and postimplementation periods). This is likely because, at our institution, medications within the same AHFS class are “grouped” together during discharge reconciliation. This function of the EHR allows providers to quickly identify duplications. Further, pharmacists at our institution are intimately involved in the discharge reconciliation process and are often able to identify errors before the provider can sign discharge orders. These potential explanations are specific to our institution; other entities may experience alternative reasons for discharge prescribing changes

The current study highlights the need for thorough and thoughtful reconciliation at the point of discharge. National accreditation bodies such as the Joint Commission consistently identify accurate medication reconciliation as a performance measure for patient safety.¹³ With this in mind, it is worrisome that TI-related discharge error rates at our institution are as high as 10% to 13% even with CDS guidance. This knowledge is one of the reasons critics of ATS protocols argue that TI is not only an irresponsible practice but also may actually contribute to patient harm.^{12,14,15} Despite such concerns, available data suggest that TI-related discharge errors, while undesirable, are not significantly associated with detrimental outcomes. In one study, Popp et al⁶ evaluated the relationship between TI, discharge medication changes, and the impact of these changes on hospital readmissions. The authors evaluated 16 therapeutic classes and tracked associated readmissions, including visits to the emergency department (ED), for 497 patient encounters. Through their analysis, the researchers concluded that neither TI nor the number of discharge medication changes was a predictor of readmission or ED visits at 30, 60, or 90 days, indicating that discrepancies

following TI are not correlated with rehospitalization. Ultimately, the evidence suggests that this practice is not only safe but beneficial in terms of hospital administration and patient care.^{2,12}

Risks from ATS-related interchanges must be appropriately weighed against benefits. In this study, CDS implementation significantly improved admission formulary adherence to ATS protocols, a finding consistent with previous publications demonstrating increased formulary and ATS protocol compliance following the implementation of CDS technology.^{3,4,10} This discovery further supports the use of CDS technology as a valuable tool in patient care delivery. EHR changes such as ATS alerts are relatively simple for informatics personnel to implement, and these efforts can translate into significant patient benefit. In fact, research shows that implementation of, and adherence to, CDS tools can significantly improve clinical outcomes and decrease costs associated with hospitalization.¹⁶ As this relates to our study, implementation of CDS-guided TI may allow practitioners to spend less time reviewing medication lists and more time on essential clinical services. This study did not evaluate either inpatient or outpatient clinical outcomes, but it is reasonable to presume that implementation had a positive impact on patient care and clinical workflow based on data from similar studies touting the impact of CDS technology.^{3,4,6,16}

This study had a number of limitations beyond the inherent confines of a retrospective study. First, owing to a large number of patients and the variability in documentation between providers, we did not review progress notes or documentation other than pharmacist interventions to identify whether discharge errors, as defined by our protocol, were intentional changes rather than discrepancies. Inpatient providers frequently change or discontinue a home medication during the course of an inpatient stay based on patient presentation and hospital course. Because of inconsistent documentation, our data were unable to identify such instances and our

results may therefore overestimate the discharge error rate. The way in which we documented inappropriate reconciliation vs duplication may also have inflated the error rate. Inappropriate reconciliation and therapeutic duplication errors did not always overlap, but it is important to note that, where they did, there was a potential for double counting. However, this limitation was systematic and applied to interchanges in the pre- and post-CDS periods; while numbers may be exaggerated, trends in error and error types are expected to be consistent with the presented data. Another limitation was that we assessed errors associated with specific ATS interchange; we did not assess errors at the encounter level. In other words, if a patient encounter was selected based on an ACE inhibitor interchange, the encounter was assessed only for errors related to the ACE inhibitor class and not for errors on the discharge medication list as a whole. Using this approach, we are unable to estimate the number of inpatient encounters that may include 1 or more ATS-related errors; further, we are unable to report, on average, how many errors were associated with an individual patient encounter. Only 9 medication classes were included in this study, some of which corresponded to very few encounters over the studied time period. The small sample size limited our ability to determine whether CDS support is more important for certain classes of medications. Additionally, because of the way data were collected, we were unable to quantify how many interchanges were accompanied by a provider-facing alert. For example, if a provider manually ordered an interchange medication after CDS implementation, that manual change would still count as a post-CDS encounter. Finally, we did not collect data on patient-specific characteristics such as age, sex, or medication list complexity; as such, we cannot draw any conclusions regarding whether a specific population is more or less vulnerable to discharge medication errors.

Conclusion

Overall, this study found that 20% to 21% of all TIs were associated with at least 1 discharge medication error. CDS implementation did not significantly improve discharge medication list accuracy. As CDS technology continues to evolve, there is opportunity for pharmacy specialists to further investigate the role of these systems in transitions of care. Future studies in this arena should focus on the impact of technology optimization, pharmacist integration, and comprehensive reconciliation services on patient-centered outcomes and customer satisfaction.

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Disclosures

The authors have declared no potential conflicts of interest.

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