Background: Potentially inappropriate medication (PIM) use in hospitalized older patients is common. Our objective was to determine whether a computerized provider order entry (CPOE) drug warning system can decrease orders for PIMs in hospitalized older patients.

Methods: We used a prospective before-and-after design among patients 65 years or older admitted to a large, urban academic medical center in Boston, Massachusetts, from June 1, 2004, through November 29, 2004 (for patients admitted before the warning system was added), and from March 17, 2005, through August 30, 2008 (patients admitted after the warning system was added). We instituted a medication-specific warning system within CPOE that alerted ordering providers at the point of care when ordering a PIM and that advised alternative medication or dose reduction. The main outcome measure was the rate of orders for PIMs before and after the warning system was deployed.

Results: The mean (SE) rate of ordering medications that were not recommended dropped from 11.56 (0.36) to 9.94 (0.12) orders per day after the implementation of a CPOE warning system (difference, 1.62 [0.33]; P < .001), with no evidence that the effect waned over time. There were no appreciable changes in the rate of ordering medications for which only dose reduction was recommended or that were not targeted after CPOE implementation. These effects persisted in autoregressive models that accounted for secular trends and season (P < .001).

Conclusion: Specific alerts embedded into a CPOE system, used in patients 65 years or older, can decrease the number of orders of PIMs quickly and specifically.

Arch Intern Med. 2010;170(15):1331-1336

Older people admitted to the hospital are especially vulnerable to adverse drug events (ADEs), which occur in up to 40% of hospital admissions. Adverse drug events increase the length of stay, the cost of caring for patients admitted to the hospital, and the risk of death.

Some medications may predispose vulnerable older patients to ADEs. Fick et al proposed a list of drugs identified by a panel of geriatric medicine experts as being medications that should be avoided in older persons. Despite the publication of the “Beers medications,” the prescription of potentially inappropriate medications (PIMs) to elderly patients remains common.

Up to 60% of ADEs during hospitalization occur at the time of ordering; the remainder occur downstream, during delivery or omission (not giving a medication as prescribed). Computerized provider order entry (CPOE) systems provide an opportunity for intervention to change prescribing practices before PIMs are ordered. However, to our knowledge, no CPOE system has previously been described that uses a warning system built around PIMs in older, hospitalized adults.

The purpose of this study was to determine whether the number of orders for PIMs in hospitalized patients 65 years or older could be decreased using a computerized warning system linked to CPOE. We studied the ordering patterns before and after the implementation of such a system for 3 groups of drugs: a larger group of drugs included in the original list of drugs compiled by Fick et al according to the Beers criteria (Beers medications) that were flagged not to be used, a second group of Beers medications that were flagged to be used at reduced doses, and a third group of Beers medications that were flagged to be used at reduced doses, and a third group of Beers medications not flagged.

METHODS

PATIENT POPULATION

We studied all inpatients 65 years or older hospitalized at a single urban academic medical center in Boston, Massachusetts. The hospital provides primary and tertiary care, with 621 inpatient beds and approximately 40,000 inpatient admis-
The CPOE system at the medical center was developed by the hospital’s CPOE system. Two screen shots illustrating the CPOE system, although dispensed medications are tracked through a separate pharmacy program. With hospital Pharmacy and Therapeutics Committee feedback, we developed medication-specific alerts that were built into the hospital’s CPOE system. Two screen shots illustrating the warnings encountered when a geriatric precaution is found.

## CPOE WARNING SYSTEM

The CPOE system at the medical center was developed by programmers at the institution and is not commercially available. All medications prescribed to inpatients are ordered through the CPOE system, although dispensed medications are tracked through a separate pharmacy program. With hospital Pharmacy and Therapeutics Committee feedback, we developed medication-specific alerts that were built into the hospital’s CPOE system. Two screen shots illustrating the warnings encountered when a geriatric precaution is found.

### Table 1. Specific Beers Medications Targeted and the Warning Received by the Ordering Physician

<table>
<thead>
<tr>
<th>Drug</th>
<th>Explanation for Warning</th>
<th>Degree of Severity</th>
<th>Conditions That Put Patients at Increased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not-Recommended Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline hydrochloride</td>
<td>Because of its strong anticholinergic and sedation properties, amitriptyline should be used rarely in the elderly.</td>
<td>High</td>
<td>Hepatic, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Chlorzepate dipotassium</td>
<td>This drug has a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.</td>
<td>High</td>
<td>Renal, hepatic, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Clonidine</td>
<td>Potential for orthostatic hypotension and CNS adverse effects.</td>
<td>Low</td>
<td>Renal or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Clorazepate dipotassium</td>
<td>This drug has a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.</td>
<td>High</td>
<td>Renal, hepatic, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Cyclobenzaprine hydrochloride</td>
<td>Most muscle relaxants and antispasmodics are poorly tolerated by elderly patients, since these cause anticholinergic side effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.</td>
<td>High</td>
<td>Renal, hepatic, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Diazepam</td>
<td>This drug has a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.</td>
<td>High</td>
<td>Hepatic or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>May cause confusion and sedation. Should not be used as a hypnotic, and, when used to treat emergency allergic reactions, it should be used in the smallest possible dose.</td>
<td>High</td>
<td>Neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Doxazosin mesylate</td>
<td>Potential for hypotension, dry mouth, and urinary problems.</td>
<td>Low</td>
<td>Renal, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Fluoxetine hydrochloride</td>
<td>Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.</td>
<td>High</td>
<td>Hepatic or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.</td>
<td>High</td>
<td>Neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Ketorolac tromethamine</td>
<td>Immediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.</td>
<td>High</td>
<td>Renal, hepatic, or cardiovascular impairment</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Has the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.</td>
<td>High</td>
<td>Renal, hepatic, or cardiovascular impairment</td>
</tr>
<tr>
<td>Oxybutynin</td>
<td>Most muscle relaxants and antispasmodics are poorly tolerated by elderly patients, since these cause anticholinergic side effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.</td>
<td>High</td>
<td>Renal, hepatic, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Has the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.</td>
<td>High</td>
<td>Renal, hepatic, or cardiovascular impairment</td>
</tr>
<tr>
<td>Propoxyphene</td>
<td>Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotic drugs.</td>
<td>Low</td>
<td>Renal, hepatic, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Greater potential for CNS and extrapyramidal adverse effects. Other antipsychotic agent might be more appropriate.</td>
<td>High</td>
<td>Renal, hepatic, cardiovascular, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td><strong>Dose-Reduction Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lorazepam</td>
<td>Because of increased sensitivity to benzodiazepines in elderly patients, smaller doses may be as effective as well as safer. Total daily dose should rarely exceed the suggested maximum of 3 mg.</td>
<td>High</td>
<td>Renal, hepatic, or neurologic/psychiatric impairment</td>
</tr>
<tr>
<td>Ferrous sulfate</td>
<td>Does not significantly increase the amount absorbed but greatly increase the incidence of constipation.</td>
<td>Low</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Unflagged Medications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amiodarone hydrochloride</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Digoxin</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Disopyramide phosphate</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CNS, central nervous system; GI, gastrointestinal; NA, not applicable.

4 All warnings also state, “Precaution is necessary for use of [drug name] in geriatric patients.” All warnings provide a reference to the updated Beers criteria in the article by Fick et al.

5 The exact wording of the explanations is given.
are available in a supplementary eAppendix (http://www.archinternmed.com).

From the larger list of PIMs listed in the article by Fick et al, we identified 3 primary classes of medications for study a priori: medications that were flagged as not recommended for use in older patients (not-recommended medications), those for which only a reduced dose was advised (dose-reduction medications), and those that were not flagged because no safer alternative was considered equally efficacious (unflagged medications [amiodarone hydrochloride, digoxin, disopyramide phosphate, and indomethacin]); the last group represented controls in our analyses. Table 1 shows the targeted drugs and the wording of the alerts used. A geriatrician (M.L.P.M.) and a pharmacist proposed the specific groups of medications, using the literature where possible to support their decisions, and the Pharmacy and Therapeutics Committee at the medical center, composed of senior hospital pharmacists and clinicians, revised and approved the list.

We did not target 2 other general categories of medications from the original list of Beers medications: (1) drug classes for which individual drugs were not consistently in the formulary throughout the study or that were extremely infrequently used among elderly inpatients and (2) drug classes with very broad and heterogeneous use (eg, nonsteroidal anti-inflammatory drugs and calcium channel blockers) that were left unflagged to minimize the number of warnings encountered by users. We included these latter 2 classes as controls in secondary analyses.

For all flagged medications, the ordering provider had the option to bypass the warning and order the medication; no prior approval was required. Each time, however, the ordering provider had to choose a reason. From March 17, 2005, through October 1, 2006, there were 3 possible reasons from which the clinician could choose: (1) “Patient stabilized on regimen; will monitor appropriate drug levels or laboratory values”; (2) “Interaction noted, regimen clinically indicated, will closely monitor”; or (3) Other. On October 2, 2006, a fourth choice was added: (4) “Warning noted, will use smaller dose and monitor for side effects.”

The warning system applied to all patients admitted to the hospital who were 65 years or older at the time of the order regardless of their location within the hospital or admitting service, although meperidine hydrochloride and promethazine hydrochloride were part of a fixed postanesthesia care unit order set that was not flagged and thus are not included. There were no other concurrent efforts made to educate providers about medication safety, and the warnings suggested no specific alternatives.

OUTCOME MEASURES

From June 1 through November 29, 2004, the 6 months before the deployment of the CPOE warning system, the number of orders in hospitalized patients 65 years or older were recorded for the selected medications. All orders, whether as-needed or standing orders, were included; the hospital does not have an electronic medication administration record, and hence we were not able to record the number or dosage of medications actually given to the patient. We excluded the period between November 30, 2004, and March 16, 2005, the period of beta testing of the warning system. We then recorded all orders after the warning system was deployed, from March 17, 2005, through August 30, 2008.

STATISTICAL ANALYSES

We computed 2 measures of the rate of prescribing of Beers medications: the daily number of medications in each class divided by either the total number of hospitalized patients 65 years or older or the number of newly admitted hospitalized patients 65 years or older each day. Because medications are differentially more likely to be prescribed on the first hospital day, these denominators represent complementary estimates of the number of patients at risk for inappropriate prescriptions.

We first plotted the daily rate of each outcome measure against calendar time and fit separate smoothed splines for the periods before and after implementation. In initial analyses, we calculated the mean daily rates of each of the 3 classes of drugs before and after the warning system was instituted and compared these with unpaired, 2-tailed t tests. Because the smoothed splines indicated that the underlying trend of the outcome rate over time was linear, we assumed linearity in time series models and fit autocorrelative regression models that accounted for the serial correlation in the measurement errors of the daily outcome rates. These models included calendar time, period (before vs after implementation), the product (or interaction) of period × time (ie, change in the secular trend after the implementation), and season. Regression analyses were performed in SAS statistical software, version 9.2 (SAS Institute Inc, Cary, North Carolina), using the PROC AUTOREG procedure.

RESULTS

During the period of study, there was a secular trend in the number of patients in the hospital 65 years or older and in the mean number of all orders, resulting in larger numbers of orders over time.

The Figure shows the temporal trends in the rate of orders of the 3 classes of medications studied. After the warning system was deployed, there was an immediate and sustained decrease in the rate of orders for the not-recommended medications. There was a modest secular trend resulting in decreased use of unflagged medications that did not change appreciably after the warning system implementation, and there was no change in the dose-reduction medications.

In before-and-after comparisons (Table 2), the mean (SE) rate of prescribing not-recommended medications dropped from 11.56 (0.36) to 9.94 (0.12) orders per day (difference, 1.62 [0.33]; P < .001). There was a modest decrease in the use of unflagged medications that was of borderline statistical significance, consistent with the observed secular trend, and we observed no change in the rate of prescribing medications in which only a dose reduction was advised.

Autoregressive models yielded similar results. There was a highly significant and immediately observed drop in the rate of use of not-recommended medications (P < .001), with no change in the secular trend after implementation of the intervention (P = .11). There were no significant changes in the absolute rate of prescribing or in the secular trend of prescribing for the other 2 classes of medications after implementation of the intervention in these models.

In secondary analyses, we also examined the rates of prescribing of all unflagged medications on the original list of Beers medications rather than the 4 medications selected a priori. In autoregressive models, there was no significant effect of the intervention on the daily rate of prescribing in absolute terms (P = .44) or on the secular trend of prescribing (P = .17).

Among the not-recommended medications, the most commonly prescribed was diphenhydramine, which accounted for approximately one-third of all prescriptions in that group before the implementation. Both its use and the use of other targeted medications dropped markedly after implementation of the warning system,
Although we had insufficient power to examine other medications individually. For example, the daily rate of orders for not-recommended medications per new admission (SE) dropped by 0.070 (0.008) \((P < .001)\) after implementation; the corresponding drops were 0.043 (0.004) \((P < .001)\) for diphenhydramine alone and 0.027 (0.006) \((P < .001)\) for other targeted medications. The drops after implementation were also significant in autoregressive models for diphenhydramine \((P < .001)\) and for other targeted medications \((P = .001)\).

All orders recorded in this study on flagged medications reflect orders in which the ordering provider bypassed the warning; the CPOE does not track prescriptions that are started but not completed. In our study, users provided “Interaction noted, regimen clinically indicated, will closely monitor” as the reason for overriding the warning half the time. “Patient stabilized on regimen; will monitor appropriate drug levels or laboratory values” was given as the second most common reason for overriding the warning (Table 3). A third option that indicated the prescriber intended to use a low dose was instituted on October 2, 2006; as intended, this option was used more frequently for dose-reduction medications (19%) than for not-recommended medications (13%; \(P < .001\) for heterogeneity across categories).

**COMMENT**

In this quasi-experimental study of a large urban medical center, the rate of orders for PIMs in older patients was markedly decreased by the use of a CPOE warning system targeting a subset of Beers medications. The intervention showed no signs of users growing weary of repeated warnings and ignoring them (“alert fatigue”), and other medications that were not flagged or flagged only for dose adjustment continued to be prescribed at unchanged rates.

**SPECIFIC FEATURES AND FINDINGS**

After our alert system was implemented, the rate of ordering of the targeted medications declined immediately in the study population. Others have found similar results in the outpatient setting.8,9 This may reflect our restriction to only a subset of medications with legitimate alternatives in a vulnerable patient population.10 In this regard, the specificity and immediacy of the drop in the use of flagged medications is reassuring and suggests that local systems can be effectively tailored to meet local standards of care. Indeed, previous research suggests that drug alerts created in internally developed CPOE systems tailor-made to an individual institution or service can reduce medication errors or orders for PIMs.11-13

We did not observe a substantial learning effect, in which one might hope to see a further reduction over time in the rate of ordering the PIMs, perhaps because of the annual turnover of house staff who order medications. On the other hand, the effect of our warning system appeared to be durable over time with no sign that users grew weary of repeated warnings.

**CPOE IN AN AGING POPULATION**

Many clinicians have not received formal education about the unique medical needs of elderly patients and, de-
spite the fact that more people are living longer, there are no geriatric medicine-specific performance standards for US medical students. This may explain why PIMs continue to be prescribed for hospitalized patients 65 years or older and provide a rich target for CPOE intervention.

Understanding this limit in training, we created a CPOE warning system to decrease the use of PIMs in older patients. These CPOE systems change the way clinicians order medications and provide new opportunities to guide behavior. Although less than 10% of US hospitals currently use CPOE, the Institute of Medicine report calling for universal adoption of CPOE heralds an increasing reliance on this technology.

Designing CPOE systems to shape best practice is an evolving field. Research suggests that CPOE systems without any decision support around medication ordering are associated with high rates of ADEs. Furthermore, general drug alerts within CPOE systems are overridden up to 90% of the time. Initial efforts to reduce ADEs with CPOE systems have focused on reducing medication errors, such as drug allergy and drug-drug interactions. Our results suggest that specific drug alerts for medications that place older patients at particular risk for ADEs could be an especially attractive addition to such systems.

NEXT STEPS AND IMPLICATIONS

Our study and some studies of outpatient drug warning systems have found a clear reduction in the use of PIMs. As such, our findings—by showing that these drugs are indeed amenable to targeted change by a straightforward ordering system—provide the first necessary step in determining whether reducing the use of these medication will ultimately improve patient outcomes. It is not yet clear whether any differences in patient outcomes can be attributed to this change in behavior, but our results provide optimism that this important research question can be addressed in the near future.

As CPOE is more widely adopted, it seems likely that most institutions will rely on commercially available (rather than internally developed) systems. Such systems will rarely be sufficiently malleable to allow the fine-tuned and circumscribed type of intervention we describe herein. Designing commercial CPOE systems to guide clinicians at the local level to adhere to the best care is challenging. To be most effective, systems should minimize generalized warnings and, like this warning system, use focused alerts to target specific patient populations where alternate treatment exists. We encourage developers of commercial CPOE systems to build in the flexibility to implement point-of-care warnings appropriate to local circumstances.

LIMITATIONS

There are several limitations to our data. For lorazepam and ferrous sulfate, the warning advised a dose reduction. The warning did not advise against the use of these medications and, consistent with this advice, the rate of ordering these medications did not change after the imple-
mentation of the warning system—suggesting that the system could provide adequate specificity. However, we lack information on the dose of medication prescribed and hence cannot be certain whether the targeted dose reductions were achieved.

Another limitation of this study is its generalizability. Our drug warning system was used at an academic medical center where medical trainees or physician extenders order most medications. We do not know whether a similar result would be seen in a system where attending physicians place most of the orders or in institutions without a firmly entrenched and multipurpose CPOE system. We also lacked the ability to determine whether ADEs were prevented by the use of this warning system.

Similarly, we are only able to comment on medications ordered. Although we recorded all orders, including as-needed and standing orders, we lacked the ability to ascertain the number of medications actually given to patients because our hospital does not have an electronic medical administration record. Nonetheless, all medications actually administered at the medical center necessarily were captured as orders, so our findings accurately reflect a decline in the number of patients exposed to a subset of potentially problematic medications.

Finally, without detailed clinical record review, we cannot determine whether the medications that were ordered were clinically required. One important area of future study is a better understanding of the scenarios in which it is clinically appropriate and reasonable to prescribe the Beers medications even to older adults.

In summary, we found that a CPOE system with specific, targeted, and straightforward warnings can dramatically yet selectively reduce the prescription of PIMs in vulnerable hospitalized older patients. Such systems can produce rapid and clinically significant change while leaving unchanged the rate of prescribing unflagged medications. This may represent a tool for improving the safety of hospitalized older adults.

Accepted for Publication: January 18, 2010.

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Financial Disclosure: None reported.

Funding Support: This study was funded in part by grant 1 U1L RR025758-01, Harvard Clinical and Translational Science Center, from the National Center for Research Resources (Dr Ngo).


Additional Contributions: Rachel Murkowski, MD, and Lisa Saubermann, PharmD, BCPS, contributed to the development of the original alert system.

REFERENCES