

Alternatives to potentially inappropriate medications for use in e-prescribing software: triggers and treatment algorithms

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ABSTRACT

Objective: To describe the development of evidence-based electronic prescribing (e-prescribing) triggers and treatment algorithms for potentially inappropriate medications (PIMs) for older adults.

Design: Literature review, expert panel and focus group.

Setting: Primary care with access to e-prescribing systems.

Participants: Primary care physicians using e-prescribing systems receiving medication history.

Interventions: Standardised treatment algorithms for clinicians attempting to prescribe PIMs for older patients.

Main outcome measure: Development of 15 treatment algorithms suggesting alternative therapies.

Results: Evidence-based treatment algorithms were well received by primary care physicians. Providing alternatives to PIMs would make it easier for physicians to change decisions at the point of prescribing.

Conclusion: Prospectively identifying older persons receiving PIMs or with adherence issues and providing feasible interventions may prevent adverse drug events.

INTRODUCTION

Among independently living adults in the USA, over a quarter experience adverse drug events (ADEs) based on one cohort study.¹ The estimates of ADEs are even higher in American adults over 65 years of age and receiving Medicare, the US federal healthcare program for older adults.² An estimated US \$887 million is spent annually on preventable ADEs among Medicare recipients in the ambulatory setting.³ Given this significant burden of ADEs, identifying feasible interventions for reducing preventable ADEs in

the private physician offices and other ambulatory care settings is important.

The medication use process includes prescribing, dispensing, administering, and monitoring the medication. The prescribing stage of the process is associated with over half of the errors associated with preventable ADEs.^{2–4} Electronic prescribing, more commonly known as e-prescribing, has been proposed as a technology-based approach for reducing potentially preventable ADEs. E-prescribing is the direct computer-to-computer transmission of prescription information from physician offices to community pharmacies. E-prescribing systems also allow for patient safety features including clinical decision support and sharing of patient pharmacy data across multiple prescribers. The technology has advanced features which allow a prescriber to access formulary information at the point of prescribing. With this technology, the physician writes a prescription for a patient using a computer, with the computer software alerting the prescriber when a potential drug–drug or drug–disease interaction might occur.

By the end of 2009, 25% of all office-based prescribers in the US were using e-prescribing and about 18% of eligible prescriptions were prescribed electronically.⁵ Most US prescribers are in solo and small group practices which have continued to lag in the use of e-prescribing and other advanced features such as accessing formulary information. These advanced features are important for efficient primary care practice. Older Americans may have one of many different types of private insurance plans that provide the drug coverage

commonly known as Medicare Part D plans.⁶ These insurance plans may have their own unique formulary of covered medications.

Continued growth in e-prescribing is anticipated with the passage of the American Recovery and Reinvestment Act in 2010. This legislation has provided governmental funding and other incentives to encourage the more widespread use of health information technology (HIT) including e-prescribing. With the growing use of e-prescribing and HIT in the USA, it has also become apparent that the technology must be clinically relevant. For example, computer alerts that commonly tell a busy prescriber about drug interactions that are clinically insignificant may result in the prescriber ignoring the alerts, including those that are very important.^{7 8}

To address previous issues with prescribing alerts, we designed tailored triggers and alternative treatment options specific for older patients as part of a larger e-prescribing study. Our goal was to improve drug use in older adults by alerting prescribers to potentially inappropriate medications (PIMs), as well as to suggest potentially safer alternatives at the point of prescribing. Focus groups were also conducted to identify healthcare providers' opinions about drug alerts embedded within e-prescribing applications. The purpose of the current paper is to describe the development of evidence-based treatment algorithms for recommending alternative treatments to PIMs, and to provide the actual treatment algorithms which are being used in a large-scale e-prescribing study.

METHODS

The study protocol was approved by the Institutional Review Boards of Virginia Commonwealth University, University of Rhode Island, and Memorial Hospital of Rhode Island.

Triggers for PIMs

PIMs were identified first by reviewing the 2003 update of the Beers criteria drugs with all drugs initially being considered.⁹ Although many medications may potentially be inappropriate for older adults, such as the use of statins at the end of life, we sought to identify medications that had well accepted concerns associated with their use, either in terms of their safety or limited efficacy.

An informal email survey of community pharmacists practicing in Rhode Island and Massachusetts was conducted. The seven pharmacists were alumni of the University of Rhode Island College of Pharmacy and served as preceptors for pharmacy students on their required community pharmacy experiential rotations. The pharmacists worked for the three major drug store

chains in the USA. The pharmacists were asked to review the list of 39 PIMs from the Beers criteria and to indicate what drugs were being dispensed in their pharmacies. This resulted in the number of PIMs being reduced from 39 to 15 based on limited prescribing of many of the identified drugs. One author (ALH) also reviewed the list for more commonly prescribed PIMs, as well as two other pharmacy faculty members with clinical and research expertise in geriatrics and one pharmacy faculty member with expertise in community pharmacy practice.

Treatment algorithms for alternatives to PIMs

An extensive literature search was conducted to provide the basis for making alternative recommendations for PIMs. The treatment algorithms were intended to serve as a quick reference for clinical decision-making. Early on in this project, one of the authors (ALH) with extensive experience in primary care geriatrics developed an initial draft algorithm for each of the 39 PIMs for older adults.⁹ After discussion with the software vendor, this initial list was reduced to the 15 which were further developed.

The authors discussed the rationale and alternative recommendations listed in the algorithms, and the evidence upon which the recommendations were made. Revisions were made to the algorithms based on these discussions. The algorithms were reviewed by two additional pharmacy faculty members with clinical and research expertise in geriatrics, as well as by a pharmacy faculty member with expertise in community pharmacy practice. These individuals provided a careful review and recommendations for modification of the treatment algorithms. The rationale for suggested changes was discussed and agreement was reached about the final treatment algorithms. The research team then reviewed the algorithms for their general content and likely effectiveness as a prescribing alert. Judging the likely effectiveness of the alert was based primarily on the appropriateness of the alternative drugs proposed by the alert. This included consideration of the alternative drug's safety and effectiveness for the condition, availability as a generic drug, likely familiarity with primary care providers, etc. This assessment was also based on the experience of research team members who were pharmacists or physicians.

Integration of trigger for PIM use in the real-time e-prescribing software

The first stage of the process included meeting with the electronic prescribing software vendor to learn about what specific medication data were available, and how the information was captured. The goal was to identify patients prescribed (or soon to be prescribed) PIMs in

the ‘real-time’ of the clinical encounter. As such, we needed to develop triggers based on information included in the commercial software. The development of triggers was focused on drugs that were potentially more serious. We also need to identify an approach within the existing software to both trigger and display the alternative suggestion without slowing down the software or adding to clinician burden to receive the messaging. We embedded the alerts into the e-prescribing software such that seeing the alerts did not require additional effort for prescribers. The alerts appeared on the main prescribing screen and as such did not require the physicians to push extra buttons to see the alerts. We had the alerts appear similarly to what appears when the physician attempts to prescribe medications that are not on the formulary of the patient’s insurer. That is, a message appears alerting the prescriber that the medication is not on the formulary along with a box of alternative medications that are on the formulary.

In addition, we wanted the messages to be relevant and concise, as well as consistent with the software display. This process required several iterations with the research team and the e-prescribing software vendor.

Physician focus groups

Setting and sample: We implemented a purposive sample for focus group participants. For the first focus group conducted in April 2008, we recruited physicians attending the annual meeting of the Rhode Island Academy of Family Physicians (RIAFP). Physician participants were recruited through an advertisement placed in the RIAFP newsletter with subsequent email follow-up. Participants eligible for the focus group used e-prescribing software, but not necessarily the software of our research partner, DrFirst (DrFirst, Inc., Rockville, Maryland, USA). The first focus group included 11 participants. For the second focus group, we included six users of DrFirst’s RCopia software from Massachusetts. For both focus groups, a US\$100 incentive was provided to participants. We originally had planned for additional focus groups; however, we reached saturation after conducting two.

Focus group script development: After conducting a systematic review of the literature, our multidisciplinary project team prepared a core list of open-ended questions to serve as the script for the focus group. Questions were included about the triggers and algorithms that were being developed including their general knowledge of the Beers criteria drugs, as well as workflow issues.

Conduct of focus groups: Standard focus group procedures were used with focus groups about 2 h in length and held over dinner.¹⁰ An experienced focus group

moderator (REG) facilitated each session and was assisted by members of the research team (CE, BQ, AH). Consent forms and anonymous demographic data forms were completed by participants. An open-ended approach was used to elicit participants’ opinions about the issues experienced with older patients and their medications from the moderator, complemented by spontaneous question probes or additional questions to follow new lines of inquiry raised by the focus group participants. Focus groups were recorded and professionally transcribed. Transcripts were checked for accuracy.

Analysis of focus group data: We conducted a group method of data analysis known as immersion/crystallisation.¹¹ We analysed each focus group discussion in its entirety, thus maintaining awareness of the overall context of each speaker’s comments within the whole of the discussion. In addition, the qualitative software NVivo was used to code the transcripts line-by-line.¹² To enable this process to go forward, research team members independently listened to the focus group recordings and/or read the transcripts multiple times. We discussed each focus group, comparing the data between them, to search for emerging themes and findings relevant to the development of algorithms for the project.

RESULTS

While physicians in the focus groups on the whole claimed that triggers and evidenced-based treatment algorithms incorporated into their electronic medical record system would be useful in their practice, they clearly indicated that the triggers must be carefully designed to promote efficiency and reduce redundancy. A physician asserted, “Something pops up, gives you a little tutorial—it has to be short and sweet, something you can read in 30 s.” And another explained, “You want to provide a little more information, but you can’t have it so long, in providing every explanation... . We don’t want that because all you’re gonna do is click on little boxes, saying ‘I don’t care, I don’t care’.

Participants described the frustration of receiving triggers and alerts about information that they were well aware of, alerts that were repetitive because of the frequency of the condition among patients or because the alert came up every time they saw particular patients, and from receiving alerts claiming that they had prescribed inappropriately when in fact they had made a specific decision to treat the patient in such a manner. Clinicians in the focus groups suggested suppressing alerts for renewals of medication combinations that patients were currently taking and tolerating, as well as for alerts related to medications that were used for short-term courses of therapy. We frequently heard the

Table 1 Actual messages in e-prescribing software—benzodiazepines and anticholinergic medications

Trigger drug	Short warning	Text displayed if prescriber presses the more button	Alternative medications shown
Alprazolam ≥2 mg/day	Warning—dose alert, increased sensitivity in the elderly ... more	'Because of increased sensitivity to benzodiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximum.'	Alprazolam <0.75 mg
Diazepam	Warning—prolonged half-life in the elderly, high fall risk ... more	'Older benzodiazepines (BZDP) such as diazepam, have a prolonged half-life due to their lipid solubility and the presence of active metabolites. In elderly patients, their half-life may potentially exceed several days, resulting in prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting BZDP are preferred if a benzodiazepine is actually required.'	Alprazolam 0.125–0.25 mg twice daily; not to exceed 2 mg every day Buspirone 5 mg twice daily, up to 20–30 mg every day; not to exceed 60 mg every day; mg twice daily; not to exceed 2 mg every day Lorazepam: 0.5 mg two to three times a day; not to exceed 3 mg/day Oxazepam: 10 mg two to three times a day; not to exceed 60 mg/day Non-drug modalities Acetaminophen or ibuprofen Naproxen short term only
Cyclobenzaprine (Flexeril, McNeil Consumer and Specialty Pharmaceuticals, Fort Washington, PA)	Warning—high risk of anticholinergic reactions in the elderly ... more	'Most skeletal muscle relaxants are poorly tolerated by elderly patients. Some drugs, including cyclobenzaprine, may have anticholinergic adverse effects as well as causing sedation and weakness. Agents such as carisoprodol are metabolised to meprobamate which has a significant abuse potential. Additionally, the effectiveness of these drugs at dosages tolerated by elderly patients is questionable. The long-term safety and efficacy of skeletal muscle relaxants for chronic low back pain is unclear and not recommended.'	
Hydroxyzine	Warning—high risk of anticholinergic reactions in the elderly ... more	'Some non-prescription and prescription antihistamines may have potent anticholinergic properties. In addition to traditional anticholinergic symptoms of constipation, urinary retention, and blurred vision, these drugs may cause confusion and delirium, especially if other drugs with anticholinergic properties are present. Non-anticholinergic antihistamines are preferred in elderly patients especially when needing to treat allergies chronically.'	Loratidine 10 mg every day; 10 mg every other day in renal or hepatic failure Cetirizine 10 mg every day; decrease by 50% in renal or hepatic failure Fexofenadine 60 mg twice daily or 180 mg every day; 60 mg every day in renal failure
Oxybutynin (regular release)	Warning—high risk of anticholinergic reactions in the elderly ... more	'Regular release products containing oxybutynin, a urinary antispasmodic agent, may be poorly tolerated by many elderly patients. Anticholinergic effects are common and include confusion and agitation in addition to traditional anticholinergic effects of constipation and tachycardia. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.'	Ditropan XL, Ortho-McNeil Pharmaceuticals, Raritan, NJ Detrol LA, Pfizer, New York, NY Solifenacin, darifenacin, trospium

Table 2 Actual messages in e-prescribing software—antidepressants

Trigger drug	Short warning	Text displayed if prescribers presses the more button	Alternative medications shown
Amitriptyline	Warning—high risk of anticholinergic reactions and sedation in the elderly ... more	‘Amitriptyline (as well as doxepin) should not be used as first-line antidepressant therapy in elderly patients because of strong anticholinergic and sedative properties. In addition, cardiac toxicity is more likely to occur in the presence of underlying cardiac disease. Amitriptyline and doxepin may cause significant orthostatic hypotension in older adults even in lower dosages, thereby increasing the risk of falls and fractures. Although nortriptyline or desipramine may be used if a TCA is required, alternatives such as sertraline or citalopram generally are preferred as they may be safer in elderly patients.’	Sertraline Citalopram Escitalopram Mirtazepine Bupropion
Doxepin	Warning—high risk of anticholinergic reactions and sedation in the elderly ... more	‘Doxepin (as well as amitriptyline) should not be used as first-line antidepressant therapy in elderly patients because of strong anticholinergic and sedative properties. In addition, cardiac toxicity is more likely to occur in the presence of underlying cardiac disease. Doxepin, and amitriptyline may cause significant orthostatic hypotension in older adults even in lower dosages, thereby increasing the risk of falls and fractures. Although nortriptyline or desipramine may be used if a TCA is required, alternative antidepressants such as sertraline or citalopram generally are preferred as they may be safer in elderly patients.’	Sertraline Citalopram, Escitalopram Mirtazepine Bupropion
Fluoxetine (daily)	Warning—prolonged half-life in elderly, high ADR risk ... more	‘Although the daily administration of fluoxetine in healthy older adults has been shown to be safe and effective in clinical trials, concern exists because of the prolonged half-life of fluoxetine and nor-fluoxetine especially in more medically complex elderly patients. In addition, a risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation exists especially with daily fluoxetine. Fluoxetine may also cause multiple drug interactions. Safer alternatives such as sertraline or citalopram exist.’	Sertraline Citalopram, Escitalopram Mirtazepine Bupropion

ADR, adverse drug reaction; CNS, central nervous system; TCA, tricyclic antidepressant.

following sentiment, “Don’t keep showing the same ones over and over again.”

Physicians repeated over and over the need for the data to be accurate and useful, “It would depend on how reliable we would perceive that data to be. Judging from other insurance data we get, it’s pretty poor in terms of the accuracy of that.”

Another physician said, “Differentiate it from the usual. There’s an interaction here, you know, non-steroidals and antihypertensives—we all know that. Quit doing that. It’s annoying. Only if it’s actually helpful. If this person has a serious side effect. And that’s the only reason it (the alert) went up, and it really meant something, then yes (it’s useful).”

A physician who approved of getting computer triggers nevertheless warned about ease of use,

I think that information would be extremely important.... So I think the information would have to be readily available, not having to be looked for, not physician-dependent, it really needs to be something brought to me by the prescreening technicians, and that information is on the chart—4/5 prescriptions filled, zero prescriptions filled... . All I need is the data.

Some physicians felt that having medication-related triggers on the computer at the time of the visit would aid them in counselling patients who were non-adherent with their medication therapy,

Table 3 Actual messages in e-prescribing software—pain medications

Trigger drug	Short warning	Text displayed if prescriber presses the more button	Alternative medications shown
Indomethacin	Warning—high risk of CNS ADRs in the elderly ...more	'Indomethacin produces the most CNS adverse effects such as headache, vertigo, and dizziness of all NSAIDs when used chronically. Although all NSAIDs may increase the risk of serious GI complications such as perforation, obstruction and haemorrhage (especially in elderly patients), potent agents such as indomethacin also have an increased risk over other NSAID and COX-2 inhibitors. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.'	Acetaminophen (\pm codeine) Lidocaine patch Celecoxib: osteoarthritis 200 mg QD or in divided doses; rheumatoid arthritis 100-200 mg BID Ibuprofen: 2400 mg/24 h (every 8–12 h) or naproxen for short-term use Tramadol Opiate such as morphine Choline magnesium trisalicylate: 5500 mg/24 h (every 8–12 h) Acetaminophen (\pm codeine) Lidocaine patch Celecoxib: osteoarthritis 200 mg every day or in divided doses; rheumatoid arthritis 100–200 mg twice daily Ibuprofen: 2400 mg/24 h (every 8–12 h) or naproxen for short-term use Tramadol Opiate such as morphine Choline magnesium trisalicylate: 5500 mg/24 h (every 8–12 h) Acetaminophen (\pm codeine) Lidocaine patch Celecoxib: osteoarthritis 200 mg every day or in divided doses; rheumatoid arthritis 100–200 mg twice daily Ibuprofen: 2400 mg/24 h (every 8–12 h) or naproxen for short-term use Tramadol Opiate such as morphine Choline magnesium trisalicylate: 5500 mg/24 h (every 8–12 h)
Ketorolac	Warning—high risk of GI bleed, renal failure, elevated BP and CHF in the elderly ...more	'Ketorolac has significant adverse effects including serious GI complications such as perforation, obstruction and haemorrhage especially in elderly patients. Ketorolac is not appropriate for chronic use. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.'	
Piroxicam	Warning—high risk of GI bleed, renal failure, elevated BP and CHF in the elderly ... more	'Piroxicam has significant adverse effects including serious GI complications such as perforation, obstruction and haemorrhage especially in elderly patients. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.'	

Continued

Table 3 Continued

Trigger drug	Short warning	Text displayed if prescriber presses the more button	Alternative medications shown
Propoxyphene	Warning—lack of efficacy in the elderly with increased risk of ADRs ... more	<p>‘Propoxyphene is an opioid analgesic that has been available for many years, despite limited efficacy even when compared with acetaminophen or aspirin.</p> <p>Propoxyphene may cause constipation and cognitive impairment, as well as other CNS effects. Several epidemiological studies have identified an association between cognitive impairment with propoxyphene and an increased risk of falls and fractures in elderly adults. In addition, many propoxyphene products also contain acetaminophen which may result in unintentional overdoses and hepatotoxicity if the elderly individual is taking other RX or OTC products containing acetaminophen.’</p>	Acetaminophen ± codeine Celecoxib Ibuprofen Naproxen short term only Opiates such as morphine

ADR, adverse drug reaction; BP, blood pressure; CHF, chronic heart failure; COX-2, cyclo-oxygenase-2; CNS, central nervous system; GI, gastrointestinal; NSAID, non-steroidal anti-inflammatory drug; OTC, over the counter; RX, prescription; TCA, tricyclic antidepressant.

“A lot of patients don’t want to bother the doctor... So a patient comes in and we see that there’s significant progression of their disease. So we’re assuming they’re not taking their medication till they come to the office, the night before. To make me happy. They’re treating me, they’re not treating themselves... . There’s some reason they’re not telling me... . So if we had some information that we could broach with them, and we could say ‘Why aren’t you filling your prescriptions?’”

Of note, many of the physicians in the focus groups were not specifically aware or knowledgeable of the term, *Beers criteria drugs*, although they recognised that the drugs were older and less commonly prescribed.

Online figures 1–15 provide the treatment algorithms for each of the targeted medications or groups of medications. For each medication, the screen initially shows a short alert in a red font such as ‘*WARNING—Dose Alert, Increased Sensitivity In The Elderly...MORE*’ (tables 1–4). Clinicians then press a button to get more information about the alert in the form of a concise explanation about the specific issue with the drug that would make it potentially inappropriate for older adults. Several alternative medications are then shown on the screen with the intent to aid prescribers in easily identifying a potentially more appropriate drug therapy for the older patient. The one group of PIMs that lack appropriate alternatives was the skeletal muscle relaxants which are only minimally effective and have safety issues in older adults. Prescribers are alerted to try non-pharmacological alternatives.

DISCUSSION

Overall, the discussion from the focus groups indicated that triggers and evidenced-based treatment algorithms would be well received by primary care physicians if the triggers were focused on highly critical information, could be trusted to provide high accuracy, and were designed to promote efficient information retrieval. These findings provide support that implementation of these algorithms as a tool for physicians in a clinical setting is feasible. Clinicians recognise that electronic alerts at the point of prescribing have the potential to improve patient safety in the ambulatory setting.^{8 13–15} A survey of Massachusetts clinicians indicated that 30% had recently modified a potentially dangerous drug as a result of an electronic alert.⁸ Despite recognising the potential value of alerts, clinicians often override e-prescribing alerts because of lack of specificity of the messages or irrelevance of the medication to the current drug regimen.^{8 13} Prior research indicates that such alerts are frequently overridden (49–96% of cases) because of poor specificity and high volume of alerts.⁷

In selecting drugs as triggers for potentially inappropriate use in older adults, we chose to use the Beers

Table 4 Actual messages in e-prescribing software—cardiovascular medications

Trigger drug	Short warning	Text displayed if prescriber presses the more button	Alternative medications shown
Amiodarone	Warning—evidence of safety and efficacy is limited in the elderly and high risk of QT prolongation and torsade ... more	'Amiodarone is an important drug in the management of arrhythmias, however, published evidence of its safety and efficacy in elderly is still limited. Major studies such as the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) have enrolled elderly patients, but the mean age was only 70 years. AFFIRM and other studies have generally not supported the superiority of rhythm over rate control in AF. In addition, adverse effects from antiarrhythmic agents have been common. Amiodarone has been associated with prolongation of the QT interval and precipitating torsade de pointes especially in the presence of risk factors such as hypokalemia and hypomagnesemia, although its risk may be lower than that of quinidine, sotalol and other antiarrhythmic agents. In addition, amiodarone carries a significant risk of hyper- or hypothyroidism (the latter especially in elderly patients), as well as pulmonary and ophthalmologic adverse effects. Drugs interactions can be common including with warfarin. Appropriate anticoagulation is a key therapy for preventing stroke in patients with AF.'	β blockers Diltiazem Verapamil Warfarin or aspirin to reduce thromboembolism from atrial fibrillation
Digoxin >0.125 mg/day	Warning—dose alert, increased risk of toxicity in the elderly ... more	'Digoxin continues to have a role in the management of heart failure and atrial fibrillation (AF). Digoxin is considered an adjunctive therapy in HF where it has been shown to reduce hospitalisations for worsening HF. However ACE inhibitors (or ARBs) and β -blockers such as carvedilol are preferred therapies because of established benefits on morbidity and mortality in patients with HF. Although digoxin may be useful for rate control in AF, β -blockers, diltiazem and verapamil are preferred for many patients with AF. (Anticoagulation remains a key therapy in AF.) Dosages of digoxin greater than 0.125 mg daily may result in toxicity due to the decreased renal function commonly present in elderly patients.'	Diltiazem, verapamil, and/or metoprolol may be appropriate alternatives depending on the individual patients Maintain digoxin concentrations between 0.5 and 1.0 ng/ml

Continued

Table 4 Continued

Trigger drug	Short warning	Text displayed if prescriber presses the more button	Alternative medications shown
Doxazosin	Warning—high risk of hypotension and dry mouth in the elderly ... more	'Doxazosin has been a useful drug for treating hypertension and BPH which are present commonly in many elderly men. Unfortunately doxazosin, similar to prazosin and terazosin, has a significant potential for dizziness and postural hypotension which may increase the risk of falls and fractures. In addition, the drug may cause dry mouth, somnolence, and asthenia. In the Medical Therapy of Prostatic Symptoms (MTOPS) study, doxazosin did not decrease the risk of acute urinary retention and the need for invasive therapy in men with progressive BPH unlike finasteride (alone or in combination with doxazosin). The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) also demonstrated a significantly increased risk of heart failure with doxazosin as compared with chlorthalidone. Although combining doxazosin with other antihypertensive agents may mitigate this risk of HF, current data suggest that it is not eliminated.'	Flomax: Boehringer-Ingelheim Pharmaceuticals, Ridgefield, CT Uroxatrol: Sanofi-Aventis Pharmaceuticals, Bridgewater, NJ

AF, atrial fibrillation; HF, heart failure; ARB, angiotensin receptor blocker; BPH, benign prostatic hyperplasia.

criteria drugs because the available e-prescribing software could easily identify these medications. Although a recent comparison between drugs—to avoid criteria such as Beers and Zhan with expert assessments of problematic prescribing—demonstrated the limitations of these criteria to measure prescribing quality,^{9 14 15} they have value in making initial prescribing decisions. In addition, a study of two large outpatient practices using electronic health records has identified that 23% of elderly patients receive at least one potentially inappropriate medication, as defined by the Beers criteria.¹⁶ The health outcomes associated with the use of the Beers criteria have been associated with ADE in independently living elderly.¹⁷ Although there were other areas of inappropriate medication use that we were interested in exploring, the available standalone e-prescribing software was limited in which medication alerts we could effectively implement because we did not have information such as diagnosis or indication of the medication.

E-prescribing alerts need to be flexible and specific. These points are consistent with desires of primary care providers in the VA system and in community settings.^{13 18} Alerts were designed so that clinicians can easily recognise the severity of the alert with the use of colours. Increasing the greater specificity of alerts or reducing alert overload may lead to less over-riding. E-prescribing software that permits the clinician to set the desired alerting threshold has lower reports of over-riding alerts.¹³ We also designed the alerts to minimise workflow disruption and so that they would not require additional clicking. We know that drug alerting systems targeting specific issues and minimising workflow disruptions increase clinician acceptance of alerts in ambulatory settings.⁷

Similar to previous reports,¹⁹ clinicians in our focus groups suggested suppressing alerts for renewals of medication combinations that patients currently tolerate. Providers noted that short-term courses of therapy would continue to arise in the alerts, suggesting that the time frame for medication history on which the drug alerts are run should be evaluated. If the e-prescribing technology has the drug-alerting component run on the entire medication history in the patient's electronic health record, it may actually exacerbate the problem of alert 'overloading' of the clinician. The best solution may be for computer software products for prescribers to run drug alerts only on the medications that the patient is currently taking (ie, an active medication list), instead of all of the medications that the patients have ever taken according to the electronic health record.

Considering the process of drug alerting at the point of prescribing in ambulatory settings is important. First, adding these alerts does not shift the work of evaluating the potential for medication harm upstream (from the

pharmacist to the prescriber). The Omnibus Budget Reconciliation Act of 1990 requires pharmacists to perform a drug use review to evaluate prescribed drug therapy before dispensing to ensure that therapy is medically necessary, appropriate, and not likely to result in an adverse event. Specifically, pharmacists evaluate therapeutic duplication, therapeutic appropriateness, drug–allergy interactions, drug–disease contraindications, drug–drug interactions, correct dosage and duration of therapy, utilisation, abuse, and appropriate use of generic products.²⁰ Thus, any product enhancements that involve alerting provide an additional layer of checking, not a substitution for checking.

The following limitations of the data should be considered. All physicians in this study were currently using e-prescribing software and represented a convenience sample. As such, the participants are likely to represent the most experienced e-prescribing users in primary care settings. Also, because scientific knowledge is dynamic, the treatment algorithms shown and alternative therapies recommended are time sensitive.

CONCLUSION

In a recent national study providing comprehensive estimates of ADE-related ambulatory visits, including visits to office-based clinics, hospital outpatient clinics, subspecialty clinics, and emergency departments, patients 65 years and older had an incidence of ADE visits as high as 1 in 20 persons.²¹ Further, ADEs in patients over 65 years of age were associated with substantial morbidity with a quarter of patients requiring admission.²¹ E-prescribing adoption in the USA is increasing because of funding initiatives and other policy initiatives of the federal government. Enhancements to e-prescribing software technology will help clinicians avoid preventable ADEs. By increasing the specificity of the alerts and providing alternative treatment suggestions, clinicians believe that such alerts will assist in clinical decision-making.

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Patient consent Obtained.

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Contributors All the authors listed made a substantial contribution to the following: conception and design, acquisition of data or analysis and interpretation of data; drafting the article or revising it critically for important intellectual content; final approval of the version published.

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Figure 1. Propoxyphene (Darvon) & Combination Products (Darvon w/ ASA, Darvon-N & Darvocet-N)

Appropriate for Use in the Elderly?

No

Propoxyphene is an opioid analgesic that has been available for many years, despite limited efficacy even when compared with acetaminophen or aspirin. Propoxyphene may cause constipation and cognitive impairment, as well as other CNS effects. Several epidemiologic studies have identified an association between cognitive impairment with propoxyphene and an increased risk of falls and fractures in elderly adults. In addition, many propoxyphene products also contain acetaminophen which may result in unintentional overdoses and hepatotoxicity if the elderly individual is taking other RX or OTC products containing this acetaminophen.

Instead

Consider acetaminophen (alone or in combination with codeine), ibuprofen, celecoxib, or short-term naproxen.

Consider narcotics such as morphine for severe pain.

Figure 2. Indomethacin (Indocin & Indocin SR)

Appropriate for use in the elderly?

No

Indomethacin produces the most CNS adverse effects such as headache, vertigo, and dizziness of all NSAIDs when used chronically. Although all NSAIDs may increase the risk of serious GI complications such as perforation, obstruction and hemorrhage (especially in elderly patients), potent agents such as indomethacin also have an increased risk over other NSAID and COX-2 inhibitors. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.

Use topical agents if appropriate(ie. Lidocaine patch)
Acetaminophen is the drug of choice for mild/moderate musculoskeletal pain, while opioid analgesics are typically for moderate/severe nociceptive pain in the elderly. Use NSAIDs with caution because of ceiling effect and renal and gastrointestinal adverse effects. **Start with lowest dose and increase gradually.**

Ibuprofen: 2400mg/24 hours (every 8 to 12 hours)

Choline magnesium trisalicylate: 5500mg/24 hours (every 8-12 hours)

Celecoxib: osteoarthritis 200mg QD or in divided doses
rheumatoid arthritis; 100-200mg BID

Consider concomitant use of a PPI to prevent peptic ulcer disease.

Tramadol is also an alternative analgesic agent.

Instead

Figure 3. Ketorolac (Toradol)

Appropriate for Use in the Elderly?

No

Ketorolac has significant adverse effects including serious GI complications such as perforation, obstruction and hemorrhage especially in elderly patients. Ketorolac is not appropriate for chronic use. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.

Instead

Use topical agents if appropriate (ie. Lidocaine patch)
Acetaminophen is the drug of choice for mild/moderate musculoskeletal pain, while opioid analgesics are typically used for moderate/severe nociceptive pain in the elderly.

Use NSAIDs with caution because of ceiling effect and renal and gastrointestinal adverse effects. **Start with lowest dose and increase gradually.**

Ibuprofen: 2400mg/24 hours (every 8 to 12 hours)

Choline magnesium trisalicylate: 5500mg/24 hours (every 8-12 hours)

Celecoxib: osteoarthritis 200mg QD or in divided doses
rheumatoid arthritis; 100-200mg BID

Consider concomitant use of a PPI to prevent peptic ulcer disease in elderly patients taking higher dosages of NSAID chronically.

Tramadol is also an alternative analgesic agent.

Figure 4. Piroxicam (Feldene)

Appropriate for Use in the Elderly?

No



Use topical agents if appropriate (ie. Lidocaine patch)
Acetaminophen is the drug of choice for mild/moderate musculoskeletal pain, while opioid analgesics are typically used for moderate to severe nociceptive pain in the elderly.

Use NSAIDs with caution because of ceiling effect and renal and gastrointestinal adverse effects. **Start with lowest dose and increase gradually.**

Ibuprofen: 2400mg/24 hours (every 8 to 12 hours)

Choline magnesium trisalicylate: 5500mg/24 hours (every 8-12 hours)

Celecoxib: osteoarthritis 200mg QD or in divided doses
rheumatoid arthritis; 100-200mg BID

Consider concomitant use of a PPI to prevent peptic ulcer disease in elderly patients taking higher dosages of NSAID chronically.

Tramadol is also an alternative analgesic agent.

Piroxicam has significant adverse effects including serious GI complications such as perforation, obstruction and hemorrhage especially in elderly patients. Acute renal failure, hypertension, and worsening heart failure also occur in elderly patients.

Instead

Figure 5. Doxazosin (Cardura)

Appropriate for Use in the Elderly?

No

Doxazosin has been a useful drug for treating hypertension and BPH which are present commonly in many elderly men. Unfortunately doxazosin, similar to prazosin and terazosin, has a significant potential for dizziness and postural hypotension which may increase the risk of falls and fractures. In addition, the drug may cause dry mouth, somnolence, and asthenia. In the Medical Therapy of Prostatic Symptoms (MTOPS) study, doxazosin did not decrease the risk of acute urinary retention and the need for invasive therapy in men with progressive BPH unlike finasteride (alone or in combination with doxazosin). The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) also demonstrated a significantly increased risk of heart failure with doxazosin as compared with chlorthalidone. Although combining doxazosin with other antihypertensive agents may lessen HF risk, current data suggest that it is not eliminated.

Instead

Tamsulosin and alfuzosin are preferred for BPH symptoms.

If doxazosin must be used for HTN, it should be used in combination with other antihypertensive drugs.

Figure 6. High Dose Digoxin (Lanoxin)
(> 0.125 mg daily)

Appropriate for Use in the Elderly?

No

Digoxin continues to have a role in the management of heart failure and atrial fibrillation (AF). Digoxin is considered an adjunctive therapy in HF where it has been shown to reduce hospitalizations for worsening HF. However ACE inhibitors (or ARBs) and beta-blockers such as carvedilol are preferred therapies because of established benefits on morbidity and mortality in patients with HF. Although digoxin may be useful for rate control in AF, beta-blockers, diltiazem and verapamil are preferred for many patients with AF. (Anticoagulation remains a key therapy in AF.) Dosages of digoxin greater than 0.125mg daily may result in toxicity due to the decreased renal function commonly present in elderly patients.

Instead

Diltiazem, verpamil, and/or metoprolol may be appropriate alternatives depending on the individual patient. Consider other drugs for rate control in atrial fibrillation

Maintain digoxin concentrations between
0.5 to 1.0 ng/ml

Figure 7. Amiodarone (Cordarone)

Appropriate for Use in the Elderly?

No

Amiodarone is an important drug in the management of arrhythmias, however, published evidence of its safety and efficacy in elderly is still limited. Major studies such as the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) have enrolled elderly patients, but the mean age was only 70 years. AFFIRM and other studies have generally not supported the superiority of rhythm over rate control in AF. In addition, adverse effects from antiarrhythmic agents have been common. Amiodarone has been associated with prolongation of the QT interval and precipitating torsade de pointes especially in the presence of risk factors such as hypokalemia and hypomagnesemia, although its risk may be lower than that of quinidine, sotalol and other antiarrhythmic agents. In addition, amiodarone carries a significant risk of hyper- or hypothyroidism (the latter especially in elderly patients), as well as pulmonary and ophthalmologic adverse effects. Drugs interactions can be common including with warfarin. Appropriate anticoagulation is a key therapy for preventing stroke in patients with AF.

Instead

Beta-blockers, diltiazem, and verapamil are preferred for rate control over antiarrhythmic agents in AF.

Use of warfarin (therapeutic INR) decreases risk of cardioembolic stroke. Aspirin may be preferred in low risk patients.

Figure 8. Amitriptyline (Elavil), Chlordiazepoxide-amitriptyline (Limbitrol), Perphenazine-amitriptyline (Triavil)

Appropriate for Use in the Elderly?

No

Amitriptyline should not be used as first-line antidepressant therapy in elderly patients because of strong anticholinergic and sedative properties. In addition, cardiac toxicity is more likely to occur in the presence of underlying cardiac disease. Amitriptyline may cause significant orthostatic hypotension in older adults even in lower dosages, thereby increasing the risk of falls and fractures. Although nortriptyline or desipramine may be used if a TCA is required, alternatives such as sertraline or citalopram generally are preferred as they may be safer in elderly patients."

Instead

Sertraline, citalopram, escitalopram, mirtazepine, and bupropion may be preferred depending on the patient's comorbid conditions.

Figure 9. Doxepin (Sinequan)

Appropriate for Use in the Elderly?

No

Doxepin should not be used as first-line antidepressant therapy in elderly patients because of strong anticholinergic and sedative properties. In addition, cardiac toxicity is more likely to occur in the presence of underlying cardiac disease. Doxepin may cause significant orthostatic hypotension in older adults even in lower dosages, thereby increasing the risk of falls and fractures. Although nortriptyline or desipramine may be used if a TCA is required, alternatives such as sertraline or citalopram generally are preferred as they may be safer in elderly patients."

Instead

Sertraline, citalopram, escitalopram, mirtazepine, and bupropion may be preferred depending on the patient's comorbid conditions.

Figure 10. Daily Fluoxetine (Prozac)

Appropriate for Use in the Elderly?

No

Although the daily administration of fluoxetine in healthy older adults has been shown to be safe and effective in clinical trials, concern exists because of the prolonged half-life of fluoxetine and nor-fluoxetine especially in more medically complex elderly patients. In addition, a risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation exists especially with daily fluoxetine. Fluoxetine may also cause multiple drug interactions. Safer alternatives such as sertraline or citalopram exist.

Instead

Sertraline, citalopram, escitalopram, mirtazepine, and bupropion may be preferred depending on the patient's comorbid conditions

Figure 11. High Dose Short-Acting Benzodiazepines [for Anxiety]

Lorazepam (Ativan) 3 mg, Oxazepam (Serax) 60 mg, Alprazolam (Xanax) 2 mg, Temazepam (Restoril) 15 mg, and Triazolam (Halcion) 0.25 mg.

Appropriate for Use in the Elderly?

No

Because of increased sensitivity to benzodiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximum.

Instead

Lorazepam < 2 mg/d
Oxazepam < 60 mg/d
Alprazolam < 0.75 mg/d

Figure 12. Long Acting Benzodiazepines
(Chlordiazepoxide [Librium], chlordiazepoxide+amitriptyline [Librax],
clidinium+chlordiazepoxide [Librax], Diazepam [Valium], Quazepam [Doral],
Halazepam [Paxipam], Clorazepate [Tranxene])

Appropriate for use in the elderly?

No

Older benzodiazepines (BZDP) such as diazepam, have a prolonged half-life due to their lipid solubility and the presence of active metabolites. In elderly patients, their half-life may potentially exceed several days, resulting in prolonged sedation and increasing the risk of falls and fractures.

Short- and intermediate-acting BZDP are preferred if a benzodiazepine is actually required.

Instead

Evaluate need for drug; Consider possible alternatives with possible gradual dosage reduction and/or discontinuation

Anxiolytics:

Alprazolam: 0.125-0.25mg BID; NTE 4mg QD

Buspirone 5mg BID; up to 20-30mg QD: NTE 60mg QD

Lorazepam: 0.5mg BID to TID; NTE 3mg/day

Oxazepam: 10mg BID to TID; NTE 60mg/day

Sedative/Hypnotics:

Zolpidem: 5mg QHS; NTE mg/day

Temazepam 7.5mg QHS; up to 15mg PRN

Zaleplon 5mg QHS; NTE 7-10 days

Figure 13. Skeletal Muscle Relaxants (Methocarbamol [Robaxin], Carisoprodol [Soma], Chlorzoxazone [Paraflex], Metaxalone [Skelaxin], Cyclobenzaprine [Flexeril])

Appropriate for use in the elderly?

No

Most skeletal muscle relaxants are poorly tolerated by elderly patients. Some drugs, including cyclobenzaprine, may have anticholinergic adverse effects as well as causing sedation and weakness. Agents such as carisoprodol are metabolized to meprobamate which has a significant abuse potential. In addition, effectiveness of these drugs at dosages tolerated by elderly patients is questionable. The long-term safety and efficacy of skeletal muscle relaxants for chronic low back pain is unclear and not recommended.

Instead

Non-drug modalities should be tried first for back pain. Acetaminophen, ibuprofen or short-term naproxen should be tried for low back pain.

Patients must be monitored individually for cause of muscle spasm. Spasticity: Multidisciplinary care and education are needed regarding factors such as proper seating, proper footwear, or underlying problems which may be worsen spasticity.

Appropriate Alternatives to Consider³:

Baclofen: 40 to 100mg daily in divided doses
Tizanidine (Zanaflex): Initial dose 4mg, may be increased by 2 to 4 mg. NTE 36mg/day.

Figure 14. Oxybutynin [Ditropan-excludes Ditropan XL]

Appropriate for use in the elderly?

No

Regular release products containing oxybutynin, a urinary antispasmodic agent, may be poorly tolerated by many elderly patients.

Anticholinergic effects are common and include confusion and agitation in addition to traditional anticholinergic effects of constipation and tachycardia. In addition, their effectiveness at dosages tolerated by elderly patients is questionable.

Instead

Use extended release or transdermal formulations of oxybutynin and newer drugs for urinary incontinence such as long-acting tolterodine (Detrol LA) and others.

Figure 15. Anticholinergic Antihistamines
(Chlorpheniramine [Chlor-trimeton], Diphenhydramin [Benadryl], Hydroxyzine [Atarax & Vistaril], Cyproheptadine [Periactin], Promethazine [Phenergan], Tripeleennamine, Dexchlorpheniramine [Polaramine])

Appropriate for use in the elderly?

No

Some nonprescription and prescription antihistamines have potent anticholinergic properties. In addition to traditional anticholinergic symptoms of constipation, urinary retention, and blurred vision, these drugs may cause confusion and delirium, especially if other drugs with anticholinergic properties are present. Nonanticholinergic antihistamines are preferred in elderly patients especially when needing to treat allergies chronically.

Consider the following alternatives

Loratidine 10mg QD; 10mg every other day in renal or hepatic failure.

Cetirizine 10mg QD; Decrease by 50% in renal or hepatic failure.

Fexofenadine 60mg BID or 180mg QD; 60mg QD in renal failure.

Instead